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Ventilator-associated pneumonia: Current management strategies

BY DAREN HEYLAND, MD

Acquired infection is a major problem for critically ill patients, resulting in increased morbidity, mortality, and health care costs.¹ The overall infection rate approaches 40% and may be as high as 80% in patients who stay in the ICU more than 5 days.² Respiratory tract infections account for 30-60% of all such infections, while urinary tract infections, bacteremia and wound infections are less common.^{2,3} Prospective cohort studies have documented the incidence of ventilator-associated pneumonia (VAP) to range from 10% to 65%. These rates vary depending upon the study population, the underlying illness, and diagnostic methods employed. Patients at highest risk of acquiring VAP are those with:

- COPD
- Burns
- Neurosurgical illness
- ARDS
- Reintubation
- Witnessed aspiration
- Receiving histamine-2 receptor antagonists or paralytic agents, or continuous enteral nutrition.^{4,5}

Microbiology

VAP can be classified as "early" (occurring within 4-7 days of onset of mechanical ventilation) or "late" (occurring after 4-7 days of ventilation). Different investigators have used different cutoffs to define early and late. Nevertheless, the distinction is important as early VAP is most often due to easily treated organisms (*Streptococcus pneumoniae*, *Hemophilus influenzae*, *Staphylococcal aureus*, and possibly lactose fermenting gram-negative bacteria). Late VAP is often due to difficult-to-treat organisms (*Pseudomonas species*, *Acinetobacter*, *Stenotrophomonas*, methicillin-resistant *Staphylococcus aureus*). Kollef and colleagues⁶ prospectively studied a group of 87 patients with late-onset pneumonia (developed after 4 days of mechanical ventilation). Twenty (23%) of these patients were infected with a difficult-to-treat organism. The mortality of this latter group was 65%, twice the mortality rate of the overall group. In a similar study, a French group examined risk factors for the development of pneumonia due to these high-risk organisms.⁷ In a single ICU, 135 consecutive episodes of VAP were observed over a 25-month period. Seventy-seven episodes were caused by these difficult-to-treat organisms. Using a logistic regression analysis, duration of mechanical ventilation ≥ 7 days (odds ratio [OR]=6.0), prior antibiotic use (OR=13.5) and prior use of broad-spectrum antibiotics (third generation cephalosporin, fluoroquinolone, and/or imipenem) (OR=4.1) were associated with infection caused by these organisms. Of patients who received prior antibiotics and were ventilated for >7 days, 58% of the organisms associated with VAP were multi-resistant.

Does VAP affect patient outcome?

There is some controversy as to whether patients die *with* or *from* pneumonia. To evaluate the attributable morbidity and mortality of VAP, we conducted a prospective, matched, cohort study.⁸ Over 1,200 patients expected to be ventilated for >48 hours were followed for the development of VAP. Compared to matched patients who did not



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develop VAP, patients with VAP stayed in the ICU 4.3 days longer (95% CI, 1.5 - 7.0) and had a trend towards an increase in the risk of death (absolute risk increase, 5.8%, 95% CI, -2.4 to 14.0; relative risk increase of 32.3%, 95% CI, -20.6 to 85.1). There are six other studies that employed a “matching” strategy to examine the excess morbidity and mortality of VAP.⁸ In all six studies, VAP was associated with a prolonged length of ICU stay (range 5-13 days). The excess mortality attributable to VAP ranged from an absolute risk increase of zero to 50%. Therefore, it would appear that VAP does prolong ICU length of stay and may increase risk of death.

Given the excess morbidity and mortality associated with VAP, every effort should be made to prevent it. Preventative measures shown to be efficacious include:

- removal of nasogastric or nasotracheal tubes as soon as possible
- use of a formal infection control program
- semi-recumbent positioning of patients
- oral versus nasal intubation
- less frequent changes of ventilator tubing
- subglottic secretion drainage
- avoidance of gastric overdistension.⁹

Diagnostic strategies

There has been considerable debate in the literature and at international scientific meetings over the past 5 years as to the optimal diagnostic strategy in critically ill patients with VAP.^{10,11} Several studies have documented that “clinical criteria” alone which rely on cultures from endotracheal aspirates result in a high misclassification rate of VAP.^{12,13} To aid in the diagnosis and to identify the infecting organisms, bronchoscopy with use of protected brush catheters (PBC) or bronchoalveolar lavage (BAL) may be more accurate than reliance on standard endotracheal aspirates. Initial reports suggest sensitivity and specificity are high (pooled estimates, 89.9% and 94.5% respectively, for PBC, and 53.3-100% and 98.6% for BAL),¹⁴ while recent studies question the accuracy of invasive techniques in patients on antibiotics prior to bronchoscopy.¹⁵⁻¹⁷ Using post-mortem examinations as the gold standard to make the diagnosis of pneumonia, previous studies have documented a high incidence of false positive and false negative results in patients on antibiotics who underwent PBC or BAL.^{18,19} In patients already receiving antibiotics, there is minimal correlation between clinical findings, microbiologic data, and postmortem examination of the lung. The utility of histopathology as the gold standard for the diagnosis of pneumonia is questionable in this setting. Regardless, from a patient outcomes perspective, the question still remains: Does a management strategy that combines clinical judgement with results from invasive diagnostic procedures improve patient outcomes compared to clinical judgement alone (regardless of which gold standard is used)?

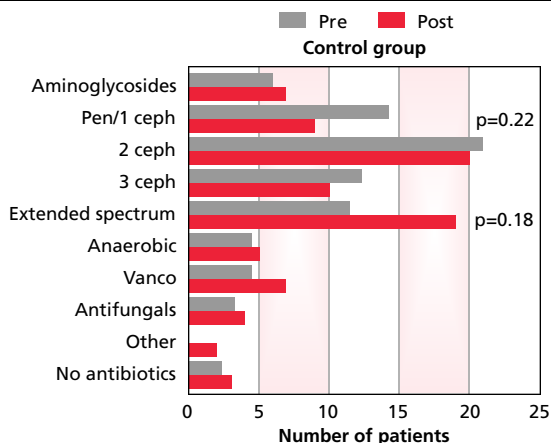
In the management of VAP, there are few controlled trials evaluating a strategy based on information derived from invasive diagnostic techniques compared to clinical judgement. Sanchez-Nieto and colleagues²⁰ randomized 51 ICU patients with a clinical suspicion of pneumonia to undergo quantitative endotracheal aspiration with bronchoscopy and PBC and BAL or quantitative endotracheal aspiration alone. They demonstrated that BAL and PBC resulted in a greater number of changes to antibiotics, but no difference in length of stay or mortality. Differences in baseline characteristics of study patients make it difficult to interpret this small study. In the group that underwent bronchoscopy, there were more patients infected with *Pseudomonas*

For years, French investigators have been proponents of invasive diagnostic techniques. Recently, they published the results of a large, multicentered, randomized, unblinded study of 413 critically ill patients with a clinical suspicion of VAP.²¹ Patients with recent antibiotic changes were excluded from the study which limits the generalizability of the results. Patients were randomized to bronchoscopy with BAL and/or PBC or non-quantitative endotracheal aspirates. Antibiotics were started based on presence of organisms on the gram stain and the clinical condition of the patient. For example, in a patient with no organisms on the gram stain and with no signs of severe sepsis, antibiotics were withheld pending culture results. If the patient did have signs of severe sepsis, empiric antibiotics were initiated. If the cultures were subsequently negative, antibiotics were discontinued. The choice of individual antibiotics was left up to the attending physician and was to follow the American Thoracic Society Consensus Conference guidelines on antibiotic choices.²²

In the intention-to-treat analysis, the results suggested that patients treated with invasive diagnostic techniques had more antibiotic-free days in a 28-day period (11.5 vs 7.5 days), fewer antibiotics per day (1.0 vs 1.3), and less organ dysfunction at day 3 and day 7 (as measured by a SOFA score). At 14 days, the mortality rate was significantly lower in the group that received invasive tests (16.2 vs. 25.8%, $p=0.022$). At 28 days, mortality rates were similar in both groups. It is difficult to explain how less exposure to antibiotics in the first few weeks of care resulted in such an early and significant treatment effect.

The non-standardized antibiotic administration in this study represents an important confounding variable. Using ATS guidelines can result in several different combinations of antibiotics and is therefore an important confounding variable. In the group that underwent invasive diagnostic techniques, there was a much lower rate of inappropriate empiric antibiotics (1 patient [0.5%] vs 24 patients [13%], $p<0.001$). Thirty-two per cent of the 25 patients who received inappropriate initial antibiotics died, compared to 20% of the 388 patients who received appropriate initial

Figure 1: Change in antibiotic prescription before and after results of endotracheal aspirates known. Pen=penicillin; ceph=cephalosporins; vanco=vancomycin.

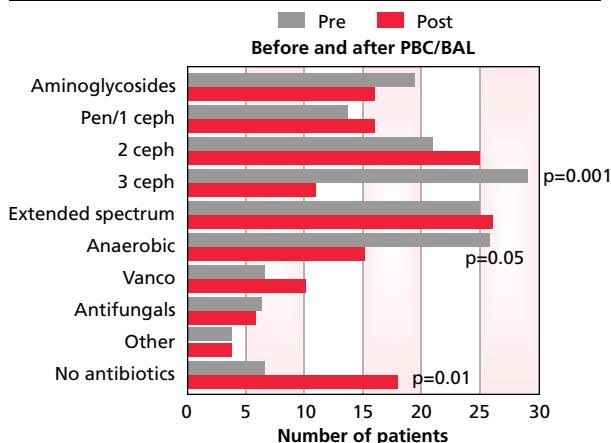


antibiotic therapy. In the patients who received inappropriate antibiotics, all of the deaths occurred before day 14. Consequently, the mortality difference between groups may have had less to do with the diagnostic strategy, and more to do with the antibiotic choices.

Furthermore, there is additional evidence that both groups may not have been treated equally in this unblinded study. There were more patients with infections other than VAP diagnosed in the invasive treated-group (22 vs 5 infections, $p < 0.001$), and we do not know if the diagnostic work-up and therapeutic interventions related to these interventions was the same in both groups.

In the absence of compelling data from large randomized trials, a reasonable, next-best approach was to examine the impact of invasive diagnostic techniques on health care workers, patient management, and patient outcome using an observational study design. In this multicenter, Canadian study, 92 mechanically ventilated patients with a clinical suspicion of VAP who underwent bronchoscopy were compared to 49 patients with a clinical suspicion of pneumonia who did not.²³ While both groups experienced a similar rate of antibiotic changes, patients who underwent PBC or BAL ended up on fewer antibiotics and a greater proportion had their antibiotics discontinued all together. Furthermore, compared to empiric antibiotics initiated at baseline, patients in the group who underwent bronchoscopy ultimately received fewer prescriptions for third-generation cephalosporins, while those in the control group showed a trend towards an increase in broad spectrum antibiotics (Figures 1 and 2). The duration of mechanical ventilation, ICU, and hospital stay was similar between the two groups; however, we observed a lower mortality rate in the group that underwent bronchoscopy with PBC or BAL (18.5 vs. 34.7%,

Figure 2: Change in antibiotic prescription before and after results of bronchoscopy are available. Pen=penicillin; ceph=cephalosporins; vanco=vancomycin.



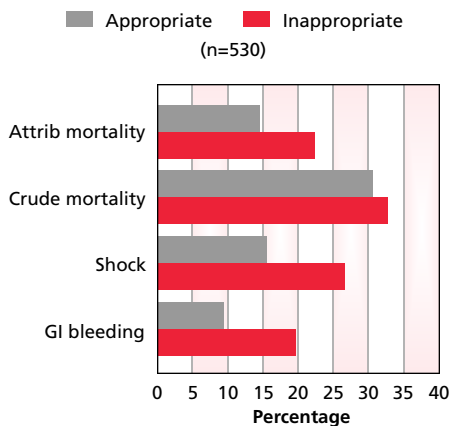
$p = 0.03$). Given that patients were not randomized to invasive or noninvasive diagnostic approaches, one cannot make strong inferences from these findings. However, a potential advantage of using invasive techniques is that antibiotic therapy may be tailored to the results of PBC or BAL. This is consistent with the findings of the French study and has important clinical implications. Reducing the unnecessary use of broad spectrum antibiotics may minimize the emergence of resistant microorganisms in the ICU and reduce antibiotic costs.

Empiric antibiotic strategies: A case for broad-spectrum antibiotics

Empiric therapy for VAP (antibiotics started prior to results of cultures) usually consists of one or two agents with activity against Gram-negative and Gram-positive organisms. Several reports that document empiric therapy based on clinical judgement in patients suspected of having pneumonia demonstrate that initial treatment was often inadequate; that is, subsequent cultures grew organisms resistant to initial antibiotics or antibiotics initially withheld and culture results subsequently positive.^{24,25} Additional studies have shown that patients treated with “inappropriate” empiric therapy have a much higher mortality rate than patients placed on “appropriate” empiric antibiotic therapy.

In a prospective, observational study in 30 ICUs in Spain, Alvarez-Lerma and colleagues studied antibiotic use in 530 patients with VAP.²⁶ Empiric antibiotics were administered in 430 (87%) of cases. In 214 (43.7%) cases, empiric therapy was modified because of isolation of organisms not covered by empiric antibiotics, lack of clinical response and/or development of resistance. Antibiotic coverage was considered to be appropriate in 284 (66%) episodes and inappropriate in 146 (34%).

Figure 3: Outcomes of patients receiving empiric treatment for suspected VAP grouped by “appropriateness” of initial antibiotics.



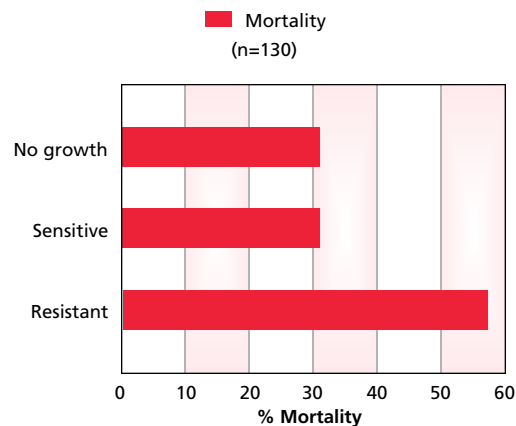
Attributable mortality and related complications (particularly shock and gastrointestinal bleeding) were higher in patients treated with inappropriate antibiotics (Figure 3).

Luna and colleagues followed 132 patients with a clinical suspicion of pneumonia and described antibiotic use prior to and after BAL results were available.²⁷ Sixty-five patients had a “positive” BAL. Of those 65 patients, only 16 (25%) were receiving adequate antibiotic therapy prior to bronchoscopy. The mortality rate in those patients receiving initial adequate therapy was significantly lower (6/16, 38%) compared to patients receiving inadequate therapy (31/34, 91%), even though this last cohort subsequently had therapy changed to an adequate agent, either established empirically or based on culture results.

Finally, Kollef and colleagues have published two studies that evaluate the relationship between inadequate antimicrobial treatment and mortality. In one study of 130 critically ill patients with suspected VAP, 60 patients had a positive mini-BAL culture.²⁴ Of those, 44 (73%) were classified as receiving inadequate antibiotics. Following the results of cultures, antibiotics remained unchanged in 51 (39%) cases, were changed in another 51 (39%) cases, and were discontinued in the remaining 28 (22%) of cases. The mortality rates for these three groups were 33.3%, 60.8%, and 14.3%, respectively, suggesting that a delay in achieving adequate antibiotic coverage is associated with a increased mortality rate (Figure 4).

In another study of 2000 consecutive admissions to a medical or surgical ICU, 655 (33.3%) were thought to have either community-acquired or nosocomial infections.²⁸ Of these, 165 (25.2%)

Figure 4: Mortality rates of patients with organisms that were resistant and sensitive to empiric treatment for a suspicion of VAP.



received inadequate antibiotics for their infection. The hospital mortality rate of infected patients with inadequate antimicrobial treatment was significantly higher than the mortality rate for patients with adequate treatment (52.1% vs 23.5%, $p < 0.0001$). The most common cause of inadequate antibiotics was the presence of an antibiotic-resistant organism.

Based on these data, the use of broad spectrum antibiotics as initial management of suspected VAP is likely to result in less microbiologic failure and improved clinical outcomes. However, in patients with more than 7 days of mechanical ventilation and prior use of antibiotics, any single broad spectrum agent (by itself) would be adequate in only <45% of cases (best case scenario).⁷ Furthermore, to prevent the development of resistance while on treatment, it is recommended that two drugs be used for infections due to *Pseudomonas*.²⁹ Whereas treatment with a third-generation cephalosporin may suffice for early onset VAP, to ensure maximal probability of adequate treatment of an infecting organism, combination therapy with two broad spectrum antibiotics is recommended for late-onset VAP.²² The American Thoracic Society (ATS) guidelines recommends that for patients with late-onset VAP with “risk factors,” empiric treatment includes the combination of aminoglycoside or ciprofloxacin plus one of the following antimicrobial agents, an antipseudomonal penicillin, a beta-lactam/beta-lactamase inhibitor combination, ceftazidime, imipenem or meropenem with or without vancomycin.²² However, there is no rigorous evidence that supports these guidelines and broad spectrum antibiotics are not without their side effects.

A case against two empiric broad-spectrum antibiotics

Observational studies that document a higher mortality rate in patients treated with “inappropriate” antibiotics or in patients who have had their antibiotics changed, may only be describing an “association,” not a “causal relationship.” Developing a multi-resistant organism or changing the antibiotics may be associated with sicker patients with a severe underlying illness. Despite therapeutic changes, these patient will likely succumb to the underlying illness. Often, antibiotics are changed because the patient is clinically deteriorating, regardless of the organisms or sensitivities. Conversely, since assessments of drug activity are *in vitro*, sometimes patients will improve on drugs that are reportedly inactive against a specific organism.

Epidemiologic data on the prevalence of multiresistant organisms comes from French and other European centers.⁷ These data are not systematically collected and published in Canada. However, in our recent study assessing the attributable morbidity and mortality of VAP, only 14/177 (13.6%) of patients with VAP were treated empirically with “inappropriate” antibiotics and the incidence of *Pseudomonas* and *Acinetobacter* was less than 25% (there were no cases of *Stenotrophomonas* documented).⁸ With respect to blood stream infections, a Canadian surveillance study documented that infections due to *Pseudomonas*, *Acinetobacter* and *Stenotrophomonas* were less than 7% of all infections.³¹ These data suggest that the prevalence of multi-resistant organisms may be lower than reported elsewhere. In addition, there is some evidence that treating serious pseudomonal infections with one antibiotic active *in vitro* may be sufficient.³² Therefore, the use of two broad spectrum agents, as recommended in the ATS guidelines may not be necessary, especially in the Canadian setting.

The use of broad-spectrum antibiotics may have serious adverse effects in critically ill patients. The overuse or indiscriminate use of broad spectrum antibiotics is implicated in the development of infections due to multi-resistant, difficult-to-treat bacteria and fungi.^{30,40,33} The highest concentration of antibiotic resistant isolates is found in the ICU.³⁴ The primary strategy for preventing antibiotic-resistant nosocomial infections is eliminating or reducing the unnecessary use of antibiotics.³⁵ In addition, overuse of antibiotics may increase the frequency of antibiotic-associated side effects (allergic reactions, diarrhea, etc.). Finally, the excessive use of broad spectrum antibiotics will certainly increase pharmacy costs. Therefore, the risks and benefits of administering two empiric

broad-spectrum antibiotics need to be evaluated in the context of a randomized clinical trial.

Conclusion

The combination of two empiric broad-spectrum antibiotics (to improve clinical outcomes) and invasive diagnostic tests (to limit antibiotic use) may be the optimal management strategy for critically ill patients with a clinical suspicion of late-onset VAP. Before strong clinical guidelines can be put forward, however, the risks and benefits of this management strategy need to be evaluated in the context of a randomized clinical trial. The Canadian Critical Care Trials Group is currently conducting a multi-center randomized clinical trial of invasive diagnostic techniques and empiric antibiotics in an attempt to provide stronger evidence as to the optimal management of the most prevalent complication of critical illness – ventilator-associated pneumonia.

References

1. Girou E, Stephan F, Novara A, Safar M, Fagon JY. Risk factors and outcome of nosocomial infections: Results of a matched case-control study of ICU patients. *Am J Respir Crit Care Med* 1998;157:1151-1158.
2. Vincent JL, Bihari D, Suter PM, Bruining HA, White J, et al. 1995. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European prevalence of infection in intensive care (EPIC) study. *JAMA* 1995; 274:639-644.
3. Kerver AJH, Rommes JH, Mevissen-Verhage EAE, Halstaert PF, Vos A, Verhoef J, Wittebol P. Colonization and infection in surgical intensive care units - a prospective study. *Intensive Care Med* 1987;13:347-351.
4. Cook DJ, Kollef MH. Risk factors for ICU-acquired pneumonia. *JAMA* 1998;279:1605-1606.
5. Cook DJ, Walter SD, Cook RJ, Griffith LE, Guyatt GH, Leasa D, Jaeschke RZ, Brun-Buisson C, for the Canadian Critical Care Trials Group. Incidence and risk factors for ventilator-associated pneumonia in critically ill patients. *Ann Intern Med* 1998;129(6):433-440.
6. 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.
7. Trouillet JL, Chastre J, Vuagnat A, et al. Ventilator-associated pneumonia caused by potentially drug-resistant bacteria. *Am J Respir Crit Care Med* 1998;157:531-539.
8. 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. The Canadian Critical Care Trials Group. *Am J Respir Crit Care Med* 1999;159:1249-1256.
9. Kollef MH, Ward S. The influence of mini-BAL cultures on patient outcomes: Implications for the antibiotic management of ventilator-associated pneumonia. *Chest* 1998;113:412-20.
10. Chastre J, Fagon JY. Invasive diagnostic testing should be routinely used to manage ventilated patients with suspected pneumonia. *Am J Respir Crit Care Med* 1994;150:570-574.
11. Niederman MS, Torres A, Sumner W. Invasive diagnostic testing is not needed routinely to manage suspected ventilator-associated pneumonia. *Am J Respir Crit Care Med* 1998;199:565-569.
12. Andrews CP, Coalsen JJ, Smith JD, Johanson Jr WG. Diagnosis of nosocomial bacterial pneumonia in acute, diffuse lung injury. *Chest* 1981;80:254-258.
13. Fagon JY, Chastre J, Hance AJ, et al. Detection of nosocomial lung infection in ventilated patients: Use of a protected specimen brush and quantitative culture techniques in 147 patients. *Am Rev Resp Dis* 1988;138:110-116.
14. Cook DJ, Fitzgerald JM, Guyatt GH, Walter S. Evaluation of the protected brush catheter and bronchoalveolar lavage in the diagnosis of nosocomial pneumonia. *J Intensive Care Med* 1991;6:196-205.

15. Rouby JJ, Martin de Lasale M, Poete P, et al. Nosocomial broncho-pneumonia in the critically ill. Histologic and bacteriologic aspects. *Am Rev Respir Dis* 1992;146:1059-1066.
16. Torres A, El-Ebiary M, Padro L, et al. Validation of different techniques for the diagnosis of ventilator-associated pneumonia: comparison with immediate postmortem pulmonary biopsy. *Am J Respir Crit Care Med* 1994;149:324-331.
17. Timsit JF, Misset B, Goldstein FW, Vaury P, Carlet J. Reappraisal of distal diagnostic testing in the diagnosis of ICU-acquired pneumonia. *Chest* 1995;108:1632-39.
18. Kirtland SH, Corley DE, Winterbauer RS, et al. The diagnosis of ventilator-associated pneumonia: A comparison of histologic, microbiologic and clinical criteria. *Chest* 1997;112:445-57.
19. Marquette CH, Copin M, Wallet F. Diagnostic tests for pneumonia in ventilated patients: prospective evaluation of diagnostic accuracy using histology as a diagnostic gold standard. *Am J Respir Crit Care Med* 1995;151:1878-1888.
20. Sanchez-Nieto JM, Torres A, Garcia-Cordoba F, et al. Impact of invasive and noninvasive quantitative culture sampling on outcome of ventilator-associated pneumonia: a pilot study. *Am J Respir Crit Care Med* 1998;157:371-376.
21. Fagon JY, Chastre J, Wolff M, et al. Invasive and noninvasive strategies for management of suspected ventilator-associated pneumonia: A randomized trial. *Ann Intern Med* 2000;132:621-630.
22. Campbell GD, Niederman MS, Broughton WA, et al. Hospital-acquired pneumonia in adults: diagnosis, assessment of severity, initial antimicrobial strategy, and preventative strategies. A consensus statement. *Am J Respir Crit Care Med* 1996;153:1711-1725.
23. Heyland DK, Cook D, Leasa D, Frietag A, for the Canadian Critical Care Trials Group. The utility of invasive diagnostic techniques in the setting of ventilator associated pneumonia. *Chest* 1999;115:1076-1084.
24. Kollef MH, Ward S. The influence of mini-BAL cultures on patient outcomes: Implications for the antibiotic management of ventilator-associated pneumonia. *Chest* 1998;113:412-20.
25. Fagon JY, Chastre J, Hance AJ, Domart Y, Trouillet JL, Gibert C. Evaluation of clinical judgement in the identification and treatment of nosocomial pneumonia in ventilated patients. *Chest* 1993;103:547-53.
26. Alvarez-Lerma F, for the ICU-Acquired Pneumonia Study Group. Modification of empiric antibiotic treatment in patients with pneumonia acquired in the intensive care unit. *Intensive Care Med* 1996;22:387-394.
27. Luna CM, Vujacich P, Niederman MS, et al. Impact of BAL data on the therapy and outcome of ventilator-associated pneumonia. *Chest* 1997;111:676-685.
28. Kollef MH, Sherman G, Ward S, Fraser VJ. Inadequate antimicrobial treatment of infections: A risk factor for hospital mortality among critically ill patients. *Chest* 1999;115:462-474.
29. Thomas JK, Forrest A, Bhavnani SM, et al. Pharmacodynamic evaluation of factors associated with the development of bacterial resistance in acutely ill patients during therapy. *Antimicro Agents and Chemotherapy* 1998;42:521-527.
30. Spencer R.C. Predominant pathogens found in the European prevalence of infection in intensive care study. *Eur J Clin Microbiol Infect Dis* 1996;15:281-285.
31. Pfaller MA, Jones RN, Doern GV, Kugler K and the Sentry Participants Group. Bacterial pathogens isolated from patients with bloodstream infection: Frequencies of occurrence and antimicrobial susceptibility patterns from the Sentry antimicrobial surveillance Program. *Antimicrobial agents and Chemotherapy* 1998;42:1762-1770.
32. Vidal F, Mensa J, Almela M, et al. Epidemiology and outcome of *Pseudomonas aeruginosa* bacteremia, with special emphasis on the influence of antibiotic treatment. *Arch Intern Med* 1996;156:2121-2126.
33. Villers D, Espaze E, Coste-Burel M, et al. Nosocomial *Acinetobacter baumannii* infections: Microbiological and clinical epidemiology. *Ann Intern Med* 1998;129:182-189.
34. Archibald L, Phillips L, Monnet D, McGowan JE, Tenover F, Gaynes R. Antimicrobial resistance in isolates from inpatients and outpatients in the United States: Increasing importance of the intensive care units. *Clin Infect Dis* 1997;24:211-215.
35. 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. *JAMA* 1996;275:234-240.

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Abstracts

The attributable morbidity and mortality of ventilator-associated pneumonia in the critically ill patient.

The Canadian Critical Trials Group.

HEYLAND DK; COOK DJ; GRIFFITH L; KEENAN SP; BRUN-BUISSON C

To evaluate the attributable morbidity and mortality of ventilator-associated pneumonia (VAP) in intensive care unit (ICU) patients, we conducted a prospective, matched cohort study. Patients expected to be ventilated for > 48 h were prospectively followed for the development of VAP. To determine the excess ICU stay and mortality attributable to VAP, we matched patients with VAP to patients who did not develop clinically suspected pneumonia. We also conducted sensitivity analyses to examine the effect of different populations, onset of pneumonia, diagnostic criteria, causative organisms, and adequacy of empiric treatment on the outcome of VAP. One hundred and seventy-seven patients developed VAP. As compared with matched patients who did not develop VAP, patients with VAP stayed in the ICU for 4.3 d (95% confidence interval [CI]: 1.5 to 7.0 d) longer and had a trend toward an increase in risk of death (absolute risk increase: 5.8%; 95% CI: -2.4 to 14.0 d; relative risk (RR) increase: 32.3%; 95% CI: -20.6 to 85.1%). The attributable ICU length of stay was longer for medical than for surgical patients (6.5 versus 0.7 d, $p < 0.004$), and for patients infected with "high risk" organisms as compared with "low risk" organisms (9.1 d versus 2.9 d). The attributable mortality was higher for medical patients than for surgical patients (RR increase of 65% versus -27.3%, $p = 0.04$). Results were similar for three different VAP diagnostic criteria. We conclude that VAP prolongs ICU length of stay and may increase the risk of death in critically ill patients. The attributable risk of VAP appears to vary with patient population and infecting organism.

Am J Respir Crit Care Med 1999;159:1249-1256.