# The Safety and Diagnostic Accuracy of Minibronchoalveolar Lavage in Patients with Suspected Ventilator-Associated Pneumonia

Marin H. Kollef, MD; Kevin R. Bock, BS, RRT; Rodger D. Richards, CRTT; and Mona L. Hearns, CRTT

■ Objectives: To assess the safety of minibronchoalveolar lavage done by respiratory therapists for the evaluation of suspected ventilator-associated pneumonia and to determine the diagnostic agreement between quantitative lower airway cultures obtained by the minibronchoalveolar lavage and protected specimen brush techniques.

■ Design: A prospective direct comparison of two diagnostic techniques.

Setting: An academic tertiary care center in St. Louis, Missouri.

■ Patients: 72 consecutive patients suspected of having ventilator-associated pneumonia on the basis of clinical evidence.

Interventions: Sampling of lower airway secretions using the protected specimen brush and minibronchoalveolar lavage techniques.

Main Outcome Measures: Clinical complications and quantitative cultures of respiratory secretions.

Results: 72 patients suspected of having ventilatorassociated pneumonia (first episode) were evaluated using minibronchoalveolar lavage. In 42 patients, lower airway secretions were also obtained using the protected specimen brush technique. No change in arterial blood oxygen saturation or heart rate occurred after minibronchoalveolar lavage (P > 0.2). Mean arterial pressure slightly increased with minibronchoalveolar lavage (baseline mean pressure, 90.1 mm Hg [CI, 88.4 to 91.7 mm Hg]; average within-person change, 2.6 mm Hg; P = 0.024). Good diagnostic agreement was shown for quantitative cultures obtained with the protected specimen brush and minibronchoalveolar lavage techniques (kappa statistic, 0.63; concordance, 83.3%); 103 colony forming units/mL was used as the threshold for a clinically significant culture result.

■ Conclusions: Minibronchoalveolar lavage is a safe and technically simple procedure for obtaining quantitative lower airway cultures in patients requiring mechanical ventilation. Quantitative culture results obtained by minibronchoalveolar lavage are similar to those obtained by the protected specimen brush technique.

Ann Intern Med. 1995;122:743-748.

From Washington University School of Medicine and Barnes Hospital, St. Louis, Missouri. For current author addresses, see end of text. Nosocomial pneumonia is the leading cause of death resulting from hospital-acquired infections among critically ill patients requiring mechanical ventilation (that is, ventilator-associated pneumonia) (1-5). Several lines of investigation have suggested that previous administration of broad-spectrum antibiotics may predispose patients to develop ventilator-associated pneumonia caused by antibiotic-resistant pathogens (2, 3, 6-8). Additionally, the reported mortality rates related to ventilator-associated pneumonia caused by antibiotic-resistant organisms are substantially greater than rates associated with antibioticsensitive pathogens (5-7). These findings have fueled a growing debate about the need for more specific diagnostic techniques for ventilator-associated pneumonia that are aimed at directing antibiotic therapy and avoiding its needless administration in order to minimize the development of antibiotic-resistant infections (9-13).

Bronchoscopic sampling of lower airway secretions (for example, the protected specimen brush technique) is an accurate and reproducible method for the evaluation of suspected ventilator-associated pneumonia (3, 14–17). As part of our ongoing quality improvement efforts (2, 8), we have developed a nonbronchoscopic technique—minibronchoalveolar lavage—for establishing the diagnosis of ventilator-associated pneumonia and potentially guiding the administration of antimicrobial agents. Therefore, we did a prospective study to investigate the safety of minibronchoalveolar lavage and to compare the results of this method with those of the protected specimen brush technique (in which bronchoscopy is used).

#### Methods

### Study Location and Patients

Our study was done in the medical intensive care unit (19 beds) of Barnes Hospital, a 900-bed private teaching hospital, between October 1993 and September 1994. All patients receiving mechanical ventilation for more than 24 hours were prospectively evaluated. Patients suspected on clinical grounds of having ventilator-associated pneumonia were eligible for entry into the study. The study protocol was approved by the Human Studies Committee of the Washington University School of Medicine, and informed consent was obtained for all patients receiving bronchoscopic procedures.

## Data Collection

The following data were prospectively collected by one of the investigators: patient age, sex, APACHE III (Acute Physiology and Chronic Health Evaluation III) score (18), Organ System Failure Index, hospital admission diagnosis, body temperature, leukocyte count, presence or absence of purulent tracheobronchial secretions, and antibiotic use at the time of the evaluation. All chest roentgenograms were prospectively reviewed by the principal investigator (MK), as were the roentgenographic reports (24 to 48 hours later) for independent confirmation of the presence or absence of pulmonary infiltrates.

We also prospectively screened each patient for possible alternative causes for fever and radiographic densities as suggested by other investigators (19, 20). Patients were also evaluated for the occurrence of complications caused by the sampling of airway secretions with either the minibronchoalveolar lavage or the protected specimen brush techniques. We also analyzed whether these procedures caused complications, including clinically significant arterial blood oxygen desaturation (< 90%), hypotension (mean arterial pressure < 60 mm Hg), tachycardia (heart rate > 120 beats/min), bradycardia (heart rate < 60 beats/min), arrhythmias, bronchial hemorrhage, pneumothorax, and death.

#### Definitions

The definition of ventilator-associated pneumonia was modified from criteria established by the American College of Chest Physicians (21). Ventilator-associated pneumonia was considered to be present when a new or progressive pulmonary infiltrate developed in conjunction with one of the following: radiographic evidence of pulmonary abscess formation (that is, cavitation within preexisting pulmonary infiltrates), histologic evidence of pneumonia in lung tissue, presence of substantial growth on a quantitative culture obtained from the lower airways using techniques that minimize contamination with upper respiratory tract flora (for example, the minibronchoalveolar lavage or the protected specimen brush technique) (15, 22, 23), or a positive blood or pleural fluid culture. Blood and pleural fluid cultures could not be related to another source, and both had to be obtained within 48 hours before or after respiratory sampling. The microorganism(s) recovered from blood or pleural fluid cultures also had to be identical to the organisms recovered from cultures of lower airway secretions.

Ventilator-associated pneumonia was considered to be absent when postmortem examination (done within 3 days of the suspicion of ventilator-associated pneumonia) showed no histologic evidence of lung infection; a definitive alternative cause was established; or no substantial growth occurred on a reliable lower airway culture in association with the resolution of one of the following: fever, infiltrate, or leukocytosis. This last criterion was required to occur without the addition of new antimicrobial therapy or without a change in preexisting antimicrobial therapy. All other cases were defined as indeterminate.

Scores from the APACHE III test were calculated in a standard manner (18), and the Organ System Failure Index was modified from that used by Rubin and coworkers (24). Minor bronchial hemorrhage was defined by the presence of new red blood streaking of airway secretions aspirated from the endotracheal tube. Major bronchial hemorrhage was defined as the aspiration of more than 30 mL of red blood from the endotracheal tube.

# Collecting Lower Airway Secretions

By local protocol, the fraction of inspired oxygen was increased to 1.0 before both minibronchoalveolar lavage and bronchoscopy were done. Patients first had bronchoscopy in which the protected specimen brush technique was used and then had minibronchoalveolar lavage. Both procedures were done within 4 hours of one another. The lung being sampled was selected by the principal investigator on the basis of the distribution of the pulmonary infiltrates. Pulse oximetry, heart rate, and arterial blood pressure were continuously monitored during and after these procedures. All respiratory therapists doing minibronchoalveolar lavage were shown how to do this technique and were supervised by the principal investigator before doing the procedure independently.

Protected specimen brush samples were obtained using bronchoscopy in a standard manner (15). Intravenous sedation with either diazepam or midazolam was administered along with 10 mL of 1% lidocaine solution instilled down the endotracheal tube before passage of the bronchoscope. The bronchoscope was then advanced through the endotracheal tube to a position proximal to the segmental orifice to be sampled. A sheathed protected catheter (Microbiology Specimen Brush: Microvasive, Boston Scientific Corporation, Watertown, Massachusetts) was advanced 3 cm out of the bronchoscope, and the inner cannula was protruded to eject the distal carbon wax plug into the large airway. The inner catheter was then advanced into the desired segmental orifice, and the brush was subsequently protruded to obtain airway secretions.

Minibronchoalveolar lavage was done using a prepackaged, commercially available telescoping catheter (BAL Cath, Ballard Medical Products, Draper, Utah). The telescoping catheter was passed through the endotracheal tube using an accompanying prepackaged access port adapter, with the curved tip of the catheter directed toward the desired lung (25). The catheter was advanced until resistance was met, after which the inner catheter was similarly advanced until resistance was again encountered, signifying that it was in a "wedged" position. Twenty-five milliliters of sterile, physiologic saline solution was then injected through the catheter and then reaspirated using the same syringe. The aspirated lavage sample and the cut end of the protected specimen brush were placed in sterile tubes containing 1 mL of sterile physiologic saline solution for transfer to the microbiology laboratory.

#### Microbiological Analysis

The tubes containing the respiratory specimens were first vortexed for 15 seconds. A 0.01-mL calibrated loop was placed into the respective specimens and then onto the center of three media plates (blood agar, chocolate agar, and MacConkey agar). The media plates were then streaked using the pin-wheel streak method and incubated in  $CO_2$  at 35 °C (23). Bacterial culture growth was quantitated according to the number of colonies observed per plate: Fewer than 10 colonies per plate represented less than 103 colony-forming units (CFU)/mL; 10 to 100 colonies per plate represented 103 to 104 CFU/mL; 100 to 1000 colonies per plate represented 104 to 105 CFU/mL; and more than 1000 colonies per plate represented greater than 105 CFU/mL. All identified microorganisms were reported with their antibiotic sensitivities. We used a previously established and validated quantitative threshold ( $\geq 10^3$  CFU/mL) for both sampling methods to support the diagnosis of ventilator-associated pneumonia (15, 22, 23).

#### Statistical Analysis

The safety of minibronchoalveolar lavage was assessed by comparing the patient's baseline heart rate, blood pressure, and pulse oximetry readings (obtained before doing the procedure during a period of inactivity) with the values most changed from baseline (obtained during the procedure and for 5 minutes after its completion). A paired statistical analysis was done using the Student *t*-test for this portion of the analysis. The individual complication rates for the two procedures were compared using the chi-square statistic. All changes in heart rate, blood pressure, and pulse oximetry are reported as average within-person changes along with their variance. All other results are expressed as mean values  $\pm$  SD (continuous variables) or as a percentage of the group value they were derived from (categorical variables).

The degree of variability for statistically significant culture results obtained by the protected specimen brush and minibronchoalveolar lavage techniques was assessed by use of the kappa statistic. Kappa values greater than 0.75 are arbitrarily considered to indicate excellent agreement, values between 0.4 and 0.75 indicate moderate agreement, and values less than 0.4 indicate poor agreement (26). *P* values less than 0.05 were considered significant.

#### Results

Respiratory therapists did minibronchoalveolar lavage in 72 patients with suspected ventilator-associated pneumonia during the study period. Forty-two patients also had bronchoscopy with protected specimen brush sampling of airway secretions. All but three of the bronchoscopic procedures were done by the principal investigator; the remaining three were done by other pulmonary attending physicians. In 30 patients, consent for bronchos-

### Table 1. Patient Characteristics\*

Characteristic	Patients Who Had Both PSB and mBAL (n = 42)	Patients Who Had Only mBAL $(n = 30)$	
Ape. v	51.6 + 19.3	$48.5 \pm 10.9$	
Women/men. n/n	20/22	17/13	
APACHE III score	41.7 + 14.6	$43.4 \pm 9.6$	
Organ System Failure Index	$2.2 \pm 1.1$	$2.0 \pm 1.1$	
Underlying medical condition, $n(\%)$			
Pulmonary disease			
Obstructive lung disease	3 (7.1)	2 (6.7)	
Pneumonia	8 (19.0)	3 (10.0)	
Noncardiogenic pulmonary edema	6 (14.3)	7 (23.3)	
Malignancy	1 (2.4)	0	
Aspiration	7 (16.7)	4 (13.3)	
Other	2 (4.8)	1 (3.3)	
Cardiac disease	- ( )		
Congestive heart failure	4 (9.5)	6 (20.0)	
Cardiogenic shock	2 (4.8)	1 (3.3)	
Neurologic disease	4 (9.5)	3 (10.0)	
Miscellaneous	5 (11.9)	3 (10.0)	

\* APACHE = Acute Physiology and Chronic Health Evaluation; mBAL = minibronchoalveolar lavage; PSB = protected specimen brush. Means are expressed  $\pm$  SD. P > 0.05 for all comparisons.

copy was denied by the patient, his or her surrogate, or the attending physician. Patient characteristics and severity of illness are shown in Table 1. Thirteen patients (31.0%) in the group receiving both minibronchoalveolar lavage and bronchoscopy died during hospitalization compared with 8 patients (26.7%) receiving minibronchoalveolar lavage alone.

No statistically significant differences were noted in the mean values for heart rate (mean baseline rate, 98.7 beats/min [95% CI, 95.4 to 101.9 beats/min]; average within-person change, 1.9 beats/min) or arterial blood oxygen saturation (mean baseline saturation, 97.2% [CI, 96.5% to 97.9%]; average within-person change, -0.5%) resulting from minibronchoalveolar lavage. A small but statistically significant change in mean arterial pressure (mean baseline pressure, 90.1 mm Hg [CI, 88.4 to 91.7 mm Hg]; average within-person change, 2.6 mm Hg; P = 0.024) occurred with minibronchoalveolar lavage. Of the 25 mL of lavage fluid that was instilled, the average amount of fluid obtained from minibronchoalveolar lavage time required for the respiratory therapists to do mini-

bronchoalveolar lavage was  $23.7 \pm 8.9$  seconds (CI, 21.6 to 25.8 seconds).

The observed clinical complications for each procedure are shown in Table 2. No significant differences in complication rates could be shown between the minibronchoalveolar lavage and protected specimen brush techniques for the 42 patients having both procedures. Among the 72 patients having minibronchoalveolar lavage, coughing was the most common complication (66.7%), followed by minor bronchial hemorrhage (8.3%), tachycardia (2.8%), and severe hypoxemia (1.4%). The two patients developing sinus tachycardia had heart rates of 130 and 159 beats/min, respectively; the one patient with severe hypoxemia had an arterial blood oxygen saturation of 87%. All observed complications occurring with minibronchoalveolar lavage were transient, resolving shortly after completion of the procedure. No patient deaths were directly attributed to the minibronchoalveolar lavage or bronchoscopy procedures.

Table 3 shows all positive quantitative cultures obtained by either sampling technique for the patients having both procedures. Seventeen (40.5%) of the paired specimens

Complication	Patients Who Had Both PSB and mBAL $(n = 42)$		Patients Who Had Only mBAL $(n = 30)$
	PSB	mBAL	
Severe hypoxemia (SaO <sub>2</sub> < 90%), $n(\%)$	4 (9.5)	1 (2.4)	0
Arrhythmias, n	0	0	0
Tachycardia (heart rate > 120 beats/min), $n(\%)$	5 (11.9)	1 (2.4)	1 (3.3)
Bradycardia (heart rate $< 60$ beats/min), n	0	0	0
Hypotension (MAP $< 60 \text{ mm Hg}$ ), n	0	0	0
Bronchial hemorrhage, n(%)			
Minor	4 (9.5)	5(11.9)	1 (3.3)
Major	0	0	0
Coughing during procedure, n(%)	24 (57.1)	29 (69.0)	19 (63.3)
Pneumothorax, n	0	0	0

Table 2. Clinical Complications\*

\* MAP = mean arterial pressure; mBAL = minibronchoalveolar lavage; PSB = protected specimen brush; SaO2 = arterial blood oxygen saturation.

Table 3. Results of Positive Quantitative Cultures\*

Patient F Number	Recovered Organism	PSB	mBAL
		CFU/mL	
1	Staphylococcus aureus	103 to 104	103 to 104
2	ORSA	103 to 104	103 to 104
3	Enterobacter cloacae	NG	103 to 104
4	Enterobacter aerogenes	NOF	<103
5	Pseudomonas aeruginosa	NG	<103
6	Pseudomonas aeruginosa	NG	103 to 104
7	ORSA	NG	103 to 104
8	Enterobacter cloacae	NG	104 to 105
9	Enterobacter cloacae	103 to 104	103 to 104
	Acinetobacter calcoaceticus		<10 <sup>3</sup>
10	ORSA	>10 <sup>5</sup>	>105
	Enterobacter cloacae	2244	<103
	Enterobacter aerogenes		$< 10^{3}$
11	ORSA	NG	104 to 105
	Enterobacter cloacae	10.000	<103
12	Klebsiella pneumoniae	NG	103 to 104
13	Escherichia coli	NG	<103
14	Candida albicans	<103	104 to 105
15	Xanthomonas maltophilia	NG	<103
16	Candida albicans	<103	<103
	B-hemolytic streptococci	2002220	0.000.000
	(non-Group A)	<103	<103
17	Streptococcus pneumoniae	104 to 105	104 to 105
Es	Escherichia coli	<10 <sup>3</sup>	<103
	Klebsiella pneumoniae		<103
18	Staphylococcus aureus	103 to 104	104 to 105
19	ORSA	103 to 104	>105
20	Staphylococcus aureus	103 to 104	103 to 104
21	Staphylococcus aureus	104 to 105	>105
	Aspergillus fumigatus	<103	
22	Staphylococcus aureus	103 to 104	104 to 105

\*mBAL = minibronchoalveolar lavage; NG = no growth; NOF = normal oral flora; ORSA = oxacillin-resistant *Staphylococcus aureus*. PSB = protected specimen brush. For all other patients, the quantitative cultures either showed no growth or only growth of normal oral flora.

were obtained from patients who had not received any antimicrobial therapy for at least 72 hours. For 20 (47.6%) of the paired specimens, existing antimicrobial therapy was unchanged for at least 72 hours before the development of suspected ventilator-associated pneumonia and before lower airway sampling. In the remaining five patients (11.9%), antimicrobial therapy was begun or was changed within 72 hours of the clinical suspicion of ventilator-associated pneumonia and lower airway sampling.

When the minibronchoalveolar lavage technique was used, almost twice as many different organisms were obtained than when the protected specimen brush technique was used (29 isolates and 15 isolates, respectively). Culture results from three of the protected specimen brush samples and two of the corresponding minibronchoalveolar lavage samples indicated that Candida albicans or Aspergillus fumigatus were potential pathogens. In two of these three patients (patients 14 and 21), transbronchial lung biopsy specimens showed direct invasion of lung tissue by fungal elements consistent with a diagnosis of nosocomial fungal pneumonia. Among the 42 patients having both diagnostic procedures, 14 (33.3%) were classified as having ventilator-associated pneumonia, 24 (57.2%) were classified as not having ventilator-associated pneumonia, and 4 patients (9.5%) could not be classified.

Table 4 shows the concordance between the quantitative lower airway cultures obtained by the protected spec-

### Discussion

Our study shows that minibronchoalveolar lavage is a safe and simple procedure for obtaining quantitative cultures of lower airway secretions. Minibronchoalveolar lavage was associated with only a small and clinically unimportant increase in mean arterial pressure. Patient complications occurring with minibronchoalveolar lavage were similar to those occurring with the protected specimen brush technique. We also observed good overall diagnostic agreement among the quantitative cultures obtained by these two methods.

Our findings are unique in two important respects. First, they show for the first time that respiratory therapists can safely do minibronchoalveolar lavage in patients with respiratory failure requiring mechanical ventilation. Second, they show that a nonphysician-directed method of obtaining quantitative lower airway cultures may have accuracy similar to that of a physician-directed bronchoscopic technique.

The use of fiberoptic bronchoscopy for the evaluation of ventilator-associated pneumonia has developed, in part, because of the proven inaccuracy of clinical judgment for establishing the presence or absence of this diagnosis (27, 28). Combining microscopic examination of cells recovered by bronchoalveolar lavage (to show the number of cells containing intracellular bacteria) with quantitative cultures obtained by the protected specimen brush technique is an approach reported to have a sensitivity of 100% and a high level of specificity (> 95%) for the diagnosis of nosocomial pneumonia (10, 29). However, other investigators have found these same bronchoscopic methods to have unacceptably high false-negative and false-positive rates (15, 30-33) that result primarily from previous antimicrobial administration (34, 35) and underlying bacterial colonization of the airways (36). These limitations, along with the lack of data showing improvements in patient outcomes after the use of these diagnostic methods, have resulted in requests for their validation in prospective clinical trials before their general acceptance (9, 11).

Nonbronchoscopic techniques have also been developed for the evaluation of ventilator-associated pneumo-

Table 4. Diagnostic Agreement betwee	n the Techniques*
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Technique	Ventilator-Associated Pneumonia		
85	$\frac{\text{Present}}{(n=14)}$	Absent $(n = 24)$	Uncertain $(n = 4)$
Protected specimen brush			
<10 <sup>3</sup> CFU/mL	4	24	4
$\geq 10^3 \text{ CFU/mL}$	10	0	0
Minibronchoalveolar lavage			
<103 CFU/mL	0	23	2
$\geq 10^3 \text{ CFU/mL}$	14	1	2
Concordance, %	71.4	95.8	50.0

\* CFU = colony-forming units.

nia, but they have the same limitations as those noted above for the bronchoscopic methods. However, nonbronchoscopic approaches have been advocated as potentially better alternatives because of their minimal invasiveness, wide availability, and relative inexpensiveness compared with fiberoptic bronchoscopy (9). The principle nonbronchoscopic techniques that have been investigated include quantitative cultures of endotracheal aspirates and blindcatheter sampling of the lower airways. Several studies (20, 22, 37-45) have now shown that these techniques have rates of diagnostic accuracy similar to those of bronchoscopy-directed sampling methods. In one of these studies (22), minibronchoalveolar lavage had a sensitivity of 70% and a specificity of 69% compared with postmortem histologic and bacteriologic analysis of lung tissue (22). These results compare favorably with the findings of an earlier investigation (46) that compared postmortem tissue examination with culture results obtained by the protected specimen brush technique.

An important consideration in our investigation was the financial implications associated with providing these diagnostic procedures. The direct patient charges at our institution for obtaining a protected specimen brush sample include \$532 for the technical support required to do bronchoscopy, \$60 for the protected specimen brush technique, and (on average) more than \$500 for physician fees. In comparison, the charges for minibronchoalveolar lavage are \$24 for the respiratory therapist and \$75 for the catheter. This represents a potential savings of almost \$1000 when minibronchoalveolar lavage is substituted for the protected specimen brush technique. However, total savings depend both on these direct savings and on the balance of false-positive and false-negative results produced by these tests with their ensuing costs and patient charges.

Several limitations of our investigation should be noted. Because of the lack of an established diagnostic criterion standard, the exact operating characteristics (sensitivity, specificity, predictive values, diagnostic accuracy) for the two procedures examined in our study could not be determined. Examination of postmortem lung tissue (bacteriologic and histologic) has been used as an independent reference (control) with which to determine the precise diagnostic yield of similar bronchoscopic and nonbronchoscopic procedures (22, 33, 46). However, histologic sampling errors, the effects of previous antibiotic administration on tissue cultures, and problems related to the timing of postmortem lung examination have substantially limited the diagnostic utility of this procedure (22, 23).

In an attempt to develop a usable reference standard, some investigators (21) have advocated that predetermined criteria for the diagnosis of ventilator-associated pneumonia be used when evaluating new diagnostic techniques. However, such an approach is flawed by the circular reasoning of establishing diagnostic criteria based, in part, on the same test results (for example, protected specimen brush cultures) that a study is attempting to assess for accuracy. Other investigators (47) have suggested that diagnostic approaches that err on the side of overdiagnosing ventilator-associated pneumonia should be clinically accepted when compared with less sensitive alternatives. This approach is based on the premise that the risk for not treating an individual patient with pneumonia probably outweighs the risk for unnecessary antibiotic administration (47). Our results indicate that minibronchoalveolar lavage is at least as sensitive as the protected specimen brush technique for diagnosing ventilator-associated pneumonia. Similar findings (38, 39) have been shown for quantitative cultures of endotracheal aspirates and samples from blind bronchial suctioning using a lower airway catheter.

Another important limitation of our investigation is that we studied a relatively small number of patients. Larger studies using independent criteria to establish the diagnosis of ventilator-associated pneumonia (for example, histologic examination and blood or pleural fluid cultures) are required to determine the exact operating characteristics of the minibronchoalveolar lavage and protected specimen brush techniques. We also obtained all protected specimen brush samples before doing minibronchoalveolar lavage. This practice may have influenced our results from minibronchoalveolar lavage culture by the introduction of contaminated upper airway secretions into the lower airways during bronchoscopy. Finally, the lack of an established diagnostic criterion standard prevented us from conducting a complete economic analysis because we could not assess the effect of patient charges associated with the treatment of false-positive culture results.

We have shown that respiratory therapists can safely and accurately do the minibronchoalveolar lavage technique. If the results of our study are confirmed by further investigations, then minibronchoalveolar lavage may become an acceptable alternative to bronchoscopy for the evaluation of suspected ventilator-associated pneumonia. These findings, including the fact that minibronchoalveolar lavage is relatively inexpensive, also suggest that it may be a useful method for the serial evaluation of suspected nosocomial pneumonia in patients requiring prolonged mechanical ventilation. Future investigations are required to validate these results, establish their general applicability, and determine the utility of quantitative cultures obtained by minibronchoalveolar lavage to influence clinical decision making and to affect patient outcomes.

Acknowledgments: The authors thank Daniel P. Schuster, MD, for review of this manuscript and Lisa Schomaker for secretarial assistance.

Requests for Reprints: Marin H. Kollef, MD, FACP, Pulmonary and Critical Care Division, Washington University School of Medicine, Box 8052, 660 South Euclid Avenue, St. Louis, MO 63110.

Current Author Addresses: Dr. Kollef: Pulmonary and Critical Care Division, Washington University School of Medicine, Box 8052, 660 South Euclid Avenue, St. Louis, MO 63110.

Mr. Bock, Mr. Richards, and Ms. Hearns: Department of Respiratory Therapy, Barnes Hospital, One Barnes Hospital Plaza, St. Louis, MO 63110.

#### References

- Meduri GU, Johanson WG Jr. International Consensus Conference: clinical investigation of ventilator-associated pneumonia. Introduction [Editorial]. Chest. 1992;102:551S-2S.
- Kollef MH. Ventilator-associated pneumonia. A multivariate analysis. JAMA. 1993;270:1965-70.
- Fagon JY, Chastre J, Domart Y, Trouillet JL, Pierre J, Darne C, et al. Nosocomial pneumonia in patients receiving continuous mechanical ventilation. Prospective analysis of 52 episodes with use of a protected specimen brush and quantitative culture techniques. Am Rev Respir Dis. 1989;139:877-84.
- Seidenfeld JJ, Pohl DF, Bell RD, Harris GD, Johanson WG Jr. Incidence, site, and outcome of infections in patients with the adult respiratory distress syndrome. Am Rev Respir Dis. 1986;134:12-6.
- 5. Fagon JY, Chastre J, Hance AJ, Montravers P, Novara A, Gibert C.

Nosocomial pneumonia in ventilated patients: a cohort study evaluating attributable mortality and hospital stay. Am J Med. 1993;94:281-8.

- Rello J, Ausina V, Ricart M, Castella J, Prats G. Impact of previous antimicrobial therapy on the etiology and outcome of ventilator-associated pneumonia. Chest. 1993;104:1230-5.
- Rello J, Torres A, Ricart M, Valles J, Gonzalez J, Artigas A, et al. Ventilator-associated pneumonia by *Staphylococcus aureus*. Comparison of methicillin-resistant and methicillin-sensitive episodes. Am J Respir Crit Care Med. 1994;150:1545-9.
- Kollef MH, Wragge T, Pasque C. Determinants of mortality and multiorgan dysfunction in cardiac surgery patients requiring prolonged mechanical ventilation. Chest. 1995; [In press].
- Niederman MS, Torres A, Summer W. Invasive diagnostic testing is not needed routinely to manage suspected ventilator-associated pneumonia. Am J Respir Crit Care Med. 1994;150:565-9.
- 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;150:570-4.
- Cook DJ, Brun-Buisson C, Guyatt GH, Sibbald WJ. Evaluation of new diagnostic technologies: bronchoalveolar lavage and the diagnosis of ventilator-associated pneumonia. Crit Care Med. 1994;22:1314-22.
- Kollef MH. Antibiotic use and antibiotic resistance in the intensive care unit: are we curing or creating disease? Heart Lung. 1994;23: 363-7.
- Wunderink RG. Mortality and ventilator-associated pneumonia. The best antibiotics may be the least antibiotics [Editorial]. Chest. 1993; 104:993-5.
- Fagon JY, Chastre J, Hance AJ, Guiguet M, Trouillet JL, Domart Y, 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 Respir Dis. 1988;138:110-6.
- Meduri GU, Chastre J. The standardization of bronchoscopic techniques for ventilator-associated pneumonia. 1992;102:5578-64S.
- Chastre J, Fagon JY, Lamer C. Procedures for the diagnosis of pneumonia in ICU patients. Intensive Care Med. 1992;18:S10-7.
- Meduri GU. Ventilator-associated pneumonia in patients with respiratory failure. A diagnostic approach. Chest. 1990;97:1208-19.
- Knaus WA, Wagner DP, Draper EA, Zimmerman JE, Bergner M, Bastos PG, et al. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. Chest. 1991; 100:1619-36.
- Meduri GU, Mauldin GL, Wunderink RG, Leeper KV Jr, Jones CB, Tolley E, et al. Causes of fever and pulmonary densities in patients with clinical manifestations of ventilator-associated pneumonia. Chest. 1994;106:221-35.
- Marquette CH, Georges H, Wallet F, Ramon P, Saulnier F, Neviere R, et al. Diagnostic efficiency of endotracheal aspirates with quantitative bacterial cultures in intubated patients with suspected pneumonia. Comparison with protected specimen brush. Am Rev Respir Dis. 1993;148:138-44.
- Pingleton SK, Fagon JY, Leeper KV Jr. Patient selection for clinical investigation of ventilator-associated pneumonia. Criteria for evaluating diagnostic techniques. Chest. 1992;102:553S-6S.
- Rouby JJ, Martin De Lassale E, Poete P, Nicolas MH, Bodin L, Jarlier V, et al. Nosocomial bronchopneumonia in the critically ill. Histologic and bacteriologic aspects. Am Rev Respir Dis. 1992;146: 1059-66.
- Baselski VS, el-Torky M, Coalson JJ, Griffin JP. The standardization of criteria for processing and interpreting laboratory specimens in patients with suspected ventilator-associated pneumonia. Chest. 1992; 102:571S-9S.
- Rubin DB, Wiener-Kronish JP, Murray JF, Green DR, Turner J, Luce JM, et al. Elevated von Willebrand factor antigen is an early plasma predictor of acute lung injury in nonpulmonary sepsis syndrome. J Clin Invest. 1990;86:474-80.
- Hart TP, Mahuette CK. Evaluation of a closed-system, directional-tip suction catheter. Respiratory Care. 1992;37:1260-5.
- Fleiss JL. Statistical Methods for Rates and Proportions. 2d ed. New York: J Wiley; 1981:212-36.
- Bell RC, Coalson JJ, Smith JD, Johanson WG Jr. Multiple organ system failure and infection in adult respiratory distress syndrome. Ann Intern Med. 1983;99:293-8.
- 28. Fagon JY, Chastre J, Hance AJ, Domart Y, Trouillet JL, Gilbert C.

Evaluation of clinical judgment in the identification and treatment of nosocomial pneumonia in ventilated patients. Chest. 1993;103:547-53.

- Chastre J, Fagon JY, Soler P, Bornet M, Domart Y, Trouillet JL, et al. Diagnosis of nosocomial bacterial pneumonia in intubated patients undergoing ventilation: comparison of the usefulness of bronchoalveolar lavage and the protected specimen brush. Am J Med. 1988;85:499-506
- Timsit JF, Misset B, Francoual S, Goldstein FW, Vaury P, Carlet J. Is protected specimen brush a reproducible method to diagnose ICUacquired pneumonia? Chest. 1993;104:104-8.
- Marquette CH, Herengt F, Mathieu D, Saulnier F, Courcol R, Ramon P. Diagnosis of pneumonia in mechanically ventilated patients. Repeatability of the protected specimen brush. Am Rev Respir Dis. 1993;147:211-4.
- Dreyfuss D, Mier L, Le Bourdelles G, Djedaini K, Brun P, Bossougant Y, et al. Clinical significance of borderline quantitative protected brush specimen culture results. Am Rev Respir Dis. 1993;147:946-51.
- Torres A, el-Ebiary M, Padro L, Gonzalez J, de la Bellacasa JP, Ramirez J, et al. Validation of different techniques for the diagnosis of ventilatorassociated pneumonia. Comparison with immediate postmortem pulmonary biopsy. Am J Respir Crit Care Med. 1994;149:324-31.
- Meduri GU, Beals DH, Maijub AG, Baselski V. Protected bronchoalveolar lavage. A new bronchoscopic technique to retrieve uncontaminated distal airway secretions. Am Rev Respir Dis. 1991;143:855-64.
- Dotson RG, Pingleton SK. The effect of antibiotic therapy on recovery of intracellular bacterial from bronchoalveolar lavage in suspected ventilator-associated nosocomial pneumonia. Chest. 1993;103:541-6.
- 36. Fagon JY, Chastre J, Trouillet JL, Domart Y, Dombret MC, Bornet M, et al. Characterization of distal bronchial microflora during acute exacerbation of chronic bronchitis. Use of the protected specimen brush technique in 54 mechanically ventilated patients. Am Rev Respir Dis. 1990;142:1004-8.
- Torres A, Martos A, Puig de la Bellacasa J, Ferrer M, el-Ebiary M, Gonzalez J, et al. Specificity of endotracheal aspiration, protected specimen brush, and bronchoalveolar lavage in mechanically ventilated patients. Am Rev Respir Dis. 1993;147:952-7.
- el-Ebiary M, Torres A, Gonzalez J, de la Bellacasa JP, Garcia C, Jimenez de Anta MT, et al. Quantitative cultures of endotracheal aspirates for the diagnosis of ventilator-associated pneumonia. Am Rev Respir Dis. 1993;148:1552-7.
  Papazian L, Martin C, Meric B, Dumon JF, Gouin F. A reappraisal of
- Papazian L, Martin C, Meric B, Dumon JF, Gouin F. A reappraisal of blind bronchial sampling in the microbiologic diagnosis of nosocomial bronchopneumonia. A comparative study in ventilated patients. Chest. 1993;103:236-42.
- Baigelman W, Bellin S, Cupples A, Berenberg MJ. Bacteriologic assessment of the lower respiratory tract in intubated patients. Crit Care Med. 1986;14:864-8.
- Pham LH, Brun-Buisson C, Legrand P, Rauss A, Verra F, Brochard L, et al. Diagnosis of nosocomial pneumonia in mechanically ventilated patients. Comparison of a plugged telescoping catheter with the protected specimen brush. Am Rev Respir Dis. 1991;143:1055-61.
- Leal-Noval SR, Alfaro-Rodriguez E, Murillo-Cabeza F, Garnacho-Montero J, Rey-Perez J, Munoz-Sanchez MA. Diagnostic value of blind brush in mechanically ventilated patients with nosocomial pneumonia. Intensive Care Med. 1992;18:410-4.
- 43. Torres A, Puig de la Bellacasa J, Rodriguez-Roisin R, Jimenez de Anta MT, Agusti-Vidal A. Diagnostic value of telescoping plugged catheters in mechanically ventilated patients with bacterial pneumonia using the Metras catheter. Am Rev Respir Dis. 1988;138:117-20.
- Middleton R, Broughton WA, Kirkpatrick MB. Comparison of four methods for assessing airway bacteriology in intubated mechanically ventilated patients. Am J Med Sci. 1992;304:239-45.
- Clarke WR, Bell LM, Conte VH, McGowan KL. Blind endobronchial cultures: an alternative respiratory culturing method in children with chronic respiratory failure. J Crit Care. 1992;7:230-5.
- Chastre J, Viau F, Brun P, Pierre J, Dauge MC, Bouchama A, et al. Prospective evaluation of the protected specimen brush for the diagnosis of pulmonary infections in ventilated patients. Am Rev Respir Dis. 1984;130:924-9.
- Baker AM, Bowton DL, Haponik EF. Decision making in nosocomial pneumonia. An analytic approach to the interpretation of quantitative bronchoscopic cultures. Chest. 1995;107:85-95.