

Does Bronchoalveolar Lavage Enhance Our Ability to Treat Ventilator-Associated Pneumonia in a Trauma-Burn Intensive Care Unit?

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Background: Recent literature supports the notion that bronchoalveolar lavage (BAL) in ventilated trauma patients may improve our ability to diagnose and treat ventilator-associated pneumonia (VAP). We hypothesized that BAL would decrease the number of cases of VAP diagnosed and impact our antibiotic use and ventilator days.

Methods: Prospective data on all infectious complications were collected for patients admitted to the trauma-burn service for the year 2001. All VAPs between January 1, 2001, through June 30, 2001, were diagnosed without BAL (No BAL group) using clinical signs of fever, sputum production, leukocytosis, chest radiographs, and

sputum culture. After July 1, 2001, VAP was diagnosed with the use of BAL.

Results: There were 37 cases of VAP in the No BAL group (11%) and 29 cases of VAP (8%) in the BAL group. There were no statistical differences in Injury Severity Score, hospital length of stay, ventilator days, or mortality between the two groups. The time to initial treatment of VAP was shorter for the BAL group, but did not reach significance. The number of patients who had their VAP pathogens correctly treated with empiric antibiotics was also the same between the two groups. There was no difference in the rate of recurrent pneumonias. The antibiotic costs and respiratory therapy/ventila-

tor costs were not statistically different between the groups for trauma patients, although antibiotic costs were higher for burn patients.

Conclusion: The routine use of BAL to diagnose VAP in our mixed trauma-burn population did not impact on clinical outcomes or antibiotic use. Our results do not justify the additional costs and potential risks of BAL for all patients. The means of VAP diagnosis may not be as important as choosing the appropriate antibiotics for common VAP organisms in any given intensive care unit.

Key Words: Bronchoalveolar lavage, Ventilator-associated pneumonia, Trauma, Burn.

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Many issues surrounding ventilator-associated pneumonia (VAP) in injured patients remain controversial,^{1–5} from how to make the diagnosis to what the correct therapy and duration of antimicrobial therapy should be.^{6–10} The clinical findings of fever, purulent sputum, abnormal chest radiograph, and elevated white blood cell count suggest the diagnosis of pneumonia in many patients. These clinical findings are often present in the trauma population without documented pneumonia. The difficulty in differentiating a true VAP from other entities, such as systemic inflammatory response syndrome (SIRS), has led many centers to use quantitative cultures performed by bronchoalveolar lavage (BAL). It has been reported that BAL reduces the number of patients diagnosed with VAP by excluding

patients with SIRS, and the cultures obtained are thought to be more reliable.¹¹

On the basis of the literature, it was our bias that BAL would substantially reduce our VAP rate by reducing the number of false-positive “pneumonia” patients, and the BAL would improve our ability to treat VAP with better culture data. We recently instituted the policy of using BAL for establishing the diagnosis of VAP in all our ventilated patients with suggestive signs of pneumonia. As part of our quality assurance and protocol use review, we looked at whether the number of cases of VAP decreased, whether the costs were lower, and how BAL compared with Gram’s stains and regular sputum cultures in making the diagnosis of VAP.

MATERIALS AND METHODS

Mechanically ventilated patients admitted to the mixed Trauma-Burn Unit at the University of Michigan Health System during 2001 were followed prospectively for development of pneumonia signs and symptoms by our hospital infection control specialist and the treating physicians. These clinical indicators included fever, elevated white blood cell count of $> 10,000/\text{mm}^3$, purulent sputum, developing infiltrate on chest radiograph, and increased oxygen requirements. Any trauma or burn patient meeting clinical criteria of VAP admitted from January 1, 2001, through June 30, 2001, had

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their VAP diagnosed using standard sputum Gram's stain and sputum culture (No BAL group). These samples were obtained by the respiratory therapists using an in-line ventilator suctioning system and small amounts of 0.9% saline lavage (20–40 mL). Specimens were sent for Gram's stain, routine culture, and sensitivities.

As part of our quality improvement process, the Division of Trauma, Burn and Emergency General Surgery opted to use BAL for diagnosis of VAP in trauma or burn patients admitted from July 1, 2001, through December 31, 2001. Standard sputum cultures were also obtained before the BAL for comparison. Either a surgical resident or the trauma attending physician performed BAL. After a period of preoxygenation, the bronchoscope was passed down the right bronchus and directed toward any involved lobe, or placed in the lower bronchus if there was no obvious abnormality or radiographic infiltrate. Fifty milliliters of sterile, nonbacteriostatic saline was instilled in aliquots and the pooled effluent suctioned into a sterile in-line specimen container. Gram's stain and quantitative bacterial cultures were performed with subsequent sensitivities as appropriate. The same procedure was repeated for the left side. A positive quantitative culture had $> 10^4$ colony-forming units (CFU)/mL. BAL with $\leq 10^4$ CFU/mL were repeated as clinically indicated.

In both time periods of the study, the development of three clinical indicators for pneumonia prompted cultures to rule out the presence of VAP. The clinical indications did not change, but the method of culture diagnosis changed from sputum culture to BAL. The results of the Gram's stain were categorized as to presence of gram-negative rods, gram-positive cocci, yeast, or mixed pathogens (which includes "oral flora"), or no organisms. The Gram's stain findings were compared with the final culture results for both the No BAL and BAL patients. The results were designated as follows: an exact match, where the Gram's stain type and final cultured organism were the same; a partial match, where the Gram's stain had either a single organism type and the culture grew both gram-negative rods and gram-positive cocci or vice versa; or no overlap, where the Gram's stain and final culture were completely different. For both parts of the study, a recurrent pneumonia was defined as a pneumonia that developed after a complete course of therapy and after a period of negative cultures. The "recurrent" pneumonia could be from either the same organism as previously treated or a different pathogen.

According to our existing protocol, patients were started on empiric antibiotics after all cultures were obtained. If patients were already on a "prophylactic" antibiotic for coverage of open fractures or intracranial pressure monitors, additional antibiotics were added at the discretion of the attending physician. This category also included antibiotics given for other therapeutic reasons (e.g., urinary tract infection, cellulitis). In both halves of the study, after sending cultures, an empiric antibiotic was started that was usually a single broad-spectrum agent such as piperacillin-tazobactam,

levofloxacin, or ampicillin-sulbactam. Once final antibiotic sensitivities were available (from 48–72 hours), the empiric antibiotics were either maintained or adjusted to provide appropriate coverage. The empiric antibiotic choices did not change between the two time periods. The final cultures for all VAPs were compared with the empiric or prophylactic antibiotic coverage given. The results were categorized as to whether the antibiotic prescribed provided activity against the cultured organism. Antibiotics were described as inadequate treatment if the organism was not sensitive to the prescribed antibiotic. Partial antibiotic coverage was classified as either an antibiotic that had only intermediate sensitivity for the organism, or the organism required double or synergistic antibiotic coverage (the Infectious Disease Service at our institution recommends double coverage for *Pseudomonas* sp., *Acinetobacter* sp., and *Enterobacter* sp.). Typical coverage for these organisms would be a third-generation cephalosporin or piperacillin-tazobactam with either an aminoglycoside or fluoroquinolone.

Information on patient-associated costs for all antibiotics and respiratory/ventilator care was obtained through the University of Michigan Health System Financial Data Warehouse. Basic demographic data on patients including gender, age, mechanism of injury, Injury Severity Score, presence of an inhalational injury and total body surface area (TBSA) burn in the burn patients, length of stay, ventilator days, timing of antibiotic therapy, and mortality were obtained retrospectively from our trauma registry and online patient records.

Continuous variables were analyzed using unpaired two-tailed *t* tests. Discrete variables were compared using χ^2 analysis. Significance was defined as $p \leq 0.05$. Approval for this study was obtained through the hospital institutional review board.

RESULTS

Over the 1-year period, there were 68 patients treated for VAP. Of these, 37 were in the No BAL group and 29 were in the BAL group. The VAP rate for admitted patients was 11% for the No BAL group and 8% for the BAL group. The VAP rate per 1,000 ventilator days was 38% for the No BAL group and 29% for the BAL group. There was no statistical difference between the two groups for VAP rates. There were three patients in the No BAL time period who met some clinical criteria for VAP but who were not treated because of the lack of leukocytes on Gram's stain (two burn patients with inhalation injuries and one trauma patient). There were six patients who did not meet quantitative culture criteria for VAP in the BAL time period, and they were not treated (two burn patients with inhalation injuries and four trauma patients). None of these nine patients were treated for a subsequent pneumonia. The Injury Severity Score, age, ventilator days, hospital length of stay (LOS), and mortality of VAP patients were not different between the two groups (Table 1). There were more burn patients in the No BAL group than in the

Table 1 Demographics of Ventilator-Associated Pneumonia Patients

Group	VAP No (%)	Age (yr)	ISS	Ventilator Days	HLOS Days	Mortality No (%)
No BAL	37 (11)	44 ± 22	27 ± 9	12.3 ± 10	24 ± 11	5 (14)
BAL	29 (8)	50 ± 8	29 ± 13	12.9 ± 6	20 ± 6	6 (21)

ISS, Injury Severity Score.

BAL group. The average LOS for the burn patients was longer than their trauma counterparts for both the No BAL (50 ± 31 vs. 17 ± 6 days) and BAL groups (31 ± 30 vs. 20 ± 9 days).

The flora of the two groups is listed in Table 2. Almost two thirds of the coagulase-positive *Staphylococcus* were methicillin-resistant *S. aureus* (MRSA) in both groups. In addition, 24% of the No BAL bacteria and 28% of the BAL bacteria were *Pseudomonas* sp., *Acinetobacter* sp., or *Enterobacter* sp., which we routinely treat with double antibiotic coverage. One patient in each group had *Enterococcus*, and one patient in each group had yeast. In total, approximately 70% of patients in either group required either double antibiotic therapy for very pathogenic gram-negative organisms or specific coverage for MRSA, *Enterococcus*, or yeast.

Comparison of the Gram's stain findings and the final culture results revealed that 62% of the No BAL and 54% of the BAL specimens had the same type of organisms grow on culture as was seen on the initial Gram's stain (Table 3). The culture results of the sputum sent before BAL grew the same pathogens as the BAL specimen in 58% of samples. An additional 33% of the sputum cultures performed before the BAL had some overlap of the cultured organisms grown on subsequent BAL cultures. Only two patients (8%) had no overlap between the sputum culture performed before BAL and the BAL culture (Table 4).

The time to initiation of empiric antibiotic therapy was not different between the groups, with a delay of 0.8 ± 0.9 days for the No BAL and 0.6 ± 0.8 days for the BAL patients. The percentage of VAP patients who were started on adequate empiric antibiotic therapy for their VAP final cul-

Table 2 Cultured Organisms in Ventilator-Associated Pneumonias by Method of Diagnosis

Organism	No BAL	BAL
<i>Staphylococcus</i> sp.	16	9
<i>Streptococcus pneumoniae</i>	6	7
<i>Enterococcus faecalis</i>	1	1
<i>Haemophilus influenzae</i>	7	5
<i>Klebsiella</i> sp.	2	5
<i>Acinetobacter</i> sp.	1	2
<i>Enterobacter</i> sp.	5	4
<i>Pseudomonas</i> sp.	3	2
<i>Serratia marcescens</i>	0	2
Other gram-negative rod	3	2
Oral flora	7	6
Yeast	1	1

* There was more than one organism per final culture.

tured organisms was 35% for the No BAL and 34% for the BAL group. The coincident use of "prophylactic" antibiotics improved the percentage of adequate coverage of No BAL organisms to 43% and BAL organisms to 41%. The inclusion of antibiotic regimens that provided at least partial antibiotic coverage of an organism increased the adequacy of the empiric drug regimens to 57% for both the No BAL and BAL groups (Table 5). For patients started on either correct or partially correct therapeutic regimens, there were 6 deaths in 33 patients. Of those patients receiving either no antibiotics or nontherapeutic agents, there were 5 deaths in 33 patients.

There were 14 cases of recurrent VAP in the No BAL group and 9 in the BAL group. The recurrence rates were not statistically different. For the No BAL subset, 7 of 14 cases were diagnosed with the same organism as the initial VAP. Ten of the 14 recurrent VAP cases for the No BAL group had incorrect or partially inadequate antibiotic therapy with their initial empiric antibiotic regimens. Seven of nine recurrent VAP cases for the BAL group had the same organism as the initial VAP. Of these seven, six had initially inadequate empiric antibiotic coverage. The duration of total antibiotic therapy for the recurrent VAP patients compared with those

Table 3 Comparison of Gram's Stain Findings to Final VAP Culture by Diagnostic Method

Gram's Stain and Culture Results	No BAL	BAL
Gram's stain, GPC; culture, GPC	6	5
Gram's stain, GNR; culture, GNR	3	5
Gram's stain, mixed flora; culture, mixed flora	14	5
Gram's stain, GNR; culture, GPC	0	0
Gram's stain, GPC; culture, GNR	2	3
Gram's stain, mixed flora; culture, either GPC or GNR	5	3
Gram's stain, either GPC or GNR; culture, mixed flora	6	6
Grams stain, no organism; culture grew any organism	1	2

GPC, gram-positive cocci;
GNR, gram-negative rods.

Table 4 Comparison of BAL Final Culture and Sputum Final Culture*

Comparison of Cultures	No.
Final cultures identical	14
Final cultures had some overlap	8
Final cultures had no overlap	2
Sputum sample not sent (BAL only)	5

* Sputum culture refers to the sputum culture performed just before BAL procedure.

Table 5 Adequacy of Empiric or Prophylactic Antibiotics for Ventilator-Associated Pneumonia Pathogens

Adequacy of Antibiotic Regimen	No BAL (n = 37)	BAL (n = 29)
Correct empiric* antibiotics	13	10
Correct prophylactic** antibiotics	3	2
Resistant to prophylactic antibiotic or no double coverage provided	8	6
Resistant to empiric antibiotic	6	4
Empiric regimen does not provide double coverage	1	3
Empiric regimen sensitive for one but not all organisms	5	4
No empiric or prophylactic antibiotics given	1	0

* Empiric antibiotic specifically prescribed for pneumonia.

** Prophylactic antibiotic prescribed for other reason (e.g., open fractures, intracranial pressure monitor).

without recurrence was not different (10.7 ± 4 days vs. 12.4 ± 4 days, *p* = 0.13)

The costs per patient for all antibiotics and for all respiratory care/ventilator use are listed in Tables 6 and 7. Although the pharmacy antibiotic costs for the No BAL and BAL groups were not statistically different (*p* = 0.38), the No BAL group had a higher average cost. In the No BAL group, there were twice as many burn patients who had higher average antibiotic costs than either the trauma patients in the No BAL group or burn patients in the BAL group. The duration of antibiotic therapy was also not different between the No BAL group and the BAL group (11.3 ± 4 vs. 12 ± 3 days). The respiratory care costs were higher for trauma patients in the BAL group compared with the No BAL group (*p* = 0.008). Because of much longer hospital LOS and more ventilatory days, the burn patients were analyzed separately. The respiratory care costs for the No BAL burn patients were higher than for the BAL burn patients (*p* = 0.01). After

Table 6 Average Antibiotic Costs by Diagnostic Method

	No BAL (n = 34)*	BAL (n = 24)*
Mean cost ± SD	\$1,157 ± 1,219**	\$843 ± 777
Median cost	\$792	\$492

* Complete cost data not available on all patients.

** *p* = 0.38.

Table 7 Respiratory Care and Ventilator Costs by Diagnostic Method and Patient Type

	Trauma (n = 53)		Burn (n = 15)	
	No BAL (n = 29)	BAL (n = 24)	No BAL (n = 10)	BAL (n = 5)
Mean cost ± SD	\$5,095 ± 3,313*	\$8,087 ± 3,779	\$15,834 ± 6,581**	\$6,518 ± 2,497
Median cost	\$4,039	\$8,636	\$15,030	\$5,212

* *p* = 0.008.

** Not significant when controlled for by total surface area burn.

controlling for TBSA burn size, the difference was no longer significant (*p* = 0.06).

DISCUSSION

Over the last few years, the literature has been replete with data supporting the advantages of BAL in the diagnosis of VAP, in terms of lower costs and fewer patients treated for VAP through reduction of false-positive cultures.^{1-5,11} We instituted the practice of BAL with the belief that we would see the same benefits as described in the literature. In our 1-year study, we did not see the expected benefits of BAL. The number of ventilator days, respiratory care costs, number of recurrent VAP, hospital LOS, and antibiotic costs per patient were not different for our trauma patients diagnosed with VAP. There were initial differences detected in the burn patients in terms of costs. However, when burn patients' costs were controlled for by TBSA burn, the costs were no longer different between the No BAL and BAL groups.

There may be several explanations for our findings. This was a small but prospective 1-year study. We estimate, on the basis of the measured differences in this study, that we would require 1,540 ventilated patients to detect a potential difference in ventilator days. A study of this magnitude would take our single center many years to complete. One must ask, if it takes years to show such a small difference, is BAL worth the extra effort? The antibiotic and respiratory costs in this current study did not appear to justify BAL for trauma patients. In fact, the ventilator-associated costs were actually higher for trauma patients in the BAL group. A potential cost benefit may be present for burn patients who have BAL to establish the diagnosis of VAP. The number of burn patients in each group was small (10 in the No BAL group and 5 in the BAL group), with even fewer inhalational injuries and a wide variety of TBSA burn sizes. More patients would be needed to clearly demonstrate cost effectiveness for BAL. However, two burn patients with inhalation injuries were excluded from treatment in the BAL period.

One of the reported advantages of BAL is the ability to distinguish between patients who have clinical stigmata of VAP but who do not have a true pneumonia.¹¹ Only six patients were placed in the SIRS category rather than the VAP group during the BAL time period. The exclusion of these six patients from the BAL VAP group certainly incurred lower costs, but it did not substantially lower the overall VAP rate for the BAL group. Croce et al. have defined VAP using a BAL result of ≥ 10⁵ CFU/mL. In their

study, up to one third of patients diagnosed with SIRS after BAL continued to have symptoms, and 13% were later diagnosed with VAP on repeat BAL that resulted in $\geq 10^5$ CFU/mL.¹¹ With implementation of a new diagnostic method and concern over undertreatment of patients with VAP, we chose the lower threshold of $\geq 10^4$ CFU/mL as used by other authors.^{8,10} Potentially, this threshold was too sensitive, and we overtreated some patients with SIRS but not VAP. Croce et al. experienced a 13% VAP rate on repeat BAL in those initially not treated.¹¹ There were no patients in our study who had an initial BAL that was $\leq 10^4$ CFU/mL who were later diagnosed with VAP.

Our method of obtaining standard sputum cultures may be different from that of other centers. A recent study supports the notion that nonbronchoscopic alveolar lavage is a safe and sensitive technique for the diagnosis of VAP.^{8,12} This technique is more similar to our method of obtaining non-BAL sputum samples. The vast majority of sputum specimens were collected by respiratory therapists who routinely perform small-volume saline lavage before suctioning for a sputum sample through an in-line catheter system. The actual sputum culture results were identical to the BAL cultures in 58%, with overlap of some but not all organisms in an additional 33%. This left only a small percentage of cases where the pathogen was not detected by sputum culture alone. The technique of blinded "minilavage" may be the reason why BAL did not substantially reduce the number of false-positives for VAP. More data from other centers may be helpful in defining the usefulness of this technique.

We agree with other studies that Gram's stain is inaccurate for VAP diagnosis.^{12,13} Because Gram's stain was correct for only 54% of our BAL specimens, we opted to begin broad-spectrum empiric antibiotic therapy, rather than base therapy on the BAL Gram's stain or sputum Gram's stain results alone. Another reason for broad-spectrum therapy in our patient population is the bacteria profile in our intensive care unit (ICU). Many of the VAP staphylococci are MRSA, and one third of VAP pathogens are *Pseudomonas* sp., *Acinetobacter* sp., or *Enterobacter* sp.

As part of the review of BAL in our ICU, we have focused on which pathogens are present and what our current antibiotic susceptibilities are. One of the most important points in this study was the finding that what we thought was "adequate" empiric antibiotic therapy was inappropriate for 40% of VAPs in our ICU. Although the institution publishes hospital-wide antibiotic susceptibilities and likely organisms, the flora in our ICU is different. The importance of treating the local flora has been highlighted in other studies, which support the belief that duration of treatment and mortality may also be lowered by the correct initial antibiotic regimen.^{6,9,14} We did not detect a difference in mortality for those treated initially with correct or partially correct empiric antibiotics compared with those who received inappropriate antibiotic therapy. Unit-specific data provide for improved antibiotic selection and may lower costs by decreasing the

number of antibiotic days that are nontherapeutic. The risk of antibiotic resistance may also be less if the number of antibiotic changes necessary for completion of an appropriate therapeutic regimen is decreased.

CONCLUSION

In this 1-year, prospective study in a mixed trauma-burn population, we did not find that BAL lowered the VAP rate or costs associated with treatment compared with sputum culture alone. Burn patients with inhalation injury may be one patient subset with lower VAP-associated costs when diagnosed with BAL, and a larger study may provide insight into this problem. Despite the technique for establishing the diagnosis of VAP, specific knowledge about potential VAP pathogens in a given ICU is a crucial part of the correct and timely treatment of VAP.

REFERENCES

1. Pugin J, Auckenthaler R, Mili N, et al. Diagnosis of ventilator-associated pneumonia by bacteriologic analysis of bronchoscopic and nonbronchoscopic "blind" bronchoalveolar lavage fluid. *Am Rev Respir Dis.* 1991;143:1121-1129.
2. Cook DJ, Burn-Buisson C, Guyatt GH, Sibbald WJ. Evaluation of new diagnostic technologies: bronchoalveolar lavage and the diagnosis of ventilator-associated pneumonia. *Crit Care Med.* 1994; 22:1314-1322.
3. Meduri GU, Baselski V. The role of bronchoalveolar lavage in diagnosing non-opportunistic bacterial pneumonia. *Chest.* 1991; 100:179-190.
4. Torres A, dela Bellacasa JP, Xaubert A, et al. Diagnostic value of quantitative cultures of bronchoalveolar lavage and telescoping plugged catheters in mechanically ventilated patients with bacterial pneumonia. *Am Rev Respir Dis.* 1989;140:306-310.
5. Fagon JY, Chastre J, Hance AJ, et al. Detection of nosocomial lung infection in ventilated patient: use of a protected specimen brush and quantitative culture techniques in 147 patients. *Am Rev Respir Dis.* 1989;139:110-116.
6. Dupont H, Mentec H, Sollet JP, Bleichner G. Impact of appropriateness of initial antibiotic therapy on the outcome of ventilator-associated pneumonia. *Intensive Care Med.* 2001;2:355-362.
7. Baughman RP, Spencer RE, Kleykamp BO, Rashkin MC, Douthit MM. Ventilator associated pneumonia: quality of nonbronchoscopic bronchoalveolar lavage sample affects diagnostic yield. *Eur Respir J.* 2000;16:1152-1157.
8. Brown DL, Hungness ES, Campbell RS, Luchette FA. Ventilator-associated pneumonia in the surgical intensive care unit. *J Trauma.* 2001;51:1207-1216.
9. Iregui M, Ward S, Sherman G, Fraser V, Kollef M. Clinical importance of delays in the initiation of appropriate antibiotic treatment for ventilator-associated pneumonia. *Chest.* 2002;122:262-268.
10. Combes A, Figliolini C, Trouillet JL, et al. Incidence and outcome of polymicrobial ventilator-associated pneumonia. *Chest.* 2002; 121:1618-1623.
11. Croce MA, Fabian TC, Schurr MJ, et al. Using bronchoalveolar lavage to distinguish nosocomial pneumonia from systemic inflammatory response syndrome. *J Trauma.* 1995;39:1134-1140.
12. Duflo F, Allaouchiche B, Debon R, et al. An evaluation of the Gram stain in protected bronchoalveolar lavage fluid for the early diagnosis of ventilator-associated pneumonia. *Anesth Analg.* 2001; 92:442-447.

13. Croce MA, Fabian TC, Wadde-Smith L, et al. Utility of Gram's stain and efficacy of quantitative culture for posttraumatic pneumonia. *Ann Surg.* 1998;227:743-751.
14. American Thoracic Society. Hospital-acquired pneumonia in adults: diagnosis, assessment of severity, initial antimicrobial therapy, and preventative strategies. *Am J Respir Crit Care Med.* 1995;153:1711-1725.

DISCUSSION

Dr. William G. Cioffi (Providence, Rhode Island): I'd like to congratulate Dr. Wahl and her colleagues for trying to help us unravel the best diagnostic method for ventilator-associated pneumonia. We all struggle with the standard Centers for Disease Control and Prevention (CDC) criteria and wonder whether they really represent the "gold standard."

Unfortunately, I'm not sure they have arrived at an answer for us. In a nonrandomized fashion, they have compared blind sputum sampling with BAL quantitative cultures and they found no differences. The real question is, is this believable? Although my biases support their conclusions, there are several issues and problems with their study.

As pointed out in the last slide, this really compared blinded versus direct sampling. Do they have data that compare standard sputum sampling rather than this undirected, blinded lavage technique used by the respiratory therapists?

More importantly, how did you arrive at the decision to use 10^4 organisms as your quantitative endpoint for the diagnosis of pneumonia? If you had used 10^5 , which is also commonly used in the literature, would you have seen a difference?

Do you have any data, as the next article will discuss, on intracellular organisms? Would this have helped and refined your technique?

Could you have a type II error here? These are small numbers of patients. How many total patients were there in each time period? How many were on the ventilator and for how long? Although you gave us ventilator rates per 1,000 days, clearly the data could be skewed if there were some patients on the ventilator for a very long time and some for a short time.

How many patients had BAL and why did you perform the BAL? Were the entrance criteria in the CDC criteria for the second 6 months and then you had the BAL sample?

Finally, this is a very heterogenous patient population that includes both burn patients and trauma patients. How many of the burn patients had inhalation injury? If you segregated those patients out, do the data change?

My final question is, what do you do now? Have you abandoned this technique in your ICU, or are you still trying to refine it? Thank you.

Dr. David A. Spain (Stanford, California): If I understood this, you were comparing patients in both groups that you treated. What was the total cost of patients that you treated for pneumonia and those that you then didn't treat because of the results of the BAL?

How many patients in the second period underwent BAL, had the diagnosis of pneumonia excluded, and had antibiotic treatment terminated? Therefore, what's the cost of that entire group versus the ones that you actually treated. Because if you only look at the treated patients, you wouldn't expect the reduction in ventilator days or costs or any other factors.

The other issue has to do with the poor choice of empiric antibiotic. The data that Nick Namias has shown is that clearly unit-specific antibiograms are crucial, and the attributable increase in mortality from pneumonia, if you pick the wrong empiric antibiotics, is at least 25%.

Dr. David J. Dries (St. Paul, Minnesota): I have a number of questions that may help clarify some of these issues. In our unit, we look very critically at early versus late pneumonia. In trauma patients, there is a significant incidence of aspiration, particularly in people who are intubated or have airway problems in the field or in the emergency department. Did you segregate those people? They may behave differently than patients who acquire pneumonia farther into their ICU course. One of the keys to this article is your definition of pneumonia. Given your criteria, I think that a number of authors would say your ability to diagnose ventilator-associated pneumonia is as good as a coin flip. That may be in part, as Dr. Cioffi indicated, a problem with what the CDC has given us so far.

You talk about the ability to BAL to improve outcome. BAL, like a pulmonary artery catheter, just provides you data. The key to improving outcome is what you do with the data. We have decreased our rate of pneumonia and decreased our ventilator days, not because we used BAL or didn't use BAL but because we put in a strictly enforced nurse- and therapist-driven ventilator weaning protocol. Could you comment?

Dr. Carol R. Schermer (Albuquerque, New Mexico): My questions relate to some of the others, but not in terms of cost. In the patients who had a BAL and in whom you were able to discontinue antibiotics, did those patients get out of the unit sooner, and did you have overall less resistance in your unit?

The other issue relating to that is, do you use different empiric therapies on the basis of how long they have been in your unit? For example, is *Staphylococcus* found earlier and *Pseudomonas* later, so you alter the empiric antibiotic, which will alter your outcome?

My other comment is that I think discontinuing antibiotics in 6 patients of a total of 30 who got pneumonia is not a small number at all. If you were to convert that into numbers needed to treat to perform BAL, that's a pretty reasonable number to treat for the cost difference.

Dr. Wendy Lynn Wahl (closing): Thank you, Dr. Cioffi. We formerly performed this as a quality assurance issue. We believed so strongly that BAL was going to help us that we decided this was the way we were going to do it. So, you're right. This was historical and not a randomized pro-

spective trial, although the data were collected in a prospective fashion.

We did use 10^4 . Mostly, this is a microbiology issue. They didn't want to do the 10^4 and 10^5 , and we felt more comfortable doing 10^4 . Potentially, we were overly sensitive in picking up pneumonias. We did not have patients that had less than 10^4 that went on to develop pneumonia, so you could say that we were overly sensitive and overtreated.

If we had picked 10^5 , we may have missed some patients, but we decided, on the basis of the data out there, that we would choose 10^4 . I don't have any data on intracellular organisms, and I'm looking forward to hearing the next presentation.

As always, this could be a type II error, and looking at our data, we would need approximately 1,500 ventilator patients to make sure that we don't have a type II error. For us, that would take quite a long time, so a multicenter study would always be helpful, but we wanted to see in our patient population, really, what worked best.

For the BAL, we didn't really change our criteria for pneumonia. We were pretty strict about if you had these clinical findings, then you would get either a sputum or a BAL. It didn't change during the time periods. We were pretty rigorous about saying you had to meet these criteria before we really started to look for a pneumonia.

In terms of the burn patients, we did break them out for the costs because it was so skewed. But basically, because our ICU is a mixed population, we wanted to look at all patients and how we deliver care to all of them and see whether there were differences.

For the burns, approximately half of them had inhalation injuries but, again, you're getting down to such small numbers that it's hard. You could be missing something. But if anybody in the population seemed to have a benefit with the BAL, it may be the burn patients because of the inhalation component.

What are we doing now? We are still in disbelief. We are still doing BAL. We're going to get another year of data and compare, particularly looking at the burn patients and see.

I think one of the things that we didn't realize was that the respiratory therapists had been doing the blind lavage the entire time without us knowing it and not random sputum

cultures, because they had read that it was a better way of doing it.

Dr. Spain, I agree. I don't have the actual cost data for how many people were not treated but I could get them. That would be easy to do, because I have all the data. In the BAL group, there are six patients who met the clinical criteria and then did not meet the culture criteria.

In the sputum culture time period, there were three patients who met all the clinical criteria but didn't meet it on a culture. Thus, in both groups we weeded out some. It would be simple enough to add that to the cost data, and I agree.

In terms of the mortality, that was a big concern when we were looking at this thing. We are doing a terrible job selecting our empirics. One of the reasons why is the data that are reported to us through the hospital—first of all, in a cost-cutting measure a few years ago, they started doing hospital-wide sensitivities and organisms that don't apply to our ICU.

Then, we started getting unit-specific data, but the way it's being reported is the respiratory cultures. Thus, you would have 100 respiratory cultures. Let's say the same patient had 10 sent and all of them showed *Pseudomonas*, so it skews your data so you don't really know what your patient population really has, because you want that person to be counted 1 time and not 10 times. Thus, we are working on a more useful reporting system and also pushing them to report it in a timely fashion so we can use it to select antibiotics.

We did look at the mortality issue because I was very concerned. Thankfully, in this small study, the number of deaths in the correctly or partially correct antibiotic group was six, and the number of deaths in the inappropriate or antibiotic group was five, so we didn't see a difference there.

Dr. Dries, I agree. I think it's not so much how you make the diagnosis but what you do with the information. We did not, for this study, look at early versus late. I could do that. The numbers are getting so small they wouldn't be helpful, but I agree that that might be helpful in determining the organisms and our empiric antibiotic usage.

There were six in the BAL and three in the no BAL groups that were not treated. We would have to go back and look at the costs because we didn't separate it out. I didn't look at the people who we didn't treat, look at their length of stay and their costs, but we could go back and look at that, in addition.