Endotracheal Aspiration in the Diagnosis of Ventilator-Associated Pneumonia*

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Abbreviations: EA = endotracheal aspiration; VAP = ventilator-associated pneumonia

The time-honored method of identifying bacterial pathogens that are potentially responsible for nosocomial pneumonia in patients receiving mechanical ventilation is the microscopic examination of specimens obtained by endotracheal aspiration (EA). This technique is the simplest noninvasive means of obtaining respiratory secretions from patients receiving mechanical ventilation; it is readily performed at the bedside and requires minimal training by health-care providers. This section focuses on clinical studies evaluating diagnostic procedures using endotracheal specimens (*ie*, cytologic examination, antibody coating, elastin fibers, Gram's stain, and culture) in immunocompetent adults with suspected VAP.

The cytologic examination of specimens containing a large number of leukocytes and a paucity of epithelial cells is likely to produce the most valid representation of infectious organisms. A test for the detection of the presence of antibody coating on bacteria has been developed in an attempt to distinguish organisms that are colonizing the lower respiratory tract from those that actually are infecting it. The test is based on the premise that an infection will elicit an antibody response in the host and that this response will be detectable on the microorganism. In addition, using 40% potassium hydroxide to detect elastin fibers has been promoted as a rapid and inexpensive way to demonstrate the destruction of lung parenchymal tissue that is caused by pneumonia.

However, an analysis of endotracheal specimens obtained by aspiration has been diagnostically inadequate. Several qualitative articles have reviewed the use of endotracheal specimens to diagnose VAP. Among the challenges for investigators and clinicians are the following: distinguishing upper from lower respiratory tract infection; distinguishing infection from colonization and contamination; standardizing aspiration collection methods and microbiological techniques; and interpreting test properties in light of the host's immune status, the pathogenic load, and the effect of prior antimicrobial therapy.

Newer bronchoscopic methods for diagnosing VAP have become the focus of recent investigations, conferences, and professional documents. Invasive approaches have not necessarily been adopted by clinicians,[2] at least in part because of procedural access, cost, and the absence of compelling evidence that treatment based on the derived data changes clinical or economic outcomes. Thus, many physicians continue to use endotracheal specimens and other clinical features in diagnosing VAP.

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Analysis

The most acceptable reference standards or "gold standards" usually include biopsy or autopsy reports. Since these often are not feasible standards, alternatives are usually used. They include cultures of pleural and blood specimens, long-term follow-up to exclude other diagnoses, and quantitative cultures of specimens obtained through bronchoscopic techniques. The use of bronchoscopic specimens makes interpretation of the reference standard particularly difficult, since the test properties of BAL and protected-specimen brush sampling still are being evaluated. Tables 9–11 cover the reference standards used in these studies.

We calculated the sensitivity and specificity of a test result on an endotracheal specimen according to formulas presented earlier in this report. In parentheses in Tables 9–11, we indicated the sensitivity and specificity estimates of the authors. The calculation of likelihood ratios requires knowledge of the number of patients with and without pneumonia, as determined by the reference standard, separated according to the culture results from endotracheal specimens. Most studies did not report data on all four groups of patients, so we could not calculate a 2×2 table and did not include likelihood ratios for these studies. Due to heterogeneous study designs and results, we did not statistically pool data in the form of a meta-analysis.

Results

The comprehensive literature search described earlier[2] yielded 12 relevant citations[2,13–15,18,23,91–96] published from 1985 to 1995. Nine studies evaluated cultures from EA, two studies evaluated antibody coating, and three studies evaluated elastin fibers. Study characteristics and the results of Gram's stain and aspiration culture appear in Table 9. The same data are recorded for antibody coating in Table 10, and for elastin fibers in Table 11. The original articles present the details of the design and results of the studies.

Most studies were prospective. Several stated that patients were enrolled consecutively. Most patients received mechanical ventilator support. Some studies profiled patients according to the duration of ventilator support. Most patients were receiving antibiotics at the time of testing. The methods of analyzing endotracheal specimens were recorded in all studies. In no studies were test results interpreted by investigators blinded to the results of other tests. In one study,[17] the reference standard was interpreted by an investigator blinded to the results of the test under evaluation. Most studies focused on sensitivity by enrolling patients with suspected VAP. A valuable study by Torres et al[23] determined specificity in patients without suspected VAP.

Most investigators acknowledged the difficulty with choosing a reference standard for VAP. For example, one

Table 9—*Study Characteristics and Results for EAs

Study/Year	Enrollment/Patients (Episodes)	Population (Antibiotic Status)	Quality of the Sample	Reference Standard	Sensitivity†	Specificity†
Villers et al[96]/1985	Prospective selected/17 (17)	Suspected VAP, not suspected VAP, ventilated > 72 h (yes)	Bacteria present/absent	PSB or blood/pleural fluid culture of serology or open-lung biopsy	100% (NR)	0% (NR)
Lambert et al[16]/1989	Prospective/22 (22)	Suspected VAP, ventilated > 72 h (yes)	Bacteria present/absent	Autopsy or clinical response to antibiotics or PSB	100% (NR)	38% (33%)
Torres et al[15]/1989	Prospective/34 (34)	Suspected VAP (yes)	Bacteria present/absent	Autopsy, favorable antibiotic response, or other diagnosis ruled out	94% (94%)	14% (14%)
El-Ebiary et al[13]/1993	Prospective/102 (102)	Suspected VAP, not suspected VAP, autopsy, ventilated > 72 h (yes)	Q, 10^5 cfu/mL	Clinical diagnosis (definite, uncertain, control)	CC (70%)	CC (72%)
Marquette et al[95]/1993	Prospective/52 (52)	Suspected VAP (yes)	Q, 10^6 cfu/mL	Clinical diagnosis	82% (82%)	83% (83%)
Sauaia et al[14]/1993	Prospective consecutive/18 (18)	Suspected VAP, ventilated > 72 h (yes)	SQ and Q, 10^5 cfu/mL, SEC	Clinical diagnosis (definite, probable, no pneumonia)	38% (NR)	100% (NR)
Torres et al[23]/1993	Prospective consecutive/27 (27)	VAP not suspected, ventilated > 72 h (yes)	Q, 10^6 cfu/mL	Clinical absence of VAP	CC (NR)	89% (78%)
Jourdain et al[94]/1995	Prospective consecutive/39 (57)	Suspected VAP, ventilated > 48 h, mean ventilation 2–3 wk (no or no change in 72 h)	Q, 10^6 cfu/mL, PMN in BAL, ICO	Clinical diagnosis, PSB or BAL	CC (68%)	CC (84%)
Marquette et al[18]/1995	Prospective consecutive/28 (28)	Suspected VAP had autopsy within 3 d of bronchoscopy, mean ventilation 2 wk	Q, 10^6 cfu/mL, SEC, PMN, ICO	Autopsy	53% (55%)	67% (85%)

*Episodes = No. of episodes of VAP considered; PSB = protected-specimen brush; NR = not reported; Q = quantitative; CC = cannot calculate; SQ = semiquantitative; SEC = squamous epithelial cells; PMN = polymorphonuclear cells; and ICO = intracellular organisms.
†Values in parentheses indicate estimates of authors.

study evaluated different cutoffs for values from endotracheal specimens, conceptualizing positive results on a spectrum (from 10^3 to 10^6 cfu/mL), rather than as a *black-and-white* phenomenon.[23] Other investigators avoided two categories (VAP present or not present) by creating three categories along the following clinical lines: definite VAP; probable VAP; and unlikely VAP.[13,14] The tables show the various reference standards.

Table 10—*Study Characteristics and Results for Antibody-Coated Bacteria

Study/Year	Enrollment/Patients (Episodes)	Population (Antibiotic Status)	Quality of the Sample	Reference Standard	Sensitivity†	Specificity†
Lambert et al[16]/1989	Prospective/22 (22)	Suspected VAP, ventilated > 72 h (yes)	ACB, EA (bacteria present/absent), PMN	Autopsy or clinical response to antibiotics or PSB	56% (NR)	50% (NR)
Wunderink[134]/1991	Prospective/36 (36)	Suspected VAP (yes)	ACB, EA (bacteria present/absent)	Clinical diagnosis or open-lung biopsy or autopsy or blood culture of DFA) (Legionella spp)	46% (46%)	69% (100%)

*ACB = antibody-coated bacteria; DFA = direct fluorescent antibody. See Table 9 for other abbreviations and explanations of data.
†Values in parentheses indicate estimates of authors.

Table 11—*Study Characteristics and Results for Elastin Fibers

Study/Year	Enrollment/Patients (Episodes)	Population (Antibiotic Status)	Quality of the Sample	Reference Standard	Sensitivity†	Specificity†
Salata[135]/1987	Prospective consecutive/51 (51)	Suspected VAP, mean ventilation 2–5 wk (yes)	Q, 10^5 cfu/mL, PMN, ICO	Clinical diagnosis (pulmonary infection, colonization, colonization with infiltrate)	52% (NR)	93% (NR)
El-Ebiary et al[13]/1993	Prospective/78 (78)	Suspected VAP, ventilated > 72 h (yes)	Q, 10^5 cfu/mL	Definite (blood/pleural fluid isolate, histopathology, or culture of pathogen) Probable (clinical diagnosis)	32% (32%)	72% (72%)
Shepherd et al[17]/1995	Prospective selected/22 (22)	Suspected VAP with ARDS (yes)	Unclear	Definite (clinical diagnosis and 1 of blood or pleural fluid isolate, or histopathology) Probable (clinical diagnosis)	58% (58%)	40% (40%)

*See Table 9 for abbreviations and explanations of data.
†Values in parentheses indicate estimates of authors.

Conclusions

- The sensitivity and specificity of quantitative tests on cultures of EA samples vary widely in their ability to diagnose VAP.
- Qualitative EA cultures usually identify organisms found by invasive tests (EA cultures have high sensitivity). However, qualitative EA cultures often recover multiple organisms, including nonpathogens (EA tests have a moderate positive-predictive value). If the result of a qualitative EA culture is negative, VAP is unlikely unless the patient has received antibiotic therapy (EA tests have a moderately high specificity).
- With initial and subsequent episodes of VAP, the results of diagnostic tests may vary with the pathogenic bacterial load, the duration of ventilator support, and antibiotic administration.
- Gram's stain and culture of endotracheal secretions obtained by aspiration may be useful in diagnosing VAP (grade D recommendation). The presence of antibody coating or elastin fibers is an unreliable indicator and is not recommended for clinical diagnostic use (grade C recommendation).

Recommendations

Current studies on VAP diagnosis evaluate the most basic, frequently used approaches to endotracheal analysis and yield insufficient data to generate strong clinical policy recommendations (recommendations based on research). Fewer than 600 patients contribute to the body of evidence. More high-quality studies are needed.

Although the studies reviewed in this report are moderately rigorous, differences between studies in designs and results make generalizations difficult. For example, in studies on endotracheal specimens, sensitivity ranged from 38 to 100%, and specificity ranged from 14 to 100%. Practitioners in most fields would not rely on such tests to diagnose or rule out disease. Findings cannot be explained with confidence on the basis of study design or chance. Such heterogeneous data preclude strong evidence-based inferences, and our recommendations are necessarily heavily augmented by opinion.