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# Sputum Gram Stain Assessment in Community-Acquired Bacteremic Pneumonia

RICHARD GLECKMAN,* JAMES DEVITA, DEBRA HIBERT, CAROL PELLETIER, AND RONALD MARTIN

*Division of Infectious Disease, Saint Vincent Hospital, 25 Winthrop Street, Worcester, Massachusetts 01604*

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**A prospective study was performed over a 4.5-year period to determine the ability of a sputum Gram stain to predict the cause of community-acquired bacterial pneumonia. A blood culture isolate, rather than a sputum culture, served as the reference standard to provide precise identification of the etiologic agent. The study population comprised 59 bacteremic adults who expectorated a valid sputum sample. Data are presented that indicate that a physician, aided by the morphology of the stained sputum, could theoretically select appropriate monotherapy approximately 94% of the time when selective, defined criteria for the microbiology of valid sputum are met. Three of the five patients with pneumonia caused by *Haemophilus influenzae*, however, had sputum stains that suggested alternative pathogens. This study reaffirms that the Gram-stained sputum is a reliable, but not infallible, guide to direct initial antibiotic therapy in adults with community-acquired bacterial pneumonia.**

Recently, concern has been expressed that physicians tend to prescribe the more expensive broad-spectrum cephalosporin antibiotics rather than make a serious effort to accurately identify the cause of a pneumonia and institute directed, organism-specific treatment with the more established, less expensive agents (4).

Techniques that provide access to lower respiratory secretions, consisting of transtracheal aspiration, lung puncture, and fiber-optic protected-catheter bronchoscopy, are uncomfortable, invasive, and expensive and necessitate considerable skill. In addition, on occasion these procedures cause major untoward events, and thus, with the exception of a few university teaching hospitals, they have not been accepted as part of the routine assessment of patients with community-acquired bacterial pneumonia.

Traditionally, an evaluation of Gram-stained expectorated sputum has served as a guide for initial selection of antibiotic therapy for patients with bacterial pneumonia. There are a number of reasons why this approach has enjoyed so much acceptance; sputum is usually readily available; this procedure entails no risk to the patient; interpretation requires no sophisticated equipment; the evaluation can be completed within a few minutes; sputum assessment is very inexpensive; and presumably, this test provides invaluable diagnostic and prognostic information (2).

A dispute currently exists in the medical literature regarding the ability of clinicians to rely on a Gram stain of sputum to guide onset treatment of community-acquired pneumonia (11). There are studies that support or refute the diagnostic specificity of Gram-stained sputum (2, 5, 7, 8, 12). These studies however, have used the culture of lower respiratory tract secretions as the reference standard, and they have not exclusively evaluated the potential impact of valid sputum. We performed a prospective study for 4.5 years in which we evaluated the correlation between valid sputum Gram stains and blood cultures for patients with community-acquired bacterial pneumonia. We decided to use blood culture isolates as the reference standard rather than cultures of sputum, transtracheal aspirate, or bronchoscopy aspirate.

* Corresponding author.

We elected not to study patients with nosocomial bacteremic pneumonia. We identified few hospitalized patients with bacteremic pneumonia who were capable of expectorating a valid sputum. These patients were invariably debilitated from advanced stages of neurological or neoplastic disease or were being managed with mechanical ventilation.

## MATERIALS AND METHODS

**Patients.** An attempt was made to collect blood cultures and sputum from all adult patients with community-acquired bacterial pneumonia admitted to Saint Vincent Hospital between January 1982 and July 1987. One hundred and forty-four adult patients with community-acquired bacteremic pneumonia who necessitated hospitalization during this 4.5-year period were candidates for this study. The definition of community-acquired bacteremic pneumonia required the following four elements: an illness necessitating hospital admission, manifested by fever, respiratory symptoms, and respiratory signs; identification of a new pulmonary infiltrate on chest X ray that was interpreted by the radiologist as most consistent with an infectious process; isolation of a bacterium from blood that is a recognized respiratory pathogen; and absence of any coexistent infection that could serve as an alternative source for the bacteremia. From the potential pool of candidates and by using rigid criteria to define valid respiratory secretions, we identified 59 patients. These latter patients are the subjects of this report. None of these 59 patients were receiving antimicrobial agents before the acquisition of blood cultures and respiratory secretions.

**Microbiology.** Blood cultures were processed by conventional microbiologic techniques (6). Spontaneously expectorated sputa were collected within 2 h of hospital admission and before any antimicrobial therapy. Sputa were incubated for 48 h on chocolate agar, on 5% sheep blood agar, and on MacConkey agar plates. For the first 24 h, the chocolate agar was incubated in 5% $CO_2$, and the sheep blood agar was incubated in an anaerobic jar. Organisms were identified by standard microbiologic techniques (9). The sputum plates were read on the day after the Gram-stained preparations were interpreted. The following organisms were considered

potential pathogens: *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Branhamella catarrhalis*, and facultatively anaerobic gram-negative bacilli.

The technologists were given no clinical information, and they interpreted the smears 1 to 2 days before detection of the bacteremia. For the purpose of this study, the Gram-stained smears had to fulfill the following two criteria to be considered valid: there had to be more than 25 polymorphonuclear leukocytes and less than 10 squamous epithelial cells on low-power (×100) magnification.

**Study design.** Once the diagnosis of bacterial pneumonia is considered, physicians are interested in confirming the diagnosis and rapidly instituting correct antimicrobial treatment. The purpose of this investigation was to determine whether a valid sputum Gram stain, supplemented by epidemiological and clinical features, could immediately guide appropriate antibiotic selection, pending identification and susceptibility determination of the respiratory pathogen. Arbitrarily, we would consider therapy ideal if penicillin was prescribed to a patient when gram-positive cocci resembled *Streptococcus pneumoniae*, *Streptococcus pyogenes*, or *Streptococcus agalactiae*; a broad-spectrum cephalosporin (cefonicid, cefuroxime, or cefamandole), a third-generation cephalosporin, or chloramphenicol was prescribed when gram-negative rods resembled *Haemophilus influenzae*; a third-generation cephalosporin, with or without an aminoglycoside, was prescribed when gram-negative rods resembled *Enterobacteriaceae*; oxacillin, a cephalosporin, or vancomycin was prescribed when gram-positive cocci appearing in clumps resembled *Staphylococcus aureus*; and amoxicillin-clavulanic acid was prescribed when gram-negative diplococci resembled either *Neisseria meningitidis* or *Branhamella catarrhalis*.

**Statistical analysis.** Statistical comparisons of groups were made by use of two-by-two contingency tables. The *P* values were determined by use of the Fisher exact probability method.

## RESULTS

The patients ranged in age from 17 to 93 years, with a medium of 66 years and a mean of 65 years. Thirty-three patients were men, and 26 patients were women.

The etiology of the pneumonia, as determined by blood cultures, included 36 infections caused by *Streptococcus pneumoniae*, 8 caused by *Haemophilus influenzae*, 7 caused by *Staphylococcus aureus*, 4 caused gram-negative facultatively anaerobic bacilli (*Escherichia coli*, 3; *Serratia marcescens*, 1), 1 caused by *Streptococcus agalactiae*, 1 caused by *Streptococcus pyogenes*, 1 caused by *Neisseria meningitidis*, and 1 in which both *Staphylococcus aureus* and *Streptococcus pyogenes* were isolated.

On the basis of the morphology and quantitative assessment of the Gram-stained sputum, we identified the following five categories of patients: category A, no organisms seen (1 patient); category B, mixed flora, in which there was no one morphotype in a concentration of >10 organisms per oil immersion (magnification ×1,000) field (7 patients); category C, mixed flora, in which there were two or more different morphotypes in a concentration of >10 organisms per oil immersion field (4 patients); category D, one morphotype in a concentration of <10 organisms per oil immersion field (9 patients); category E, one morphotype in a concentration that exceeded 10 organisms per oil immersion field, with or without an additional morphotype in a concentration of <5 organisms per oil immersion field (38 patients).

We elected not to assess sputa from patients in categories A, B, or C because, by definition, these respiratory secretions do not provide clinicians with precise therapeutic guidance to initiate appropriate selective therapy, and these exudates would, therefore, require administration of multiple or broad-spectrum antimicrobial agents until the true pathogens were identified, if possible, by alternative methods. These sputa demonstrated either no bacteria or a polymicrobic flora. We decided to analyze sputa exclusively from patients in categories D and E because, presumably, the morphotypes observed traditionally are considered presumptive guides for onset, directed antimicrobial treatment.

Table 1 depicts the Gram stain morphology, blood culture isolate, and sputum culture isolate obtained from each patient in categories D and E, those patients with sputa that demonstrated a single predominant morphotype. Collectively, these two categories comprise 47 patients. Disorders that predispose to development of pneumonia were identified in 29 of the 47 patients. There were 14 patients with chronic pulmonary diseases, 8 with malignant disorders, 4 with neurologic impairments, and 3 with miscellaneous diseases. The Gram-stained sputum precisely predicted the blood culture isolate results for 67.7% (6 of 9) of the patients in category D and 89.5% (34 of 38) of the patients in category E, for an overall sensitivity of 85.1%. There was no significant difference ($P = 0.49$) in sensitivity when specimens from patients in category D were compared with specimens from patients in category E.

It is apparent (Table 1) that if a clinician had been guided by the valid Gram-stained sputum specimens and offered monotherapy, previously outlined and appropriate, to patients in categories D and E, initial treatment would have been ideal for 40 patients, acceptable for 4 patients, and inappropriate for 3 patients. There was no significant difference ($P = 0.17$) in terms of inappropriate treatments when misleading smears from patients in category D (2 of 9) were compared with misleading smears (1 of 38) from patients in category E.

Four patients would have received acceptable initial antibiotic treatment, including the patient who had both *Staphylococcus aureus* and *Streptococcus pneumoniae* isolated from blood cultures. Oxacillin, a cephalosporin, and vancomycin would be considered appropriate therapies for community-acquired bacterial pneumonia caused by *Streptococcus pneumoniae* and *Streptococcus agalactiae*, but penicillin would be preferred.

For three patients, the interpretation of the Gram-stained sputa would have directed a clinician to prescribe inappropriate treatment. The smears from two patients in category D suggested pneumococci, but both patients had pneumonia caused by *Haemophilus influenzae*. One smear from a patient in category E revealed gram-positive cocci that resembled *Streptococcus pneumoniae*, but the patient had *Staphylococcus aureus* recovered from the blood. It is of interest, however, that both organisms were isolated from sputum, suggesting the possibility of mixed or polymicrobic pneumonia.

## DISCUSSION

Clinicians are interested in rapid, simple, inexpensive, and readily available tests that will assist them in prescribing proper medications for life-endangering infections and, in the present era of prospective payment, will guide them in

TABLE 1. Correlation of Gram stain, blood isolate, and sputum culture

| Category and organism traits | Organism(s) from blood isolate (no.) | Organism(s) from sputum isolate (no.) |
|---|---|---|
| Category D | | |
| Gram-positive cocci in pairs and chains | *Streptococcus pneumoniae* (5)<br>*Haemophilus influenzae* (2) | *Streptococcus pneumoniae* (4)<br>*Haemophilus influenzae* (2)<br>Normal flora (1) |
| Gram-positive cocci in clusters | *Staphylococcus aureus* (1)<br>*Streptococcus pneumoniae* (1) | *Streptococcus aureus* (1)<br>Normal flora (1) |
| Category E | | |
| Gram-positive cocci in pairs and chains | *Streptococcus pneumoniae* (20)<br>*Streptococcus pyogenes* (1)<br>*Staphylococcus aureus* (1) | *Streptococcus pneumoniae* (20)<br>*Streptococcus pyogenes* (1)<br>*Staphylococcus aureus* and (1) *Streptococcus pneumoniae* |
| Gram-positive cocci in clusters | *Staphylococcus aureus* (5)<br>*Staphylococcus aureus* and (1) *Streptococcus pyogenes*<br>*Streptococcus pneumoniae* (2)<br>*Streptococcus agalactiae* (1) | *Staphylococcus aureus* (6)<br>*Staphylococcus aureus* and (1) *Streptococcus pyogenes*<br>*Streptococcus pneumoniae* (1)<br>Normal flora (1) |
| Small gram-negative coccobacilli | *Haemophilus influenzae* (2) | *Haemophilus influenzae* (2) |
| Gram-negative bacilli | *Escherichia coli* (2)<br>*Serratia* sp. (1)<br>*Haemophilus influenzae* (1) | *Escherichia coli* (2)<br>*Serratia* sp. (1)<br>*Haemophilus influenzae* (1) |
| Gram-negative diplococci | *Neisseria meningitidis* (1) | *Neisseria meningitidis* (1) |

the selection of cost-effective treatments. For management of community-acquired pneumonia, the sputum Gram strain has traditionally served this function. When comparing it with conventional culture techniques as the reference standard to determine the cause of the pneumonia, some investigators have, however, questioned the reliability of the sputum Gram stain (7, 12).

To enhance the diagnostic value of a sputum sample and to preclude assessment of respiratory secretions contaminated by oropharyngeal flora, microbiologists, infectious disease consultants, and pulmonary disease specialists recommend that only valid respiratory secretions be processed (10). We elected to correlate the interpretation of the sputum Gram stain with the decision regarding initial antibiotic therapy for patients with community-acquired bacterial pneumonia. We attempted to accomplish this by using only valid sputum, substituting a blood culture for a sputum culture as the reference standard, and offering acceptable antibiotic guidelines for initial treatment. We elected to use a blood isolate as the reference standard because recovery of an acknowledged respiratory pathogen from blood cultures provides precise etiologic information (1).

Our experience underscores the difficulty of collecting valid respiratory secretions from adult patients with pneumonia. This was achieved with 59 (41%) of 144 patients. Further analysis indicated that a predominant and exclusive morphotype was detected in 47 specimens or 79% of the valid specimens. The data from this study indicate that if a clinician is guided by the morphology of a valid, stained sputum sample he or she can select appropriate monotherapy for the treatment of community-acquired bacterial pneumonia when there is a single morphotype. In our experience, unacceptable antibiotic treatment would have been prescribed for only 3 (6.4%) of 47 patients. In fact, for one of the latter patients, the sputum culture suggested the possibility of a polymicrobic infection (3).

Our study was performed on patients with bacteremic community-acquired pneumonia, which represents approximately 15% of the adult patients with pneumonia who are admitted to our hospital. We are unaware of any published study that precludes us from extrapolating our findings to the larger patient population, namely, adults with community-acquired pneumonia unassociated with bacteremia.

Although we used different criteria and a new approach, our prospective study confirms the observation made by Boerner and Zwadyk that a sputum Gram stain is a reliable indicator to guide initial antibiotic therapy (2). It is essential to emphasize, however, that our data are applicable exclusively to that segment of the adult population with community-acquired pneumonia who have disease caused by conventional bacterial respiratory pathogens, can expectorate a valid sputum, and do not have a polymicrobic infection. There remains a need to develop alternative tests to the sputum Gram stain to guide onset treatment for patients who are not capable of expectorating valid sputum.

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