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Nonvalue of Sputum Culture in the Management of Lower Respiratory Tract Infections

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Establishment of the microbiological etiology of bacterial pneumonia by sputum culture is confounded by both lack of recovery of fastidious pathogens and contamination of specimens with oropharyngeal flora. We reviewed the clinical records from 249 patients over a 3-month period for evidence of pneumonia. Gram staining and cultures were performed on 381 specimens isolated from this population of patients. Recovery of respiratory tract pathogens was accomplished with 354 specimens from 226 patients; 27 specimens yielded normal flora in culture but were smear positive. An additional 256 specimens submitted to our microbiology laboratory did not meet smear criteria for purulence nor did they yield respiratory tract pathogens in culture. A total of 637 specimens submitted to the microbiology laboratory were evaluated for sputum purulence by the criteria of Bartlett. Of the total 354 specimens which were positive in culture for a pathogen, 182 (52%) were submitted from 150 patients with no objective evidence of pneumonia. The majority of specimens obtained from patients without pneumonia were nonpurulent. However, 71 of 182 culture-positive specimens obtained from 50 patients without pneumonia were purulent. Approximately half of these patients (31 of 50) had other pulmonary or upper respiratory tract pathology which could account for the sputum purulence. Among the 172 culture-positive specimens from 76 patients with pneumonia, only 100 (58%) were acceptable by smear criteria. An additional 23 patients provided expectorated purulent sputum from which no respiratory tract pathogen could be isolated. Of these 23, 7 had pneumonia. We conclude that sputum culture and Gram staining are neither specific nor sensitive as diagnostic tools. Objective criteria for purulence of Gram-stained specimens must be applied before their inoculation into culture media. Specimens should be sought only from patients with objective evidence of pneumonia.

The reliance on sputum culture to establish the microbiological etiology of bacterial pneumonia remains a matter of great controversy. Previous studies have recorded positive sputum cultures in patients with bacteremic pneumococcal pneumonia at frequencies between 48 to 98% (1, 6, 8). In patients with bacteremic *Haemophilus influenzae* pneumonia, simultaneous isolation of the pathogen from sputum specimens was accomplished for 55 to 66% of the patients (20, 32). Conversely, the rapid acquisition of gram-negative enteric flora in the oropharynx of critically ill hospitalized patients (17) may yield sputum culture results discordant with the true pulmonary pathogen.

The potential complications of transtracheal aspiration (13, 19) and the known contamination of bronchoscopically obtained specimens with oropharyngeal flora (18) have resulted in an overreliance on expectorated sputum cultures for the diagnostic and therapeutic management of pneumonia. The inherent difficulties in the interpretation of expectorated sputum culture results may lead to selection of inappropriate therapy. More frequently, physicians may empirically choose broad-spectrum antimicrobial agents or potentially toxic antibiotic combinations because of the uncertain relevance of expectorated sputum culture results.

The present study was undertaken to evaluate the role that expectorated sputum culture results played in the management of patients with pneumonia at our institution. We also investigated the frequency of discordance between the clinical status of patients and the recovery of pulmonary pathogens from cultures of their expectorated sputum specimens.

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MATERIALS AND METHODS

Evaluation of patients. Between 1 January 1985 and 31 March 1985, 226 patients whose expectorated sputum in culture yielded potential pathogens were evaluated for clinical and radiologic evidence of upper or lower respiratory tract infection. An additional 23 patients were identified as producing purulent sputum which was negative for respiratory pathogens in culture. Patients were considered to have pneumonia if they had new or changing pulmonary infiltrates shown by chest X ray plus at least three of the following signs or symptoms: fever (>38°C), productive cough, dyspnea, and physical findings compatible with pneumonia, i.e., rales, egophony, pectoriloquy, decreased breath sounds, dullness, increased tactile fremitus, or bronchial breath sounds. The physicians caring for the individual patients were contacted; their clinical diagnosis and the influence that positive sputum culture had in the therapeutic management of the patient were noted.

All but two patients were males, hospitalized at the Edward Hines, Jr., Veterans Administration Hospital. There were 179 patients who submitted a single purulent specimen during the study period; 40 patients submitted two purulent specimens, 12 patients submitted three, 8 patients submitted four, 6 patients submitted five, and 4 patients submitted six purulent specimens. Only one purulent sputum per patient per day was analyzed in the study. An additional 256 nonpurulent specimens from 217 patients were cultured during the period of the study. These patients were investi-

gated only for evidence of lower or upper respiratory tract infection, retrospectively. Of the 70 patients with multiple sputum specimens from which respiratory pathogens were recovered, 56 received antibiotics appropriate to their clinical status. The effect of antibiotic therapy on respiratory flora was evaluated among these patients.

Microbiologic studies. Sputum specimens were generally obtained under the supervision of a nurse or a respiratory therapist. All sputum Gram stains were read at low (×100) magnification and evaluated according to the criteria described by Bartlett (2) by a single observer (D. A. L.) before clinical evaluation of the patient. Specimens were scored 0, +1, or +2 according to the number of leukocytes seen per field and 0, −1, and −2 according to the number of squamous epithelial cells seen per field. Specimens with total scores of zero or less were considered inadequate and heavily contaminated with oropharyngeal flora. Those containing greater than 25 leukocytes and fewer than 10 squamous epithelial cells per field were optimal specimens. All specimens were submitted to the microbiology laboratory of our institution. During the period of this study, regardless of Gram stain score, each sputum specimen submitted was cultured. This was the standard practice of the clinical laboratory up to the completion of this study.

Specimens were incubated overnight in an atmosphere containing 5% CO_2 in air on sheep blood, chocolate, and eosin-methylene blue agars (GIBCO Diagnostics, Madison, Wis.) in standard fashion (16). Organisms were identified by standard microbiologic techniques (5). Viridans group streptococci, diphtheroids, coagulase-negative staphylococci, and some *Neisseria* species were considered normal respiratory flora (24). *Streptococcus pneumoniae*, *H. influenzae*, *Neisseria meningitidis*, beta-hemolytic streptococci, *Staphylococcus aureus*, and enteric gram-negative bacilli were considered to be potential pathogens. All cultures from which these organisms were obtained were considered to be positive.

Definitions. We determined the specificity, sensitivity, and negative and positive predictive values for all patients, including those with negative sputum smears and cultures and for that subgroup of patients with either a positive sputum culture or a purulent sputum smear. The following definitions were applied irrespective of culture findings: true-positive, results from patients with pneumonia and purulent sputum; false-positive, results from patients with no evidence of pneumonia but with purulent sputum; true-negative, results from patients with no evidence of pneumonia and with nonpurulent sputum; and false-negative, results from patients with pneumonia but with nonpurulent sputum.

Statistical analysis. Comparisons of groups were performed by chi-square analysis. A probability value of ≤ 0.05 was considered statistically significant.

RESULTS

Pathogens were recovered from 354 sputum specimens submitted for culture from 226 patients. From an additional 23 patients there were 27 specimens which were considered to be purulent on review of the Gram stains, but which yielded normal respiratory flora in culture. These patients and specimens were similarly evaluated for clinical and radiologic evidence of upper or lower respiratory tract infection. The clinical data correlating with these microbiologic results are presented in Table 1. Of the 354 culture-positive specimens, 172 were obtained from 76 patients with evidence of pneumonia, whereas 182 culture-positive specimens (52%) were submitted from 150 patients with no objective evidence of pneumonia. Of the 27 purulent specimens yielding normal respiratory flora, 7 were obtained from 7 patients with evidence of pneumonia, whereas 20 purulent specimens were submitted from 16 patients with no objective evidence of pneumonia. Among the 179 specimens from patients with pneumonia, only 107 (60%) were acceptable specimens; the other 72 specimens (40%) were inadequate by the criteria of Bartlett. The majority (111 of 202 specimens [55%]) recovered from patients without pneumonia were judged to be nonpurulent. However, 91 of 202 (45%) specimens from 66 of these patients were purulent sputum specimens upon review of Gram stains. Because none of these 66 patients had evidence of pneumonia, the significance of these purulent sputum specimens was uncertain.

We reviewed the charts of these 66 patients in detail and noted a diagnosis other than pneumonia which could explain the presence of polymorphonuclear leukocytes in 43 patients. Fourteen patients had chronic obstructive pulmonary disease. Six patients had suffered a cardiopulmonary arrest requiring intubation. Four patients each had either postoperative atelectasis or carcinoma of the lung. Three patients had the adult respiratory distress syndrome. Two patients each had acute tracheobronchitis, sinusitis, or unexplained hemoptysis. One patient each had tuberculosis, a pulmonary embolus, interstitial fibrosis, rheumatoid lung, a bronchopleural fistula, and a mucus plug.

There were 23 patients with no evidence of lower respiratory tract disease; 17 of these were febrile and 7 were without evidence of any overt infectious process. We suspected but could not prove that they may have had an upper respiratory tract infection. Six patients were not febrile, nor did they have an active pulmonary disorder, yet they produced purulent sputum. Sputum purulence was significantly associated with respiratory tract pathology but not with pneumonia per se ($\chi^2 = 1.8$, df = 1, $P > 0.10$).

Therapeutic intervention was retrospectively reviewed with reference to the results of sputum Gram staining. Of the 381 specimens reviewed, 198 (51.9%) were judged to be purulent by the criteria of Bartlett. Of these specimens, 107 were obtained from 50 patients with pneumonia for which antibiotic therapy was given. A total of 91 purulent specimens were recovered from 66 patients without pneumonia. Therapy was given if other infections were noted to be present (see above). The data correlating pathogen recovery and antibiotic therapy among the patients who produced two or more sputum specimens are shown in Table 2. There were 179 patients who submitted a single specimen; 70 patients submitted multiple specimens. Of these 70 patients, 56 received antibiotic therapy for pneumonia or other infections as noted. Recovery of the same pathogen or normal flora in

TABLE 1. Correlation of sputum specimen purulence with clinical status of patients

Lung and sputum status of patients	No. (%) of patients	No. (%) of specimens
Pneumonic	83 (33.4)	179 (47.0)
Purulent	50 (20.2)	107 (28.1)[a]
Nonpurulent	33 (13.2)	72 (18.9)
Nonpneumonic	166 (66.6)	202 (53.0)
Purulent	66 (26.5)	91 (23.9)[b]
Nonpurulent	100 (40.1)	111 (29.1)

[a] Of 107 specimens, 7 yielded normal flora.
[b] Of 91 specimens, 20 yielded normal flora.

TABLE 2. Effect of antibiotic therapy upon recovery of respiratory pathogens from patients with multiple sputum specimens

No. of specimens/ patient	No. of specimens	No. of patients	No. of patients with antibiotic therapy	Pathogen recovered/treated patient		
				Same	New	NF[a]
2	80	40	37	25	4	8
3	36	12	7	5	2	0
4	32	8	5	3	2	0
5	30	6	5	3	2	0
6	24	4	2	1	0	1

[a] NF, Normal flora.

subsequent specimens was noted most frequently among those patients from whom two sputum specimens were obtained. There were no differences in the frequency of recovery of the same pathogen or a new pathogen among those patients from whom three or more specimens were obtained.

Gram-positive cocci were more frequently associated with purulent sputum than with nonpurulent sputum specimens from patients with pneumonia. Among gram-negative bacilli, only *Proteus mirabilis* was more frequently recovered from purulent sputum than from nonpurulent sputum.

Among the 76 patients with pneumonia from whose expectorated sputum a pathogen could be recovered, the most frequently isolated organism was *S. pneumoniae*. Data correlating positive sputum culture results with initial Gram stain smear interpretations for the 76 patients with pneumonia are shown in Table 3. An additional seven patients with pneumonia whose sputum cultures yielded normal respiratory flora were found by Gram staining to have mixed flora (two patients), streptococci (two), gram-negative bacilli (one), or no bacteria (two), along with many polymorphonuclear leukocytes.

From the 183 nonpurulent, culture-positive sputum specimens, 72 were recovered from 33 patients with clinical evidence of pneumonia. Antimicrobial therapy was empirically chosen for these patients. An additional 111 nonpurulent, culture-positive sputum specimens were obtained from 100 patients with no evidence of pneumonia. Many of these specimens were routinely submitted as part of the evaluation of a febrile episode. The majority (108 of 111 [97.3%]) of these cultures were ignored by the managing physicians when it was apparent that the patients did not have pneumonia. Therapy, when given, was directed toward eradication of infection arising from sites other than the lower respiratory tract in 39 patients. No therapy was given to 58 patients from whom no evidence of infection could be found. On three separate occasions, the recovery of sputum pathogens inappropriately led to the treatment of patients with antibiotics, despite the absence of clinical or radiologic evidence of pneumonia. The value of a positive result from sputum Gram staining, culture, or both in the diagnosis of pneumonia is presented in Table 4.

TABLE 3. Correlation of respiratory pathogen recovery with sputum purulence among patients with pneumonia

Pathogen recovered	No. of patients with sputum smear result	
	Purulent	Nonpurulent
Streptococcus pneumoniae	13	5
Staphylococcus aureus	9	4
Beta-hemolytic streptococci	2	3
Pseudomonas aeruginosa	6	5
Escherichia coli	2	1
Serratia marcescens	1	0
Klebsiella species	1	4
Enterobacter cloacae	0	2
Citrobacter diversus	0	1
Morganella morganii	0	1
Proteus mirabilis	5	2
Haemophilus influenzae	2	2
Mixed gram-negative bacilli	2	3

TABLE 4. Value of sputum culture and gram staining in the diagnosis of pneumonia

Parameter	Value (%)[a] for diagnosis of patients testing:	
	Positive by one method alone[b]	Positive and negative, both methods[c]
Positive predictive value	43.1	43.1
Negative predictive value	75.1	88.5
Sensitivity	60.2	56.8
Specificity	60.2	82.5

[a] Defined as ratios of patient groups: positive predictive value, true-positive/true-positive plus false-positive; negative predictive value, true-negative/true-negative plus false-negative; sensitivity, true-positive/true-positive plus false-negative; and specificity, true-negative/true-negative plus false-positive.

[b] $n = 249$.

[c] $n = 466$ (249 patients with either positive sputum smear or culture results and 217 patients with both negative sputum smear and culture results).

Among the 217 patients with nonpurulent specimens from which only normal respiratory flora was identified in culture, we found five additional patients with pneumonia. The remaining 212 patients had no documentation for pneumonia in their hospital records. Incorporating these patients into the group that could be evaluated reduces the sensitivity of testing only minimally, whereas it increases the specificity and negative predictive value (Table 4). Purulent sputum was significantly more frequently recovered from patients with respiratory tract pathology than from those without it ($\chi^2 = 11.25$, df = 1, $P < 0.001$). Pneumonia per se could not be evaluated by sputum purulence alone.

DISCUSSION

The value of sputum cultures has long been a subject of uncertainty and debate. Significantly greater numbers of bacterial species are present in expectorated sputum specimens compared with those obtained by transtracheal aspiration (6). To minimize the effect of oropharyngeal contamination on lower respiratory tract secretions, Bartlett (2) and Murray and Washington (23) devised screening criteria based on quantitation of leukocytes and squamous epithelial cells. Our survey demonstrated that 48.0% of the culture-positive sputum specimens submitted to our clinical microbiology laboratory were inadequate by objective criteria. It is important to note that these criteria were not used to screen sputa from neutropenic patients. Furthermore, only 198 of 637 specimens (31%) submitted were found to be purulent.

The recovery of purulent sputum from patients without pneumonia presents a diagnostic challenge to clinicians. In the final analysis of our patients, 66 of 249 patients (26.5%) produced purulent sputum in the absence of overt radiologic or clinical evidence for pneumonia. Forty-three patients had

other pulmonary pathology to explain sputum purulence in the absence of pneumonia. One could argue that patients with lung cancer or adult respiratory distress syndrome (4) could have coexisting pulmonary infection. There were 2 patients each with sinusitis (9) or acute tracheobronchitis (28) and 14 patients with exacerbations of chronic obstructive pulmonary disease (3, 25). Even with these exceptions, 23 patients with no evidence of pulmonary pathology produced purulent sputum. We made no attempt to isolate *Mycoplasma pneumoniae* (22, 33), *Legionella* species (26), or viruses (14, 29) of the upper respiratory tract, nor did we perform serologic testing for these respiratory tract pathogens. Several reviews have addressed the contribution of these pathogens to adult pneumonia (10, 21).

From the patients with pneumonia, 72 of 179 sputum specimens were not deeply expectorated. Consequently, cultures of these secretions were more reflective of oropharyngeal flora than of pulmonary pathogens (17, 30). Age (11, 12, 27), nutritional status, and level of cognitive function (15) all contribute to the ability of a patient to clear pulmonary secretions. Physiologic changes of aging, such as decreased mucociliary clearance, diminished glottic closure, loss of alveolar elasticity, and decreased cough velocity due to diminished respiratory muscle tone impair the nonimmune respiratory defense mechanisms (7). The inability to expectorate sputum when pneumonia is present not only contributes to the pathogenesis of the infection (31) but also decreases the diagnostic value of specimen cultures.

From our results it is apparent that sputum examination by culture and Gram staining is neither specific nor sensitive as a screen to evaluate pulmonary infections. Even with the inclusion of all the smear-negative and pathogen-negative specimens, the sensitivity of the combined methods was only minimally decreased. Specificity, on the other hand, increased from 60 to 82.5%. However, as most laboratories do not routinely culture nonpurulent specimens, the data from these patients are of little importance in the management of lower respiratory tract infections. The negative predictive value of both methods increased from 75 to 88.5%; however, no change was noted in the positive predictive value of these combined results. This further demonstrates the valueless outcome of routine culturing of nonpurulent sputum specimens. The incidence of pneumonia among 350 patients producing nonpurulent sputum was 10.8%. Of 38 patients, 33 were noted to have pathogens in cultures of their sputa whereas specimens from 5 were culture negative. These patients would be missed by screening sputa before culture. Purulent sputum, on the other hand, was as frequently recovered from patients with other respiratory tract infections or pathology as it was from patients with pneumonia. Among the patients with pneumonia, 50 of 88 (56.8%) produced purulent sputum. The reliability of sputum as the sole diagnostic tool for the presence of pneumonia is extremely limited. Clinicians use clinical and radiographic evidence, as we did, to determine the presence or absence of the disease process. Thus, it is unlikely that among patients producing nonpurulent sputum, the diagnosis would be missed. Consequently, we feel that the increased cost of diagnosing a single case of pneumonia by culturing all specimens received would be excessive. Without strict objective criteria for evaluation of sputum specimens, considerable waste in manpower and financial resources may be incurred. Sputum cultures are labor intensive and time consuming for the laboratory. The Medicare reimbursement for a sputum culture and sensitivity is $25.40. By screening for purulence and eliminating the culturing of sputum specimens without purulence, our hospital alone would realize estimated annual savings of $31,700.00.

Our data support the notion that clinical microbiology laboratories may reject for culture those sputum specimens from nonneutropenic patients which fail to meet the criteria of Bartlett for purulence. If sputum cultures are to be used to provide meaningful data, they must be ordered judiciously for documented episodes of lower respiratory tract infection. The microbiology laboratory must use objective criteria, by Gram stain screening, for purulence before inoculation of culture media. Only if these minimal guidelines are met will meaningful data be provided.

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