

# Assessment of the Usefulness of Sputum Culture for Diagnosis of Community-Acquired Pneumonia Using the PORT Predictive Scoring System

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**Background:** The usefulness of sputum culture in guiding microbiological diagnosis of community-acquired pneumonia is controversial. We evaluate and assess it using the Patients Outcome Research Team (PORT) predictive scoring system.

**Methods:** A cohort of 1669 patients with community-acquired pneumonia was studied. Before administering antibiotic therapy, sputum was collected and its quality evaluated. Samples were gram stained and those of good quality were assessed for a predominant morphotype (PM). Sputum cultures were processed according to standard protocols.

**Results:** A sputum sample was obtained from 983 (59%) of the 1669 patients and 532 (54%) of the samples were of good quality. There was a PM in 240 (45%) of the latter samples (ie, for 14.4% of the 1669 patients) and there was no PM in 292 (55%). Culture yielded a microorganism in

207 (86%) of the 240 samples with PM and 57 (19.5%) of the 292 samples without PM ( $P < .05$ ). Rates of sputum obtained, good-quality sputum specimens, PM identification, and positive culture were not significantly different among the PORT-score groups of patients ( $P > .05$ ). The sensitivity and specificity of the gram-positive diplococci identification in the sputum culture of *Streptococcus pneumoniae* were 60% and 97.6%, and the positive and negative predictive values were 91% and 85.3%, respectively.

**Conclusions:** Good-quality sputum with PM could be obtained in only 14.4% of all patients. A PORT-score group in which sputum could be of greater usefulness in identifying the causative organism could not be identified. The presence of gram-positive diplococci in gram-stained sputum culture was highly specific for *S pneumoniae*.

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**C**OMMUNITY-ACQUIRED pneumonia (CAP) remains a major cause of morbidity and mortality. A causative agent is identified in 30% to 40% of cases, and the most common is *Streptococcus pneumoniae*. The clinical and radiographic microbiological diagnoses of pneumonia lack accuracy,<sup>1,2</sup> cultures take at least 24 hours to produce a positive result, and specific rapid tests based on the detection of soluble antigens of *S pneumoniae* or *Legionella pneumophila* in body fluids are not always available. Therefore, initial antibiotic therapy is usually empirically chosen.<sup>3,4</sup>

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The role of sputum culture as a rapid diagnostic tool that could direct antimicrobial treatment of CAP is a matter of controversy.<sup>5-11</sup> Some of its limitations are the difficulty to obtain good-

quality samples, its lack of reliability due to possible sputum contamination by the flora of the upper airways, its low diagnostic yield (ie, sensitivity), and, therefore, its low impact on treatment decisions. The Infectious Diseases Society of America guidelines recommend gram staining and culture of sputum in immunocompetent patients requiring hospitalization<sup>12</sup>; however, the American Thoracic Society guidelines recommend obtaining sputum samples only if a drug-resistant pathogen or an organism not susceptible to usual empirical treatment is suspected.<sup>13,14</sup>

The relationship between the severity of CAP and the usefulness of blood cultures has been analyzed,<sup>15,16</sup> but there are no studies analyzing the relationship between the severity of CAP and the usefulness of sputum gram staining. The aim of this prospective study of hospitalized patients and outpatients is to evaluate the usefulness of routine sputum gram staining in the microbiological diagnosis of CAP and

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to assess it according to the Patients Outcome Research Team (PORT) predictive scoring system.<sup>17</sup>

## METHODS

From October 1996 to April 2002, 1669 consecutive patients older than 14 years with acute symptoms consistent with CAP were studied according to a standard protocol in the Respiratory and Infectious Diseases Services at the Hospital Clinic in Barcelona, Spain, a 800-bed university teaching hospital.

Community-acquired pneumonia was defined by clinical history and physical signs of lower respiratory tract infection plus the presence of a new infiltrate on a chest radiograph in patients who had not been hospitalized within the previous month and in whom no alternative diagnosis had emerged during follow-up. Clinical, laboratory, and radiologic findings at presentation as well as other epidemiological data were recorded on a specific questionnaire and entered in a computer database. Disease severity was assessed within the first day of admission using the PORT scores. Part of this study population has been previously described.<sup>18,19</sup>

Patients with neutropenia (neutrophil count  $<1.0 \times 10^9/L$ ), human immunodeficiency virus infection, tuberculosis, or fungal infection, and those treated with steroids in a prednisone-equivalent dosage of more than 20 mg/d for 2 weeks or longer since the onset of disease, were not included.

## MICROBIOLOGICAL EVALUATION

The standard process included 1 sputum and 2 blood sample cultures, plus evaluation of 2 serum samples, 4 to 8 weeks apart. Pleural puncture, transthoracic needle puncture, tracheobronchial aspiration (in mechanically ventilated patients), and protected specimen brush or bronchoalveolar lavage sampling were performed as needed according to clinical indication or the judgment of the attending physician.

Expectorated sputum samples were collected before administering antibiotic therapy at the hospital's emergency department. All patients were asked by the nurse or the attending physician to produce, if possible, sputum samples; no special attempt was requested or technique used, however, to reflect as much as possible standard routine practice in medical settings. Samples were gram stained and examined, and accepted as suitable for culture if there were less than 10 squamous epithelial cells and more than 25 polymorphonuclear cells per low-power field, independent of the presence of a predominant morphotype (PM). Suitable sputum, blood culture samples, undiluted and serially diluted tracheobronchial aspirates, and fluid samples obtained from bronchoalveolar lavage and protected specimen brush were plated on the following media: sheep blood agar, CDC (Centers for Disease Control and Prevention) agar, chocolate agar, and Sabouraud agar. Undiluted samples from protected specimen brush and bronchoalveolar lavage fluids were cultured on charcoal-yeast extract agar. Identification of microorganisms was done according to standard methods. From 2001 on, urine was also collected in the acute phase for detection of *L pneumophila* antigen by enzyme immunoassay (Bartels Legionella Urinary Antigen Test Kit; Trinity Biotech, Bray, Ireland).

The presence of a PM was considered when gram staining showed bacteria only or mainly corresponded to the gram morphotype revealed by standard microbiological criteria.

The etiology of pneumonia was considered definitive if 1 of the following criteria was met: (1) blood cultures yielding a bacterial pathogen in the apparent absence of an extrapulmonary focus; (2) cultures of pleural fluid or transthoracic needle aspiration fluids yielding a bacterial pathogen; (3) seroconversion (ie, a 4-fold increase in IgG titer for *Chlamydia pneumoniae*, *Chlamydia psittaci*, *L pneumophila*, *Coxiella burnetii*, and certain res-

piratory viruses (ie, type A and type B influenza viruses; types 1, 2, and 3 parainfluenza viruses; respiratory syncytial virus; and adenovirus); (4) single IgM titers greater than 1:32 for *C pneumoniae* and greater than 1:80 for *C burnetii*, and of any value for *Mycoplasma pneumoniae*; (5) a positive urinary antigen for *L pneumophila*; and (6) a quantitative bacterial growth of  $10^5$  cfu/mL or greater in tracheobronchial aspirates,  $10^3$  cfu/mL or greater in the protected specimen brush fluid, and  $10^4$  cfu/mL or greater in the bronchoalveolar lavage fluid.

The recorded end points were (1) number of patients who could produce sputum, (2) microscopic validity of sputum samples, (3) identification of a PM, (4) microbiological results of sputum cultures, (5) influence of prior ambulatory antimicrobial treatment, and (6) relation of these end points to PORT scores. A subanalysis was carried out for patients with bacteremic pneumococcal CAP and for patients with *C pneumoniae*, *M pneumoniae*, or *L pneumophila* pneumonia.

## STATISTICAL ANALYSIS

Descriptive data are presented as means  $\pm$  SD for continuous variables and as rates for categorical variables. Statistical comparisons of categorical variables were made by  $\chi^2$  analysis or the Fisher exact test, when appropriate. Statistical significance was defined as  $P < .05$  (2-tailed).

Performance characteristics of gram-positive diplococci identification for culture of *S pneumoniae* in sputum were also analyzed. Diagnostic parameters such as sensitivity, specificity, and positive and negative predictive values were calculated according to standard equations.

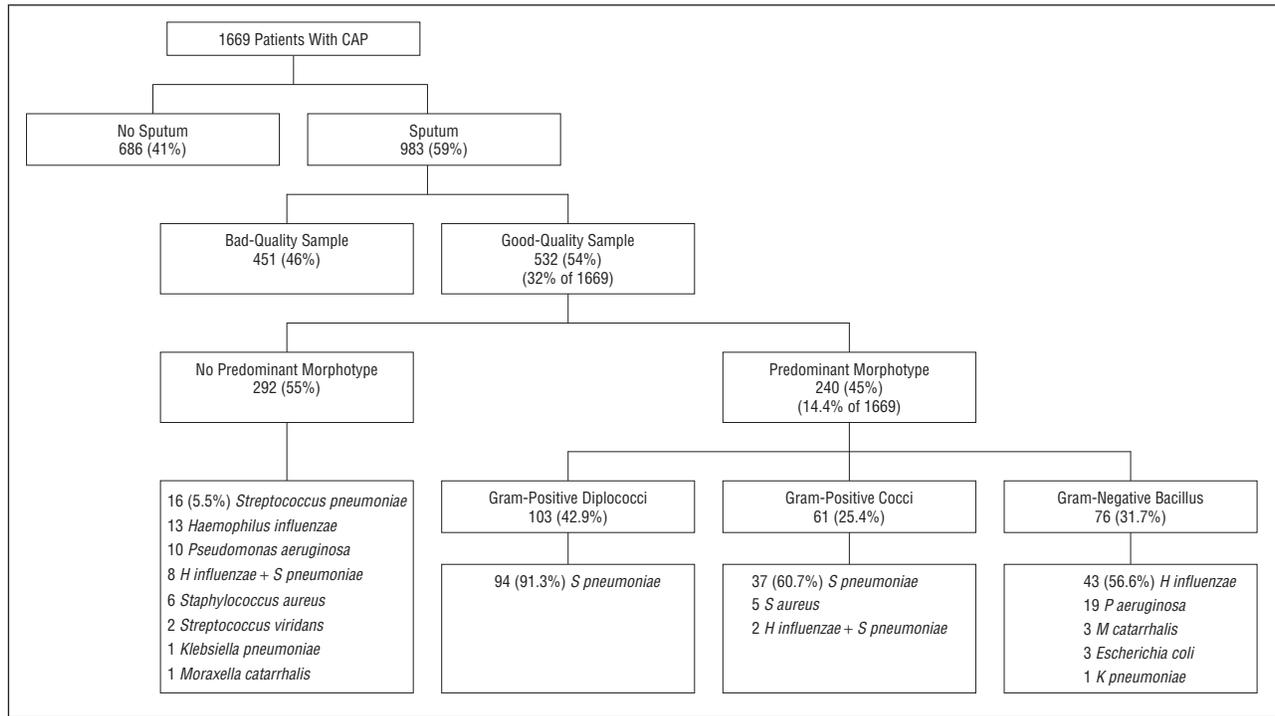
All statistical values were calculated using the SPSS software package, version 9.0 (SPSS Inc, Chicago, Ill).

## RESULTS

The study population of 1669 consecutive patients with bacterial CAP consisted of 1095 men (65.6%) and 574 women (34.4%) ranging in age from 15 to 101 years (mean,  $67 \pm 18.17$  years).

Sputum samples were obtained from 983 patients (59%). Of the 532 samples (54%) that were of good quality, 240 (45%, ie, representing 14.4% of the initial 1669 patients) showed a PM. There were 61 gram-positive cocci, 76 gram-negative bacilli, and 103 gram-positive diplococci. Sputum culture yielded a causative organism in 207 (86%) of the 240 samples with a PM and in 57 (19.5%) of the 292 good-quality samples with no PM ( $P < .05$ ). *Streptococcus pneumoniae* was the microorganism cultured in 133 (81%) of the 164 samples with a gram-positive PM and in 24 (8%) of the 292 samples with no PM ( $P < .05$ ) (**Figure**).

Among the 133 patients who had bacteremic pneumococcal CAP, 77 (58%) could provide a sputum sample. Of the 77 samples, 39 (50.6%) were considered of good quality and 14 (36%) showed gram-positive diplococci as the PM. *Streptococcus pneumoniae* was cultured in only 13 samples (**Table 1**). Results for patients with atypical CAP or previous antibiotic treatment are also shown in Table 1, as well as microbiological results of sputum sample cultures. Overall, sputum cultures were positive in 264 (49.6%) of 532 good-quality samples. In the case of patients with previous antibiotic treatment, sputum cultures were positive in 56 (53.8%) of 104 of good-quality samples ( $P > .05$ ). However, in these cultures, 51% of the PMs were gram-negative bacilli ( $P < .05$ ), compared with 32% in the general sample.



In a study of 1669 patients with community-acquired pneumonia (CAP), bacterial pathogens could be identified in only 264 cultured sputum samples.

**Table 1. Pathogen Distribution in the Sputum Samples of 1669 Patients With Community-Acquired Pneumonia (CAP)\***

	All Patients With CAP	Patients With Bacteremic Pneumococcal CAP (n = 133)	Patients With Atypical CAP (n = 123)	Patients With Previous Antibiotic Treatment (n = 299)
Sputum	983 (59)	77 (58)	73 (59)	192 (64)
Good-quality sample	532 (54)	39 (51)	37 (51)	104 (54)
Predominant morphotype	240 (45)	24 (62)	14 (38)	47 (46)
Gram-positive diplococci	103 (43)	14 (58)	6 (43)	13 (28)
Gram-positive cocci	61 (25)	10 (42)	4 (29)	10 (21)
Gram-negative bacilli	76 (32)	...	4 (29)	24 (51)
Positive culture†	264	23	11	56
<i>Streptococcus pneumoniae</i>	147	22	7	19
<i>Haemophilus influenzae</i>	56	...	3	18
<i>Moraxella catarrhalis</i>	4	...	...	1
<i>Klebsiella pneumoniae</i>	2	...	...	2
<i>Pseudomonas aeruginosa</i>	29	...	1	10
<i>Streptococcus viridans</i>	2	1	...	...
<i>H influenzae + S pneumoniae</i>	10	...	...	2
<i>Escherichia coli</i>	3	...	...	...
<i>Staphylococcus aureus</i>	11	...	...	4

\*Data are given as number or number (percentage); ellipses indicate that no pathogen was found.

Therefore, sputum culture contributed to identify *S pneumoniae* in 157 (9.4%) and blood culture in 133 (8%) of the 1669 patients (Table 1).

**Table 2** shows the results according to severity of CAP using PORT scores. Rates of sputum obtained, good-quality status of sputum, PM identification, and positive culture were not significantly different among the PORT groups of patients ( $P > .05$ ).

The sensitivity and specificity of the gram-positive diplococci identification in the sputum culture of *S pneumoniae* were 60% and 97.6%, and the positive and negative predictive values were 91% and 85.3%, respectively

(for 532 patients who provided good-quality samples, there were 103 samples with gram-positive diplococci and 157 with *S pneumoniae*).

#### COMMENT

The role of sputum as a tool in the diagnostic workup of patients with CAP remains controversial.<sup>20</sup> Rosón et al<sup>7</sup> concluded that a good-quality sample could be obtained in 39% of the patients with CAP and that gram staining was highly specific for the diagnosis of pneumococcal and *H influenzae* pneumonia, and therefore useful in guiding

**Table 2. Usefulness of Sputum Culture According to the Patients Outcome Research Team (PORT) Predictive Score for 1669 Patients With Community-Acquired Pneumonia\***

	No. (%)	PORT Score		
		I-II	III	IV-V
Sputum samples obtained	983 (59)	61	69	59
Good-quality samples	532 (54)	53	53.5	55
Predominant morphotype present	240 (45)	47	46.5	46

\*P Values were not significant.

pathogen-oriented antimicrobial therapy. Cordero et al<sup>9</sup> found that sputum culture is a useful technique in human immunodeficiency virus–infected patients for the diagnosis of bacterial pneumonia because of its good correlation with culture results of sterile samples. Bandyopadhyay et al<sup>21</sup> compared induced and expectorated sputum for the microbiological diagnosis of CAP. The diagnostic yield of induced sputum was 20%, compared with 24% for spontaneously expectorated sputum. While these and other authors<sup>22–26</sup> consider gram staining useful in the initial evaluation of patients with CAP, others<sup>21,27–31</sup> have pointed out that sputum samples have a low value as a diagnostic tool in pneumonia because of its lack of sensitivity and specificity. More recently, Ewig et al<sup>8</sup> have shown that in primary care hospitals sputum has low diagnostic yield (9%) and does not contribute significantly to patient management. Besides, the yield of gram staining has proven to be highly dependent on a skilled microbiologist applying strict criteria.<sup>21–33</sup>

In our study, we analyzed a large series of patients with CAP, which provided a good assessment of sputum gram staining and culture in daily medical practice. Sputum samples submitted for culture are often improperly collected and contain predominantly upper respiratory or oropharyngeal flora (46% of the sputum samples were considered bad-quality specimens). Furthermore, our results show a limited value of sputum as a diagnostic tool in the initial evaluation of patients with CAP, as a PM could be identified in only 45% (240/532) of the patients with a good-quality sputum sample. Therefore, the identification of a PM by the microbiologist could have guided initial antibiotic choice in only 240 (14.4%) of the 1669 patients who were evaluated. Even in patients with a bacteremic pneumococcal CAP, a PM informative of *S pneumoniae* infection (presence of gram-positive diplococci or gram-positive cocci) was identified in only 24 (18%) of the 77 patients with bacteremia who could provide sputum. It is also of consideration that in patients with atypical CAP (*C pneumoniae*, *M pneumoniae*, *C burnetii*, or *L pneumophila*) mixed infections can occur (as it did in 11 of the 73 patients who could expectorate sputum). Thus, the identification of a PM in a gram-stained sample cannot rule out an atypical CAP and selective antipneumococcal empirical treatment might not be appropriate.

The presence of gram-positive diplococci in gram-stained samples was highly specific (with a specificity of 97.6% and a positive predictive value of 91%) for the per-

sence of *S pneumoniae* in sputum culture; however, even in patients with bacteremia, sputum provided a diagnosis in only 17.3% of the cases.

The usefulness of sputum culture in CAP diagnosis was not significantly different according to disease severity assessed using PORT scores. We could not identify a PORT-score group of patients in whom information provided by gram staining could be especially useful in guiding initial empirical antibiotic choice. Young patients (PORT I and II risk class) may have been expected to have greater difficulty expectorating sputum, and patients from groups with associated comorbidities, such as chronic bronchitis, and higher PORT scores, may have been expected to produce a more purulent sputum. However, we could not identify such differences.

Furthermore, the availability of any test for the presumptive diagnosis of a causative organism of pneumonia in the emergency department may be less of a need if, as recommended, a macrolide is systematically included as part of the empirical regimen given to patients with CAP who require hospitalization, or if a new quinolone is chosen as a single therapy.<sup>34</sup> The recommendation of including a macrolide is based not only on the frequency of atypical microorganisms as causative agents of CAP, but also on recent evidence suggesting that patients with pneumococcal pneumonia fare better with a  $\beta$ -lactam–macrolide combination than with a  $\beta$ -lactam alone.<sup>35,36</sup>

The value of sputum samples might be epidemiological, as a tool in providing information about microbiological and antibiotic susceptibility trends in patients with CAP, but not in the emergency department. As the microbiological usefulness of good-quality sputum samples with no bacterial PM was significantly lower than that of samples in which a PM could be identified (19.5% of positive cultures vs 86%;  $P < .05$ ), we would probably not recommend obtaining for culture samples in which a PM could not be identified.

The rates of good-quality samples and PM in the gram-stained sample were similar in patients who had taken antibiotic medications before collection of the sputum sample and in the overall group of patients who could produce sputum (Table 1); however, in the former, 51% of the PMs were gram-negative bacilli, compared with 32% in the overall group. The value of sputum samples might therefore be dubious in persons who have been taking antibiotics before admission.

In conclusion, gram staining of sputum samples was useful in guiding microbiological diagnosis of CAP in only 14.4% of a total of 1669 patients. The culture of good-quality sputum samples with no PM or of samples obtained from patients who have received antibiotic treatment is probably not cost-effective. A PORT-score group of patients in whom sputum could be of greater usefulness in guiding diagnosis of the causative organism was not identified. The presence of gram-positive diplococci/cocci was highly specific for culture of *S pneumoniae* in sputum, but even in patients with bacteremia, a marker of severe illness, sputum provided diagnosis in only 23 (17.3%) of 133 cases. This low sensitivity could probably be improved by encouraging proper sputum collection techniques and providing correct instructions to the patient,<sup>37</sup> but is it worthwhile?<sup>38</sup>

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