Contribution of a Pleural Antigen Assay (Binax NOW) to the Diagnosis of Pneumococcal Pneumonia*

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Study objectives: **To determine whether the detection of pneumococcal antigen in pleural fluid augments conventional microbiological methods used for the etiologic diagnosis of pneumonia.**
Methods: **In this retrospective study, a rapid immunochromatographic test (ICT) [NOW *Streptococcus pneumoniae* assay; Binax; Scarborough, ME] was performed on pleural fluid samples from 34 patients with pneumonia due to *S pneumoniae*, 89 patients with effusions of nonpneumococcal origin, and 17 patients with pneumonia of unknown etiology. Data on blood cultures, pleural fluid cultures, and urinary antigen tests were recorded.**
Results: **The ICT test result was positive in 24 of 34 patients (70.6%) with pneumococcal pneumonia and negative in 83 of 89 patients (93.3%) without pneumococcal pneumonia. The sensitivity of the pleural ICT test was higher than that obtained for blood (37.5%) and pleural fluid cultures (32.3%), but lower than the detection of pneumococcal antigen in urine samples (82.1%). However, three patients with pneumococcal pneumonia and a negative ICT urine test result had a positive pleural fluid antigen detection result test. Previous antibiotic exposure did not influence pneumococcal antigen detection in either pleural fluid or urine specimens. Six additional patients with empyema due to anaerobes (three patients), *Streptococcus viridans* (two patients), and *Enterococcus faecalis* (one patient) had false-positive pleural ICT test results. Finally, the ICT assay finding was also positive in 5 of 17 patients (29.4%) with pneumonia without a definite microbiological cause.**
Conclusions: **The ICT test performed on pleural fluid samples augments the standard diagnostic methods of blood and pleural fluid cultures, even in the case of prior antibiotic therapy, and enhances the ICT urinary antigen assay.** ***(CHEST 2007; 131:1442–1447)***

Key words: empyema; immunochromatographic test; pleural effusion; pneumococcal pneumonia

Abbreviations: CAP = community-acquired pneumonia; CI = confidence interval; ICT = immunochromatographic test

Community-acquired pneumonia (CAP) represents the most frequent cause of hospital admission and mortality of infectious origin in developed countries,[1] and *Streptoccoccus pneumoniae* ranks first in the order of pathogens causing CAP.[2]

In clinical practice, there are a number of problems associated with demonstrating the microbial etiology of CAP by conventional methods. For instance, only one third of patients produce sputum suitable for culture, and results lack specificity due to nasopharyngeal carriage of pneumococci in healthy individuals.[3] In addition, blood cultures are specific, but they have a low positivity rate (< 10%).[4,5] About 10% of pneumonia cases are associated with pleural effusion,[6] although a pathogen is recovered in less than half of those persons who undergo diagnostic thoracentesis.[7] Finally, one third of patients with CAP have received antibiotics before the collection of biological specimens for microbial analysis,[8] which may decrease the diagnostic yield by such conventional methods.[9]

The need for improved speed and accuracy during etiologic diagnosis of CAP has led to the development of a rapid urinary assay for detecting pneumococcal cell wall components common to all serotypes, namely, the NOW assay (Binax; Scarborough,

ME).[10] Until now, the test has been validated for urine and cerebrospinal fluid samples only. However, three recent studies have evaluated the NOW urinary antigen assay in pleural fluid samples from children[11,12] and adults[13] with CAP. In all of them, the sensitivity of the pleural test was higher than that of pleural cultures, and authors suggested that the NOW test could be a valuable tool for the etiologic study of CAP, although a thorough comparison of the NOW operating characteristics between pleural and urine samples could be inferred from only one of these series.[13]

The aim of the present study was to ascertain whether the NOW test when performed on pleural fluid samples can add information to the findings of conventional methods (*ie*, blood cultures, pleural fluid cultures, and urinary antigen assay) for the identification of *S pneumoniae* as the cause of CAP.

Materials and Methods

Subjects and Study Design

The Ethics Committee of the Arnau de Vilanova University Hospital in Lleida, Spain, approved this retrospective study. We examined 140 pleural fluid samples that had been collected from patients who had undergone thoracentesis in our hospital between 2002 and 2006. Pleural fluids were selected randomly from our pleural fluid bank, where they were stored frozen at −80°C. The basis for randomization was a random number generator (http://www.randomization.com). Patients with pleural effusion were classified into the following three groups: group 1 included 34 patients with pneumococcal pneumonia; group 2 consisted of 89 patients with effusions of nonpneumococcal origin (nonpneumococcal pneumonia, 29 patients; tuberculosis, 20 patients; neoplasm, 23 patients; heart failure, 15 patients; cirrhosis, 1 patient; and post-coronary-artery bypass surgery, 1 patient); and group 3 comprised 17 patients with pneumonia of unknown etiology. Data on blood cultures, pleural fluid cultures, and urinary antigen tests were obtained from medical records.

Diagnostic Criteria

A parapneumonic effusion was defined as any pleural exudate associated with bacterial pneumonia. A diagnosis of CAP due to *S pneumoniae* was established when this microorganism was isolated from an uncontaminated sample (blood or pleural fluid), or when pneumococcal antigen was detected in unconcentrated urine samples by the NOW assay described in the next section. Sputum culture was not used as a "gold standard" test due to concerns regarding its specificity.[14]

A diagnosis of nonpneumococcal CAP was made on the basis of the identification of a microorganism other than *S pneumoniae* in blood or pleural fluid. The diagnosis of pneumonia of unknown etiology was based on negative results of all of the following: blood cultures; pleural fluid cultures; urinary antigen tests for *S pneumoniae* and *Legionella pneumophila*; and antibody testing for *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *L pneumophila*, *Chlamydia psittaci*, *Coxiella burnetti*, and Influenza A virus in paired serum samples.

Tuberculous pleuritis was diagnosed if the results of Ziehl-Neelsen or Löwenstein cultures of pleural fluid, sputum, or pleural biopsy tissue samples were positive, or a pleural biopsy specimen showed granulomas in the parietal pleura. A pleural effusion was said to be malignant if malignant cells were demonstrated to be present on cytologic examination of pleural fluid or biopsy specimens. Finally, the diagnosis of heart failure was based on medical history, physical examination results, chest radiograph, ECG, or echocardiogram findings, and the response to diuretic therapy.

Pneumococcal Antigen Test

An immunochromatographic test (ICT) [NOW *S pneumoniae* antigen test; Binax] was used to detect *S pneumoniae* C-polysaccharides in urine and pleural fluid samples. Briefly, a swab was dipped into 200 μL of pleural fluid and inserted into the ICT device, according to the manufacturer's instructions. Results were assessed by visual inspection after 15 min. A pink-to-purple color on both the sample and control lines indicates a positive antigen test result, whereas color on the control line alone indicates a negative test result. An absence of color on the control line indicates an invalid test. The reading of ICT results was performed and interpreted under blinded conditions by experienced personnel from the Department of Clinical Microbiology.

Statistical Analysis

Data are presented as proportions or means, as deemed appropriate. The sensitivity, specificity, and likelihood ratios of the pleural ICT test were calculated according to standard formulas using results obtained from groups 1 and 2. For between-group comparisons of proportions, the χ^2 test or Fisher exact test were used when appropriate.

Results

The study population included 140 patients with pleural effusion, of whom 92 were men and 48 were women (age range, 18 to 93 years; mean [± SD] age, 56 ± 20 years). There were no differences in the patients' mean age between study groups (group 1, 52 ± 20 years; group 2, 57 ± 20 years; and group 3, 58 ± 18 years; $p = 0.22$). However, men predominated in group 3 (16 patients; 94%) compared with groups 1 (19 patients; 56%), and 2 (57 patients; 65%; $p = 0.02$).

The ICT test result was positive in 24 of 34 pleural

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Authors have neither personal or financial support nor any conflict of interest
Manuscript received July 30, 2006; revision accepted January 4, 2007.

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DOI: 10.1378/chest.06-1884