Comparison of Latex Agglutination and Counterimmunoelectrophoresis in the Diagnosis of Acute \textit{Streptococcus pneumoniae} Infections

P. Van der Auwera\textsuperscript{1*}, A. Andr\textsuperscript{2}, G. Bulliard\textsuperscript{1}, J. C. Legrand\textsuperscript{3}, B. Gordts\textsuperscript{4}, H. Van Landuyt\textsuperscript{5}, F. Schuyteneer\textsuperscript{1}

The ability of latex agglutination (Slidex Pneumokit) and counterimmunoelectrophoresis to detect \textit{Streptococcus pneumoniae} antigen in body fluids was evaluated. The patients were classified as having proven \textit{Streptococcus pneumoniae} infection, suspected \textit{Streptococcus pneumoniae} infection, acute superinfection of chronic bronchitis or non-pneumococcal respiratory infection. Sixty-two non-pneumococcal meningitis patients were also included in the study. Latex agglutination and counterimmunoelectrophoresis tests were performed on serum, urine and cerebrospinal fluid specimens when indicated and repeated each week until the patient was discharged. Latex agglutination was done on samples boiled for 10 min. In vitro sensitivity of counterimmuno-electrophoresis and latex agglutination were 10 and 1 ng/ml respectively for type three antigen. In pulmonary disease (proven and suspected \textit{Streptococcus pneumoniae} infection) counterimmuno-electrophoresis and latex agglutination had a clinical sensitivity of 72.9 and 87.5 % respectively, a specificity of 96.3 and 92.6 %, a predictive value for a positive test of 97.2 and 95.4 % and for a negative test of 66.6 and 80.6 %. Latex agglutination may offer an alternative to counterimmunoelectrophoresis in the rapid diagnosis of \textit{Streptococcus pneumoniae} infections since it is easier to perform and gives a reliable result within 15 min.

\textit{Streptococcus pneumoniae} remains a major cause of acute meningitis and pneumonia (1). Moreover, the spectrum of lung infections due to \textit{Streptococcus pneumoniae} has recently changed, patients now presenting with a bronchopneumonic pattern rather than the classical lobar pattern (2). The difficulty in establishing a specific etiologic diagnosis in pneumonia on the basis of results of bacterial cultures of sputum is well documented (1, 2). Sputum culture is positive in only 30–60% of the patients having pneumococcal pneumonia, and contamination from the mouth is difficult to avoid unless special aggressive techniques are used like transtracheal aspiration or bronchoscopy. On the other hand, between 40 and 50% of the normal population are healthy carriers of \textit{Streptococcus pneumoniae} without any previous contact with an acute case (3).

Despite potent antibiotic treatment, the mortality of pneumococcal pneumonia remains as high as 20% in uncomplicated cases (1), while in patients with bacteremia and severe underlying diseases or patients over 70 years, mortality may increase dramatically (3–5). Meningitis due to \textit{Streptococcus pneumoniae} also has a very high mortality of up to 68% (1). Usually CSF Gram stain and culture are positive; however, in the case of previous antibiotic treatment they may be falsely negative. As death occurs mostly during the first few days of illness in both diseases, it is essential to obtain a specific diagnosis within hours after the patient's admission to the hospital as early penicillin treatment may reduce the mortality and the rate of complications.
Counterimmunoelectrophoresis (CIE) has frequently been reported to be a reliable method for detecting *Streptococcus pneumoniae* antigen in various body fluids of patients with acute *Streptococcus pneumoniae* infections (6–8). CIE is a very specific method but lacks sensitivity, being positive in urine of 60% of patients with septicemic pneumonia and of at most 40% of patients with non-septicemic pneumonia (6). CIE gives better results in the testing of CSF from patients with acute meningitis, virtually all patients being positive (7). But, there are other limitations. Unless special conditions are used, CIE fails to detect capsular antigens type 7 and 14. Moreover, other capsular types may not be detected with the same sensitivity as type 3 antigen. Cross-reactions may occur with other bacteria, e.g. *Neisseria meningitidis* B, *Haemophilus influenzae* a,b, *Escherichia coli* K 1, *Klebsiella pneumoniae* (9). Other drawbacks are the need for special equipment and training and the high cost of the procedure, rendering CIE unsuitable for field diagnosis in developing countries. An advantage of CIE is that it can be used to evaluate semi-quantitatively the amount of antigen present in body fluids. Some authors have reported that large amounts of antigen correlate with poor outcome (3, 6).

Recently a commercialized latex agglutination kit (Silixed Pneumokit, Pneumoslide) has become available for identifying isolated colonies of *Streptococcus pneumoniae*. Theoretically, this test can detect all serotypes with the same sensitivity, and thus should compensate for the lack of sensitivity of CIE in detecting types 7 and 14. The purpose of this study was to evaluate latex agglutination (LA) as a method for the rapid diagnosis of acute infections due to *Streptococcus pneumoniae* in comparison with CIE.

### Materials and Methods

**Patients.** Patients suspected of having either acute broncho-pulmonary, pulmonary infection, or acute meningitis were admitted to the study. They were classified into the following five clinical categories.

1) **Proven Pneumococcal Disease.** Thirty-three patients presenting with acute meningitis (nine patients) or pneumonia (22 patients) with positive blood and/or CSF cultures for *Streptococcus pneumoniae* were considered to have proven pneumococcal disease. Two patients were added to this group. The first was a case of acute meningitis secondary to acute sinusitis treated before admission with high doses of ampicillin (CIE of the CSF was positive, CSF Gram stain and blood cultures were negative). The second was a patient with metapneumonic pleuresy who had a positive culture of the pleural fluid with a non-typable strain of *Streptococcus pneumoniae* and negative blood cultures. All patients had repeated chest X-rays and were treated with 12–20 million units of penicillin G i.v.

2) **Possible Pneumococcal Disease.** Twenty-five patients presenting with an acute bronchopulmonary or pulmonary infection confirmed by X-ray, with a temperature over 38.5 °C, partial or complete response to penicillin G, and no pathogen identified by culture or serology other than *Streptococcus pneumoniae*, were considered to have possible pneumococcal pulmonary infection. Sputum and blood cultures were obtained before treatment; 13 of them had a positive sputum culture, and in the remaining 12 no significant pathogen was isolated from the sputum. Chest X-rays were repeated twice a week.

3) **Chronic Obstructive Pulmonary Disease.** Twenty-four patients presenting with acute superinfection of chronic obstructive pulmonary disease (COPD) were included in this category. Most of them had a low grade fever (37.5–38.2 °C). Chest X-rays did not reveal lung consolidation. Some of these patients did not receive any antibiotic. All of them received intensive respiratory kinesitherapy and bronchodilators i.v. or orally. Thirteen had positive sputum culture for *Streptococcus pneumoniae*.

4) **Negative Controls for Pulmonary Disease.** Twenty-seven patients with miscellaneous acute broncho-pulmonary diseases were included in this category as negative controls when the following criteria were met: negative blood and sputum cultures for *Streptococcus pneumoniae* with isolation or serological evidence of another significant pathogen, or pathological proof of a non-infectious cause for the pulmonary infiltrate. Infectious causes included acute viral infections (three patients), necrotizing bronchopneumonia due to *Haemophilus influenzae* (two patients), bronchopneumonia due to *Mycoplasma pneumoniae* (two patients), septicemia due to *Streptococcus* species (two patients), post-operative atelectasis (three patients), and purulent empyema of unknown etiology (one patient). Other causes were pulmonary embolism (three patients), carcinoma or leukemic infiltrates (six patients), and cardiac failure (five patients).

5) **Negative Controls for Meningitis.** Sixty-two patients with proven or suspected viral meningitis (50 patients) or non-pneumococcal bacterial meningitis (seven patients with *Haemophilus influenzae*, four with *Neisseria meningitidis* B, and one with *Neisseria meningitidis* C) were included in this category.