# Use of Latex Agglutination Testing in Diagnosing Pediatric Meningitis

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*Background.* Latex agglutination (LA) tests are ordered frequently on cerebral spinal fluid (CSF) specimens obtained from pediatric patients to identify pathogenic bacteria as early as possible in an acute infection.
*Methods.* Six hundred ten LA tests were performed on 176 patients suspected of having meningitis.
*Results.* Five patients with meningitis had positive LA tests. We found that the CSF white blood cell (WBC) count, and differential were the best predictors of meningitis.
*Conclusions.* By limiting the use of LA tests to those patients having CSF with abnormal WBC counts or with positive Gram stains, the number of tests ordered would have been reduced. This practice would greatly reduce laboratory expense.
*Key words.* Latex fixation tests; meningitis; pediatrics; cerebrospinal fluid. *J Fam Pract 1992; 34:176-179.*

Frequently, the primary care physician is presented with the clinical problem of evaluating a febrile child. The extent of the workup and aggressiveness of initial treatment is based on the child's presenting signs, symptoms, and age. Whether the child is hospitalized usually depends on the results of the physician's workup. The typical workup includes a complete blood count, blood cultures, urinalysis with culture, chest radiograph, and cerebral spinal fluid (CSF) specimen. After this initial evaluation, the physician must decide whether to use antibiotics while waiting 48 to 72 hours for the culture results to return.

Laboratory techniques have been developed that allow for rapid, same-day identification of bacterial antigens from various body fluid samples. These testing methods include immunoelectrophoresis, radioimmunoassay, and latex agglutination (LA). Commercially available LA tests (Wellcogen, Wellcome Diagnostics, Triangle Park, North Carolina) can be used to identify the presence of any one of the four common bacterial antigens: *Streptococcus pneumoniae, Hemophilus influenzae, group B streptococcus,* and *Neisseria meningitidis.* The LA test procedure consists of mixing the body fluid specimen with the test reagent that contains beads coated with antibodies to the specific polysaccharide surface antigen. If the antigen is present in the patient's specimen, then antigen-antibody "clumping" appears on the test slide.

The four Wellcogen tests have reported sensitivities of 96% to 100%.[1,2,3] The sensitivities of the LA tests vary depending upon the type of fluid tested: blood, urine, or cerebrospinal fluid. This variability can be the result of different concentrations of antigens in various fluid specimens. The *H influenzae* antigen can be identified in CSF specimens with a 99% sensitivity.[1,4–7] *Streptococcus pneumoniae* antigen can be detected with a 96% sensitivity in serum, but with only an 82% to 87% sensitivity in CSF.[1,4,5,7] Serum samples are best for identifying *N meningitidis* with sensitivities of 99%, as compared with only 77% to 88% in CSF samples.[1,4,5,7] Group B streptococcus is most easily identified in urine with a sensitivity of 99% as compared with 90% in CSF.[1,8,9]

At our medical center, Wellcogen tests are frequently ordered by physicians to screen for bacterial antigens in the CSF specimens of children being evaluated for meningitis. In many cases, these tests are ordered in spite of a low suspicion of meningitis. Furthermore, antibiotics are started even when the Wellcogen tests are negative. The purpose of this study was to develop a better use of the Wellcogen tests.

## Methods

A total of 176 children admitted to the pediatric ward and pediatric intensive care unit at our medical center

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Table 1. Discharge Diagnosis of Pediatric Patients Who Received Lumbar Punctures (N = 176)

| Diagnosis (Category) | No. of Cases |
|---|---|
| Respiratory illness | 34 |
| Seizure | 31 |
| Gastrointestinal illness | 19 |
| "Viral" | 18 |
| "Fever" | 13 |
| Meningiitis | 16 |
| Urinary tract infection | 9 |
| Bacteremia | 4 |
| No diagnosis given | 2 |
| Other | 30 |

between September 1, 1988, and September 1, 1989, received lumbar punctures during their hospital stay. We reviewed the roster of inpatient cultures kept by the microbiology department within the medical center laboratory to identify all patients. The data obtained from each patient's chart included: patient age, CSF culture results, LA results, CSF glucose and protein, CSF cell count and differential, antibiotics used (if any), and final diagnosis. Results of the first lumbar puncture were used if a patient had more than one lumbar puncture during the hospital stay.

We determined how many cases of meningitis were diagnosed from the accumulated data. Next, from this subgroup, we attempted to determine which CSF abnormalities, if any, were good predictors of meningitis. We reviewed the use and results of the LA tests to determine the sensitivities and specificities within this study group. We wanted to see how frequently the test was used, and to see if the results of the LA tests had any effect on whether the physician used antibiotics during the interim between lumbar puncture and the final culture results. Finally, a financial analysis determined the cost of routine use of LA testing.

## Results

A total of 176 patients, aged 2 weeks to 16 years, received lumbar punctures during the period included in the study. The laboratory received spinal fluid specimens on 175 of these patients. Administration of empiric antibiotics was begun in 144 patients at the time cultures were obtained. The final diagnoses of these patients are categorized in Table 1. Sixteen cases of meningitis were diagnosed (the ages of these patients ranged from 2 weeks to 8 years).

At least one LA test was ordered for 161 of 175 patients. Physicians ordered a total of 610 LA tests (some patients were not screened for group B streptococcus). Administration of antibiotics was started in 132 of these 161 patients at the time of lumbar puncture. Five positive LA tests were obtained from CSF: four *H influenzae* and one *S pneumoniae*. All five cases had positive Gram stains as well. There were neither false-positive nor false-negative LA results as proven by culture. Thus, the remaining 605 tests were true negatives. There were two cases of bacterial meningitis in which the causative agent could not be identified by latex agglutination. These organisms were identified by culture as *Listeria* and *Staphylococcus*. The physicians assumed that the remaining nine cases of meningitis were viral because bacterial cultures were negative. Table 2 gives the laboratory results obtained for 16 patients with meningitis.

We reviewed the results of the CSF chemistries and cell counts to determine which values were seen in infected CSF. The spinal fluid glucose tests were ordered for 15 patients with infected CSF, and 7 were normal. Spinal fluid protein tests were ordered in 15 patients with infected CSF, and 5 were normal. However, there were also 24 patients with noninfected CSF specimens but with elevated serum protein levels. All specimens from patients with meningitis had elevated WBC counts ($>10$ WBC/mm$^3$).

In this study, only 42 of 175 patients had elevated CSF WBC counts. If we look at this subgroup of 42 patients, 33 of these were placed on antibiotics at the time of lumbar puncture (111 patients with normal WBC counts in CSF were started on antibiotics as well). The admitting physicians ordered a total of 139 LA tests on 37 of these patients. All 5 positive LA tests and all 12 meningitis cases were included within this group. A further breakdown of this subgroup is possible by screening only those CSF specimens having elevated WBC counts that also contain polymorphonuclear cells. Thirty-four of the 42 patients met this criterion. All cases of meningitis were again contained within this group. A total of 114 LA tests were ordered on 34 patients to obtain the 5 positive results. In addition, 99 children over the age of 3 months were screened for group B streptococcus. No cases of group B streptococcal meningitis were noted in our study group.

## Discussion

In our hospital, LA tests are usually ordered simultaneously with other CSF tests rather than after preliminary test results that may be suggestive of an infection are obtained. As a result, 610 LA tests were performed to confirm 5 cases of meningitis. By limiting the use of LA testing to only those CSF specimens with elevated WBC counts, we could reduce the total number of patients

Table 2. Laboratory Results of 16 Meningitis Cases

| Culture Results | CSF WBC ($mm^3$) | % PMN | CSF Protein g/L | CSF Protein (mg/dL) | CSF Glucose mmol/L | CSF Glucose (mg/dL) |
|---|---|---|---|---|---|---|
| *Hemophilus influenzae* | 6100 | 98 | 2.54 | (254) | 1.51 | (27) |
| *H influenzae* | 5800 | 92 | 1.85 | (185) | 0.72 | (13) |
| *H influenzae* | 2750 | 53 | 0.52 | (52) | 1.18 | (21) |
| *H influenzae* | 288 | 44 | 0.47 | (47) | 3.02 | (54) |
| *Streptococcus pneumoniae* | 69 | 26 | 2.35 | (235) | 1.46 | (26) |
| Viral | 40 | 0 | 0.46 | (16) | 2.74 | (49) |
| Encephalitis (viral) | 9000 | 97 | 1.50 | (150) | 2.63 | (47) |
| Viral | 4850 | 41 | 0.93 | (93) | 6.16 | (110) |
| Listeria | 2850 | 66 | 1.75 | (175) | 1.96 | (35) |
| Viral | 93 | 40 | 0.31 | (21) | 4.37 | (78) |
| Viral | 49 | 56 | 0.33 | (33) | 4.31 | (77) |
| Staphylococcus* | — | — | — | — | — | — |
| Viral | 186 | 74 | 0.47 | (47) | 3.08 | (55) |
| Viral | 173 | 77 | 0.21 | (21) | 3.64 | (65) |
| Viral | 18 | 1 | 0.15 | (15) | 3.42 | (61) |
| Viral | 25 | 5 | 0.39 | (39) | 2.97 | (53) |

**Patient had infected ventriculoperitoneal shunt; culture and sensitivity were the only tests ordered by physician.*
*CSF denotes cerebrospinal fluid; WBC, white blood cell count; PMN, polymorphonuclear cells.*

tested to 37 of 175 (21% of the previous total) and reduce the total number of LA tests to 104, instead of 610 (19% of the previous total). These reductions could have been made without excluding any of the confirmed cases of meningitis.

We propose several other methods that can reduce the use of LA tests. First, the group B streptococcus Wellcogen test is greatly overused. Group B streptococcus causes infections in children, typically in those under the age of 3 months.[10] In this study group, 74 of 99 children over the age of 3 months were screened for group B streptococcus. By using age as a criterion for exclusion, this step alone would have reduced the total number of LA tests by 12%. Second, the Gram stain obtained from the CSF can be used to determine which, if any, LA tests need to be ordered. Ballard and colleagues[11] have noted that the Gram stain can be as reliable as latex agglutination. For example, if gram-negative rods are seen on Gram stain, then a test for *H influenzae* could be performed to confirm the pathogen. In this particular example, screening for streptococcus (gram-positive) would not be appropriate. However, the Gram stain and culture may be misleading in the case of a child to whom antibiotics were already being administered at the time of lumbar puncture, resulting in a sterile CSF. In these cases, a negative Gram stain would not exclude the need to perform LA tests, especially if WBCs were present. Third, and most important, is that in most cases the physician elected to place the child on antibiotics until the culture results came back negative in spite of the negative LA results obtained initially. This would suggest that the physicians placed little credence in the LA results in their decision making. One hundred fifty-six patients with negative LA tests were also on antibiotics. There are several possible explanations for this. The physician may have suspected that an organism not detectable by LA (as was the case in two of seven bacterial meningitis cases) was present, and he or she needed the culture to confirm that suspicion. Also, as in Table 1, most of the cases were not meningitis. The use of antibiotics in some of these cases was to treat another diagnosed infection such as otitis or a pneumonia. Another possibility for antibiotic use even when negative LA test results had been obtained is that the physician was unaware of the test's high sensitivity and therefore was not willing to base his decision on these results.

The use of Wellcogen tests as a screening tool is not cost-effective and it considerably increases patient expense. The initial test group of 176 patients who had 610 LA tests ordered were charged a total of $20,425 for LA testing. This averages out to a cost of $120 per patient and an expenditure of $4216 per positive result. If the 176 patients had been tested according to the criteria outlined above, $801 would have been expended per positive result.

At our hospital, although LA tests are known to have high sensitivities and specificities, their use as an initial screening tool is unwarranted. The CSF WBC count and differential is most useful in identifying those patients most likely to have meningitis. The CSF Gram stain can then possibly identify an organism by its morphology. By limiting the use of latex agglutination testing to only those CSF specimens with elevated WBC counts and/or positive Gram stains, or to patients who were previously treated with antibiotics, we can reduce the total number of tests ordered and decrease patient expense. Gerber[12] and Williams and Hart[13] have suggested limiting the use of the latex agglutination test to

CSF specimens with abnormal indices. The results of our study substantiate their suggestions.

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