Quality Assurance Study of Bacterial Antigen Testing of Cerebrospinal Fluid

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Bacterial antigen testing (BAT) of cerebrospinal fluid (CSF) by latex agglutination is a low-yield procedure in patients whose CSF specimens have normal laboratory parameters. Between August 1992 and August 1994, we evaluated 287 bacterial antigen (BA) test requests to determine whether yields could be improved and whether patient costs could be reduced by canceling BAT for those patients with normal CSF parameters (cell count, protein, glucose) after consultation with physicians. A total of 171 (68%) BA tests were canceled by this approach. None of these CSF specimens was culture positive for an organism detectable by BAT. Of the remaining 116 CSF specimens tested, only 3 were positive by BAT, one each for Neisseria meningitidis, Streptococcus pneumoniae, and group B streptococcus. Only 43 of the CSF specimens tested had at least two abnormal parameters; the 3 positive CSF specimens were included in this group. In light of the low rate of positivity, the number of BA tests can be further reduced by establishing criteria that must be met before a CSF specimen is accepted for BAT. After review of our data and the literature concerning this topic, we concluded that only specimens with leukocyte counts of ≥50 cells per mm3 should be tested. Of 287 specimens evaluated in our study, only 36 met this criterion, including the 3 BA-positive specimens. Enacting such a restriction would have reduced the total number of BA tests by 251 (87%) without compromising patient care. A laboratory cost savings of $6,500 per year would have been realized, with a substantial reduction in the cost per positive test. Patient charges would have been reduced by $12,500 per year.

In the early 1970s, immunodiagnostic methods for the detection of bacterial antigens (BAs) in cerebrospinal fluid (CSF) emerged to fill the need for prompt identification of common agents of bacterial meningitis (5, 11, 31). Numerous assays and commercial kits, including counterimmunoelectrophoresis, coagglutination, and latex particle agglutination, were rapidly developed to serve as adjuncts to routine culture and Gram staining (3, 8, 9, 17). During this era, chloramphenicol was used as empiric therapy for meningitis to ensure adequate staining (3, 8, 9, 17). During this era, chloramphenicol was originally designed to be used in patients who demonstrated laboratory and clinical findings consistent with meningitis (3, 5, 8, 11). Despite these initial intentions, this test has been used much too often as a screening tool in cases of suspected meningitis in patients whose CSF specimens have normal chemistries and cell counts. The indiscriminate use of BAT without consideration of the chemical and cytological profiles of the CSF is a misuse of valuable resources.

In view of the present emphasis in the health care community on the cost-effective use of laboratory services and the changing epidemiology of bacterial meningitis, we felt that it was prudent to formulate a policy concerning the judicious use of BAT. We prospectively evaluated 287 BA test requests over a 2-year period in an effort to determine whether unnecessary testing could be reduced by recommending to physicians that the test be canceled if the CSF analysis was normal. We also determined whether certain CSF parameters would be reliable predictors of BA test positivity and, thus, would allow us to limit our testing to such specimens.

**MATERIALS AND METHODS**

**Study design.** We prospectively studied the use of BAT of CSF in our institution from August 1992 to August 1994. All CSF specimens submitted to our laboratory for BAT were included in the study if the following CSF tests were done: protein, glucose, cell count, Gram staining, and bacterial culture. In order to reduce the number of unnecessary BA tests, we consulted the ordering physician and recommended that BAT be canceled if no abnormal CSF parameters (protein, glucose, cell count) were noted or if only one abnormal parameter was present. Normal values for these parameters at our institution are as follows: leukocyte (WBC) count, 0 to 5 cells per mm3; protein concentration, 15 to 45 mg/dL; glucose concentration, 5 to 60 mg/dL; Gram staining, no more than a few intracellular gram-negative rods; and culture, negative.

In our laboratory, CSF specimens are accepted for BAT only if the following tests were done: protein, glucose, cell count, Gram staining, and bacterial culture. Only if that specimen is accepted for BAT is a BA test performed. In patients whose CSF specimens have normal laboratory parameters, the number of BA tests can be further reduced by establishing criteria that must be met before a CSF specimen is accepted for BAT. We concluded that only specimens with leukocyte counts of ≥50 cells per mm3 should be tested. Of 287 specimens evaluated in our study, only 36 met this criterion, including the 3 BA-positive specimens. Enacting such a restriction would have reduced the total number of BA tests by 251 (87%) without compromising patient care. A laboratory cost savings of $6,500 per year would have been realized, with a substantial reduction in the cost per positive test. Patient charges would have been reduced by $12,500 per year.

The value of BAT for detecting H. influenzae type b in CSF was in cases of invasive H. influenzae disease. Over the past 22 months, no cases of invasive H. influenzae disease have been seen at our institution.

Although BAT has been used for more than a decade, much controversy has arisen over the proper use of this test. BAT was originally designed to be used in patients who demonstrated laboratory and clinical findings consistent with meningitis (3, 5, 8, 11). Despite these initial intentions, this test has been used much too often as a screening tool in cases of suspected meningitis in patients whose CSF specimens have normal chemistries and cell counts. The indiscriminate use of BAT without consideration of the chemical and cytological profiles of the CSF is a misuse of valuable resources.
mg/dl, and glucose concentration, 50 to 75 mg/dl. During this initial phase of the study, age-related variations in protein concentrations and cell counts were not taken into account in determining when to call a physician concerning cancellation of the test. If the physician insisted that BAT be done, despite normal CSF parameters, he or she was asked to provide a brief explanation as to why such testing was deemed necessary. Upon completion of the study, the data were analyzed to determine if a further reduction in BAT could be achieved by establishing which CSF parameter(s) was indicative of bacterial meningitis and predictive of a positive antigen test. In this final analysis, age-related variations in protein concentrations and cell counts were taken into consideration in determining whether the parameter was abnormal. WBC counts also were adjusted on the basis of the number of erythrocytes in the CSF in instances of traumatic lumbar tap. One WBC per 700 erythrocytes was subtracted from the total WBC count in the CSF (4).

**TABLE 2. Characteristics of patients with positive BA results**

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>80</td>
<td>36</td>
<td>15</td>
</tr>
<tr>
<td>Glucose concn (mg/dl)</td>
<td>6</td>
<td>47</td>
<td>7</td>
</tr>
<tr>
<td>Protein concn (mg/dl)</td>
<td>1,358</td>
<td>147</td>
<td>180</td>
</tr>
<tr>
<td>Cell count (% PMNs)</td>
<td>21,525 (%)</td>
<td>2,300 (87)</td>
<td>1,850 (86)</td>
</tr>
<tr>
<td>Gram stain result</td>
<td>No organisms seen, moderate PMNs</td>
<td>Few gram-positive cocci, heavy PMNs</td>
<td>Rare gram-negative cocci, moderate PMNs</td>
</tr>
<tr>
<td>Culture result</td>
<td>Negative</td>
<td>Rare group B strep</td>
<td>Few N. meningitidis</td>
</tr>
<tr>
<td>Antigen result</td>
<td>S. pneumoniae</td>
<td>Group B streptococci</td>
<td>N. meningitidis C, W135</td>
</tr>
<tr>
<td>Previous antibiotic treatment</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

a) PMNs, polymorphonuclear cells.
CSF in a logical sequence, relying on standard tests such as cell count, differential, protein and glucose concentrations, and Gram staining to guide the decision to order additional testing (10, 19, 25, 27, 29). The cell count and differential in CSF have been shown to be sensitive indicators of bacterial meningitis, more so than glucose and protein concentration estimations, which are often nonspecific and of limited diagnostic value (13, 19, 29, 34–36). Using a WBC count of ≥50 cells per mm³ as a criterion for performing BAT, Werner and Kruger (36) achieved 100% sensitivity in predicting BA-positive specimens (36). Others have used both higher and lower cell counts with similar results (7, 29). In applying any biochemical or cytologic criterion for screening CSF, there is always the argument that immunosuppression or prior antibiotic therapy will alter the CSF picture. Clearly, immunosuppression can affect the cell count in CSF. Fishbein et al. (14) found that 6% of patients with meningitis seen over a 13-year period demonstrated an absence of CSF pleocytosis (<6 cells per mm³). All of these patients had underlying conditions which were considered to contribute to a decreased immune response. Therefore, one must be cautious in applying any CSF screening procedure to such patients.

The effect of prior antimicrobial therapy on the CSF tends not to be as clear-cut as that of immunosuppression. Many of the normal CSF specimens that we tested for BA were tested at the insistence of physicians who were concerned that prior therapy had altered the bacterial picture of the CSF. In reviewing the literature, we were not convinced that prior therapy so drastically altered the cell count in CSF that it could not be used as a criterion for testing. In many pediatric patients with meningitis, prior therapy typically consists of antibiotics administered orally for otitis media, usually within 1 week of hospital admission. These partially treated patients may have a decreased likelihood of a positive CSF culture or Gram stain result, but the therapy has minimal effect on CSF parameters such as cell count (4, 6, 12, 15, 18, 20–23, 25, 28, 30, 32, 33, 35, 36). Even after institution of appropriate therapy for meningitis, the CSF picture can remain abnormal for 48 to 72 h (1). Persistent pleocytosis (>60 cells per mm³) has been observed after 7 days of therapy in 50% of children treated for bacterial meningitis (4). With this information in mind, we sought to establish a criterion based on the cell count in CSF as a means of eliminating unnecessary BAT.

In reviewing numerous studies addressing various durations and types of antibiotic pretreatment, the cell count in CSF remained ≥50 cells per mm³ in almost every clinical setting and was typically much higher (6, 12, 20–23, 28, 30, 32, 36). Therefore, we chose to adopt a cell count of ≥50 cells per mm³ to distinguish those specimens most likely to be positive by BAT. Of a total of 287 specimens in the study, only 36 met this criterion, including the 3 specimens positive by BAT (Table 3).

<table>
<thead>
<tr>
<th>No. of specimens</th>
<th>Physician consultation</th>
<th>Total Canceled</th>
<th>Tested Positive</th>
<th>Positive Patient</th>
<th>Laboratory</th>
</tr>
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<tbody>
<tr>
<td>WBC count*</td>
<td>287</td>
<td>171</td>
<td>116</td>
<td>3</td>
<td>8,550</td>
</tr>
<tr>
<td></td>
<td>287</td>
<td>251</td>
<td>36</td>
<td>3</td>
<td>12,550</td>
</tr>
</tbody>
</table>

WBC count, ≥50 cells per mm³.

REFERENCES