

## CSF BACTERIAL ANTIGEN DETECTION TESTING IN THE DIAGNOSIS OF MENINGITIS

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Bacterial meningitis carries a high mortality and morbidity if untreated or treated late. The success of parenteral antibiotic therapy depends on early diagnosis. Although cerebral spinal fluid (CSF) studies allow early presumptive diagnosis prior to initiation of treatment, broad spectrum parenteral antibiotics are currently administered, regardless of initial CSF results, if a bacterial cause is suspected, with the inherent risk of drug side effects and induction of bacterial resistance. CSF culture allows bacteriological diagnosis, but results are not immediate. Rapid identification of the offending organism by Gram's stain characteristics or bacterial antigen detection testing (BADT) allows chemoprophylaxis of contacts whenever indicated.

The value of these two tests in CSF analysis has been contradictory in the literature, especially in patients with meningitis who received antibiotic therapy before the lumbar puncture was carried out.<sup>1-10</sup> The clinical usefulness of these tests should, therefore, be reassessed in light of the local epidemiology, immunization programs (*Haemophilus influenzae* type b [Hib] and *Neisseria meningitidis*) and the cost containment imperatives that all health care systems are currently encountering.

We undertook to assess the clinical usefulness of CSF BADT and Gram's stain studies in children diagnosed as having meningitis in our institution, focusing on the bacterial cases and on all those who had been treated with antibiotics prior to lumbar puncture.

### Methods

All cases of meningitis diagnosed in children under 14 years of age in our institution between January 1983 and June 1995 were analyzed. Patients were considered to have bacterial meningitis if the clinical presentation was suggestive and if parenteral antibiotic therapy for bacterial

meningitis was given for at least seven days, with either a positive CSF culture or BADT, or if organisms were seen on Gram's stain, or in the presence of meningococcal septicemia with purpura and CSF pleocytosis in the absence of a positive CSF culture.

All medical records were reviewed and data collected included age, sex, antibiotic therapy before lumbar puncture, results of CSF analysis (total white blood cells [WBC] and differential, protein, glucose, Gram's stain, culture and BADT). CSF pleocytosis was defined as CSF WBC over  $6 \times 10^{-6}/L$  ( $6 \text{ WBC}/\text{mm}^3$ ). BADT was carried out with Wellcogen<sup>®</sup> Bacterial Antigen Kit, Murex Diagnostics Limited, Dartford, England. This kit uses rapid qualitative latex agglutination technique to detect specific polysaccharide surface antigens for *Haemophilus influenzae* type b (Hib), *Streptococcus pneumoniae* (*Strep. pneumoniae*), *Escherichia coli* (*E. coli*) K1, group B streptococcus and *Neisseria meningitidis* (*N. meningitidis*) groups A, B, C, Y and W135 antigens.

### Results

During the study period, a total of 98 cases of meningitis were diagnosed: 63 were aseptic (64.3%) and 35 bacterial (35.7%). A total of 20 children (20.4%) had received antibiotics prior to diagnosis. Gram's stain showed organisms in 22 of the 27 bacterial cases and none in the 55 aseptic cases tested (sensitivity of 81.5%, specificity of 100%, positive predictive value of 100%, negative predictive value of 91.6%). BADT was positive in 12 of the 21 bacterial cases and negative in all 29 aseptic cases tested (sensitivity of 57.1%, specificity of 100%, positive predictive value of 100%, negative predictive value of 76.3%). CSF culture was positive in 28 of the 35 bacterial cases and negative in all 63 aseptic cases (sensitivity of 80%, specificity of 100%, positive predictive value of 100%, negative predictive value of 90%). Blood culture was positive in 25 of the 30 bacterial cases and two of the 60 aseptic cases (sensitivity of 83.3%, specificity of 96.7%, positive predictive value of 92.5%, negative predictive value of 92.3%).

Bacterial meningitis was diagnosed in 35 patients, 12 of whom had received antibiotics prior to diagnosis. Age

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ranged from three days to 13 years (mean 2.62 years). Twenty-eight cases had a positive CSF culture: *Haemophilus influenzae* type b grew in the CSF of 11 (and blood culture of 13) patients, *Streptococcus pneumoniae* in eight CSF (and five blood) cultures, *Neisseria meningitidis* in two CSF (and four blood) cultures, *E. coli* and *Staphylococcus coagulase* positive each in two CSF (and one blood) cultures, *Enterobacter* in two and *Bacteroides* in one CSF (and one blood) culture. CSF cultures were negative in seven cases of bacterial meningitis, six of whom had a positive blood culture (four had *Haemophilus influenzae* type b and two had *Neisseria meningitidis*), six had received antibiotics prior to diagnosis. BADT was positive in three cases and negative in three other cases with a sensitivity of 50%, Gram's stain showed organisms in five cases and was negative in one, showing a sensitivity of 83.3%.

Sixty-three patients had aseptic meningitis with negative CSF cultures in all, of whom eight had received antibiotics prior to diagnosis

A total of 20 children (20.4%) had received antibiotics prior to diagnosis: eight had aseptic and 12 had bacterial meningitis. CSF culture was positive in six of the 12 bacterial cases and negative in all eight aseptic cases. Blood culture was negative in all aseptic cases, positive in 10 of the 12 bacterial cases, not available in one patient and negative in only one case. Gram's stain showed organisms in nine, but was negative in one bacterial and in the seven aseptic cases tested (sensitivity of 90%, specificity of 100%, positive predictive value of 100%, negative predictive value of 87.5%). BADT was positive in seven and negative in three bacterial cases. It was negative in all five aseptic cases tested. It therefore had a sensitivity of 70%, specificity of 100%, a positive predictive value of 100% and a negative predictive value of 62.5%.

### Discussion

In our experience, Gram's stain of the CSF was more sensitive than BADT in diagnosing the bacterial or viral nature of meningitis (81.5% versus 57.1%), especially in bacterial cases, where the CSF culture did not show any organism (83.3% versus 50%) and also in patients who received antibiotic therapy prior to diagnosis (90% versus 70%). Its negative predictive value also reflects the same findings.

BADT is positive only in the presence of specific polysaccharide surface antigens for *Haemophilus influenzae* type b, *Streptococcus pneumoniae*, *Escherichia coli* K1, group B *Streptococcus* and *Neisseria meningitidis* groups A, B, C, Y and W135 antigens, while any other bacteria remain undetected. Gram's stain does not suffer from this limitation.

Some studies do not recommend routine BADT in all CSF studies, but only in cases where Gram's stain does not identify an organism, or if it suggests a meningococcal infection.<sup>5,8,9</sup> This has not been our experience, as only one out of five cases where Gram's stain was negative had a positive BADT. All cases with meningococcal meningitis had organisms on the Gram's stain, while BADT was only positive in half the cases tested. This is in accordance with studies showing Gram's stain to be more sensitive than BADT in diagnosing meningococcal meningitis.<sup>6,7</sup>

Previous reports recommended that BADT be performed in patients who had previously received antibiotics.<sup>4</sup> We found it to have a positive predictive value of only 62.5% in these cases, compared to 100% for Gram's stain. Out of the 12 patients with bacterial meningitis who had received antibiotics prior to diagnosis, nine had organisms on Gram's stain (only six of them had positive BADT), one had no organisms on Gram's stain (with a negative BADT) and in no case was BADT positive without organisms seen on Gram's stain.

In conclusion, our data indicate that Gram's stain of CSF in patients suspected of having meningitis is superior to BADT in diagnosing a bacterial etiology, even in cases where the CSF culture fails to demonstrate the organism, and also in patients who were treated with antibiotics prior to diagnosis. Adding to its value is its relatively low cost when compared to BADT and its wide availability throughout laboratories across the world.

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