JOURNAL OF CLINICAL MICROBIOLOGY, Apr. 2010, p. 1504–1505 Vol. 48, No. 4
0095-1137/10/$12.00 doi:10.1128/JCM.00153-10

Letters to the Editor

Comparison of Bacterial Antigen Test and Gram Stain for Detecting Classic Meningitis Bacteria in Cerebrospinal Fluid▽

The bacterial antigen test (BAT) screens cerebrospinal fluid (CSF) or other body fluids for antigens of classic bacterial meningitis pathogens (i.e., *Streptococcus pneumoniae*, *Haemophilus influenzae* type b [Hib], group B *Streptococcus* species, *Neisseria meningitidis*, and *Escherichia coli* K1) (7). The utility of the BAT has been questioned in several published reports (2, 5, 6, 8, 12, 15). Furthermore, changes in the epidemiology of bacterial meningitis related to the pneumococcal, meningococcal, and Hib vaccines have likely affected the positive predictive value of the BAT (1, 3, 9, 10, 12, 16). Consequently, many laboratories have discontinued use of the BAT. However, in the absence of clear recommendations, some laboratories may continue to offer the BAT due to conflicting evidence in the literature (5, 11, 14) or the possibility that the BAT may be valuable in diagnosing bacterial meningitis caused by culture-negative organisms (8).

We retrospectively analyzed 918 CSF specimens from adults and children tested at our institution (Mayo Clinic, Rochester, MN) with the BAT (Wellcogen bacterial antigen kit; Remel, Inc., Lenexa, KS), Gram stain, and culture between January 2000 and March 2009. We further analyzed a subset of these in which at least one of the following criteria was met: (i) positive BAT result, (ii) positive Gram stain result consistent with a classical bacterial meningitis pathogen, or (iii) classical bacterial meningitis pathogen identified by culture from CSF. Forty-two cases were identified.

Results of the BAT and Gram stain were compared (Table 1). In 9 of the culture-negative CSF specimens, the culture of samples (blood or ear drainage) from other sterile body sites yielded classic meningitis organisms. For specimens from CSF, blood, or ear drainage with positive culture results, the results of the BAT and Gram stain were analyzed by organism (Table 2).

For the 3 specimens in which the BAT was positive and the Gram stain was negative, the culture was also positive, rendering the BAT redundant. None of the culture-negative cases were missed by the Gram stain, again making the BAT unnecessary.

To increase the sensitivity of the CSF Gram stain, a cytocentrifugation procedure was implemented in January 2007 (4, 13). All five (12%) Gram stain-negative specimens with classic bacterial meningitis pathogens present (including those in which the BAT was positive) were tested prior to the implementation of the cytocentrifugation procedure. Had these Gram stains been performed using the more sensitive cytocentrifugation protocol, the results may have been positive.

Kiska et al. (8) proposed screening criteria based on CSF indices to decrease unnecessary use of the BAT. Their findings suggested that in cases of previous antibiotic treatment in which culture and Gram stain results may be negative, the BAT still may play a role in the diagnosis of bacterial meningitis. However, the findings of our large, retrospective study indicate that the BAT provides no substantial benefit beyond the Gram stain in screening for bacterial meningitis, even in cases with culture-negative results. Although the BAT may be faster than culture in the Gram stain-negative cases, routine antimicrobials are recommended until all test results are available. This moderate benefit must be contrasted with the risk of a false sense of security with a false-negative BAT, or the risk of a false-positive BAT, which would complicate care decisions.

TABLE 1. Comparison of BAT and Gram stain results[a]

Gram stain result	No. (%) of specimens	
	BAT positive	BAT negative
Positive	26 (62)	11 (26)
Negative	3 (7)[a]	2 (5)

[a] Forty-two specimens were tested. The results of the BAT and the Gram stain were not statistically significantly different from one another ($P = 0.64$, Fisher's exact test). All three Gram stain-negative specimens were culture positive.

TABLE 2. Specimens with and without classic bacterial meningitis-causing organisms and number not detected by BAT and Gram stain

Organism	Total no. of specimens	No. (%) of specimens not detected by:	
		BAT	Gram stain
Detected by culture[a]			
Streptococcus pneumoniae	22	6 (27)	3 (14)
Group B *Streptococcus* species	7	3 (43)	0 (0)
Neisseria meningitidis	7	3 (43)	1 (14)
Haemophilus influenzae type b	2	0 (0)	1 (50)
Not detected by culture[b]	4	1 (25)	0 (0)
Total	42	13 (31)	5 (12)

[a] Growth from cerebrospinal fluid, blood, or ear drainage specimens.
[b] Results of both the BAT and the Gram stain were positive for three specimens, with results indicating *N. meningitidis* in two and *S. pneumoniae* in one. In one specimen, the Gram stain showed Gram-positive cocci resembling streptococci, the BAT was negative, and the urine pneumococcal antigen test was positive.

We gratefully acknowledge the staff in the Mayo Clinic bacteriology laboratory for performing the microbiologic tests described and Thomas E. Grys for his thoughtful review of this letter.

REFERENCES

1. **Azzari, C., and M. Resti.** 2008. Reduction of carriage and transmission of *Streptococcus pneumoniae*: the beneficial "side effect" of pneumococcal conjugate vaccine. Clin. Infect. Dis. **47:**997–999.
2. **Barlow, J. F.** 1996. Is BAT BAD in CSF? S. D. J. Med. **49:**85.
3. **CDC.** 2008. Invasive pneumococcal disease in children 5 years after conjugate vaccine introduction—eight states, 1998–2005. MMWR Morb. Mortal. Wkly. Rep. **57:**144–148.
4. **Chapin-Robertson, K., S. E. Dahlberg, and S. C. Edberg.** 1992. Clinical and laboratory analyses of cytospin-prepared Gram stains for recovery and diagnosis of bacteria from sterile body fluids. J. Clin. Microbiol. **30:**377–380.

5. **Das, B. K., R. L. Gurubacharya, T. M. Mohapatra, and O. P. Mishra.** 2003. Bacterial antigen detection test in meningitis. Indian J. Pediatr. **70:**799–801.
6. **Finlay, F. O., H. Witherow, and P. T. Rudd.** 1995. Latex agglutination testing in bacterial meningitis. Arch. Dis. Child. **73:**160–161.
7. **Hayden, R. T., and L. D. Frenkel.** 2000. More laboratory testing: greater cost but not necessarily better. Pediatr. Infect. Dis. J. **19:**290–292.
8. **Kiska, D. L., M. C. Jones, M. E. Mangum, D. Orkiszewski, and P. H. Gilligan.** 1995. Quality assurance study of bacterial antigen testing of cerebrospinal fluid. J. Clin. Microbiol. **33:**1141–1144.
9. **Laval, C. A., F. C. Pimenta, J. G. de Andrade, S. S. Andrade, and A. L. de Andrade.** 2003. Progress towards meningitis prevention in the conjugate vaccines era. Braz. J. Infect. Dis. **7:**315–324.
10. **Makwana, N., and F. A. Riordan.** 2007. Bacterial meningitis: the impact of vaccination. CNS Drugs **21:**355–366.
11. **Mirdha, B. R., U. Gupta, and R. A. Bhujwala.** 1991. Latex agglutination test: an adjunct to the laboratory diagnosis of pyogenic bacterial meningitis. Indian J. Pediatr. **58:**521–524.
12. **Perkins, M. D., S. Mirrett, and L. B. Reller.** 1995. Rapid bacterial antigen detection is not clinically useful. J. Clin. Microbiol. **33:**1486–1491.
13. **Shanholtzer, C. J., P. J. Schaper, and L. R. Peterson.** 1982. Concentrated Gram stain smears prepared with a cytospin centrifuge. J. Clin. Microbiol. **16:**1052–1056.
14. **Surinder, K., K. Bineeta, and M. Megha.** 2007. Latex particle agglutination test as an adjunct to the diagnosis of bacterial meningitis. Indian J. Med. Microbiol. **25:**395–397.
15. **Tarafdar, K., S. Rao, R. A. Recco, and M. M. Zaman.** 2001. Lack of sensitivity of the latex agglutination test to detect bacterial antigen in the cerebrospinal fluid of patients with culture-negative meningitis. Clin. Infect. Dis. **33:**406–408.
16. **Theodoridou, M. N., V. A. Vasilopoulou, E. E. Atsali, A. M. Pangalis, G. J. Mostrou, V. P. Syriopoulou, and C. S. Hadjichristodoulou.** 2007. Meningitis registry of hospitalized cases in children: epidemiological patterns of acute bacterial meningitis throughout a 32-year period. BMC Infect. Dis. **7:**101.

Tess Karre
Emily A. Vetter
Division of Clinical Microbiology
Department of Laboratory Medicine and Pathology

Jayawant N. Mandrekar
Division of Biomedical Statistics and Informatics

Robin Patel*
Divisions of Clinical Microbiology and Infectious Diseases
Department of Medicine
Mayo Clinic
200 First St. SW
Rochester, Minnesota 55905

*Phone: (507) 538-0579
Fax: (507) 284-4272
E-mail: patel.robin@mayo.edu

▽ Published ahead of print on 10 February 2010.