Critical Review Form

Diagnostic Test

CSF Findings in Aseptic Versus Bacterial Meningitis, *Pediatrics* 2000; 105; 316-319

Objectives: "To assess the characteristics of the cerebrospinal fluid (CSF) white blood cell differential findings in children with aseptic meningitis and to examine the influence of duration of illness on these findings." (p. 316)

Methods: Retrospective chart review of "all patients outside of the neonatal age group" at Children's Hospital Pittsburgh with a diagnosis of meningitis from April to October 1992-1997. Definitions included

CSF pleocytosis - > 20 CSF WBC/mm^3

Aseptic meningitis – CSF pleocytosis and absence of any bacterial growth on CSF culture.

Bacterial meningitis – growth of CSF culture or CSF pleocytosis AND blood culture growth of bacterial organism known to cause pediatric bacterial meningitis.

PMN predominance – neutrophils + bands > 50%.

Exclusion criteria included age < 30 days, antibiotics within five days before lumbar puncture (LP), concurrent bacterial infection, neurosurgical procedure, CNS shunt, or immunodeficiency. A prodromal period of illness was estimated to the nearest multiple of 12 (hours) by recorded reports of any first symptoms: fever, headache, cough, irritability, change in behavior or feeding habits, diarrhea, or vomiting. Patient disposition and follow-up were not reported (pp 316-317).

Guide		Comments
I.	**Are the results valid?**	Answer questions IA, IB, & IC below
A.	**Did clinicians face diagnostic uncertainty?**	Treating physicians → YES Data abstractors & authors → NO, as they had all of the data concurrently thus introducing the potential for bias.
B.	**Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group?**	There were no treatment and control groups in this study. All subjects had the gold standard CSF culture, but as noted above, the data abstractors and authors were not blinded to these variables.
C.	**Did the results of the test being evaluated influence the decision to perform the gold standard?**	No, all subjects had the gold standard CSF culture obtained without exception.

<table>
<tr><td>II.</td><td>What are the results?</td><td>Answer questions IIA below.</td></tr>
<tr><td>A.</td><td>What likelihood ratios were associated with the range of possible test results?</td><td>The data provided in the paper permit one to derive the following 2x2 Tables.

<table>
<tr><td></td><td>Growth</td><td>No growth</td><td>TOTALS</td></tr>
<tr><td>CSF % PMN</td><td></td><td></td><td></td></tr>
<tr><td>> 50</td><td>18</td><td>78</td><td>96</td></tr>
<tr><td>< 50</td><td>2</td><td>60</td><td>62</td></tr>
<tr><td>TOTALS</td><td>20</td><td>138</td><td>158</td></tr>
</table>

One can then calculate a sensitivity (90%), specificity (43%), positive Likelihood Ratio (1.58), and negative Likelihood Ratio (0.23) for bacterial meningitis. Note that one could also re-arrange the table with the top column being presence or absence of aseptic meningitis to yield the following for the detection of aseptic meningitis: sensitivity 57%, specificity 10%, LR+ 0.63, LR- 4.3.

Therefore, PMN predominance is a weak predictor to rule-in or rule-out either bacterial meningitis or aseptic meningitis among children with a CSF pleocytosis exceeding 20 wbc/mm^3.</td></tr>
<tr><td>III.</td><td>How can I apply the results to patient care?</td><td>Answer questions III A-D below.</td></tr>
<tr><td>A.</td><td>Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?</td><td>I am uncertain whether the pediatric population CSF response to CNS pathogens equates to that of adult populations, but lacking similar evidence in adults will assume so for the present.</td></tr>
<tr><td>B.</td><td>Are the results applicable to the patients in my practice?</td><td>Among non-immunocompromised children without a concurrent bacterial illness or CNS procedure presenting during enteroviral season, most definitely. Extending these conclusions to adults is shaky at best, but probably best available evidence presently.</td></tr>
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C.	**Will the results change my management strategy?**	Yes, I will be less confident that PMN pleocytosis identifies a bacterial etiology or that lack thereof excludes a bacterial etiology.
D.	**Will patients be better off as a result of the test?**	Yes, if false negatives (those sent home with bacterial meningitis) are eliminated.

Limitations

1) **Retrospective chart review without clearly stated methods.**
    a. **How were cases identified (by physician recall, ICD-9 codes, or other)?**
    b. **How was the data abstraction undertaken? Were reviewers blinded to the study hypothesis? How was abstractor reliability assessed?**
    c. **How was missing or conflicting data managed?**
2) **No sample size calculation reported so uncertain of the possibility of a Type II error (failing to detect a statistically significant difference when one truly exists).**
3) **How was follow-up arranged for those discharged? Was any follow-up attempted?**
4) **Aseptic meningitis cases are likely a mix of viral and non-viral etiologies. The gold standard of viral cultures or polymerase chain reaction was not uniformly performed.**
5) **Only 13% (20/158) were bacterial meningitis. Given the lack of case-capture method reporting, it is reasonable to assume that not all of the bacterial meningitis cases were captured during a six-year period spanning seven months of each year. Future studies should report what portion of those with PMN < 50% have bacterial meningitis, as these are the cases you do not want to miss.**

Bottom Line

A retrospective chart review without clearly stated methods over a six-year period at one urban academic pediatric medical center showed that during the peak season for viral meningitis, CSF PMN predominance (whether >50%, >60% or >90%) among those aged 30 days to 18 years with CSF pleocytosis exceeding 20 WBC/mm^3 is more likely to represent aseptic than bacterial meningitis. PMN predominance alone discriminates poorly between aseptic and bacterial etiologies, even beyond 24-hours since the reported onset of illness.