Critical Review Form

Diagnostic Test

Accuracy and Test Characteristics of Ancillary Tests of CSF for Predicting Acute Bacterial Meningitis in Children with Low WBC Counts in CSF, *Acad EM* 2005; 12: 303-309

Objectives: **To "investigate the accuracy of total protein concentration, glucose concentration, and percentage neutrophils in cerebrospinal fluid (CSF) for predicting acute bacterial meningitis in children with low CSF white blood cell counts (WBC) and provide estimates of the degree to which to adjust the pre-test odds of acute bacterial meningitis based on the results of these tests." (pp 303-304)**

Methods: **Retrospective study of children aged 29 days to 18 years seen in the ED of Children's Hospital Boston from January 1993 to July 1999 (a second cohort of 11 patients from January 1984 to December 1992 was added due to the low number of bacterial meningitis cases meeting their criteria) who had CSF WBC < 30 wbc/mm3 with CSF sent for other routine markers of CNS infection. Exclusion criteria included certain bacterial pathogens (Haemophilus influenza, tuberculosis), leukemia, immunodeficiency, or CNS shunts. Bacterial meningitis was defined as a CSF culture identifying a pathogen known unequivocally to cause CNS infection in children. CSF that isolated probable contaminants were considered not to be infected, but were retained in the data set. The authors analyzed pre-set intervals for protein, glucose, and PMN percentage to compute interval Likelihood Ratios and Receiver Operator Curve Area Under the Curve (AUC).**

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
B.	**Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group?**	No treatment and control group. All had gram stain and CSF culture or they were excluded from the study.
C.	**Did the results of the test being evaluated influence the decision to perform the gold standard?**	No – all had CSF cultures.

<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>See Table 3 (p 308).
<table>
<tr><th></th><th>LR+</th><th>AUC</th><th>Pre</th><th>Post</th></tr>
<tr><td>PMN > 75</td><td>57</td><td>0.90</td><td>0.1%</td><td>5.4%</td></tr>
<tr><td>Gluc >120</td><td>20</td><td>0.69</td><td>0.1%</td><td>2%</td></tr>
<tr><td>Gluc <20</td><td>15</td><td>0.69</td><td>0.1%</td><td>1.5%</td></tr>
<tr><td>Protein > 200</td><td>22</td><td>0.61</td><td>0.1%</td><td>2.2%</td></tr>
</table>

The pre-test probability was obtained from this sample's prevalence of bacterial meningitis (10/7701 = 0.001 = 0.1%). The post-test probability reflects the likelihood of bacterial meningitis in a patient with that pre-test probability and a "positive" test with that LR (a "positive" protein, for example is any level above 200 mg/dL).</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 of the reproducibility of these results to adults, but lacking contradictory 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>To non-immuncompromised children within the age range 29 days to 3 years with CSF WBC < 30 cells/mm^3, yes. To adults, debatable.</td></tr>
<tr><td>C.</td><td>Will the results change my management strategy?</td><td>Yes, diminished concern about missed bacterial meningitis with CSF WBC < 30 cells/mm^3 unless extreme values of ancillary tests (20>glucose>120, protein >200, or PMN >75%).</td></tr>
<tr><td>D.</td><td>Will patients be better off as a result of the test?</td><td>Yes, if less iatrogenic injury (antibiotic adverse drug reactions), unnecessary hospitalizations, and decreased worrying while awaiting cultures is the end result of an increased confidence of post-disease probability of bacterial meningitis.</td></tr>
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Limitations

1) **Retrospective chart review without clearly stated methods.**
    a. **How were cases identified?**
    b. **Were data abstractors trained and supervised?**
    c. **Were data abstractors blinded to the study hypothesis?**
    d. **Were standardized data abstraction forms utilized?**
2) **Children pre-treated with antibiotics were not excluded.**
3) **No attempt to assess the utility of CSF glucose:serum glucose ratio was made, although this was probably by design as it is difficult to control for large variations in timing of CSF being obtained and serum glucose being measured.**
4) **The authors added a cohort of patients without clearly stating methods of how cases were identified or how co-morbidities were compared.**
5) **The authors do not discuss why traumatic LP's were excluded or why they did not utilize previously described, widely utilized correction formulas.**
6) **Arbitrary definition of CSF pleocytosis at 30 wbc/mm^3. Might have been interesting to see how results varied when pleocytosis set at 20 wbc/mm^{3}or 10 wbc/mm^3.**
7) **Insufficient power for multivariable analysis or subgroup analysis.**

Bottom Line

No single value of CSF glucose, protein, or percentage PMN has sufficient discriminatory value to definitively diagnose acute bacterial meningitis in children with CSF WBC < 30 wbc/mm^3, although extreme values (protein > 200 mg/dL, CSF neutrophils >75%, or CSF glucose >120 mg/dL or < 20 mg/dL) should substantially heighten the concern for bacterial meningitis in this population.