4.3 Findings Suggestive of Meningitis in Children

Although vaccination has significantly reduced its incidence, the possibility of bacterial meningitis (a bacterial infection of the area around the brain) remains scary for clinicians seeing young children with fevers. Israeli investigators reported on the diagnostic accuracy of clinical symptoms and signs of meningitis in children.[1] They enrolled 108 patients 2 months to 16 years old who underwent lumbar puncture (also called a spinal tap; using a needle in the back to remove spinal fluid) for suspected meningitis and correlated signs and symptoms with the diagnosis of meningitis. The gold standard for meningitis was a white blood cell count of 6 or higher per microliter of cerebrospinal fluid (CSF).

(Clinical information: *bacterial* meningitis is more severe and less common than *aseptic* (viral) meningitis, and CSF white blood cell (WBC) counts with meningitis are typically much higher than 6 WBC/μL, especially in those with bacterial meningitis.)

From the abstract:

RESULTS: Meningitis was diagnosed in 58 patients (53.7%; 6 bacterial and 52 aseptic). Sensitivity and specificity were 76% and 53% for headache (among the verbal patients)… Photophobia {pain or discomfort from bright light} was highly specific (88%) but had low sensitivity (28%). Clinical examination revealed nuchal rigidity {stiff neck} (in patients without open fontanel) in 32 (65%) of the patients with meningitis and in 10 (33%) of the patients without meningitis.

These are disappointing results for some of the main symptoms and signs we use to decide whether to do a lumbar puncture.

Consider clinical findings such as headache as the index tests and the CSF cell count ≥ 6 as the gold standard for meningitis.

For each of the following statements, answer whether it is true or false and explain your answer.

a. The low sensitivity of the findings could be due to *partial verification bias*, because only subjects who received a lumbar puncture were included in the study. [2]

False. Partial verification bias increases sensitivity. In this study, patients with negative index tests were probably less likely to get a lumbar puncture. If some of them had ≥ 6 WBC/μL in the CSF they would have been false negatives, if they had received a lumbar puncture. Thus excluding them would be expected to falsely raise sensitivity, not lower it.

b. The higher specificity of photophobia could be due to *partial verification bias*, if clinicians deciding to do a lumbar puncture were particularly influenced to do so because photophobia was present. [2]

False. The described scenario would indeed cause partial verification bias, but that

would decrease specificity. Patients with < 6 WBC/ μL in the CSF would be more likely to get a lumbar puncture and be included in the study if they had photophobia. These false positives would lower specificity because they would make photophobia less likely to be "negative in health."

c. If we wished to use this study to estimate the sensitivity of clinical findings for *bacterial* meningitis, we would have to be concerned about falsely low sensitivity due to *spectrum bias*: sensitivity probably would have been higher if more of the meningitis group had bacterial meningitis. [2]

True. The D+ patients in this study had milder disease and were therefore probably less likely to be positive on the index tests. Some of the patients characterized as D+ may not have had meningitis at all and this makes apparent false negatives (that should be true negatives) more likely. Usually spectrum bias means that the D+ group consists of the sickest of the sick and sensitivity is biased up, but in this case, the D+ group included patients who weren't that sick and may not have truly been D+, so sensitivity, especially for bacterial meningitis, was probably biased down.

d. The low specificity of these tests could be due to *spectrum bias*: specificity probably would have been higher if more of the meningitis group had bacterial meningitis. [2]

False. Specificity does not depend on the spectrum of *disease*, it depends on the spectrum of *non-disease.*

Assume that the photophobia results were as in the following table:

	CSF WBC Count per μL		
Photophobia	**>30**	**7-30**	**≤6**
Yes	6	10	6
No	0	42	44
	6	52	50

e. If the authors had used a WBC cutoff of ≥ 30/μL for the meningitis gold standard, both sensitivity and specificity would have been higher. [2]

False. Sensitivity would have been higher because the D+ group would have more severe disease. Based on the table above, sensitivity for photophobia with a D+ cutoff of 30 WBC/μL would have been 100%.

However, a cutoff for D+ of 30 WBC/ μL would make specificity (42+44)/(52+50) = 86/102 = 84%, which is lower than the 88% reported in the abstract. This makes sense because now the nondiseased group includes some of the sickest of the well (those with WBC 7-30).

This is the problem with using an arbitrary cutoff to define D+. A strict cutoff often makes sensitivity higher by making the D+ group the sickest of the sick, but it makes the specificity lower by including the sickest of the well in the D− group. A lax cutoff, like 6 WBCs to define meningitis, makes sensitivity low

and specificity high.

1. Amarilyo G, Alper A, Ben-Tov A, Grisaru-Soen G. Diagnostic accuracy of clinical symptoms and signs in children with meningitis. Pediatr Emerg Care. 2011;27(3):196-9.