How to use clinical signs of meningitis

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ABSTRACT

Meningitis is a critical diagnosis not to miss in children presenting with fever. Since the early 20th century, classical clinical signs have been used to aid the diagnosis of meningitis. These classical signs are nuchal rigidity, Kernig's sign and Brudzinski's sign. Each of these relies on the principle that stretching the inflamed meningeal membranes causes clinically detectable irritation. Several primary studies have quantified the diagnostic performance of clinical examination in detecting meningitis in children. The results of these studies vary significantly due to methodological differences, clinical heterogeneity and interobserver variability. However, their findings demonstrate that positive meningitic signs increase the likelihood of a diagnosis of meningitis, and the absence of meningitic signs reduces this probability. These signs have greatest utility when combined with other features in the history and examination to contribute to a comprehensive clinical assessment.

BACKGROUND

Meningitis describes inflammation of the meninges, which can be subclassified by aetiology (box 1). The most critical diagnosis to identify is bacterial meningitis as this has a poor prognosis when unrecognised.

> **Box 1   Key definitions**
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> ► Meningitis—a disease characterised by inflammation of the meninges. Meningitis may be due to bacterial, tuberculous, viral or fungal infections, or may be aseptic. Causes of aseptic meningitis include partially treated infections, neoplastic disease, drug administration and systemic inflammatory diseases.
> ► Meningism—a clinical syndrome of signs and symptoms that are suggestive of meningeal irritation. Symptoms may include headache, photophobia, neck stiffness and seizures. Signs may include nuchal rigidity, Kernig's sign, Brudzinski's sign or jolt accentuation headache.

Definitive diagnosis of meningitis is made on examination of cerebrospinal fluid obtained at lumbar puncture (LP). Clinical assessment plays an important role in stratification of patients before LP according to pretest probability of meningitis. Traditionally, the identification of clinical signs on examination is used to assess likelihood of meningitis. Nuchal rigidity, Kernig's sign and Brudzinski's sign are classical signs that date from the early 20th century but are still used routinely in paediatric practice.[1]
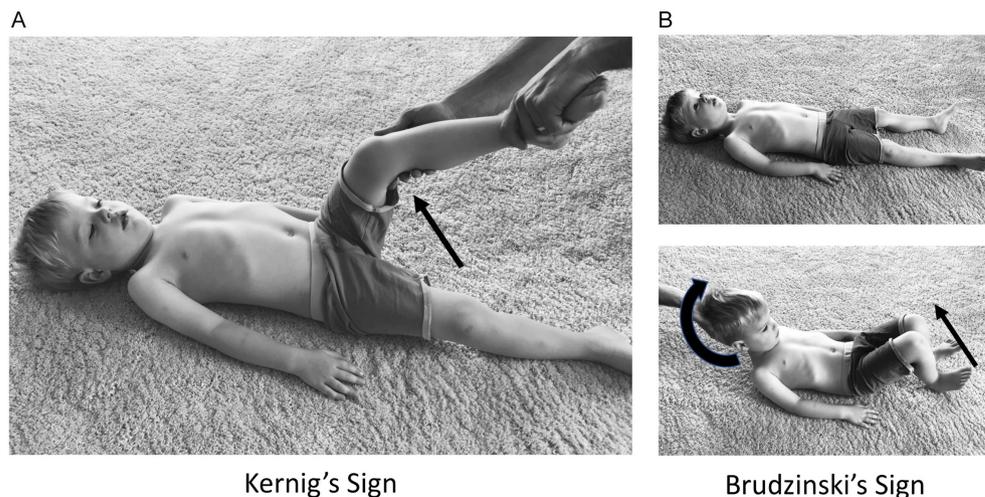

Figure 1   How to examine for clinical signs of meningism. (A) Kernig's sign. (B) Brudzinski's sign.

Table 1 A summary of studies quantifying the diagnostic performance of clinical signs of meningitis

	Study setting	Study design	Inclusion criteria	Exclusion criteria	Sample size	Level of evidence (OCEBM)	Key results
Berkley et al[6]	Rural district hospital, Kenya	Cross sectional	All paediatric patients older than 60 days admitted during 13-month study period.		4582 patients (91 bacterial meningitis cases)	2	**Neck stiffness** LR+ 13.3, LR− 0.74
Lehmann et al[4]	Rural hospital, Papua New Guinea	Cross sectional	Children aged 1–59 months admitted during normal working hours with suspected meningitis.	CSF not collected for analysis.	697	2	**Neck stiffness** Sensitivity 53%, specificity 81% PPV 39% [NPV 80%]
Offringa et al[11]	Urban hospital, Netherlands	Cross sectional	All children between 3 months and 6 years of age who presented with first episode of seizure with fever at two urban hospitals during 2-year period.		309 (23 cases)	2	**Nuchal rigidity** OR 128 if 'definite' OR 2.1 if 'dubious' **Combined history and examination features to define 'major features of meningitis'** LR+=∞ LR−=0.3 PPV 100% NPV 98%
Curtis et al[2]	Global	Systematic review of prospective studies	Studies that described history and examination features of children with meningitis confirmed on LP compared with an LP-negative comparison group. Data collected prospectively and amenable to calculation of accuracy estimates. Not pretreated with antibiotics.	Not prospective. No comparison group. No data or mixed data. Pretreated with antibiotics.	10 studies	1	**Meningeal signs** (any one of NR, KS or BS) Sensitivity 64%, specificity 89% LR+ 4.5 (2.4–8.3), LR− 0.41 (0.3–0.57) **Neck stiffness** Sensitivity 51%, specificity 89% LR− 4 (2.6–6.3), LR− 0.56 (0.43–0.72) **Kernig's sign** Sensitivity 53%, specificity 85% LR+ 3.5 (2.1–5.7), LR− 0.56 (0.41–0.75) **Brudzinski's sign** Sensitivity 66%, specificity 74% LR+ 2.5 (1.8–3.6), LR− 0.46 (0.31–0.68)
Bilavsky et al[7]	Urban hospital, Israel	Prospective cohort study	All children aged 3 months to 17 years who were diagnosed with bacterial meningitis in a 4-year period. Control group were children who were suspected to have bacterial meningitis but ruled out on LP.	Antibiotic therapy before arrival to ED.	86 (40 in study group)	2	**Nuchal rigidity** Sensitivity 64.9%, specificity 53.5% LR+ 1.39, LR− 0.66 **Brudzinski's sign** Sensitivity 52.6%, specificity 77.5% **Nuchal rigidity** LR+ 2.34, LR− 0.61 **Kernig's sign** Sensitivity 51.3%, specificity 95% LR+ 10.27, LR− 0.51
Amarilyo et al[5]	Urban tertiary hospitals, Israel	Cross sectional	Included patients with clinically suspected meningitis between the ages of 2 months and 16 years.	Severe chronic disease, immune deficiency or any neurological condition, patients in whom LP was not performed.	108 (58 cases of meningitis, 6 confirmed bacterial)	2	**Nuchal rigidity** Sensitivity 65%, specificity 67% PPV 0.8 [NPV 0.62] **Brudzinski's sign** Sensitivity 51%, specificity 80% PPV 0.81 [NPV 0.58] **Kernig's sign** Sensitivity 27%, specificity 0.87 PPV 0.77 [NPV 0.51] Prevalence 53.7%

Predictive values in square brackets were not reported by the original study but have been calculated by the authors for the purposes of this review. 95% CIs are given in brackets.

CSF, cerebrospinal fluid; ED, emergency department; LP, lumbar puncture; LR+, positive likelihood ratio; LR−, negative likelihood ratio; NPV, negative predictive value; OCEBM, Oxford Centre for Evidence-Based Medicine; PPV, positive predictive value.

See appendix for search strategy used to identify studies for inclusion (online supplementary file 1).

Interpretations

Table 2 Negative predictive values and likelihood ratios for clinical signs of meningitis

Clinical sign	Negative predictive values*	Likelihood ratios of negative result*
Nuchal rigidity	0.62 to 0.80	0.56 to 0.74
Kernig's sign	0.51	0.51 to 0.56
Brudzinski's sign	0.58	0.46 to 0.61

A quantitative summary of how effectively the absence of each clinical sign alone rules out a diagnosis of meningitis.

*Predictive values and likelihood ratios derived from studies summarised in table 1.[2 4–7]

The physiological principle underlying these tests is that meningeal irritation can be elicited by performing certain movements. In each test, the clinician aims to stretch the meninges and thus elicit features of meningeal irritation (box 2).

To test for nuchal rigidity, the examiner flexes the patient's neck and the test is positive if there is palpable resistance to passive flexion. To test for Kernig's sign, the patients are positioned supine with their hips flexed to 90°. Kernig's sign is present if there is pain on passive knee extension. To elicit Brudzinski's sign, the patients lie supine and their necks are passively flexed by the examining clinician. The test is positive if this causes reflex flexion of the hip and knee. Figure 1 and online supplementary figure 2 demonstrates how to test for Kernig's sign and Brudzinski's sign.

SCENARIOS

Case 1: In febrile children over the age of 1 year, can the absence of clinical signs of meningism rule out meningitis?

Studies reporting the diagnostic accuracy of clinical signs of meningitis are summarised in table 1. Of note, these studies were performed in different populations, using inconsistent reference standards across a range of healthcare contexts including high and low-resource settings (box 3).

Even with these variations in study design and setting, all studies demonstrated that the absence of clinical signs of meningism reduced the likelihood of meningitis, with a combined negative likelihood ratio of 0.41 (95% CI 0.3 to 0.57).[2] Table 2 further summarises the performance of different signs in isolation.

As with all diagnostic tests, it is necessary to consider the pretest probability when applying the test to clinical practice. A recent prospective study of 5517 paediatric hospital attendances with acute illness (excluding trauma, intoxication and exacerbation of chronic conditions) found that only 0.308% of children were diagnosed with meningitis.[3] Using this as a pretest probability, the risk of meningitis in a child presenting with an acute illness without signs of meningism is 0.1% (table 4).

In summary, absence of clinical signs of meningitis suggests a very low risk of meningitis assuming a low pretest probability. The absence of clinical signs

Box 2 How to test for clinical signs of meningitis

► Neck stiffness: Passively flex the patient's neck. This test is positive if there is palpable resistance.
► Kernig's sign: Position the patients supine with their hips flexed to 90°. This test is positive if there is pain on passive extension of the knee.
► Brudzinski's sign: Position the patients supine and passively flex their neck. This test is positive if this manoeuvre causes reflex flexion of the hip and knee.

Box 3 Limitations of research on diagnostic value of clinical signs of meningitis

► Inconsistent diagnostic reference standard.
► Uncertain microbiology, which is sometimes confounded by pretreatment with antibiotics.
► Low patient numbers, often making it impossible to test the performance of each sign for identification of bacterial meningitis per se.
► Interobserver variability.
► Variability between study settings, for example, developed versus developing world.

is reassuring in low-risk children, but meningitis can occur without clinical signs of meningism.

Case 2: In febrile children over the age of 1 year, does the presence of clinical signs of meningism confirm the diagnosis of meningitis?

As summarised in table 3, the positive predictive values for each clinical sign vary between 0.39 and 0.81.[4 5] The likelihood ratios for positive results range from 1.39 to 13.3.[2 6 7] These data demonstrate that the presence of clinical signs of meningism increases the likelihood of meningitis.

However, as shown in table 4, the risk of meningitis remains under 1% even in the presence of signs of meningism. This is due to the low prevalence of meningitis in febrile children. Although the overall risk remains low in children aged over 1 year, the presence of clinical signs of meningism confers an increased risk of meningitis. In this situation, further investigation including LP is likely to be required.

Table 3 Positive predictive values and likelihood ratios for clinical signs of meningitis

Clinical sign	Positive predictive values*	Likelihood ratios of positive result*
Nuchal rigidity	0.39 to 0.8	1.39 to 13.3
Kernig's sign	0.77	3.5 to 10.27
Brudzinski's sign	0.81	2.34 to 2.5

A quantitative summary of the likelihood of a diagnosis of meningitis given positive clinical signs.

*Predictive values and likelihood ratios derived from studies summarised in table 1.[2 4–7]

Table 4 Pretest and post-test probabilities of meningitis

Pre-test probability of meningitis in children with acute illness (%)	Clinical examination finding		Post-test probability of meningitis (%)
	Absent	Nuchal rigidity	0.200
		Kernig's sign	0.200
		Brudzinski's sign	0.170
0.308	Present	Nuchal rigidity	0.640
		Kernig's sign	0.609
		Brudzinski's sign	0.527

A summary of pretest and post-test probability of meningitis (bacterial and viral) according to clinical examination findings. Pretest probability derived from ref [3]. Post-test probabilities calculated using likelihood ratios from ref [2].

Case 3: Are clinical signs of meningism useful in children under the age of 1 year?

Children below the age of 2 months were not included in any study that quantified the performance of clinical signs of meningitis (table 1). Consensus opinion is that these examination findings are unreliable in infants.[8]

Furthermore, the risks of meningitis are much higher in young infants than in older children. For example, a prospective study of infants under the age of 90 days who presented with fever without source found the prevalence of bacterial meningitis to be 0.458%.[9] Therefore, it is necessary to maintain a higher index of suspicion for meningitis when infants present with fever.

For this reason, the National Institute for Health and Care Excellence guidelines recommend LP in febrile infants under the age of 1 month, and in febrile infants aged 1–3 months who appear unwell.[10]

Clinical bottom line

► Bacterial meningitis is uncommon in children over the age of 1 year.
► Meningitis can be difficult to detect clinically.
► The absence of Kernig's sign, Brudzinski's sign and nuchal rigidity is reassuring in low-risk settings but cannot fully exclude meningitis.
► The presence of Kernig's sign, Brudzinski's sign and nuchal rigidity confers enough risk to justify further investigation.

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