

# Does This Adult Patient Have Acute Meningitis?

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## CLINICAL SCENARIOS

### Case 1

A 30-year-old man presents to the emergency department with a 24-hour history of chills and a stiff neck. On clinical examination, he is afebrile and has normal mental status. He can fully flex his neck although he complains of pain over his cervical spine when doing so. Kernig and Brudzinski signs are absent.

### Case 2

A previously healthy 70-year-old woman presents to the emergency department with a 3-day history of fever, confusion, and lethargy. She is unable to cooperate with a full physical examination, but she has neck stiffness upon neck flexion. The findings from a chest radiograph and urinalysis are normal.

## WHY IS CLINICAL EXAMINATION IMPORTANT?

*If, in a fever, the neck be turned awry on a sudden, so that the sick can hardly swallow, and yet no tumour appear, it is mortal.*

—Aphorism XXXV of Hippocrates

As early as the 5th century BC clinicians recognized the seriousness of infectious meningitis.<sup>1</sup> In the 20th century, the annual incidence of bacterial meningitis ranges from approximately 3 per 100 000 population in the United States,<sup>2</sup> to 45.8 per 100 000 in Brazil,<sup>3</sup> to 500 per 100 000 in the “meningitis belt” of Africa.<sup>4</sup> In one county in Minnesota, there was an incidence

**Context** Early clinical recognition of meningitis is imperative to allow clinicians to efficiently complete further tests and initiate appropriate therapy.

**Objective** To review the accuracy and precision of the clinical examination in the diagnosis of adult meningitis.

**Data Sources** A comprehensive review of English- and French-language literature was conducted by searching MEDLINE for 1966 to July 1997, using a structured search strategy. Additional references were identified by reviewing reference lists of pertinent articles.

**Study Selection** The search yielded 139 potentially relevant studies, which were reviewed by the first author. Studies were included if they described the clinical examination in the diagnosis of objectively confirmed bacterial or viral meningitis. Studies were excluded if they enrolled predominantly children or immunocompromised adults or focused only on metastatic meningitis or meningitis of a single microbial origin. A total of 10 studies met the criteria and were included in the analysis.

**Data Extraction** Validity of the studies was assessed by a critical appraisal of several components of the study design. These components included an assessment of the reference standard used to diagnose meningitis (lumbar puncture or autopsy), the completeness of patient ascertainment, and whether the clinical examination was described in sufficient detail to be reproducible.

**Data Synthesis** Individual items of the clinical history have low accuracy for the diagnosis of meningitis in adults (pooled sensitivity for headache, 50% [95% confidence interval {CI}, 32%-68%]; for nausea/vomiting, 30% [95% CI, 22%-38%]). On physical examination, the absence of fever, neck stiffness, and altered mental status effectively eliminates meningitis (sensitivity, 99%-100% for the presence of 1 of these findings). Of the classic signs of meningeal irritation, only 1 study has assessed Kernig sign; no studies subsequent to the original report have evaluated Brudzinski sign. Among patients with fever and headache, jolt accentuation of headache is a useful adjunctive maneuver, with a sensitivity of 100%, specificity of 54%, positive likelihood ratio of 2.2, and negative likelihood ratio of 0 for the diagnosis of meningitis.

**Conclusions** Among adults with a clinical presentation that is low risk for meningitis, the clinical examination aids in excluding the diagnosis. However, given the seriousness of this infection, clinicians frequently need to proceed directly to lumbar puncture in high-risk patients. Many of the signs and symptoms of meningitis have been inadequately studied, and further prospective research is needed.

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rate of viral meningitis of 10.9 per 100 000 person-years from 1950 to 1981, with most cases occurring in the summer months.<sup>5</sup>

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Despite the availability of antimicrobial therapy, meningitis-related case fatality rates remain high, with a 17% all-cause mortality rate between 1980

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**Table 1.** Pathophysiology of Clinical Findings in Meningitis

Pathophysiology	Clinical Features
Systemic infection	Fever, myalgia, rash
Meningeal inflammation	Neck stiffness, Kernig sign, Brudzinski sign, jolt accentuation of headache, cranial nerve palsies
Cerebral vasculitis secondary to meningeal inflammation	Focal neurologic abnormalities, seizures
Elevated intracranial pressure secondary to meningeal inflammation and cerebral edema	Change in mental status, headache, cranial nerve palsies, seizures

and 1988 reported for community-acquired and nosocomial bacterial meningitis among patients aged 16 years and older.<sup>6</sup> Among previously healthy patients who survive pneumococcal meningitis, up to 18% may experience long-term sequelae including dizziness, excessive fatigue, and gait ataxia.<sup>7</sup> Clinical signs and symptoms at presentation may predict prognosis.<sup>8</sup> Thus, early clinical recognition of meningitis is imperative to allow clinicians to efficiently complete further investigations and initiate appropriate therapy with a goal of minimizing these adverse outcomes.

The purpose of this systematic review is to provide clinicians with an understanding of the literature from which the current clinical approach to meningitis is derived. Optimal use of the clinical examination aids physicians in identifying patients at sufficient risk for meningitis to require further definitive diagnostic testing with a lumbar puncture. Patients in whom meningitis is suspected require this invasive procedure to effectively establish or refute the diagnosis. In addition, evaluation of the cerebrospinal fluid may help direct antimicrobial therapy.<sup>9</sup> To avoid unnecessary invasive procedures, it would be useful to identify clinical features that could distinguish patients at high and low risk of meningitis. Clinical findings with a high specificity will assist clinicians in the decision to proceed to lumbar puncture. Conversely, clinical findings with a high

sensitivity will aid clinicians in deciding against invasive investigation, particularly for those patients for whom the clinical suspicion of meningitis is relatively low.

This systematic review will focus on the features of history taking and physical examination that clinicians use to identify adult, immunocompetent patients at risk for acute meningitis for whom further diagnostic testing is indicated. We use the term *meningitis* to refer to acute infections of the meninges of either bacterial or viral origin.

### Pathophysiology of Meningitis

The brain is protected from infection by the skull; the pia, arachnoid, and dural meninges covering its surface; and the blood-brain barrier. When any of these defenses are breached by a pathogen, infection of the meninges and subarachnoid space can occur, resulting in meningitis.<sup>10</sup> Predisposing factors for the development of community-acquired meningitis include preexisting diabetes mellitus, otitis media, pneumonia, sinusitis, and alcohol abuse.<sup>6</sup>

The clinical features of meningitis are a reflection of the underlying pathophysiologic processes (TABLE 1). Systemic infection generates nonspecific findings such as fever, myalgia, and rash. Once the blood-brain barrier is breached, an inflammatory response within the cerebrospinal fluid occurs. The resultant meningeal inflammation and irritation elicit a protective reflex to prevent stretching of the inflamed and hypersensitive nerve roots, which is detectable clinically as neck stiffness or Kernig or Brudzinski signs.<sup>11,12</sup> The meningeal inflammation may also cause headache and cranial nerve palsies.<sup>13</sup> If the inflammatory process progresses to cerebral vasculitis or causes cerebral edema and elevated intracranial pressure, then alterations in mental status, headache, vomiting, seizures, and cranial nerve palsies may ensue.<sup>10</sup>

### Examination for the Signs and Symptoms of Meningitis

The classic clinical presentation of acute meningitis is the triad of fever, neck

stiffness, and an altered mental state. However, less than two thirds of patients present with all 3 clinical findings.<sup>6</sup> While taking the patient's history, clinicians suspecting meningitis will examine for general symptoms of infection (such as fever, chills, and myalgias), as well as symptoms suggesting central nervous system infection (photophobia, headache, nausea and vomiting, focal neurologic symptoms, or changes in mental status).

The physical examination must include checking the vital signs and a brief mental status examination. General inspection may reveal a rash. In patients with severe meningeal irritation, the patient may spontaneously assume the tripod position (also called Amoss sign or Hoyne sign) with the knees and hips flexed, the back arched lordotically, the neck extended, and the arms brought back to support the thorax.<sup>14</sup>

Physical examination specifically for meningitis includes assessing neck stiffness, testing for Kernig and Brudzinski signs, and assessing jolt accentuation of headache. Neck stiffness is assessed by examining the neck for rigidity by gentle forward flexion with the patient in the supine position.

Like neck stiffness, Kernig and Brudzinski signs also indicate meningeal irritation. Vladimir Kernig, a Russian physician, first published the description of the sign that bears his name in 1884,<sup>11,15</sup> although the sign had been previously described by Lazarevic in 1880 and by Forst in 1881.<sup>14</sup> In Kernig's original description, when patients sat on the edge of a bed with their legs dangling, an attempt to extend the knee joint more than 135°, or in severe cases more than 90°, elicited spasm of the extremity that disappeared when the patient lay supine or stood up. Today, the maneuver is most commonly performed with the patient lying supine and the hip flexed at 90°. A positive sign is present when extension of the knee from this position elicits resistance or pain in the lower back or posterior thigh.

In 1909, Josef Brudzinski, a Polish physician, described many meningeal signs in children.<sup>11,16</sup> His best known

“nape of the neck” sign (Brudzinski sign) is present when passive neck flexion in a supine patient results in flexion of the knees and hips. A separate sign, the contralateral reflex, is present if passive flexion of one hip and knee causes flexion of the contralateral leg.

An additional maneuver in assessing for meningitis is to elicit jolt accentuation of the patient’s headache by asking the patient to turn his or her head horizontally at a frequency of 2 to 3 rotations per second. Worsening of a baseline headache represents a positive sign.<sup>17</sup>

A complete neurologic examination follows these more specific tests for meningitis, including examination of the cranial nerves, the motor and sensory systems, reflexes, and testing for Babinski reflex. A general examination follows, with an emphasis on the ears, sinuses, and respiratory system.

## METHODS

### Literature Search and Selection

We searched MEDLINE for articles from 1966 to July 1997 using a structured search strategy (available from the authors on request) to retrieve English- and French-language articles describing the precision and accuracy of the clinical examination in the diagnosis of meningitis. This search strategy yielded 139 abstracts, which were reviewed by one of us (J.A.) for relevance. Full-text articles were retrieved for abstracts that potentially met the inclusion criteria. Additional references were identified by searching the reference lists of pertinent articles.

Explicit inclusion and exclusion criteria were applied to the retrieved articles. We included articles that were original studies describing the accuracy or precision of the clinical examination in the diagnosis of meningitis in which the majority of patients had objectively confirmed bacterial or viral meningitis. We excluded studies that enrolled only children or immunocompromised adults; described mixed patient populations from which adult data could not be extracted; or focused only

on metastatic meningitis, or meningitis of a single specific microbial origin (ie, *Listeria meningitidis* or *Mycobacterium tuberculosis*). Tuberculous meningitis was also excluded on the grounds that this infection is more prevalent in patients with human immunodeficiency virus infection<sup>18</sup> and children, neither of which represent our target population. However, in 2 studies in which there were insufficient data to separate the patients with tuberculous meningitis, we have retained them in our analyses<sup>17,19</sup> (TABLE 2).

### Study Characteristics

This systematic review differs from previous Rational Clinical Examination articles in that all but 1<sup>17</sup> of the 10<sup>6,19-26</sup> articles that met our inclusion criteria were retrospective chart reviews. These studies assessed the clinical presentation of a total of 845 patient-episodes (824 patients), in patients aged 16 to 95 years, with meningitis confirmed by lumbar puncture or autopsy (Table 2).

Because no quality grading system for chart reviews has been widely established, we assessed the validity of these studies by critically appraising several components of the study design (Table 2). These components included an assessment of the reference standard used to diagnose meningitis (lumbar puncture or autopsy), the completeness of patient ascertainment, and whether the clinical examination was described in sufficient detail to be reproducible. The major limitation common to all these studies was the lack of a control population, which means that only sensitivities were available for most of the clinical findings. In addition, the reported sensitivities may overestimate the true sensitivities (as could be established in a prospective study) because the clinical examinations recorded in the charts could have been performed with knowledge of the lumbar puncture results.

The single prospective study included 54 inpatients and outpatients presenting with fever and headache to a Japanese center (Table 2).<sup>17</sup> A standardized clinical examination was per-

formed by an examiner before lumbar puncture was undertaken and clinical findings were compared with those of cerebrospinal fluid pleocytosis.

### Data Analysis

Clinical examination findings that differ between viral and bacterial causes are explicitly indicated. Sensitivities for the various signs and symptoms of meningitis were calculated from the data in each study. Pooled sensitivities were calculated for each feature of the clinical examination, using a random effects model.<sup>27</sup> Clinical features are included in the tables and text of the “Results” section.

Because control groups of patients without meningitis were not included in the 9 retrospective studies, specificities for many features of the clinical examination were unavailable. For the findings assessed in the prospective study, specificities and likelihood ratios were calculated and included.<sup>17</sup>

## RESULTS

### Precision of Symptoms and Signs of Meningitis

Data on the precision of the clinical examination for meningitis were not available from the retrospective studies. In the prospective study, a single clinician completed all clinical examinations.<sup>17</sup>

### Accuracy of the Clinical History in the Diagnosis of Meningitis

The individual components of the clinical history have low sensitivity for the diagnosis of meningitis, as indicated in TABLE 3. In addition to symptoms of headache and nausea and vomiting, neck pain was reported to have a sensitivity of 28% among patients with meningitis.<sup>22</sup> Data from the prospective trial suggest that the clinical history also lacks specificity for the diagnosis of meningitis, with reported specificities of 15% for a nonpulsatile headache, 50% for a generalized headache, and 60% for nausea and vomiting.<sup>17</sup> Thus, clinical history alone is not useful in establishing a diagnosis of meningitis. The inaccuracy of the clini-

cal history may relate to the frequently impaired mental status of patients with meningitis (pooled sensitivity, 67%; 95% confidence interval [CI], 52%-82%; TABLE 4), who are relatively incapable of providing an accurate clinical history.<sup>23,24</sup>

### Accuracy of the Physical Examination in the Diagnosis of Meningitis

In contrast to the clinical history, elements of the physical examination have sensitivities that are clinically useful. The frequency with which patients pre-

sented with the classic clinical triad of fever, neck stiffness, and a change in mental status (or headache<sup>26</sup>) was assessed in 3 studies. Although the pooled sensitivity for the presence of all 3 symptoms was low (Table 4), 95% of patients had 2 or more symptoms,<sup>26</sup> and 2 studies reported between 99% and 100% of patients had at least 1 of these clinical findings.<sup>6,20</sup> Thus, the diagnosis of meningitis may be effectively eliminated in adult patients presenting without any of the symptoms of fever, neck stiffness, or a change in mental status.

As indicated in Table 4, documentation of fever has a pooled sensitivity of 85% (95% CI, 78%-91%) for the diagnosis of meningitis. As would be expected of a single physical finding common to many disorders, fever has a low specificity of 45%.<sup>17</sup> Normal body temperature may significantly lower the likelihood that a patient has meningitis, although the presence of a fever does not definitively establish the disease. The relationship between body temperature and meningitis may be U-shaped because hypothermic patients with sepsis are more likely to

**Table 2.** Studies Assessing Clinical Presentation of Patients

Source, y	Clinical Setting, Years	No. of Patients	Age, Mean (Range), y	Type of Meningitis*	Patient Identification	Clinical Findings Defined
Sigurdardottir et al, <sup>20</sup> 1997	All hospitals in Iceland, 1975-1994	119	44% >45 (16-?)	Bacterial	All patients with bacterial isolates from cerebrospinal fluid or meningococemia, processed at national central laboratory, complete hospital records for 119 of 132 patient-episodes	No
Durand et al, <sup>6</sup> 1993	University hospital, 1962-1988	259	56% >50 (16-88)†	Bacterial	Hospital diagnosis of acute bacterial meningitis, including transferred patients	No
Uchihara and Tsukagoshi, <sup>17</sup> 1991‡	General hospital, dates not specified	34	38.6 (15-71)	Aseptic (n = 28), bacterial/tuberculous (n = 1), other§	Patients presenting to outpatient or emergency department with headache and fever	Yes
Genton and Berger, <sup>21</sup> 1988	University hospital, 1977-1982	112	Women: 41, men: 40 (16-89)	Bacterial	Patients admitted and discharged with a diagnosis of meningitis	No
Gorse et al, <sup>22</sup> 1984§	University and Veterans Affairs hospitals, 1970-1982	54	64 (50-95)	Bacterial	Patients with a discharge diagnosis of meningitis	No
Gorse et al, <sup>22</sup> 1984	University hospital, 1970-1982	32	(15-49)¶	Bacterial	Patients with a discharge diagnosis of meningitis	No
Massanari, <sup>23</sup> 1977	University hospital, 1965-1975	17	>65#	Bacterial	Patients with a chart diagnosis of meningitis	No
Magnussen, <sup>24</sup> 1980	Community hospital, 1969-1978	59	39**	Aseptic (n = 34), bacterial	Patients with a discharge diagnosis of acute meningitis	No
Domingo et al, <sup>25</sup> 1990	Hospital, 1974-1988	59	71 (65-87)	Bacterial	Not indicated	No
Behrman et al, <sup>26</sup> 1989	University hospital, 1970-1985	31	72 (65-89)	Aseptic (n = 4), bacterial	Patients with a discharge diagnosis of meningitis, subdural empyema, brain abscess, or epidural abscess	Yes
Rasmussen et al, <sup>19</sup> 1992	Community hospitals, 1976-1988	48	69¶ (60-88)††	Tuberculous (n = 6), bacterial	Computer search of hospital records for patients with a diagnosis of acute bacterial meningitis	No

\*Infections included in calculations of sensitivities for clinical findings.

†Community-acquired meningitis.

‡Prospective study design, assessing clinical findings compared with cerebrospinal fluid pleocytosis in patients presenting with headache and fever.

§Predominantly aseptic meningitis (28/54 patients). Other includes subarachnoid hemorrhage (n = 2), acute monocytic leukemia (n = 1), Sjögren syndrome (n = 1), upper respiratory tract infection (n = 11), infectious diarrhea (n = 3), edentulous (n = 2), glaucoma (n = 1), and not specified (n = 3).

||Two patient groups were included in this study: 54 patients older than age 50 years and 32 patients between 15 and 49 years. Each age group is reported separately.

¶Mean age not reported.

#Mean age and range not reported.

\*\*Mean age calculated from data in study, range not reported.

††Median age.

be severely ill than normothermic patients.<sup>28</sup>

Neck stiffness is also a relatively useful clinical finding, with a pooled sensitivity of 70% (95% CI, 58%-82%, Table 4). Other signs of meningeal irritation, namely Kernig and Brudzinski signs, have not been well studied, although in Brudzinski's original description of 42 cases of meningitis (including 21 cases of tuberculous meningitis), Kernig sign had a sensitivity of 57%, while Brudzinski nape of the neck sign had a sensitivity of 97% and the contralateral re-

flex sign had a sensitivity of 66%.<sup>11</sup> Brudzinski himself claimed to confirm the specificity of his nape of the neck sign by attempting (and failing) to elicit it in children with other neurological conditions.<sup>11</sup> Uchihara and Tsukagoshi's prospective study<sup>17</sup> of younger adult patients (mean age, 39 years) reported a sensitivity of 9% and a specificity of 100% for the Kernig sign, while neck stiffness had a sensitivity of 15% and a specificity of 100%. Because this study enrolled patients presenting with fever and headache, and excluded those with

mental status abnormalities or focal neurologic findings, the low reported sensitivities may result from excluding those patients with the highest likelihood of having meningeal signs.

Considering that these signs of meningeal irritation have been in use for almost a century, assessment of their accuracy has been limited. Indirect evidence of poor specificity comes from a case series of<sup>29</sup> 74 acute-care and 287 geriatric patients (hospitalized patients in the acute-care or rehabilitation geriatric wards) aged 17 to 92 years.

**Table 3.** Sensitivity of Clinical History in the Diagnosis of Meningitis

Source, y	No. of Patient Episodes	Headache, %	Nausea and Vomiting, %*	Neck Pain, %
Uchihara and Tsukagoshi, <sup>17</sup> 1991†	34	27	32	NA
Gorse et al, <sup>22</sup> 1984‡	54	43	30	28
Massanari, <sup>23</sup> 1977	17	41	NA	NA
Magnussen, <sup>24</sup> 1980	59	78	NA	NA
Domingo et al, <sup>25</sup> 1990	59	81	NA	NA
Behrman et al, <sup>26</sup> 1989	32§	31	NA	NA
Rasmussen et al, <sup>19</sup> 1992	48	46	29	NA
Pooled sensitivity (95% confidence interval)		50 (32-68) [n = 303]	30 (22-38) [n = 136]	NA

\*NA indicates the clinical finding was not assessed.

†Only study patients with pleocytosis were included in the calculation of sensitivity.

‡Data reported only for patients older than 50 years.

§Thirty-one patients with 32 patient-episodes.

||Number in brackets is patients included in calculation of sensitivity.

**Table 4.** Sensitivity of the Physical Examination in the Diagnosis of Meningitis<sup>a</sup>

Source, y	No. of Patient Episodes	Fever	Neck Stiffness	Altered Mental Status	Fever, Neck Stiffness, and Altered Mental Status	Focal Neurologic Findings <sup>b</sup>	Rash	Kernig Sign	Jolt Accentuation of Headache
Sigurdardottir et al, <sup>20</sup> 1997	119	97	82	66	51	10	52	NA	NA
Durand et al, <sup>6</sup> 1993	279 <sup>c</sup>	95	88	78	66	29	11	NA	NA
Uchihara and Tsukagoshi, <sup>17</sup> 1991 <sup>d</sup>	34	71	15	NA	NA	NA	NA	9 <sup>e</sup>	97 <sup>f</sup>
Genton and Berger, <sup>21</sup> 1988	112	NA	NA	32	NA	10	NA	NA	NA
Gorse et al, <sup>22</sup> 1984 <sup>g</sup>	54	91	81	89	NA	39	NA	NA	NA
Gorse et al, <sup>22</sup> 1984 <sup>g</sup>	32	75	66	53	NA	22	NA	NA	NA
Massanari, <sup>23</sup> 1977	17	88	76	88	NA	NA	NA	NA	NA
Magnussen, <sup>24</sup> 1980	59	42	81	20 <sup>h</sup>	NA	10	NA	NA	NA
Domingo et al, <sup>25</sup> 1990	59	95	92 <sup>i</sup>	88	NA	37	NA	NA	NA
Behrman et al, <sup>26</sup> 1989	32 <sup>j</sup>	94	59	88	18 <sup>k</sup>	38	NA	NA	NA
Rasmussen et al, <sup>19</sup> 1992	48	79	54	69	NA	21	4	NA	NA
Pooled sensitivity (95% confidence interval)		85 (78-91) (n = 733)	70 (58-82) (n = 733)	67 (52-82) (n = 811)	46 (22-69) (n = 426)	23 (15-31) (n = 794)	22 (1-43) (n = 446)		

<sup>a</sup>All data are presented as percentage unless otherwise noted. NA indicates finding was not assessed.

<sup>b</sup>Focal neurologic findings include bilateral Babinski reflexes, pupillary abnormalities, hemiparesis, cranial nerve abnormalities, nystagmus, convulsion and/or seizure, and tremor.

<sup>c</sup>There were 279 patient-episodes in 259 patients.

<sup>d</sup>Only study patients with pleocytosis were included in the calculation of sensitivity.

<sup>e</sup>Specificity of 100%; Brudzinski sign was not assessed.

<sup>f</sup>Specificity of 60%.

<sup>g</sup>Two patient groups were included in this study: 54 patients older than 50 years and 32 patients between 15 and 49 years. Sensitivities were calculated separately for each age group.

<sup>h</sup>Moderate or severe alteration in mental status.

<sup>i</sup>Authors refer to this clinical finding as "meningeal signs."

<sup>j</sup>Thirty-two patient-episodes in 31 patients.

<sup>k</sup>For this triad, assessed only in patients (n = 28) with bacterial meningitis. The authors of this study described the triad of symptoms as fever, neck stiffness, and headache.

Puxty et al<sup>29</sup> found that 13% of the acute-care patients and 35% of the geriatric patients had nuchal rigidity despite the absence of meningitis. Kernig sign was present in 1.5% of the acute-care and 12% of the geriatric populations. The low specificity of the meningeal signs may be due to the frequent presence of cervical arthritis and spondylosis among older patients. Clearly, a well-designed prospective study in which patients suspected of having meningitis are observed prospectively is necessary to definitively establish the accuracy of meningeal signs.

Alterations in mental status, ranging from confusion to coma, have a pooled sensitivity of 67% (95% CI, 52%-82%, Table 4), indicating that normal mental status may be helpful in ruling out meningitis in low-risk patients. One study directly comparing aseptic with bacterial meningitis reported that moderate to severe mental status abnormalities were more common in patients with bacterial meningitis than with aseptic meningitis (44% vs 3%, respectively).<sup>24</sup> Similarly, a second study reported that all patients with bacterial meningitis had a change in mental status, while none of the aseptic meningitis patients did.<sup>26</sup>

One of the most sensitive maneuvers in the diagnosis of meningitis is jolt accentuation of headache as described by Uchihara and Tsukagoshi.<sup>17</sup> Of 34 patients with pleocytosis in this study, 30 had meningitis and 4 had other conditions. Jolt accentuation of headache was present in 33 of these patients compared with 8 of 20 patients without pleocytosis, yielding a sensitivity of 97% and a specificity of 60%. The associated positive likelihood ratio was 2.4, and the negative likelihood ratio was 0.05. If we calculate the likelihood ratios specifically for those patients with meningitis, we obtain a sensitivity of 100%, a specificity of 54%, a positive likelihood ratio of 2.2, and a negative likelihood ratio of 0. In patients presenting with fever and headache, a lack of jolt accentuation of headache on physical examination may essentially exclude meningitis. The main limitation to widespread application of these

results is the small sample of patients assessed in this study.

Rashes occurred most frequently in the presentation of meningitis due to *Neisseria meningitidis*, with prevalences of 63%<sup>6</sup> and 80%.<sup>19</sup> A petechial rash occurred in 73% of patients with meningococcemia, whereas purpura was described in only 20% of these patients.<sup>6</sup> Petechial, purpuric, and ecchymotic rashes also occurred, with lower frequency, in infections caused by *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Listeria monocytogenes*. Since the overall incidence of *N meningitidis* among patients with community-acquired bacterial meningitis was low (14% in 1 series<sup>6</sup>), the pooled sensitivity of a rash for the diagnosis of meningitis was poor (Table 4).

One or more focal neurologic abnormalities were described in many of the case series, including bilateral Babinski reflexes, pupillary abnormalities, hemiparesis, cranial nerve abnormalities, nystagmus, convulsion or seizure, and tremor. As summarized in Table 4, the pooled sensitivity for these signs is low, and they are not clinically useful in ruling out meningitis.

### SCENARIO RESOLUTION

The first scenario described a 30-year-old man with chills, who complained of a stiff neck but had no fever or meningeal signs on examination. We would ask the patient about a headache, and, if present, assess for jolt accentuation. His lack of fever, normal mental status, and lack of jolt accentuation would be sufficient to assure us that this patient does not have meningitis.

In the second scenario, a 70-year-old woman presented with fever, confusion, and neck stiffness. Although we do not know the specificity of these findings, their presence causes us to suspect that she may have meningitis. To establish or refute the diagnosis in this scenario, we would proceed to definitive testing by lumbar puncture.

### THE BOTTOM LINE

Assessment of the accuracy of the clinical examination in the diagnosis of

meningitis is severely limited by the paucity of prospective data on this topic. Despite classic descriptions of meningeal signs and sweeping statements about clinical presentations in generations of textbooks, the signs and symptoms of meningitis have been inadequately studied and the conclusions of this systematic review are that more prospective research is required. Based on the limited studies included in this systematic review, we suggest the following to make optimal use of the clinical examination.

1. The absence of all 3 signs of the classic triad of fever, neck stiffness, and an altered mental status virtually eliminates a diagnosis of meningitis.

2. Fever is the most sensitive of the classic triad of signs of meningitis and occurs in a majority of patients, with neck stiffness the next most sensitive sign. Alterations in mental status also have a relatively high sensitivity, indicating that normal mental status helps to exclude meningitis in low-risk patients. Changes in mental status are more common in bacterial than viral meningitis.

3. Among the signs of meningeal irritation, Kernig and Brudzinski signs appear to have low sensitivity but high specificity.

4. Jolt accentuation of headache may be a useful adjunctive maneuver for patients with fever and headache. In patients at sufficient risk of meningitis, a positive test result may aid in the decision to proceed to lumbar puncture, whereas a negative test result essentially excludes meningitis.

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### REFERENCES

1. Sprengell C. *The Aphorisms of Hippocrates, and the Sentences of Celsus*. 2nd ed. London, England: R Wilkin; 1735.
2. Tunkel AR, Scheld WM. Pathogenesis and pathophysiology of bacterial meningitis. *Clin Microbiol Rev*. 1993;6:118-136.
3. Bryan JP, de Silva HR, Tavares A, Rocha H, Scheld WM. Etiology and mortality of bacterial meningitis in northeastern Brazil. *Rev Infect Dis*. 1990;12:128-135.
4. Scheld WM. Meningococcal diseases. In: Warren KS, Mahmoud AAF, eds. *Tropical and Geographical Medicine*. 2nd ed. New York, NY: McGraw-Hill; 1990: 798-814.
5. Nicolosi A, Hauser WA, Beghi E, Kurland LT. Epi-

- demology of central nervous system infections in Olmsted County, Minnesota, 1950-1981. *J Infect Dis*. 1986;154:399-408.
6. Durand ML, Calderwood SB, Weber DJ, et al. Acute bacterial meningitis in adults: a review of 493 episodes. *N Engl J Med*. 1993;328:21-28.
  7. Bohr V, Paulson OB, Rasmussen N. Pneumococcal meningitis: late neurologic sequelae and features of prognostic impact. *Arch Neurol*. 1984;41:1045-1049.
  8. Aronin SI, Peduzzi P, Quagliarello VJ. Community-acquired bacterial meningitis: risk stratification for adverse clinical outcome and effect of antibiotic timing. *Ann Intern Med*. 1998;129:862-869.
  9. Spanos A, Harrell FE, Durack DT. Differential diagnosis of acute meningitis: an analysis of the predictive value of initial observations. *JAMA*. 1989;262:2700-2707.
  10. Lindsay KW, Bone J, Callander R. *Neurology and Neurosurgery Illustrated*. New York, NY: Churchill Livingstone; 1991.
  11. Brody IA, Wilkins RH. The signs of Kernig and Brudzinski. *Arch Neurol*. 1969;21:215-218.
  12. O'Connell JEA. The clinical signs of meningeal irritation. *Brain*. 1946;69:9-21.
  13. Harvey AM, Johns RJ, McKusick VA, Owens AH, Ross RS, eds. *The Principles and Practice of Medicine*. Norwalk, Conn: Appleton & Lange; 1988.
  14. Sapira JD. *The Art and Science of Bedside Diagnosis*. Baltimore, Md: Urban & Schwarzenberg Inc; 1990.
  15. Kernig W. Ueber ein Wenig bemerktes Meningitis-Symptom. *Berl Klin Wochenschr*. 1884;21:829-832.
  16. Brudzinski J. Un signe nouveau sur les membres inferieurs dans les meningites chez les enfants (signe de la nuque). *Arch Med Enfants*. 1909;12:745-752.
  17. Uchihara T, Tsukagoshi H. Jolt accentuation of headache: the most sensitive sign of CSF pleocytosis. *Headache*. 1991;31:167-171.
  18. Berger JR. Tuberculous meningitis. *Curr Opin Neurol*. 1994;7:191-200.
  19. Rasmussen HH, Sorensen HT, Moller-Petersen J, Mortensen FV, Nielsen B. Bacterial meningitis in elderly patients: clinical picture and course. *Age Ageing*. 1992;21:216-220.
  20. Sigurdardottir B, Bjornsson OM, Jonsdottir KE, Erlendsdottir H, Gudmundsson S. Acute bacterial meningitis in adults: a 20-year overview. *Arch Intern Med*. 1997;157:425-430.
  21. Genton B, Berger JP. Les méningites de l'adulte au centre hospitalier universitaire vaudois: diagnostique, prise en charge et évolution de 112 cas. *Rev Med Suisse Romande*. 1988;108:795-803.
  22. Gorse GJ, Thrupp LD, Nudleman KL, Wyle FA, Hawkins B, Cesario TC. Bacterial meningitis in the elderly. *Arch Intern Med*. 1984;144:1603-1607.
  23. Massanari RM. Purulent meningitis in the elderly: when to suspect an unusual pathogen. *Geriatrics*. 1977;32:55-59.
  24. Magnussen CR. Meningitis in adults: ten-year retrospective analysis at a community hospital. *N Y State J Med*. 1980;80:901-906.
  25. Domingo P, Mancebo J, Blanch L, Coll P, Net A, Nolla J. Acute bacterial meningitis in the elderly. *Arch Intern Med*. 1990;150:1546-1547.
  26. Behrman RE, Meyers BR, Mendelson MR, Sacks HS, Hirschman SZ. Central nervous system infections in the elderly. *Arch Intern Med*. 1989;149:1596-1599.
  27. Fleiss JL. The statistical basis of meta-analysis. *Stat Methods Med Res*. 1993;2:121-145.
  28. Lewin S, Brettman LR, Holzman RS. Infection in hypothermic patients. *Arch Intern Med*. 1981;141:920-925.
  29. Puxty JAH, Fox RA, Horan MA. The frequency of physical signs usually attributed to meningeal irritation in elderly patients. *J Am Geriatr Soc*. 1983;31:590-592.

Times change and forms and their meanings alter. Thus new poems are necessary. Their forms must be discovered in the spoken, the living language of their day, or old forms, embodying exploded concepts, will tyrannize over the imagination, depriving us of its greatest benefits. In the forms of new poems will lie embedded the essences of future enlightenment.

—William Carlos Williams (1883-1963)