Bacterial Meningitis in Aging Adults

Chester Choi
Departments of Medicine, St. Mary Medical Center, Long Beach, and the UCLA School of Medicine, Los Angeles, California

Bacterial meningitis remains a highly lethal disease in older adults, with mortality rates averaging >20% despite modern antibiotic therapy. In this population, more variable presentations are seen, with fewer patients manifesting fever, neck stiffness, and headache than among younger adults. In addition, many older adults (aged ≥ 60 years) may have other underlying diseases causing symptoms that may be confused with those of meningitis. The spectrum of etiologic bacterial organisms is more broad than that for a younger population, in part because of the increased frequency of severe underlying diseases and in part as a result of immunosenescence. Therapy is complicated by both the range of possible causative organisms and the increasing antibiotic resistance manifested by some. These difficulties, contrasted with the success of vaccination in the pediatric population, highlight the need for improved preventive strategies for older adults. This review outlines some key clinical points in the management of bacterial meningitis in the older adult.

In recent years, bacterial meningitis has radically changed to become a disease largely of adults—in particular, of older adults. This circumstance highlights key problem areas in the management of the disease: (1) recognition of the disease in older patients who present with fewer of the classic symptoms of meningitis or for whom there are other explanations for these symptoms; (2) the greater number of possible causative organisms; (3) the prompt initiation of appropriate therapy against organisms with increasing antibiotic resistance; and (4) the prevention of this disease through effective vaccinations.

EPIDEMIOLOGY

In a summary of bacterial meningitis prior to the widespread use of the Haemophilus influenzae vaccine, Gotschlich indicated that of a cohort of 1000 newborns, approximately 1 or 2 would develop neonatal meningitis, 3 or 4 would develop H. influenzae meningitis, and 1 would develop either Streptococcus pneumoniae or Neisseria meningitidis meningitis. Thus, a total of about 6 cases of meningitis would occur in this cohort, and 1 patient would die and 2 patients would have severe neurological sequelae [1]. Since that time, widespread use of the H. influenzae vaccine has markedly changed the demographics of this disease. A comprehensive survey of meningitis in the United States in 1995 showed a marked decrease in the incidence of H. influenzae meningitis, to 0.2 per 100,000 persons (0.002 per 1000 persons) and a change in the median age of patients from 15 months to 25 years. Approximately 20% of the cases were projected to involve individuals ≥ 60 years of age, as opposed to the 8.6% involving older adults in a similar 1986 survey [2].

Several epidemiological studies indicate that a greater variety of organisms may be responsible for meningitis in the older adult and that viral etiologies are distinctly less common [3–6]. The responsible bacterial organisms include S. pneumoniae; Listeria monocytogenes; gram-negative bacilli such as Escherichia coli and Klebsiella pneumoniae; Streptococcus agalactiae; and, less commonly, N. meningitidis or H. influenzae [7, 8]. Table 1 lists the attack and case fatality rates for some of these organisms. In addition, comparative studies reveal significant complication rates of 85% for older adults, versus 41% for a younger group of adults with bacterial meningitis [6].

This increased risk of bacterial meningitis for older adults is likely multifactorial and includes both a greater propensity for underlying acute and chronic diseases and immunosenescence, a decline in immune function related to aging. Many of these epidemiological studies document that pneumonia, diabetes, renal or hepatic failure, or other chronic underlying diseases are associated with bacterial meningitis in older adults, particularly with S. pneumoniae, L. monocytogenes, and S. agalactiae.
CLINICAL SYMPTOMS

Suspecting bacterial meningitis in the older adult is the initial, major challenge, as there is considerable variability in the clinical findings (table 2). Since febrile responses are often blunted or absent in older adults in general [14], it is not surprising that fever is not a universal symptom, varying in occurrence from 59% in a study by Gorse et al. [6] and 67% in a recent study in Brazil [15] to 100% in other studies [5, 7]. Similarly, headache and nuchal rigidity have been noted in only about 50% of older adults with meningitis and depressed levels of consciousness such as stupor or coma are often but not universally present [5–7].

An evidence-based review of the clinical examination for identifying adults with meningitis, based on data predominantly from studies of older adults, concluded that no single finding was sufficiently sensitive or specific to prompt a diagnosis. However, 1 of 3 findings—fever, neck stiffness, or altered mental status—was present in virtually all patients with meningitis (sensitivity of 99%–100% for the presence of 1 of these findings); thus, the absence of any of the 3 findings essentially excluded the diagnosis, with a high negative predictive value. The presence of all 3 findings was not common in these patients with meningitis (pooled sensitivity of 46%) [16].

Nuchal rigidity and other signs of meningeval irritation such as Kernig or Brudzinski signs should be sought, but these are not universal findings and may also require interpretation. Neck stiffness was found in 35% of older adults (aged ≥60 years) without meningitis and may be caused by prior cerebrovascular accident, cervical arthritis, Parkinson’s disease, or certain drugs [17]. A sometimes helpful clinical sign is that with cervical arthritis, in particular, passive flexion of the neck may elicit resistance more at the extremes of range of motion, whereas with meningeval irritation, resistance may be felt more immediately.

“Jolt” accentuation of headache was purported, in 1 small study [16], to be 97% sensitive for identifying meningitis; this is elicited by asking the patient to rapidly rotate the head horizontally from side to side (2–3 rotations/s). This may be a helpful adjunctive finding, but its sensitivity and specificity for the diagnosis of meningitis require further confirmation.

Thus, in the clinical assessment for possible bacterial meningitis, older adults who present without fever, neck stiffness, or altered mental function probably do not have this disease. Those individuals with 2 or 3 of the 3 classic findings are more likely to have meningitis, but even the presence of all 3 findings is not entirely specific. Headache is present in 21%–81% and nuchal rigidity in 57%–92% [5–7].

Differential diagnosis and initial evaluation

Given the lack of specificity or sensitivity of symptoms and signs, the basis for the diagnosis of meningitis is the lumbar puncture (LP), with analysis of the CSF. For other age groups, a major distinction must often be made between viral and bacterial meningitis; however, the former is relatively uncommon in older adults [6]. A more common clinical problem in the geriatric population is distinguishing between bacterial meningitis and infection at another site as the cause of fever and acutely depressed mental function.

In a study of hospitalized patients who had not undergone a neurosurgical procedure, these 2 symptoms, in the absence of others such as meningeval signs or headache, were not due to nosocomially-acquired bacterial meningitis; however, the sample size of 51 patients was too small to allow a firm con-

Table 1. Data from surveillance studies of bacterial meningitis in older adults (aged >60 years).

<table>
<thead>
<tr>
<th>Organism</th>
<th>AR</th>
<th>CFR</th>
<th>AR</th>
<th>CFR</th>
<th>AR</th>
<th>CFR</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>1.5</td>
<td>31</td>
<td>0.5</td>
<td>54</td>
<td>1.9</td>
<td>20</td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
<td>0.5</td>
<td>—</td>
<td>0.1</td>
<td>41</td>
<td>0.6</td>
<td>—</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>0.2</td>
<td>—</td>
<td>0.09</td>
<td>24</td>
<td>0.07</td>
<td>—</td>
</tr>
<tr>
<td><em>Neisseria meningitidis</em></td>
<td>0.1</td>
<td>—</td>
<td>0.2</td>
<td>29</td>
<td>0.1</td>
<td>—</td>
</tr>
<tr>
<td>Group B <em>Streptococcus</em></td>
<td>0.2</td>
<td>51</td>
<td>0.02</td>
<td>23</td>
<td>0.1</td>
<td>18</td>
</tr>
</tbody>
</table>

NOTE. AR, attack rate per 100,000; CFR, case fatality rate (percentage).

* Incomplete data on CFRs for some organisms.

Table 2. Frequency of signs and symptoms of meningitis in the older adult.

<table>
<thead>
<tr>
<th>Sign or symptom</th>
<th>Frequency, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>59–100</td>
</tr>
<tr>
<td>Confusion</td>
<td>57–96</td>
</tr>
<tr>
<td>Headache</td>
<td>21–81</td>
</tr>
<tr>
<td>Nuchal rigidity</td>
<td>57–92</td>
</tr>
</tbody>
</table>

NOTE. Adapted from [5–7].

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In the older adult, however, fever and altered mental status are less frequently seen on Gram-stained smears. The findings on testing of the CSF help differentiate bacterial meningitis from other conditions (table 3). A profile of purulence with >500 WBCs, lowered glucose level of less than one-third of the simultaneous peripheral glucose level, and differential count with >85% polymorphonuclear leukocytes is highly suggestive of bacterial meningitis, but patients may not have these classic CSF signs, particularly early in the course of the disease [8, 7, 23]. Newer surrogate markers such as CSF lactate, serum procalcitonin, or cytokine levels are under study as diagnostic aids [24]. Whether these tests have particular relevance to an older adult population is unstudied.

Gram-stained smears are positive in up to 85% of untreated cases and may indicate the identity of the causative organism; however, prior antibiotic therapy may significantly reduce the rate of positivity. L. monocytogenes and gram-negative bacilli, more frequent causes of bacterial meningitis in older adults than in younger patients, are less frequently seen on Gram-

### Table 3. CSF findings indicative of meningitis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal CSF</th>
<th>Acute bacterial</th>
<th>Viral</th>
<th>Tuberculous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opening pressure</td>
<td>6–20 cm H2O</td>
<td>Usually elevated</td>
<td>Normal to moderately elevated</td>
<td>Usually elevated</td>
</tr>
<tr>
<td>CSF WBCs, cells per mm³</td>
<td>0–5 (~85% lymphocytes)</td>
<td>Usually several hundred to &gt;80,000 PMNs predominate</td>
<td>5 to a few hundred, but may be &gt;1000; lymphocytes predominate but may be &gt;80% PMNs in first few days</td>
<td>Usually 25–100, rarely &gt;800; lymphocytes predominate except in early stages, when PMNs may account for &gt;80% of cells</td>
</tr>
<tr>
<td>Protein, mg/dL</td>
<td>18–45</td>
<td>Usually 100–500; occasionally &gt;1000</td>
<td>Frequently normal or slightly elevated; &lt;100, may show greater elevation in severe cases</td>
<td>Nearly always elevated; usually 100–200 but may be much higher if dynamic block</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>45–80, or 0.6 × serum glucose</td>
<td>Usually 5–40, or &lt;0.3 × serum glucose</td>
<td>Usually normal but can be low with mumps, HSV 2</td>
<td>Usually reduced; &lt;45 in 75% of cases</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>For traumatic LP, add 1 WBC and 1 mg/dL protein for each 1000 RBCs</td>
<td>Gram stain positive in ~60–80%¹</td>
<td>Usually do not need to find specific causal virus</td>
<td>AFB-positive stain in &lt;25%, culture-positive in &gt;2/3 of cases (but may take 4–8 weeks for growth)</td>
</tr>
</tbody>
</table>

**NOTE.** Adapted from [7, 8, 23]. AFB, acid-fast bacilli; HSV 2, herpes simplex virus type 2; LP, lumbar puncture; PMNs, polymorphonuclear leukocytes.

¹ Gram-positive diplococci; gram-negative diplococci; gram-positive rods.
stained smears of CSF, and improved, rapid diagnostic tests for these organisms are needed [7, 8, 12].

The use of bacterial antigen detection for diagnosis can be helpful, particularly when a patient has received antibiotics before LP, when bacterial meningitis is suspected but the Gram stain of CSF is unrevealing, and when the CSF is otherwise nondiagnostic. Tests are commercially available for *S. pneumoniae*, *N. meningitidis*, *H. influenzae* type B, *E. coli*, and *S. agalactiae* but not for *L. monocytogenes*. The costs of these tests generally mitigate against their routine use, and their sensitivities range from 50% to 75%, whereas their specificities approach 95%–100%. Thus, a positive test is helpful, but a negative test does not rule out a particular pathogen. It is anticipated that newer diagnostic tests such as PCR or DNA probes will significantly improve our diagnostic abilities [25].

**EMPIRICAL TREATMENT**

The increased frequency of resistance of *S. pneumoniae* to penicillin and other antibiotics and the increased frequency of *L. monocytogenes* infection in older adults significantly complicate empirical antibiotic therapy. In a recent nationwide surveillance study, ~25% of strains of *S. pneumoniae* were resistant to penicillin, with 14% demonstrating high-level resistance (≥2.0 μg/mL) and 10% demonstrating intermediate resistance (1.2–2.0 μg/mL) [26]. If the Gram stain of CSF is highly suggestive of nonstreptococcal organisms, the use of ceftriaxone or cefotaxime plus ampicillin (to cover *L. monocytogenes*) should provide adequate initial coverage; however, if organisms consistent with *S. pneumoniae* are seen or if the bacterial antigen test is positive for this organism, vancomycin plus ceftriaxone or cefotaxime should be instituted until sensitivity data are available [22].

Penicillin allergy also complicates the decision regarding antibiotic administration. For individuals with such an allergy, vancomycin with rifampin may be the appropriate choice against *S. pneumoniae*, and the addition of trimethoprim-sulfamethoxazole would provide treatment against *L. monocytogenes*, an organism which occasionally is not adequately susceptible to vancomycin [7, 8].

A more problematic scenario is that of CSF findings that are consistent with bacterial meningitis, but with a CSF Gram stain that is unrevealing. Bacterial antigen tests should be performed, but administration of vancomycin, ampicillin, and ceftriaxone or cefotaxime should be instituted until these tests or standard cultures reveal the causative organism, allowing therapy to be narrowed.

**SPECIFIC TREATMENT AND ANCILLARY MEASURES**

The choice of specific antibiotics should be governed by the degree of penetration of the agent through the blood-brain barrier and by the bactericidal effect of the agent(s). The degree of penetration to the CSF and the suggested dosing regimens and indications are listed in tables 4 and 5 [7, 8, 22, 27].

There are few studies of the optimal duration of therapy for bacterial meningitis, particularly for older adults. In general, treatment against *S. pneumoniae* should extend for 10–14 days, whereas treatment against *L. monocytogenes*, *S. agalactiae*, and gram-negative bacilli should be for 14–28 days; *N. meningitidis* meningitis generally can be treated for ~7 days with effective antibiotics [22].

There are no convincing data to support the routine use of corticosteroids such as dexamethasone to decrease the complication rate in the treatment of meningitis in older adults, as there are for the management of *H. influenzae* meningitis in the pediatric age group [28]. However, there are experimental data that would support the use of dexamethasone in the setting of increased intracranial pressure to combat the development or worsening of vasogenic and cytotoxic cerebral edema. If dexamethasone is used in adjunctive therapy for bacterial meningitis, evidence of the penetration and efficacy of the antibiotic therapy—particularly if cell-wall-active agents are used—should be sought, since these drugs depend upon meningeal inflammation to achieve significant levels in the CSF. This may entail the measurement of antibiotic levels in the CSF or, more practically, a repeated assay of the CSF at 24–48 h and perhaps at further intervals to determine improvements in glucose levels and WBC counts as markers of antibacterial efficacy [7, 8].

**PREVENTION**

Since a significant number of cases of bacterial meningitis in older adults are caused by *S. pneumoniae*, prevention of this form should be a high priority for clinicians. Surveys from 1993 showed that fewer than one-third of patients for whom *S. pneumoniae* vaccine was indicated had received it. Whether this vaccine can adequately prevent invasive forms of *S. pneu-
moniae disease has been controversial, but the vaccine does appear to be at least partially effective (56%–81% for invasive disease, including meningitis) and to be both safe and well-tolerated. Thus, increased utilization of pneumococcal vaccine is a major health care goal of the Centers for Disease Control and Prevention (Atlanta) and a number of other agencies, with an aim to achieve 60% vaccination rates among eligible persons and 80% among institutionalized older adults [29].

The development of an improved pneumococcal vaccine is also a major goal, and a protein conjugate vaccine using elements of the capsule of S. pneumoniae is currently licensed for administration to infants. Early test results suggest improved protection in the pediatric population, and it is hoped that similar results may be obtained among older adults and immunocompromised individuals [29].

H. influenzae is an uncommon cause of meningitis in the older adult, and since the vaccine protects against only type B, the use of this vaccine in the geriatric population would not be expected to have a significant impact. Similarly, N. meningitidis vaccine is available and utilized for outbreaks of invasive disease or to protect some travelers and longer-term visitors and residents in areas where the disease is highly endemic. However, there are no recommendations for its routine use in the older-adult population [30]. Vaccination is recommended, however, for those individuals who have had prior serious infections with this organism and those with complement deficiencies.

Current preventive efforts against L. monocytogenes focus on decreasing exposure to this pathogen by improving food safety and awareness. Research efforts toward the development of an S. agalactiae vaccine are under way and are largely directed toward its use to prevent perinatal transmission of this organism and subsequent invasive disease in the neonate. No trials involving older adults, including those with risk factors such as diabetes or renal failure, have been reported [31].

**FUTURE ENDEAVORS**

Future improvements in the management of bacterial meningitis in older adults should probably focus on three areas. First, improved diagnostic testing would be beneficial. Meningeal imaging that could reliably document the presence of meningitis would help delineate those patients who require LP. Alternatively, a serum test for a marker unique to bacterial meningitis could also be helpful. Improved, rapid diagnostic CSF tests could lead to more targeted and effective antibiotic therapy.

Second, improved antibiotic regimens may be needed. High-dose quinolone therapy may be useful, since these drugs do seem to achieve significant CSF levels and may be valuable in treatment against resistant organisms such as S. pneumoniae. Clinical trials are needed. The use of dexamethasone or other agents to decrease the adverse effects of meningitis holds the promise of altering the significant complication rate of this disease among older adults. The results of a large European multicentered trial are pending. Third, improved prevention strategies are essential. The successes of H. influenzae vaccination in the pediatric population could be repeated and substantially decrease the incidence of bacterial meningitis among older adults.

**References**


3. Wenger JD, Hightower AW, Facklam RR, et al. Bacterial meningitis in...