Several rapid diagnostic tests have been developed to aid in the etiologic diagnosis of bacterial meningitis. Latex agglutination techniques detect the antigens of *H. influenzae* type b, *S. pneumoniae, N. meningitidis, E. coli* K1, and the group B streptococci. However, because bacterial antigen testing does not appear to modify the decision to administer antimicrobial therapy and false-positive results have been reported, routine use of this modality for rapid determination of the bacterial cause of meningitis is not recommended. It can be considered for patients who have been pretreated with antimicrobial therapy and when CSF Gram stain and culture results are negative.

TABLE 90-2 CEREBROSPINAL FLUID TESTS FOR PATIENTS WITH SUSPECTED CENTRAL NERVOUS SYSTEM INFECTION

ROUTINE TESTS
WBC count with differential
RBC count*
Glucose concentration†
Protein concentration
Gram stain
Bacterial culture
SELECTED TESTS BASED ON CLINICAL SUSPICION
Viral culture‡
Smears and culture for acid-fast bacilli
Venereal Disease Research Laboratory (VDRL) test
India ink preparation
Cryptococcal polysaccharide antigen
Fungal culture
Antibody tests (IgM or IgG, or both)§
Nucleic acid amplification tests (e.g., PCR)‖
Cytology¶
Flow cytometry

From Tunkel AR: Approach to the patient with central nervous system infection. In Bennett JE, Dolin R, Blaser M, editors: Mandell, Douglas, and Bennett's principles and practice of infectious diseases, ed 8, Philadelphia, 2015, Saunders.

CSF, Cerebrospinal fluid; IgG, immunoglobulin G; IgM, immunoglobulin M; PCR, polymerase chain reaction; RBCs, red blood cells; WBCs, white blood cells.

*Check in the first and last tubes; in patients with a traumatic tap, there should be a decrease in the number of RBCs with continued flow of CSF. The following formula can be used for determining whether the numbers of CSF red blood cells and white blood cells are consistent with a traumatic tap (all units are number of cells/cubic mm):

$$\text{Adjusted WBCs in CSF} = \text{Actual WBCs in CSF} - \frac{\text{WBCs in blood} \times \text{RBCs in CSF}}{\text{RBCs in blood}}$$

†Compare with serum glucose concentration measured just before lumbar puncture.
‡Yield of viral culture may be low.
§May be useful for specific causes of meningitis and encephalitis.
‖Most useful for specific viral causes of encephalitis and causes of chronic meningitis.
¶In patients with suspected malignancy.

Nucleic acid amplification tests, such as polymerase chain reaction (PCR), have been used to amplify DNA from patients with meningitis caused by several meningeal pathogens. The test characteristics for broad-based bacterial PCR demonstrated a sensitivity of 100%, a specificity of 98.2%, a positive predictive value of 98.2%, and a negative predictive value of 100%.

Differentiation of Bacterial from Viral Meningitis

In patients without a positive CSF Gram stain or culture, the diagnosis of acute bacterial meningitis is often difficult to establish or reject. A combination of clinical features, with or without test results, has been assessed to develop models in an attempt to accurately predict the likelihood of bacterial meningitis compared with other potential causes (most often viruses). In a published meta-analysis of bacterial meningitis score validation studies in which 5312 patients were identified from eight studies, 4896 (92%) had sufficient clinical data to calculate the bacterial meningitis score, which identified children with CSF pleocytosis who were at very low risk for bacterial meningitis. Low-risk features were a negative CSF Gram stain, a CSF absolute neutrophil count less than 1000 cells/mm^3, a CSF protein level less than 80 mg/dL, and a peripheral absolute neutrophil count less than 10,000 cells/mm^3. Despite the positive results of this meta-analysis and other studies, clinical judgment should continue to be used in decisions about the need for administration of empirical therapy in patients with suspected bacterial meningitis.

Several proteins have been examined for their usefulness in the diagnosis of acute bacterial meningitis. C-reactive protein (CRP) detected in serum or CSF and serum procalcitonin concentrations have been elevated in patients with acute bacterial meningitis and may be useful in discriminating between bacterial and viral meningitis. In patients with meningitis in whom the CSF Gram stain result is negative and analysis of other parameters is inconclusive, serum concentrations of CRP or procalcitonin that are normal or below the limit of detection have a high negative predictive value in the diagnosis of bacterial meningitis.

PCR is the most promising alternative to viral culture for the diagnosis of enteroviral meningitis. Enteroviral reverse transcription PCR (RT-PCR) has been tested in clinical settings by numerous investigators and found to be more sensitive than culture for the detection of the enterovirus; the sensitivity has ranged from 86% to 100% and specificity from 92% to 100% for the diagnosis of enteroviral meningitis. For patients with HSV-2 meningitis, PCR appears promising for the diagnosis. In patients

TABLE 90-3 CEREBROSPINAL FLUID FINDINGS FOR PATIENTS WITH INFECTIOUS CAUSES OF MENINGITIS

CAUSE OF MENINGITIS	WHITE BLOOD CELL COUNT (cells/mm^3)	PRIMARY CELL TYPE	GLUCOSE (mg/dL)	PROTEIN (mg/dL)
Viral	50-1000	Mononuclear*	>45	<200
Bacterial	1000-5000†	Neutrophilic‡	<40§	100-500
Tuberculous	50-300	Mononuclear‖	<45	50-300
Cryptococcal	20-500¶	Mononuclear	<40	>45

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*May be neutrophilic early in presentation.
†May range from <100 to >10,000 neutrophils/mm^3.
‡About 10% of patients have a cerebrospinal fluid (CSF) lymphocyte predominance.
§Should always be compared with a simultaneous serum glucose level; ratio of CSF to serum glucose is ≤0.4 in most cases.
‖A therapeutic paradox may exist in which a mononuclear predominance becomes neutrophilic during antituberculosis therapy.
¶More than 75% of patients with acquired immunodeficiency syndrome have <20 cells/mm^3.