TABLE 90-7 RECOMMENDED DOSAGES OF ANTIMICROBIAL AGENTS FOR MENINGITIS IN ADULTS WITH NORMAL RENAL AND HEPATIC FUNCTION

ANTIMICROBIAL AGENT	TOTAL DAILY DOSE*	DOSING INTERVAL (hr)
Amikacin†	15 mg/kg	8
Amphotericin B deoxycholate	0.7-1.0 mg/kg	24
Ampicillin	12 g	4
Cefepime	6 g	8
Cefotaxime	8-12 g	4-6
Ceftazidime	6 g	8
Ceftriaxone	4 g	12-24
Ethambutol§	15 mg/kg	24
Fluconazole	400-800 mg‡	24
Flucytosine§,‖	100 mg/kg	6
Gentamicin†	5 mg/kg	8
Isoniazid§,¶	300 mg	24
Liposomal amphotericin B	3-4 mg/kg	24
Meropenem	6 g	8
Nafcillin	9-12 g	4
Oxacillin	9-12 g	4
Penicillin G	24 million units	4
Pyrazinamide§	15-30 mg/kg	24
Rifampin§	600 mg	24
Tobramycin†	5 mg/kg	8
Sulfamethoxazole-trimethoprim	10-20 mg/kg**	6-12
Vancomycin††	30-60 mg/kg	8-12

*Unless indicated, therapy is administered intravenously.
†Need to monitor peak and trough serum concentrations.
‡Dose of 800-1200 mg is recommended for patients with coccidioidal meningitis.
§Oral administration.
‖Maintain serum concentrations of 50-100 µg/mL.
¶Initiate therapy at a dose of 10 mg/kg.
**Dosage based on trimethoprim component.
††Maintain serum trough concentrations of 15-20 µg/mL.

for 14 days (range, 10 to 28 days); no evidence supports treatment durations longer than 4 weeks.

In patients with tuberculous meningitis, the most important principle of therapy is early initiation on the basis of strong clinical suspicion; it should not be delayed until proof of infection has been obtained. The American Thoracic Society, in conjunction with the CDC and the Infectious Diseases Society of America, recommends 2 months of isoniazid, rifampin, ethambutol, and pyrazinamide, followed by 7 to 10 months of isoniazid and rifampin for patients with drug-sensitive tuberculous meningitis. Therapy for tuberculous meningitis may need to be individualized, with longer durations of therapy used for patients with more severe illness or HIV.

Therapy for cryptococcal meningitis in patients with AIDS is usually an amphotericin B preparation (i.e., amphotericin B deoxycholate, liposomal amphotericin B, or amphotericin B lipid complex) plus flucytosine for 2 weeks, followed by consolidation therapy with fluconazole for 8 weeks. For non-AIDS patients with cryptococcal meningitis, the optimal use of fluconazole is less clear. In a retrospective review of HIV-1–negative patients with CNS cryptococcosis, the patients were more likely to receive an induction regimen containing amphotericin B and subsequent therapy with fluconazole. Most experts recommend high-dose fluconazole (800 to 1200 mg daily) as first-line therapy for coccidioidal meningitis.

The current recommendation is to treat *Histoplasma* meningitis with liposomal amphotericin B over 4 to 6 weeks, followed by itraconazole for at least 1 year. Amphotericin B, alone or in combination with flucytosine, also is the treatment of choice for *Candida* meningitis.

Adjunctive Therapy

For adult patients with bacterial meningitis, adjunctive dexamethasone should be administered to those with suspected or proven pneumococcal meningitis. This recommendation is based on a prospective, randomized, double-blind trial enrolling 301 adults with bacterial meningitis. Adjunctive dexamethasone was associated with a reduction in the proportion of patients who had unfavorable outcomes (15% vs. 25%, $P = .03$) and in the proportion of patients who died (7% vs. 15%, $P = .04$). The benefits were most striking for the subgroup of patients with pneumococcal meningitis and those with moderate to severe disease as assessed by the admission Glasgow Coma Scale.

Dexamethasone is administered at a dosage of 10 mg intravenously every 6 hours (with the first dose given concomitant with or just before the first dose of an antimicrobial agent for maximal attenuation of the subarachnoid space inflammatory response) for 4 days. Adjunctive dexamethasone should not be used in patients who have already received antimicrobial therapy or the meningitis is found not to be caused by *S. pneumoniae*. Despite the positive benefits of adjunctive dexamethasone for adults with bacterial meningitis described previously, the routine use of adjunctive dexamethasone for patients with bacterial meningitis in the developing world has been controversial.

Tuberculous meningitis is associated with persistent morbidity and mortality despite the availability of effective antituberculous chemotherapy. Use of adjunctive corticosteroids has abrogated the signs and symptoms of disease, and early treatment with adjunctive dexamethasone should be used in all patients with tuberculous meningitis.

Patients with cryptococcal meningitis may have increased intracranial pressure or hydrocephalus, or both. Therapeutic modalities for these complications include shunting of CSF and frequent, high-volume lumbar punctures.

Encephalitis

Definition

Encephalitis is inflammation of the brain parenchyma that is associated with neurologic dysfunction. In the absence of pathologic evidence of brain inflammation, an inflammatory response in the CSF or parenchymal abnormalities on neuroimaging are often used as surrogate markers of brain inflammation; however, encephalitis can occur without significant CSF pleocytosis or demonstrable neuroimaging abnormalities. Encephalitis and meningitis share many features. Both syndromes can manifest with fever, headache, and altered mental status, although the encephalitis patient suffers from more severe alterations in mental status.

There is also clinical overlap between encephalitis and encephalopathy. Patients with encephalopathy, however, exhibit confusion early in the course of their illness that can quickly progress to obtundation. Causes of encephalopathy include metabolic disturbances, hypoxia, ischemia, intoxications, organ dysfunction, paraneoplastic syndromes, and systemic infections.