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ANTIBIOTIC ESSENTIALS

Cheston B. Cunha, MD
Burke A. Cunha, MD

Antimicrobial Drug Summaries
Clinical Pharmacokinetics

Antimicrobial Stewardship

Infectious Disease Essentials

Differential Diagnosis

EIGHTEENTH EDITION

2024

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COLOR ATLAS OF CSF, SPUTUM, AND URINE GRAM STAINS & FUNGAL STAINS Center of Book

Chapter 2

Empiric Therapy Based on Clinical Syndrome

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- *Clinical summaries immediately follow each treatment grid*.
- **Therapeutic recommendations are based on antimicrobial effectiveness, resistance potential, and clinical experience.**
- Antimicrobial dosages in this section represent the usual dosages for normal renal and hepatic function in adults.
- **In any given grid category, drug choices are equivalent alternatives.**
- Dosage adjustments, side effects, drug interactions, and other prescribing information are described in individual Drug Summaries (Chapter 11).

UNDER PROOFERS

- *Use of any drug should be preceded by careful review of the package insert, which provides indications and dosing approved by the U.S. Food and Drug Administration.*
- "*PO Therapy or IV-to-PO Switch*" entry in the treatment grids indicates the clinical syndrome can be treated, PO therapy alone, or IV followed by PO therapy.
- *Most patients on IV therapy should be switched to equivalent PO therapy after clinical improvement.*

Empiric Therapy of CNS Infections

Acute Bacterial Meningitis (ABM) (see Color Atlas for CSF Gram stains)

Subset	Usual Pathogens	Preferred IV Therapy	Alternate IV Therapy	IV-to-PO Switch
Normal host	N. meningitidis H. influenzae S. pneumoniae	Ceftriaxone 2 gm (IV) q12h × 2 weeks	Meropenem 2 gm (IV) q8h × 2 weeks	Chloramphenicol 500 mg (PO) q6h × 2 weeks
Elderly or malignancy	Listeria monocytogenes N. meningitidis H. influenzae S. pneumoniae	Before culture results Ceftriaxone 2 gm (IV) q12h **plus** Ampicillin 2 gm (IV) q4h *Listeria present* after culture results Ampicillin 2 gm (IV) q4h × 3 weeks *Listeria not present* Ceftriaxone 2 gm (IV) q12h × 2 weeks	After culture results *Listeria present* TMP–SMX 5 mg/kg (IV) q6h × 3 weeks **or** Meropenem 2 gm (IV) q8h × 3 weeks **or** Chloramphenicol 500 mg (IV) q6h × 2 weeks **or** Linezolid 600 mg (IV) q12h × 3 weeks *Listeria not present* Ceftriaxone 2 gm (IV) q12h × 2 weeks	For Listeria meningitis only TMP–SMX 5 mg/kg (PO) q6h × 3 weeks **or** Chloramphenicol 500 mg (PO) q6h × 3 weeks **or** Linezolid 600 mg (PO) q12h × 3 weeks For usual meningeal pathogens Chloramphenicol 500 mg (PO) q6h × 2 weeks

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Acute Bacterial Meningitis (ABM) (see Color Atlas for CSF Gram stains) *(cont'd)*

Subset	Usual Pathogens	Preferred IV Therapy	Alternate IV Therapy	IV-to-PO Switch
CNS shunt infections (VA shunts)	S. aureus S. epidermidis (CoNS)	MSSA/MSSE Meropenem 2 gm (IV) q8h* MRSA/MRSE Linezolid 600 mg (IV) q12h*	MSSA/MSSE Cefepime 2 gm (IV) q8h* MRSA/MRSE Vancomycin 2 gm (IV) q12h* **plus** Vancomycin 20 mg (IT) q24h (until shunt removal)	MSSE/MRSE Linezolid 600 mg (PO) q12h* MSSA/MRSA Minocycline 200 mg (PO) × 1, then 100 mg (PO) q12h* **or** Linezolid 600 mg (PO) q12h*
CNS shunt infections (VP shunts)	E. coli K. pneumoniae Enterobacter S. marcescens	Ceftriaxone 2 gm (IV) q12h × 2 weeks (after shunt removal)	TMP–SMX 5 mg/kg (IV) q6h × 2 weeks (after shunt removal)	TMP–SMX 5 mg/kg (PO) q6h × 2 weeks (after shunt removal)
Ventriculitis (EVD associated)	MDR P. aeruginosa	Meropenem 2 gm (IV) q8h ± Colistin 5 mg/kg (IV) q8h **plus** Colistin 10 mg (IT) q24h × 2 weeks (after shunt removal)	Meropenem 2 gm (IV) q8h ± Amikacin 1 gm (IV) q24h **plus** Amikacin 10 mg (IT) q24h × 2 weeks (after shunt removal)	
	MDR Acinetobacter	Ampicillin/Sulbactam 4.5 gm (IV) q6h × 2 weeks (after shunt removal) **plus either** Meropenem 2 gm (IV) q8h × 2 weeks (after shunt removal) **or** Colistin 10 mg (IT) q12h × 2 weeks (after shunt removal)	Meropenem 2 gm (IV) q8h × 2 weeks (after shunt removal) **or** Ampicillin/Sulbactam 4.5 gm (IV) q6h × 2 weeks (after shunt removal) **plus** Colistin 10 mg (IT) q12h × 2 weeks (after shunt removal)	

MSSA/MRSA = methicillin-sensitive/resistant S. aureus; MSSE/MRSE = methicillin-sensitive/resistant S. epidermidis.

* Treat for 1 week after shunt removal.

Clinical Presentation: Abrupt onset of fever, headache, stiff neck.
Diagnosis: CSF gram stain/culture.

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Acute Bacterial Meningitis (Normal Hosts)

Diagnostic Considerations: Gram stain of centrifugated CSF is still the best diagnostic test. CSF antigen/CIE are unhelpful in establishing the diagnosis (many false-negatives). In ABM, typical CSF findings include a WBC count of 100–5000 cells/mm^3, elevated opening pressure, variably elevated protein and CSF lactic acid levels (> 6 mmol/L). After the Gram stain, the single most important CSF Dx test is the CSF lactic acid level. In ABM, CSF LA levels >6 mmol/L. In partially treated ABM, CSF LA levels 4-6 mmol/L. ABM is effectively ruled out with CSF LA <4 mmol/L. If the WBC is extremely high (> 20,000 cells/mm^3), suspect brain abscess with rupture into the ventricular system, and obtain a CT/MRI to confirm.

Pitfalls: If ABM is suspected, always perform lumbar puncture (LP) before obtaining a CT scan, since early antibiotic therapy is critical. A CT/MRI should be obtained before LP only if a mass lesion is a primary concern. A stiff neck on physical examination has limited diagnostic value in the elderly, since nuchal rigidity may occur without meningitis (e.g., cervical arthritis) and meningitis may occur without nuchal rigidity. Recurrence of fever during the first week of H. influenzae meningitis is commonly due to subdural effusion, which usually resolves spontaneously over several days. Meningococcal meningitis may occur with or without meningococcemia. On Gram stain, S. pneumoniae may be mistaken for H. influenzae, and Listeria may be mistaken for S. pneumoniae.

Therapeutic Considerations: Do not reduce "meningeal" antibiotic dosing as the patient improves. Repeat LP if the patient is not responding to antibiotics after 48 hours; lack of response may be due to therapeutic failure, relapse, or noninfectious CNS disorder. For S. pneumoniae meningitis, penicillin-resistant strains are susceptible to meningeal doses of beta-lactam antibiotics e.g., ceftriaxone. Highly resistant pneumococcal strains (rare in the CSF) may be treated for 2 weeks with meropenem 2 gm (IV) q8h or linezolid 600 mg (IV) q12h. Dexamethasone 0.15 mg/kg (IV) q6h × 4 days may be given to reduce the incidence/severity of neurologic sequelae. If used, give dexamethasone 30 minutes before the initial antibiotic dose.

Prognosis: Often fatal without treatment. Case-fatality rates in treated adults are 10–20%. Neurological deficits on presentation are associated with a poor prognosis. Permanent neurological deficits are more frequent with S. pneumoniae than H. influenzae, even with early therapy. In meningococcal meningitis, there are no neurological deficits in survivors.

Acute Bacterial Meningitis (Elderly/Malignancy)

Diagnostic Considerations: Diagnosis by CSF Gram stain/culture and CSF LA (see above). ABM pathogens include usual pathogens in normal hosts plus Listeria monocytogenes, a gram-positive, aerobic, bacillus. Listeria is the most common ABM pathogen in patients with malignancies, and is a common pathogen in the elderly. With Listeria meningitis, CSF cultures are positive in 100%, but CSF gram stain is negative in 50%. Meningeal carcinomatosis is suggested by multiple cranial nerve abnormalities.

Pitfalls: "Diphtheroids" isolated from CSF should be speciated to rule out Listeria. Listeria are motile and hemolytic on blood agar, but diphtheroids are not.

Therapeutic Considerations: Elderly patients and cancer patients with ABM require empiric coverage of Listeria plus other ABM pathogens in normal hosts (N. meningitidis, H. influenzae, S. pneumoniae). Third-generation cephalosporins are not active against Listeria.

Prognosis: Related to underlying immunocompetence of the host.

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Acute Bacterial Meningitis (CNS Shunt Infections)/Ventriculitis (EVD infections)
Diagnostic Considerations: Diagnosis by CSF Gram stain/culture and ↑ CSF lactic acid levels >6 nmol/L.
Pitfalls: Blood cultures are usually negative shunt pathogens. VA shunt infections usually due to skin organisms. VP shunt infections may be due to GNB from GI tract.
Therapeutic Considerations: In addition to systemic antibiotics in meningeal doses, adjunctive intraventricular (IVT)/intrathecal (IT) antibiotics are sometimes given to control shunt infections before shunt removal. Cure requires VA/VP shunt or EVD removal.
Prognosis: Good if EVD or CNS shunt is removed.

Acute Nonbacterial Meningitis/Chronic Meningitis

Subset	Usual Pathogens	Preferred IV Therapy	Alternate IV Therapy	PO Therapy or IV-to-PO Switch
Viral (aseptic)	EBV, LCM, Parvo B19, mumps, enteroviruses, WNE. No effective therapy for most.			
	HSV-1* HSV-2*	IV Therapy: Acyclovir 10 mg/kg (IV) q8h × 10 days Ganciclovir 5 mg/kg (IV) q12h × 10 days PO Therapy: Valacyclovir 1 gm (PO) q8h × 10 days		
	VZV	IV Therapy: Acyclovir 10 mg/kg (IV) q8h × 10 days PO Therapy: Valacyclovir 2 gm (PO) q6h × 10 days		
	HHV-6	Gangciclovir: 5 mg/kg (IV) q12h × 2 weeks **or** Foscarnet 90 mg/kg (IV) q12h × 2 weeks		
Primary amebic meningo-encephalitis (PAM)	Naegleria fowleri	Amphotericin B 1 mg/kg (IV) q24h until cured **plus** Amphotericin B 1 mg (IVT) via Ommaya reservoir q24h until cured		
Granulomatous amebic meningo-encephalitis (GAM)	Acanth-amoeba	Amphotericin B 1 mg/kg (IV) q24h until cured		
Lyme neuroborreliosis	Borrelia burgdorferi	Ceftriaxone 2 gm (IV) q24h × 2 weeks **or** Minocycline 200 mg (IV) × 1, then 100 mg (IV) q12h × 2 weeks **or** Doxycycline 200 mg (IV) q12h × 3 days, then 100 mg (IV) q12h × 11 days		Minocycline 200 mg (PO) × 1, then 100 mg (PO) q12h × 2 weeks **or** Doxycycline 200 mg (PO) q12h × 3 days, then 100 mg (PO) q12h × 11 days

* For patients with HIV: Therapy optional depending on severity and immune status.

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Acute Nonbacterial Meningitis/Chronic Meningitis *(cont'd)*

Subset	Usual Pathogens	Preferred IV Therapy	Alternate IV Therapy	PO Therapy or IV-to-PO Switch
Leptospirosis	Leptospira interrogans	Ceftriaxone 2 gm (IV) q12h × 1 weeks **or** Doxycycline 200 mg (IV) q12h × 3 days, then 100 mg (IV) q12h × 4 days		Doxycycline 200 mg (PO) q12h × 3 days, then 100 mg (PO) q12h × 11 days
Neuro-brucellosis	Brucella sp.	Ceftriaxone 2 gm (IV) q12h **plus** Doxycycline 100 mg (PO) q12h **plus** Rifampin 600 mg (PO) q24h × 4 weeks, then Doxycycline **plus** Rifampin (same doses) × 4 weeks		
TB	M. tuber-culosis	INH 300 mg (IV/PO) q24h × 6 months **plus** Rifampin 600 mg (IV/PO) q24h × 6 months **plus** PZA 25 mg/kg (PO) q24h × 2 months **plus** EMB 15 mg/kg (PO) q24h (until susceptibilities known)		
		Treat with 4 drugs, as for pulmonary TB, but extend treatment for 9–12 months. Corticosteroids tapered over 1–2 months helpful.		
Fungal *Non-HIV*	Cryptococcus neoformans, C. gatti	Isavuconazole 200 mg (IV) q8h × 48 h, then 200 mg (IV/PO) q24h × 4–6 weeks **or** Liposomal amphotericin (L-amb) 6 mg/kg (IV) q24h × 4–6 weeks **followed by** Fluconazole 800 mg (IV or PO) × 1 dose, then 400 mg (PO) q24h × 8 weeks*	Amphotericin B 0.7–1 mg/kg (IV) q24h × 4–6 weeks* **plus** Flucytosine 25 mg/kg (PO) q6h × 6 weeks* **followed by** Fluconazole 800 mg (IV or PO) × 1 dose, then 400 mg (PO) q24h × 8 weeks* **or** Liposomal amphotericin (L–amb) 6 mg/kg (IV) q24h × 4–6 weeks	PO therapy alone Fluconazole may be given PO*
HIV	Cryptococcus neoformans (see Chapter 5)			
Chronic meningitis	Coccidioidomycosis, Histoplasmosis, Neurocysticercosis (see Chapter 4)			Do not treat empirically

* May need suppressive fluconazole 200 mg (PO) q24h × 12 months.

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Viral (Aseptic) Meningitis

Clinical Presentation: Headache, low-grade fever, mild meningismus, photophobia. Natalizumab (NTZ) predisposes to HSV and VZV meningitis or meningoencephalitis.

Diagnostic Considerations: Diagnosis by specific serological tests, or CSF viral PCR. CSF LA levels are < 4 mmol/L. HSV-1, usually more severe than HSV-2. HSV, HHV-6, and WNE meningitis is indistinguishable clinically from other causes of viral meningitis. EBV meningitis is usually associated with clinical/laboratory features of EBV infectious mononucleosis; suspect the diagnosis in a patient with a positive monospot and unexplained meningoencephalitis. VZV meningitis is typically associated with cutaneous vesicular lesions (H. zoster). VZV meningitis may later (weeks/months) be followed by a CVA. LCM meningitis begins as a "flu-like" illness usually in the fall after hamster contact, and may have low CSF glucose. Enterovirus meningitis is often associated with a maculopapular rash, non-exudative pharyngitis, diarrhea, and rarely low CSF glucose. Aseptic meningitis due to mumps may present without parotid swelling ± acute deafness and decreased CSF glucose. Drug-induced aseptic meningitis usually have eosinophils in the CSF and little/no fever.

Pitfalls: Consider NSAIDs, TMP–SMX, and IV immunoglobulin as causes of drug induced aseptic meningitis.

Therapeutic Considerations: Usually no need to treat mild HSV-1 or HSV-2 meningitis in normal hosts.

Prognosis: Without neurological deficits, full recovery is the rule.

Primary Amebic Meningoencephalitis (PAM) (Naegleria fowleri)

Clinical Presentation: Acquired by freshwater exposure containing the protozoa, often by jumping into a lake/pool. Affects healthy children/young adults. Organism penetrates cribriform plate and enters CSF. Symptoms occur within 7 days of exposure and may be indistinguishable from fulminant bacterial meningitis, including headache, fever, anorexia, vomiting, signs of meningeal inflammation, altered mental status, coma. May complain of unusual smell/taste sensations early in infection. CSF has RBCs and low glucose.

Diagnostic Considerations: Diagnosis by demonstrating organism in CSF. Worldwide distribution. Free-living freshwater amoeba flourish in warmer climates. Key to diagnosis rests on clinical suspicion based on history of freshwater exposure in previous 1–2 weeks.

Pitfalls: CSF findings resemble bacterial meningitis, but RBCs present.

Therapeutic Considerations: Often fatal despite early treatment.

Prognosis: Frequently fatal.

Granulomatous Amebic Meningoencephalitis (GAM) (Acanthamoeba sp.)

Clinical Presentation: Insidious onset with focal neurologic deficits ± mental status changes, seizures, fever, headache, hemiparesis, meningismus, ataxia, visual disturbances. May be associated with Acanthamoeba keratoconjunctivitis, skin ulcers, or disseminated disease. Usually seen only in immunocompromised/debilitated patients.

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Diagnostic Considerations: Diagnosis by demonstrating organism in brain biopsy specimen. CT/MRI shows mass lesions. "Stellate cysts" characteristic of Acanthamoeba. Worldwide distribution. Strong association with extended wear of contact lenses. Differentiate from N. fowleri by culture.
Pitfalls: Not associated with freshwater exposure, unlike primary amebic meningoencephalitis (Naegleria fowleri). Resembles subacute/chronic meningitis. No trophozoites in CSF. Skin lesions may be present for months before onset of CNS symptoms.
Therapeutic Considerations: No proven treatment. Often fatal despite early treatment.
Prognosis: Usually fatal.

Neuroborreliosis (CNS Lyme Disease)
Clinical Presentation: May have mild neck stiffness not frank nucal rigidity. Low grade fever < 102˚F usually ~ 100–101˚F. Recent tick exposure. Often without rash. Sore throat in some, WBC count WNL, mildly ↑ AST/ALT in some.
Diagnostic Considerations: Diagnosed by demonstrating B. burgdorferi antibody production in the CNS. A CSF : serum IgM ELISA Lyme titer ratio > 1:1 is diagnostic.
Pitfalls: If CNS symptoms present with acute Lyme disease, rash may be absent and serology may be negative early. Neuroborreliosis cannot be reliably diagnosed using CSF : serum IgM if antibiotics given before the LP (antibiotics change the CSF : serum ratio and render the test useless).
Therapeutic Considerations: Preferred Oral Options: doxycycline or minocycline.
Prognosis: Related to underlying health of host. Prognosis with neuroborreliosis is good even with delayed treatment.

Leptospirosis Meningitis (Leptospira interrogans)
Clinical Presentation: Abrupt onset of fever, no chills, severe headache, conjunctival suffusion, cough, intense myalgias (gastroc/back). Meningitis (early) CSF + for leptospires; aseptic meningitis (late) → CSF – for leptospires.
Diagnostic Considerations: Diagnosis by blood/urine culture, PCR or ↑ MAT IgM titers.
Pitfalls: CSF glucose normal and WBCs < 500/hpf. Only ID with CSF bilirubin > serum.
Therapeutic Considerations: β-lactam or doxycycline may result in a Jarish-Herxheimer reaction.
Prognosis: Excellent if treated early.

TB Meningitis (Mycobacterium tuberculosis)
Clinical Presentation: Subacute onset of nonspecific symptoms. Fever usually present ± headache, nausea, vomiting. Acute presentation and cranial nerve palsies uncommon.
Diagnostic Considerations: Diagnosis by CSF AFB smear/culture; CSF PCR is specific but not very sensitive. CSF may be normal, but if TB suspected, obtain serial LPs. CSF in TB typically shows a mild lymphocytic pleocytosis, ↓ glucose, highly ↑ protein, and few RBCs. CSF lactic acid levels slightly elevated ↑ CSF adenosine deaminase (ADA) levels diagnostically helpful. ADA levels more highly elevated in TB than in ABM, listeria ABM or neurobrucellosis.
Pitfalls: CSF may have PMN predominance early, before developing typical lymphocytic predominance. Eosinophils in CSF is not a feature of TB, and should suggest another diagnosis. Chest x-ray, PPD, and CSF smear/culture may be negative.

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Therapeutic Considerations: Dexamethasone 4 mg (IV or PO) q6h × 4–8 weeks is useful to reduce CSF inflammation if given early. Proteinaceous TB exudates may obstruct ventricles and cause hydrocephalus, which is diagnosed by CT/MRI and may require shunting.
Prognosis: Poor prognostic factors include delay in treatment, neurologic deficits, or hydrocephalus.

Fungal (Cryptococcal) Meningitis (Cryptococcus neoformans)
Clinical Presentation: Insidious onset of nonspecific symptoms. Headache most common. Chronic cases may have CNS symptoms for weeks to months with intervening asymptomatic periods. Acute manifestations are more common in AIDS, chronic steroid therapy, lymphoreticular malignancies. 50–80% of patients are abnormal hosts.
Diagnostic Considerations: C. neoformans is the most common cause of fungal meningitis, and the only encapsulated yeast in the CSF to cause meningitis. Diagnosis by CSF India ink preparations showing encapsulated yeasts/cryptococcal latex antigen by latex agglutination/culture. Consider HIV.
Pitfalls: False + crytococcal antigen may occur with BBL Port-A-Cul transport vials. CSF latex antigen titer may not return to zero. Continue treatment until titers decline/do not decrease further, and until CSF culture is negative for cryptococci. India ink preparations showing encapsulated yeasts of CSF are useful for initial infection, but should not be relied on to diagnose recurrent episodes, since smears may be positive despite negative CSF cultures (dead cryptococci may remain in CSF for years). Diagnosis of recurrences rests on CSF culture.
Therapeutic Considerations: Treat until CSF is sterile or CSF latex antigen titer is zero or remains near zero on serial lumbar punctures. After patient defervesces on amphotericin B/5FC, switch to oral fluconazole × 10 weeks. Lipid amphotericin may be used if amphotericin B cannot be tolerated. HIV patients require life-long suppressive therapy with fluconazole 200 mg (PO) q24h.
Prognosis: Good. Poor prognostic factors include no CSF pleocytosis, many organisms in CSF, and altered consciousness on admission.

Encephalitis

Subset	Usual Pathogens	IV-to-PO Switch
Herpes simplex	HSV-1 HSV-2	IV Therapy: Acyclovir 10 mg/kg (IV) q8h × 10 days* **or** Ganciclovir 5 mg/kg (IV) q12h × 10 days.* PO Therapy: Valacyclovir 1 gm (PO) q8h × 10 days*
Herpes zoster (VZV)	VZV	IV Therapy: Acyclovir (IV) q8h 10 mg/kg × 10 days.* PO Therapy: Valacyclovir 2 gm (PO) q6h × 10 days*

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Encephalitis *(cont'd)*

Subset	Usual Pathogens	IV-to-PO Switch	
	HHV-6	Ganciclovir 5 mg/kg (IV) q12h × 2 weeks **or** Foscarnet 90 mg/kg (IV) q12h × 2 weeks	
Arboviral	Mosquito borne: California encephalitis (CE), La Crosse encephalitis (LE) Western equine encephalitis (WEE), Venezuelan equine encephalitis (VEE), Eastern equine encephalitis (EEE), St. Louis encephalitis (St. LE), Japanese encephalitis (JE), Jamestown canyon virus (JCV), Nipah virus, West Nile encephalitis (WNE) dengue, chikungunya, zika virus Tick borne: Powassan (POWV), TBE (RSSE/CCE) IV/PO Therapy: None		
Mycoplasma	M. pneumoniae	Doxycycline 200 mg (IV) q12h **or** Azithromycin 500 mg (IV) × 1, then 250 mg (IV) q24h × 2 weeks	Doxycycline 200 mg (PO) q12h **or** Azithromycin 500 mg (PO) × 1, then 250 mg (PO) q24h × 2 weeks
Rickettsial	R. rickettsii (RMSF) Candidatus Rickettsia tarasevichiae (CRT)	Doxycycline 200 mg (IV) q12h × 3 days, then 100 mg (IV) q12h × 2 weeks	Doxycycline 200 mg (PO) q12h × 3 days, then 100 mg (PO) q12h × 2 weeks
Listeria	L. monocytogenes	Treat as for Listeria meningitis (see p. 18) but treat for ~6 weeks	
HIV	see Chapter 5		
Transplants, HIV	CMV HHV-6 Toxoplasma	Transplants (see p. 174), HIV (see Chapter 5)	

* Severe HSV encephalitis may require a longer duration of therapy, i.e., 14-21 days.

Herpes Encephalitis (HSV-1)

Clinical Presentation: Acute onset of fever and change in mental status without nuchal rigidity. Natalizumab (NTZ) predisposes to HSV meningitis, meningoencephalitis, or encephalitis.

Diagnostic Considerations: EEG is best early (< 72 hours) presumptive test, showing unilateral temporal lobe abnormalities. Brain MRI is abnormal before CT scan, which may require several days before a temporal lobe focus is seen. Definitive diagnosis is by CSF PCR for HSV-1 DNA. Usually presents as encephalitis or meningoencephalitis; RBCs in CSF ~ CNS damage early/mild HSE may have no RBCs in CSF. CSF may have PMN predominance and low glucose levels, unlike other viral causes of meningitis.

Pitfalls: HSV-2 HSE rare in young adults; HSV-2 aseptic menigitis common. HSV-2 HSE occurs in the elderly/immunosuppresed. In normal hosts, HHV-6 may mimic HSV-1 encephalitis with a frontal/temporal focus on EEG.

Therapeutic Considerations: HSV is treatable. Treat as soon as possible, since neurological deficits may be mild and reversible early on, but severe and irreversible later.

Prognosis: Related to extent of brain injury and early anti-HSV therapy.

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Rickettsial Encephalitis

Clinical Presentation: RMSF: Acute onset of fever (with relative bradycardia), headache, change/decrease in mental status days after tick bite. RMSF suggested by wrist/ankle MP rash that later becomes petechial with periorbital edema with edema of the dorsum of hands/feet, normal WBC count with thrombocytopenia encephalitis. Candidatus Rickettsia tarasevichiae (CRT): Presents with a flu-like illness in China. Fever/chills, malaise, myalgias, dry cough. CNS symptoms include headache, dizziness, mental confusion. N/V/D common generalized adenopathy common; rash rare. Eschar in some, bleeding in some hemoptysis, hematuria, epistaxis, petechiae/ecchymoses. ↑ LDH, CPK, AST/ALT. Leukopenia, relative lymphopenia, thrombocytopenia. Many (2/3) co-infected with SFTS (severe fever with thrombocytopenia syndrome).
Diagnostic Considerations: RMSF: Diagnosis by specific serology. CRT: PCR.
Pitfalls: Usually occurs in summer/fall. Easily confused with enteroviral exauthems.
Therapeutic Considerations: Doxycycline should be started immediately before dx test results reported.
Prognosis: Good if treated early.

Mycoplasma Encephalitis

Clinical Presentation: Acute onset of fever and change in mental status without nuchal rigidity.
Diagnostic Considerations: Diagnosis suggested by CAP with sore throat, otitis, E. multiforme, soft stools/diarrhea, with elevated IgM mycoplasma titers, and very high (≥ 1:512) cold agglutinin titers. CSF shows mild mononucleosis/pleocytosis and normal/low glucose.
Pitfalls: CNS findings may overshadow pulmonary findings.
Therapeutic Considerations: Among macrolides, only azithromycin effective in encephalitis. Doxycycline rapidly ↓ mycoplasma shedding in oropharyngeal secretions (vs. prolonged shedding with macrolides). "High dose" doxycycline more effective than with usual doses.
Prognosis: With early treatment, prognosis is good without neurologic sequelae.

Listeria Encephalitis

Clinical Presentation: Fever/mental confusion (encephalitis/cerebritis) ± nuchal rigidity (meningoencephalitis).
Diagnostic Considerations: Diagnosis by LP. Suspect Listeria if CSF with "purulent profile" plus RBCs. Listeria seen on CSF Gram stain in 50%; but CSF cultures positive in 100%.
Pitfalls: Not to be confused with other Gram-positive bacilli (GPB) isolated from CSF (diphtheroids). Listeria are motile and hemolytic on blood agar vs. other GPB from the skin.
Therapeutic Considerations: 3rd generation cephalosporins not active against Listeria. In penicillin-tolerant patients, use (meningeal dosed) ampicillin. TMP-SMX, meropenem, or linezolid are alternatives in penicillin allergic patients.
Prognosis: Good with early/adequate treatment. Related to degree of T-lymphocyte dysfunction.

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CMV Encephalitis (see Chapter 5)

Toxoplasma Encephalitis (see Chapter 5)

Brain Abscess/Subdural Empyema/Cavernous Vein Thrombosis/Intracranial Suppurative Thrombophlebitis

Subset	Usual Pathogens	Preferred IV Therapy	Alternate IV Therapy	IV-to-PO Switch
Brain Abscess (Single Mass Lesion)				
Open trauma	S. aureus (MSSA) GNB P. aeruginosa	Meropenem 2 gm (IV) q8h × 2 weeks **or** Cefepime 2 gm (IV) q8h × 2 weeks		Not applicable
Neurosurgical procedures	S. aureus S. epidermidis (CoNS)	MSSA Nafcillin 2 gm (IV) q4h × 2 weeks **or** MRSA/MSSE/MRSE Linezolid 600 mg (IV) q12h × 2 weeks **or** Minocycline 200 mg (IV) × 1, then 100 mg (IV) q12h × 2 weeks		MSSA/MRSA/MSSE/MRSE Linezolid 600 mg (PO) q12h × 2 weeks **or** Minocycline 200 mg (PO) × 1, then 100 mg (PO) q12h × 2 weeks
Mastoid/otitic source	Enterobacter Proteus	Treat the same as for open trauma (see above)		
Dental source	Oral anaerobes Actinomyces	Ceftriaxone 2 gm (IV) q12h × 2 weeks		Doxycycline 200 mg (PO) q12h × 3 days, then 100 mg (PO) q12h × 2 weeks
Subdural empyema/ sinus source	Oral anaerobes H. influenzae	Treat the same as for dental source (see above)		
Cardiac source (ABE; right-to-left shunt)	S. aureus (MSSA) S. pneumoniae H. influenzae	Ceftriaxone 2 gm (IV) q12h × 2 weeks **or** Meropenem 2 gm (IV) q8h × 2 weeks		
	S. aureus (MRSA)	Linezolid 600 mg (IV) q12h × 2 weeks **or** Minocycline 200 mg (IV) × 1, then 100 mg (IV) q12h × 2 weeks		Minocycline 200 mg (PO) × 1, then 100 mg (PO) q12h × 2 weeks
Pulmonary source	Oral anaerobes Actinomyces	Ceftriaxone 2 gm (IV) q12h × 2 weeks		Ceftizoxime 3 gm (IV) q6h × 2 weeks
Bacteremic source	Listeria monocytogenes	TMP–SMX 5 mg/kg (IV) q6h × 6 weeks **or** Meropenem 2 gm (IV) q8h × 6 weeks **or** Linezolid 600 mg (IV) q12h × 6 weeks		TMP–SMX 5 mg/kg (PO) q6h × 6 weeks **or** Linezolid 600 mg (PO) q12h × 6 weeks

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