

Encephalitis

Subset	Usual Pathogens	IV-to-PO Switch	
Herpes	HSV-1	Acyclovir 10 mg/kg (IV) q8h x 7 days, then if able to take oral medications, complete 14-21 days of total therapy with acyclovir 400 mg (PO) 5x/day or valacyclovir 1 gm (PO) q8h or famciclovir 500 mg (PO) q8h	
Arbovirus	<p><u>Usual Pathogens</u> California encephalitis (CE), Western equine encephalitis (WEE), Venezuelan equine encephalitis (VEE), Eastern equine encephalitis (EEE), St. Louis encephalitis (SLE), Japanese encephalitis (JE), West Nile encephalitis (WNE)</p> <p><u>IV/PO Therapy</u> Not applicable</p>		
Mycoplasma	M. pneumoniae	<p><u>Preferred IV Therapy</u> Doxycycline 200 mg (IV) q12h x 3 days, then 100 mg (IV) q12h x 2-4 weeks</p> <p><u>Alternate IV Therapy</u> Minocycline 100 mg (IV) q12h x 2-4 weeks</p> <p><u>IV-to-PO Switch</u> Doxycycline 200 mg (PO) q12h x 3 days, then 100 mg (PO) q12h x 2-4 weeks*</p> <p style="text-align: center;">or</p> <p>Minocycline 100 mg (PO) q12h x 2-4 weeks</p>	
Solid organ transplants, HIV/AIDS	Toxoplasma gondii	<p><u>Preferred Therapy</u> Sulfadiazine 1.5-2 gm (PO) q6h + pyrimethamine 200 mg (PO) x 1 dose then 50 mg (PO) q6h + folinic acid 10 mg (PO) q24h x 6-8 weeks until good clinical response. Follow with life-long suppressive therapy** with sulfadiazine 1 gm (PO) q12h + pyrimethamine 50 mg (PO) q24h + folinic acid 10 mg (PO) q24h</p>	<p><u>Alternate Therapy</u> Clindamycin 600 mg (IV or PO) q6h + pyrimethamine 200 mg (PO) x 1 dose then 50 mg (PO) q6h + folinic acid 10 mg (PO) q24h x 6-8 weeks until good clinical response. Follow with life-long suppressive therapy** with sulfadiazine 1 gm (PO) q12h + pyrimethamine 50 mg (PO) q24h + folinic acid 10 mg (PO) q24h</p>
	CMV	<p><u>Preferred Therapy</u> Ganciclovir 5 mg/kg (IV) q12h x 3 weeks, followed by valganciclovir 900 mg (PO) q24h indefinitely†. For severe cases, consider ganciclovir + foscarnet</p>	<p><u>Alternate Therapy</u> Foscarnet 60 mg/kg (IV) q8h or 90 mg/kg (IV) q12h x 3 weeks ± ganciclovir 5 mg/kg (IV) q12h x 3 weeks. Follow with valganciclovir 900 mg (PO) q24h indefinitely†</p>

Duration of therapy represents total time IV or IV + PO. Most patients on IV therapy able to take PO meds should be switched to PO therapy after clinical improvement

* Loading dose is not needed PO if given IV with the same drug

* Consider discontinuation of therapy if CD₄ > 200 for ≥ 6 months in response to antiretroviral therapy

† Consider discontinuation of therapy if CD₄ > 100-150 for ≥ 6 months in response to antiretroviral therapy

Herpes Encephalitis (HSV-1)

Clinical Presentation: Acute onset of fever and change in mental status without nuchal rigidity

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; presentation as meningitis alone is uncommon. Profound decrease in sensorium is characteristic of HSV meningoencephalitis. CSF may have PMN predominance and low glucose levels, unlike other viral causes of meningitis

Pitfalls: Rule out non-infectious causes of encephalopathy

Therapeutic Considerations: HSV is the only treatable common cause of viral encephalitis in normal hosts. 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 antiviral therapy

Arboviral Encephalitis

Clinical Presentation: Acute onset of fever, headache, change in mental status days to weeks after inoculation of virus through the bite of an infected insect (e.g., mosquito/tick). May progress over several days to stupor/coma

Diagnostic Considerations: Diagnosis by specific arboviral serology

Pitfalls: Usually occurs in summer/fall. Diagnosis suggested by arboviral contact/travel history. Electrolyte abnormalities due to syndrome of inappropriate antidiuretic hormone (SIADH) may occur

Therapeutic Considerations: Only supportive therapy is available at present

Prognosis: Permanent neurological deficits are common, but not predictable. May be fatal

Mycoplasma Encephalitis

Clinical Presentation: Acute onset of fever and change in mental status without nuchal rigidity

Diagnostic Considerations: Diagnosis suggested by CNS and extra-pulmonary manifestations—sore throat, otitis, E. multiforme, soft stools/diarrhea—in a patient with community-acquired pneumonia, elevated IgM Mycoplasma titers, and very high ($\geq 1:1024$) cold agglutinin titers. CSF shows mild mononucleosis/pleocytosis and normal/low glucose

Pitfall: CNS findings may overshadow pulmonary findings

Therapeutic Considerations: Macrolides will treat pulmonary infection, but not CNS infection (due to poor CNS penetration)

Prognosis: With early treatment, prognosis is good without neurologic sequelae

Toxoplasma Encephalitis (T. gondii)

Clinical Presentation: Wide spectrum of neurologic symptoms, including sensorimotor deficits, seizures, confusion, ataxia. Fever/headache are common

Diagnostic Considerations: Diagnosis by characteristic radiographic appearance and response to empiric therapy in a Toxoplasma seropositive patient

Pitfalls: Use folinic acid 10 mg (PO) daily with pyrimethamine-containing regimens, not folate. Radiographic improvement may lag behind clinical response

Therapeutic Considerations: Alternate agents include atovaquone, azithromycin, clarithromycin, minocycline (all with pyrimethamine if possible). Decadron 4 mg (PO or IV) q6h is useful for edema/mass effect

Prognosis: Usually responds to treatment if able to tolerate drugs. Clinical response is evident by 1 week in 70%, by 2 weeks in 90%. Radiographic improvement is usually apparent by 2 weeks. Neurologic recovery is variable

CMV Encephalitis

Clinical Presentation: Fever, mental status changes, and headache evolving over 1-2 weeks. True meningismus is rare. CMV encephalitis occurs in advanced HIV disease ($CD_4 < 50/mm^3$), often in patients with prior CMV retinitis

Diagnostic Considerations: CSF may show lymphocytic or neutrophilic pleocytosis; glucose is often decreased. Characteristic findings on brain MRI include confluent periventricular abnormalities with variable degrees of enhancement. Diagnosis is confirmed by CSF CMV PCR (preferred), CMV culture, or brain biopsy

Pitfalls: A wide spectrum of radiographic findings are possible, including mass lesions (rare). Obtain ophthalmologic evaluation to exclude active retinitis

Therapeutic Considerations: Ganciclovir plus foscarnet may be beneficial as initial therapy for severe cases. Consider discontinuation of valganciclovir maintenance therapy if CD_4 increases to $> 100-150/mm^3$ x 6 months or longer in response to antiretroviral therapy

Prognosis: Unless immune reconstitution occurs, response to therapy is usually transient, followed by progression of symptoms

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 Entero-bacteriaceae P. aeruginosa	Cefepime 2 gm (IV) q8h x 2 weeks	Meropenem 2 gm (IV) q8h x 2 weeks	Not applicable
Neurosurgical procedure (Treat initially for MSSA; if later identified as MRSA, MSSE or MRSE, treat accordingly)	S. aureus S. epidermidis	<u>MSSA/MSSE</u> Nafcillin 2 gm (IV) q4h x 2 weeks or Ceftizoxime 3 gm (IV) q6h x 2 weeks or Cefepime 2 gm (IV) q8h x 2 weeks <u>MRSA/MRSE</u> Linezolid 600 mg (IV) q12h x 2 weeks		<u>MSSA/MRSA</u> Linezolid 600 mg (PO) q12h x 2 weeks
Mastoid/otitic source	Enterobacter Proteus	Cefepime 2 gm (IV) q8h x 2 weeks	Meropenem 2 gm (IV) q8h x 2 weeks	Not applicable
Dental source	Oral anaerobes Actinomyces	Ceftizoxime 3 gm (IV) q6h x 2 weeks	Ceftriaxone 2 gm (IV) q12h x 2 weeks plus Metronidazole 1 gm (IV) q24h x 2 weeks	Not applicable

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

Subset	Usual Pathogens	Preferred IV Therapy	Alternate IV Therapy	IV-to-PO Switch
Subdural empyema/sinus source	Oral anaerobes H. influenzae	Ceftizoxime 3 gm (IV) q6h x 2 weeks	Ceftriaxone 2 gm (IV) q12h x 2 weeks plus Metronidazole 1 gm (IV) q24h x 2 weeks	Not applicable
Brain Abscess (Multiple Mass Lesions)				
Cardiac source (ABE; right-to-left shunt)	S. aureus S. pneumoniae H. influenzae	Cefepime 2 gm (IV) q8h x 2 weeks	Cefotaxime 3 gm (IV) q6h x 2 weeks or Meropenem 1 gm (IV) q8h x 2 weeks	Not applicable
Pulmonary source	Oral anaerobes Actinomyces	Ceftizoxime 3 gm (IV) q6h x 2 weeks	Ceftriaxone 2 gm (IV) q12h x 2 weeks plus Metronidazole 1 gm (IV) q24h x 2 weeks	Not applicable

MSSA/MRSA = methicillin-sensitive/resistant S. aureus; MSSE/MRSE = methicillin-sensitive/resistant S. epidermidis. Duration of therapy represents total time IV or IV + PO. Most patients on IV therapy able to take PO meds should be switched to PO therapy after clinical improvement

Clinical Presentation: Variable presentation, with fever, change in mental status, cranial nerve abnormalities ± headache

Diagnostic Considerations: Diagnosis by CSF gram stain/culture. If brain abscess is suspected, obtain head CT/MRI. Lumbar puncture may induce herniation

Pitfalls: CSF analysis is negative for bacterial meningitis unless abscess ruptures into ventricular system

Therapeutic Considerations: Treatment with meningeal doses of antibiotics is required. Large single abscesses may be surgically drained; multiple small abscesses are best treated medically

Prognosis: Related to underlying source and health of host

Brain Abscess (Mastoid/Otitic Source)

Diagnostic Considerations: Diagnosis by head CT/MRI demonstrating focus of infection in mastoid

Pitfalls: Rule out associated subdural empyema

Therapeutic Considerations: ENT consult for possible surgical debridement of mastoid

Prognosis: Good. May require mastoid debridement for cure

Brain Abscess (Dental Source)

Diagnostic Considerations: Diagnosis by panorex x-rays/gallium scan of jaw demonstrating focus in mandible/erosion into sinuses

Pitfalls: Apical root abscess may not be apparent clinically

Therapeutic Considerations: Large single abscess may be surgically drained. Multiple small abscesses are best treated medically. Treat until lesions on CT/MRI resolve or do not become smaller on therapy

Prognosis: Good if dental focus is removed

Brain Abscess (Subdural Empyema/Sinus Source)

Diagnostic Considerations: Diagnosis by sinus films/CT/MRI to confirm presence of sinusitis/bone erosion (cranial osteomyelitis/epidural abscess). Usually from paranasal sinusitis

Pitfalls: Do not overlook underlying sinus infection, which may need surgical drainage

Therapeutic Considerations: Obtain ENT consult for possible surgical debridement of sinuses

Prognosis: Good prognosis if sinus is drained

Brain Abscess (Cardiac Source; Acute Bacterial Endocarditis)

Diagnostic Considerations: Diagnosis by blood cultures positive for acute bacterial endocarditis (ABE) pathogen and multiple brain lesions on head CT/MRI

Pitfalls: Do not overlook right-to-left cardiac shunt (e.g., patent foramen ovale, atrial septal defect) as source of brain abscess. Cerebral embolization results in aseptic meningitis in SBE, but septic meningitis/brain abscess in ABE (due to high virulence of pathogens)

Therapeutic Considerations: Multiple lesions suggest hematogenous spread. Use sensitivity of blood culture isolates to determine coverage. Meningeal doses are the same as endocarditis doses

Prognosis: Related to location/size of CNS lesions and extent of cardiac valvular involvement

Brain Abscess (Pulmonary Source)

Diagnostic Considerations: Diagnosis suggested by underlying bronchiectasis, empyema, cystic fibrosis, or lung abscess in a patient with a brain abscess

Pitfalls: Brain abscesses are associated with chronic suppurative lung disease (e.g., bronchiectasis, lung abscess/empyema), not chronic bronchitis

Therapeutic Considerations: Lung abscess may need surgical drainage

Prognosis: Related to extent/location of CNS lesions, drainage of lung abscess/empyema, and control of lung infection