

Central Nervous System Infections

Meningitis

Treatment

- **Bacterial meningitis is a MEDICAL EMERGENCY. ANTIBIOTICS SHOULD BE STARTED AS SOON AS THE POSSIBILITY OF BACTERIAL MENINGITIS BECOMES EVIDENT, IDEALLY WITHIN 30 MINUTES.**
- **DO NOT WAIT FOR CT SCAN OR LP RESULTS TO START ANTIBIOTICS. IF LP MUST BE DELAYED, GET BLOOD CULTURES AND START THERAPY.**
- Adjust therapy once pathogen and susceptibilities are known.
- Consider penicillin desensitization for pathogen-specific therapy in patients with severe allergies (see section on approach to patient with penicillin allergy).
- **Antibiotic doses are higher for CNS infections, see dosing table below.**
- Infectious Diseases consultation is recommended for all CNS infections, particularly those in which the preferred antibiotic cannot be used or in which the organism is resistant to usual therapy.
- Practice guidelines are available through the IDSA at:
http://www.idsociety.org/IDSA_Practice_Guidelines/

Empiric Therapy

Host	Pathogens	Preferred Abx (see dosing table)	Alternative for serious PCN allergy, i.e. anaphylaxis (ID consult advised)
Immunocompetent, age < 50*	<i>S. pneumo</i> , <i>N meningitidis</i> , <i>H influenza</i>	Vancomycin PLUS Ceftriaxone	Vancomycin PLUS Meropenem
Immunocompetent, age > 50*	<i>S. pneumo</i> , <i>Listeria</i> , <i>H. influenzae</i> , <i>N. meningitidis</i> , Group B streptococci	Vancomycin PLUS Ceftriaxone PLUS Ampicillin	Vancomycin PLUS Meropenem PLUS TMP/SMX
Immunocompromised*	<i>S. pneumo</i> , <i>N. meningitidis</i> , <i>H. influenzae</i> , <i>Listeria</i> , (Gram-negative rods)	Vancomycin PLUS Cefepime PLUS Ampicillin	Vancomycin PLUS TMP/SMX PLUS Meropenem
Post-neurosurgery or penetrating head trauma	<i>S. pneumo</i> (if CSF leak), <i>H. influenzae</i> , Staphylococci (MRSA, CoNS), Gram-negatives	Vancomycin PLUS EITHER Cefepime OR Meropenem	Vancomycin PLUS Meropenem
Infected Shunt	<i>S. aureus</i> , CoNS, <i>P. acnes</i> , gram-negatives (rare)	Vancomycin PLUS Cefepime	Vancomycin PLUS Meropenem

Immunocompromised is defined as HIV or AIDS, receipt of immunosuppressive therapy, or after transplantation. In patients with HIV infection, non-bacterial causes of meningitis must be considered, particularly cryptococcal meningitis.

*Use of Dexamethasone

- Addition of dexamethasone is recommended in all adult patients with suspected pneumococcal meningitis (most community-acquired adult patients)
- Dose: 0.15 mg/kg IV q6h for 2-4 days
- The first dose must be administered 10-20 minutes before or concomitant with the first dose of antibiotics.
- Administration of antibiotics should not be delayed to give dexamethasone.
- Dexamethasone should not be given to patients who have already started antibiotics.
- Continue dexamethasone only if the CSF gram stain shows Gram-positive diplococci or if blood or CSF grows *S. pneumoniae*.
- Consider adding rifampin for suspected *S. pneumoniae*, pending susceptibilities, if dexamethasone is used. If *S. pneumoniae* is beta-lactam susceptible, rifampin may be discontinued.

Pathogen-Specific Therapy

Pathogens	Preferred	Alternatives for serious PCN allergy (ID consult advised)
<i>S. pneumo</i> PCN MIC \leq 0.06 AND/OR Ceftriaxone MIC < 0.5	Penicillin OR Ceftriaxone	Vancomycin OR Linezolid, consider PCN desensitization
<i>S. pneumo</i> PCN MIC >0.1 - 1 AND Ceftriaxone MIC < 1 (ID consult advised)	Ceftriaxone	Linezolid
<i>S. pneumo</i> PCN MIC >1 AND/OR Ceftriaxone MIC \geq 1 (ID consult advised)	Ceftriaxone PLUS Vancomycin PLUS Rifampin	Linezolid
<i>N. meningitidis</i> PCN susceptible (MIC < 0.1)	Penicillin* OR Ceftriaxone	Ciprofloxacin OR Meropenem, consider PCN desensitization
<i>H. influenzae</i> Non-beta lactamase producer	Ampicillin OR Ceftriaxone	Meropenem OR Ciprofloxacin, consider PCN desensitization
<i>H. influenzae</i> Beta-lactamase producer	Ceftriaxone	Meropenem OR Ciprofloxacin, consider PCN desensitization
<i>Listeria</i>	Ampicillin \pm Gentamicin	TMP/SMX
<i>P. aeruginosa</i> (ID consult advised)	Cefepime OR Meropenem	Any 2 of the following: Ciprofloxacin, Gentamicin, Aztreonam
<i>E. coli</i> and other Enterobacteriaceae	Ceftriaxone \pm Ciprofloxacin OR Meropenem	Aztreonam OR Ciprofloxacin OR TMP/SMX

<i>S. aureus</i> - methicillin-susceptible (MSSA)	Oxacillin	Vancomycin
<i>S. aureus</i> - methicillin-resistant (MRSA)	Vancomycin OR Linezolid	
Coagulase-negative staphylococci if oxacillin MIC ≤ 0.25	Oxacillin	Vancomycin
Coagulase-negative staphylococci if oxacillin MIC > 0.25	Vancomycin OR Linezolid	
<i>Enterococcus</i>	Ampicillin OR Vancomycin PLUS Gentamicin	Vancomycin PLUS Gentamicin, Linezolid

*Must give Ciprofloxacin 500 mg once to eradicate carrier state if PCN used as treatment

Recommended Doses of Select Antimicrobial Agents for Treatment of Meningitis in Adults with Normal Renal and Hepatic Function

Antimicrobial Agent	Dose
Ampicillin	2 g q4h
Aztreonam	2 g q6h
Cefepime	2 g q8h
Ceftriaxone	2 g q12h
Ciprofloxacin	400 mg q8h
Meropenem	2 g q8h
Metronidazole	500 mg q6h
Oxacillin	2g q4h
Penicillin G	20-24 million units per day as continuous infusion
Rifampin	600 mg q24h
TMP/SMX	15-20 mg/kg/24h divided q6-12h
Vancomycin	Load with 25-35 mg/kg, then 15-20 mg/kg q8-12h (goal trough 15-20 mcg/mL)

TREATMENT NOTES

Indications for head CT prior to LP (do **NOT** delay initiation of antimicrobial therapy for CT)

- History of CNS diseases (mass lesions, CVA)
- New-onset seizure (≤ 1 week)
- Papilledema
- Altered consciousness
- Focal neurologic deficit

Duration

- STOP treatment if LP culture obtained prior to antibiotic therapy is negative at 48 hours
OR no PMNs on cell count
- *S. pneumoniae*: 10-14 days
- *N. meningitidis*: 7 days
- *Listeria*: 21 days
- *H. influenzae*: 7 days
- Gram-negative bacilli: 21 days

Adjunctive therapy

- Consider intracranial pressure monitoring in patients with impaired mental status.

Encephalitis

- Herpes viruses (HSV, VZV) remain the predominant cause of treatable encephalitis.
- CSF PCRs are rapid diagnostic tests and appear quite sensitive and specific.
- Have a low threshold to treat if suspected, as untreated mortality exceeds 70%
- **Treatment: Acyclovir 10 mg/kg IV q8h for 14-21 days**

Brain Abscess

- Empiric treatment is guided by suspected source and underlying condition.
- **While therapy should be adjusted based on culture results, anaerobic coverage should ALWAYS continue even if none are grown.**

Source/Condition	Pathogens	Preferred (see dosing section above)	Alternative for serious PCN allergy (Infectious Disease consult advised)
Unknown	<i>S. aureus</i> , Streptococci, Gram-negatives, Anaerobes	Vancomycin PLUS Ceftriaxone PLUS Metronidazole	Vancomycin PLUS Ciprofloxacin PLUS Metronidazole
Sinusitis	Streptococci (including <i>S. pneumoniae</i>), Anaerobes	[Penicillin OR Ceftriaxone] PLUS Metronidazole	Vancomycin PLUS Metronidazole
Chronic Otitis / Mastoiditis	Gram-negatives, Streptococci, Anaerobes	Cefepime PLUS Metronidazole	Vancomycin PLUS Aztreonam PLUS Metronidazole
Post-neurosurgery	Staphylococci, Gram-negatives	Vancomycin PLUS Cefepime	Vancomycin PLUS Ciprofloxacin
Cyanotic heart disease	Streptococci (esp. <i>S. viridans</i>)	Penicillin OR Ceftriaxone	Vancomycin

CNS Shunt Infection

Diagnosis

- Culture of cerebrospinal fluid remains the mainstay of diagnosis. Clinical symptoms may be mild and/or non-specific, and CSF chemistries and WBC counts may be normal.

Empiric Therapy (see dosing section for CSF dosing)

- Vancomycin **PLUS** Cefepime
- OR**
- PCN Allergy: Vancomycin **PLUS** Ciprofloxacin

TREATMENT NOTES

- **Infectious Diseases consult recommended for assistance with timing of shunt replacement and duration of therapy.**
- Removal of all components of the infected shunt with external ventricular drainage or intermittent ventricular taps in combination with the appropriate intravenous antibiotic therapy leads to the highest effective cure rates. Success rates are substantially lower when the infected shunt components are not removed.
- Intraventricular antibiotics are occasionally used, particularly when there has been no improvement after 48 hours, for refractory cases, or cases in which shunt removal is not possible. Intraventricular injection should be administered only by experienced practitioners, such as the Neurocritical care service.

REFERENCES

IDSA Guidelines for the Management of Bacterial Meningitis: Clin Infect Dis 2004;39:1267.

Dexamethasone in adults with bacterial meningitis: N Eng J Med 2002;347:1549.

Therapy in cerebrospinal fluid shunt infection. Neurosurgery 1980;7:459.