# 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. 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* | *S. pneumo, N meningiditis, H influenzae* | Vancomycin **PLUS** Ceftriaxone | Vancomycin **PLUS** Meropenem |
| Immunocompetent, age > 50* | *S. pneumo, Listeria, H. influenzae, N. meningiditis,* Group B streptococci | Vancomycin **PLUS** Ceftriaxone **PLUS** Ampicillin | Vancomycin **PLUS** Meropenem **PLUS** TMP/SMX |
| Immunocompromised* | *S. pneumo, N. meningiditis, H. influenzae, Listeria, (*gram-negatives) | Vancomycin **PLUS** Cefepime **PLUS** Ampicillin | Vancomycin **PLUS** TMP/SMX **PLUS** Meropenem |
| Post-neurosurgery or | *S. pneumo* (if CSF | Vancomycin **PLUS** | Vancomycin **PLUS** |

| | | | |
|---|---|---|---|
| penetrating head trauma | leak), *H. influenzae,* Staphylococci (MRSA, CoNS), Gram-negatives | **EITHER** Cefepime **OR** Meropenem | Meropenem |
| Infected Shunt | *S. aureus*, CoNS, *P. acnes*, 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)** |
|---|---|---|
| *S. pneumo* PCN MIC ≤ 0.06 **AND/OR** Ceftriaxone MIC < 0.5 | Penicillin **OR** Ceftriaxone | Vancomycin **OR** Linezolid, consider PCN desensitization |
| *S. pneumo* PCN MIC >0.1 - 1 **AND** Ceftriaxone MIC < 1 (ID consult advised) | Ceftriaxone | Linezolid |
| *S. pneumo* PCN MIC >1 **AND/OR** Ceftriaxone MIC ≥ 1 (ID consult advised) | Ceftriaxone **PLUS** Vancomycin **PLUS** Rifampin | Linezolid |
| *N. meningitidis* PCN | Penicillin* **OR** Ceftriaxone | Ciprofloxacin **OR** |

| | | |
|---|---|---|
| susceptible (MIC < 0.1) | | Meropenem, consider PCN desensitization |
| *H. influenzae*<br>Non-beta lactamase producer | Ampicillin **OR** Ceftriaxone | Meropenem **OR** Ciprofloxacin, consider PCN desensitization |
| *H. influenzae*<br>Beta-lactamase producer | Ceftriaxone | Meropenem **OR** Ciprofloxacin, consider PCN desensitization |
| *Listeria* | Ampicillin ± Gentamicin | TMP/SMX |
| *P. aeruginosa* (ID consult advised) | Cefepime **OR** Meropenem | Any 2 of the following: Ciprofloxacin, Gentamicin, Aztreonam |
| *E. coli* and other Enterobacteriaceae | Ceftriaxone ± Ciprofloxacin **OR** Meropenem | Aztreonam **OR** Ciprofloxacin **OR** TMP/SMX |
| *S. aureus* - methicillin-susceptible (MSSA) | Oxacillin | Vancomycin |
| *S. aureus* - methicillin-resistant (MRSA) | Vancomycin **OR** Linezolid | |
| Coagulase-negative staphylococci if oxacillin MIC ≤ 0.25 | Oxacillin | Vancomycin |
| Coagulase-negative staphylcocci if oxacillin MIC > 0.25 | Vancomycin **OR** Linezolid | |
| *Enterococcus* | 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. meningiditis:* 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 threshhold 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 | *S. aureus,* Streptococci, Gram-negatives, Anaerobes | Vancomycin **PLUS** Ceftriaxone **PLUS** Metronidazole | Vancomycin **PLUS** Ciprofloxacin **PLUS** Metronidazole |
| Sinusitis | Streptococci (including *S. pneumoniae)*, 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. *S. viridans)* | 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.