CENTRAL NERVOUS SYSTEM INFECTIONS

Acute Bacterial Meningitis

Community-acquired Acute Bacterial Meningitis
• Acute bacterial meningitis is an inflammatory disease of the leptomeninges, the tissues surrounding the brain and spinal cord as proven by a positive bacterial CSF culture, PCR, gram stain or antigen test; or suspected by clinical characteristics and/or CSF markers of inflammation (an abnormal number of white blood cells, elevated protein and low glucose levels)
• In children, common signs and symptoms include fever, irritability, poor feeding, bulging fontanel and seizures. In neonates, signs and symptoms are subtler and may resemble neonatal sepsis. There is no single or combination of signs which are diagnostic of bacterial meningitis. If bacterial meningitis is suspected, CSF analysis and culture should be performed to confirm the diagnosis.
• In adults, the classic triad of acute bacterial meningitis consists of fever, nuchal rigidity, and a change in mental status.
• Once suspected and awaiting laboratory results, empiric therapy should be started right away to prevent complications and mortality.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Preferred regimen</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli, Streptococcus pneumoniae</em>, <em>Klebsiella</em>, <em>Enterobacter</em>, Group B Streptococcus (rare)</td>
<td><strong>P:</strong>&lt;br&gt;&lt; 2 months old&lt;br&gt;Ampicillin or Cefotaxime IV/IM using the following dose:</td>
<td>Adjust therapy based on culture. Early onset usually due to maternal transmission.</td>
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<tr>
<td></td>
<td>Age 0-7 days</td>
<td>May use Ceftriaxone if Cefotaxime is not available and the neonate is not jaundiced.</td>
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<tr>
<td></td>
<td>Age &gt;7 days</td>
<td>Repeat lumbar tap in the neonate is necessary to verify sterilization of the CSF in gram-negative meningitis. Duration of therapy is dependent on the etiology of bacterial meningitis.</td>
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<tr>
<td></td>
<td>Body weight &lt;2 kg 50 mg/kg q12h</td>
<td>50 mg/kg q8h</td>
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<tr>
<td></td>
<td>Body weight at least 2 kg 50 mg/kg q8h</td>
<td>50 mg/kg q6h</td>
</tr>
<tr>
<td>S. pneumoniae, Haemophilus influenzae Neisseria meningitidis (less common)</td>
<td>PLUS</td>
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<tr>
<td><strong>Amikacin</strong></td>
<td>15 mg/kg/d q24h IV/IM</td>
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<tr>
<td><strong>Gentamicin</strong></td>
<td>5mg/kg/d q24h IV/IM</td>
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</table>

>2 months to 5 yrs
**Ceftriaxone** 100 mg/kg/d IV q12-24h; max dose 4 g/d

OR
**Chloramphenicol** 100 mg/kg/d IV q8h Max dose: 4 g/d

Duration of Therapy (regardless of age):
* S. pneumoniae: 10-14 d
* H. influenzae B: 7-10 d
* N. meningitidis: 7 d
* Culture negative: 10-14 d

Dexamethasone has no role in neonatal meningitis.

Antibiotic therapy should be started immediately after lumbar puncture or, if this is delayed, after obtaining blood cultures.

Add vancomycin if penicillin- or cephalosporin-resistant *H. influenzae* is suspected.

Cefuroxime should not be used for the treatment of bacterial meningitis because of delayed sterilization and a greater incidence of hearing loss.

Dexamethasone is of proven value for children with *H. influenzae B* meningitis in children less than 5 years old at a dose of 0.15 mg/kg (max 10 mg) q6h x 4 d. It should be started along or shortly before the 1st antibiotic dose. The first dose should be administered within 4 hours of starting antibiotic. Do not start dexamethasone >12h after starting antibiotics.
<table>
<thead>
<tr>
<th>Disease Combination</th>
<th>Age Group</th>
<th>Antibiotic Treatment</th>
<th>Duration of Therapy (regardless of age)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. pneumoniae, N. meningitidis</td>
<td>&gt;5 yrs - 18 yrs</td>
<td><strong>Ceftriaxone</strong> 100 mg/kg/d IV q12h; max dose 4 g/d OR <strong>Chloramphenicol</strong> 100 mg/kg/d IV q8h; max dose 4 g/d</td>
<td><strong>S. pneumoniae:</strong> 10-14 d <strong>N. meningitidis:</strong> 7 d <strong>Culture negative:</strong> 10-14 d</td>
<td>Repeat lumbar puncture (LP) is recommended in patients with poor clinical response despite 36 hours of appropriate antibiotic treatment, or those with gram-negative meningitis. For <em>H. influenzae</em> and <em>S. pneumoniae</em> meningitis, if patient is improving, repeat LP is not necessary. Patients &lt;10 yrs with confirmed Hib meningitis should receive Rifampin prophylaxis to eradicate the carrier state. Recommended rifampicin dose for prophylaxis: <strong>&lt;3 yrs old:</strong> 10 mg/kg/d x 4 d <strong>&gt;3-10 yrs:</strong> 20 mg/kg/d x 4 d Max dose: 600 mg Patients with confirmed meningococcal meningitis and not treated with Ceftriaxone should receive either: <strong>Rifampicin</strong> 10 mg/kg/d x 2 d (max dose 600 mg) OR</td>
</tr>
<tr>
<td>S. pneumoniae, N. meningitidis, Listeria monocytogenes, aerobic Gram-negative bacilli</td>
<td>18 yrs - 50 yrs</td>
<td><strong>Ceftriaxone</strong> 2 g IV q12h</td>
<td><strong>S. pneumoniae:</strong> 10-14 d <strong>N. meningitidis:</strong> 7 d <strong>Culture negative:</strong> 10-14 d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;50 yrs</td>
<td><strong>Ampicillin</strong> 2 g IV q4h</td>
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</tbody>
</table>
**Central and Nervous System Infections**

**National Antibiotic Guidelines**

### Ceftriaxone 2g IV q12h

For severe penicillin allergy:

**Vancomycin 15-20 mg/kg IV q8-12h**

PLUS

### Aztreonam 2g IV q6-8h

OR

**Ciprofloxacin 400mg IV q12h**

Duration of Therapy (regardless of age):

- *S. pneumoniae*: 10-14 d
- *H. influenzae*: 7 d
- *N. meningitidis*: 7 d
- *L. monocytogenes*: 21 d
- Gram-negative enteric bacilli: 21 d
- Culture negative: 10-14 d

### Ceftriaxone: <15 yrs: 125 mg IM once >15 yrs: 250 mg IM once

OR

**Ciprofloxacin 500 mg PO once**

For household contacts:

**Hib meningitis**: give same regimen as for patient with *N. meningitidis*

For adults, dexamethasone should be started before or given with the first dose of antibiotics at 0.15 mg/kg q6h IV x 2-4 d.

### Staphylococcus aureus, Staphylococcus epidermidis, Gram-negative bacilli including *Pseudomonas aeruginosa*

Anatomic defects, neurosurgical complications and open head trauma

**P:**

**Vancomycin**

60 mg/kg/d IV/IM q6h

PLUS
Staphylococcus aureus, 
Staphylococcus epidermidis, 
Gram-negative bacilli including 
Pseudomonas aeruginosa

<table>
<thead>
<tr>
<th><strong>Ceftazidime</strong></th>
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<tbody>
<tr>
<td>2g/d q8h</td>
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<tr>
<td>Duration of treatment is 3-6 weeks</td>
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</table>

**Brain abscess**
- Brain abscess is a focal collection of pus within the brain parenchyma. The etiology may be trauma, direct spread of infection or hematogenous spread from a distant site of infection.
- Imaging studies such as CT scan and MRI are necessary for diagnosis although this cannot determine the etiology.
- Etiology and treatment depends on the source of infection.

<table>
<thead>
<tr>
<th><strong>Etiology</strong></th>
<th><strong>Preferred regimen</strong></th>
<th><strong>Comments</strong></th>
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</table>
| In the presence of dental infection: Streptococci (viridans and anaerobic), *Fusobacterium, Bacteroides* | P: 
**Penicillin G**
400,000 U/kg/d IV/IM q6h 
PLUS 
**Ceftriaxone**
100 mg/kg/d IV/IM q12h; max dose: 4 g/d 
OR 
Chloramphenicol 
100 mg/kg/d IV/IM q6h 
A: 
**Penicillin G**
4 Million U IV/IM q4h 
PLUS | Consult a neurosurgeon; aspiration of abscess is usually required if lesion is >2.5 cm |
In the presence of dental infection:
Streptococci (viridans and anaerobic), *Fusobacterium*, *Bacteroides*

<table>
<thead>
<tr>
<th>P: Penicillin G</th>
<th>400,000 U/kg/d IV/IM q6h</th>
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<tbody>
<tr>
<td>PLUS</td>
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<tr>
<td>Ceftriaxone</td>
<td>100 mg/kg/d IV/IM q12h; max dose: 4 g/d</td>
</tr>
<tr>
<td>OR</td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td></td>
<td>100 mg/kg/d IV/IM q6h</td>
</tr>
<tr>
<td>A: Penicillin G</td>
<td>4 Million U IV/IM q4h</td>
</tr>
<tr>
<td>PLUS</td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>2 g IV q12h</td>
</tr>
<tr>
<td>OR</td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td></td>
<td>1 g IV/IM q6h</td>
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Duration of treatment is unclear, usually 6-8 weeks.

Consult a neurosurgeon; aspiration of abscess is usually required if lesion is >2.5 cm.

In the presence of chronic otitis media, sinusitis, or mastoiditis

<table>
<thead>
<tr>
<th>P: Ceftazidime</th>
<th>150 mg/kg/d IV/IM q8h</th>
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<tbody>
<tr>
<td>PLUS</td>
<td></td>
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<tr>
<td>Ceftriaxone</td>
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<td></td>
<td></td>
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<tr>
<td>Chloramphenicol</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Duration of treatment is unclear, usually 6-8 weeks.</td>
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</tbody>
</table>
In the presence of head trauma:
Streptococci (aerobic and anaerobic), *Haemophilus influenzae*,
Gram-negative enteric bacilli, *Bacteroides* spp, *P. aeruginosa*

<p>| | | |</p>
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<tbody>
<tr>
<td><strong>PLUS</strong></td>
<td><strong>Metronidazole</strong></td>
<td>7.5 mg/kg q6h IV/IM or 15 mg/kg IV/IM q12h</td>
</tr>
<tr>
<td><strong>A:</strong></td>
<td><strong>Ceftazidime</strong> 2g/d IV/IM q8h</td>
<td></td>
</tr>
<tr>
<td><strong>PLUS</strong></td>
<td><strong>Metronidazole</strong></td>
<td>7.5 mg/kg q6h or 15 mg/kg IV/IM q12h</td>
</tr>
<tr>
<td><strong>P:</strong></td>
<td><strong>Vancomycin</strong> 60 mg/kg/d IV q6h</td>
<td></td>
</tr>
<tr>
<td><strong>PLUS</strong></td>
<td><strong>Ceftriaxone</strong> 100 mg/kg/d IV/IM q12h; max dose: 4 g/d</td>
<td></td>
</tr>
<tr>
<td><strong>A:</strong></td>
<td><strong>Vancomycin</strong> 15-20mg/kg IV q8-12h</td>
<td></td>
</tr>
<tr>
<td><strong>PLUS</strong></td>
<td><strong>Ceftriaxone</strong> 2g IV q12h</td>
<td></td>
</tr>
</tbody>
</table>

If methicillin-sensitive *S. aureus* is documented, shift to oxacillin.
| In the presence of endocarditis (native valve): S. aureus, aerobic streptococci, Gram-negative enteric bacilli | P: Ceftriaxone  100 mg/kg/d q12h IV or IM; max dose: 4 g/d  
PLUS Gentamicin 3-6mg/kg/d IV/IM q24h  
(If Enterococcus faecalis is documented, give q8h)  
A: Ceftriaxone  2 g IV q12h  
PLUS Gentamicin 3-6mg/kg/d IV/IM q24h  
(If Enterococcus faecalis is documented, give q8h)  
P: Vancomycin  60 mg/kg/d q6h IV  
PLUS Gentamicin 3-6mg/kg/d IV/IM q24h  
(If Enterococcus faecalis is documented, give q8h) | If methicillin-sensitive S. aureus is documented, shift to oxacillin. |

In the presence of endocarditis (prosthetic valve): Streptococcus viridans, S. aureus
| A: Vancomycin  
15-20mg/kg q8-12h  
PLUS  
Gentamicin  
3-6mg/kg/day IV/IM q24h  
(If *Enterococcus faecalis* is documented, give q8h) |
|-----------------|-----------------|
| P: Ceftriaxone  
100 mg/kg/d IV/IM q12h; max dose: 4 g/d  
PLUS  
Metronidazole  
7.5 mg/kg IV q6h or 15 mg/kg IV q12h |
| A: Ceftriaxone  
2 g IV q12h  
PLUS  
Metronidazole  
7.5 mg/kg IV q6h or 15 mg/kg IV q12h |

In the presence of congenital heart disease:  
*S. viridans, Haemophilus* spp.
No focus
*S. pneumoniae, H. influenzae*

**P:**

1st line:
**Ceftriaxone**
100 mg/kg/d IV/IM q12h; max dose: 4 g/d

PLUS

**Metronidazole**
7.5 mg/kg/ IV q6h or 15 mg/kg IV q12h

2nd line:
**Penicillin G**
400,000U/kg/d IV q6h

PLUS

**Chloramphenicol**
100 mg/kg/d IV q6h

**A:**

1st line:
**Ceftriaxone**
2 g IV q12h

PLUS

**Metronidazole**
7.5 mg/kg/ IV q6h or 15 mg/kg q12h
### Spinal Abscess

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Preferred regimen</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus, Streptococci</td>
<td><strong>P:</strong> Vancomycin 60 mg/kg/d IV q6h</td>
<td>If methicillin-sensitive S. aureus is documented, shift to oxacillin.</td>
</tr>
<tr>
<td></td>
<td><strong>A:</strong> Vancomycin 15-20mg/kg IV q8-12h</td>
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</table>

### Encephalitis

- Encephalitis is an inflammation of the brain usually caused by viral infections. The classic presentation is encephalopathy with diffuse or focal neurologic symptoms, including the following: behavioral and personality changes, with decreased level of consciousness, neck pain, stiffness, photophobia, generalized or focal seizures.
- Findings of herpes simplex virus (HSV) infection in neonates may include the following: herpetic skin lesions over the presenting surface from birth or with breaks in the skin, oropharyngeal involvement, keratoconjunctivitis, seizure, irritability, bulging fontanels. Severe signs include jaundice, hepatomegaly and shock.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Preferred regimen</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral including, measles, influenza,</td>
<td>Supportive treatment</td>
<td>Children should be immunized with measles</td>
</tr>
<tr>
<td>enteroviruses, arboviruses</td>
<td></td>
<td>vaccine at 9</td>
</tr>
</tbody>
</table>
months, and measles, mumps, rubella (MMR), and varicella vaccines at 12 months. A booster of MMR is given at 4-6 years old.

<table>
<thead>
<tr>
<th>Herpes simplex</th>
<th><strong>P:</strong> Acyclovir (&lt;12 years): 20 mg/kg IV infused over 1 hour q8h</th>
<th>Early diagnosis and treatment is necessary.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>A:</strong> Acyclovir 10 mg/kg IV infused over 1 hour q8h</td>
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<tr>
<td></td>
<td>Duration of treatment is 14-21 days</td>
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</table>

### Fungal Meningitis
- *Candida* may enter the central nervous system by hematogenous spread, at the time of craniotomy, or through a ventricular shunt. Manifestations of *Candida* meningitis may be similar to those of acute bacterial meningitis. Culture of the CSF is the gold standard for diagnosis.
- Infection with the encapsulated yeast *Cryptococcus neoformans* can result in harmless colonization of the airways, meningitis or disseminated disease, especially in persons with defective cell-mediated immunity. Cryptococcal meningitis is usually fatal without appropriate therapy, and death may occur from 2 weeks to several years after symptom onset. The most common symptoms include headache and altered mental status, personality changes, confusion, lethargy, obtundation, and coma.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Preferred regimen</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td><em>Candida</em> meningitis</td>
<td><strong>Amphotericin B deoxycholate</strong> 0.6-1 mg/kg/d IV over 2-6h</td>
<td>BUN, creatinine and K+ should be monitored at least weekly.</td>
</tr>
<tr>
<td></td>
<td>Start with test dose of 0.1 mg/kg/dose IV to a maximum dose of 1 mg over 20-60 min.</td>
<td>Removal of shunts is recommended.</td>
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<tr>
<td>Indication</td>
<td>Treatment Plan</td>
<td></td>
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<td>------------</td>
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</tr>
</tbody>
</table>
| **Cryptococcal meningitis (non-AIDS)** | **Induction:**

Amphotericin B deoxycholate 0.7-1 mg/kg/d IV over 2-6h

Duration of treatment: until patient is afebrile and cultures are negative (approximately 6 weeks)

**Consolidation phase:**

Fluconazole 200 mg PO od

Duration of treatment: 10-12 weeks after CSF culture is negative

OR

(for less severely ill)

Fluconazole

\[P: 6-12 \text{ mg/kg/d od} \]

\[A: 400 \text{ mg od} \]

Duration of treatment: 10-12 weeks after CSF culture is negative |

If CSF pressure >25 cm H\(_2\)O, repeat the lumbar tap to drain fluid and control pressure.

The ideal regimen includes flucytosine in the induction phase, but this drug is not available in the Philippines.
| Cryptococcal meningitis associated with HIV/AIDS | **Induction:**  
**Amphotericin B deoxycholate**  
0.7-1 mg/kg/d IV over 2-6h  
PLUS  
**Fluconazole**  
P: 6-12 mg/kg/d IV od  
A: 800 mg IV or po od  
Duration of treatment: at least 2 weeks  
**Consolidation phase:**  
**Fluconazole**  
P: 6-12 mg/kg/d IV once daily  
A: 400 mg IV or po once daily  
Duration of treatment: at least 8 weeks  
**Suppression (chronic maintenance therapy):**  
**Fluconazole**  
P: 3 mg/kg/d IV once daily  
A: 200 mg po once daily  
Duration: at least 1 year | Defer ART to allow for 5 weeks of antifungal therapy.  
Repeat lumbar tap daily until signs and symptoms of increased intracranial pressure consistently improve.  
Begin after successful induction therapy (defined as substantial clinical improvement and negative CSF culture on repeat tap).  
May stop once CD4 > 100 cells/μL x at least 3 months and with undetectable viral load. |
Central and Nervous System Infections National Antibiotic Guidelines

REFERENCES:


• Tropical Diseases and Other Diseases, Manila 2012, 214, Section of Infectious and Immunization Practices (AIP). MMWR 2013; 62 (No. 2).


• Tropical Diseases and Other Diseases, Manila 2012, 214, Section of Infectious and Immunization Practices (AIP). MMWR 2013; 62 (No. 2).


• Tropical Diseases and Other Diseases, Manila 2012, 214, Section of Infectious and Immunization Practices (AIP). MMWR 2013; 62 (No. 2).
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• Research Institute of Tropical Medicine. Antimicrobial Resistance Surveillance Program 2014 Annual Report


• Southwick FS. Treatment and Prognosis of Bacterial Meningitis in Children. PIDSP and CNSP Bacterial Meningitis in Children. PIDS. Journal 2015; 16 (2): 2-42.


• Research Institute of Tropical Medicine. Antimicrobial Resistance Surveillance Program 2014 Annual Report


• Research Institute of Tropical Medicine. Antimicrobial Resistance Surveillance Program 2014 Annual Report
