Infectious Diseases

PY-3 Fall 2011

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**Meningitis**

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Educational Outcomes

1. Explain how the drug characteristics, the anatomy of the CNS and the organism impact the most appropriate route of administration for antibiotic therapy when treating CNS infections
2. Explain how pathogens invade the CNS to cause infection.
3. Explain why patients experience neurologic sequelae following CNS infections.
4. List the clinical manifestations associated with meningitis
5. Given the results of the LP, determine if the patient has a bacterial or viral infection.
6. Discuss the role of steroids in the treatment of CNS infections.
7. Given a patient case recommend an appropriate empiric and/or definitive treatment regimen including drugs, dose, route and duration of therapy.
8. Develop a monitoring plan for a patient being treated for bacterial meningitis
9. Identify strategies for preventing bacterial meningitis

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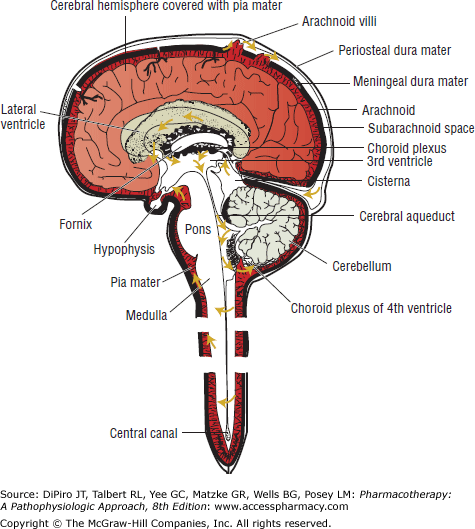
**What has had the greatest impact on the incidence of meningitis in the U.S.?**

Vaccines

I. Epidemiology – Why the treatment of meningitis is considered an emergency.

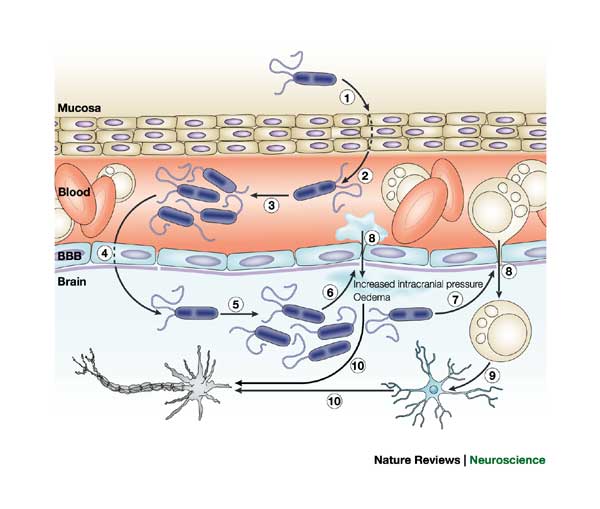
1. Mortality Rates: 2-30%
2. Neurologic Sequelae: 30-50%

II. Anatomy of the CNS – treatment implications



II. Pathophysiology of CNS Infections

1. Sequence of events



The different steps include mucosal colonization (1), invasion of bloodstream (2), survival and multiplication (3) causing high levels of bacteraemia, crossing of the blood–brain barrier (4), and invasion of the meninges and the central nervous system (5). Subsequently, bacteria can induce an increased permeability of the blood–brain barrier (BBB; 6) and pleocytosis (7), leading to edema and increased intracranial pressure (8), and to the release of proinflammatory compounds from infiltrated white blood cells and other host cells (9). Ultimately, these process lead to neuronal injury (10)

Kwang Sik Kim Nature Reviews Neuroscience 4, 376-385 (May 2003)

1. Neurologic Sequelae See Figure 115-3 in Dipiro

Key Concept: Neurologic sequelae are not due to the presence of the bacteria, but due to inflammation resulting from the activation of the patient’s inflammatory pathways by the pathogen or their products

Clinical Relevance:

III. Risk Factors

1. Exposure to cigarette smoke – Meningococcal disease
2. Children with Cochlear Implants – Pneumococcal meningitis
3. Respiratory Tract Infections
4. Otitis Media
5. Mastoiditis
6. Head Trauma
7. Immunoglobulin deficiency
8. Immunosuppression (Disease and/or drug induced)
9. Patients who are unable to activate the alternate complement pathway

**??** Who?

Asplenic patients

Do not have spleen

Sickle cell

**??** These patients are at increased risk of developing meningitis secondary to which pathogens

H. influenzae B

Pneumococcal

meningococcal

IV. Clinical Manifestations

1. General
2. Varies with age
3. Viral vs bacterial indistinguishable based on symptoms
4. Signs and Symptoms

Fever

Altered mental status

Irritability

Drowsiness, Lethargy

Chills

Vomiting

Photophobia

Severe Headache

Seizures

Most common in children

Delirium

Coma

1. Physical Findings

Bulging Fontanel in infants

Nuchal Rigidity: stiff neck

Kernig’s Sign: if lift leg, then pt lifts head

Brudzinski’s Sign

Petichial/purpuric rash

? Associated with which type of infection

1. Diagnostic Studies
2. Lumbar Puncture (LP) Key diagnostic test

* Gram Stain
* Culture
* Antigen Detection Tests (Latex Agglutination, latex fixation, enzyme immunoassay (EIA)

**?? When and why?**

Faster results

* Chemistry: Protein, Glucose
* Hematology: RBC, WBC with differential

Top of Form

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|  | CSF Analysis Normal and Abnormal CSF (Do not memorize values, but know the relative changes)   |  |  | | --- | --- | | |  | | --- | | Mean Values of the Components of Normal and Abnormal Cerebrospinal Fluid | | | | **Type** | **Normal** | **Bacterial** | **Viral** | **Fungal** | **Tuberculosis** | | --- | --- | --- | --- | --- | --- | | WBC (cells/mm3) | <5 | 1,000–5,000 | 100–1,000 | 40–400 | 100–500 | | Differential (%) | >90 *a* | > 80 PMNs | 50 *b*, *c* | >50 *b* | >80 *b*, *c* | | Protein (mg/dL) | <50 | 100–500 | 30–150 | 40–150 | 40–150 | | Glucose  (mg/dL) | 50%–66% simultaneous serum value | <40  (<60% simultaneous serum value) | <30–70 | <30–70 | <30–70 | | | *a* Monocytes, *b* Lymphocytes, *C* Initial CSF-WBC differential may show a predominance of polymorphonuclear cells (PMNs)  From: Pharmacotherapy: A Pathophysiologic Approach, 8e  Chapter 115. Central Nervous System Infections | |  | |  |

B. Blood

1. Culture
2. WBC with differential

VI. Treatment

1. Antibiotic Penetration into the CNS
2. Factors Affecting CNS Concentration in the CSF

Characteristics of the drug

* LMW
* Lipid soluble
* Non-ionized at physiologic pH
* Not highly protein bound

Increased permeability of the BBB

1. Penetration of Antimicrobial Agents into the CSF

|  |  |  |  |
| --- | --- | --- | --- |
| **Therapeutic levels in CSF with or without inflammation** | **Therapeutic levels in CSF with inflammation of meninges** | | **Non-therapeutic levels in CSF with or without inflammation** |
| Choramphenicol  [Cycloserine](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5960');)  [Ethionamide](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6159');)  [Isoniazid](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6407');)  [Metronidazole](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6573');)  Pyrazinamide  Rifampin  Sulfonamides  Trimethoprim | [Acyclovir](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5569');)  [Ampicillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5637');) ± sulbactam  [Aztreonam](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5693');)  [Carbenicillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5813');)  [Cefotaxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5840');)  [Ceftazidime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5845');)  [Ceftizoxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5847');)  [Ceftriaxone](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');)  [Cefuroxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5849');)  [Ciprofloxacin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5904');)  Colistin  [Daptomycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5979');)  [Ethambutol](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6149');)  [Fluconazole](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6203');)  [Flucytosine](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6204');)  [Foscarnet](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6235');) | [Ganciclovir](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6253');)  Imipenem  [Levofloxacin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6454');)  [Linezolid](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6467');)  [Meropenem](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6538');)  Mezlocillin  [Moxifloxacin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6608');)  [Nafcillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6619');)  [Ofloxacin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6675');)  Penicillin G  [Piperacillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6783');)  [Pyrimethamine](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6880');)  Quinupristin/dalfopristin  Ticarcillin ± clavulanic acid  [Vancomycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7141');)  Vidarabine | Aminoglycosides  Amphotericin B  Cefoperazone  Cephalosporins (1st gen)  Cephalosporins (2nd gen) 1  Clindamycin  Itraconazole  Ketoconazole |

1 Cefuroxime is an exception 2 Achieves therapeutic brain tissue concentrations. 3 Achieves therapeutic concentrations for Cryptococcus neoformans therapy

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From: Pharmacotherapy: A Pathophysiologic Approach, 8e > Section 16. Infectious Diseases > Chapter 115. Central Nervous System Infections

1. Empiric Therapy

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| |  | | --- | | Bacterial Meningitis: Most Likely Pathogens and **Empirical** Therapy by Age Group | |
| | **Age Commonly Affected** | **Most Likely Organisms** | **Empirical Therapy** | | --- | --- | --- | | Newborn–1 mo | Group B *Streptococcus*  Gram-negative enterics  E.coli  Klebsiella  *Listeria monocytogenes* | Ampicillin + cefotaxime or an aminoglycoside | | 1 mo– 29 y | *S. pneumoniae*  *N. meningitidis*  *H. influenzae* 1 | Vancomycin 2 and cefotaxime or ceftriaxone | | 30–60 y | *S. pneumoniae*  *N. meningitidis* | Vancomycin 2 and cefotaxime or ceftriaxone | | >60 y | *S. pneumoniae*  Gram-negative enterics  E.coli  Klebsiella spp  Enterobactor spp  *L monocytogenes* | Vancomycin 2 and ampicillin and cefotaxime or ceftriaxone | |
| 1If not immunized with HIB vaccine. 2Vancomycin use should be based on local incidence of penicillin-resistant *S. pneumoniae* and until cefotaxime or cefotaxime minimum inhibitory concentration results are available. |

Adapted from; Pharmacotherapy: A Pathophysiologic Approach, 8ed.Section 16. Chapter 115. Central Nervous System Infections

Bottom of Form

1. Definitive Therapy

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| |  | | --- | | **Antimicrobial Agents of First Choice and Alternative Choice in the Treatment of Meningitis Caused by Gram-Positive and Gram-Negative Microorganisms** | |
| | **Organism** | **Antibiotic of First Choice** | **Alternative Antibiotics** | **Recommended Duration of Therapy** | | --- | --- | --- | --- | | **Gram-positive** | | | | | *Streptococcus pneumoniae* |  | | 10–14 days | | Penicillin susceptible | Penicillin G or [Ampicillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5637');) (A-III) | [Cefotaxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5840');) (A-III), [Ceftriaxone](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');) (A-III), [Chloramphenicol](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5867');) (A-III) |  | | Penicillin intermediate | [Cefotaxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5840');) or [Ceftriaxone](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');) (A-III) | [Cefepime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5838');) (B-II), [Meropenem](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6538');) (B-II), [Moxifloxacin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6608');) (B-II), [Linezolid](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6467');) (C-III) |  | | Penicillin resistant | [Vancomycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7141');) *a*plus [Cefotaxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5840');) or [Ceftriaxone](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');) (A-III) | [Cefepime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5838');) (B-II), [Meropenem](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6538');) (B-II), [Moxifloxacin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6608');) (B-II), [Linezolid](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6467');) (C-III) |  | | Group B *Streptococcus* | Penicillin G or [Ampicillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5637');) ± [Gentamicin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6261');) *a*(A-III) | [Cefotaxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5840');) (B-III), [Ceftriaxone](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');) (B-III), [Chloramphenicol](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5867');) (B-III) | 14–21 days | | **Antimicrobial Agents of First Choice and Alternative Choice in the Treatment of Meningitis Caused by Gram-Positive and Gram-Negative Microorganisms (continued)** | | | | | *Staphylococcus aureus* |  |  | 14–21 days*e* | | Methicillin susceptible | [Nafcillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6619');) or [Oxacillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6691');) (A-III) | [Vancomycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7141');) *a*(A-III), [Meropenem](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6538');) (B-III) |  | | Methicillin resistant | [Vancomycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7141');) *a*(A-III) | [Trimethoprim](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7111');)-sulfamethoxazole (A-III), [Linezolid](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6467');) (B-III) |  | | *Staphylococcus epidermidis* | [Vancomycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7141');) *a*(A-III) | [Linezolid](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6467');) (B-III) | 14–21 days*d* | | *Listeria monocytogenes* | Penicillin G or [Ampicillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5637');) ± [Gentamicin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6261');) *a*(A-III) | [Trimethoprim](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7111');)-sulfamethoxazole (A-III), [Meropenem](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6538');) (B-III) | http://www.accesspharmacy.com/images/special/greaterorequal.gif21 days | | **Gram-negative** | | | | | ***Neisseria meningitis*** |  |  | 7 days | | Penicillin susceptible | Penicillin G or [Ampicillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5637');) (A-III) | [Cefotaxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5840');) (A-III), [Ceftriaxone](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');) (A-III), [Chloramphenicol](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5867');) (A-III) |  | | Penicillin resistant | [Cefotaxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5840');) or [Ceftriaxone](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');) (A-III) | [Chloramphenicol](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5867');) (A-III), [Meropenem](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6538');) (A-III), [Fluoroquinolone](javascript:windowReference('drugInfo','drugClassification.aspx?catid=1009');) (A-III) |  | | *Haemophilus influenzae* |  |  | 7 days | | *http://www.accesspharmacy.com/images/special/betalower.gif*-Lactamase negative | [Ampicillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5637');) (A-III) | [Cefotaxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5840');) (A-III), [Ceftriaxone](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');) (A-III), [Chloramphenicol](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5867');) (A-III), [Cefepime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5838');) (A-III), [Fluoroquinolone](javascript:windowReference('drugInfo','drugClassification.aspx?catid=1009');) (A-III) |  | | *http://www.accesspharmacy.com/images/special/betalower.gif*-Lactamase positive | [Cefotaxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5840');) or [Ceftriaxone](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');) (A-I) | [Cefepime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5838');) (A-I), [Fluoroquinolone](javascript:windowReference('drugInfo','drugClassification.aspx?catid=1009');) (A-III), [Chloramphenicol](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5867');) (A-III) |  | | ***Enterobacteriaceae* (E.coli, and Klebsiella spp)** | [Cefotaxime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5840');) or [Ceftriaxone](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5848');) (A-II) | [Cefepime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5838');) (A-III), [Fluoroquinolone](javascript:windowReference('drugInfo','drugClassification.aspx?catid=1009');) (A-III), [Meropenem](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6538');) (A-III), [Aztreonam](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5693');) (A-III) | 21 days | | ***Pseudomonas aeruginosa*** | [Cefepime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5838');) or [Ceftazidime](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5845');) (A-II) ± [Tobramycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7065');) *a*,*b*(A-III) | [Ciprofloxacin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5904');) (A-III), [Meropenem](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6538');) (A-III), [Piperacillin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6783');) plus [Tobramycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7065');) *a*,*b*(A-III), [Colistin sulfomethate](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5944');) *a*,*c*(B-III), [Aztreonam](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5693');) (A-III) | 21 days | |
|  |
| *a*Monitor drug levels in serum. *b*Direct central nervous system administration may be added; *c*Should be reserved for multidrug-resistant pseudomonal or *Actinetobacter* infections for which all other therapeutic options have been exhausted. *e*Based on clinical experience; no clear recommendations. |

|  |  |  |
| --- | --- | --- |
| Antibiotic Doses | | |
| Antimicrobial Agent | **Infants and Children** | **Adults** |
| Ampicillin | 75 mg/kg every 6 h | 2 g every 4 h |
| Aztreonam |  | 2 g every 6–8 h |
| Cefepime | 50 mg/kg every 8 h | 2 g every 8 h |
| Cefotaxime | 75 mg/kg every 6–8 h | 2 g every 4–6 h |
| Ceftazidime | 50 mg/kg every 8 h | 2 g every 8 h |
| Ceftriaxone | 100 mg/kg once daily | 2 g every 12–24 h |
| Chloramphenicol | 25 mg/kg every 6 h | 1–1.5 g every 6 h |
| Ciprofloxacin | 10 mg/kg every 8 h | 400 mg every 8–12 h |
| Colistin a,c | 5 mg/kg once daily | 5 mg/kg once daily |
| Gentamicin a,b | 2.5 mg/kg every 8 h | 2 mg/kg every 8 h |
| Levofloxacin | 10 mg/kg once daily | 750 mg once daily |
| Linezolid | 10 mg/kg every 8 h | 600 mg every 12 h |
| Meropenem | 40 mg/kg every 8 h | 2 g every 8 h |
| Oxacillin/Nafcillin | 50 mg/kg every 6 h | 2 g every 4 h |
| PenicillinG | 0.05 mUnits/kg every 4–6 h | 4 mUnits every 4 h |
| Piperacillin | 50 mg/kg every 4–6 h | 3 g every 4–6 h |
| Tobramycin | 2.5 mg/kg every 8 h | 2 mg/kg every 8 h |
| TMP-SMZ d | 5 mg/kg every 6–12 h | 5 mg/kg every 6–12 h |
| Vancomycin | 15 mg/kg every 6 h | 15 mg/kg every 8–12 h |

*a*Monitor drug levels in serum. *b*Direct central nervous system administration may be added *c*Should be reserved for multidrug-resistant pseudomonal or *Actinetobacter* infections for which all other therapeutic options have been exhausted. *d*Dosing based on [trimethoprim](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7111');) component.

1. The role of Dexamethasone in the Management of Patients with Meningitis
2. Theoretical Rationale
3. Pros/Cons
4. Conflicting data
5. Current Recommendations
6. Pediatric Patients:

* American Academy of Pediatrics: Consider administration of dexamethasone 0.15 mg/kg Q 6 h for 4 days in infants and children older than 2 months suspected of having HIB or pneumococcal meningitis. The first dose must be administered before the first dose of antibiotics. Alternative dose 0.4 mg/kg Q 12 h for 2 days
* Repeat LP in 24-48 h

1. Adults

* Benefits: In patients suspected of having pneumococcal meningitis administer dexamethasone 0.15 mg/kg Q 6 h for 2-4 days

1. Monitoring Therapy

VII. Prevention of Meningitis

1. Vaccines

|  |  |  |  |
| --- | --- | --- | --- |
|  | Hemophilus Influenza B  Hib (several vaccines marketed | Pneumococcal | Meningococcal |
| Primary Series | 2,4,6,12-15 months | **PCV-13**  2,4,6,12-15 months | **MCV4**  11-12 yr repeat at 16 yr |
| Adults | Anatomic or functional asplenia | **PPSV**  65 yr  Smoker  Chronic diseases  Asplenia  Cochlear Implant  HIV or other immunosuppressive condition | **MCV4**  Asplenia, compliment component deficiency |

B. Antibiotic Prophylaxis

**Meningococcal Meningitis**

1. Indication: Close contacts of the index case- day care center contacts, household contacts, and individuals who had contact with respiratory or oral secretions.
2. Prophylactic Regimens

Rifampin

Infants < 1 month 5 mg/kg Q 12 h for 2 days

>1month 10 mg/kg/dose Q 12 h for 2 days

Adults 600 mg Q 12 h for 2 days

Ciprofloxacin PO 500 mg one dose adults and children > 12 y

Ceftriaxone

Children 125 mg IM one dose

Adults 2250 mg IM one dose

**Hemophilus influenza B**

1. Indications: Household contacts, individuals sharing sleeping quarters, day care center contacts, nursing home residents, and

crowded confined populations.

2. Prophylactic regimen

Rifampin Children 20 mg/kg/day for 4 days; Adults 600 mg daily for 4 days.