



## Chapter 109 – CNS Infections

### Episode Overview:

1. Provide a differential diagnosis (10) for acute, non-infectious meningitis.
2. What is the pathophysiology of acute infectious meningitis? (eg. n. meningitidis)
3. List 8 host factors predisposing to meningitis
4. List 6 immediate and 6 delayed complications of bacterial meningitis
5. What is the clinical presentation of cryptococcal meningitis? Who is at risk?
6. Describe the inoculation patterns of brain abscesses.
7. What are typical presenting findings of encephalitis?
8. List 6 potential causes of viral meningitis. What is the treatment?
9. What is the morbidity of viral meningitis / encephalitis?
10. List 10 causes of aseptic meningitis
11. Which pts with suspected meningitis need a CT?
12. What are indications for LP in CNS infection? What are contraindications to LP?
13. List analysis tests of CSF.
  - a. Describe expected CSF findings in normal, bacterial meningitis, and viral meningitis.
  - b. List 6 other tests of CSF or CSF findings suggestive of specific disease processes
14. What are Gram's Stain Characteristics of Selected Meningeal Pathogens:
  - a. Staphylococci
  - b. Strep. Pneumoniae
  - c. Listeria monocytogenes
  - d. Neisseria meningitidis
  - e. Haemophilus influenzae
  - f. Escherichia coli
  - g. Pseudomonas aerug.
15. What are the antimicrobial therapies recommended for presumed bacterial meningitis in the following age groups/populations:
  - a. < 1 month
  - b. 1 month – 2 yrs
  - c. 2 yrs – 50 yrs
  - d. > 50 yrs
  - e. Head trauma: basilar skull fracture, penetrating trauma
  - f. Post neurosurgery
  - g. CSF shunt
16. Describe the management of suspected bacterial meningitis? What is the evidence supporting the use of corticosteroids in bacterial meningitis? When should it be given?
17. For whom is chemoprophylaxis indicated in bacterial meningitis? What is an appropriate regimen?



## Wisecracks

1. What percentage of patients have classic presentation of meningitis? (Fever, nuchal rigidity, altered)
2. What are 3 atypical presentations of meningitis?
3. What is Kernig's sign? What is Brudzinski's sign?
4. What are five typical bacterial pathogens for purulent meningitis in the following age groups/populations:
  - a. < 1 month
  - b. 1 month – 2 yrs
  - c. 2 yrs – 50 yrs
  - d. > 50 yrs
  - e. Head trauma: basilar skull fracture, penetrating trauma
  - f. Post neurosurgery
  - g. CSF shunt
5. Provide the differential diagnosis of a ring-enhancing lesion.
6. What is the schedule for pneumococcal vaccination (conjugated vaccine) in healthy children? Which strains of *n. meningitidis* are covered by the meningococcal vaccine?

## Key Points:

- CNS infection should be considered in all patients with headache, neck stiffness, fever, altered sensorium, or diffuse or focal neurological findings.
- S. pneumoniae* is one of the two leading causes of bacterial meningitis in adults. Mortality from *S. pneumoniae* is 30%.
- pay close attention to cranial nerves 2, 3, 4, and 6
- Altered mental status in a patient with suspected meningitis can be a sign of increased ICP or encephalitis.
- You've got to get the LP! Only true way to assess for meningitis
- Early initiation of empirical antimicrobial therapy is recommended in cases of suspected acute CNS infection. Antibiotic administration should not be delayed for CSF analysis or performance of neuroimaging studies.
- Antibiotic chemoprophylaxis should be assured for close contacts of patients with meningitis resulting from *N. meningitidis* or *H. influenzae*.
- Concomitant CNS infection should be strongly considered in any symptomatic patient with another severe systemic infection, such as urinary tract infection or pneumonia.
- First line treatment for bacterial meningitis is ceftriaxone plus vancomycin.
- Acyclovir is recommended for patients with suspected meningoencephalitis.
- Dexamethasone is recommended prior to treatment with antibiotics in adults (controversial)



## 1. Provide a differential diagnosis (10) for acute, non-infectious meningitis.

We'll review this in question 10, but here is a quick list!

1. Postinfectious / postvaccine
  - a. Rubella
  - b. Varicella
  - c. Rabies vaccine
  - d. Pertussis vaccine
  - e. Influenza vaccine
  - f. Yellow fever vaccine
2. Drugs
  - a. NSAIDS
  - b. Septra
  - c. Azathioprine
  - d. IVIG
  - e. Isoniazid
  - f. Intrathecal methotrexate
  - g. Allopurinol
  - h. Carbamazepine
3. Systemic disease
  - a. Collagen vasc. Diseases
    - i. SLE, GPanG, RA, Kawasaki's
  - b. Sarcoidosis
  - c. Behcet's disease
4. Neoplastic disease
  - a. Leukemia
  - b. Carcinomatous meningitis
5. Inflammation of neighboring structures
  - a. Brain / epidural abscess
6. Misc.
  - a. Migraine

## 2) What is the pathophysiology of acute infectious meningitis? (eg. n. meningitidis)

- The predominant pathogens are Strep. Pneumoniae and N. meningitidis (<45 yrs).
- Common pathogenic sequence:
  - Nasopharyngeal colonization → mucosal invasion → virulent microbes freeze the mucosal cilia and evade the immune system (IgA proteases, capsular properties help bacteria remain undercover) → enter the BBB and enter CSF.
  - CSF is unable to protect against invasion due to low levels of immune cells to fight infection.



- Bacteria proliferate → cytokine storm and inflammation in the CSF leads to BBB breakdown → vasculitis, edema, increased ICP → **decreased cerebral blood flow. = hypoxia and cellular metabolic failure due to GLUCOSE depletion.**

### 3) List 8 host factors predisposing to meningitis

#### BOX 99.1

##### Host Factors Predisposing to Meningitis

- Age younger than 5 years old / Age older than 60 years old
- Male gender / African-American race
- Low socioeconomic status / Crowding (eg, military recruits)
- Splenectomy / Sickle cell disease / Thalassemia major
- Alcoholism and cirrhosis / Diabetes / Malignancy
- Immunologic defects
- Recent colonization
- Dural defect (eg, traumatic, surgical, congenital)
- Continuous infection (eg, sinusitis)
- Household contact with meningitis patient
- Intravenous (IV) drug abuse
- Bacterial endocarditis
- Ventriculoperitoneal shunt

### 4) List 6 immediate and 6 delayed complications of bacterial meningitis

#### BOX 99.2

##### Complications of Bacterial Meningitis

- IMMEDIATE
  - Coma
  - Loss of airway reflexes
  - Seizures
  - Cerebral edema
  - Vasomotor collapse
  - Disseminated intravascular coagulation (DIC)
  - Respiratory arrest
  - Dehydration
  - Pericardial effusion
  - Death
  - Others
- DELAYED
  - Seizure disorder
  - Focal paralysis
  - Subdural effusion
  - Hydrocephalus
  - Intellectual deficits



- Sensorineural hearing loss
- Ataxia
- Blindness
- Bilateral adrenal hemorrhage
- Death
- Cerebral venous thrombosis
- Others

## **5) What is the clinical presentation of cryptococcal meningitis? Who is at risk?**

This fungal infection usually occurs post pulmonary exposure in an immunocompromised host.

## **6) Describe the inoculation patterns of brain abscesses.**

Can occur at any age and any time of year. They are associated with local spread (e.g. post-op bone fragments in the brain tissue) or hematogenous spread from a remote source (pulmonary infection, endocarditis).

Other risk factors: IVDU, post neuro sx, CNS trauma, post-otitis media/sinusitis/dental infection.

People at very high risk are immunocompromised (HIV or post organ transplant).

## **7) What are typical presenting findings of encephalitis?**

Encephalitis = an inflammation of the brain

- Alteration of consciousness
- Personality changes
- Confusion
- Disorientation
- Hallucinations / bizarre behaviour
  - May progress to focal neurological findings
- Seizures
- Delirium
- Fevers / h/a

## **8) List 6 potential causes of viral meningitis. What is the treatment?**

There is a long list; so just get to know a few!



## Viruses

- Enteroviruses—polio, Coxsackie, echovirus
- Herpes group of viruses
- Herpes simplex virus (HSV) types 1 and 2
- Varicella zoster virus
- Cytomegalovirus
- Epstein-Barr virus
- Human herpes virus 6 (HHV-6)
- Respiratory viruses
- Adenovirus
- Rhino virus
- Influenza virus types A and B
- Arboviruses
- Mumps virus
- Lymphocytic choriomeningitis
- Human immunodeficiency virus (HIV)

**There is no specific agent to treat most types of viral meningitis.** They usually are benign and self-limited. The most important role we play is to exclude a more serious form of meningitis.

**Viral encephalitis** - suspected herpes meningoencephalitis - should be treated with IV acyclovir: 10 mg/kg q8 hrs.

Other antivirals for encephalitis caused by HHV6 and enteroviral disease can be administered. Many of the insect borne encephalitis (West Nile Virus) are best prevented by insecticide use - no perfect treatment exists yet...

“Some patients with suspected viral meningitis merit hospitalization. These include patients with more severe disease with refractory headache, immunocompromise, and suspicion of HSV meningitis. **Although local practices vary, we recommend managing patients with classical presentations of viral meningitis as outpatients with close follow-up within 24 hours.**” - Rosen’s

## 9) What is the morbidity of viral meningitis / encephalitis?

- Overall, the prognosis from viral meningitis is excellent with few complications (there are of course exceptions with very virulent viruses).
- HSV encephalitis is an exception, where pre-acyclovir mortality was 65%, and with the use of antivirals is 30%.
  - These survivors are at risk for:
    - Seizures, motor deficits, mentation changes.
- Other “killer” viruses with high mortality:
  - Japanese encephalitis
  - Eastern equine virus
  - St. Louis encephalitis virus
  - West Nile virus
- Measles virus encephalitis - at risk for post-infectious encephalomyelitis



## 10) List 10 causes of aseptic meningitis

**This comes from Box 99.3.** It's a huge list. So think of it in terms of categories! And remember, just because we say aseptic, doesn't mean it's non-infectious!

Causes of Aseptic Meningitis

(From Kumar R: Aseptic meningitis: diagnosis and management. Indian J Pediatr 72:57–63, 2005.)

Infectious causes	Non-infectious
<p>Viruses</p> <ul style="list-style-type: none"> <li>● Enteroviruses—polio, Coxsackie, echovirus</li> <li>● Herpes group of viruses</li> <li>● Herpes simplex virus (HSV) types 1 and 2</li> <li>● Varicella zoster virus</li> <li>● Cytomegalovirus</li> <li>● Epstein-Barr virus</li> <li>● Human herpes virus 6 (HHV-6)</li> <li>● Respiratory viruses</li> <li>● Adenovirus</li> <li>● Rhino virus</li> <li>● Influenza virus types A and B</li> <li>● Arboviruses</li> <li>● Mumps virus</li> <li>● Lymphocytic choriomeningitis</li> <li>● Human immunodeficiency virus (HIV)</li> </ul>	<p>Postinfectious/Postvaccinial</p> <ul style="list-style-type: none"> <li>● Rubella</li> <li>● Rubella</li> <li>● Varicella</li> <li>● Variola</li> <li>● Rabies vaccine</li> <li>● Pertussis vaccine</li> <li>● Influenza vaccine</li> <li>● Vaccinia</li> <li>● Yellow fever vaccine</li> </ul>
<p>Bacteria</p> <ul style="list-style-type: none"> <li>● Partially treated meningitis</li> <li>● Parameningeal infection</li> <li>● Endocarditis</li> <li>● Mycoplasma pneumonia</li> <li>● Mycobacterium tuberculosis</li> <li>● Ehrlichiosis</li> <li>● Borrelia burgdorferi</li> <li>● Treponema pallidum</li> <li>● Brucella</li> <li>● Leptospirosis</li> </ul>	<p>Drugs</p> <ul style="list-style-type: none"> <li>● Nonsteroidal anti-inflammatory drugs (NSAIDs)</li> <li>● Trimethoprim-sulfamethoxazole, amoxicillin</li> <li>● Muromonab CD3 (OKT3)</li> <li>● Azathioprine</li> <li>● Intravenous (IV) immunoglobulin</li> <li>● Isoniazid</li> <li>● Intrathecal methotrexate</li> <li>● Intrathecal cytosine arabinoside</li> <li>● Allopurinol</li> <li>● Carbamazepine</li> <li>● Sulfasalazine</li> </ul>
<p>Fungi</p> <ul style="list-style-type: none"> <li>● Cryptococcus neoformans</li> <li>● Histoplasma capsulatum</li> <li>● Coccidioides immitis</li> </ul>	<p>Systemic Disease</p> <ul style="list-style-type: none"> <li>● Collagen vascular disorders</li> <li>● Systemic lupus erythematosus</li> <li>● Wegener's granulomatosis</li> </ul>



<ul style="list-style-type: none"> <li>• Blastomyces dermatitides</li> <li>• Candida</li> </ul>	<ul style="list-style-type: none"> <li>• Central nervous system (CNS) vasculitis</li> <li>• Rheumatoid arthritis</li> <li>• Kawasaki's disease</li> <li>• Sarcoidosis</li> <li>• Leptomeningeal cancer</li> <li>• Post-transplantation lymphoproliferative disorder</li> <li>• Behçet's disease</li> <li>• Vogt-Koyanagi syndrome</li> </ul>
<p>Parasites</p> <ul style="list-style-type: none"> <li>• Toxoplasma gondii</li> <li>• Neurocysticercosis</li> <li>• Trichinosis</li> <li>• Naegleria</li> <li>• Hartmannella</li> <li>• Bartonella henselae</li> </ul>	<p>Neoplastic Disorders</p> <ul style="list-style-type: none"> <li>• Leukemia</li> <li>• Carcinomatous meningitis secondary to primary or secondary tumors of the brain</li> </ul>
<p>Rickettsiae</p> <ul style="list-style-type: none"> <li>• Rocky Mountain spotted fever</li> <li>• Typhus</li> </ul>	<p>Inflammation of Neighboring Structures</p> <ul style="list-style-type: none"> <li>• Brain abscess</li> <li>• Epidural abscess</li> <li>• Miscellaneous</li> <li>• Arachnoiditis</li> <li>• Migraine</li> <li>• Urinary tract infection</li> </ul>

### 11) Which pts with suspected meningitis need a CT?

We want to get a CT (with contrast) or MRI in anyone who we suspect may have ICH, mass lesions, or an abscess.

But regarding a non-contrast CT pre-LP...

- Anyone with signs of increased ICP
  - Fundoscopy
    - Papilledema
    - Loss of venous pulsations
  - Coma
  - Focal neurological signs
  - Seizures
  - Depressed mental status

“It has been conventionally asserted that an LP in the presence of increased ICP may be harmful or fatal to the patient. **Up to 30% of patients with bacterial meningitis will herniate even if they do not have an LP**, suggesting that the herniations observed in some studies are the result of the underlying disease process and not the test. “





You should also consider getting an MRI to evaluate for cases of viral HSV encephalitis. In fact...”In subtle cases, LP can create meningeal enhancement on a subsequent MRI. If viral encephalitis is suspected and treatment has already been initiated, we recommend performing the LP after the MRI.” - Rosen’s 9th Ed.

Uptodate 2017 says it this way:

“Based upon these observations and in agreement with the 2004 Infectious Diseases Society of America (IDSA) guidelines for the management of bacterial meningitis, a CT scan of the head before LP should be performed in adult patients with suspected bacterial meningitis who have one or more of the following risk factors [27-29]:

- Immunocompromised state (eg, HIV infection, immunosuppressive therapy, solid organ or hematopoietic stem cell transplantation)
- History of central nervous system (CNS) disease (mass lesion, stroke, or focal infection)
- New onset seizure (within one week of presentation)
- Papilledema
- Abnormal level of consciousness
- Focal neurologic deficit

Patients with these clinical risk factors should have a CT scan to identify a possible mass lesion and other causes of increased intracranial pressure.

However, it has been suggested that a normal CT scan does not always mean that performance of an LP is safe and that certain clinical signs of impending herniation (ie, deteriorating level of consciousness, particularly a Glasgow coma scale <11; brainstem signs including pupillary changes, posturing, or irregular respirations; or a very recent seizure) may be predictive of patients in whom an LP should be delayed.”

## **12) What are indications for LP in CNS infection? What are contraindications to LP?**

### **Indications:**

- Whenever a CSF infection is suspected: remember that typical signs and symptoms may be absent!

**Contraindications:** There are no absolute contraindications, just relative contraindications (need to weigh the risk benefits out!):

The bottom line according to Rosen’s is: “we recommend against LP in patients who have rapid neurological deterioration, seizures, or signs of herniation.”



Here's the longer version:

- SSTI at the puncture site (cellulitis or spinal epidural abscess)
- Anyone with signs of increased ICP
  - Fundoscopy
    - Papilledema
    - Loss of venous pulsations
  - Coma
  - Focal neurological signs
  - Seizures
  - Depressed mental status
- Spinal epidural abscess
- Thrombocytopenia (<50-80k plts)
- Bleeding diathesis (including ACTIVE therapeutic anticoagulation)

From UptoDate: "Thus, at present the only guidepost is "clinical judgment." We generally advise NOT performing an LP in patients with coagulation defects who are actively bleeding, have severe thrombocytopenia (eg, platelet counts <50,000 to 80,000/ $\mu$ L), or an INR >1.4, without correcting the underlying abnormalities."

### 13) List analysis tests of CSF.

Draw 4 tubes, each with 1-2 ml per tube. Labelled in order.

Test	Normal analysis
Opening pressure	5-20 cm H <sub>2</sub> O (applies ONLY to the lateral recumbent position) Elevated in: TB, bacterial, fungal meningitis Falsely elevated: obese, tense pts.
Turbidity	Clear and colourless
Xanthochromia	Absent
Glucose	2-4 mmol/L
Protein	150 - 450 mg/L (or 0.15 - 0.45 g/L)
Cell count and differential (tubes 1 and 3)  (unaffected by pretreatment with ABx)	< 5 leukocytes / mm <sup>3</sup> <= 1 PMN **any more than 1 PMN or 5 leuks = evidence of CNS infection** Presence of these are always abnormal: <ul style="list-style-type: none"> <li>● Basophils, eosinophils</li> </ul> See formula below table in question 14 for calculating true CSF WBC in cases of a traumatic tap
Gram stain, and bacterial culture	No organisms



(affected by pretreatment with ABx)	
Antigen testing <ul style="list-style-type: none"> <li>• Cryptococcal antigen (replaced India-ink stain)</li> <li>• Stain for acid-fast bacilli</li> <li>• VDRL (syphilis test)</li> </ul>	May be measured in CSF, serum or urine.
Lactic Acid	> 2.8 mmol/L may indicate bacterial meningitis (<2.8 mmol/L may indicate viral) Little current role for this test
CSF to serum glucose ratio	Normal = 06 : 1. A CSF-to-serum glucose ratio of less than 0.5 in normoglycemic subjects or 0.3 in hyperglycemic subjects is abnormal and may represent the impaired glucose transport mechanisms and increased CNS glucose use associated with pyogenic meningitis.
Others with unclear roles: <ul style="list-style-type: none"> <li>• CRP</li> <li>• Chloride</li> <li>• NAAT's with PCR for H.flu S.pneumoniae, N.meningitidis</li> </ul>	

**a) Describe expected CSF findings in normal, bacterial meningitis, and viral meningitis.**

Test	Normal analysis	Bacterial Meningitis	Viral Meningitis
Opening pressure	5-20 cm H2O	Normal to elevated	Often normal
Turbidity	Clear and colourless	Clear to turbid	Often clear
Glucose	2-4 mmol/L	Often low	Normal
Protein	150 - 450 mg/L (or 0.15 - 0.45 g/L)	Often very elevated* Often 1 to 5 g/L.	Often elevated Often 0.5 to 3 g/L.
Cell count and differential (tubes 1 and 3)  (unaffected by pretreatment with ABx)	< 5 leukocytes / mm <sup>3</sup> <= 1 PMN **any more than 1 PMN or 5 leuks = evidence of CNS infection** Presence of these are always abnormal: <ul style="list-style-type: none"> <li>• Basophils, eosinophils</li> </ul>	Usually very high > 500 cells/mm <sup>3</sup> +granulocyte shift +mostly PMN leukocytes  Initial CSF can show 50% of lymphocytes in 10% of cases	Usually < 500 cells/mm <sup>3</sup>  Nearly 100% of cells mononuclear
Gram stain, and bacterial culture (affected by pretreatment with ABx)	None	Diminished from 80% to 50-60% with pre-treatment Abx	None



**Important to know that early presentations (<48Hrs) of either bacterial or viral meningitis can have a lot of overlapping CSF features on cell count, protein and glucose levels...**a repeat LP in 8-12 hrs may be necessary. And normal CSF studies in high risk patients do not rule out the disease - these patients should be treated with Abx, admitted and get a repeat LP.

\*In the presence of a traumatic LP, one may estimate the true degree of CSF white blood cell (WBC) pleocytosis with the following formula:

[https://www.merckmanuals.com/medical-calculators/CSF\\_WBC.htm](https://www.merckmanuals.com/medical-calculators/CSF_WBC.htm)

Alternatively, when peripheral cell counts are normal, the CSF from a traumatic LP should contain about 1 WBC per 700 RBCs.

When a traumatic LP has occurred, the CSF protein can be corrected for the presence of blood by subtracting 1 mg/dL (10 mg/L) of protein for each 1000 RBCs.

See for more helpful tips.

[https://meds.queensu.ca/central/assets/modules/lumbar\\_puncture/what\\_to\\_do\\_with\\_this\\_csf.html](https://meds.queensu.ca/central/assets/modules/lumbar_puncture/what_to_do_with_this_csf.html)

#### **b) List 6 other tests of CSF or CSF findings suggestive of specific disease processes**

- **Brain abscess/parameningeal infection** - CSF studies can be normal or look like a viral meningo-encephalitis picture.
- **Fungal meningitis:** VERY elevated proteins: > 10,000 mg/L
- **HSV encephalitis:**
  - ELISA test can detect HSV antibody production (late finding)
  - PCR for HSV DNA (very sensitive and specific)
  - Similar PCR tests can be done for enteroviruses
- **SAH:** Xanthochromia
- **TB meningitis** = +ve PCR study; elevated lactate; positive acid fast stain (>10 ml of fluid needed!)
- **Cryptococcus** = blood, urine or CSF antigen for cryptococcus; very high opening pressure; positive India Ink Stain
- Vasculitis, syphilis, neoplasms, demyelinating syndromes = very high protein

#### **14) What are Gram's Stain Characteristics of Selected Meningeal Pathogens:**

- a. Staphylococci
- b. Strep. Pneumoniae
- c. Listeria monocytogenes
- d. Neisseria meningitidis
- e. Haemophilus influenzae
- f. Escherichia coli
- g. Pseudomonas aeruginosa



**TABLE 99.2**

**Gram's Stain Characteristics of Selected Meningeal Pathogens**  
**PATHOGEN TYPICAL CHARACTERISTICS**

- **Staphylococci** Gram-positive cocci: Singles, doubles, tetrads, clusters
- **Streptococcus pneumoniae** Gram-positive cocci: Paired diplococci
- **Other streptococci** Gram-positive cocci: Pairs and chains
- **Listeria monocytogenes** Gram-positive rods: Single or chains
- **Neisseria meningitidis** Gram-negative cocci: Negative paired diplococci; kidney or coffee bean appearance
- **Haemophilus influenzae** Gram-negative coccobacilli: "Pleomorphic" bacilli
- **Enterobacteriaceae (including Escherichia coli)** Gram-negative rods
- **Pseudomonas aeruginosa** Gram-negative rods

**15) What are the antimicrobial therapies recommended for presumed bacterial meningitis in the following age groups/populations:**

"Early initiation of antimicrobial therapy should not be delayed pending an LP. The algorithmic alternatives are:

- (1) immediate LP followed by initiation of antibiotic treatment before obtaining the results, or
- (2) initiation of antibiotic treatment followed by a head CT scan and then an LP.
- (3) a third option could be considered: antibiotics and no LP despite an unremarkable CT scan." [this is because a plain CT scan isn't perfect at identifying patients with increased ICP, and the patient could still herniate despite a normal CT head]. - Rosen's.

**< 1 month** (doses from Uptodate and Lexicomp Neonatal Meningitis)

- Ampicillin 300 mg/kg/**day** divided every 6 hours
- Cefotaxime 150 mg/kg/**day** divided every 8 hours
- Gentamicin 4 to 5 mg/kg/dose every 24 hours

**1 month – 2 yrs**

- Vancomycin (15 mg/kg/dose every 6 hours)
- Third generation cephalosporin (Ceftriaxone 100 mg/kg per day IV)

**2 yrs – 50 yrs**

- Vancomycin (15 mg/kg/dose every 6 hours)
- Third generation cephalosporin (Ceftriaxone 100 mg/kg per day IV)

**> 50 yrs**

- Ceftriaxone 2 g IV
- Vancomycin 15 mg/kg IV
- Consider ampicillin 100 mg/kg if concerned about Listeria (elders)



If allergic to penicillins / cephalosporins:

- Meropenem 2 g IV
- Vancomycin 15 mg/kg IV

#### Head trauma:

Basilar skull fracture

- Vancomycin plus a third-generation cephalosporin

Penetrating trauma

- Vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem

#### Post neurosurgery

- Vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem

#### CSF shunt

- Vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem

### 16) Describe the management of suspected bacterial meningitis? What is the evidence supporting the use of corticosteroids in bacterial meningitis? When should it be given?

See question 15 for ABX options!

**The evidence is poor for steroids in adult bacterial meningitis, but Rosen's recommends it. Don't use steroids in children though** (unless perhaps the child is unvaccinated and *S. pneumoniae* is highly suspected).

**“In adult bacterial meningitis, an absolute risk reduction of 10% for unfavorable outcome is seen when dexamethasone is given either 15 minutes before or concomitantly with antibiotics and continued for 4 days at 6-hour intervals.** This benefit is greatest in those with *S. pneumoniae*. Despite uncertainty from conflicting trials, we recommend an initial dose of dexamethasone 10 mg IV prior to or concurrent with empirical antibiotics in patients with suspected community acquired meningitis and without signs of septic shock. Given the potential adverse effects of high dose corticosteroids in patients with septic shock, the use of low dose hydrocortisone at 50 mg IV instead of high dose dexamethasone is a reasonable approach, although clear benefit has not be demonstrated.

In pediatric meningitis, the evidence supporting adjunctive dexamethasone is even less compelling. Invasive Hib and pneumococcal infections have drastically been reduced by vaccination. Consequently, we do not recommend adjunctive dexamethasone at this time in the treatment of pediatric meningitis.” - Rosen's 9th Ed.



## 17) For whom is chemoprophylaxis indicated in bacterial meningitis? What is an appropriate regimen?

“The reported attack rate for close contacts of patients with sporadic meningococcal disease is approximately 4 in 1000 persons exposed (0.4 percent), which is 500 to 800 times higher than the general population” - UptoDate 2017

“In addition, these contacts should be advised to watch for fever, sore throat, rash, or any symptoms of meningitis. They should be hospitalized with appropriate IV antimicrobial therapy if there are signs that active meningococcal disease is developing, because rifampin is ineffective against invasive meningococcal disease.”

**Here are the CLOSE CONTACT\* groups:** Chemoprophylaxis is only for meningococcus (*N. meningitidis*) and Hib meningitis^ (NOT pneumococcal meningitis)

1. Household contacts with confirmed cases of meningococcus
2. Intimate, non-household contacts with mucosal exposure to oral secretions
3. Health care workers with DIRECT mucosal contact with patients secretions:
  - a. Mouth-to-mouth resuscitation
  - b. Intubation
  - c. Nasotracheal suctioning

“Although "close contact" has not been clearly defined, it generally refers to individuals who have had prolonged (>8 hours) contact while in close proximity (<3 feet) to the patient or who have been directly exposed to the patient's oral secretions during the seven days before the onset of the patient's symptoms and until 24 hours after initiation of appropriate antibiotic therapy” - UPTODATE

^Rifampin prophylaxis for the contacts of patients with Hib meningitis is recommended for nonpregnant household contacts when there are children younger than 4 years old in the household (adults, 600 mg by mouth; children, 20 mg/kg by mouth daily for 4 days).

**Recommended chemoprophylaxis regimens for protection against meningococcal disease – Advisory Committee on Immunization Practices (ACIP), United States, 2012**

Drug	Age group	Dose	Duration and route of administration*
Rifampin ¶	Children aged <1 month	5 mg/kg every 12 hours	Two days
	Children aged ≥1 month	10 mg/kg every 12 hours	Two days
	Adults	600 mg every 12 hours	Two days
Ciprofloxacin Δ	Adults	500 mg	Single dose
Ceftriaxone	Children age <15 years	125 mg	Single IM dose
Ceftriaxone	Adults	250 mg	Single IM dose

IM: intramuscular.

\* Oral administration unless indicated otherwise.

¶ Rifampin is not recommended for pregnant women because the drug is teratogenic in laboratory animals. Because the reliability of oral contraceptives might be affected by rifampin therapy, consideration should be given to using alternative contraceptive measures while rifampin is being administered.

Δ Ciprofloxacin is not generally recommended for persons aged <18 years or for pregnant and lactating women because the drug causes cartilage damage for immature laboratory animals. However, ciprofloxacin may be used for chemoprophylaxis of children when no acceptable alternative therapy is available. A review identified no reports of irreversible cartilage toxicity or age-associated adverse events in children and adolescents<sup>[1]</sup>.

**\*\*ciprofloxacin-resistant *N. meningitidis* in has been described....**





## Wisecracks

### 1) What percentage of patients have classic presentation of meningitis? (Fever, nuchal rigidity, change in mental status)

Only 44% of pts in one study had the classic triad. [15509818](#) (PMID)

“The constellation of symptoms that may classically occur in an acute CNS infection consists of fever, headache, photophobia, nuchal rigidity, lethargy, malaise, altered sensorium, seizures, vomiting, and chills.

**However, good quality literature suggests that the absence of fever, stiff neck, and mental status change excludes meningitis in immunocompetent adults.**

A systematic review of prospective data **in children found clinical factors useful in increasing the likelihood of bacterial meningitis included bulging fontanel, neck stiffness, and seizures in children outside the age typical for febrile convulsions.** No combination of factors have been identified that rule in or rule out the disease, which is not surprising given the diversity of presentations in children.”

**“Petechiae and cutaneous hemorrhages are widely reported with meningococemia but also occur with Hib, pneumococcal organisms, L. monocytogenes, and echovirus infections, in addition to staphylococcal endocarditis.”**

### 2) What are 3 atypical presentations of meningitis?

- The geriatric or immunosuppressed population:
  - Isolated altered mental status
- Fungal meningitis:
  - h/a, low fever, lassitude, weight loss
- TB meningitis
  - Vague nonspecific symptoms, fever, night sweats, malaise

### 3) What is Kernig’s sign? What is Brudzinski’s sign?

**These are not very reliable tests...**

A well-designed prospective study until a 2002 report of 297 patients with suspected meningitis done found When meningitis was defined as  $\geq 6$  white cells/microL of cerebrospinal fluid (CSF), **the sensitivity was extremely low (5 percent for each sign and 30 percent for nuchal rigidity)**; the specificity was 95 percent for each sign and 68 percent for nuchal rigidity. Neither Kernig nor Brudzinski signs performed much better among the 29 patients with moderate meningeal inflammation or the four patients with severe meningeal inflammation, defined as  $\geq 100$  and  $\geq 1000$  white cells/microL, respectively. Nuchal rigidity was present in all four patients with severe meningeal inflammation but had a specificity of only 70 percent. (compiled from Uptodate).





See: <https://www.ncbi.nlm.nih.gov/pubmed?term=12060874>

**However, in kids these signs may be MORE reliable than adults....Rosen’s states:** “On the other hand, at least in children, the 2010 National Institute for Health and Clinical Excellence guidelines found that 85% to 95% of children with meningitis had fever, 66% had Brudzinski’s sign, 53% had Kernig’s sign or neck stiffness, and 83% had at least one of the three objective findings.”

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**Signs of meningeal irritation**

Signs of meningeal irritation	Maneuver	Positive test
Kernig sign	Place patient supine with hip flexed at 90 degrees. Attempt to extend the leg at the knee.	The test is positive when there is resistance to extension at the knee to >135 degrees or pain in the lower back or posterior thigh.
Brudzinski sign	Place patient in the supine position and passively flex the head toward the chest.	The test is positive when there is flexion of the knees and hips of the patient.
Jolt accentuation of headache	Patient rotates his/her head horizontally two to three times per second.	The test is positive if the patient reports exacerbation of his/her headache with this maneuver.

Graphic 82677 Version 4.0

**The Jolt Accentuation test isn’t amazing either...**sensitivity varies depending on the study, one review reported it as high as 97%, however recurrent validation studies found it less promising at 21-60% sensitive...therefore the absence of jolt accentuation of headache cannot exclude the possibility of meningitis in adults.

**4) What are five typical bacterial pathogens for purulent meningitis in the following age groups/populations:**

- a. < 1 month
  - i. GEL: (Gonorrhea/E.Coli/Listeria)
- b. 1 month – 2 yrs
  - i. Strep. Pneumo (Most Common / Neisseria / H. Flu / Listeria / E.Coli)
- c. 2 yrs – 50 yrs
  - i. Neisseria / Strep Pneumo / H. Flu / Listeria / E.coli
- d. > 50 yrs
  - i. Same as above, emphasize Listeria and Strep
- e. Post neurosurgery & Head trauma: basilar skull fracture, penetrating trauma
  - i. The usual plus MRSA / MSSA / Pseudomonas
- f. CSF shunt
  - i. Add GI bugs if VP shunt

**5) Provide the differential diagnosis of a ring-enhancing lesion.**

**The differential for peripheral or ring enhancing cerebral lesions includes:**

- Cerebral abscess
- Tuberculoma
- Neurocysticercosis
- Metastasis



Glioblastoma  
Subacute infarct /haemorrhage /contusion  
Demyelination (incomplete ring)  
Tumefactive demyelinating lesion (incomplete ring)  
Radiation necrosis  
Postoperative change  
Lymphoma - in an immunocompromised patient

A helpful mnemonic is MAGIC DR

**6) What is the schedule for pneumococcal vaccination (conjugated vaccine) in healthy children? Which strains of n. meningitidis are covered by the meningococcal vaccine?**

See: <https://www.canada.ca/en/public-health/services/provincial-territorial-immunization-information/provincial-territorial-routine-vaccination-programs-infants-children.html>

For your provincial plan!

Pneumococcal: Pneu-C-13 [Pneumococcal](#) conjugate (13-valent) vaccine Age: **2, 4, 12 months** (BC + AB)

Men-C-C [Meningococcal](#) conjugate (Strain C) vaccine Age:

- 2, 12 months Age (BC):
- 4, 12 months (AB)