

MEDICINE

432 Team

45 CNS Infections



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COLOR GUIDE: • Females' Notes • Males' Notes • Important • Additional

Objectives

1. Definitions
2. Causes of Meningitis
3. Aseptic Meningitis
4. Bacterial Meningitis
5. Listeria Monocytogenes
6. Brain Abscess
7. Subdural Empyema

Definitions

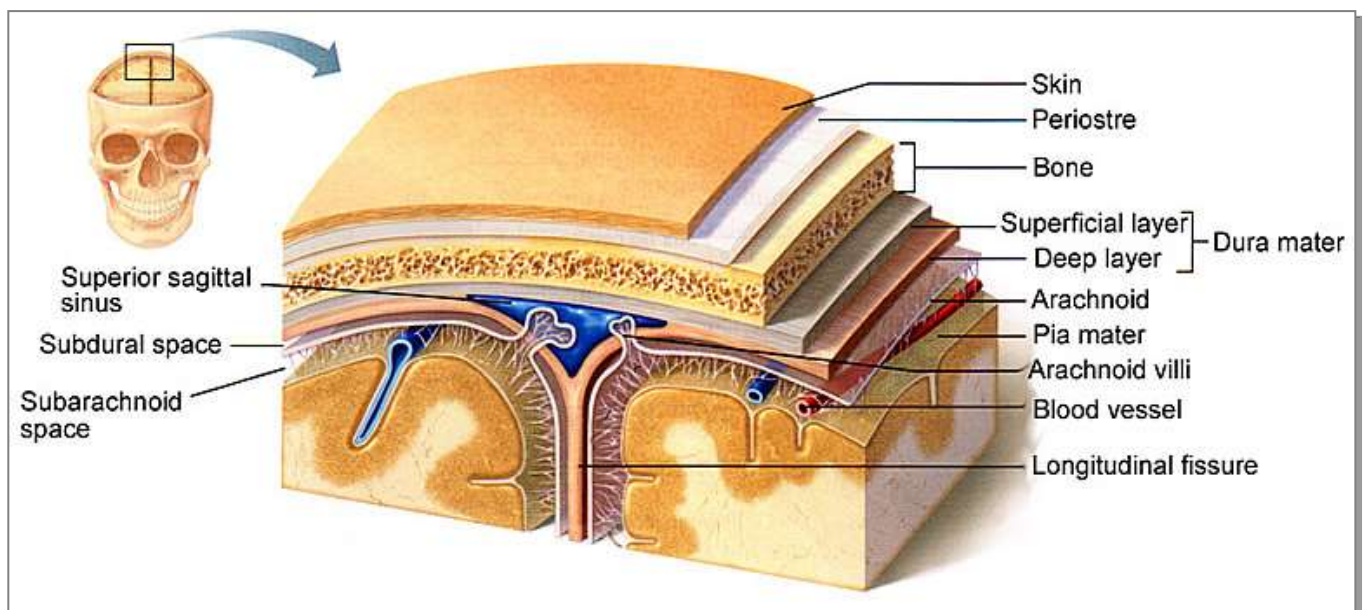
Meninges: The meninges are three layers of protective tissue called the dura mater, arachnoid mater, and pia mater that surround the neuraxis. The meninges of the brain and spinal cord are continuous, being linked through the magnum foramen⁽¹⁾.

Meningitis: inflammation of the meninges. (pia mater, arachnoid and surrounding CSF)

Encephalitis: infection of the brain parenchyma.

Meningoencephalitis: inflammation of the brain parenchyma and meninges.

Aseptic meningitis: inflammation of the meninges with sterile CSF (-ve culture).



http://www.corpshumain.ca/en/images/Neuro_Meninges_F_en.jpg

Causes of Meningitis

Infectious	Non-infectious
Viral	Aseptic meningitis
Bacterial	Malignancy
Mycobacterial	Sarcoid
Brucella	Behcet disease
Fungal	SLE

Encephalitis and encephalopathy: “External information”

Encephalitis is inflammation of the brain. Viral infections are the most common cause of the condition ⁽²⁾. A common cause of sporadic encephalitis is **herpes simplex virus type 1**. Uncommon causes include varicella-zoster virus, Epstein-Barr virus, HIV, and human herpes virus-6⁽³⁾.

Clinical features: acute onset of headache, fever, focal neurological signs (aphasia and/or hemiplegia, visual field defects) and seizures ⁽⁴⁾.

Encephalopathy is a broad term used to describe abnormal brain function or brain structure. The abnormality may be transient, recurrent, or permanent. The loss of brain function may be reversible, static and stable, or progressive with increasing loss of brain activity over time ⁽⁵⁾. The major symptom of encephalopathy is an altered mental state. The causes of encephalopathy are numerous and varied; they include infections, anoxia, metabolic problems, toxins, drugs, physiologic changes, trauma, and other causes⁽⁶⁾.

MENINGITIS VERSUS ENCEPHALITIS: The presence or absence of normal brain function is the important distinguishing feature between encephalitis and meningitis. Patients with meningitis may be uncomfortable, lethargic, or distracted by headache, but their cerebral function remains normal. In encephalitis, however, abnormalities in brain function are expected, including altered mental status, motor or sensory deficits, altered behavior and personality changes, and speech or movement disorders. Seizures and postictal states can be seen with meningitis alone and should not be construed as definitive evidence of encephalitis ⁽³⁾.

Aseptic Meningitis

Definition: The term aseptic meningitis refers to patients who have clinical and laboratory evidence for meningeal inflammation with negative routine bacterial cultures⁽⁶⁾.

Causes ⁽⁸⁾:

Common causes: Enteroviruses (most common 80 %), Mumps virus, Herpes Simplex subtype 2, and Epstein-Barr virus.

Rare causes: Lymphocytic Choriomeningitis, HIV, and West Nile virus.

Clinical signs and symptoms ⁽⁸⁾:

Prodromal phase: Fever, malaise, and sore throat.

Meningeal phase: Headache, photophobia, and drowsiness.

Signs: Neck stiffness, Kernig's sign, skin rashes, myalgia, with/without diarrhea.

Investigations ⁽⁸⁾:

- ✓ **CSF analysis:** elevated cell count (lymphocytes or monocytes) with normal glucose and protein.
- ✓ **PCR detection of viral DNA/RNA in the CSF is diagnostic.**
- ✓ **Virus culture from throat swab or stool.**

Treatment: Treatment is needed for fungal or mycobacterial causes of aseptic meningitis. Herpes virus or varicella (chickenpox) virus may be treated with antiviral medicines. Treatment for noninfectious causes consists of pain medications and managing complications, if they occur.

No specific treatment is available for enteroviral or most other viral forms of aseptic meningitis ⁽⁹⁾.

If somebody was on oral Abx presented to you with meningitis then you do CSF and find it –ve culture you have to think of Aseptic meningitis

Bacterial Meningitis

Overview:

In most of the cases the infection causing meningitis arises in the nasopharynx; intravascular invasion (bacteremia) and penetration of the blood-brain barrier follow mucosal involvement with entry into the CSF ⁽⁸⁾.

Causative organisms ⁽⁴⁾ ⁽⁸⁾:

In neonates: Gram-negative bacilli, E.coli, Haemophilus Influenza.

In adults: Streptococcus Pneumonia, Neisseria Meningitis.

In children: Haemophilus Influenza, Streptococcus Pneumonia, Neisseria Meningitis.

Clinical signs and symptoms ⁽⁴⁾ ⁽⁸⁾:

Prodromal features: respiratory infection, otitis media or pneumonia associated with muscle pain.

Meningitic symptoms: Severe frontal/occipital headache, photophobia, altered consciousness and rash.

Signs: neck stiffness and Kernig's sign.

Note: absence of all three signs of classical triad of meningitis which are

-Fever

-Stiff neck

-Changes in mental status (more common in bacterial than viruses) - ((Makes the diagnosis – of meningitis unlikely))

Investigations ⁽⁴⁾⁽⁸⁾:

1. If the patient has altered consciousness, or was drowsy, or has undergone recent neurological surgery = **obtain CT scan to exclude mass lesion.**
2. If the above signs were absent, confirm the diagnosis by **lumbar puncture.**
3. **However, don't delay treatment, take blood cultures and start the antibiotics prior to scanning.**

ABNORMAL FINDINGS OF CSF IN SOME PATHOLOGICAL CONDITIONS			
Parameter	Condition		
	Bacterial Meningitis (pyogenic)	Tuberculous Meningitis	Viral Meningitis
Appearance	Often turbid	Often fibrin web	Usually clear
Predominant cell	Polymorphs	Mononuclear	Mononuclear
Cell count/mm³	90-1000+	10-1000	50-1000
Bacteria	In smear & culture	Often none in smear	None seen or cultured
Protein (0.15-0.45 g/L)	>1.5 (↑ ↑)	1-5 (↑ ↑)	<1 (Normal)
Glucose (2.8-4.2 mmol/L)	<1/2 plasma (↓ ↓)	<1/2 plasma (↓ ↓)	>1/2 plasma (Normal or slightly ↓)
Chlorides (115 - 130 mmol/L)	↓↓	↓↓	Normal or ↓

http://ksumsc.com/download_center/Archive/2nd/432/01%20CNS%20BLOCK/432%20Teams%20Work/Biochemistry/lecture-

Emergency Department Empiric Therapy for Adults With Suspected Bacterial Meningitis

Intravenous Therapy	Adults Age <50	Adults Age ≥50
Third-Generation Cephalosporin	Ceftriaxone 2 g IV or cefotaxime 2 g IV	Ceftriaxone 2 g IV or cefotaxime 2 g IV
Ampicillin (coverage for <i>Listeria</i>)	Not recommended*	Ampicillin 2 g IV
Vancomycin (coverage for resistant <i>S. pneumoniae</i>)	Vancomycin 1 g IV	Vancomycin 1 g IV
Dexamethasone (given before or with antibiotics)	Dexamethasone 10 mg IV	Dexamethasone 10 mg IV

*Consider coverage with ampicillin in patients younger than 50 who have additional risk factors such as alcohol abuse, immunodeficiencies, or CSF leak.

Note: Providers should use local resistance data and infection patterns to guide antibiotic choices, which may differ from these general guidelines.

Source: Dr. Michael T. Fitch

ACEP

<http://www.acep.org/Clinical---Practice-Management/Focus-On--Meningitis---Beyond-Fever,-Stiff-Neck,-and-Altered-Mental-Status/>

Table 4. Recommendations for Antimicrobial Therapy for Pathogen-Specific Acute Meningitis

Microorganism	First Choice ^a	Alternative Agents ^a
<i>Streptococcus pneumoniae</i>	Vancomycin plus ceftriaxone or cefotaxime	Meropenem, fluoroquinolone
<i>Neisseria meningitidis</i>	Ceftriaxone or cefotaxime	Penicillin G, ampicillin, fluoroquinolones, aztreonam
GBS (<i>Streptococcus agalactiae</i>)	Ampicillin or penicillin G +/- aminoglycoside	Cefotaxime or ceftriaxone
<i>Listeria monocytogenes</i>	Ampicillin or penicillin G +/- aminoglycoside	Meropenem
<i>Haemophilus influenzae</i>	Ceftriaxone or cefotaxime	Chloramphenicol, cefepime, meropenem, fluoroquinolone
<i>Staphylococcus aureus</i> : Methicillin-sensitive Methicillin-resistant	Nafcillin or oxacillin Vancomycin +/- rifampin	Vancomycin, meropenem, linezolid, daptomycin Trimethoprim-sulfamethoxazole, linezolid, daptomycin
Enterococcus: Ampicillin-sensitive Ampicillin-resistant Vancomycin-resistant	Ampicillin + gentamicin Vancomycin +/- rifampin Linezolid	NA NA NA
<i>Escherichia coli</i> and other <i>Enterobacteriaceae</i>	Ceftriaxone or cefotaxime	Cefepime, meropenem, fluoroquinolone, trimethoprim-sulfamethoxazole, aztreonam
<i>Pseudomonas aeruginosa</i>	Ceftazidime or cefepime +/- aminoglycoside	Aztreonam, fluoroquinolone, meropenem +/- aminoglycoside

*Note: Choice of specific antimicrobial should be guided by in vitro susceptibility information, once available.
GBS: group B streptococcus; NA: not applicable.
Source: References 1, 12.*

http://www.uspharmacist.com/continuing_education/ceviewtest/lessonid/108112/

Prevention and vaccines:

- Vaccines are available for most meningococcal subgroups except group B ⁽⁴⁾.
- **Chemoprophylaxis:** Close contacts of patients with meningococcal infection should be given 2 days of **oral rifampicin**. In adults, a single dose of **ciprofloxacin** is an alternative.

vaccines	for
NEW Haemophilus influenzae type b (Hib) vaccine	Haemophilus influenzae type b (Hib) bacterium, a leading cause of bacterial meningitis in children . In routine childhood immunization , greatly reduced cases of this type of meningitis.
Pneumococcal polysaccharide vaccine (PPSV)	for older children and adults
Meningococcal conjugate vaccine	requirement for people going to Hajj.

http://ksumsc.com/download_center/Archive/2nd/432/01%20CNS%20BLOCK/432%20Teams%20Work/Pharmacology/L%289%29menineitis.pdf

Listeria Monocytogenes

Listeria Monocytogenes is an important bacterial pathogen in neonates, immunosuppressed patients, older adults, pregnant women, and, occasionally, previously healthy individuals. The most common central nervous system manifestation of listerial infection is Meningoencephalitis. The clinical presentation of Listeria Meningoencephalitis ranges from a mild illness with fever and mental status changes to a fulminant course with coma⁽¹⁰⁾.

Routes of transmission: **mainly food borne, transplacental/ vertical, cross contamination (nursery), inoculation (skin) farmers.** Treated with IV Ampicillin.

Brain Abscess

Organisms: **Streptococci (60-70%)**, Bacteroides (20-40%), Enterobacteriaceae (25-33%), S.Aureus (10-15%), and S.Milleri.

CT brain: If the abscess is more than 2.5cm, **then surgical drainage.** And if the patient is neurologically unstable or has decreased level of consciousness, drain regardless of the size.

Antimicrobials: empirically **Ceftriaxone** with **Metronidazole.**

Duration until response by neuroimaging.

Subdural Empyema

In adults 60-90% are extension of: Sinusitis or Otitis media.

Surgical emergency: must be drained.

Treatment: as brain abscess

SUMMARY

1. CNS infections vary from a mild self-limiting infection to a potentially fatal infection requiring emergent treatment. It can be encephalitis, meningitis or meningioencephalitis.

2. Meningitis can be:

- **Bacterial** (Cloudy CSF) or **Aseptic** (Clear CSF)
- **Acute** (Within hours to days) or **Chronic** (Within weeks to months)

3. **Aseptic meningitis:** Meaning meningitis not caused by pyogenic bacteria. The cause can be from a **non-infectious process** (Autoimmune, Drug-Induced, Neoplastic and Immune-mediated) or from an **infectious agent** (Viral, Mycobacterial, Parasitic and Fungal).

4. **Bacterial Meningitis:** Caused by bacteria inducing a pyogenic inflammatory response in the CSF.

5. **Clinical Presentation** (It may be difficult to differentiate between aseptic and bacterial clinically):

- **Symptoms:** (The **characteristic triad for Acute Bacterial Meningitis:** Fever, Nuchal Rigidity & Change in mental status). **Other Symptoms:** Photophobia, Headaches, N/V and Seizures.
- **Signs:** Rashes, Cranial nerve palsies, Kerning's sign & Brudzinski's sign (Both highly specific) and Jolt Accentuation Maneuver (100% sensitivity).
- Look for **signs and symptoms of increased ICP** (N/V, seizures, Papilledema, Ocular Palsies, Headaches, Back Pain and altered mental status).

6. Complications of Bacterial Meningitis:

- **Local:** Seizures, Coma, Brain Abscess and Subdural Empyema
- **Distant:** DIC, Respiratory Arrest, Waterhouse-Friderichsen syndrome.
- **Permanent:** CNS palsies (Deafness), Hydrocephalus and Brain Damage.

7. **Investigations:** Routine blood work, Blood culture (Before Antibiotics), CXR, Head CT and CSF Examination (LP).

8. **CSF findings in bacterial meningitis** show a pyogenic inflammatory response: Cloudy appearance, Elevated WBC count (PMNs), low glucose, high protein and positive gram stain.

Findings in **Aseptic meningitis** show a non-pyogenic response: Lymphocytic pleocytosis, normal or slightly elevated protein, normal glucose, CSF appears normal (May be positive in: serology, PCR, AFB smear or culture)

9. **Organisms in Acute Bacterial Meningitis:** (The most common cause of meningitis is Strept. Pneumoniae)

- **Neonates:** Group B strept., E.coli, Listeria Monocytogenes
- **Infants & Children:** N. meningitidis, Strept. Pneumoniae and H. Influenza.
- **Adults:** Strept. Pneumoniae, N. meningitidis and H. Influenza.
- **Elderly:** Strept. Pneumoniae, N. meningitidis and Listeria.

10. The **Empiric Treatment** for Bacterial Meningitis = **Dexamethasone + 3 Antibiotics** (Ceftriaxone, Ampicillin & Vancomycin).

11. The **most common cause of Encephalitis is HSV**. It is diagnosed by **PCR** and treated with **Acyclovir** (2-3 weeks).

12. A **Brain Abscess** is mostly caused by **Streptococci**. A **subdural empyema** requires **emergent** drainage. Both are treated with the same Antibiotics (Metronidazole and Ceftriaxone).

13. **Meningococcal Meningitis:** Meningitis caused by **N. Meningitidis** (Gram -Ve diplococcic). Purpura rashes are classic for Meningococcal meningitis. Transmissible by throat and respiratory secretions. **Tx:** Ceftriaxone.

14. **Pneumococcal meningitis:** The most common cause of meningitis is **Strept. Pneumoniae** (Gram +ve diplococcic). It has the highest mortality rate (20-30%). **Tx:** Ceftriaxone, Penicillin G or Vancomycin.

15. Only **Listeria and TB** meningitis cause **6Th Cranial Nerve Palsy**. **Listeria** is most commonly food borne (bowls) and is common in elderly, neonatal and immunocompromised (70%) patients. **Tx:** Ampicillin. **TB Meningitis** gives CSF a xanthochromic appearance. **Tx:** isoniazid, rifampicin, pyrazinamide and streptomycin.

16. **Brucella** species are common in shepherders. Detected by PCR or culture. **Tx:** Doxycycline, Rifampin, TMP-SMX.

IMPORTANT NOTES FROM EXTERNAL RESOURCES

Notes

- | | |
|------|---|
| (1) | http://www.csuchico.edu/~pmccaffrey//syllabi/CMSD%20320/362unit3.html |
| (2) | http://www.mayoclinic.org/diseases-conditions/encephalitis/basics/definition/con-20021917 |
| (3) | http://www.uptodate.com/contents/viral-encephalitis-in-adults#H4 |
| (4) | Davidson's Principles and Practice of Medicine, 22 nd edition, Neurological diseases chapter. |
| (5) | http://www.emedicinehealth.com/encephalopathy/article_em.htm |
| (6) | http://www.medicinenet.com/encephalopathy/article.htm |
| (7) | http://www.uptodate.com/contents/aseptic-meningitis-in-adults |
| (8) | Neurology and Neurosurgery Illustrated, 5 th edition, Multifocal Neurological Disease and its Management. |
| (9) | http://www.nytimes.com/health/guides/disease/aseptic-meningitis/overview.html#Treatment |
| (10) | http://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-listeria-monocytogenes-infection |

Questions

1) A 35-year-old Patient walked into the ER with a 3-day history of neck stiffness and fever. The patient appeared to be disoriented and soon lost consciousness. You need to order a LP to confirm bacterial meningitis as the diagnosis. You were informed that the procedure was delayed several hours. What is your next step?

- A. Order a blood culture to confirm diagnosis.
- B. Wait for LP.
- C. Treat for Bacterial Meningitis until LP can be obtained.
- D. A&B

2) The characteristic triad of symptoms in acute bacterial meningitis is:

- A. Malaise, photophobia and back pain
- B. Fever, photophobia and headaches.
- C. Fever, alteration in mental status and neck stiffness.
- D. Headaches, nausea and vomiting.

432 Medicine Team Leaders

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Answers:

1st Questions: C

2nd Questions: C