

INTERNAL MEDICINE MENINGITIS AND ENCEPHALITIS

BY

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Introduction

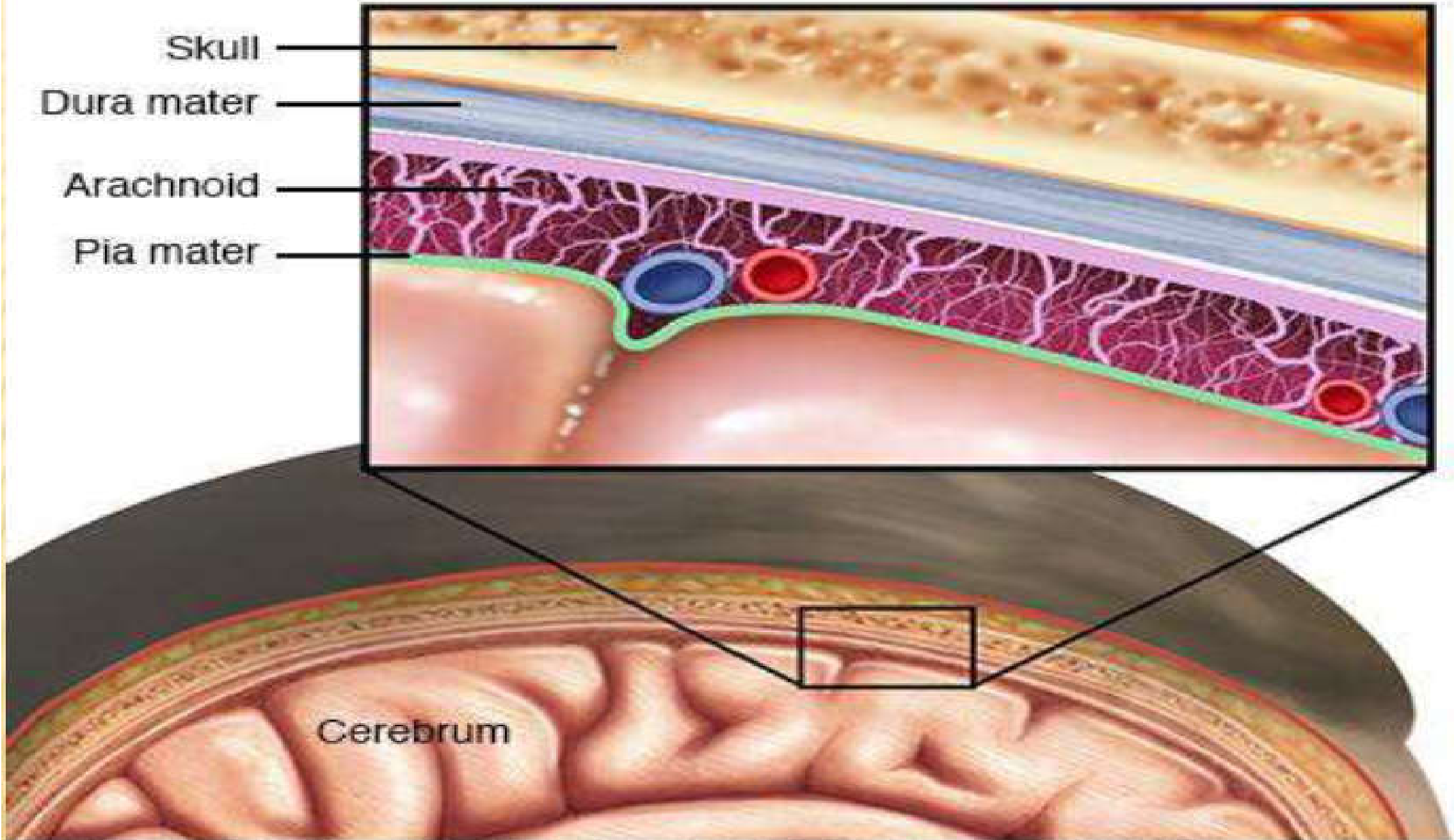
- Central nervous system infections are classified into 2 major groups:
 1. Meningitis → which is the infection of the protective layers of the brain
 2. Encephalitis → which is the infection of the parenchyma of the brain
- The clinical features of nervous system infections depend on
 1. **The location of the infection** (the meninges or the parenchyma of the brain and spinal cord)
 2. **The causative organism** (virus, bacterium, fungus or parasite)
 3. **Whether the infection is acute or chronic.**

MENINGITIS

- Introduction
- Types and causes of meningitis
 1. Bacterial meningitis
 2. Viral meningitis
 3. Fungal meningitis
 4. Tuberculosis meningitis (next seminar)
 5. Aseptic meningitis
 6. Malignant meningitis
- Clinical features of meningitis
- Diagnosis
- Management

MENINGITIS → Introduction

- The brain is covered by 3 protective layers: Dura matter, arachnoid matter and pia matter
- **Meningitis is inflammation of the leptomeningeal layers (pia and inner surface of arachnoid mater) and pachymeningeal layer (the outer surface of arachnoid matter and dura matter)**
- Meningitis can be classified according to the cause to:
 1. **Bacterial meningitis**
 2. **Viral meningitis**
 3. **Fungal meningitis**
 4. **Tuberculosis meningitis**
 5. **Non-infective meningitis (Aseptic meningitis)**
 6. **Malignant meningitis**



MENINGITIS → **Viral meningitis**

- **Viruses are the most common cause of meningitis**, usually resulting in a benign and self-limiting illness requiring no specific therapy.
- It is much less serious than bacterial meningitis unless there is associated encephalitis (which is rare).
- Viruses that might be causative organisms:
 1. **Enteroviruses (echo, Coxsackie, polio) → The most common viruses that cause viral meningitis**
 2. **Mumps → The most common cause in state of unimmunization**
 3. Influenza
 4. Herpes simplex
 5. Varicella zoster
 6. Epstein–Barr
 7. HIV
 8. Lymphocytic choriomeningitis
 9. Herpes simplex virus type 2 → Mollaret's meningitis

- **Age group** → Viral meningitis occurs mainly **in children or young adults**.
- **Pathology** →
- Predominant lymphocytic infiltration for subarachnoid space with pus formation and adhesions.
- **There is no or little cerebral edema unless encephalitis develops.**
- **N.B** → Meningitis may also occur as a complication of a systemic viral infection such as mumps, measles, infectious mononucleosis, herpes zoster and hepatitis.

MENINGITIS

→ Bacterial meningitis

- Many bacteria can cause meningitis, but geographical patterns vary, as does age-related sensitivity.

Age group	Common bacteria	Less common bacteria
Neonates	Gram-negative bacilli (Escherichia coli, Proteus) Group B streptococci	Listeria monocytogenes
Preschool	Haemophilus influenzae Neisseria meningitidis Streptococcus pneumoniae	Mycobacterium tuberculosis
Older children and adults	Neisseria meningitidis Streptococcus pneumoniae	Listeria monocytogenes Mycobacterium tuberculosis Staphylococcus aureus (skull fracture) Haemophilus influenzae

- **Streptococcus pneumoniae(pneumococcus)** → This bacterium is the most common cause of bacterial meningitis in infants, young children and adults in the United States. It more commonly causes pneumonia or ear or sinus infections. A vaccine can help prevent this infection.
- **Neisseria meningitidis(meningococcus)** → This bacterium is another leading cause of bacterial meningitis. These bacteria commonly cause an upper respiratory infection but can cause meningococcal meningitis when they enter the bloodstream. This is a highly contagious infection that affects mainly teenagers and young adults. A vaccine can help prevent infection.
- **Haemophilus influenzae(haemophilus)** → Haemophilus influenzae type b (Hib) bacterium was once the leading cause of bacterial meningitis in children. But new Hib vaccines have greatly reduced the number of cases of this type of meningitis.
- **Listeria monocytogenes(listeria)** → These bacteria can be found in unpasteurized cheeses, hot dogs and lunchmeats. Pregnant women, newborns, older adults and people with weakened immune systems are most susceptible. Listeria can cross the placental barrier, and infections in late pregnancy may be fatal to the baby.

- **Pathology** →

- The infection stimulates an immune response, causing the pia– arachnoid membrane to become **congested and infiltrated with inflammatory cells (mainly neutrophils)**. Pus then forms in layers, which may later organize to form adhesions.

- **These may obstruct the free flow of CSF, leading to hydrocephalus**, or they may damage the cranial nerves at the base of the brain. Hearing loss is a frequent complication.

- **The CSF pressure rises rapidly, the protein content increases.**

- **Mode of transmission** →

- Bacterial meningitis is usually part of a **bacteremic illness** (the bacteria reaches CSF indirectly through the blood) **or direct spread from an adjacent focus of infection** in the ear (otitis media) or nasopharynx and sinuses (sinusitis), **skull fracture (trauma), congenital malformations or iatrogenically during intracranial manipulation.**

MENINGITIS → **Fungal meningitis**

- Fungal meningitis is relatively uncommon **and usually causes chronic meningitis** but it may mimic acute bacterial meningitis. Fungal meningitis isn't contagious from person to person.
- **Fungal meningitis usually occurs in patients who are immunosuppressed** and is a recognised complication of HIV infection.
- **Most common fungi that cause meningitis:**
 - Cryptococcus neoformans (most common)
 - Candida albicans
 - Coccidioides immitis, Histoplasma capsulatum, Blastomyces dermatitidis

MENINGITIS → Malignant meningitis

- **Carcinomatous meningitis** is the dissemination of malignant cells from the primary tumor sites to leptomeningeal layers of the CNS. It occurs in the advanced stage of any cancer, solid as well as hematological malignancies.
- **The most common tumors to cause malignant meningitis:**
 1. **Breast cancer**
 2. **Bronchial cancer**
 3. **Leukemia**
 4. **Lymphoma**

MENINGITIS → Aseptic meningitis

- **Aseptic meningitis** is the inflammation of the meninges in patients whose CSF test result is negative with routine bacterial cultures. Aseptic meningitis is caused by viruses (most commonly), mycobacteria, spirochetes, fungi, medications, inflammatory diseases (SLE, Behçet's disease or sarcoidosis) and cancer malignancies.
- When the cause of aseptic meningitis is discovered, the disease can be reclassified according to its etiology. **If appropriate diagnostic methods are performed, a specific viral etiology is identified in 55-70% of cases of aseptic meningitis.**

MENINGITIS → Clinical features

- Acute infection of the meninges presents with a triad of pyrexia, headache and meningism.
- Meningism consists of headache, photophobia and stiffness of the neck, often accompanied by other signs of meningeal irritation, including Kernig's sign (extension at the knee with the hip joint flexed causes spasm in the hamstring muscles) and Brudzinski's sign (passive flexion of the neck causes flexion of the hips and knees).
- Meningism is not specific to meningitis and can occur in patients with subarachnoid haemorrhage.



Positive Kernig's sign and Brudzinski's sign

Clinical features → Bacterial meningitis

- **Headache, drowsiness, fever and neck stiffness are the usual presenting features.**
- In severe bacterial meningitis the patient may be comatose and later there may be focal neurological signs.
- Ninety percent of patients with meningococcal meningitis will have two of the following: fever, neck stiffness, altered consciousness and rash.
- When accompanied by septicemia, it may present very rapidly, with abrupt onset of obtundation (reduced level of alertness or consciousness) due to cerebral oedema
- **Generally, if the bacterial meningitis is left untreated, the most important complications that might develop is cerebral edema with increased intracranial pressure (can be detected with fundoscopy which shows papilledema) and bacterial encephalitis.**

- **In meningococcal meningitis** there is rash (morbilliform, petechial or purpuric)
- **In pneumococcal and Haemophilus infections** there may be an associated otitis media.
- **Pneumococcal meningitis** may be associated with pneumonia
- **Listeria monocytogenes** is an increasing cause of meningitis and rhombencephalitis (brainstem encephalitis) in the immunosuppressed, people with diabetes, alcoholics and pregnant women

- **Complications of bacterial meningitis:**

1. Deafness
2. mental retardation
3. spasticity or paresis
4. seizures.
5. Shock
6. Intravascular coagulation → DIC
7. Renal failure
8. Peripheral gangrene
9. Arthritis (septic or reactive)
10. Pericarditis (septic or reactive)

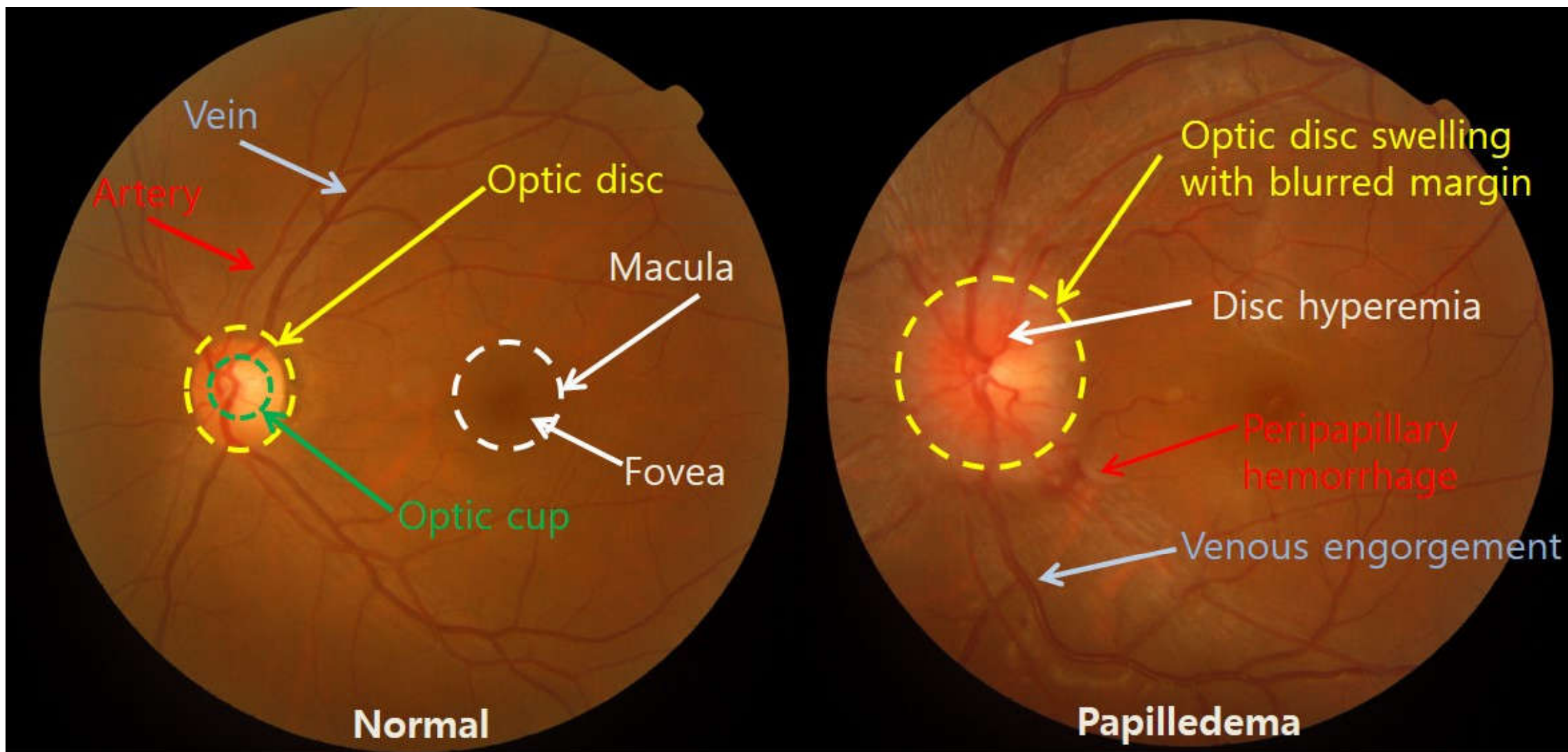


Mostly associated with meningococcal meningitis

- **Untreated bacterial meningitis has a mortality rate of 50% .**
- Even with early treatment 5-10% of the patients die within the first 24-48 hours since the onset of symptoms .
- **The mortality rate varied by organism, ranging from 3.8% for H. influenzae to 7.5% for N. meningitidis to 15.3% for S. pneumoniae.**

- **Meningococcal rash**





Clinical features → Viral meningitis

- Viral meningitis shows **acute onset of headache and irritability and the rapid development of meningism.**
- **The headache is usually the most severe feature.**
- There may be a high pyrexia but focal neurological signs are rare.
- **Complications of viral meningitis:**
 1. Seizures
 2. Encephalitis
 3. Sensorineural Deafness (mumps)
 4. Hydrocephalus
 5. Persistent cognitive deficits interfering with school/work
 6. Weakness
 7. Paralysis
 8. Cranial nerve palsy
 9. Behavior disorders

- **In summary, acute meningitis shows a triad of: Headache, fever and meningism.**
- The following findings and conditions might help in determining the causative organism:
- **Petechial rash → Meningococcal infection**
- **Skull fracture, Ear disease, congenital CNS lesion → Pneumococcal infection**
- **Immunocompromised patients → HIV and opportunistic fungal infections**
- **Rash or pleuritic pain → Enterovirus infection**
- **International travel → Malaria**

MENINGITIS → Diagnosis


- **Diagnosis is made by CSF analysis + clinical presentation.**
- CSF is collected via lumbar puncture unless there are contraindications. Three tubes are obtained, one for the chemistry lab, one for the hematology lab and one for the microbiology lab.
- **LP is contraindicated if there is any clinical suggestion of raised intracranial pressure (papilledema), depressed level of consciousness, or focal neurological signs suggesting a cerebral lesion, until imaging (by CT or MRI) has excluded a space-occupying lesion or hydrocephalus.**
- **Other laboratory tests may help in diagnosis:**
 1. Blood cultures (can support the result of CSF culture)
 2. Special studies, such as serum serology and nucleic acid amplification (PCR), may also be performed, depending on clinical suspicion of the offending organism.

LP procedure



Adult Spinal Tap Procedure Video

CSF interpretation

 26.5 How to interpret CSF results

	Normal	Subarachnoid haemorrhage	Acute bacterial meningitis	Viral meningitis	Tuberculous meningitis
Pressure	50–250 mm of water	Increased	Normal/ increased	Normal	Normal/increased
Colour	Clear	Blood-stained Xanthochromic	Cloudy	Clear	Clear/cloudy
Red cell count ($\times 10^6/L$)	0–4	Raised	Normal	Normal	Normal
White cell count ($\times 10^6/L$)	0–4	Normal/slightly raised	1000–5000 polymorphs	10–2000 lymphocytes	50–5000 lymphocytes
Glucose	> 50–60% of blood level	Normal	Decreased	Normal	Decreased
Protein	< 0.45 g/L	Increased	Increased	Normal/ increased	Increased
Microbiology	Sterile	Sterile	Organisms on Gram stain and/or culture	Sterile/virus detected	Ziehl–Nielson/auramine stain or tuberculosis culture positive
Oligoclonal bands	Negative	Negative	Can be positive	Can be positive	Can be positive

N.B → Fungal meningitis causes high increases in intracranial pressure (the hallmark of fungal meningitis → very high opening pressure)

- **Other diagnostic investigations:**
- **Sedimentation rate, antinuclear antibody, rheumatoid factor** :for autoimmune meningitis
- **VDRL, fluorescent treponemal antibody absorption test** :for syphilis (atypical bacteria)
- **Lyme titer ELISA**
- **Imaging studies: chest x-ray, CT-scan, MRI:** for tumor

MENINGITIS → Management

- **Bacterial meningitis** →
- If bacterial meningitis is suspected, **we collect 3 CSF tubes then the patient should be given parenteral benzylpenicillin immediately (intravenous is preferable) or other empirical antibiotics (in the next slide) depending on the clinical presentation/age of the patient** and prompt hospital admission should be arranged.
- Adjunctive corticosteroid therapy is useful in both children and adults → **Corticosteroids significantly reduce hearing loss and neurological sequelae**, but do not reduce overall mortality..
- **Once CSF analysis results are illustrated, we shift to the suitable antibiotic for the causative bacteria (in the next slides)**
- **In meningococcal disease**, mortality is doubled if the patient presents with features of septicemia rather than meningitis. Individuals likely to require intensive care facilities and expertise include those with cardiac, respiratory or renal involvement, and those with CNS depression prejudicing the airway. Early endotracheal intubation and mechanical ventilation protect the airway and may prevent the development of the acute respiratory distress syndrome



26.78 Treatment of pyogenic meningitis of unknown cause

1. Adults aged 18–50 yrs with or without a typical meningococcal rash

- Cefotaxime 2 g IV 4 times daily *or*
- Ceftriaxone 2 g IV twice daily

2. Patients in whom penicillin-resistant pneumococcal infection is suspected, or in areas with a significant incidence of penicillin resistance in the community

As for (1) but add:

- Vancomycin 1 g IV twice daily *or*
- Rifampicin 600 mg IV twice daily

3. Adults aged > 50 yrs and those in whom *Listeria monocytogenes* infection is suspected (brainstem signs, immunosuppression, diabetic, alcoholic)

As for (1) but add:

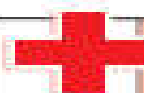
- Ampicillin 2 g IV 6 times daily *or*
- Co-trimoxazole 50 mg/kg IV daily in two divided doses

4. Patients with a clear history of anaphylaxis to β -lactams

- Chloramphenicol 25 mg/kg IV 4 times daily *plus*
- Vancomycin 1 g IV twice daily

5. Adjunctive treatment (see text)

- Dexamethasone 0.15 mg/kg 4 times daily for 2–4 days



26.79 Chemotherapy of bacterial meningitis when the cause is known

Pathogen	Regimen of choice	Alternative agents
<i>N. meningitidis</i>	Benzylpenicillin 2.4 g IV 6 times daily for 5–7 days	Cefuroxime, ampicillin Chloramphenicol*
<i>Strep. pneumoniae</i> (sensitive to β -lactams, MIC < 1 mg/L)	Cefotaxime 2 g IV 4 times daily <i>or</i> ceftriaxone 2 g IV twice daily for 10–14 days	Chloramphenicol*
<i>Strep. pneumoniae</i> (resistant to β -lactams)	As for sensitive strains but add vancomycin 1 g IV twice daily <i>or</i> rifampicin 600 mg IV twice daily	Vancomycin <i>plus</i> rifampicin* Moxifloxacin Gatifloxacin
<i>H. influenzae</i>	Cefotaxime 2 g IV 4 times daily <i>or</i> ceftriaxone 2 g IV twice daily for 10–14 days	Chloramphenicol*
<i>L. monocytogenes</i>	Ampicillin 2 g IV 6 times daily <i>plus</i> gentamicin 5 mg/kg IV daily	Ampicillin 2 g IV 4-hourly <i>plus</i> co-trimoxazole 50 mg/kg daily in two divided doses
<i>Strep. suis</i>	Cefotaxime 2 g IV 4 times daily <i>or</i> ceftriaxone 2 g IV twice daily for 10–14 days	Chloramphenicol*

*For patients with a history of anaphylaxis to β -lactam antibiotics.
(MIC = minimum inhibitory concentration)

• Prophylaxis in meningococcal infection →

- 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. If not treated with ceftriaxone, the index case should be given similar treatment to clear infection from the nasopharynx before hospital discharge.
- Vaccines are available for most meningococcal subgroups but not group B, which is among the most common serogroup isolated in many countries.

i 26.81 Chemoprophylaxis following meningococcal exposure	
Close contacts warranting chemoprophylaxis	
<ul style="list-style-type: none">• Household contacts (including persons who ate or slept in the same dwelling as the patient during the 7 days prior to disease onset)• Child-care and nursery-school contacts• Persons having contact with patient's oral secretions during the 7 days prior to disease onset<ul style="list-style-type: none">• Kissing• Sharing of toothbrushes• Sharing of eating utensils• Mouth-to-mouth resuscitation• Unprotected contact during endotracheal intubation• Aircraft contacts for persons seated next to the patient for > 8 hrs	
Persons at low risk in whom chemoprophylaxis is not recommended	
<ul style="list-style-type: none">• Casual contact (e.g. at school or work) without direct exposure to patient's oral secretions• Indirect contact only (contact with a high-risk contact and not a case)• Health-care worker without direct exposure to patient's oral secretions	

- **Viral meningitis** →

- There is no specific treatment and the condition is usually benign and self-limiting.
- The patient should be treated symptomatically in a quiet environment → **plenty of fluids, over-the-counter pain medications** to help reduce fever and relieve body aches **corticosteroids** to reduce swelling in the brain, and an anticonvulsant medication to control seizures. **If a herpes virus caused your meningitis, an antiviral medication is available.**
- Recovery usually occurs within days, although a lymphocytic pleocytosis may persist in the CSF.

- **Fungal meningitis** →

- Intravenous amphotericin B or fluticasone.

- **Aseptic meningitis** →

- If the cause classifies the patient in the previous 3 types → same ttt
- If the cause is inflammatory disease → corticosteroids

A 19-year old architectural student is admitted from university halls of residence with a 24-hour history of headache, nausea, vomiting and listlessness. There is neck stiffness on physical examination. Which physical sign would preclude the taking of a cerebrospinal fluid via lumbar puncture?

- a) A positive Kernig's sign
- b) Tachycardia, i.e. heart rate above 150 per minute, and hypotension
- c) Purpuric skin rash
- d) Blurred disc on ophthalmoscopy
- e) Systolic murmur on auscultation

The mother of a 5-year-old girl realizes that her child has spent all of Saturday in bed. The girl is listless and not arousable. At the emergency department the examining nurse practitioner notes a temperature of 38.8°C and nuchal rigidity. A lumbar puncture yields slightly cloudy CSF with a protein of 61 mg/dL and glucose 19 mg/dL (serum glucose 83 mg/dL). A culture of CSF is most likely to yield which of the following organisms?

- A Streptococcus pneumoniae
- B Cryptococcus neoformans
- C Aspergillus fumigatus
- D Histoplasma capsulatum
- E Mumps virus

THANKS FOR LISTENING QUESTIONS?

- **References:**

- 1. Kumar and Clarks clinical medicine 8th edition**
- 2. Davidson principles and practice in medicine 22th edition**
- 3. Medscape**
- 4. Pubmed**