Lecture 9
Meningitis

PATHOLOGY TEAM 435

{ ومن لم يذق مرّ التعلُّمِ ساعةً.. تجرع ذلَّ الجهل طوال حياتهِ }

Revised by
هشام الغفيلي & خولة العماري

Red: Important. Grey: Extra Notes Doctors Notes will be in text boxes

Objectives:

The student should:

- Revise the spectrum of organisms that can cause meningitis.
- Explain the terms used in the description of CNS infections patterns.
- Understand the pathology of acute bacterial and tuberculous meningitis and the information that can be obtained from investigation of cerebrospinal fluid in suspected meningitis.

Background:

The brain and its coverings, as with all other parts of the body, can be affected by infections.
Damage to nervous tissue may be the consequence of direct injury of neurons or glia by the infectious agent or it may occur indirectly through the elaboration of microbial toxins, the destructive effects of the inflammatory response or the influence of immune-mediated mechanisms.

Key principles to be discussed:

- Meningitis and meningoencephalitis: definition and a list of the possible infectious etiologies.
- Ports of entry of infection into the CNS.
- Pyogenic meningitis: etiology, clinic-pathological features and CSF findings.
- Viral (aseptic) meningitis: clinic-pathological features and CSF findings.
- Tuberculous Meningitis: clinic-pathological features and CSF findings.
- The definition and pathogenesis of epidural abscess, subdural empyema and brain abscess.

Take home messages:

- Different pathogens may use distinct routes to reach the brain, and will cause different patterns of disease.
- Bacterial infections may cause meningitis, cerebral abscesses or a chronic meningoencephalitis. Viral infections can cause meningitis or meningoencephalitis.
- Lumbar puncture plays an important role in the diagnostic process of some CNS infections.

Key words:

CNS infection, virus, bacteria, meningitis, cerebral abscesses, chronic meningoencephalitis, viral meningitis, epidural abscess, subdural empyema and tuberculosis.

References:

Robbins, Lecture & Kaplan Lecture Notes

The blood brain barrier is important for the protection of the brain
Middle ear infections when left untreated will cause meningitis
Remember that we see Negri bodies in the cytoplasm in rabies

CNS Infections:

Portals of entry of infection into the CNS:

- Hematogenous spread: The most common.
- Direct implantation: Traumatic or in congenital CNS malformation.
- Local extension:

  Occurs secondary to an established infection in a near by organ (air sinus, an infected tooth or middle ear).
- Through the peripheral nervous system into the CNS.
- Certain viruses, such as rabies and herpes zoster.

Epidural and Subdural Infections:

- These spaces can be involved with bacterial or fungal infections, usually as a consequence of direct local spread.
- Epidural abscess, commonly associated with osteomyelitis, arises from an adjacent focus of infection, such as sinusitis or a surgical procedure.
- When the process occurs in the spinal epidural space, it may cause spinal cord compression and constitute a neurosurgical emergency.

Empyema:

- Infections of the skull or air sinuses may also spread to the subdural space, producing subdural empyema.
- The underlying arachnoid and subarachnoid spaces are usually unaffected, but a large subdural empyema may produce a mass effect.
- In addition, thrombophlebitis may develop in the bridging veins that cross the subdural space, resulting in venous occlusion and infarction of the brain.
- Symptoms include those referable to the source of the infection. Most patients are febrile, with headache and neck stiffness, and if untreated may develop focal neurologic signs, lethargy, and coma.
- With treatment, including surgical drainage, resolution of the empyema occurs from the dural side; if resolution is complete, a thickened dura may be the only residual finding. With prompt treatment, complete recovery is usual

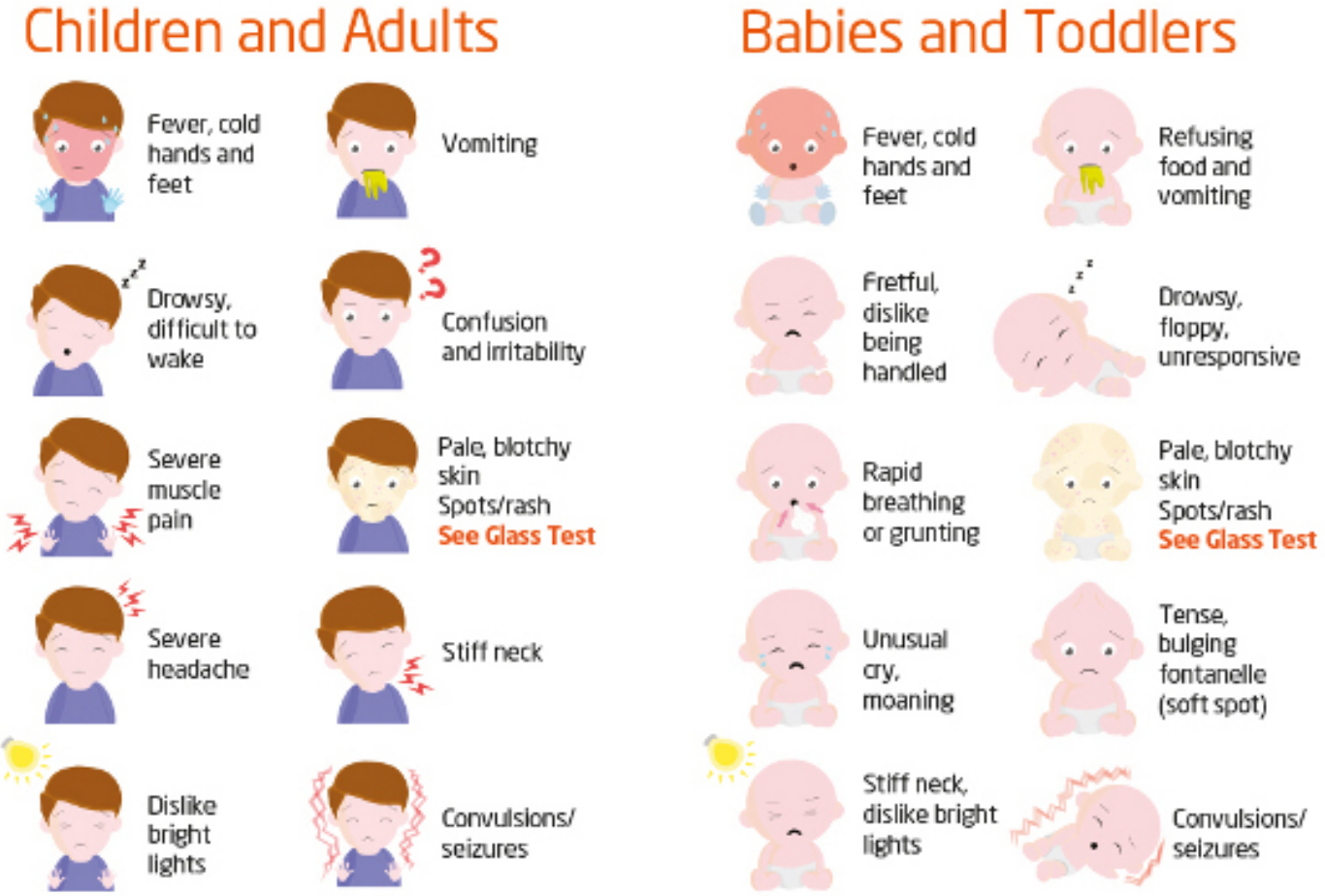
Mucormycosis is a kind of infection in diabetics can cause direct local spread and cause epidural and subdural infections.
Epidural and subdural infections are commonly caused by trauma (bullet, stab or car accident)

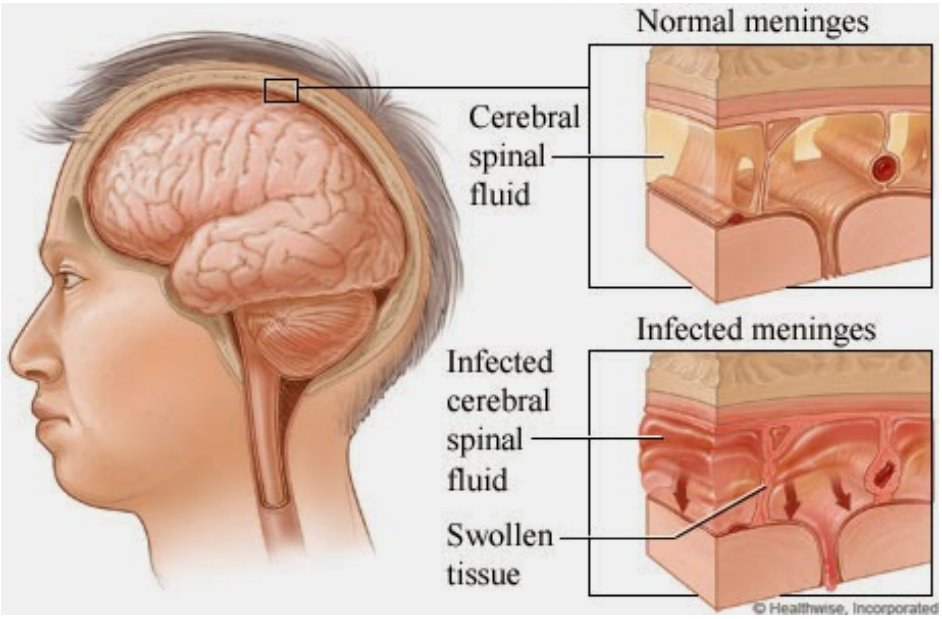
Meningitis:

An inflammatory process of the leptomeninges and CSF within the subarachnoid space. (Inflammation of the 2 inner meningeal layers, the pia and the arachnoid.)

We have different types of Meningitis; examining the CSF helps us distinguish between them. Those types are:

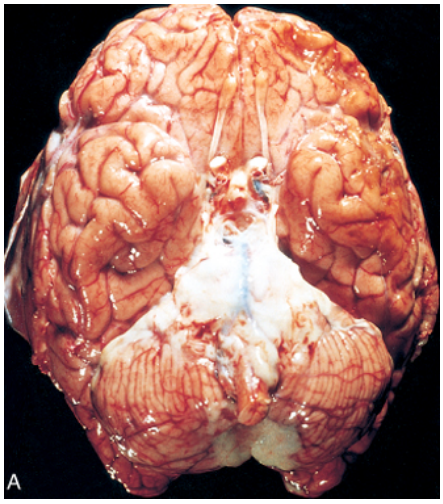
- Acute Pyogenic.
- Aseptic.
- Chronic.





Since its an emergency you never send the patient back home- vaccination for strep pneumonia Is given to elderly (older than 50) – the protein and glucose levels are compared to the blood at the same time

Acute Pyogenic Meningitis (Bacterial):



- Medical emergency
- The causative microorganisms:
  - Neonates: Escherichia coli and group B streptococci. Most frequently with group B streptococci but E. coli causes a greater number of fatalities.
  - Adolescents and young adults: Neisseria meningitidis (Meningococcal meningitis) Often associated with a maculopapular rash.
  - Elderly: listeria monocytogenes and Streptococcus pneumoniae

CSF Findings

- Cloudy or frankly purulent CSF.
- As many as 90,000 neutrophils /mm.
- Raised protein level & markedly reduced glucose content.
- Bacteria may be seen on a Gram stained smear or can be cultured, sometimes a few hours before the neutrophils appear.

Clinical Features

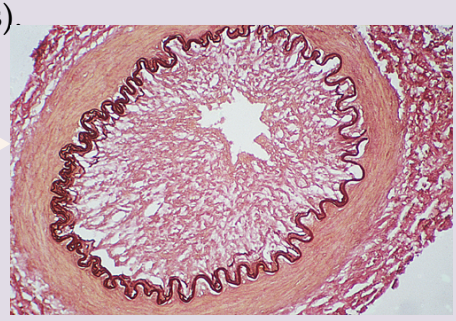
- Systemic non-specific signs of infection.
- Meningeal irritation signs and neurologic impairment: Headache, photophobia, irritability, clouding of consciousness and neck stiffness.
- Untreated, pyogenic meningitis can be fatal.
- Effective antimicrobial agents markedly reduce mortality associated with meningitis.
- The classic triad of bacterial meningitis is **fever, nuchal rigidity, and altered mental status.**

Complications

- Phlebitis[1] → venous occlusion → hemorrhagic infarction of the underlying brain.
- Leptomeningeal fibrosis [2]→ hydrocephalus.
- Septicemia → hemorrhagic infarction of the adrenal glands and cutaneous petechiae[3] (known as Waterhouse-Friderichsen syndrome, particularly common with meningococcal and pneumococcal meningitis).
- Focal cerebritis & seizures.
- Cerebral abscess.
- Cognitive deficit.
- Deafness.

Meningeal vessels are engorged and prominent

The adrenal glands hemorrhagic infarction is bilateral



[1] Inflammation of a vein, usually in the legs. It most commonly occurs in superficial veins.
[2] A fibrous reaction within the subarachnoid space
[3] A small red or purple spot caused by bleeding into the skin.

Aseptic Meningitis (Viral Meningitis):

It is a clinical term for an illness comprising meningeal irritation, fever, and alterations of consciousness of relatively acute onset **without** recognizable organisms.
Aseptic meningitis is a misnomer[4].

CSF Findings	○ Increased number of lymphocytes (pleocytosis[5]) ○ Protein elevation is only moderate ○ Glucose content is nearly always normal
Clinical Features	○ The clinical course is less fulminant than in pyogenic meningitis, is usually self-limiting, and most often is treated symptomatically. ○ Viral meningitis carries a better prognosis than bacterial meningitis. Mortality is low. ○ Symptoms resolve after 1 month with supportive care. ○ Acute viral meningitis is the most common neurologic symptom associated with primary HIV infection.
Morphology	○ In approximately 70% of cases, a pathogen can eventually be identified, most commonly **an enterovirus.** ○ There are no distinctive macroscopic characteristics except for brain swelling, seen in only some instances. ○ On microscopic examination, there is either no recognizable abnormality or a mild to moderate infiltration of **the leptomeninges** with **lymphocytes.**

Table 20-1. CSF Parameters in Different Forms of Meningitis

Condition	Cells/μL	Glucose (μg/dL)	Proteins (mg/dL)	Pressure (mm H_2O)
Normal values	<5 lymphocytes	45–85 (50–70% glycemia)	15–45	70–180
Purulent (bacterial)	Up to 90,000 neutrophils	Decreased (<45)	Increased (>50)	Markedly elevated
Aseptic (viral)	100–1,000 most lymphocytes	Normal or decreased	Normal or slightly increased (>50)	Normal or slightly elevated
Granulomatous (mycobacterial/fungal)	100–1,000 most lymphocytes	Decreased (<45)	Increased (>50)	Moderately elevated

[4] A wrong or inaccurate name or designation.
[5] An increased WBC count in CSF. Increased white blood cell count in the blood is called leukocytosis.

Under the microscope we see caseating necrotizing granulomatous inflammation and giant cells consistent with tuberculosis. Acid fast stain is done and the bacilli are usually found between the area of necrosis and the viable area for each bacteria you see there is 10^9 in the body.

Chronic Meningitis (Tuberculosis):

CSF Findings

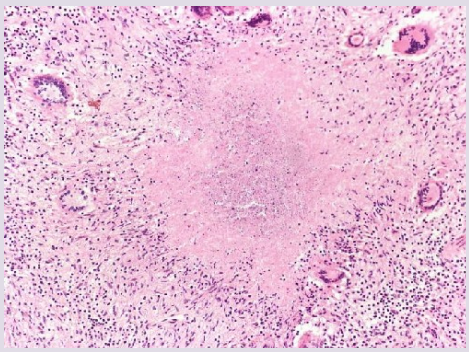
- There is only a moderate increase in cellularity of the CSF (pleocytosis) made up of mononuclear cells, or a mixture of polymorphonuclear and mononuclear cells.
- The protein level is elevated.
- The glucose content typically is moderately reduced or normal.

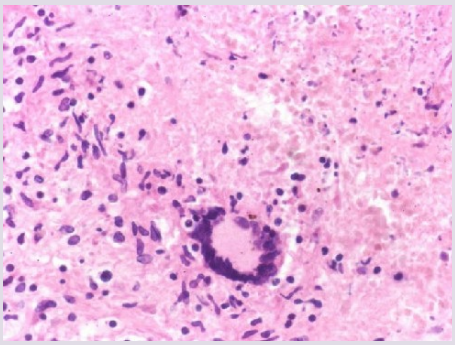
Clinical Features

- Manifests with generalized signs and symptoms of headache, malaise, mental confusion, and vomiting.
- It's a cause of arachnoid fibrosis, which may produce hydrocephalus.

Morphology

- The subarachnoid space contains a **fibrinous exudate**, most often at the base of the brain.
- Mycobacterium tuberculosis also may result in **Tuberculoma** which is a well-circumscribed intraparenchymal mass.
- A tuberculoma may be up to several centimeters in diameter, causing significant mass effect.
- Rupture of tuberculoma into subarachnoid space results in **tuberculous meningitis.**
- Always occurs after hematogenous dissemination of organism from **primary pulmonary infection.**
- On microscopic examination, there is usually a **central core of caseous necrosis** surrounded by a typical tuberculous **granulomatous** reaction.





Meningoencephalitis:

If the infection spreads into the underlying brain it is termed *Meningoencephalitis.*

It occurs in patients who have reactivation of latent infection and immunocompromised patients such as AIDS patients. It usually involves the basal surface of the brain, and may cause characteristic tuberculomas within the brain and dura mater

TB meningitis
Exudate at the base of the brain

Abscess is a mass and by definition it is a space occupying lesion that's why we have increase intracranial pressure. The CSF is not in close relation with the bacteria so its not really effected like in pyogenic.

Parenchymal infections (Brain abscess):

Can occur as a result of either hematogenous dissemination or direct spread from contiguous foci.

Predisposing conditions:

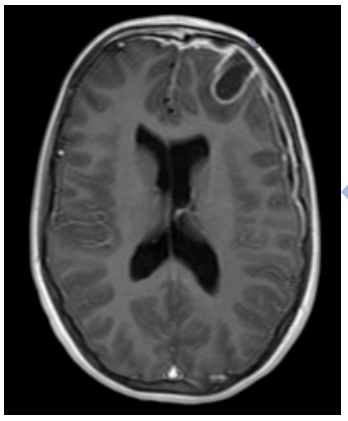
→ **Systemic:**

- Acute bacterial endocarditis (usually give multiple microabscesses[6])
- Cyanotic congenital heart disease in which there is a right-to-left shunt
- Loss of pulmonary filtration of organisms (e.g., bronchiectasis)

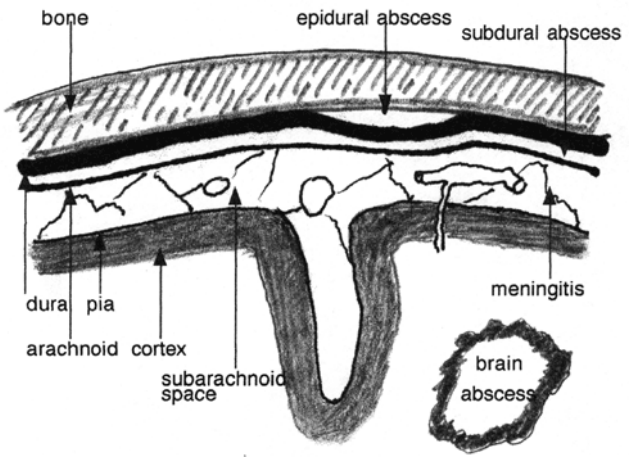
→ **Local:**

Mastoiditis, paranasal sinusitis, acute otitis, open fracture, and previous neurosurgery.

CSF Findings	○ Contains only scanty cells. ○ ↑ protein. ○ Normal level of glucose.
Clinical Features	○ Most common on cerebral hemispheres ○ Present clinically with progressive focal neurologic deficits (vary depending on the site of lesion) in addition to the general signs of raised intracranial pressure (headache, vomiting, and papilledema)
Compli-cations	○ Herniation (Diffuse cerebral edema carries a risk of fatal herniations). ○ Rupture of abscess into subarachnoid space or ventricle .
Morphology	○ **Streptococci and staphylococci** are the most common organisms identified in non-immunosuppressed populations. ○ Liquefactive necrosis. ○ The surrounding brain is **edematous**, congested & contains reactive astrocytes & perivascular inflammatory cells.



Subdural Empyema (enhancing) and brain abscess in a patient with sinusitis



[6] A small collection of neutrophils within or under the stratum corneum.

Homework

Create a table of CSF findings in Meningitis, aseptic meningitis, TB meningitis, Brain abscess and multiple sclerosis.

Disease	CSF Findings
Acute Pyogenic Meningitis	○ Cloudy or frankly purulent CSF. ○ As many as 90,000 neutrophils /mm. ○ Raised protein level & markedly reduced glucose content. ○ Bacteria may be seen on a Gram stained smear or can be cultured, sometimes a few hours before the neutrophils appear.
Aseptic Meningitis	○ Increased number of lymphocytes (pleocytosis) ○ Protein elevation is only moderate Glucose content is nearly always normal
TB Meningitis	○ There is only a moderate increase in cellularity of the CSF (pleocytosis) made up of mononuclear cells, or a mixture of polymorphonuclear and mononuclear cells. ○ The protein level is elevated. ○ The glucose content typically is moderately reduced or normal.
Brain abscess	○ Contains only scanty cells. ○ ↑ protein. ○ Normal level of glucose.
MS	○ It shows mildly elevated protein level with an increased proportion of γ-globulin ○ In one-third of cases there is moderate pleocytosis.

Check Your Understanding

MCQs:

1. **Which of the following people is most likely to develop bacterial meningitis?**
   A. An obese women
   B. A newborn baby
   C. A college student
   D. None of the above

2. **Typical signs and symptoms of meningitis include all of these EXCEPT:**
   A. Headache
   B. Painful or stiff neck
   C. Fever
   D. RBCs in CSF

3. **Meningitis results from meninges become affected through:**
   A. Virus
   B. Bacteria
   C. Fungi
   D. All the above

4. **Death can result due to meningitis caused by:**
   A. Virus
   B. Bacteria
   C. Fungi
   D. Amoeba

5. **Life is not threatened if meningitis is caused by:**
   A. Virus
   B. Bacteria
   C. Fungi
   D. Amoeba

6. **Meningitis refers to inflammation of the brain:**
   A. True
   B. False

7. **Which procedure is done to test for meningitis?**
   A. Artery bypass
   B. Spinal tap (Lumbar puncture)
   C. BiPap
   D. Brain perfusion scan

1:B 2: D 3:D 4: B 5:A 6:B 7:B

Contact us: Pathology435@gmail.com

Team Members:

فهد العبداللطيف	نوف التويجري
محمد الدغيثر	الجوهرة المزروع
معاذ باعشن	بدور جليدان
عبدالناصر الوابل	دانيا الهنداوي
عبدالرحمن الزامل	ديما الفارس
محمد الزاحم	كيان كعكي
عبدالعزيز الزيدان	كوثر الموسى
عبدالله الفريح	لميس آل تميم
ابراهيم الشايع	لينا إسماعيل
تركي الناصر	لولو الصغيّر
محمد الفضل	مريم سعيدان
	منيرة السلولي
	منيرة العمري
	نجود الحيدري
	نورة الخراز
	هديل الغرير

قال صلى الله عليه وسلم: {من سلك طريقًا يلتمس فيه علمًا سهَّل الله له بهِ طريقًا إلى الجنة}

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