Pathology

437's team work

Meningitis

important | Extra Explanation / Dr's note | Examples | Terminology

Meningitis:

#What is it? An inflammatory process of the **leptomeninges** and **CSF** within the **subarachnoid space.**

*Dr.maha's note: **leptomeninges** is the inner two meninges, the arachnoid and the pia mater, between which circulates the cerebrospinal fluid.

#Types of Meningitis

Meningoencephalitis	•if the infection spreads into the underlying **brain** it is termed
chemical meningitis 1	•a medical condition characterised by sterile **meningitis** that usually develops in certain patients after neurosurgical procedures. Its acute clinical course and standard laboratory findings are indistinguishable from those of bacterial **meningitis**.
carcinomatous meningitis:	•A serious problem that may occur in cancer in which cancer cells spread from the original (primary) tumor to the meninges causing inflammation

Dr.maha's note: example of chemical meningitis is epidermoid inclusion cysts which contain keratin There will be a rupture of cyst contents(keratin) into subarachnoid space resulting in inflammation and aseptic chemical meningitis.

#Pattern of infection:

acute pyogenic (usually bacterial) → **aseptic** (usually viral) → **chronic** (usually tuberculous, spirochetal, or cryptococcal) subtypes.

- **Bacterial infections** → may cause **meningitis**, **cerebral abscesses** or a **chronic meningoencephalitis.**
- **Viral infections** → can cause **meningitis** or **meningoencephalitis**

INFECTIONS OF THE NERVOUS SYSTEM

The brain and its coverings, as with all other parts of the body, can be sites of infections The Infection agent of nervous system could be either **relative to the nervous system** (e.g., rabies), while others **can affect many other organs** as well as the brain (e.g., Staphylococcus aureus)

Portals of entry of infection into the CNS:

1. **Hematogenous spread**: the most common and can by either **arterial** or **venous** system1
2. **Direct implantation: traumatic** or in **congenital** CNS malformation. 2
3. **Local extension:** occurs secondary to an **established** infection in a nearby organ (air sinus, an infected tooth or middle ear.)3
4. **Through the peripheral nervous system into the CNS:** certain viruses, such as rabies and herpes zoster.

*further notes from robbins :

1-* There can also be retrograde venous spread, through the **anastomoses between veins of the face**

2-* In rare cases it can be **iatrogenic** (relating to illness caused by medical examination or treatment.) **how ?** as when microbes are introduced with **a lumbar puncture needle.**

3-* Local extension can occur with infections of the **skull** or **spine**. Sources include air sinuses, most often the mastoid or frontal; infected teeth; cranial or spinal osteomyelitis; and congenital malformations, such as meningomyelocele.

A) Pyogenic meningitis :

It's a medical emergency the most likely organisms vary with patient age:

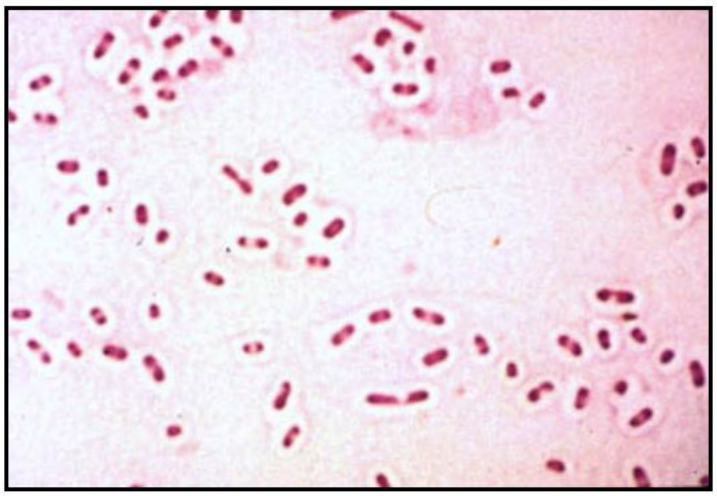
The causative microorganisms Imp.		
Neonates:	Escherichia coli	group B streptococci
Adolescents and young adults:	Neisseria meningitidis (Meningococcal meningitis)	
Elderly:	listeria monocytogenes	Streptococcus pneumoniae

▪ **Meningitis Clinical Features:**	• **Systemic non-specific signs** of infection. Like Fever. • **Meningeal irritation signs and neurologic impairment:** Headache, photophobia, irritability, clouding of consciousness and neck stiffness. • **Lumbar puncture reveals an increased pressure** • If untreated -< pyogenic meningitis can be **fatal.** • **treatment :** Effective **antimicrobial agents** IV injection markedly reduce mortality associated with meningitis.

▪ **CSF Findings in spinal tap: imp**	• **Cloudy or frankly purulent CSF.** Why? Because of high WBCs 'neutrophils'. And the pus. • **As many as 90,000 neutrophils /mm.** • **Raised protein level.** • **Markedly reduced glucose content**. Logic? Bacteria consume glucose & produce protein. • **Bacteria may be seen on a Gram stained smear or can be cultured, sometimes a few hours before the neutrophils appear.**

A) Pyogenic meningitis :

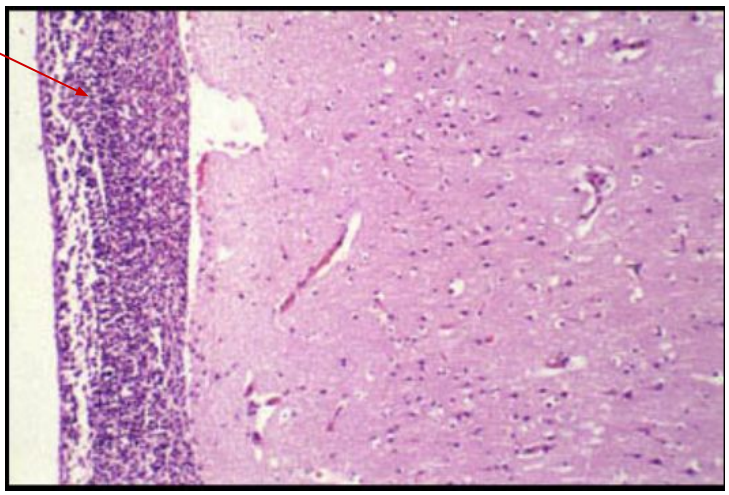
CSF Gram stain :
This gram stain shows multiple gram-positive diplococci, is characteristic of Streptococcus pneumoniae



filled with neutrophils

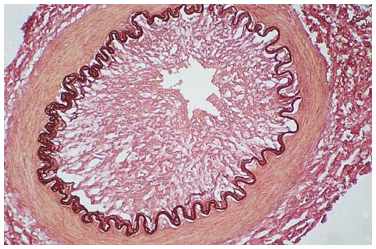
Arachnoid

Pia



The exudate expands the meningeal space between the pia and arachnoid and may extend into the perivascular Virchow-Robin spaces. However, direct extension into the brain is rare

purulent gray-white exudate over the meningeal surface of the brain(around the blood vessels)

▪ **Meningitis Complications:**	• **Phlebitis May** -> venous occlusion –> hemorrhagic infarction of the underlying brain. • leptomeningeal fibrosis ->**hydrocephalus**. • septicemia ->hemorrhagic infarction of the adrenal glands and **cutaneous petechiae** (***known as Waterhouse-Friderichsen syndrome,*** particularly common with **meningococcal** and **pneumococcal meningitis**). • Focal cerebritis & seizures. • Cerebral abscess. • Cognitive deficit • **Deafness**. 

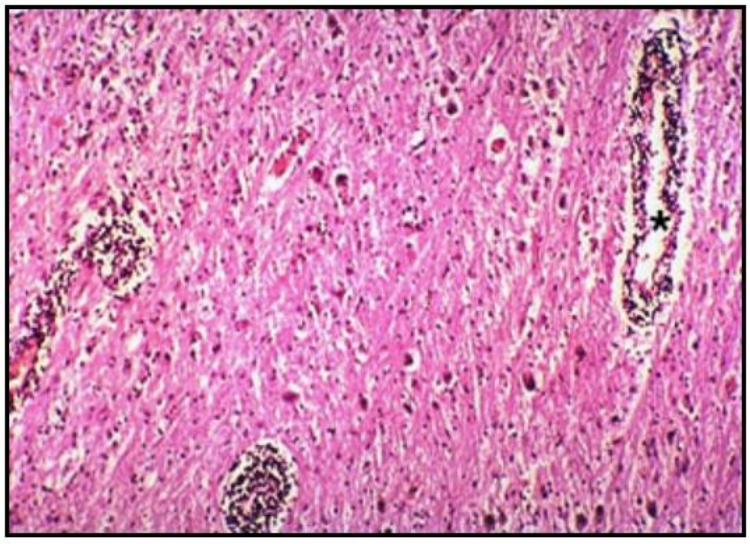
*Dr.maha's note : how does septicemia lead to *Waterhouse-Friderichsen syndrome?*

*-Septicemia -> will inciate heavily coagulation كأنه الجسم يحاول يصد البكتيريا -> **causes Disseminated intravascular coagulation (DIC)** which is a condition in which small blood clots develop throughout the bloodstream, blocking small blood vessels. The increased clotting -> **depletes the platelets and clotting factors** needed to control bleeding, -> **causing excessive bleeding** throughout the whole body . ->most important : bleeding in the skin (**cutaneous petechiae**) and bleeding in the adrenal gland (**Waterhouse-Friderichsen syndrome**) which will cause sudden failure of adrenal gland -> decrease or no steroid /adrenaline and Noradrenaline / low Na and high Ca -> SHOCK and could die.*

B) Aseptic Meningitis (Viral Meningitis):

Affects only cns	• The nervous system is particularly susceptible to certain viruses such as rabies virus and poliovirus
Affects other regions including CNS	• Other viral infections could affect CNS such as HSV, Enteroviruses, Measles or Influenza virus

- CNS viral infections could lead to **meningitis**, **encephalitis** or **brain stem and spinal cord syndromes.**
- **Intrauterine viral infection** following **transplacental spread of rubella and CMV** may cause destructive lesions, and **Zika** virus causes developmental abnormalities of the brain.
- CNS can be injured **by immune mechanisms** after systemic viral infections.
- Aseptic meningitis is a misnomer. = Inaccurate name or a misleading name
- **What is it ?** It is a clinical term **for an illness comprising meningeal irritation**, **fever**, and alterations **of consciousness** of relatively **acute onset without** recognizable organisms.
- The clinical course is less fulminant than in pyogenic meningitis, is usually **self-limiting**, and most often **is treated symptomatically**



In viral meningitis, clusters of lymphocytes surround cerebral blood vessels

B) Aseptic Meningitis (Viral Meningitis):

The CSF findings :

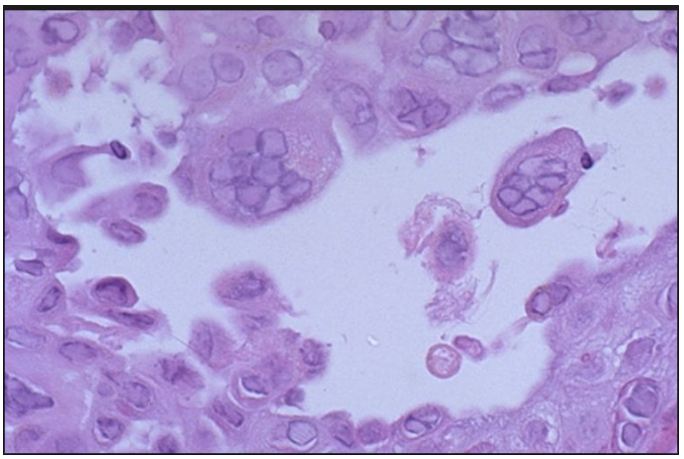
- No bacteremia in fluid culture
- Increased number of **lymphocytes** ***(pleiocytosis).***
- **Protein elevation** is only **moderate**. Could be **normal.**
- **Glucose** content is nearly always **normal**. (because viruses don't need energy)
- In approximately 70% of cases, a pathogen can eventually be identified, most commonly an enterovirus

On microscopic examination, there is either:

1. **Macroscopic :** There are no distinctive characteristics except for **brain swelling,** seen in only some instances
2. **On microscopic examination :** there is either **no recognizable abnormality** or a mild to moderate infiltration of **the leptomeninges with lymphocytes.** (Because viral lymphocytes will deal with it). Dr.maha: there is NO necrosis
3. **In viral meningitis, clusters of lymphocytes surround cerebral blood vessels**

Example of viruses : 1. Herpes simplex virus (HSV)

- HSV produces a hemorrhagic meningoencephalitis with inflammation in both the meninges and the brain parenchyma.
- The hemorrhage surrounding the **perivascular lymphocytic infiltrate.**
- The virus directly infects cells in the **cerebral cortex**, causing necrosis and a glial reaction.
- This reaction **produces a glial nodule.**

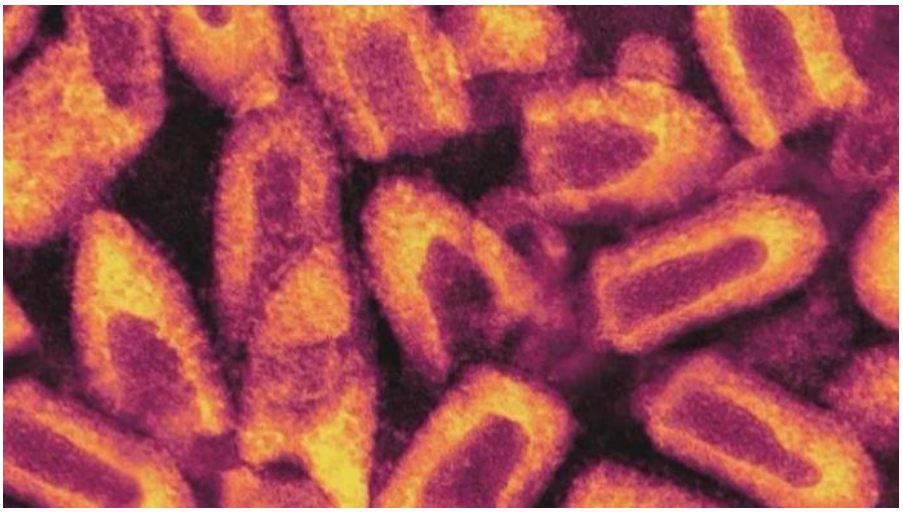


Example of viruses : 2. Varicella-zoster virus (VZV)

- Varicella-zoster virus (VZV) causes **chickenpox** during primary infection, usually without any evidence of neurologic involvement.
- The virus establishes latent infection **in neurons of dorsal root ganglia**.
- Reactivation in adults manifests as a painful, vesicular skin eruption in the distribution of one or a few dermatomes ***(shingles).***
- This usually is a self-limited process, but there may be a persistent pain syndrome in the affected region ***(postherpetic neuralgia)***

Example of viruses : 3. Rabies

- Rabies is a **fatal** encephalitic infection transmitted to humans from rabid animals, usually by a **bite**.
- The virus enters the CNS by ascending along the peripheral nerves
- Contracture of the pharyngeal musculature may create an aversion to swallowing even water ***(hydrophobia)***
- It progress to coma and eventually death



Tuberculosis:

- The **subarachnoid space** contains a fibrinous exudate (fluid full of protein), most often at the base of the brain. It may form something called: Tuberculoma.
- ***Tuberculoma*** is well-circumscribed **intraparenchymal mass** Not neoplastic it's due to infection.

Rupture of tuberculoma into **subarachnoid space** results in tuberculous meningitis. *(not tuberculoma itself because it is a mass not meningitis yet unless in case of rapture)

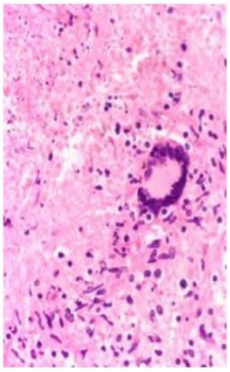
A tuberculoma may be up to several centimeters in diameter before, causing significant mass effect. *(depending on the structure it is pressing on)

Always occurs after **hematogenous** dissemination of organism from **primary pulmonary** infection.

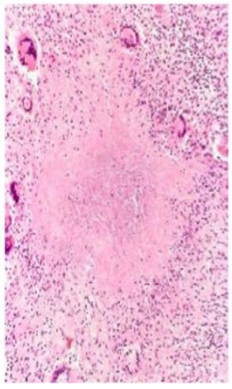
Microscopic examination:

-examination, there is usually a central core of **caseous necrosis** surrounded by a typical tuberculous **granulomatous reaction**. With Langhans Giant cells.

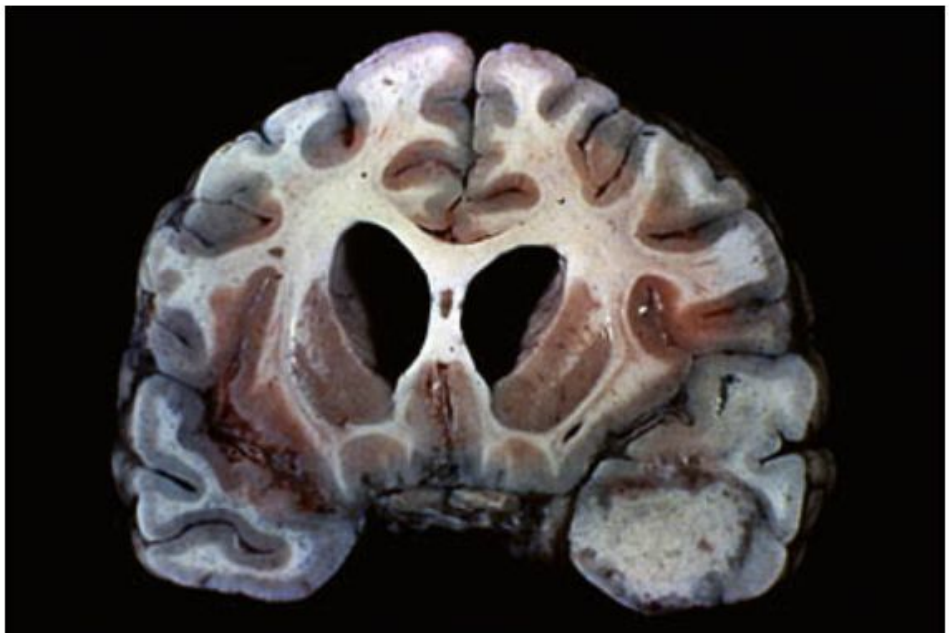
The subarachnoid space contains a **fibrinous exudate, most often at the base of the brain**.



Surrounded by a typical **tuberculous granulomatous reaction**



Central core of **caseous necrosis**



- A tuberculoma is shown in the **temporal lobe.**
- It is seen as a **well-circumscribed** intraparenchymal mass that may have effects similar to those caused by any other intracranial mass, and may therefore mimic a tumor.
- It is a destructive lesion.

Well circumscribed and it is space occupying lesions "like tumor"

CSF in TB :

There is only a **moderate increase in cellularity** of the CSF (pleiocytosis) made up of **mononuclear** cells (mainly), or a mixture of **polymorphonuclear** and mononuclear cells. *

The **protein level is elevated.**

The glucose content typically is moderately reduced or normal*why ? (because bacteria need energy) Because TB is intracellular bacteria. ما هي برا عشان تأكل الجلوكوز.

Remember:In pyogenic"PMN" , Glucose will be reduced

*Mainly: Monocytes, Lymphocytes, Macrophages.
May have some neutrophils

3- Brain abscess:

Brain abscesses are most often caused by bacterial infections.

It's a localized collection of pus in brain tissue

1. • **direct implantation of organisms**
2. • **local extension from adjacent foci** (mastoiditis, paranasal sinusitis)
3. • **hematogenous spread** (usually from a primary site in the heart, lungs, or distal bones, or after tooth extraction)

Predisposing conditions :

Acute bacterial endocarditis (usually give multiple **micro-abscesses** in the brain coming from the heart through the circulation).

Cyanotic congenital heart disease in which there is a **right-to-left shunt**[1]

Loss of pulmonary filtration of organisms **(e.g, bronchiectasis).**

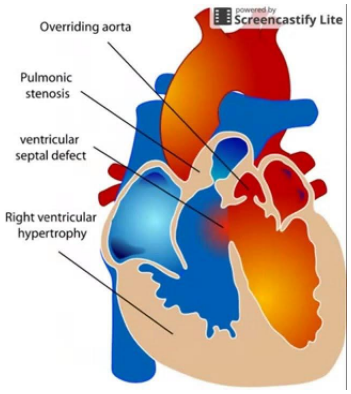
Causative agent:

- ***Streptococci*** and ***staphylococci*** are the most common organisms identified in **non-immunosuppressed** populations. It's most common on cerebral hemispheres.

1- A right-to-left shunt is an abnormal communication between the right and left sides of the heart allows deoxygenated systemic venous blood to bypass the lungs and return to the body.

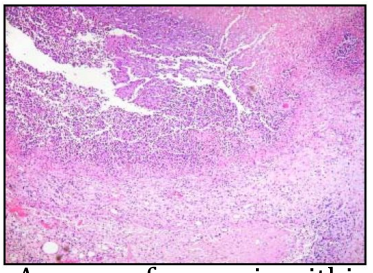
***Dr.maha's note :** normally after the blood goes from the Heart to the lung, the lung will get rid of most infectious organisms by the alveolar macrophages, that will prevent formation of septicemia. So if the blood bypass the Lung there will be a high chance for septicemia to form..

***Dr.maha's note :** in bronchiectasis there will be high amount of mucus production preventing the macrophages form getting rid of microorganisms

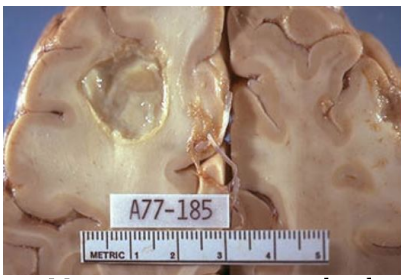


3- Brain abscess:

Morphologically:	• In the center **Liquefactive necrosis.** "Cyst containing pus" • The surrounding brain is **edematous**, **congested** & contains **reactive astrocytes** & perivascular inflammatory cells. *Present clinically with progressive **focal neurologic deficits** in addition to the general signs of **raised intracranial pressure.**
The CSF findings:	• Contains only **scanty cells.** "Small amount" • Increased levels of protein. • Normal level of glucose. Why? Because there is no bacteria in the CSF. It's abscess Only!
Complications of Brain abscess:	• Herniation. Dr.maha :through foramen magnum due to increase intracranial pressure. • Rupture of abscess into subarachnoid space or ventricle. Dr.maha : leading the bacteria to spread along the csf pathway



An area of necrosis within a brain abscess



Most common on cerebral hemispheres

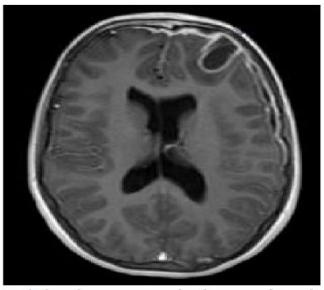
4 Epidural and Subdural Infections:

These spaces can be involved with **bacterial** "usually" or **fungal** infections, usually as a consequence of **direct local spread.**

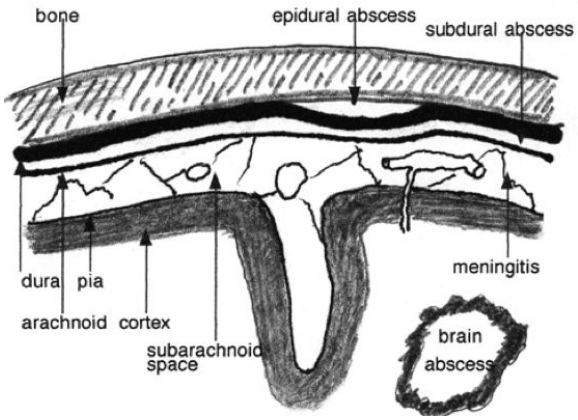
- Epidural abscess, commonly associated with **osteomyelitis***, arises from an adjacent focus of infection, such as **sinusitis** (especially chronic) or **a surgical procedure.** (when there is no good sterilization)
- When the process occurs in the **spinal epidural space**, it may cause spinal cord compression and constitute **a neurosurgical emergency.**

Susceptible patients: Elderly, immunocompromised, diabetic.

*Remember that epidural space is the area between dura mater and the bone.



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



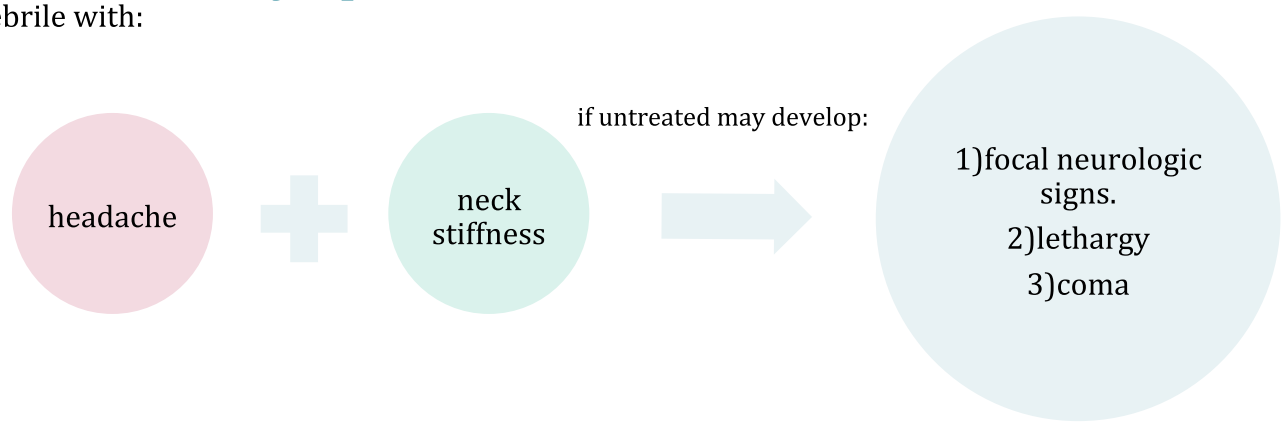
Empyema: We will have a cavity filled with Pus not Blood

#What is it ? Infections of the **skull** or **air sinuses** may also spread to **the subdural space**, producing subdural empyema

Subdural Infection -< it spreads.
Subdural Empyema <- it forms a collection

- 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.**

#What are the symptoms? include those referable to the source of the infection. Most patients are febrile with:



#What is the prognosis

- With treatment, including surgical drainage, resolution of the empyema occurs from the dural side and resolution is complete, a thickened dura may be the only residual finding.

- With prompt treatment, complete recovery is usual

HOMEWORK + SUMMARY most important points!

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

CSF findings	Meningitis	Aseptic meningitis	TB meningitis	Brain abscess	MS
Cellular infiltration	polymorphs	Pleiocytosis MOSTLY lymphs		Scanty cells	- Pleiocytosis - Increased IgG
Protein	Increased	Moderate increase	Increased	Increased	Normal or slightly increased (oligoclonal bands of gamma globulins)
Glucose	Markedly decreased	Normal	Normal or slight decrease	Normal	

SUMMARY

	Pyogenic meningitis	**Aseptic meningitis**
Causative organism:	- Neonates: E.coli + Group B streptococci. - Adolescents: Neisseria meningitides. - Elderly: listeria monocytogenes + strept. Pneuomoniae.	- Viral infection (enterovirus). - Usually self-limiting
Clinical features:	Headache, photophobia, neck stiffness.	Meningeal irritation, fever, altered consciousness.
Complications:	Hydrocephalus, Waterhouse-friderichsen syndrome, Deafness.	

Tuberculosis	**Brain Abscess**	**Epi&sub-dural infections**	**Empyema**
- Fibrinous exudate in the base of the brain. - Tuberculoma: well-circumscribed intraparenchymal mass, and the rupture of it will lead to tuberculous meningitis.	Causative organism: Streptococci & staphylococci. Predisposing conditions: Acute endocarditis & bronchiectasis. - Liquefactive necrosis.	- Consequence of direct local spread of bacterial or fungal infections. - May cause spinal cord compression.	- Infections of the skull may spread to the subdural space, producing **subdural empyema.** - Thrombophlebitis may develop in the bridging veins that cross the subdural space, infarction

MENINGITIS

I. BASIC PRINCIPLES

A. Inflammation of the leptomeninges

1. Meninges consist of three layers (dura, arachnoid, and pia) that lie between the brain and the skull.
2. Pia and arachnoid together are termed leptomeninges.

Table 17.1: Spinal Cord Tracts

TRACT	FIRST-ORDER NEURON	SECOND-ORDER NEURON	THIRD-ORDER NEURON
Spinothalamic (pain and temperature sensation)	Peripheral nerves to posterior horn; cell body is in dorsal root ganglion.	Arises from posterior horn, immediately crosses over in anterior white commissure, and ascends via the spinothalamic tract to thalamus	Thalamus to cortex
Dorsal column-medial lemniscus (pressure, touch, vibration, and proprioception)	Peripheral nerves to medulla via dorsal column; cell body is in dorsal root ganglion.	Arises from medulla, crosses over, and ascends via the medial lemniscus to thalamus	Thalamus to cortex
Lateral corticospinal (voluntary movement)	Pyramidal neurons in cortex descend, cross over in medullary pyramids, and synapse on the anterior motor horn of the cord (upper motor neuron).	Arises from the anterior motor horn and synapses on muscle (lower motor neuron)	(None)
Hypothalamospinal (sympathetic input of the face)	Arises from the hypothalamus and synapses on the lateral horn at T1	Arises from lateral horn at T1 and synapses on the superior cervical ganglion (sympathetic)	Superior cervical ganglion to eyelids, pupil, and skin of face

B. Most commonly due to an infectious agent

I. Group B streptococci, E coli, and Listeria monocytogenes (neonates)

2. N meningitidis (children and teenagers), Streptococcus pneumoniae (adults and elderly), and H influenzae (nonvaccinated infants)

3. CoxsackieVirus (children; fecal-oral transmission)

4. Fungi (immunocompromised individuals)

C. Presents with classic triad of headache, nuchal rigidity, and fever; photophobia, vomiting, and altered mental status may also be present.

D. Diagnosis is made by lumbar puncture (sampling of CSF).

l. Performed by placing a needle between L4 and LS (level of the iliac crest). Spinal cord ends at L2 , but subarachnoid space and cauda equina continue to S2.

2. Layers crossed include skin, ligaments, epidural space, dura, and arachnoid.

E. CSF findings

1. Bacterial meningitis- neutrophils with J- CSF glucose; gram stain and culture often identify the causative organism .

2. Viral meningitis- lymphocytes with normal CSF glucose

3. Fungal meningitis-lymphocytes with J- CSF glucose

F. Complications are usually seen with bacterial meningitis.

1. Death- herniation secondary to cerebral edema

2. Hydrocephalus, hearing loss, and seizures-sequelae related to fibrosis.

MCQ's.

Q1: Meningitis refers to inflammation of the brain

A: True B: False

Ans: B

Explanation: The term encephalitis refers to an inflammation of the brain. Meningitis is an inflammation of the membranes (called meninges) that surround the brain and spinal cord.

Q2: Meningitis in a 4 days old neonate is most likely to be caused by which organism:

A. Group B streptococcus B. Mycobacterium

C. Staphylococcus

D. Herpes simplex

Ans: A

Explanation: Bacterial infections by GBS result from swallowing of infected amniotic fluid or maternal secretions during delivery by infants of mothers who have vaginal colonization of GBS, although later infections may be acquired through nosocomial transmission.

Q3: Causes of aseptic meningitis include:

A. Antibiotic treated Haemophilus influenzae B. Mycobacterium tuberculosis

C. Fulminant Neisseria meningitidis infection D. Cryptococcus neoformans

E. A serious Enterovirus infection

Ans: E

Explanation: Aseptic meningitis is also known as viral meningitis. The name is derived from the original failure to (i) observe turbidity in CSF samples from viral meningitis patients and (ii) culture microorganisms from infected CSF.

Q4: The most common route of infection in meningitis is:

A. via peripheral nerves.

B. via the paranasal sinuses. C. via the ears.

D. through the skin.

E. via the bloodstream.

Ans: E

Explanation: The critical step in the pathogenesis of meningitis is for the microorganisms to be able to cross the blood-brain barrier. The most common method for this to occur is from the presence of significant numbers of microorganisms in the bloodstream.

Q5: A cerebrospinal fluid specimen was examined and the following preliminary results were obtained: Description: 3x 2.4mL, clear
- Protein: 0.55 g/L
-Glucose: 2.9 mmol/L
-WCC: 6 x 108 /L
-30% PMN
-70% Monocytes
This report is consistent with:

A. a poorly collected specimen B. an uninfected CSF specimen C. bacterial meningitis
D. viral meningitis
E. a normal CSF

Ans: D
Explanation: Several results indicate that this may be a viral infection. Firstly, the CSF is clear. This either means that a viral infection is present or,indeed, that there is no infection. The protein level is higher than normal (normal range 0.15 - 0.45 g/L). The glucose level is in the normal range, which suggests that it is not bacterial in nature. Noticeably, the WBC count is also above the threshold for infection. This data combined suggests a viral infectious agent.

Q6: All of the following CSF findings are present in tuberculous meningitis, except:

A. Raised protein levels B. Low chloride levels C. Cob web formation D. Raised sugar levels

Ans: D
Explanation: Glucose levels are decreased in tuberculous meningitis.

Q7: Which of the following is a morphologic feature of brain abscesses?
A: wedge shaped areas of infarction
B: meningeal fibrosis
C: reactive astrocytes and perivascular inflammatory cells D: A+B
Answ: C

Q8: William Mountain, age 65, arrives at the emergency department with fever, headache, and stiff neck. His wife tells you he has also been experiencing nausea, vomiting, photophobia, and an altered mental status.
Which of the following organisms is most likely causing the disease?
A: E. coli
B: Neisseria meningitidis
C: Listeria monocytogenes
D: Group B streptococci
Ans: C

كل الشكر والتقدير للجهود العظيمة من قبل أعضاء فريق علم الأمراض الكرام:

- قادة فريق علم الأمراض :

- منصور العبرة
- بثينة الماجد

- أعضاء فريق علم الأمراض :
  - رناد الفرم
  - ليلى الصباغ
  - عهد القرين
  - رزان الزهراني
  - بلقيس الراجحي
  - بتول الرحيمي
  - مها العمري

Kindly contact us if you have any questions/comments and suggestions:

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References:

-Slides