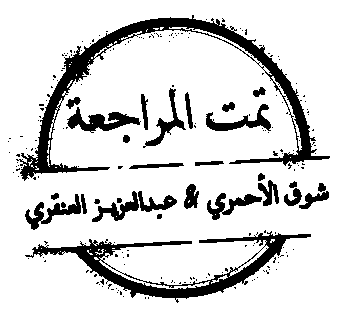
**Meningitis**





**Objectives:**

1- Revise the spectrum of organisms that can cause meningitis.

2- Explain the terms used in the description of CNS infections patterns.

3- Understand the pathology of acute bacterial and tuberculous meningitis and the information that can be obtained from investigation of cerebrospinal fluid in suspected meningitis.

**Key principles to be discussed:**

1- Meningitis and meningoencephalitis: definition and a list of the possible infectious etiologies.

2- Ports of entry of infection into the CNS.

3- Pyogenic meningitis: etiology, clinic-pathological features and CSF findings.

4- Viral (aseptic) meningitis: clinic-pathological features and CSF findings.

5- Tuberculous Meningitis: clinic-pathological features and CSF findings.

6- The definition and pathogenesis of epidural abscess, subdural empyema and brain abscess.

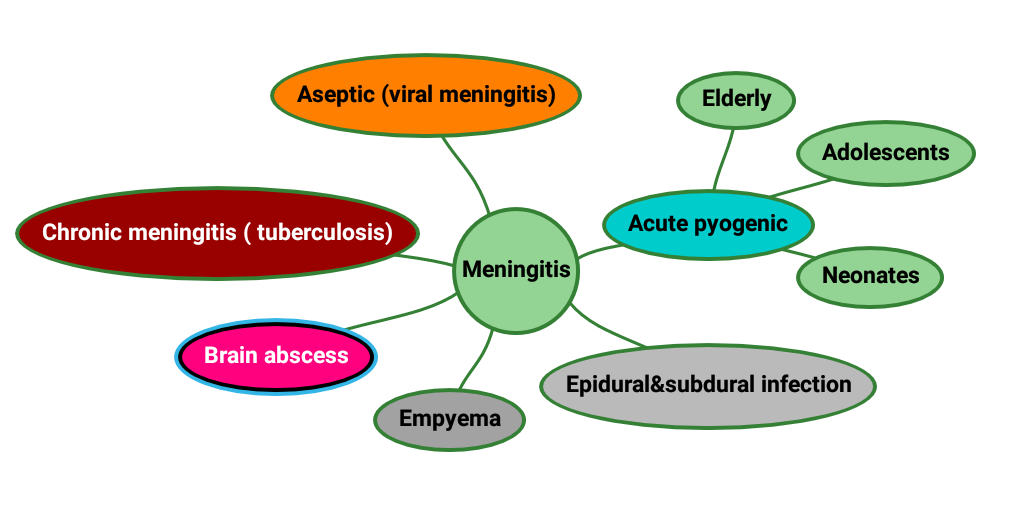
Black: Doctor’s slides.

Red or **black bold**: important!

Green: Doctor’s notes.

Grey: Extra.

*Italic black: New terminology.*



Lecture outlines:

**CNS Infections:**

Portals of entry of infection into the CNS:

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

1- *Meningitis:*

An inflammatory process of the leptomeninges and CSF within the subarachnoid space.

Meningoencephalitis 🡪 The infection when it spreads into the brain then it's called meningoencephalitis. Both brain + meninges.

Chemical meningitis: may occur in response to a nonbacterial irritant introduced into the subarachnoid space.

1. *Pyogenic meningitis* :

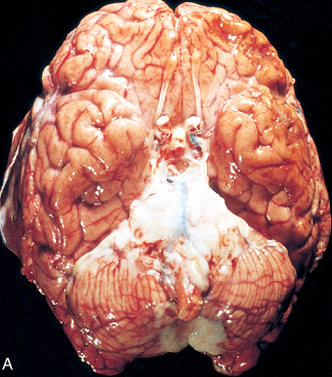
* It’s a medical emergency.

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

* CSF Findings in spinal tap:

1. Cloudy or frankly purulent CSF. Why? Because of WBCs ‘neutrophils’.
2. As many as 90,000 neutrophils /mm.
3. Raised protein level.
4. Markedly reduced glucose content. Logic? Bacteria consume glucose & produce protein.
5. Bacteria may be seen on a Gram stained smear or can be cultured, sometimes a few hours before the neutrophils appear.

If not treated will lead to death, that’s why it’s imp.

- Meningitis Clinical Features:

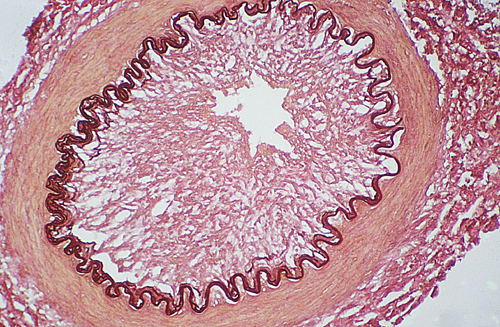
* Systemic non-specific signs of infection. Fever.
* Meningeal irritation signs and neurologic impairment:

Headache, photophobia, irritability, clouding of consciousness and neck stiffness.

* If untreated 🡪 pyogenic meningitis can be fatal.
* Effective antimicrobial agents IV injection markedly reduce mortality associated with meningitis.

Acute meningitis

- Meningitis Complications:

* Phlebitis[[1]](#footnote-1) 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**[[2]](#footnote-2), particularly common with meningococcal and pneumococcal meningitis).
* Focal cerebritis & seizures.
* Cerebral abscess.

\*لما الطفل يجيه ميننجايتيس بنلاحظ التغيّر لكنّه بيكون شوي مرة يكاد يكون غير مُلاحَظ.

* Cognitive deficit\*.
* Deafness.

What is this complication🡩?

* Meningeal vessels are engorged and prominent.
* The adrenal glands hemorrhagic infarction is bilateral.

B) *Aseptic Meningitis (Viral Meningitis):* The most common, more light.

* Aseptic meningitis is a misnomer[[3]](#footnote-3).
* 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.
* The CSF: No bacteremia in fluid culture. أهم شيء تعرفونه بهذي المحاضرة هو الفايندينقز!
* 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.
* There are no distinctive macroscopic characteristics except for brain swelling, seen in only some instances.
* On microscopic examination, there is either:

1. No recognizable abnormality. (because you need electron microscope to see viruses).
2. A mild to moderate infiltration of the leptomeninges with lymphocytes. (Because viral lymphocytes will deal with it).

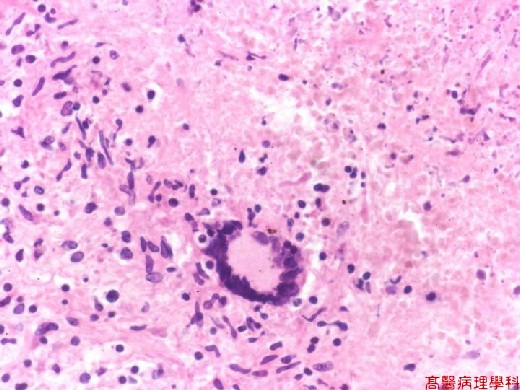
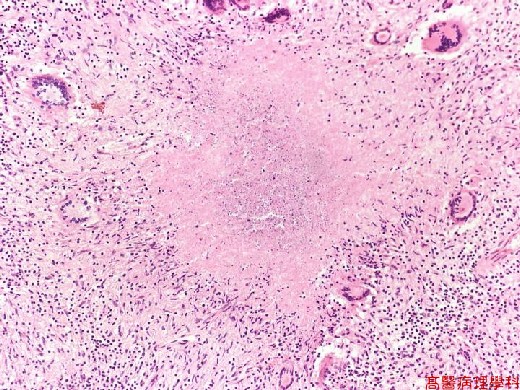
2- Tuberculosis: Caseous type of necrosis. “Specific infection”.

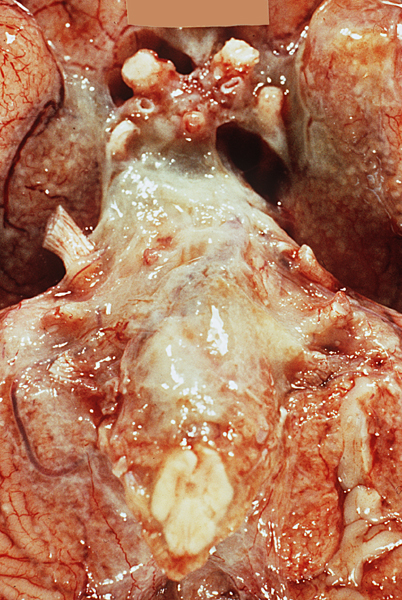
* The subarachnoid space contains a fibrinous exudate (fluid full of protein), most often at the **base** of the brain. It may form something called: Tuberculoma.
* ***Tuberculoma*** is well-circumscribed intraparenchymal **mass** Not neoplastic it’s due to infection.
  + Rupture of tuberculoma into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

تجي التيوبركلوما من الهيماتوجينس سبريد صح؟ فعادةً تكون فالبيشنتس اللي عندهم:

1- Miliary TB. 2- Primary pulmonary infection.

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



* 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\*. (because bacteria need energy)

TB meningitis: Exudate at the base of the brain.

\*Why? Because TB is intracellular bacteria. ما هي برا عشان تأكل الجلوكوز.

3- Brain abscess: (within the brain tissue)

* **Streptococci** and **staphylococci** are the most common organisms identified in **non-immunosuppressed** populations.
* Predisposing conditions:
  + Acute bacterial endocarditis (usually give multiple microabscesses).
  + Cyanotic congenital heart disease in which there is a right-to-left shunt.
  + Loss of pulmonary filtration of organisms (e.g, bronchiectasis)
* Most common on **cerebral hemispheres.**

- Morphologically:

* + In the center **Liquefactive** **necrosis.**
  + 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:

⦁ Contains only ***scanty cells***.

⦁ increased levels of protein.

⦁ Normal level of glucose. Why? Because bacteria not in the CSF. It’s in the abscess Only!

- Complications of Brain abscess:

○ Herniation. Occurs because of increased intracranial pressure.

○ Rupture of abscess into subarachnoid space or ventricle.

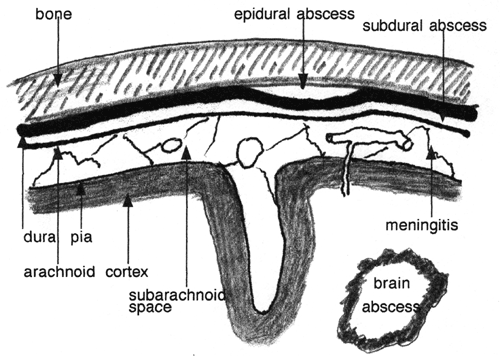
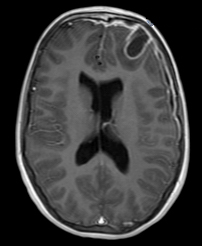
4- Epidural and Subdural Infections:

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[[4]](#footnote-4),** arises from an adjacent focus of infection, such as **sinusitis** or a **surgical procedure**.

Because it close to it أكيد الإيبيدورال بتصير بالأوستيومايلايتس

* When the process occurs in the **spinal epidural** space, it may cause spinal cord compression and constitute **a neurosurgical emergency.**





**Where it happened انتبهوا كل وحدة**

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

Infections of the skull or air sinuses may also spread to the subdural space, producing **subdural empyema.** Be aware it has nothing to do with epidural area.

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.**

\*أكثر شيء يخوّف!

○ 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. Antibiotics 🡪 may not heal!

**\*Homework** **VERY VERY IMPORTANT**

- 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 |  |

**\*Questions:**

**Q1:** A 65 years old patient admitted to ER suffering from very severe headache and witnessed tonic-clonic seizure, further investigation revealed that she had a medical history of sinusitis. What could we find in this case?

A. Presence of scanty cells in CSF.B. Thrombophlebitis of subdural veins.

C. leptomeninges with lymphocytes.

*(B) Is the correct answer*

**Q2:**What’s the most common rote of infections in CNS?

A. Hematogenous spread. B. Trauma. C. Through the peripheral nervous system.

D. local extension.

*(A) Is the correct answer*

**Q3:** Rupture in tuberculoma will lead to:

A. Subarachnoid meningitis. B. Dura meningitis. C. Subdural meningitis. D. Epidural meningitis.

*(A) Is the correct answer*

**Q4:** What is the most common organism in aseptic meningitis?

A. HIV Virus. B. Herpes zoster. C. Enterovirus. D. Rabies virus.

*(C) Is the correct answer*

**Q5:** What is the most common organism in Brain abscess?

A. Streptococci. B. Staphylococci. C. E.coli. D. A and B.

*(D) Is the correct answer*

**Q6:** What is the level of glucose in TB meningitis?

A. Low. B. Normal. C. High. D. Very high.

*(B) Is the correct answer*

**Q7:** Typical signs and symptoms of meningitis include all of these EXCEPT:

h

A. Headache. B. Stiff neck. C. Fever. D. RBCs in CSF.

*(D) Is the correct answer*

**Q8:** Life is not threatened by which of the following?

A. Bacteria. B. Fungi. C. Virus. D. Amoeba.

*(C) Is the correct answer*

**\*Summary**

|  |  |  |
| --- | --- | --- |
| **Pyogenic meningitis** | **Aseptic meningitis** | **Tuberculosis** |
| \*Causative organism:  - Neonates: E.coli + Group B streptococci.  - Adolescents: Neisseria meningitides.  - Elderly: listeria monocytogenes + strept. Pneuomoniae.  \*Clinical features:  Headache, photophobia, neck stiffness.  \*Complications:  Hydrocephalus, Waterhouse-friderichsen syndrome, Deafness. | - Viral infection (enterovirus).  - Usually self-limiting.  \* Clinical features:  Meningeal irritation, fever, altered consciousness. | - Fibrinous exudate in the base of the brain.  - Tuberculoma:  well-circumscribed intraparenchymal mass, and the rupture of it will lead to tuberculous meningitis.  - Occurs after primary pulmonary infections.  - Granulomatous reactions. |

|  |  |  |
| --- | --- | --- |
| **Brain Abscess** | **Epi&sub-dural infections** | **Empyema** |
| \*Causative organism:  Streptococci & staphylococci.  \*Predisposing conditions:  Acute endocarditis & bronchiectasis.  - Liquefactive necrosis.  - The surrounding of the brain is edematous & congested and contains reactive astrocytes. | - Consequence of direct local spread of bacterial or fungal infections.  - May cause spinal cord compression.  - Epidural abscess, commonly associated with **osteomyelitis,** arises from an adjacent focus of infection, such as **sinusitis** or a **surgical procedure**. | - 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  \*Symptoms:  headache, lethargy, coma and death. |



"اللهم لا سهل إلا ما جعلته سهلًا و أنت تجعل الحزن إذا شئت سهلًا"

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**القادة**

**نوره السهلي طراد الوكيل**

**الأعضاء**

**عبدالله أبوعمارة ريان القرني**

**صقر التميمي مبشر الأسمري**

**سالم العماري إبراهيم الديري**

**References:** Doctor’s slides + notes, Robbins basic pathology 10th edition.

1. Inflammation of the walls of the veins. [↑](#footnote-ref-1)
2. Waterhouse–Friderichsen syndrome (WFS), hemorrhagic adrenalitis or fulminant meningococcemia is defined as adrenal gland failures due to bleeding because of severe infections. [↑](#footnote-ref-2)
3. Inaccurate name or a misleading name [↑](#footnote-ref-3)
4. Inflammation of bone or bone marrow. [↑](#footnote-ref-4)