

Pathology

Meningitis



439

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تجعل الحزن اذا شئت سهلا

Color index

- Important
- Doctor's note
- Extra info
- Main text
- ★ Male's slide
- ★ Female's slide



Objective

- 01 Define meningitis, and describe its location and character
- 02 List possible routes of access of infectious organisms into the CNS
- 03 Describe the clinical presentation and pathology of acute bacterial meningitis, and its sequelae
- 04 Define the relationship between patient age and the most common etiologic organisms for bacterial meningitis
- 05 Describe the CSF findings in various causes of meningitis
- 06 Define the conditions that predispose to the development of a brain abscess, and describe the clinical and pathologic features
- 07 Describe the clinical and pathologic findings in TB in the CNS
- 08 List the common causes of viral encephalitis, and describe the pathologic changes in encephalitis due to herpes simplex virus
- 09 Recognize the importance of lumbar puncture and its role in diagnosis

★ = Only in girl's slides

Overview

CNS infections

Introduction to CNS infections

Pyogenic meningitis

Brain Abscess

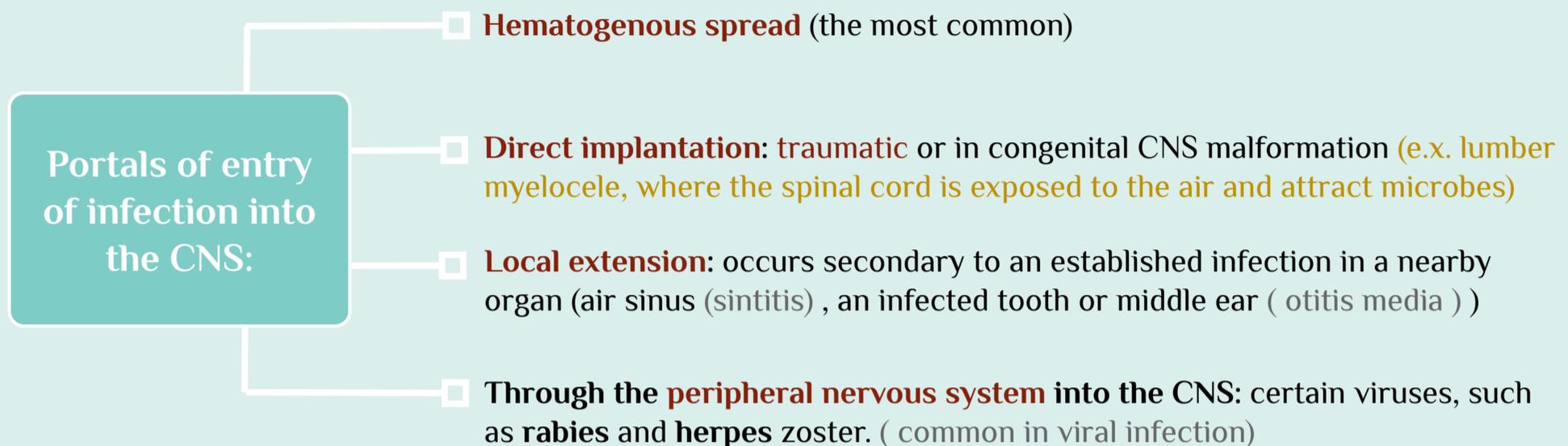
Empyema

Tuberculous meningitis

CNS viral infection

CNS infections

- ❖ The brain and its coverings, as with all other parts of the body, can be sites of infections. Some infectious agents have a relative or absolute predilection for the nervous system (e.g., rabies), while others can affect many other organs as well as the brain (e.g., Staphylococcus aureus). Damage to nervous tissue may be the consequence of direct injury of neurons or glial cells by the infectious agent or microbial toxins, or may be a consequence of the host innate or adaptive immune response.



Meningitis

An inflammatory process involving the leptomeninges (**arachnoid & pia mater**) and **CSF** within the subarachnoid space. **Infection of subdural space isn't called meningitis**

Meningoencephalitis

Is infection spreads into the underlying brain . Both brain and meninges

Etiology of meningitis : usually caused by an infection

01 Infectious meningitis ★

Could be :

- ❖ **Acute pyogenic** (bacteria)
- ❖ **Aseptic** (usually viral)
- ❖ **Chronic** (usually tuberculous, spirochetal, or fungal) subtypes
 - Examination of the CSF is often useful in distinguishing between various causes of meningitis.

Pattern of infection

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

02 Non-Infectious meningitis

Extra from guyton but the headlines were mentioned in **girl's slides**

- ❖ **Chemical meningitis:**

Is a response to a nonbacterial irritant such as debris from a ruptured epidermoid cyst.

- ❖ **Carcinomatous meningitis:**

the spread of metastatic cancer cells to the subarachnoid space.

Acute Pyogenic meningitis (bacterial meningitis)

Pyogenic = produce pus

★ Causative microorganisms

-Many bacteria can cause acute pyogenic meningitis, but the most likely organisms vary with patient age

- ❖ **Neonates:** Escherichia coli and group B streptococci
- ❖ **Adolescents and young adults:** Neisseria meningitidis is the most common pathogen (Meningococcal meningitis)
- ❖ **Elderly:** listeria monocytogenes and Streptococcus pneumoniae are more common

Clinical features

In all age group patient typically show Systemic signs (non-specific) infection along with **meningeal irritation** signs and neurologic impairment, including:



Headache



★ Photophobia



Irritability



Clouding of consciousness



★ Neck stiffness



Lumbar puncture reveals an increased pressure

- ❖ Considered a medical emergency
- ❖ Untreated, pyogenic meningitis can be fatal , but with prompt diagnosis and administration of appropriate antibiotics, many patients can be saved.
- ❖ Effective antimicrobial agents markedly reduce mortality associated with meningitis

CSF findings in spinal tap

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

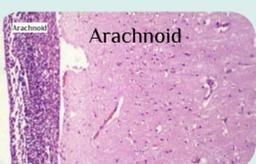
- ❖ CSF Gram stain - e.g. this gram stain shows multiple gram-positive diplococci, is characteristic of **Streptococcus pneumoniae**



- ❖ Macroscopic : **purulent** gray-white **exudate** over the meningeal surface of the brain

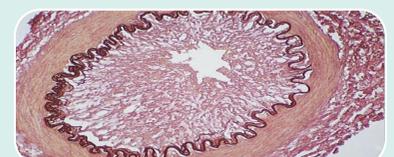


- ❖ Microscopic : We will see **large number of neutrophils in the subarachnoid space** , The exudate expands the meningeal space between the pia and arachnoid and may extend into the perivascular Virchow-Robin spaces. However, direct extension into the brain is rare



Complications

- ❖ Blood vessel could undergo to Phlebitis → 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 ***Also, pyogenic meningitis can be a complication of cerebral abscess**
- ❖ Cognitive deficit
- ❖ Deafness **when it affects temporal lobe or auditory nerves**



What is this complication?

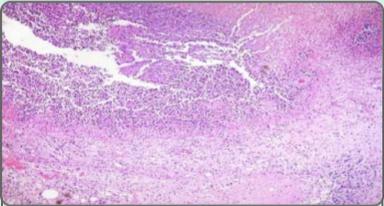
- Meningeal vessels are engorged and prominent.
- The adrenal glands hemorrhagic infarction is bilateral.

Brain abscess

(within the brain tissue)

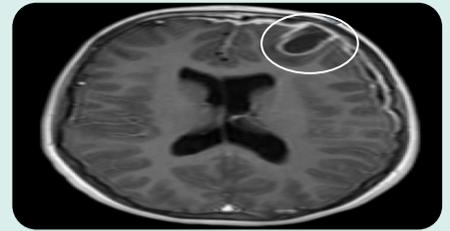
★ Overview

- ❖ Brain abscesses are most often caused by **bacterial infections**.
- ❖ These can arise by:
 - direct implantation of organisms
 - local extension from adjacent foci (mastoiditis, paranasal sinusitis)
 - hematogenous spread (usually from a primary site in the heart, lungs, or distal bones, or after tooth extraction)

Causative agent	Streptococci and staphylococci are the most common organisms identified in non-immunosuppressed populations.
Predisposing conditions	<ul style="list-style-type: none"> ❖ Acute bacterial endocarditis (usually give multiple microabscesses) ❖ Cyanotic congenital heart disease in which there is a right-to-left shunt and Loss of pulmonary filtration of organisms (e.g, bronchiectasis) ❖ Loss of Chronic pulmonary infections for example bronchiectasis
Clinical features	Present clinically with progressive focal neurologic deficits in addition to the general signs of raised intracranial pressure .
CSF examination	<ul style="list-style-type: none"> ❖ Contain only scanty cells ❖ Increased level of protein (the same as meningitis) ❖ Normal level of glucose Why? Because bacteria is not in the CSF. It's in the abscess Only! <p>Because the Brain abscess is away from the CSF , so you will not find too much cells in the spinal tap. And like MS you will find raised amount of Proteins</p>
Morphology	<ul style="list-style-type: none"> ❖ Liquefactive necrosis In the center ❖ The surrounding brain is <ul style="list-style-type: none"> ➤ Edematous ➤ Congested ➤ Contains reactive astrocytes & perivascular inflammatory cells <div style="display: flex; justify-content: space-around; align-items: flex-end;"> <div style="text-align: center;">  <p>A77-185 METRIC 1 2 3 4 5</p> <p>Most common on cerebral hemisphere</p> </div> <div style="text-align: center;">  <p>An area of necrosis within a brain abscess</p> </div> </div>
Complications	<ul style="list-style-type: none"> ❖ Herniation Occurs because of increased intracranial pressure ❖ Rupture of abscess into subarachnoid space or ventricle leading to meningitis. So both, meningitis can cause brain abscess and the other way around

Epidural and subdural infections

- ❖ These spaces can be involved by bacterial usually or fungal infection, usually as a consequence of **direct local spread**.
- ❖ When the abscesses occur in the **spinal epidural space**, they may cause spinal cord compression and constitute a **neurosurgical emergency**.
- ❖ epidural abscess is a collection of pus (infected material) and germs between the outer covering of the brain and spinal cord and the bones of the skull or spine. The abscess causes swelling in the area.



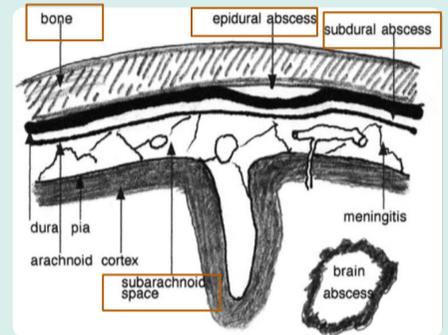
Subdural empyema (enhancing) and brain abscess in patient with sinusitis

Inflammation of CSF (subarachnoid space) = **Meningitis**

Inflammation in Parenchyma (inside brain substance) = **Brain abscess (with pus) / Encephalitis (W.O puss)**

Abscess b.w dura and arachnoid = **subdural abscess (Empyema)**

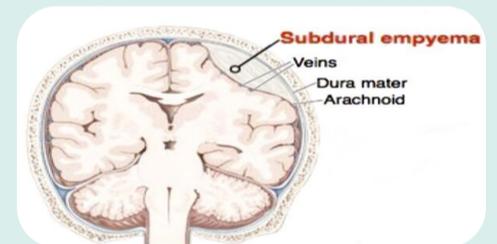
Abscess b.w dura and bone = **epidural abscess (extradural abscess)**



Empyema

We will have a cavity filled with Pus

- ❖ Infections of the skull or air sinuses may also spread to the **subdural space** producing **subdural empyema** Collection of pus in the subdural space between the dura mater and the underlying arachnoid mater
- ❖ 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

Depends on the primary disease (sinusitis, osteomyelitis,.. etc)

- ❖ Symptoms include those referable to the source of the infection.
- ❖ Most patients are :

01 febrile (fever)

02 Headache

03 Neck stiffness

- ❖ if untreated, focal neurological signs, lethargy and coma may develop.
- ❖ With Prompt treatment usually leads to complete recovery.

Prognosis

- ❖ With Treatment, including **surgical** drainage, leads to the resolution of the empyema from the dural side , if resolution is complete, a thickened dura may be the only residual finding.

Tuberculosis (tuberculous meningitis)

Caseous type of necrosis. "Specific infection"

- ❖ **Tuberculoma:** is a well-circumscribed intraparenchymal mass, which may be up to several centimeters in diameter causing a significant mass effect, and may therefore mimic a tumor. It is a destructive lesion.

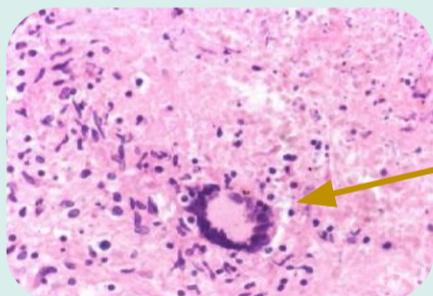


A tuberculoma is shown in the temporal lobe.

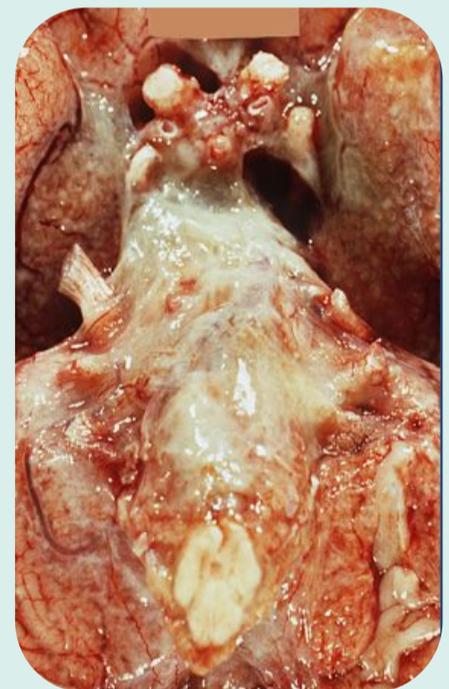
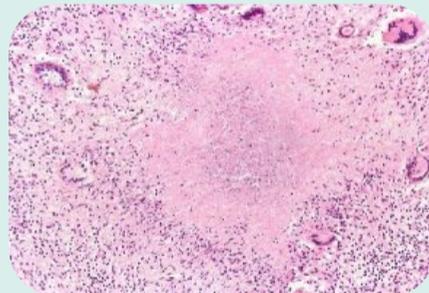
Rupture of tuberculoma into subarachnoid space results in **tuberculous meningitis**. It always occurs after hematogenous dissemination of organism from primary pulmonary infection.

Morphology

- ❖ The subarachnoid space contains a fibrinous exudate, most often at the **base** of the brain.
- ❖ On microscopic examination there is usually a central core of caseous necrosis surrounded by a typical tuberculous granulomatous reaction.



Langhan type giant cells



TB meningitis: Exudate at the base of the brain.

Symptoms

- ❖ Usually manifests with generalized signs and symptoms of
 - Malaise (fever)
 - Headache
 - Mental confusion
 - Vomiting

CSF in Tuberculosis:

Moderate increases in cellularity of the CSF (pleiocytosis) made up of mononuclear cells, or a mixture of polymorphonuclear and mononuclear cells.

Elevated protein levels (**often strikingly so**) The most CNS infection that increase the proteins amount in CSF

Glucose content typically is moderately reduced or normal. **Unlike bacterial meningitis where it is markedly reduced**

CNS viral infections

★ The nervous system is particularly susceptible to certain viruses such as rabies virus and poliovirus, and other viral infections could affect the CNS such as HSV, Enterovirus, Measles or influenza virus.

★ Intrauterine viral infection following transplacental spread of rubella and CMV may cause destructive lesions, and zika virus causes developmental abnormalities of the brain.

CNS viral infections could lead to meningitis, encephalitis or brain stem spinal cord syndromes

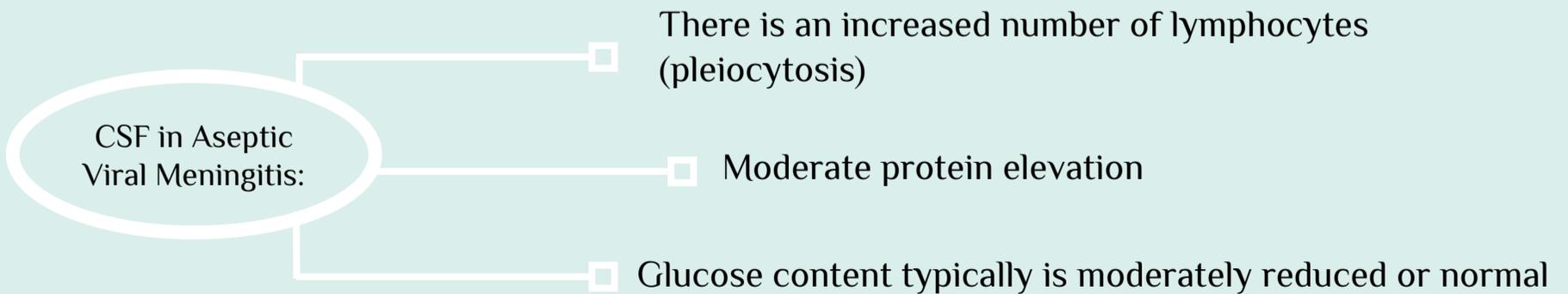
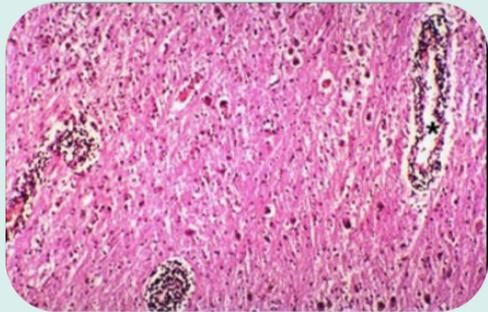
CNS can be injured by immune mechanisms after systemic viral infections

Viral/aseptic Meningitis:

- ❖ The name aseptic meningitis is a misnomer, it is a clinical term for an illness comprising of:
 - Meningeal irritation
 - Fever
 - Alterations of consciousness
- ❖ These are relatively acute onset without recognisable organisms
- ❖ The clinical course is less fulminant than in pyogenic meningitis. It is usually **self-limiting**, so treatment is most often symptomatically.

★ **Microscopically:** there is either no recognizable abnormality or a mild to moderate infiltration of leptomeninges with lymphocytes in clusters surrounding cerebral blood vessels.

Viral Infections ★		
Meningitis	Acute aseptic meningitis	Enteroviruses
		Measles (subacute sclerosing panencephalitis)
		Influenza species
		Lymphocytic choriomeningitis virus
Encephalitis	Encephalitic syndromes	Herpes simplex (HSV-1, HSV-2)
		Cytomegalovirus
		Human immunodeficiency virus
	Arthropod-borne encephalitis	West Nile virus, other arboviruses
Brain stem and spinal cord syndromes	Rhombencephalitis	Rabies
	Spinal poliomyelitis	Polio
		West Nile virus



- ❖ In approximately 70% of cases, a pathogen, most commonly an **enterovirus**, can eventually be identified.
- ❖ There is no distinctive macroscopic characteristics except for brain swelling, seen in only some instances

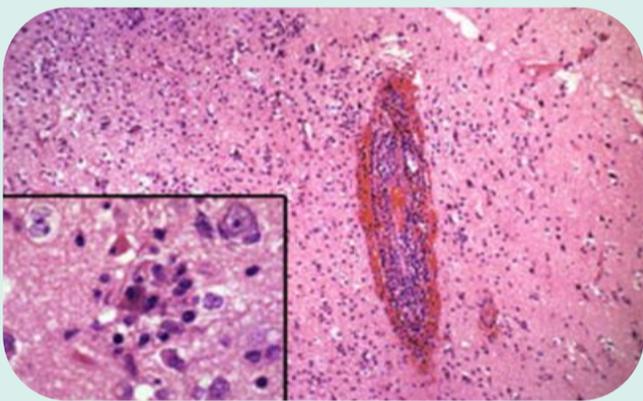
Herpes Simplex Virus (HSV)

- ❖ It produces a **hemorrhagic meningoencephalitis** with inflammation in both the meninges and the brain parenchyma.
- ❖ The virus directly infects cells in the cerebral cortex, causing necrosis and a glial reaction, which produces a microglial nodule

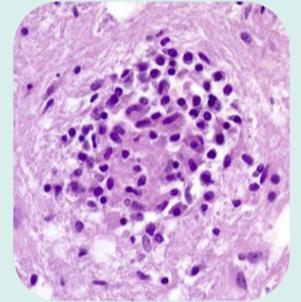
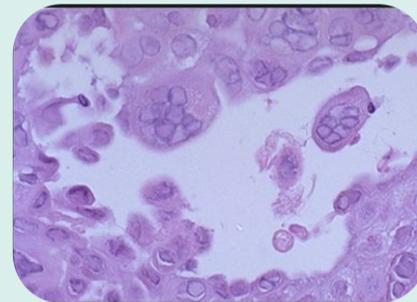
Microglial nodules: Are activated microglial cells encircling the degenerating neurons, neuronophagia, and form clusters around small foci of necrotic brain tissue).

* microglial nodules can also be seen in HIV encephalitis.

The hemorrhage surrounds the perivascular lymphocytic infiltrate



The virus may be identified by H&E stain as viral inclusion, culture or PCR amplification



Varicella-zoster Virus (VZV) meningitis

- ❖ 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**).
- ❖ Usually is self-limiting, but there may be a persistent pain syndrome in the affected region (postherpetic neuralgia)

Rabies

- ❖ It is a fatal encephalitis 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 progresses to coma and eventually death.



Homework !

IMPORTANT

Q1 - Create a table of CSF findings in Meningitis, aseptic meningitis, TB meningitis, Brain abscess and multiple sclerosis

CSF findings	Acute bacterial 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	



The CSF white blood cells content :

- Viral meningitis → Lymphocytes only
- TB → Mixture or lymphocytes
- Pyogenic meningitis → Neutrophils



MCQs

01 What is the most common route for CNS infections?			
A) Hematogenous spread	B) Direct implantation	C) Local extension	D) Through peripheral nervous system
02 Which of the following is seen in the CSF findings of pyogenic meningitis?			
A) increased glucose	B) decreased glucose	C) normal protein	D) decreased protein
03 What is the morphology of brain abscess?			
A) Caseous necrosis	B) Liquefactive necrosis	C) Microglial nodules	D) Granulomas
04 Select the symptom specific to empyema:			
A) Febrile patients	B) Headaches	C) Mental confusion	D) Neck stiffness
05 Viral meningitis is mostly caused by:			
A) TB	B) Enterovirus	C) HSV	D) Cytomegalovirus
06 Tuberculoma is:			
A) fibrinous transudate mostly at the base of the brain	B) well-circumscribed extraparenchymal mass	C) fibrinous exudate at the base of the brain	D) Well-circumscribed non destructive mass

MCQs Answer key	01	02	03	04	05	06
	A	B	B	D	B	C



Summary

Meningitis

Definition

inflammatory process involving the leptomeninges and CSF within the subarachnoid space.

Acute Pyogenic meningitis (bacterial meningitis)

-Causative organism:

Neonates: E.coli + Group B streptococci.

Adolescents: Neisseria meningitidis.

Elderly: listeria monocytogenes + strep. Pneumonia.

-Clinical features:

Headache, photophobia, neck stiffness.

-Complications:

Hydrocephalus, Waterhouse Friderichsen syndrome, Deafness

aseptic Meningitis (Viral meningitis)

-Causative organism:

Viral infection (enterovirus).

- Usually self-limiting.

-Clinical features:

Meningeal irritation, fever, altered consciousness.

Chronic meningitis (tuberculous meningitis)

-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**.

Infectious meningitis

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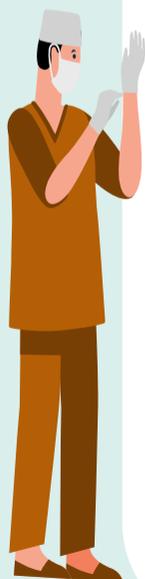
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