



Lecture 9: Meningitis

objectives

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

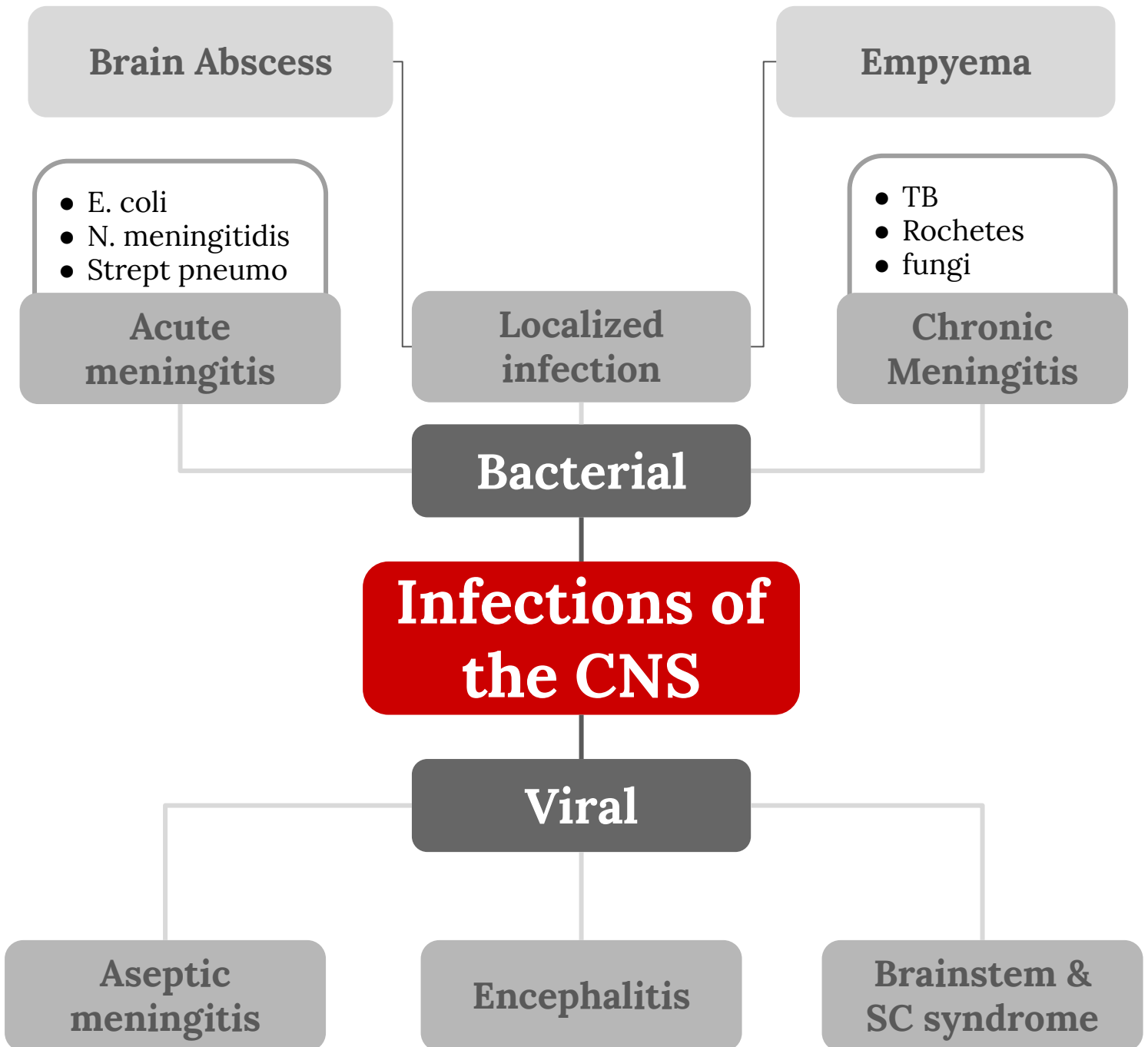
Black: original content
Red: Important
Blue: only found in boys slides

Dark orange: Doctor notes
Grey: Extra/Robbins
Pink: Only found in girls slides



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Content



Meningitis

Definition: An inflammatory process involving the leptomeninges¹ and CSF within the subarachnoid space.

meningoencephalitis: when the infection spreads into the underlying brain.

Pattern of infection:

- **Bacterial** infections may cause:
 - Meningitis².
 - Cerebral abscesses.
 - Chronic meningoencephalitis.
- **Viral** infections can cause meningitis or meningoencephalitis.

Portals of Entry into the CNS:

Hematogenous	Direct Implant	Local extension	Through the PNS
- Most common	- Trauma - Congenital malformation ex; Myelomeningocele	Secondary to infection in near organ: - Air sinus - Tooth - Middle ear	Travel from the PNS into the CNS: - Rabies - Herpes zoster

Pyogenic Meningitis

- Considered a **Medical emergency**

Causative Organisms: by population		
Neonates	Young Adults	Elderly
<ul style="list-style-type: none"> ○ E. coli ○ Group B. strept 	<ul style="list-style-type: none"> ○ Neisseria meningitidis (Meningococcal meningitis) 	<ul style="list-style-type: none"> ○ Listeria monocytogenes ○ Strept. pneumonia

Prognosis

- Untreated, pyogenic meningitis can be **fatal**.
- Effective antimicrobial agents markedly reduce mortality associated with meningitis.

¹- Leptomeninges¹ is the inner two meninges, the arachnoid and the pia mater, between which circulates the CSF.

²-Usually in arachnoid mater and subarachnoid space.

Pyogenic Meningitis

Clinical Features

- Systemic non-specific signs of infection.
- Meningeal irritation signs and neurologic impairment including¹:



Headache



Photophobia



Irritability



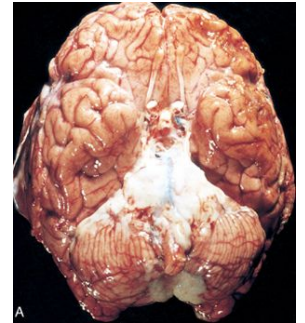
Clouding of
consciousness



Neck stiffness

CSF Findings in spinal tap:

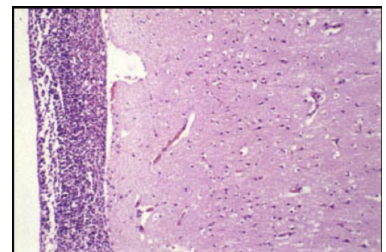
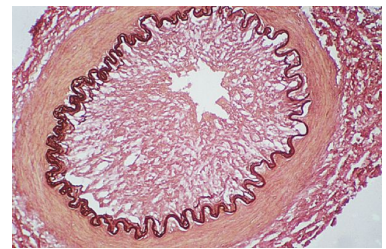
- **Cloudy** or frankly **purulent** CSF.
- As many as **90,000 neutrophils /mm**.
- **Raised protein** level.
- **Markedly reduced**² glucose content.
- Bacteria may be seen on a Gram stained smear or can be cultured, sometimes a few hours before the neutrophils appear.
- Lumbar puncture reveal **increased ICP**.



Purulent gray-white exudate over the meningeal surface of the brain

Complications untreated may lead to death

- Phlebitis (Inflammation of a vein) may cause venous occlusion→hemorrhagic infarction of the underlying brain.
- Leptomeningeal fibrosis→hydrocephalus due to closure of CSF flow
- Focal cerebritis & seizures.
- Cerebral abscess.
- Cognitive deficit.
- **Deafness**.
- **Septicemia**→**hemorrhagic** infarction of the adrenal glands and cutaneous petechiae (known as **Waterhouse Friderichsen** syndrome, particularly common with meningococcal and pneumococcal meningitis).
- **Encephalitis**
- **thrombosis**



The exudate may extend into the perivascular Virchow-Robin spaces³, neutrophilic infiltration in the subarachnoid space

1- And starring eyes in children.

2- Reduced because the need for glucose as fuel by infiltrating immune cells in response to infection.

3- Pial-lined interstitial fluid-filled spaces in the brain that surround perforating vessels

Brain abscess

Brain abscess

- Are most often caused by bacterial infections **usually in cerebral hemisphere..**

Caused by

- Direct implant of organism.
- Local extension for adjacent foci (Mastoiditis, paranasal sinus).
- Hematogenous Spread; primary site is usually:
 - Heart
 - Lung
 - Distal bones
 - After tooth extraction

Predisposing conditions

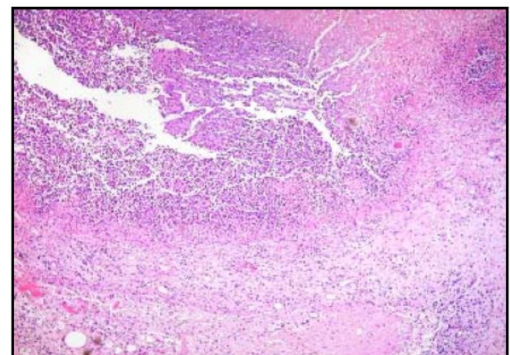
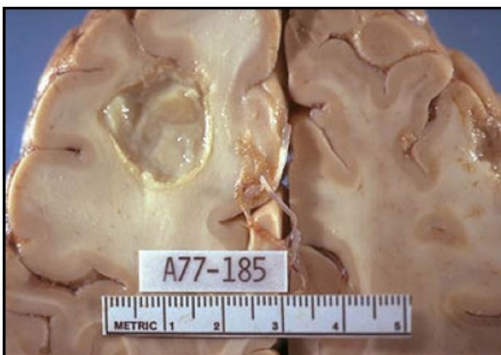
- **Acute bacterial endocarditis**, from which septic emboli are released that produce multiple microabscesses.
- **Cyanotic congenital heart disease** associated with a right-to-left shunt and lost of pulmonary filtration of organisms.
- **Chronic Pulmonary infections** (e.g, bronchiectasis).

Causative agent

- **Streptococci** and **staphylococci** are the most common organisms identified in non-immunosuppressed populations.

Morphology

- Most common on cerebral hemisphere
- Liquefactive necrosis.
- The surrounding brain is edematous, congested & contains reactive astrocytes & perivascular inflammatory Cells.



An area of necrosis within a brain abscess

Brain abscess cont.

Clinical presentation:

With progressive focal neurologic deficits in addition to the general signs of **raised intracranial pressure**.

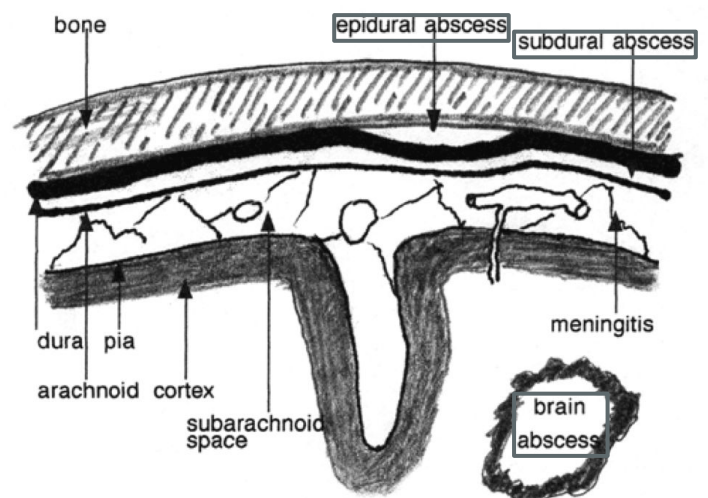
- **The CSF:**
 - Contains only scanty cells. **Important to differentiate from other infections**
 - ↑ protein.
 - Normal level of glucose.

Complications of Brain abscess:

- Herniation **Caused by mass that leads to increased intracranial pressure.**
- Rupture of abscess into subarachnoid space or ventricle

► Epidural and Subdural Infections

- Can be involved with bacterial or fungal infections.
 - usually by direct local spread.
- Epidural abscess, usually arise from an adjacent focus of infection such as:
 - **Sinusitis**
 - **Osteomyelitis**
 - Or in a surgical procedure
- When abscess occurs in the spinal epidural space, it may cause spinal cord compression and cause a neurosurgical emergency.



Empyema

- Infections of the skull or air sinuses may also spread to the **subdural space**, producing subdural empyema. **CSF is not affected**
 - Arachnoid and subarachnoid spaces are usually **unaffected**, but a large subdural empyema may produce a mass effect.
 - In addition, **thrombophlebitis** (one or more blood clots in a vein that cause inflammation) may develop in the bridging veins that cross the subdural space, resulting in venous occlusion and infarction of the brain.

Symptoms

Symptoms include those referable to the source of the infection.

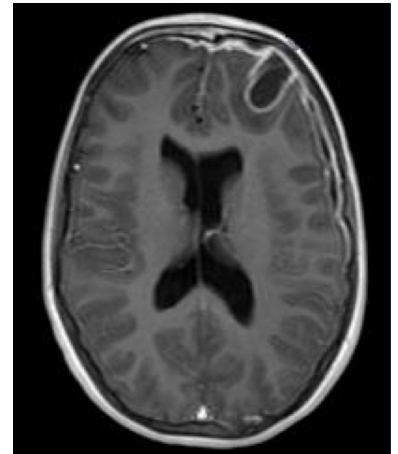
- Febrile patient²
- Headache and neck stiffness

if **untreated** may develop:

- Focal neurologic signs
- Lethargy
- Coma

Prognosis

- With treatment, including surgical **drainage**, resolution of the empyema occurs from the dural side & resolution is complete.
 - A **thickened dura** may be the only residual finding.
- With prompt treatment³, **complete recovery** is usual



Subdural empyema and brain abscess in patient with sinusitis.

Empyema vs Abscess (extra)

An empyema is a collection of pus within an naturally existing cavity such as the pleural cavity. An abscess however, is a collection of pus in a newly formed cavity.

Empyema means a lot of puss & necrosis.
2- Having or showing the symptoms of a fever.
3- Treatment performed without delay.

Tuberculous meningitis

- Chronic Infection caused by *Mycobacterium tuberculosis*.

Symptoms:

- Headache
- Malaise
- Mental confusion
- Vomiting

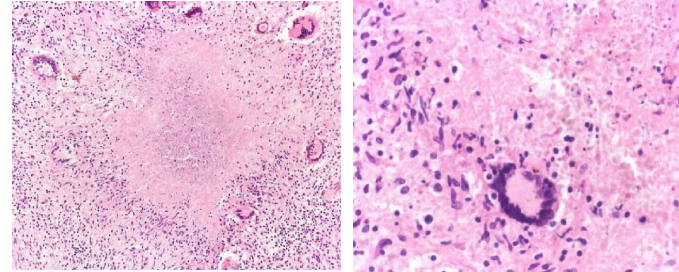
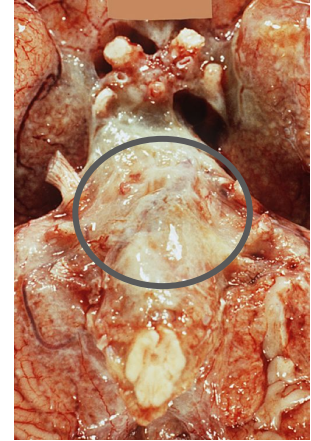
Morphology

Macroscopic Features:

- Subarachnoid space contain fibrinous exudate, most often at **base of brain**.

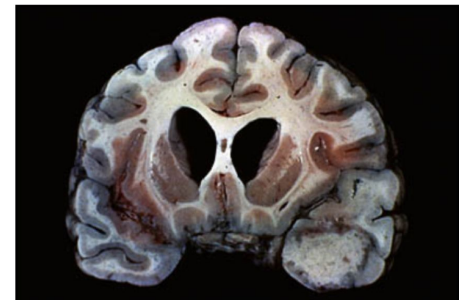
Microscopic Features:

- **Central** core of **Caseous necrosis**¹.
- **Surrounded** by a typical **granulomatous reaction**.



▶ Tuberculoma brain abscess of tuberculosis

- Is well-circumscribed **intraparenchymal mass**
- Rupture of tuberculoma into subarachnoid space results in **tuberculous meningitis**.
- A tuberculoma may be up to several centimeters in diameter, causing significant mass effect.
- **Always occurs after hematogenous** dissemination² of organism from primary pulmonary infection.



Tuberculoma in temporal lobe

CSF in Tuberculous Meningitis

- Moderate increase in cellularity of the CSF (pleocytosis) made up of mononuclear cells, or a mixture of polymorphonuclear and mononuclear cells. **lymphocytes is more because its chronic**
- The protein level is markedly **elevated**.
- The **glucose** content typically is moderately **reduced or normal**.

1- the doctor mentioned that in microscopic features the term caseous is not used, and only used in macroscopic

2- Hematogenous dissemination of TB occurs in **Miliary TB**

CNS Viral infections

- **Aseptic meningitis** is a misnomer
- 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 self-limiting & **less fulminant** (less severe) than in pyogenic, and most often **treated symptomatically**. Symptoms is like pyogenic.
- Eventually, A pathogen is identified in 70% of cases most commonly an **enterovirus**.

Pathogenesis

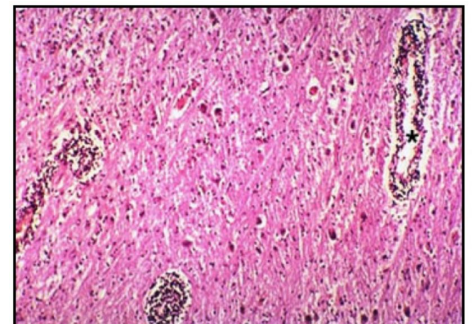
- **The CNS is specifically susceptible to certain viruses such as rabies and poliovirus.**
- Could also be infected with HSV, Enteroviruses, measles, or influenza virus.
- Intrauterine¹ infections following transplacental spread include:
 - Rubella & Cytomegalovirus (CMV) may cause destructive lesion
 - Zika virus cause **developmental abnormalities** of the brain.
- Injury could also be caused by **immune mechanism** after systemic viral infections.
- **Could lead to:**
 - Meningitis
 - Encephalitis
 - Brain stem or spinal cord syndrome

Morphology

- There are no distinctive **macroscopic** characteristics except for **brain swelling**, only in some instances.
- On **microscopic** examination, there is either no recognizable abnormality or a mild to moderate infiltration of the leptomeninges with lymphocytes.

CSF in Aseptic Meningitis:

- Increased number of lymphocytes (**pleocytosis**).
- Moderate protein elevation.
- Glucose content is nearly always normal.



Perivascular **lymphocytic** infiltrate

¹- Within the uterus.

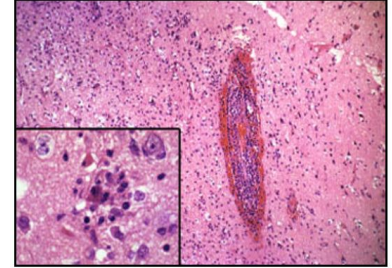
CNS Viral infections



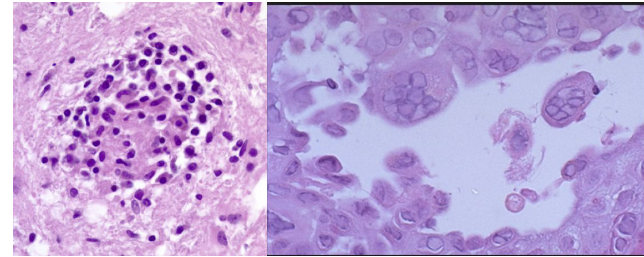
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► Herpes Simplex Virus (HSV)

- HSV produces a **hemorrhagic meningoencephalitis** with inflammation in both the meninges and the brain parenchyma.
- Virus may be identified by H&E stain as viral inclusion, culture or PCR amplification.
- The virus directly infects the cerebral cortex causing:
 - Necrosis.
 - **Glial reaction** which produce microglial nodules.
- **Microglial nodules**: Activated microglial cells encircle degeneration neurons (neurophagia) and form small foci of necrotic brain tissue.
 - Also seen in HIV encephalitis.



Hemorrhage surrounding the perivascular lymphocytic infiltrate



Microglial nodules

► Varicella-zoster virus Meningitis (VZV)

- VZV causes chickenpox during primary infection, usually with no neurological involvement
- The virus establishes latent infection in neurons of **Dorsal root ganglia**
- Reactivation in **adults** shows **painful, vesicular skin eruption** in the distribution of one or a few dermatomes (*shingles*¹)
- Usually self-limiting process, but may persist a pain syndrome in affected region (*postherpetic neuralgia*)

► Rabies

- **Rabies** is a fatal **encephalitis infection** transmitted to humans from rabid animals, usually by a bite².
- 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**

1- الحزام الناري

2- Through the infected animal's saliva (e.g. dog, cat) the virus travels to brain (usually spinal cord and brainstem) along the nerves => leading to neuronal injury.

CNS Viral infections cont.

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

Homework

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 only	-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

Bacterial meningitis

<p>Pyogenic meningitis</p>	<p>Considered a Medical emergency</p> <ul style="list-style-type: none"> • Causative Organisms: by population: <ul style="list-style-type: none"> - Neonates (<i>E. coli</i>) - Young Adults (<i>Neisseria meningitidis</i>) - Elderly (<i>Strep. pn</i>) • Prognosis: if Untreated, it can be fatal • Clinical Features: <ul style="list-style-type: none"> Headache -Photophobia -Irritability- Clouding of consciousness -Neck stiffness • CSF Findings: <ul style="list-style-type: none"> Cloudy CSF -90,000 neutrophils/mm -Raised protein level -low glucose • Complications: <ul style="list-style-type: none"> - Hydrocephalus - Focal cerebritis & seizures - Cerebral abscess - Cognitive deficit - Deafness - Hemorrhagic infarction - Waterhouse Friderichsen syndrome
<p>Brain abscess</p>	<ul style="list-style-type: none"> • Caused by: Direct implant - Local extension for foci - Hematogenous Spread • Predisposing conditions: Acute bacterial endocarditis - Cyanotic congenital heart disease - Chronic Pulmonary infections • Causative agent: <i>Streptococci and staphylococci</i> • CSF: Contains only scanty cells - ↑ protein - Normal level of glucose • Complications: Herniation - Rupture abscess into subarachnoid space/ventricle
<p>Empyema</p>	<p>Infections of the skull or air sinuses may also spread to the subdural space.</p> <ul style="list-style-type: none"> - Thrombophlebitis may develop. • Symptoms: Febrile patient - Headache and neck stiffness. • Complications: Focal neurologic signs - Lethargy - Coma.
<p>Tuberculous meningitis</p>	<ul style="list-style-type: none"> • Symptoms: • Headache • Malaise • Mental confusion • Vomiting • Tuberculoma: Is well-circumscribed intraparenchymal mass. <ul style="list-style-type: none"> - Rupture of tuberculoma into subarachnoid space results in tuberculous meningitis. - Always occurs after hematogenous dissemination. • CSF Findings: Glucose normal or low -↑ Protein -Moderate increase in cellularity

Viral meningitis

<p>Intro</p>	<ul style="list-style-type: none"> • Aseptic meningitis is a misnomer • Clinical Features: irritation, fever, and altered consciousness without recognizable organisms and it is treated symptomatically and usually self limiting. • Pathogenesis: - The CNS is specifically susceptible to certain viruses such as rabies and poliovirus - Intrauterine infections following transplacental spread - Injury caused by immune mechanism. • CSF Findings: - pleiocytosis -↑ Protein - Normal glucose level
<p>HZV</p>	<ul style="list-style-type: none"> • Produces a hemorrhagic meningoencephalitis -Infects the cerebral cortex causing: ○Necrosis ○ Glial reaction • Microglial nodules.
<p>VZV</p>	<p>Causes chickenpox during primary infection, usually with no neurological involvement.</p>
<p>Rabies</p>	<p>Is a fatal encephalitis infection transmitted to humans from rabid animals, usually by a bite.</p>

Quiz

Q1: Which of these viruses can cause hemorrhagic meningoencephalitis?

- A. Herpes Simplex Virus (HSV)
- B. Varicella
- C. Rabies
- D. MERS-CoV

Q2: Cyanotic congenital heart disease is a predisposing factor to which of these conditions?

- A. Pyogenic meningitis
- B. Brain abscess
- C. Empyema
- D. Tuberculous meningitis

Q3: In pyogenic meningitis the glucose would be:

- A. Increased
- B. Normal
- C. Slightly decreased
- D. Markedly decreased

Q4: which of these is considered a medical emergency?

- A. Pyogenic meningitis
- B. Tuberculous meningitis
- C. Poliomyelitis
- D. Fungal meningitis

Q5 :What's the most common route of infections in CNS?

- A. Hematogenous spread
- B. Trauma
- C. Through the peripheral nervous system
- D. local extension

Q6: Rupture in tuberculoma will lead to:

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

Q7: Which of the following people is most likely to develop bacterial meningitis?

- A. An obese women
- B. A newborn baby
- C. college student
- D. None of the above

Q8: Typical signs and symptoms of meningitis include all of these EXCEPT:

- A. Headache
- B. Painful or stiff neck
- C. Fever
- D. RBCs in CSF

1=A
2=B
3=D
4=A
5=A
6=A
7=B
8=D

Team Leaders

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#حتو حشونا

