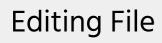


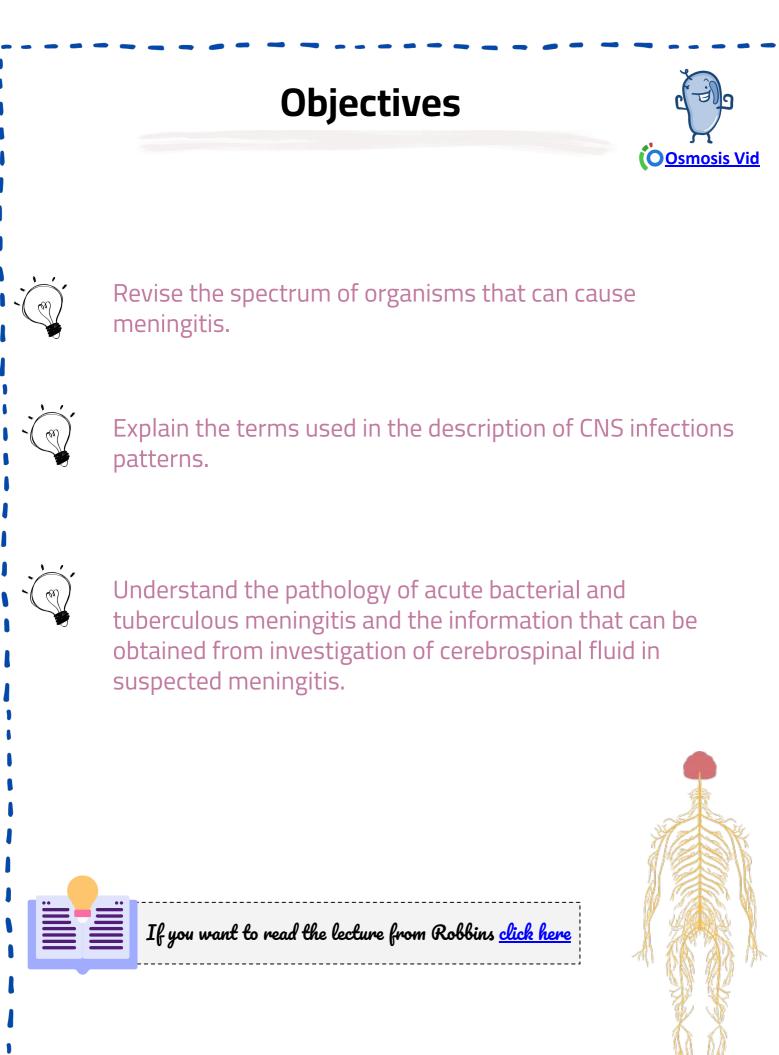
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# Pathology of meningitis and its complications





Color index : Main text ( black) Female Slides (Pink) Male Slides (Blue) Important ( Red) Dr's note (Green) Extra Info ( Grey)



# Meningitis



## Definition

Meningitis is an inflammatory process involving the leptomeninges and CSF within the subarachnoid space.

### FEMALES SLIDES

If the infection spreads into the underlying brain, it is termed meningoencephalitis.

## It can be:

• Infectious: acute pyogenic (usually bacterial), aseptic (usually viral), and chronic (usually tuberculous, spirochetal, or fungal).

• Non-infectious: chemical meningitis (a response to a nonbacterial irritant such as debris from a ruptured epidermoid cyst) and carcinomatous meningitis (the spread of metastatic cancer cells to the subarachnoid space).

## \*

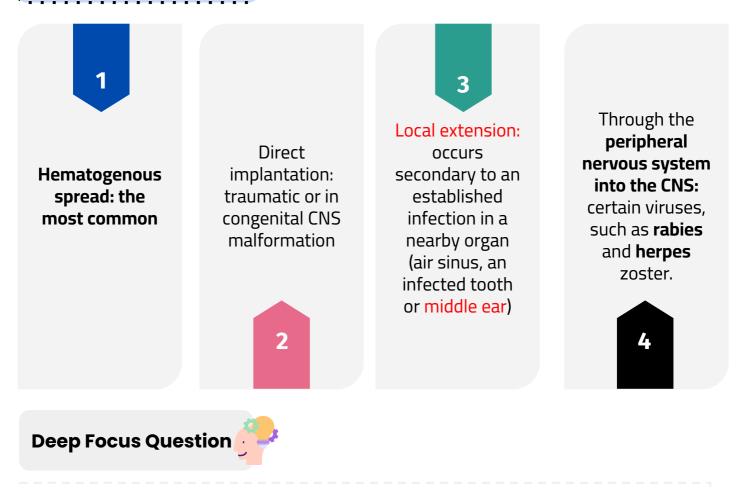
SLIDES

- Examination of the CSF is often useful in distinguishing among the various causes of meningitis.
- It is a medical emergency. Untreated pyogenic meningitis is often fatal, but with prompt diagnosis and administration of antibiotics, most patients can be saved.
- If treated early and effectively, resolved meningitis may leave little or no residuum.

Table 23.2 Common Central Nervous System Infections			
Type of Infection	Clinical Syndrome	Common Causative Organisms	
Bacterial Infe	ctions		
Meningitis	Acute pyogenic meningitis Chronic meningitis	Escherichia coli or group B streptococci (infants) Neisseria meningitidis (young adults) Streptococcus. pneumoniae or Listeria monocytogenes (older adults) Mycobacterium tuberculosis	
Localized	Abscess	Streptococci and	
infections	Empyema	staphylococci Polymicrobial (staphylococci, anaerobic gram-negative)	
Viral Infection	าร		
Meningitis	Acute aseptic meningitis	Enteroviruses Measles (subacute sclerosing parencephalitis) Influenza species Lymphocytic choriomeningitis virus	
Encephalitis	Encephalitic syndromes Arthropod-borne encephalitis	Herpes simplex (HSV-1, HSV-2) Cytomegalovirus Human immunodeficiency virus JC polyomavirus (progressive multifocal leukoencephalopathy) West Nile virus, other arboviruses	
Brain stem and spinal cord syndromes	Rhombencephalitis Spinal poliomyelitis	Rabies Polio West Nile virus	
-	irochetes, and Fung		
Meningitic syndromes	Rocky Mountain spotted fever Neurosyphilis	Rickettsia rickettsii Treponema pallidum	
	Lyme disease (neuroborreliosis)	Borrelia burgdorferi	
	Fungal meningitis	Cryptococcus neoformans Candida albicans	
Protozoa and	Metazoa		
Meningitic syndromes	Cerebral malaria Amebic encephalitis	Plasmodium falciparum Naegleria species	
Localized infections	Toxoplasmosis Cysticercosis	Toxoplasma gondii Taenia solium	

# Meningitis

# Route of entry



Which of the following statements about bacterial meningitis is TRUE?

- A. It constitutes an infection of the meninges only.
- B. It constitutes an infection of the subarachnoid space and the meninges.
- C. It refers to the infection of the cerebral cortex.
- D. Much like viral meningitis, it is a benign and self-limited disease.
- E. In constitutes an infection of the subarachnoid space only.

Answer: B

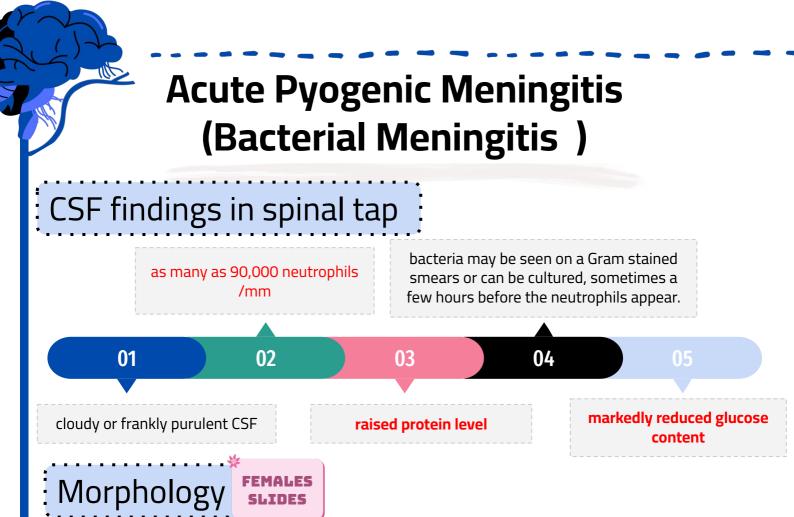
# Acute Pyogenic Meningitis (Bacterial Meningitis )

Organisms

-1015

The most likely causes of bacterial meningitis vary with patient age:

neonates	adolescents and young adults	older adults
common organisms are Escherichia coli and group B streptococci	Neisseria meningitidis ( Meningococcal meningitis) is the most common pathogen.	Streptococcus pneumoniae and Listeria monocytogenes are more common
Clinical Feature	S	MALES
<ul> <li>Systemic non-specific s</li> <li>Untreated, pyogenic m</li> <li>Effective antimicrobial meningitis</li> </ul>		<b>SLIDES</b> ity associated with
headache	1 Patients typically show systemic signs of infection along with meningeal irritation	2 Photophobia
neck stiffness 5	and neurologic impairment, including:	3 irritability
Lumbar puncture reveals an increased pressure.	clouding of consciousness	



Γ				
	Microscopic	Macroscopic		
	This gram stain shows multiple gram- positive diplococci, which is characteristic of Streptococcus pneumoniae. (1)	a Thick of suppurative exudate covers the brainstem and cerebellum and thickens the leptomeninges (1)		
	neutrophils may fill the entire subarachnoid space. Gram stain reveals varying numbers of the causative organisms	Cerebral abscesses in the frontal lobe white matter (2)		
	neutrophils may fill the entire subarachnoid space.	_		
	An exudate is evident within the leptomeninges on the surface of the brain	_		
	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. (2)	_		
	Arachnoid Pia (1) (2)	(1) (2)		

# Acute Pyogenic Meningitis (Bacterial Meningitis )

# Complication

-dbr

1	Severe involvement of leptomeningeal veins (phlebitis) may lead to venous occlusion and hemorrhagic infarction of the underlying brain.
2	Leptomeningeal fibrosis → hydrocephalus.
3	Extension to the ventricles $\rightarrow$ ventriculitis.
4	Focal cerebritis → seizures and cerebral abscess
5	Cognitive deficit
6	Deafness
7	Septicemia → hemorrhagic infarction of the adrenal glands and cutaneous petechiae (known as <mark>Waterhouse-Friderichsen syndrome</mark> , particularly common with Neisseria meningitidis and pneumococcal meningitis)
	Contraction of the second seco

more del

# **Brain Abscess**

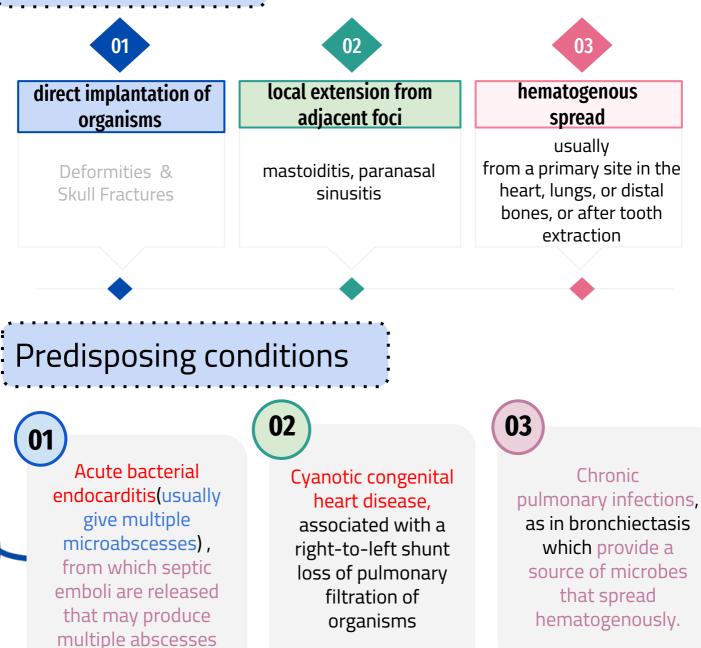
Organisms



## **Causative agent:**

- Brain abscesses are most often caused by bacterial infections.
- Streptococci and Staphylococci are the most common organisms identified in non-immunosuppressed populations.

# Routes Of Entry



# **Brain Abscess**

# Morphology

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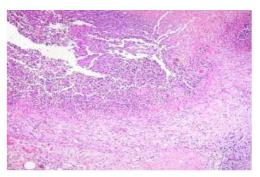
Abscesses are discrete destructive lesions with central **liquefactive necrosis** surrounded by a rim of vascularized granulation and fibrous tissue.

Outside the fibrous capsule is a zone of reactive gliosis.

The surrounding brain is edematous,congested & contains reactive astrocytes & perivascular inflammatory cells

Most common on cerebral hemispheres





# **Clinical Features**





## Neurological

Patients present clinically with progressive focal neurologic deficits in addition to the general signs of raised intracranial pressure.

## CSF

- Contains only scanty cells
- ↑ protein
- Normal level of glucose

## Complications of Brain abscess

- Herniation
- Rupture of abscess into subarachnoid space or ventricle

# **Epidural And Subdural Infections**

## Definition

The epidural and subdural spaces can be involved by bacterial or fungal infections, usually as a consequence of direct local spread.

Epidural abscesses commonly associated with osteomyelitis arise from an adjacent focus of infection, such as sinusitis or osteomyelitis or a surgical procedure

When abscesses occur in the spinal epidural space, they 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.

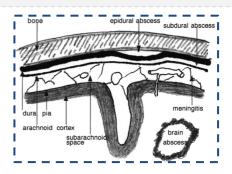
The underlying arachnoid and subarachnoid spaces are usually unaffected, but a large subdural empyema may produce a mass effect.

In addition, **Thrombophlebitis** may develop in the **bridging veins** that cross the subdural space, resulting in venous occlusion and infarction of the brain.

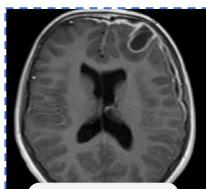
Symptoms include those referable to the source of the infection. Most patients are febrile, with headache and neck stiffness, and if untreated may develop focal neurologic signs, lethargy, and coma

## Prognosis:

• 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







brain abscess in patient with sinusitis

# **TUBERCULOUS MENINGITIS**



### Symptoms

 It usually manifests with generalized signs and symptoms of headache, malaise, mental confusion, and vomiting.

### Macroscopic findings

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



### Н H-C-ӨН H CH-0 C ӨН H C H C ӨН H C C ӨН H C H ӨН

• there is usually a

central core of caseous

necrosis surrounded by

granulomatous reaction

a typical tuberculous

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

## The protein level is markedly elevated often strikingly so

The **glucose** content typically is **moderately reduced or normal** 

## Deep Focus Question

## Deep Focus Question

What is the test of choice for bacterial meningitis?

- A. Computed tomography (CT) scan
- B. Complete metabolic panel
- C. Blood and urine cultures
- D. Lumbar puncture

Answer: D

What is a common cause of chronic bacterial meningitis?

- A. Neisseria meningitides
- B. Streptococcus agalactiae
- C. Haemophilus influenzae

D. Mycobacterium tuberculosis Answer: D

# TUBERCULOMA

It is a well-circumscribed intraparenchymal mass by a Mycobacterium tuberculosis.

Morphology

Rupture of tuberculoma into subarachnoid space results in tuberculous meningitis Always occurs after hematogenous dissemination of organism from a primary pulmonary infection

1

A tuberculoma is shown in the temporal lobe. -It is a destructive lesion A tuberculoma may be up to several centimeters in diameter,causing significant mass effect 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.



meninges.

- Bacteria usually reach the meninges via the bloodstream from the nasal cavity, often following a viral upper respiratory tract infection.
- Both the meningococcus and the pneumococcus have capsules which render them resistant to phagocytosis and complement.
- The bacteria enter the subarachnoid space where the blood-brain barrier is weak, e.g. the choroid plexus.
- Once in the CSF, the bacteria multiply rapidly and stimulate an acute inflammatory response within the





**EO** 

# **Viral Meningitis**

The nervous system is particularly susceptible to certain viruses such as rabies virus and poliovirus. Other viral infections could affect CNS such as HSV, Enteroviruses, 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.

SLIDES

CNS can be injured by immune mechanisms after systemic viral infections. CNS viral infections could lead to meningitis, encephalitis or brain stem and spinal cord syndromes.

## Deep Focus Question



How do you perform Kernig's test in a patient with suspected meningitis?

- A. With the patient prone, extend their neck backward by one inch.
- B. With the patient standing, flex their neck with the chin toward the chest.
- C. With the patient supine, flex the leg at the hip and then extend the knee.

Answer: C

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

# Aseptic meningitis

## Definition

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Misnomer, it is a clinical term for an illness comprising meningeal irritation, fever, and alterations of consciousness. The symptoms are usually of an **acute onset without recognizable organisms.** 

Clinical course	Self-limiting & <b>less fulminant</b> than pyogenic & often treated symptomatically			
Most Common Cause	A pathogen is identified in 70% of cases most commonly an <b>enterovirus.</b>			
CSF	<ul> <li>Increased number of lymphocytes (pleiocytosis).</li> <li>Moderate protein elevation.</li> <li>Glucose content is nearly always normal.</li> </ul>			
	Macroscopic			
	There are no distinctive <b>macroscopic</b> characteristics			
Morphology	except for brain swelling, only in some instances.			
	Microscopic			
	There is either no recognizable abnormality or a mild to moderate infiltration of the leptomeninges with lymphocytes. In viral meningitis, clusters of			
$\sim$	lymphocytes surround cerebral blood vessels.			

# Herpes Simplex Virus (HSV)

## HSV

HSV produces a hemorrhagic meningoencephalitis with inflammation in both the meninges and the brain parenchyma.

## HSV-1

Cause encephalitis may occur in any age group but is most common in children and young adults

## HSV-2

SLIDES

also affects the nervous system, usually in the form of meningitis in adults

# Microscopic

The infection is necrotizing and often hemorrhagic in severely affected regions.

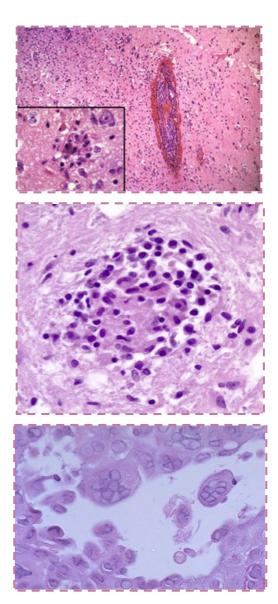
Perivascular inflammatory infiltrates usually are present.

The virus directly infects cells in the cerebral cortex, causing necrosis and a glial reaction. This reaction produces a microglial nodule.

Large eosinophilic intranuclear viral inclusions **(Cowdry type A bodies)** can be found in both neurons and glial cells.

**Microglial nodule**: activated microglial cells encircle degenerating neurons (neuronophagia) and form clusters around small foci of necrotic brain tissue. Such nodules can be seen also in HIV encephalitis.

The virus may be identified by H&E stain as viral inclusion, culture or polymerase chain reaction amplification.



# Varicella-zoster virus (VZV) Meningitis

Varicella-zoster virus (VZV) causes chickenpox during primary infection, usually without any evidence of neurologic involvement. Reactivation in adults manifests as a painful, vesicular skin eruption in the distribution of one or a few dermatomes (shingles).

SLIDES

The virus establishes latent infection in neurons of dorsal root ganglia.

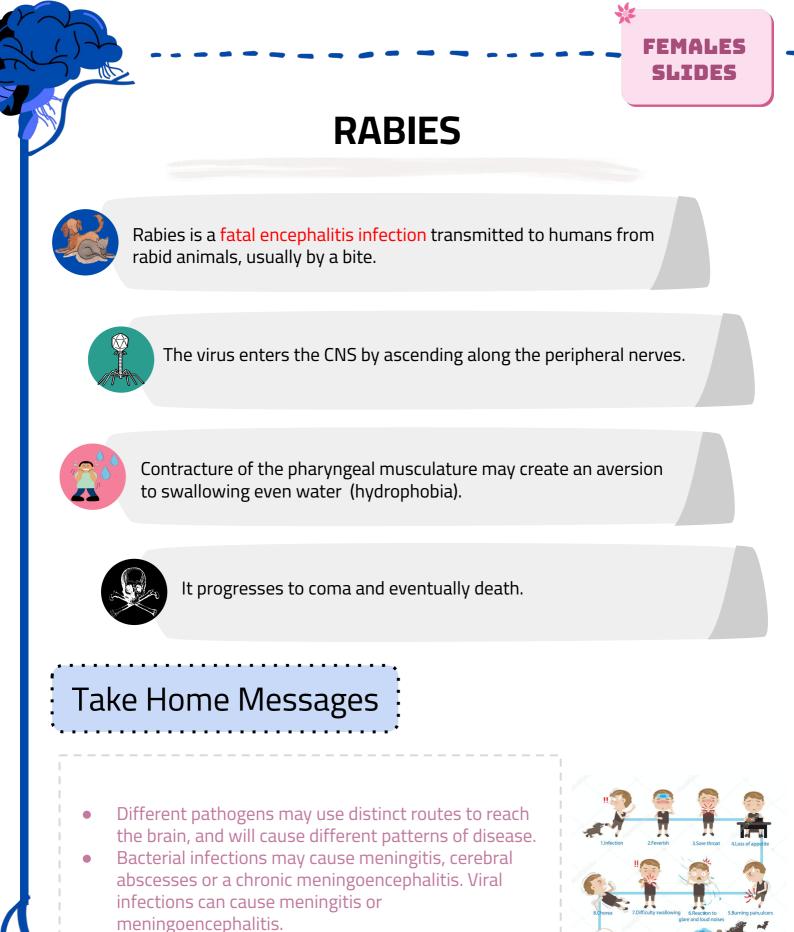
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This usually is a self-limited process, but there may be a persistent pain syndrome in the affected region (postherpetic neuralgia).

Chickenpox is usually a milder illness that affects children. Shingles results from a reactivation of the virus long after the chickenpox illness has disappeared.



CEREBROSPINAL	NORMAL	MENINGITIS			
FLUID		BACTERIAL	VIRAL	FUNGAL	TUBERCULOUS
OPENING PRESSURE (mm H <sub>2</sub> 0)	< 200	> 200	> 200	> 200	> 200
WBC COUNT	5 WBCs	1000s WBCs	100s WBCs	100s WBCs	100s WBCs
(per mm <sup>3</sup> )	70% lymphocyte	neutrophilic	lymphocytic	mononuclear	mononuclear
DIFFERENTIAL	30% monocytes	pleocytosis	pleocytosis	pleocytosis	pleocytosis
	few neutrophils	> 80%	> 50%	> 50%	> 50%
PROTEIN LEVEL ( mg/dL )	15 - 20	100 - 500	15 - 200	15 - 200	100 - 500
GLUCOSE LEVEL	45 - 100	< 40		< 40	< 40
( mg/dL )	<sup>2</sup> / <sub>3</sub> of serum		normal		
GLUCOSE CSF : SERUM	< 0.4		normal		



• Lumbar puncture plays an important role in the diagnostic process of some CNS infections.

# Keywords

-111

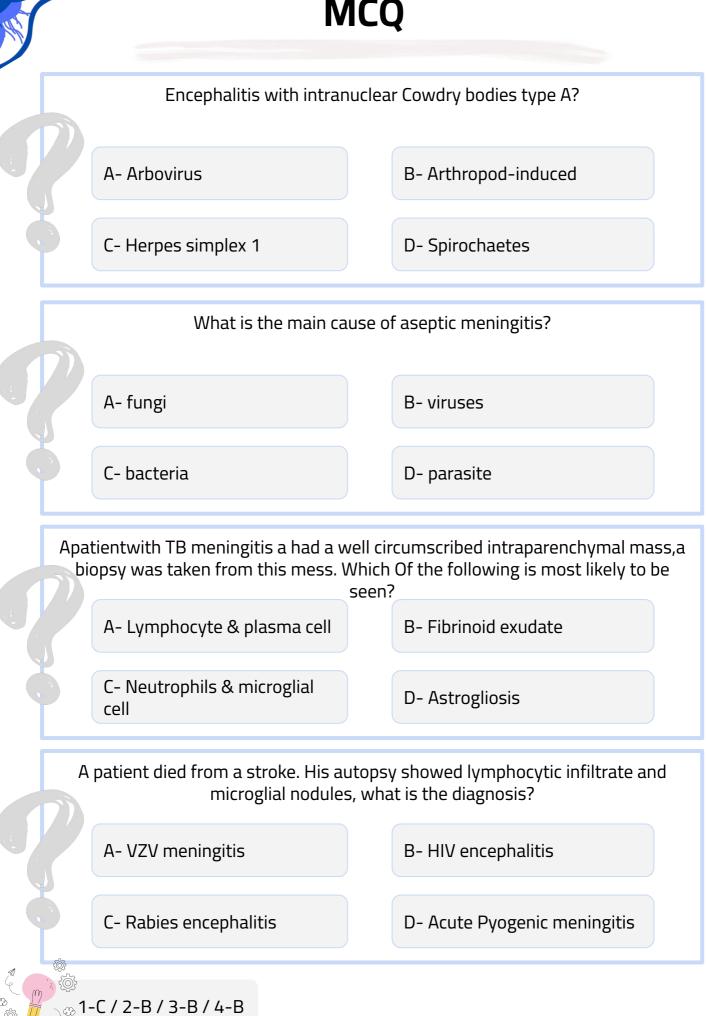
Acute Pyogenic meningitis	<ul> <li>neonates : E.coli , group B streptococci</li> <li>Adults : Neisseria meningitidis</li> <li>older adults: Streptococcus pneumoniae , Listeria monocytogenes</li> <li>Neck stiffness</li> <li>Headache</li> <li>Fever</li> <li>Increase protein level</li> <li>reduced glucose levels</li> <li>exudate</li> </ul>
Brain Abscesses	<ul> <li>Streptococci , Staphylococci</li> <li>bacterial endocarditis</li> <li>Cyanotic congenital heart disease</li> <li>Increased ICP</li> <li>scanty cells</li> <li>Increase proteins level</li> <li>Normal glucose</li> <li>central liquefactive necrosis</li> </ul>
Epidural and Subdural infections	<ul> <li>direct local spread.</li> <li>Epidural abscesses : sinusitis or osteomyelitis.</li> <li>empyema</li> <li>Thrombophlebitis : in bridging veins</li> <li>Headache</li> <li>Fever</li> <li>neck stiffness</li> </ul>
Tuberculous meningitis	<ul> <li>Malaise</li> <li>fibrinous exudate</li> <li>central core of caseous necrosis</li> <li>Increase mononuclear</li> <li>elevated protein level</li> <li>Normal glucose</li> <li>Tuberculoma</li> <li>Negative gram stain</li> </ul>

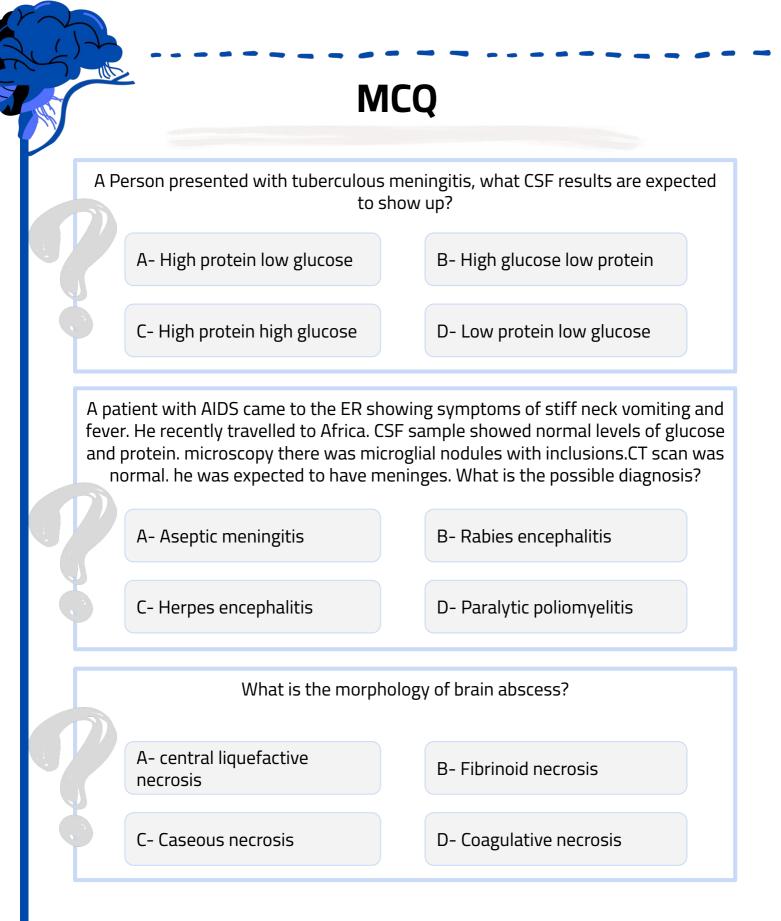
	Keywa	ords
	<ul> <li>Self-limiting</li> <li>enteroviru</li> <li>brain swell</li> </ul>	Is Iling tes infiltration protein
Aseptic meningitis	Herpes Simplex Virus (HSV)	<ul> <li>Hemorrhagic meningoencephalitis</li> <li>Necrosis</li> <li>HSV-1 encephalitis : children</li> <li>HSV-2 meniginits : adult</li> <li>Perivascular inflammatory</li> <li>Microglial nodule</li> <li>Cowdry type A bodies</li> </ul>
	Varicella-zoste r virus Meningitis (VZV) "HSV"	<ul> <li>chickenpox</li> <li>Dorsal root ganglia</li> <li>shingles</li> <li>postherpetic neuralgia</li> </ul>
	Rabies	<ul> <li>encephalitis infection</li> <li>Animal bite</li> <li>coma &amp; death</li> </ul>



## Need a SUMMARY ? <u>Click here</u>

# MCQ







# Cases

1.A 32-year-old woman presents with a 2-day history of headache, vomiting, and fever. Physical examination reveals cervical rigidity and knee pain with hip flexion. Lumbar puncture demonstrates an abundance of neutrophils and decreased levels of glucose. Which of the following diseases is most likely associated with these clinical laboratory findings?

A.Meningococcal	B.Staphylococcal	C.Tuberculous	D.Viral meningitis
meningitis	meningitis	meningitis	

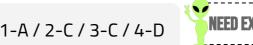
2.A 3-day-old infant presents with a fever of 38.7°C (103°F) and convulsions. The infant is started on broad-spectrum antibiotics and antiviral medications but slips into a coma and died. At autopsy, the brain shows a purulent exudate in the subarachnoid space at the base of the brain (shown in the image). What was the most likely cause of suppurative meningitis in this neonate?



	A.Candida albicans	B.Cryptococcus neoformans	C.Escherichia coli	D.Neisseria meningitidis
--	--------------------	------------------------------	--------------------	-----------------------------

3.A 59-year-old woman presents with headache and mild fever of 3 days in duration. On physical examination, the patient appears confused and inattentive. On the following day, she is rushed to the emergency room after suffering a generalized seizure. Lumbar puncture shows increased levels of CSF protein, but cultures are negative, and the white cell count is not elevated. PCR analysis of the CSF fluid shows evidence of herpes simplex type 1. This infection most likely involves which of the following anatomic regions of the patient's brain?

	A.Basal ganglia	B.Brainstem nuclei	C.Temporal lobes	D. None
4.The patient described in Question 3 is started on antiviral medication but becomes increasingly unresponsive and expires. Examination of affected brain tissue at autopsy would most likely reveal which of the following pathologic findings?				
	A.Charcot-Bouchard aneurysms	B.Focal plaques of demyelination	C.Neurofibrillary tangles	D.Perivascular cuffs of lymphocytes



# Cases

## **EXTRA CASES REQUIRE EXTRA INFO**

1.An 18-day-old boy is brought to the emergency department due to fever and irritability. The boy was healthy at birth; however, 2-days ago, he developed a fever and decreased appetite. In addition, the patient has become increasingly irritable. Blood testing reveals leukopenia and cerebrospinal fluid (CSF) analysis reveals low glucose concentration and elevated proteins. Gram culture of the blood and CSF is positive for Streptococcus agalactiae. Which of the following is true regarding this pathogen?

A.Demonstrates sensitivity to bacitracin	B.Produces a factor that enhances Staphylococcus aureus hemolysis on blood agar	C.Produces α-hemolysis on blood agar	D.Produces an enzyme that converts hydrogen peroxide to oxygen and water

2.A 45-year-old man presents to the emergency department due to intense headaches and difficulty with bright lights. The patient developed new genital lesions about a week ago. Brain imaging shows no abnormalities. Lumbar puncture is performed, and the CSF profile shows pleocytosis with a predominance of lymphocytes and a normal CSF glucose concentration. Which is the most likely cause of this patient's condition?

A.Herpes simplex virus-2	B.Herpes simplex virus-1	C.Cytomegalovirus	D.Cryptococcus

3.A 20-year-old man is brought to the emergency department due to altered mental status and headaches for the past day. His roommate states that he was in his usual state until yesterday, when he started complaining of headaches, fever, and abnormal behavior. Temperature is 38.5°C (101.3°F), pulse is 100/min, and blood pressure is 124/80 mmHg. On physical examination, the patient is lethargic but arousable. The neck is supple with full range of motion. The patient responds to questions, but the speech is incomprehensible. Hyperreflexia is present. MRI of the head shows edema and hyperintensities in the temporal lobes. Which of the following is the most likely explanation for these findings?

A.Encephalitis

**B.Myelitis** 

C.Aseptic meningitis

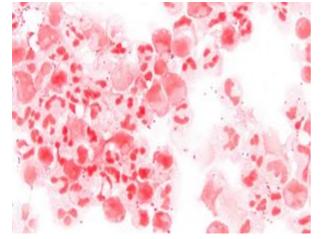
D.Meningitis



# Cases

## **EXTRA CASES REQUIRE EXTRA INFO**

3.A 19-year-old man comes to the emergency department with a severe headache, vomiting, and fever. The patient is a military recruit who is three weeks into bootcamp. His friend states that he appeared normal 12 hours ago. Temperature is 39.5 °C (103.1 °F), pulse is 120/min, respirations are 19/min, and blood pressure is 110/75 mmHg. The patient is markedly disoriented and unable to answer questions. Physical examination shows positive Kernig and Brudzinski signs. Serum glucose concentration is 90 mg/dL. A lumbar puncture is performed, and the cerebrospinal fluid gram stain is shown below:



Cerebrospinal Fluid	Reference Range
Cell count	0-5/mm³
Chloride	118-132 mEq/L
Gamma globulin	3%-12% of total proteins
Glucose	40-70 mg/dL
Pressure	70-180 mm H2O
Proteins, total	<40 mg/dL

Cerebrospinal fluid analysis is most likely to reveal which of the following sets of findings?

А.	Cell count/mm3	Protein level (mg/dL)	Glucose level (mg/dL)	В.	Cell count/mm3	Protein level (mg/dL)	Glucose level (mg/dL)
	50	500	20		1100	300	15
2. [	Cell count/mm3	Protein level (mg/dL)	Glucose level (mg/dL)	D.	Cell count/mm3	Protein level (mg/dL)	Glucose level (mg/dL)

The difference between A & B that A CSF analysis is consistent with tuberculosis (TB) meningitis, as characterized by slightly elevated lymphocyte count, markedly elevated protein level, and usually low glucose. Routine bacterial cultures would be negative.



