Meningitis

Pathology

Objectives

1. Define meningitis, and describe its location and character
2. List possible routes of access of infectious organisms into the CNS
3. Describe the clinical presentation and pathology of acute bacterial meningitis, and its sequelae
4. Define the relationship between patient age and the most common etiologic organisms for bacterial meningitis.
5. Describe the CSF findings in various causes of meningitis.
6. Define the conditions that predispose to the development of a brain abscess, and describe the clinical and pathologic features.
7. Describe the clinical and pathologic findings in tuberculosis of the central nervous system.
8. List the common causes of viral encephalitis, and describe the pathologic changes in encephalitis due to herpes simplex virus.
9. Recognize the importance of lumbar puncture and its role in the diagnostic process of some CNS infections.
10. Contrast the CSF findings characteristic of bacterial meningitis, aseptic (viral) meningitis, and chronic meningoencephalitis (tuberculous meningitis).

Ref:

- Meningitis
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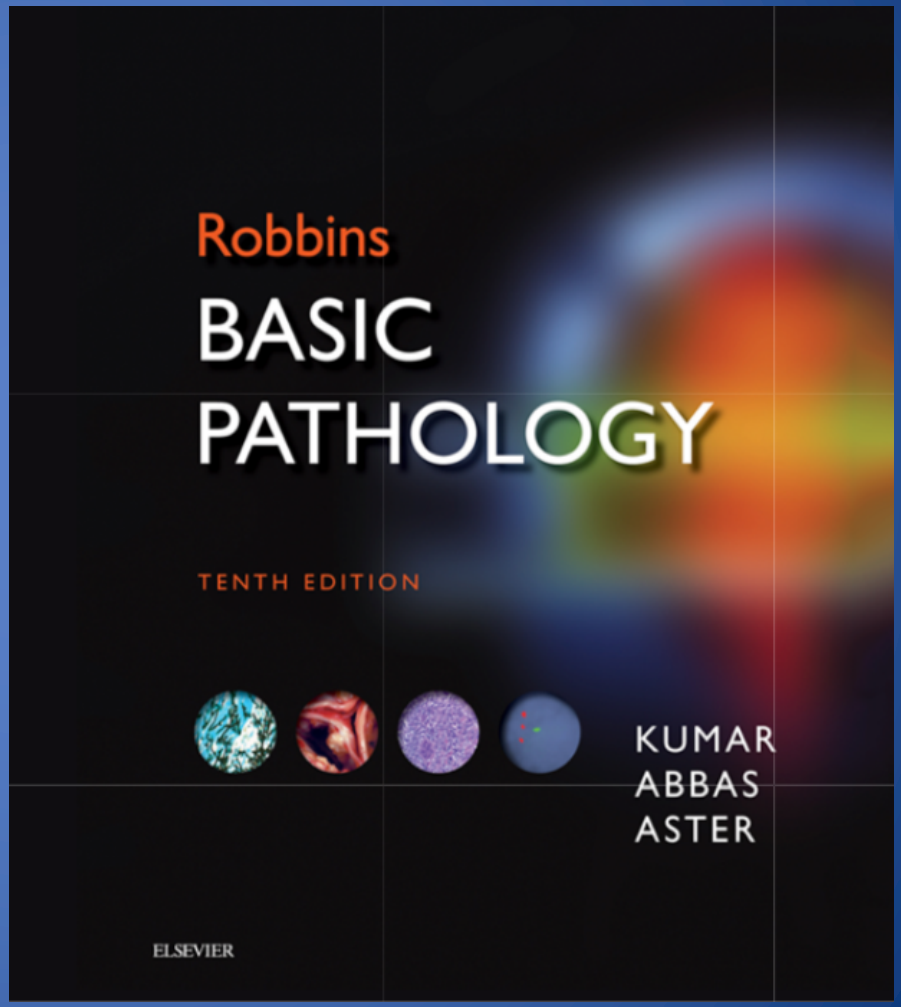


Define meningitis, and describe its location and character

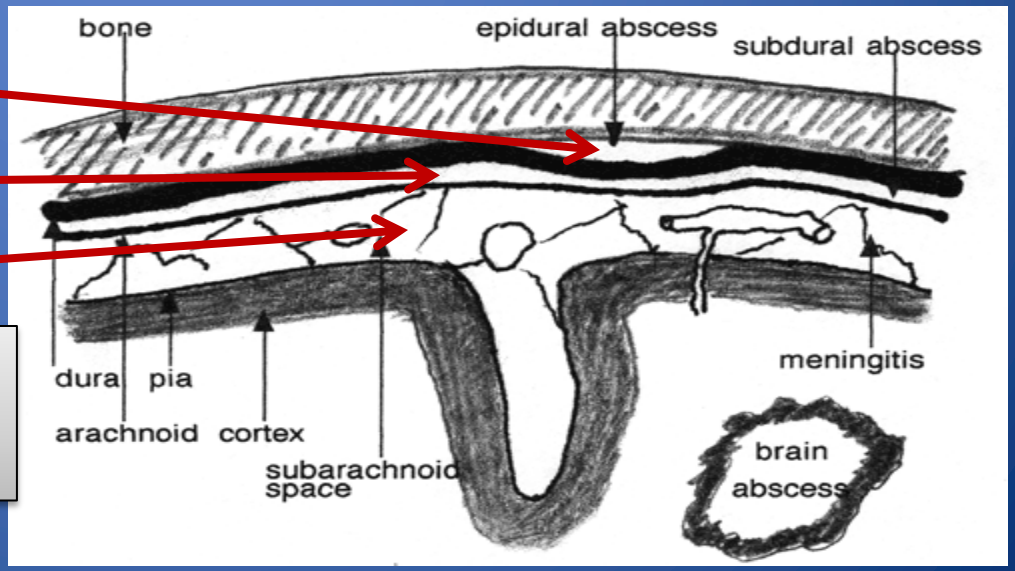
- Meningitis is an inflammatory process involving the leptomeninges and CSF within the subarachnoid space
- Meningoencephalitis is infection spreads into the underlying brain

Epidural space

Subdural space

Subarachnoid space

chemical meningitis
carcinomatous meningitis



Infectious meningitis

Could be:

- **Acute pyogenic**
- **Aseptic (usually viral)**
- **Chronic (usually tuberculous, spirochetal, or fungal) subtypes**

Pattern of infection:

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

List possible routes of access of infectious organisms into the CNS

CNS Infections

- Portals of entry of infection into the CNS:
  - ***Hematogenous spread***
    - the most common
  - ***Direct implantation***
    - traumatic or in congenital CNS malformation
  - ***Local extension***
    - occurs secondary to an established infection in a near by organ (air sinus, an infected tooth or middle ear)
  - ***Through the peripheral nervous system into the CNS***
    - certain viruses, such as rabies and herpes zoster.

Define the relationship between patient age and the most common etiologic organisms for bacterial meningitis.

CNS Infection: Pyogenic meningitis

- Medical emergency
- The causative microorganisms

(10th edition, Robbins):

- **Neonates :**
  Escherichia coli and *group B streptococci*
- **Adolescents and young adults:**
  Neisseria meningitidis (Meningococcal meningitis)
- **Elderly and older adults:**
  Listeria monocytogenes and *Streptococcus pneumoniae*

Describe the clinical presentation and pathology of acute bacterial meningitis, and its sequelae

Pyogenic meningitis

Clinical features

- Systemic signs of infection along with meningeal irritation and neurologic impairment, including:
  - Headache
  - Photophobia
  - Irritability
  - Clouding of consciousness
  - Neck stiffness.
  - Lumbar puncture reveals an increased pressure

CNS Infections

Pyogenic meningitis

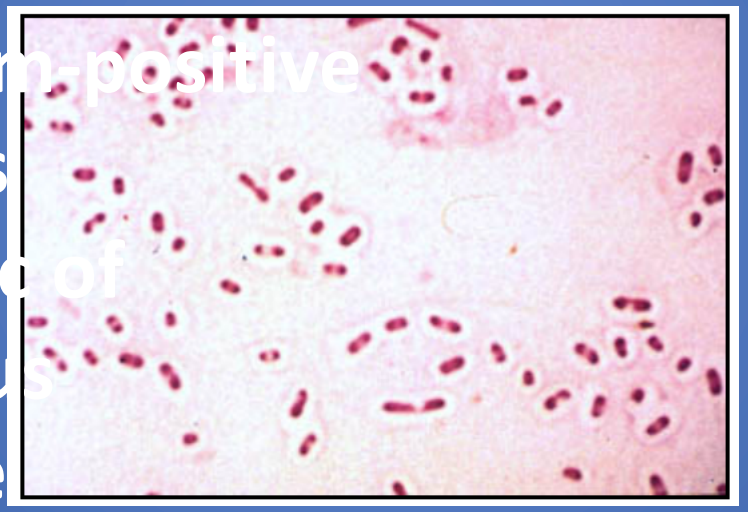
- **CSF Findings in spinal tap:**
  - cloudy or frankly purulent CSF
  - as many as 90,000 neutrophils /mm
  - raised protein level
  - markedly reduced glucose content
  - bacteria may be seen on a Gram stained smear or can be cultured, sometimes a few hours before the neutrophils appear

CNS Infections

Pyogenic meningitis

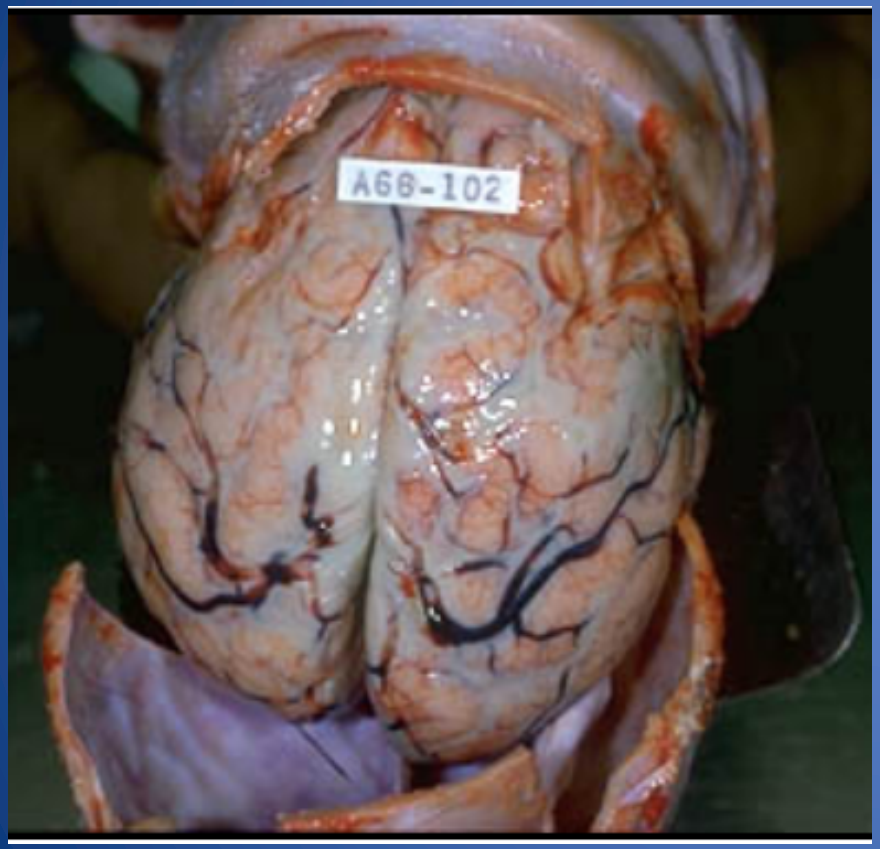
CSF Gram stain -

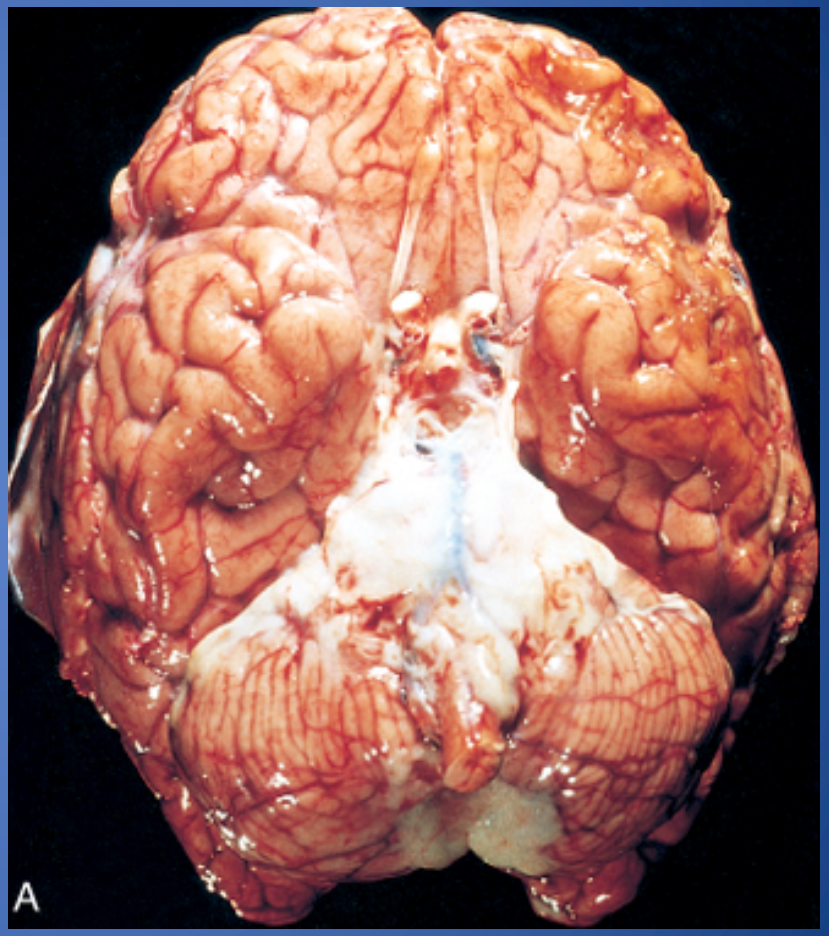
e.g. this gram stain shows multiple gram-positive diplococci, is characteristic of Streptococcus pneumoniae



Describe the clinical presentation and pathology of acute bacterial meningitis, and its sequelae

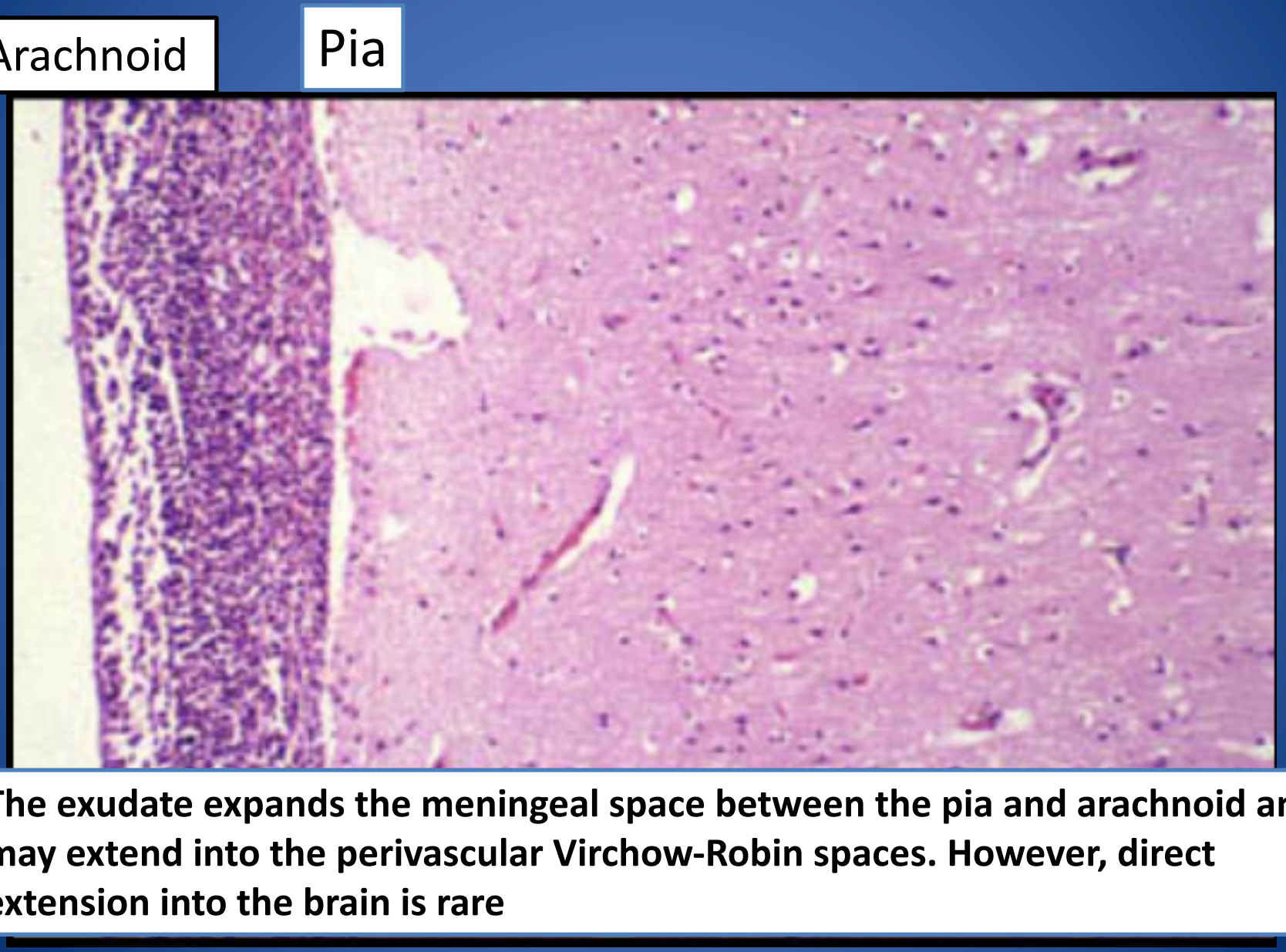
Pyogenic meningitis: Acute meningitis





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

Pyogenic meningitis: Acute meningitis



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

Describe the clinical presentation and pathology of acute bacterial meningitis, and its sequelae

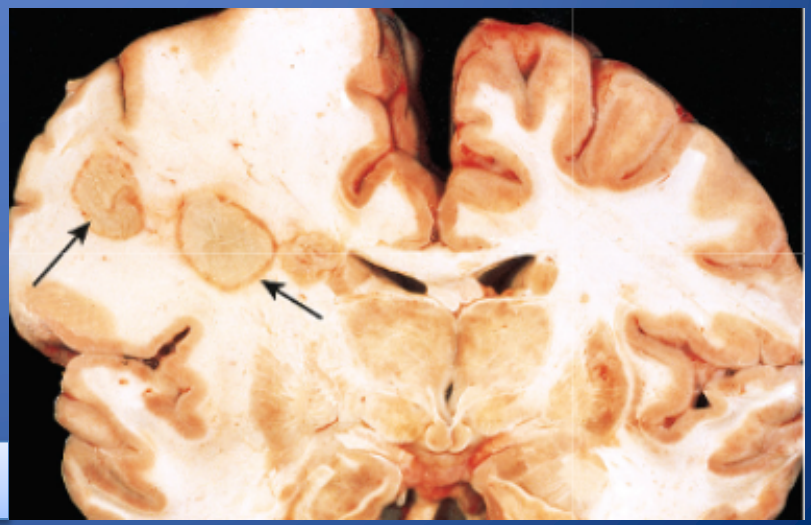
Pyogenic Meningitis: outcome

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

Describe the clinical presentation and pathology of acute bacterial meningitis, and its sequelae

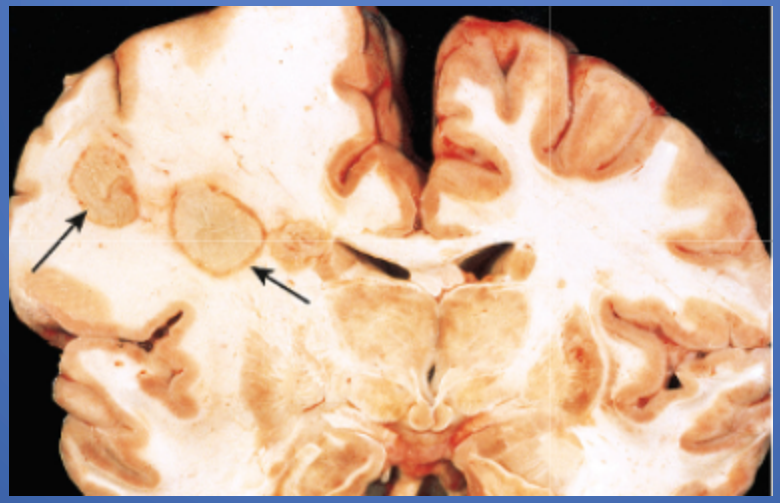
Pyogenic meningitis: **Complications**

- 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 *Neisseria meningitidis* and pneumococcal meningitis)
- Focal cerebritis & seizures
- Cerebral abscess
- Cognitive deficit
- Deafness



What is this complication →

Brain abscess



Define the conditions that predispose to the development of a brain abscess, and describe the clinical and pathologic features

Brain abscess

- **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)

CNS Infections
Brain abscess

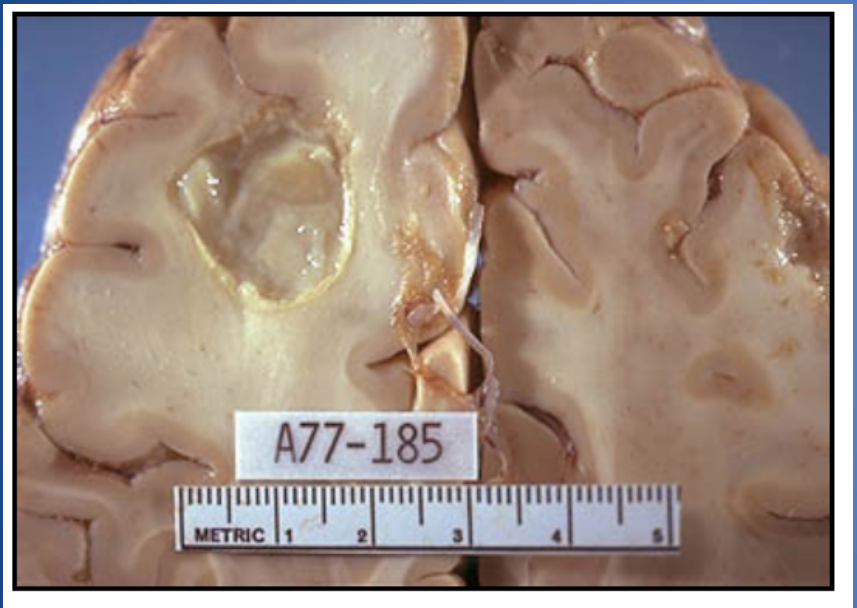
- Predisposing conditions:
  - ***Acute bacterial endocarditis:*** usually give multiple microabscesses
  - ***Cyanotic congenital heart disease***: There is a right-to-left shunt and Loss of pulmonary filtration of organisms
  - ***Chronic pulmonary infections:*** e.g, bronchiectasis

➢ Causative agent:

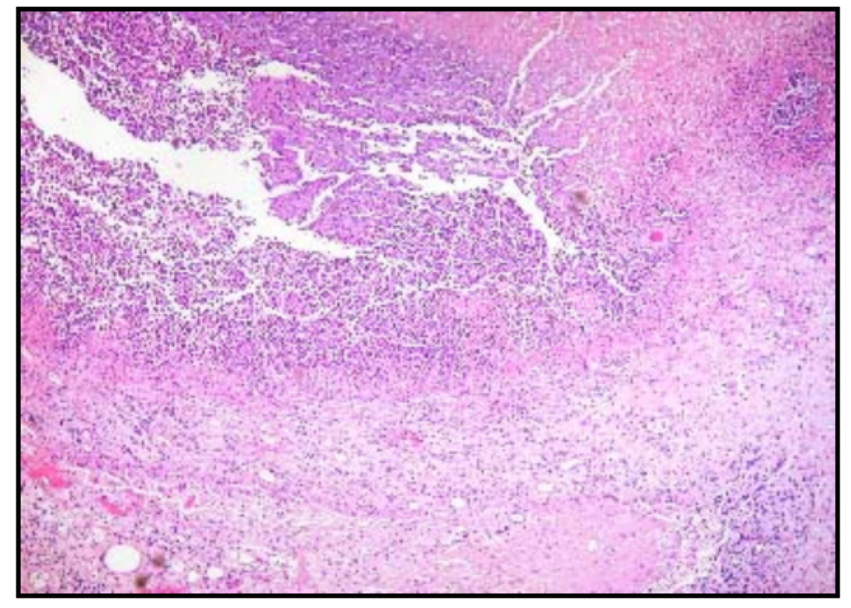
Streptococci and *Staphylococci* are the most common organisms identified in non-immunosuppressed populations

CNS Infections: Brain abscess Morphology

Most common on cerebral hemispheres



An area of necrosis within a brain abscess



–Liquefactive necrosis

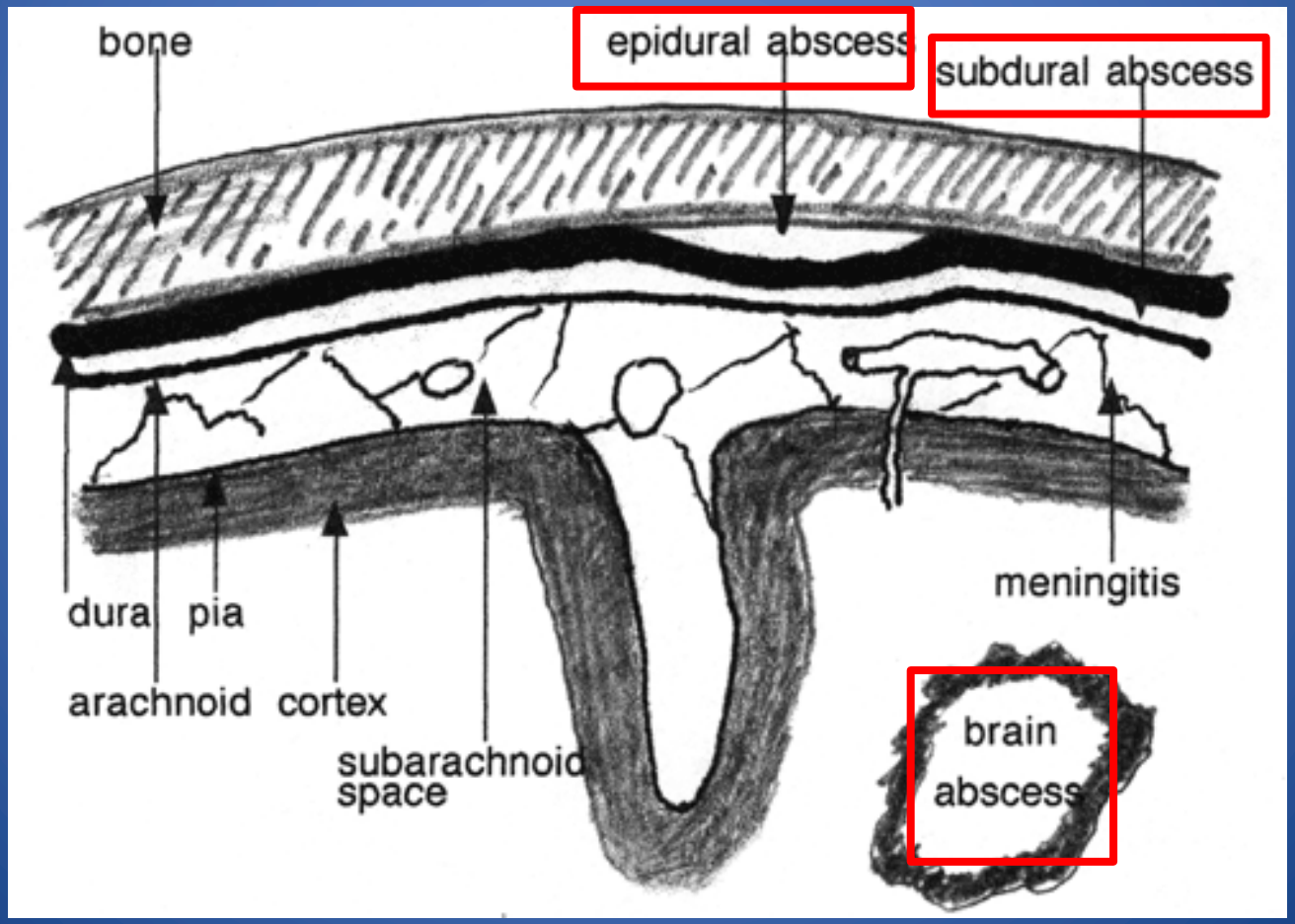
–The surrounding brain is edematous , congested & contains reactive astrocytes & perivascular inflammatory cells

CNS Infections

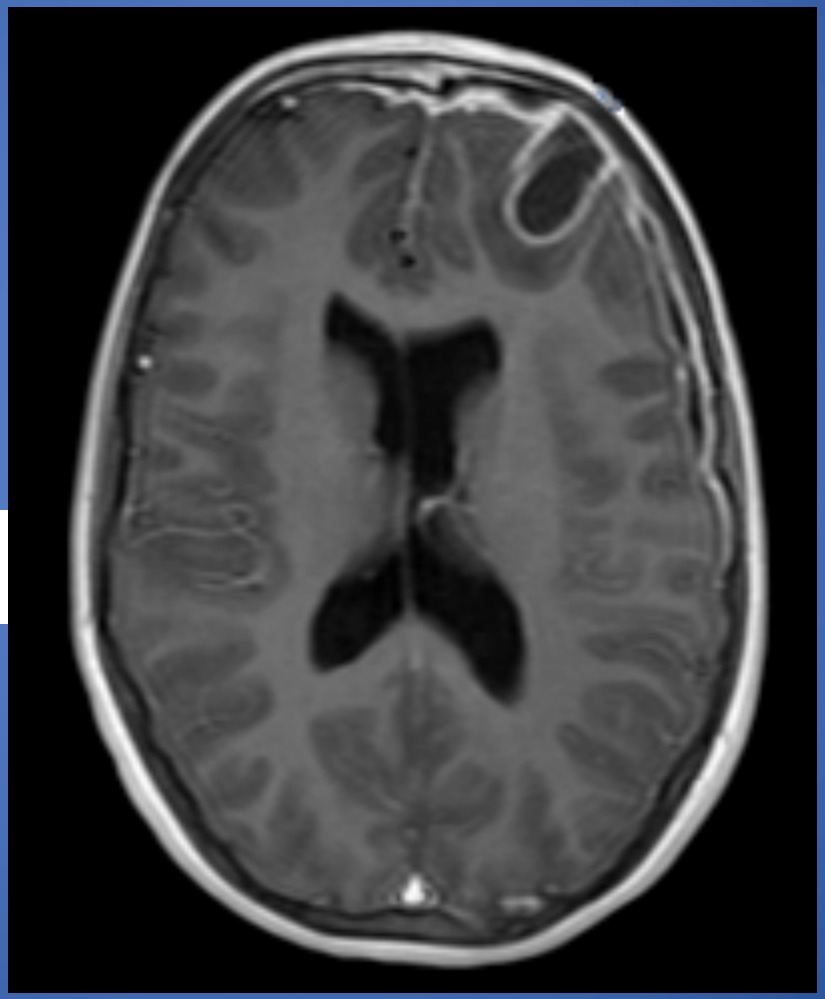
Brain abscess

- Present clinically with progressive focal neurologic deficits in addition to the general signs of raised intracranial pressure
- The 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



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



Epidural and Subdural Infections

- These spaces can be involved with bacterial 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 or a surgical procedure
- When the process occurs in the spinal epidural space, it 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
  - Thrombophlebitis may develop in the bridging veins that cross the subdural space, resulting in venous occlusion and infarction of the brain

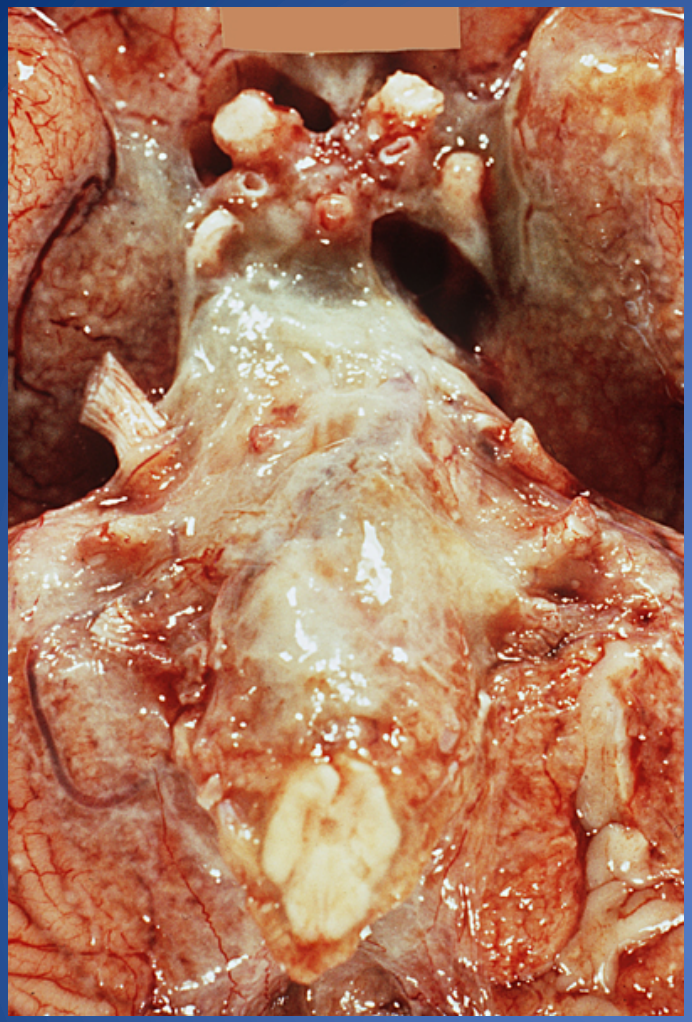
Empyema

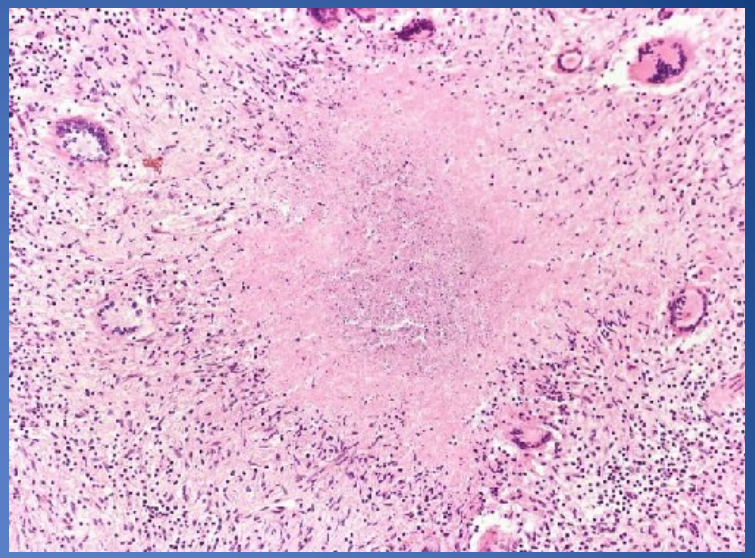
- Symptoms:
  - most patients are febrile, with headache and neck stiffness, and if untreated may develop focal neurologic signs, lethargy, and coma
- Prognosis:
  - With treatment, including surgical drainage, resolution of the empyema occurs from the dural side and resolution is complete, a thickened dura may be the only residual finding.
  - With prompt treatment, complete recovery is usual

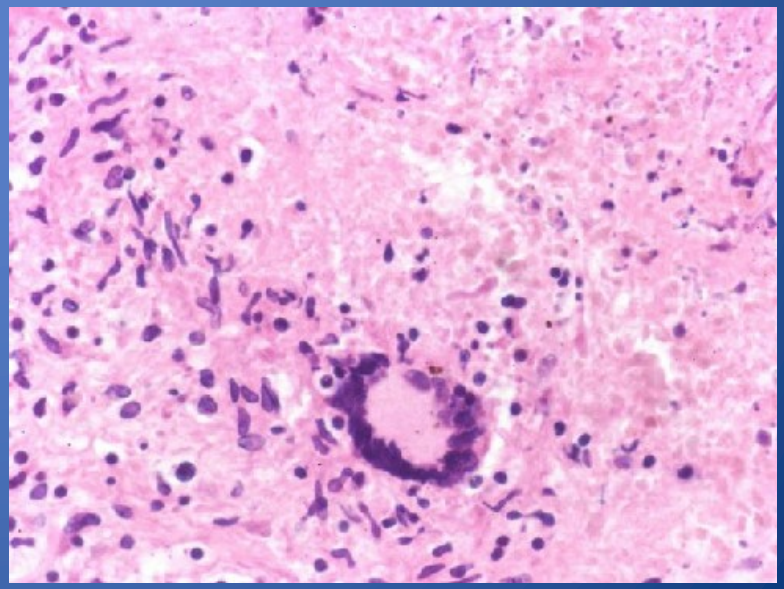
CNS Infections
Tuberculous meningitis

CNS Infections
Tuberculous meningitis

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





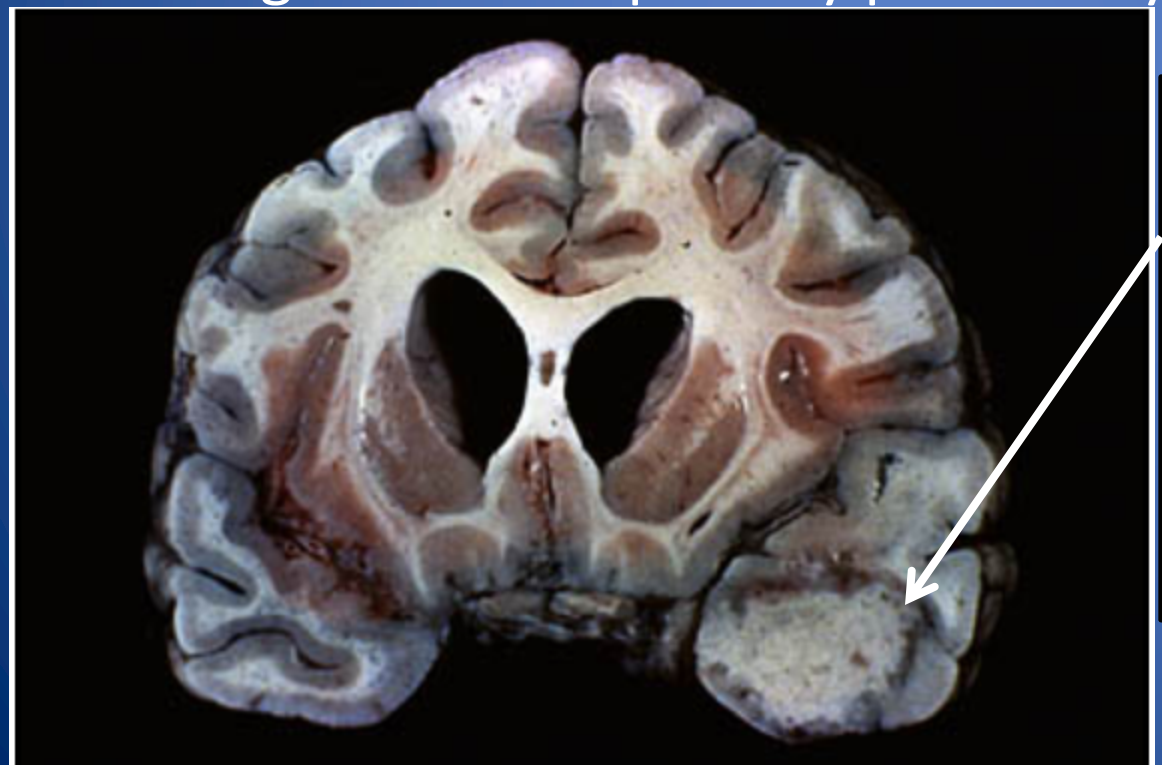


TB meningitis

Exudate at the base of the brain

Tuberculoma

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



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.

CNS Infections
CSF in TB

- 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
- The glucose content typically is moderately reduced or normal

CNS viral infections

1. Viral (aseptic) Meningitis
2. Encephalitis
3. Brain stem and spinal cord syndromes

CNS viral infections

- 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.
- 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

CNS viral infections

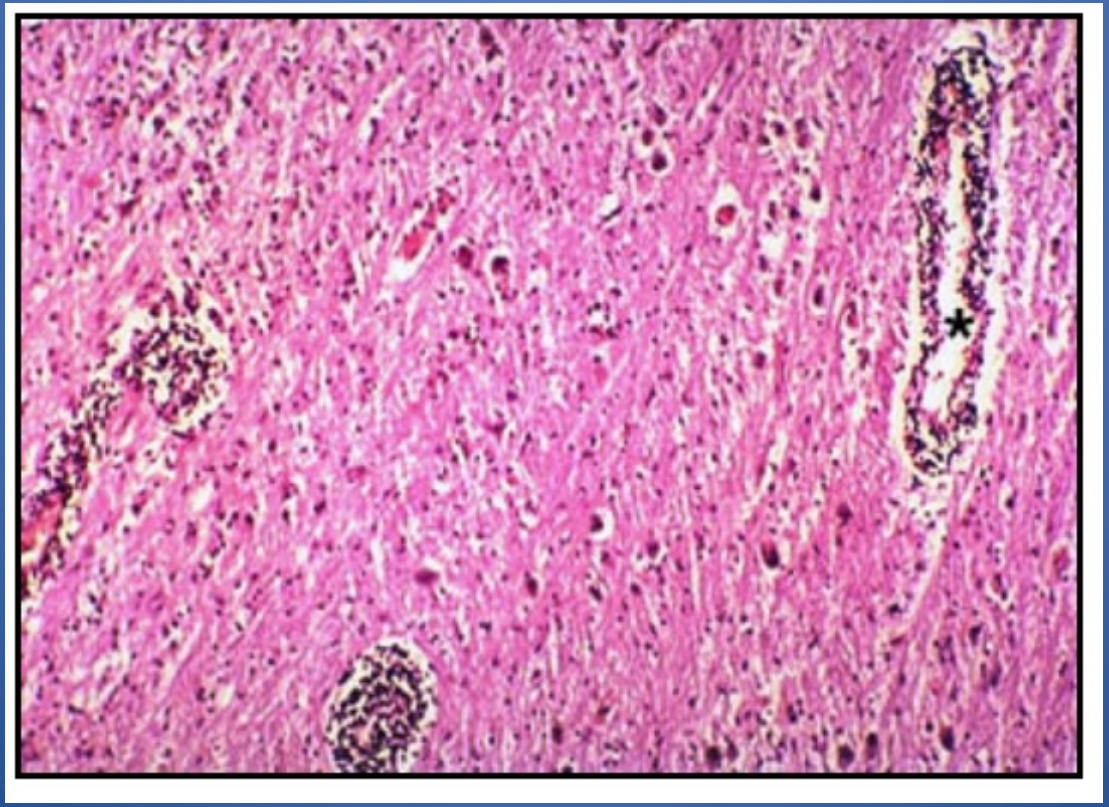
Viral Infections		
Meningitis	Acute aseptic meningitis	Enteroviruses
		Measles (subacute sclerosing panencephalitis)
		Influenza species
		Lymphocytic choriomeningitis virus
Encephalitis	Encephalitic syndromes	Herpes simplex (HSV-1, HSV-2)
		Cytomegalovirus
		Human immunodeficiency virus
		JC polyomavirus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

Aseptic Meningitis (Viral Meningitis)

- Aseptic meningitis is a misnomer
- It is a clinical term for an illness comprising:
  - meningeal irritation
  - fever
  - alterations of consciousness
  - These are relatively acute onset without recognizable organisms
- The clinical course is less fulminant than in pyogenic meningitis (is usually self-limiting)
- It is most often treated symptomatically

Aseptic Meningitis (Viral Meningitis)

In viral meningitis, clusters of lymphocytes surround cerebral blood vessels



Aseptic Meningitis (Viral Meningitis)

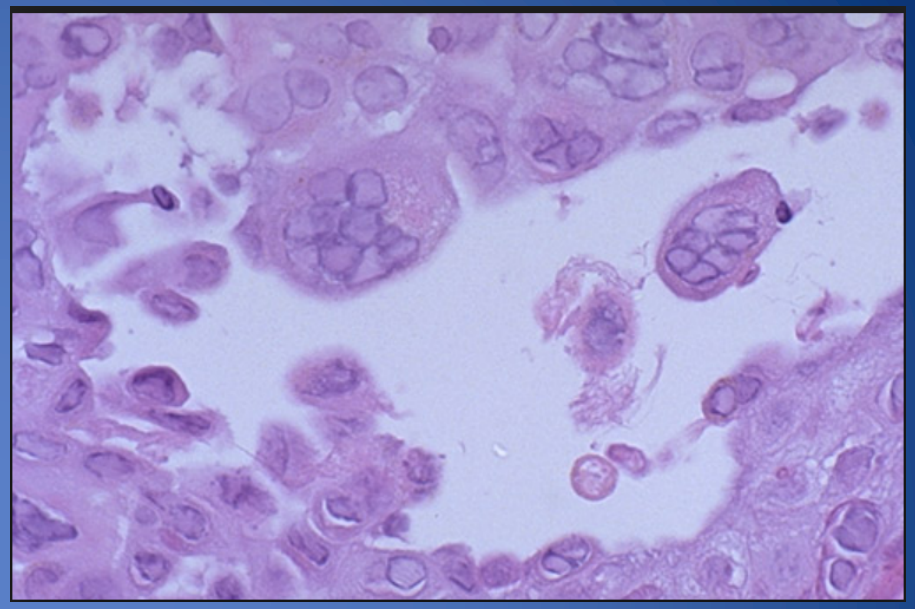
- CSF:
  - increased number of lymphocytes (pleiocytosis)
  - protein elevation is only moderate
  - glucose content is nearly always normal
- In approximately 70% of cases, a pathogen can eventually be identified, most commonly an enterovirus
- There are no distinctive macroscopic characteristics except for brain swelling, seen in only some instances
- On microscopic examination, there is either no recognizable abnormality or a mild to moderate infiltration of the leptomeninges with lymphocytes.

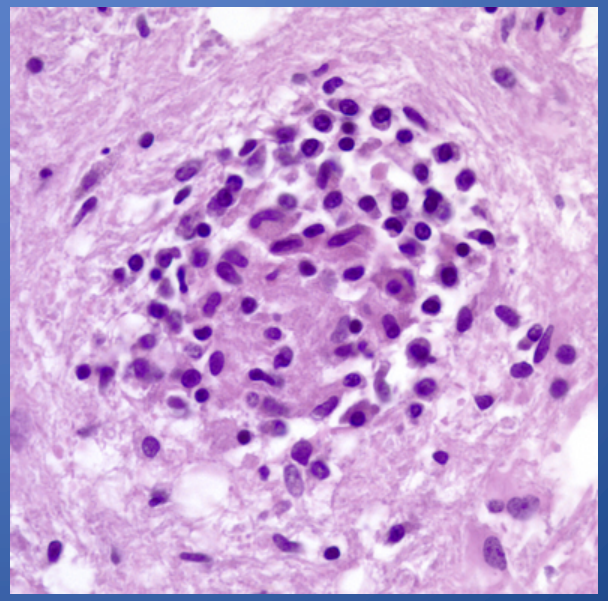
Herpes simplex virus (HSV)

- 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 microglial nodule.

Herpes simplex virus

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





Varicella-zoster virus (VZV) Meningitis

- 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)*

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

Homework

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