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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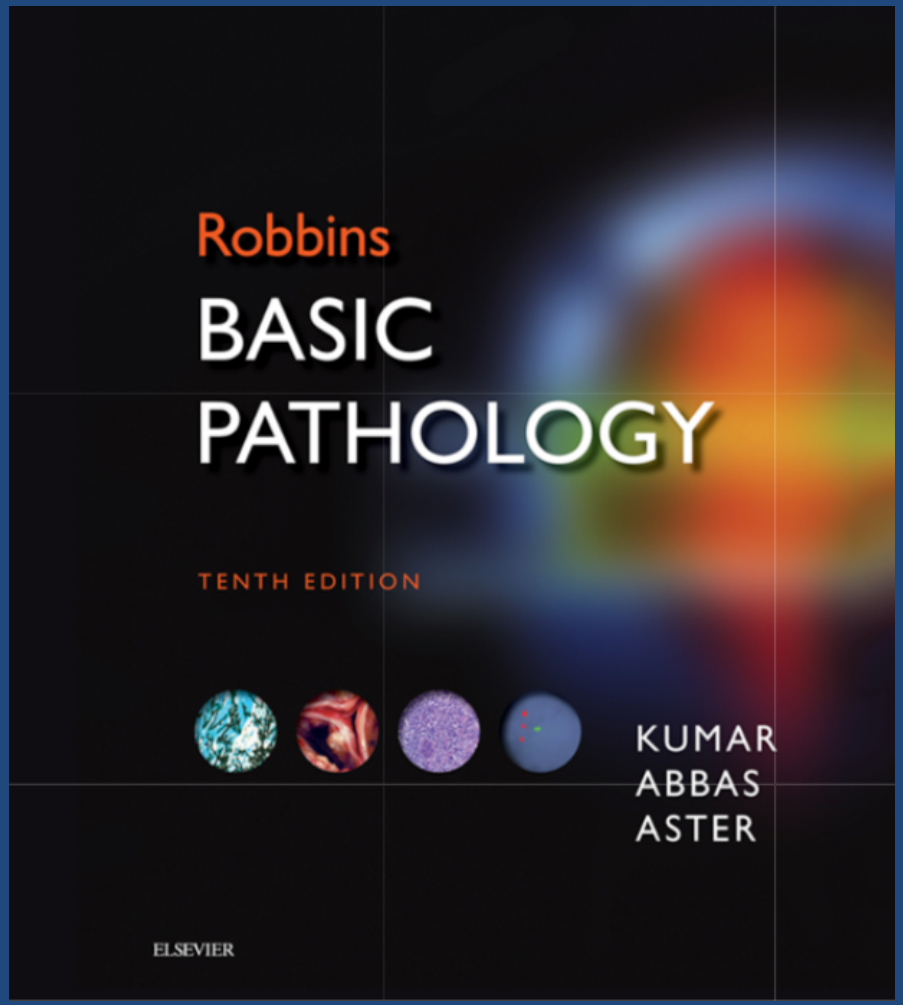


Define meningitis, and describe its location and character

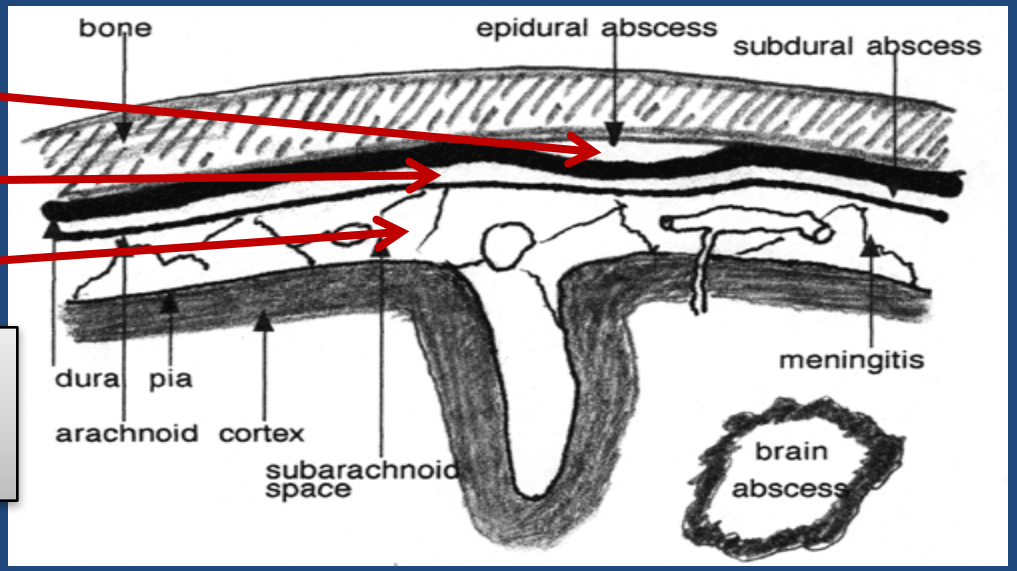
- Meningitis is an inflammatory process involving the leptomeninges and CSF within the subarachnoid space
- Meningoencephalitis is infection spreads into the underlying brain

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:**
  Listeria monocytogenes and *Streptococcus pneumoniae*

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

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

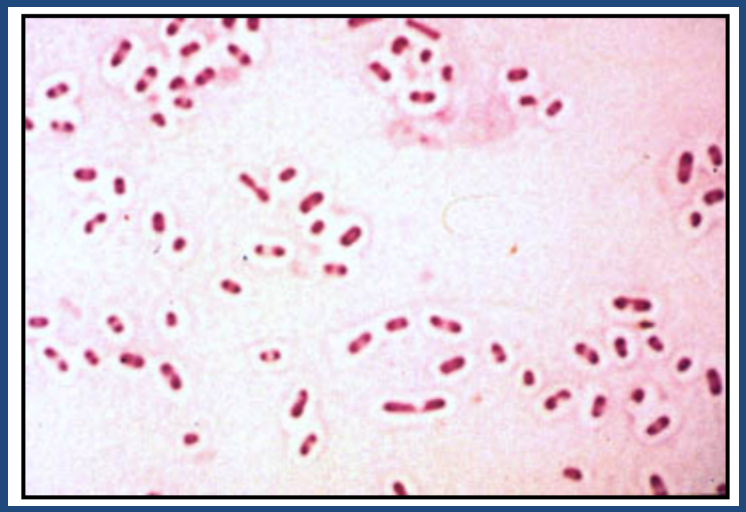
CNS Infections

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

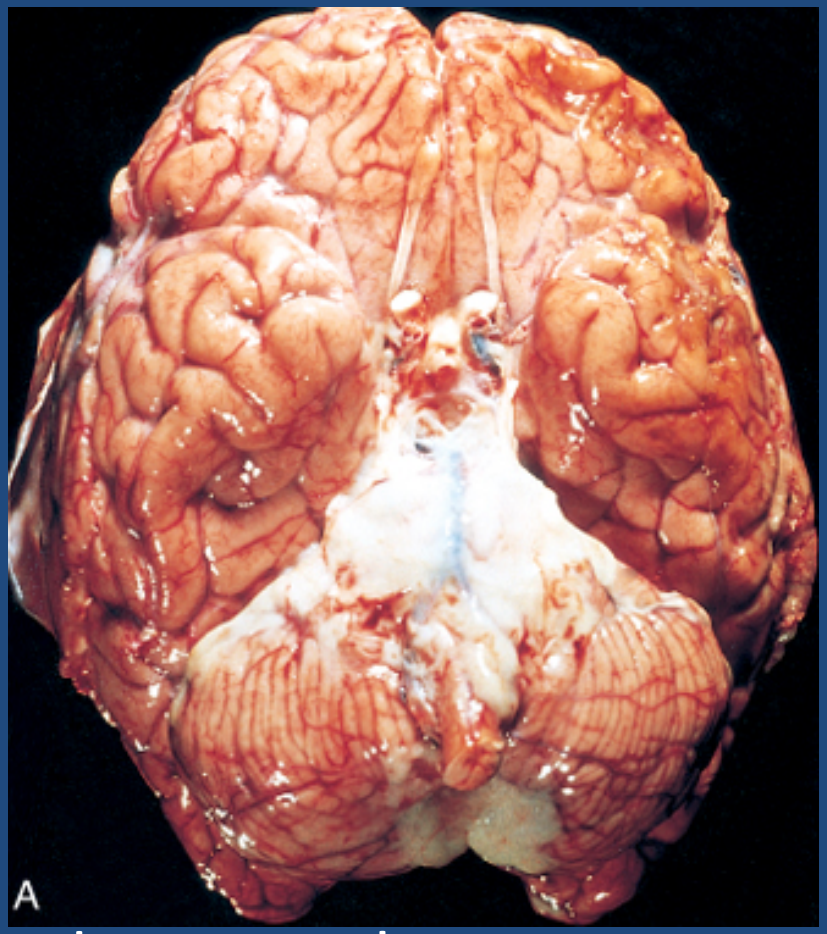
CNS Infections
Pyogenic meningitis

CSF Gram stain -
This gram stain shows multiple gram-positive diplococci, is characteristic of Streptococcus pneumoniae



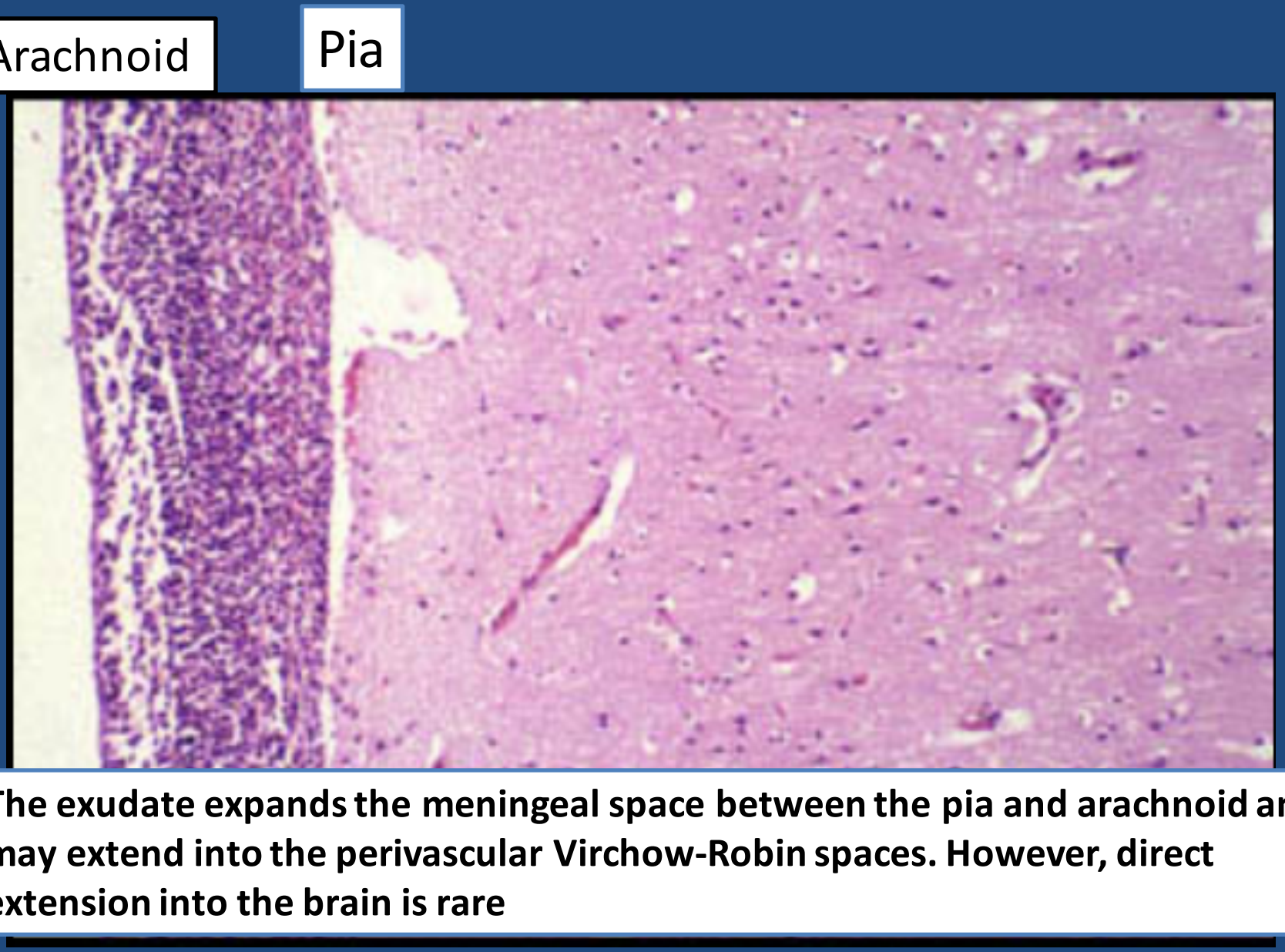
Describe the clinical presentation and pathology of acute bacterial meningitis, and its sequelae

Acute meningitis



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

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

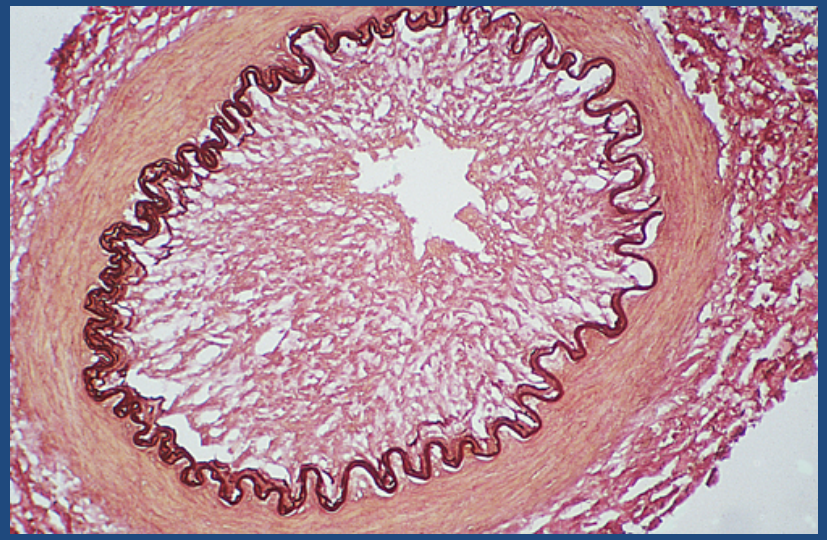
- Untreated, pyogenic meningitis can be fatal
- Effective antimicrobial agents markedly reduce mortality associated with meningitis

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

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 meningococcal and pneumococcal meningitis)
- Focal cerebritis & seizures
- Cerebral abscess
- Cognitive deficit
- Deafness

What is this complication →



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

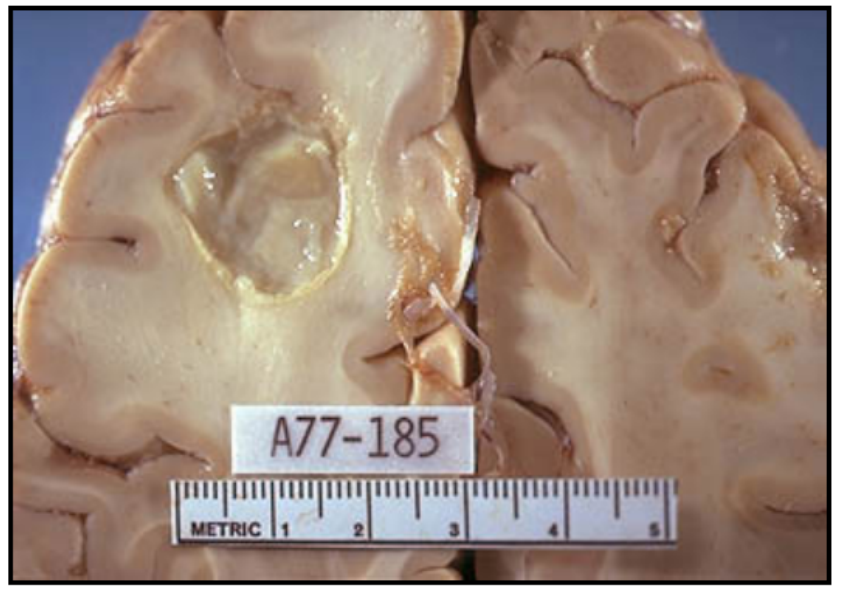
- Predisposing conditions:
  - Acute bacterial endocarditis (usually give multiple microabscesses)
  - Cyanotic congenital heart disease in which there is a right-to-left shunt
  - Loss of pulmonary filtration of organisms (e.g, bronchiectasis)

➢ Causative agent:

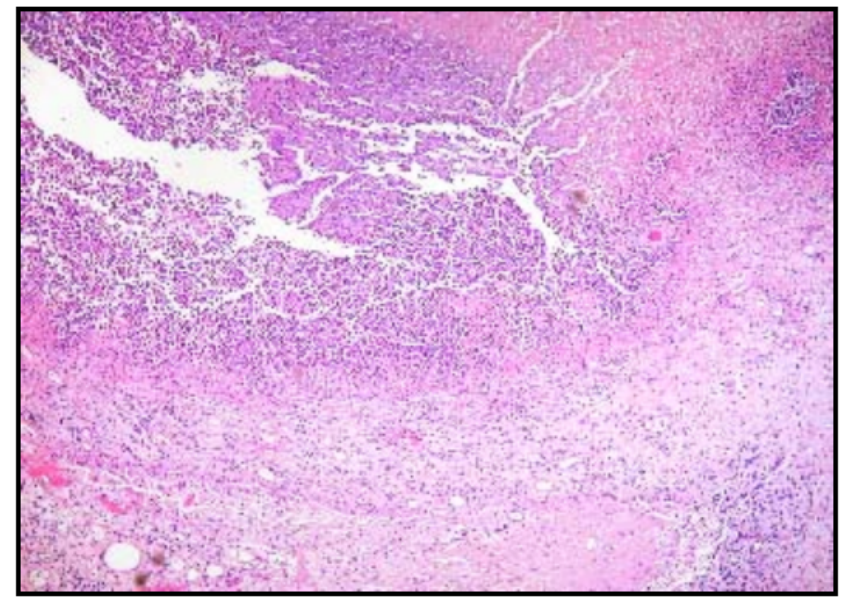
Streptococci and *Staphylococci* are the most common organisms identified in non-immunosuppressed populations

CNS Infections: Brain abscess Morphology

Most common on cerebral hemispheres



An area of necrosis within a brain abscess



–Liquefactive necrosis

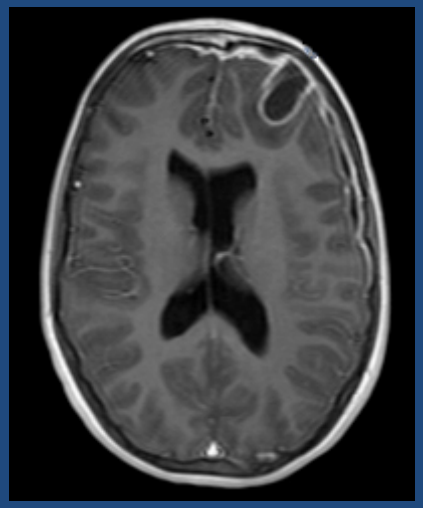
–The surrounding brain is edematous , congested & contains reactive astrocytes & perivascular inflammatory cells

CNS Infections

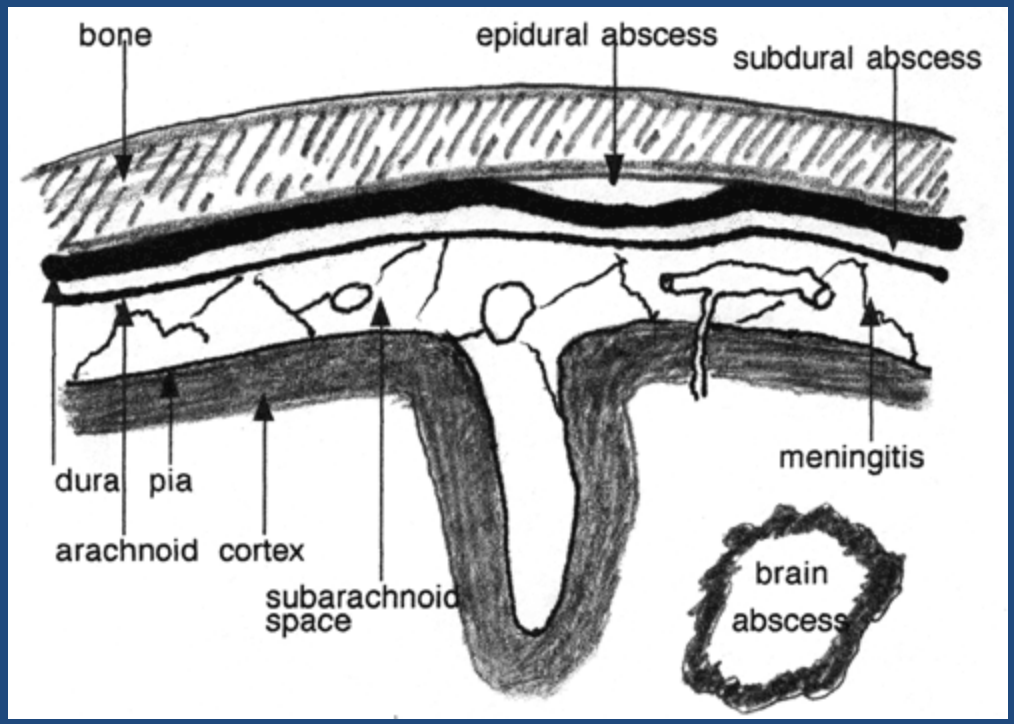
Brain abscess

- 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

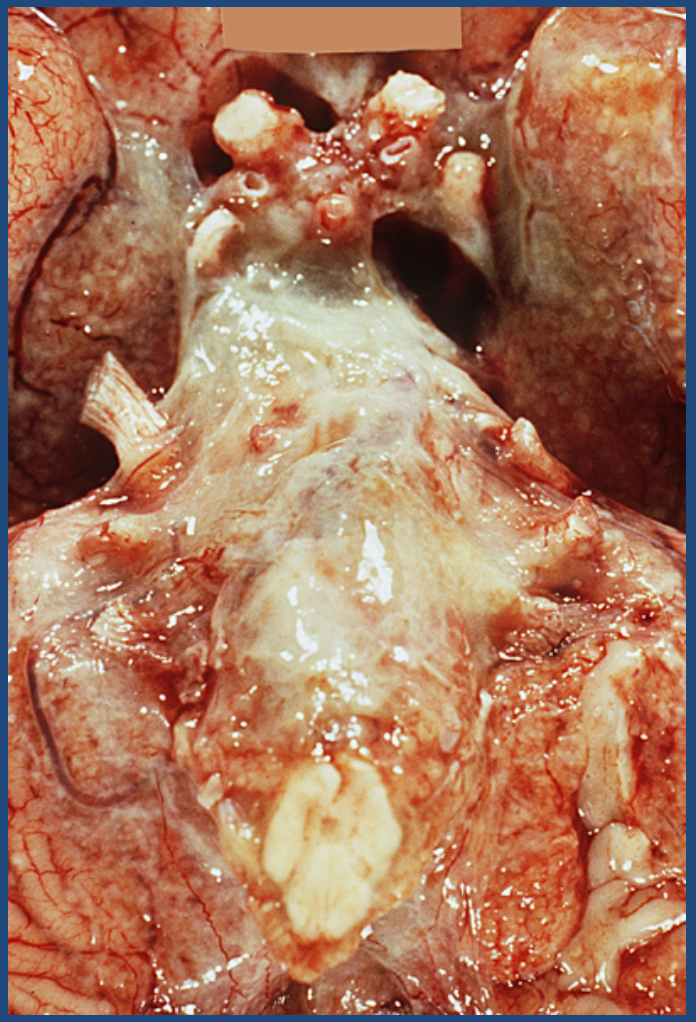
- Infections of the skull or air sinuses may also spread to the subdural space, producing subdural empyema
  - The underlying arachnoid and subarachnoid spaces are usually unaffected, but a large subdural empyema may produce a mass effect
  - In addition, thrombophlebitis may develop in the bridging veins that cross the subdural space, resulting in venous occlusion and infarction of the brain

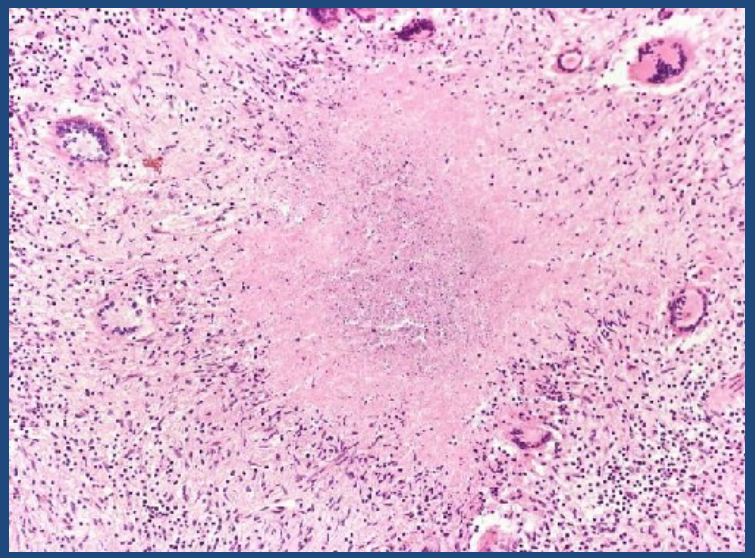
Empyema

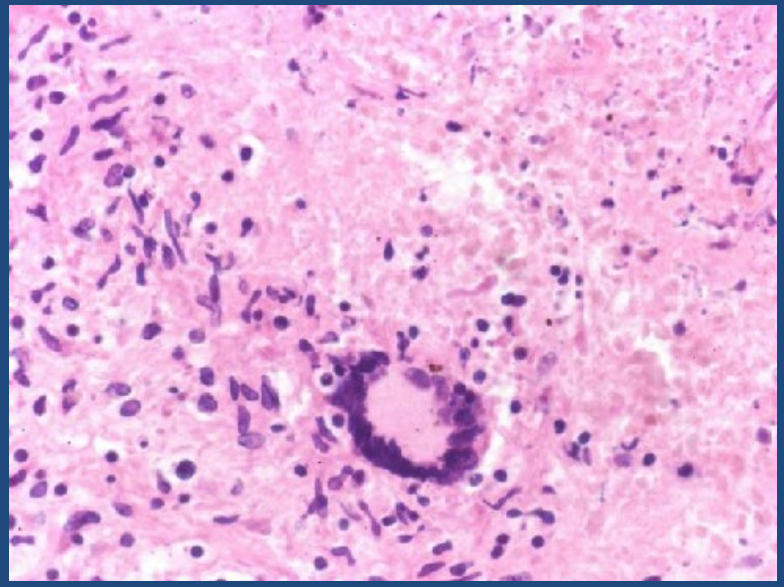
- Symptoms:
  - most patients are febrile, with headache and neck stiffness, and if untreated may develop focal neurologic signs, lethargy, and coma
- Prognosis:
  - With treatment, including surgical drainage, resolution of the empyema occurs from the dural side and resolution is complete, a thickened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

CNS Infections
Tuberculous meningitis

- 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





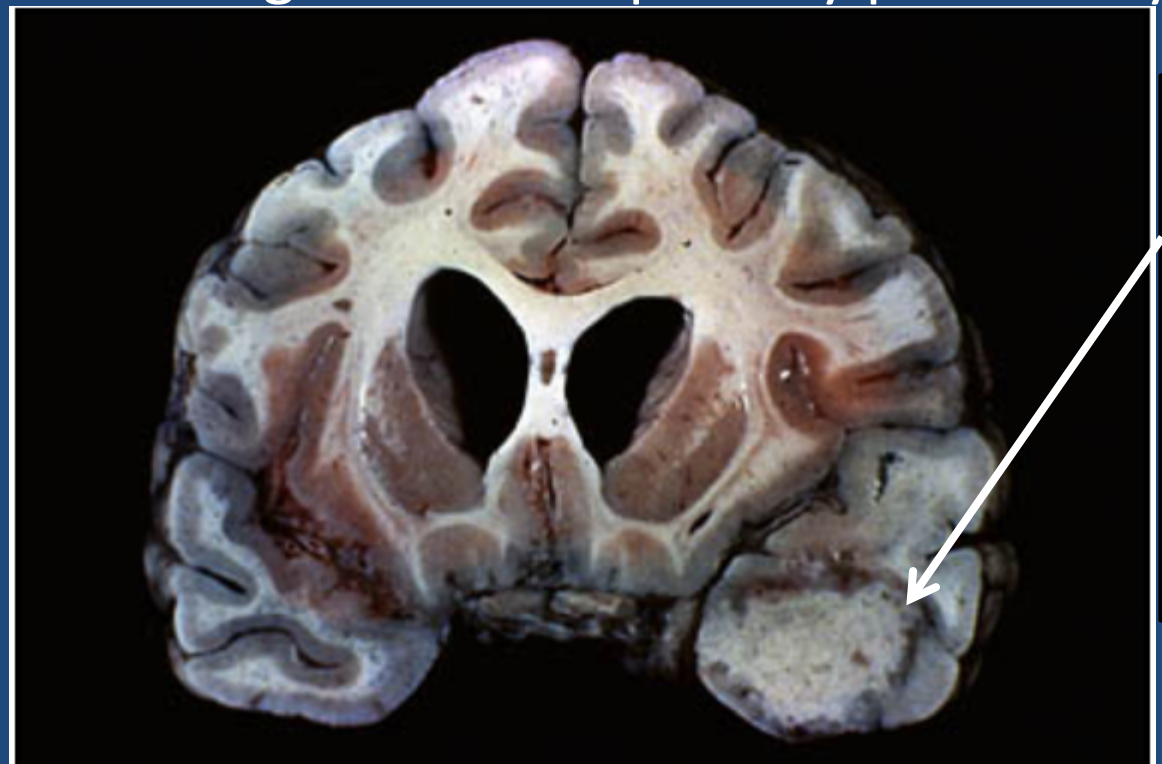


TB meningitis

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 elevated, often strikingly so
- The glucose content typically is moderately reduced or normal

List the common causes of viral encephalitis, and describe the pathologic changes in encephalitis due to *Herpes Simplex Virus*

Aseptic Meningitis (Viral Meningitis)

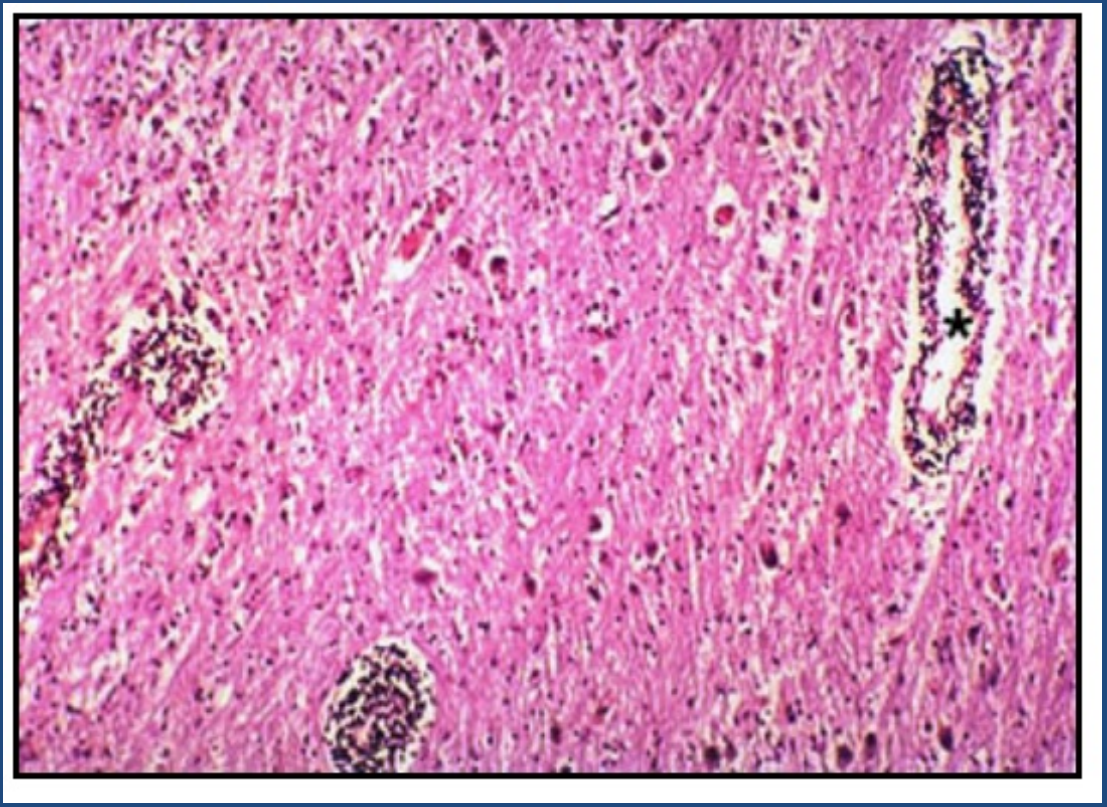
- The nervous system is particularly susceptible to certain viruses such as rabies virus and poliovirus.
- Other viral infections could affect CNS such as HSV, Enteroviruses, Measles or Influenza virus
- CNS viral infections could lead to meningitis, encephalitis or brain stem and spinal cord syndromes
- 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.

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)

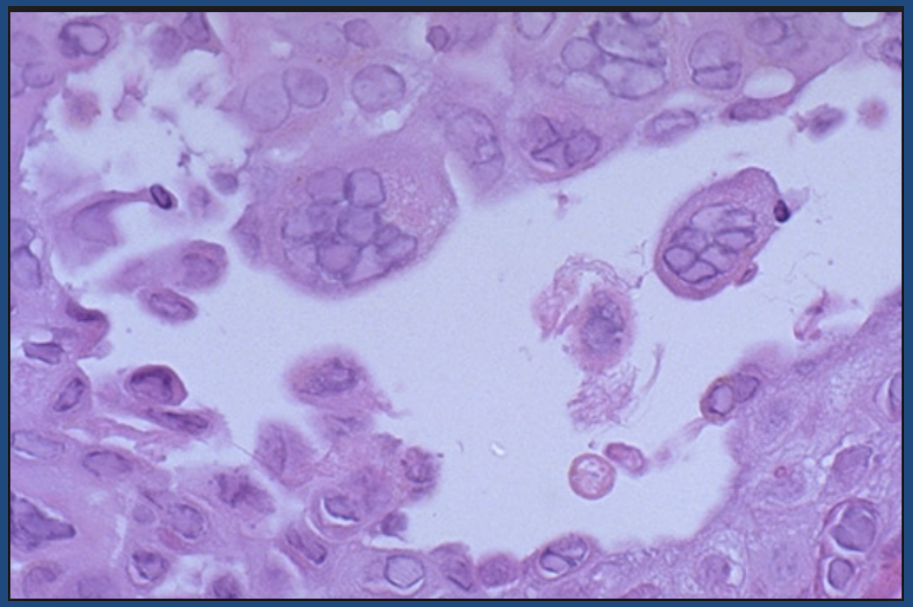
- CSF:
  - increased number of lymphocytes (pleiocytosis)
  - protein elevation is only moderate
  - glucose content is nearly always normal
- In approximately 70% of cases, a pathogen can eventually be identified, most commonly an enterovirus
- There are no distinctive macroscopic characteristics except 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 glial nodule.

Herpes simplex virus

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



Aseptic Meningitis (Viral 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)*

Aseptic Meningitis (Viral Meningitis)

- 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!