

Pathology of CNS infections

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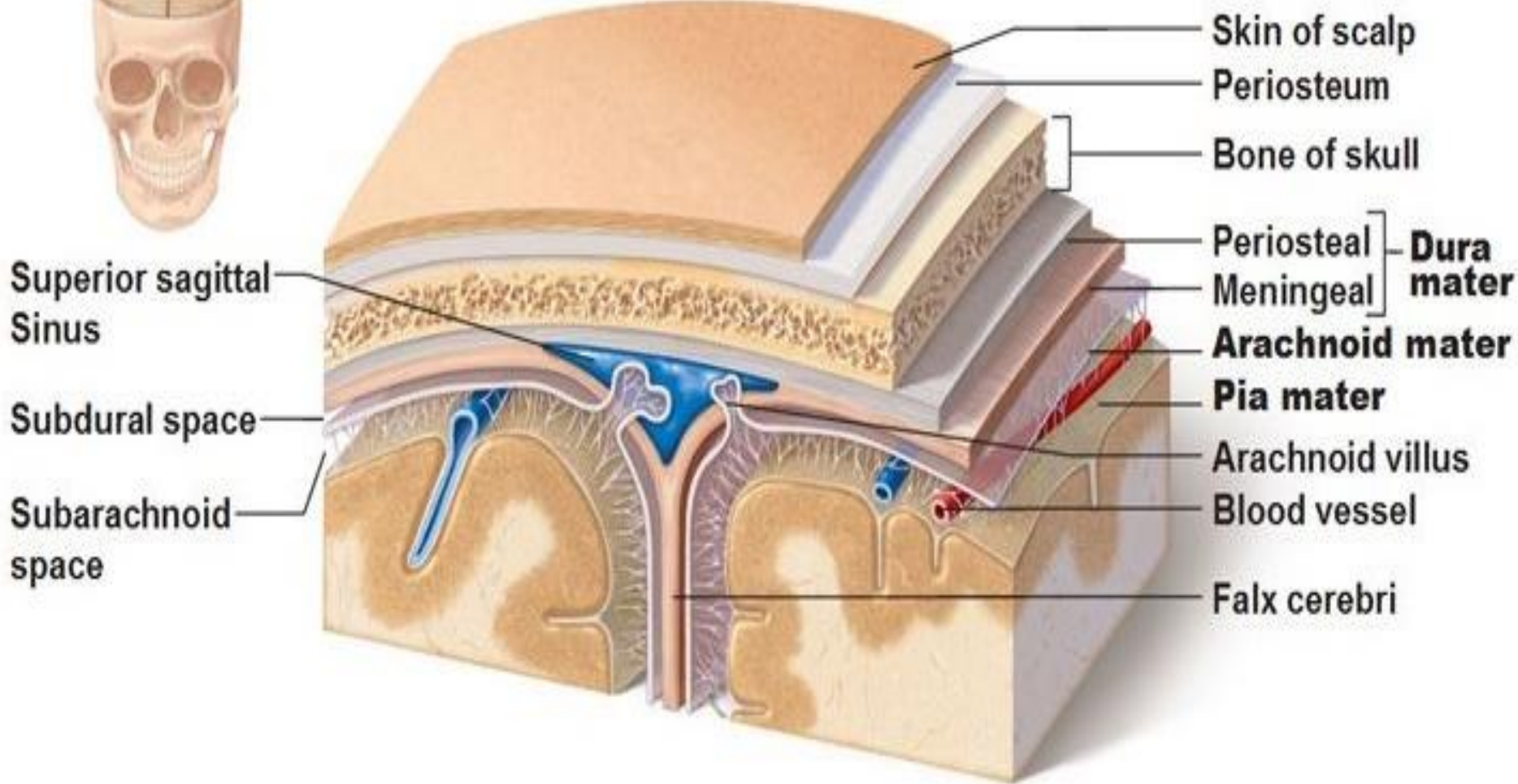
Dept of Pathology

At the end of this lecture student should be able to:

- Describe the pathogenesis and pathology of the brain in bacterial meningitis, viral meningitis and tuberculous meningitis.
- Differentiate CSF parameters of bacterial, viral and tuberculous meningitis
- Enumerate the complications of meningitis
- Name the aetiological agents and describe the pathology of encephalitis
- Describe the pathogenesis and pathology of brain abscesses

Infections of the CNS

- Meningitis -diffuse inflammation of the meninges
- Encephalitis -inflammation of the brain matter
- Meningo-encephalitis
- Cerebral abscess –focal suppuration of brain matter
- Other inflammatory lesions
 - Epidural abscess
 - Subdural empyema
 - Septic thromboembolism of dural sinuses
 - Encephalomyelitis



Superior sagittal
Sinus

Subdural space

Subarachnoid
space

Skin of scalp

Periosteum

Bone of skull

Periosteal
Meningeal

**Dura
mater**

Arachnoid mater

Pia mater

Arachnoid villus

Blood vessel

Falx cerebri

Routes of CNS infections

- The CNS is sterile, but once the organisms get into it, rapid spread of infection occurs.

➤ Routes

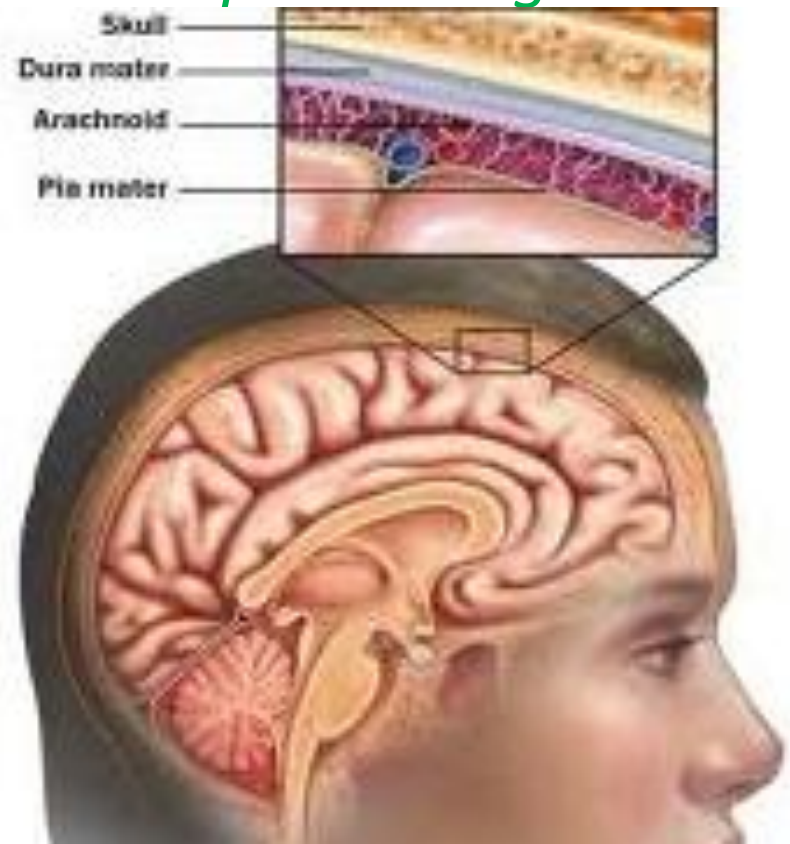
1. Haematogenous – septicaemia/septic emboli
2. Direct extension from adjacent sites
3. Iatrogenic
4. Along the peripheral nerves

Risk factors for infections of nervous system

- Trauma eg : compound fractures
- Congenital malformations eg: spina bifida
- Iatrogenic eg: neurosurgical procedures, lumbar puncture
- Local foci of infections eg: mastoid and middle ear infections
- Blood-born infections
- Immunodeficiency states

Meningitis

- Diffuse inflammation of the meninges
 - Inflammation of the dura- *pachymeningitis*
 - Inflammation of pia-arachnoid –*leptomeningitis*
- By convention “meningitis” means leptomeningitis*



Meningitis (*leptomeningitis*)

1. Acute bacterial meningitis
 2. Sub acute meningitis caused by tuberculosis and fungi
 3. Aseptic meningitis/ viral meningitis
- Infrequently meningitis may caused by
 - Chemicals -chemical meningitis
 - Malignant cell infiltration -carcinomatous meningitis

Acute bacterial meningitis

- Acute infection of pia-arachnoid and the CSF enclosed within the subarachnoid space
- Spread through cerebrospinal fluid and the ventricles

Commonest organisms

- *Streptococcus agalactiae*, *Escherichia coli* in neonates and infants
- *Haemophilus influenza* in children
- *Neisseria meningitides* in young
- *Streptococcus pneumoniae* in elderly
- Refer Microbiology

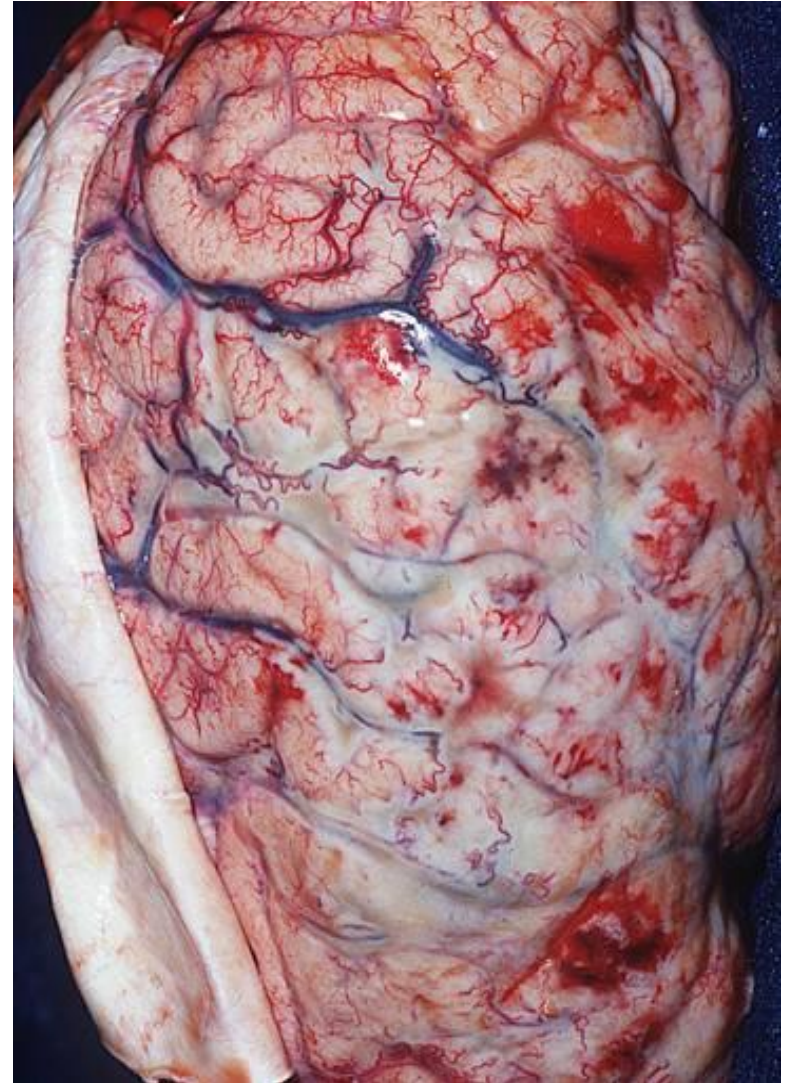
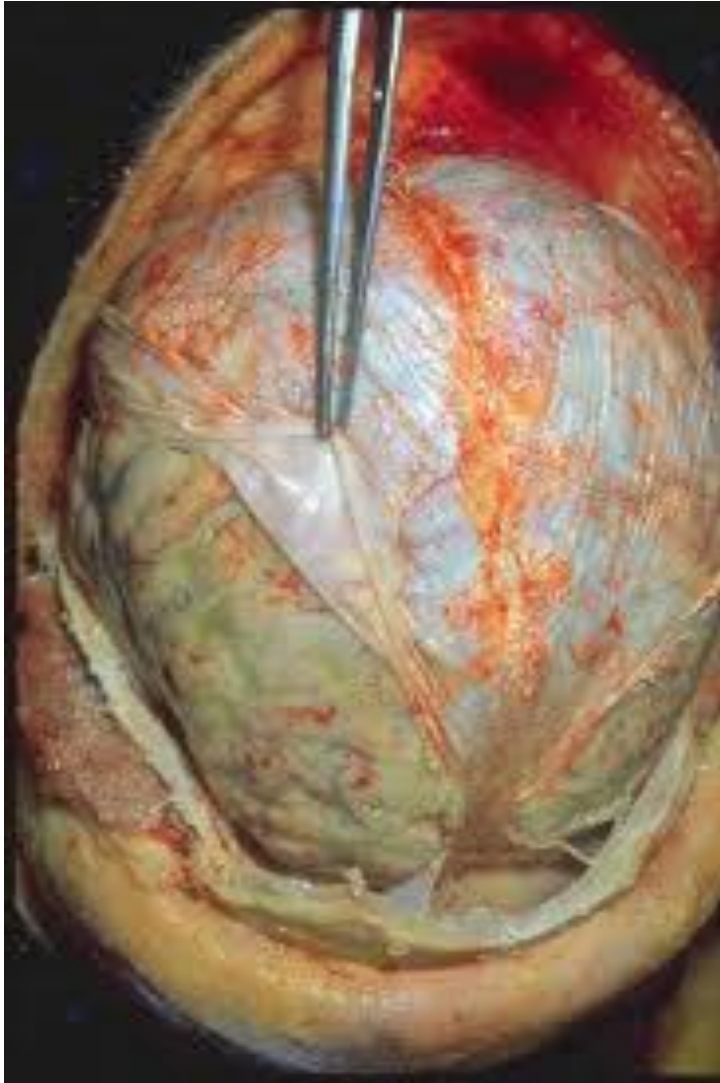
Routes of spread

- Haematogenous spread
- Direct spread from infections in the skull bones
- Compound fractures
- Neurosurgery or LP

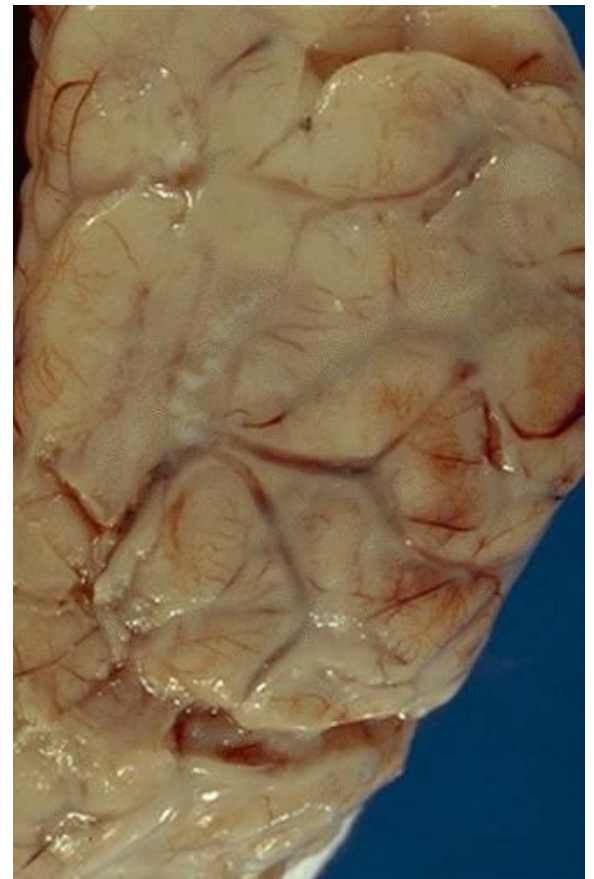
Acute bacterial meningitis - Macroscopy

- Oedema of the brain
- Inflammatory exudate (pus) fills the subarachnoid space
- Clear CSF becomes turbid
- Meninges looks opaque
- The sulci are filled with pus
- Vessels are prominent
- Changes are more marked on the base of the brain.

Acute bacterial meningitis - Macroscopy



The yellow-tan exudate
obscures the sulci



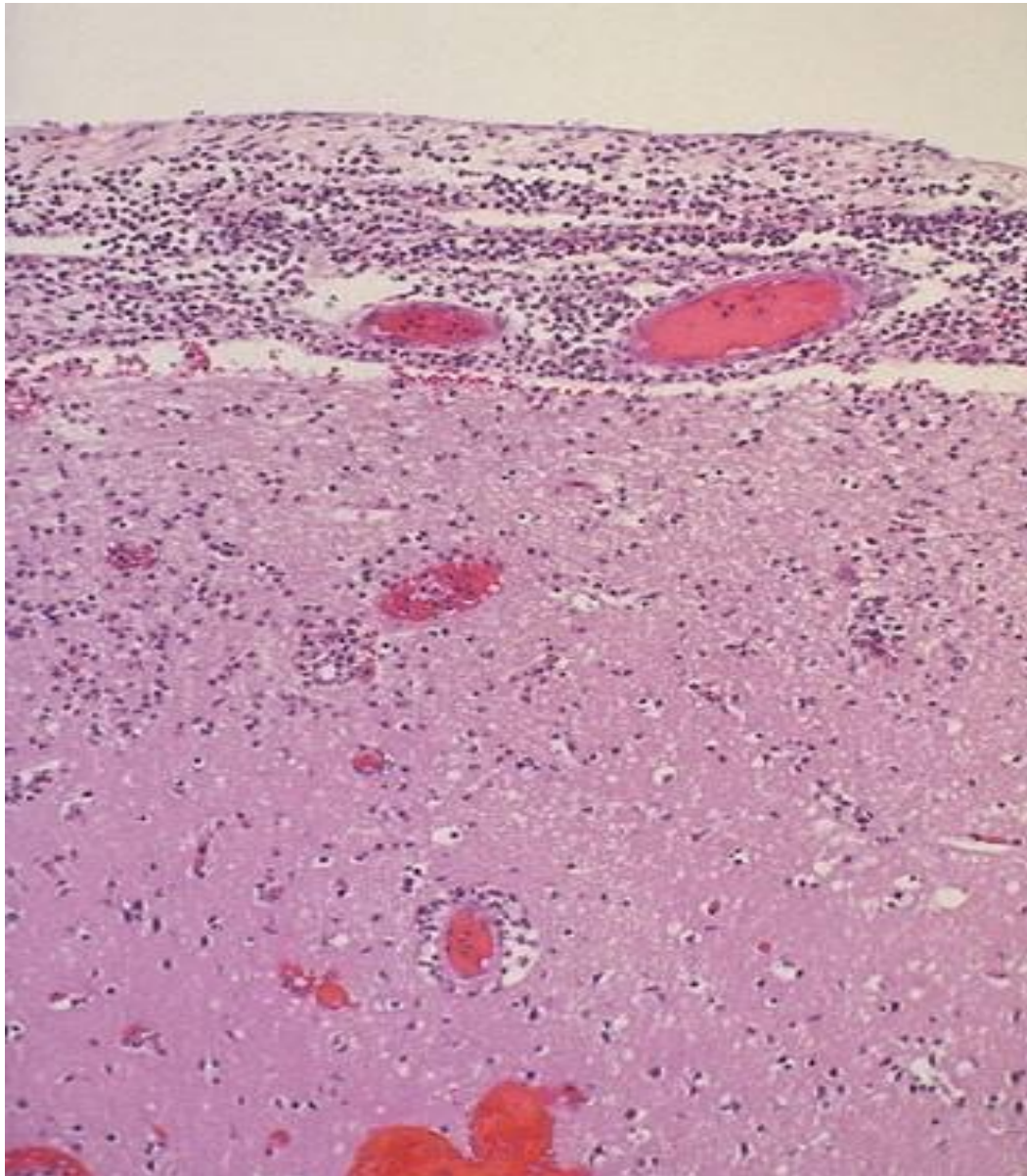
Acute bacterial meningitis - Macroscopy

- Later the layer of pus organizes and causes fibrous adhesions
- This can result in compression of cranial nerves and hydrocephalus.

Acute bacterial meningitis - Microscopy

- Acute inflammatory exudate containing many neutrophils in the subarachnoid space and in the meninges.
- Prominent dilated vessels
- Oedema and focal inflammation (extending down via the Virchow-Robin space) in the cerebral cortex.
-

Acute bacterial meningitis - Microscopy



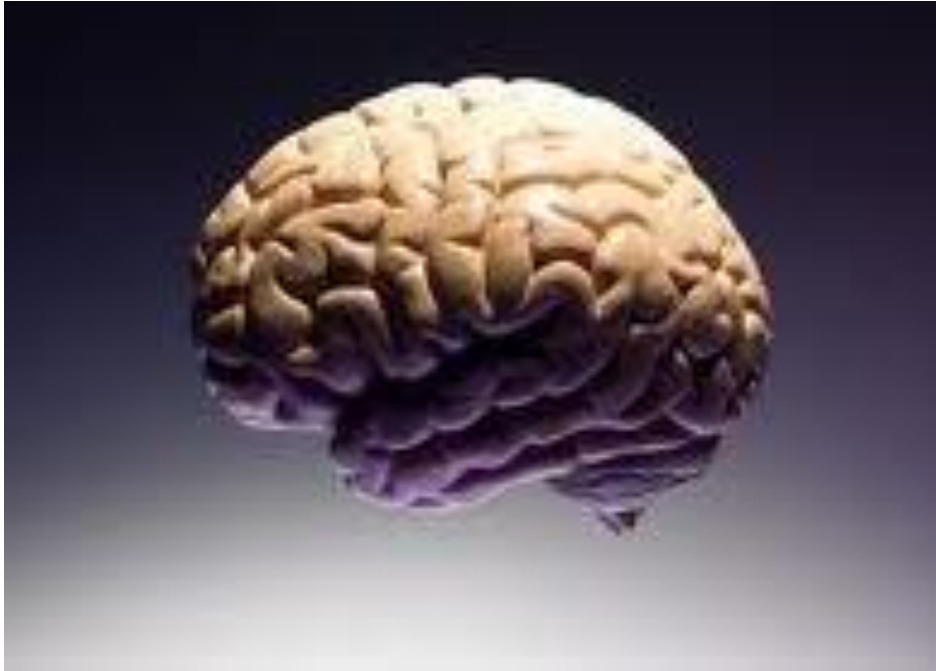
Complications of acute bacterial meningitis

- Obstructive hydrocephalus
- Cerebral infarcts
- Cerebral abscess
- Subdural empyema
- epilepsy

Viral/ aseptic meningitis

- Also known as acute lymphocytic meningitis
- Aetiology -
 - Enterovirus
 - Echo
 - Coxsackie
 - Mumps
 - Epstein-Barr
 - HSV
 - HIV
- Haematogenous spread

Viral/ septic meningitis



Morphological changes are not so marked as in bacterial meningitis

Microscopically

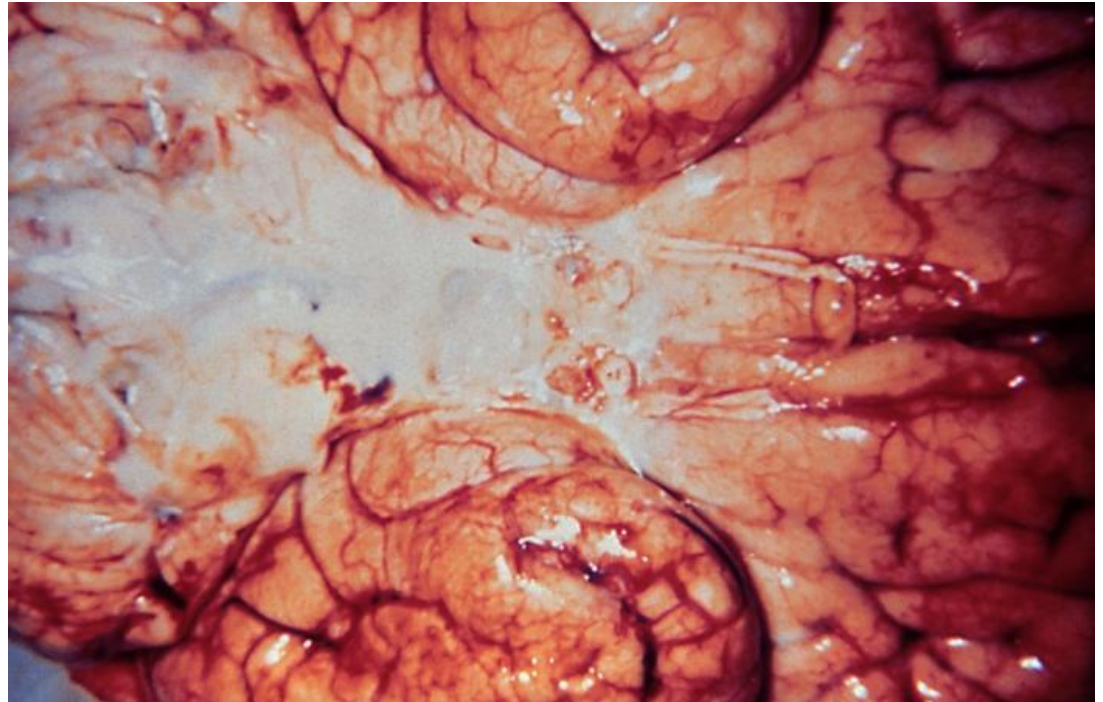
- lymphocytic infiltrate in the leptomeninges.
- Perivascular lymphocytic infiltration of meningeal vessels

Tuberculous meningitis

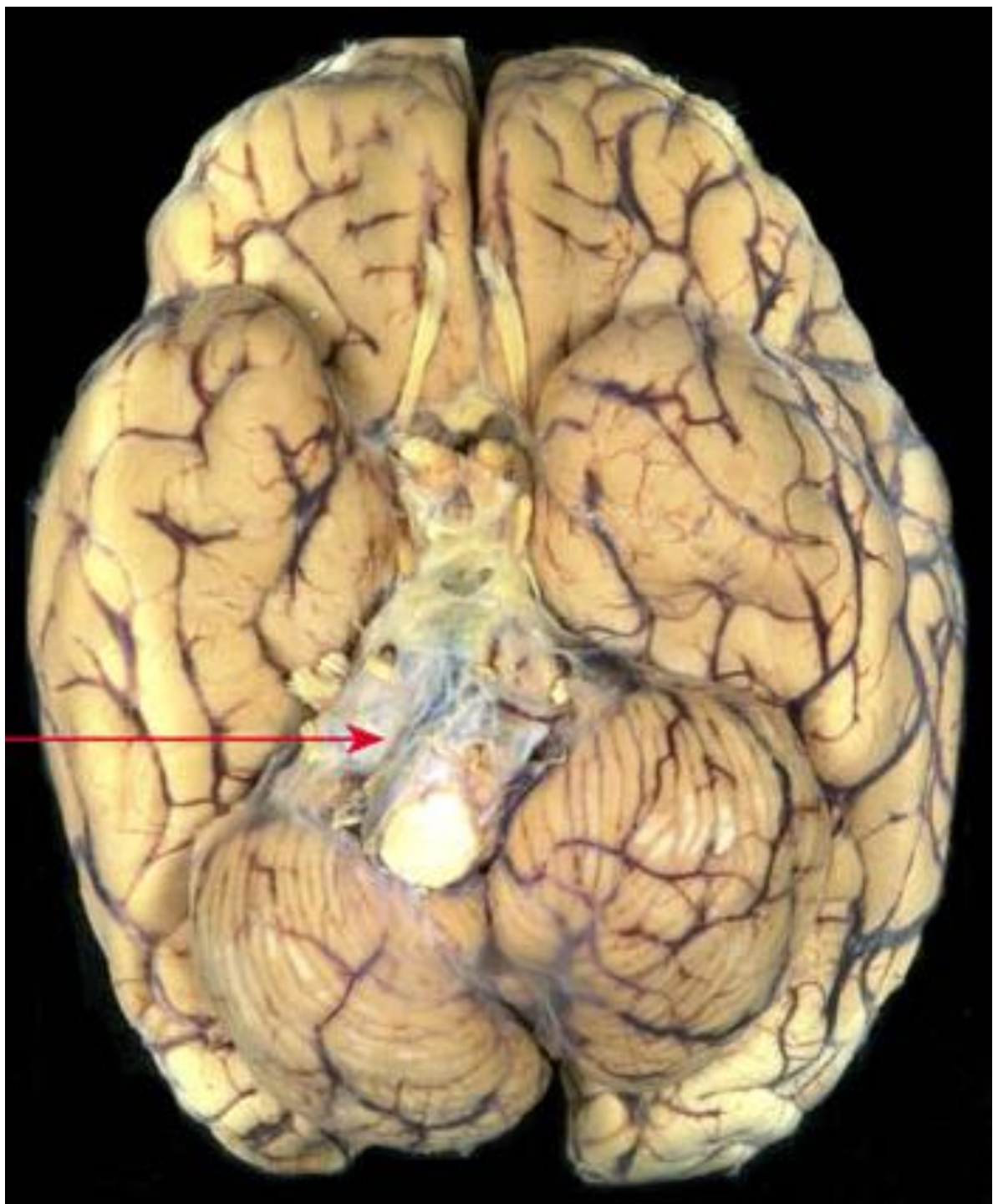
- Routes of spread
 - Haematogenous
 - As a part of milliary tuberculosis
 - Less commonly direct spread from TB of vertebral body
- This is subacute/chronic meningitis.

Tuberculous meningitis -macroscopy

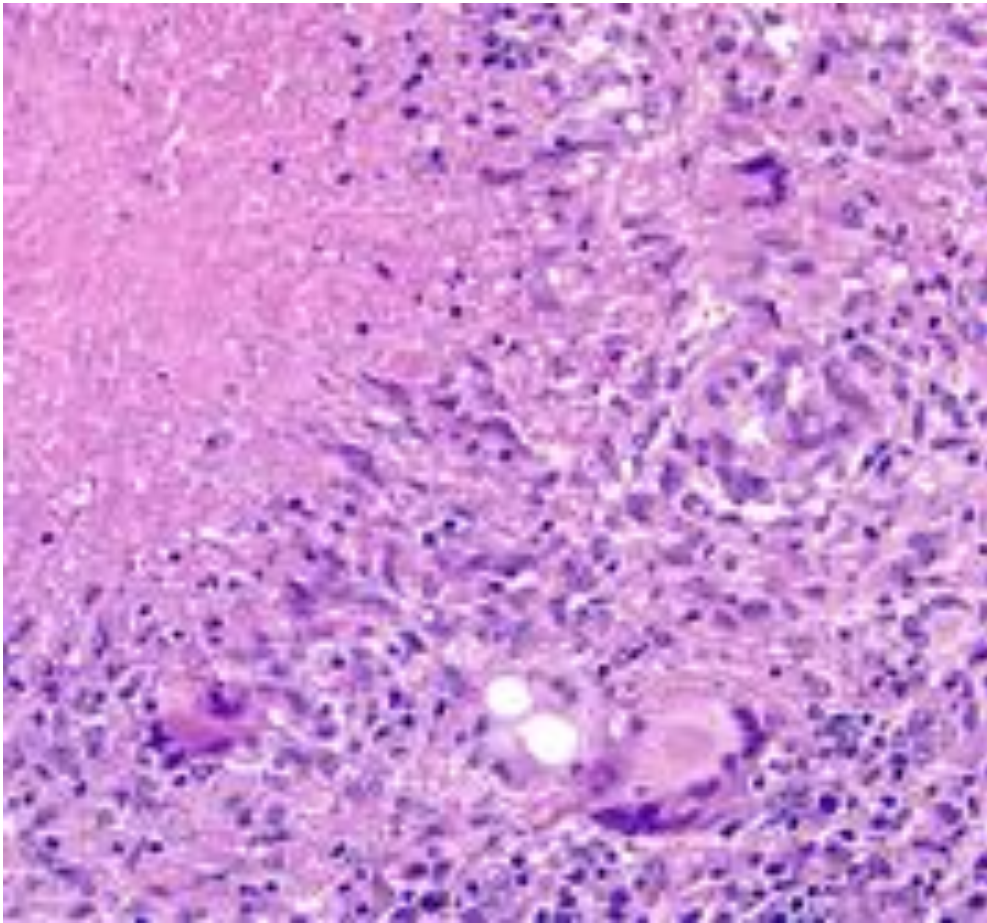
- Thick exudate obscuring the sulci particularly at the base of the brain.
- **Tubercles** of 1-2 mm mainly closer to the blood vessels.
- Adhesions are invariable



Thick grey
exudate
encasing
the cranial
nerves and
blood
vessels



Tuberculous meningitis -microscopy



Tuberculous meningitis -microscopy

- Chronic inflammatory cell infiltrate
- Few neutrophils may be seen
- Granuloma formation with giant cell
- With or without caseation
- When the treatment is delayed fibrous adhesions in the subarachnoid space

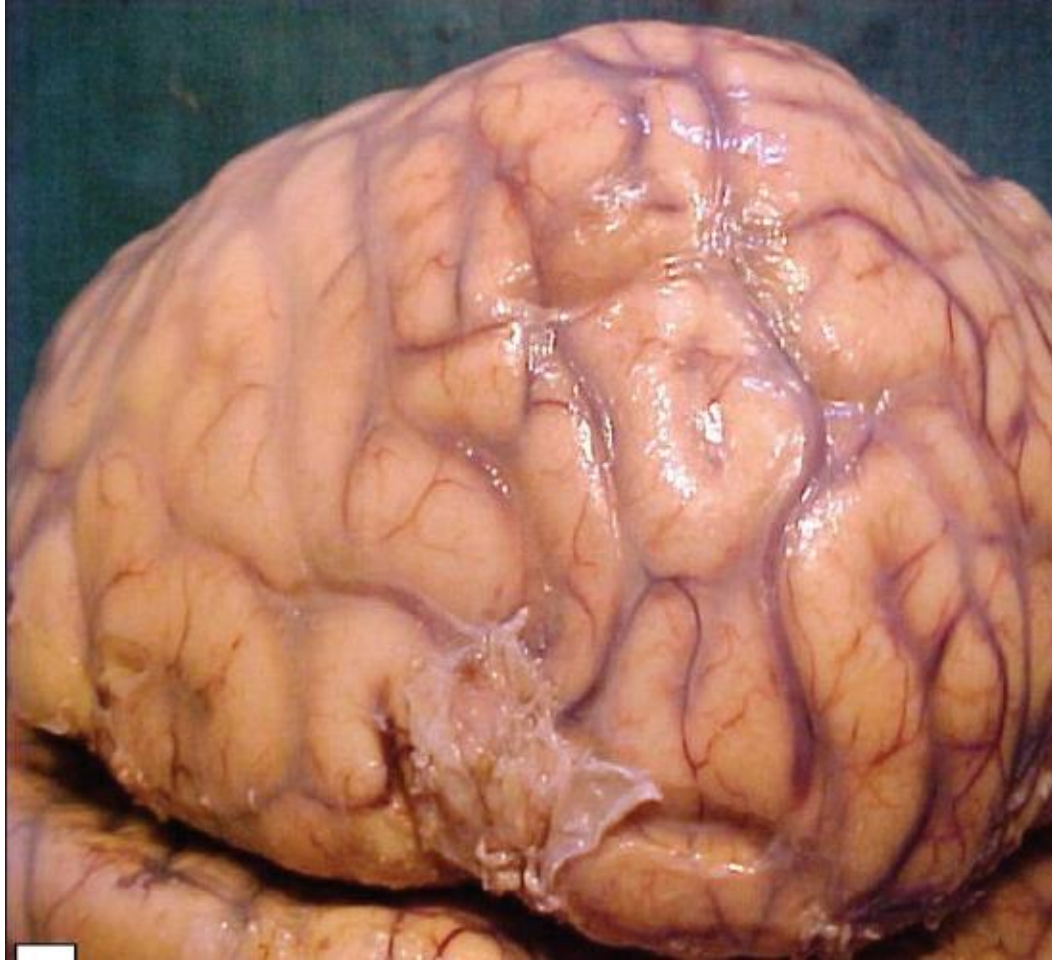
Tuberculoma

- Focal areas of granulomatous inflammation with caseation, surrounded by a dense fibrous rim
- Rare to present as meningitis
- Acts as a space occupying lesion
- Cerebellum is the most frequent site.

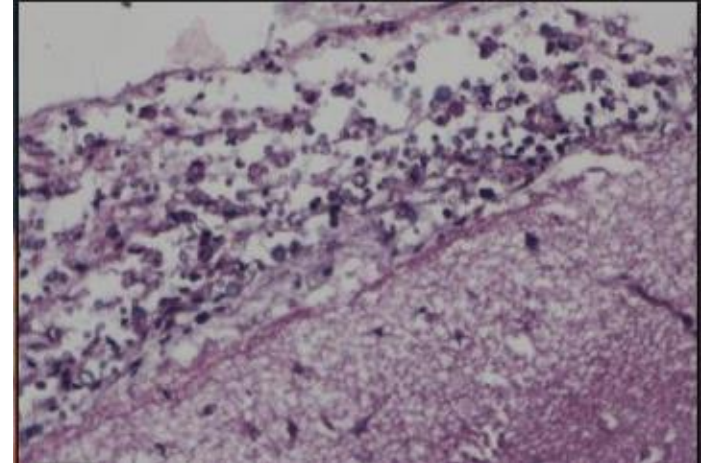
Fungal meningitis

- Mainly in debilitated or immunocompromized patients
- An important cause for meningitis in HIV/AIDS
- Haematogenous spread from infections at distant sites
- Organisms
 - *Cryptococcus neoformans*
 - *Candida albicans*
 - *Aspergillus fumigatus*
 - *Coccidioides immitis*

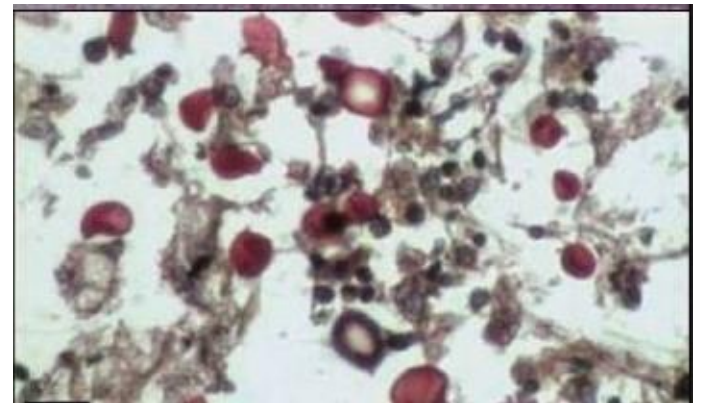
Fungal meningitis



Brain showing opaque meninges in cryptococcal meningitis



lymphomononuclear inflammation over meninges with scattered yeast like fungal organisms



yeast like forms of Cryptococcus highlighted by mucicarmine stain

CSF findings in different types meningitis

| Feature | Normal | Bacterial meningitis | Viral meningitis | Tuberculous meningitis |
|------------------------|-----------------------|---------------------------|--------------------|--|
| Naked eye appearance | Clear/colourless | Cloudy/purulent | Clear /turbid | Turbid/viscous Fibrin coagulum on standing (cob-web) |
| Cells /mm ³ | 0-4 Ly 0 N | 200-thousands N <50 Ly | 10-100 Ly 0 N | 100-300 Ly 0-200 N |
| Proteins | 15-45 mg/dl | Markedly raised | Raised | Raised |
| Glucose | 2/3-1/2 blood glucose | <1/2 blood glucose | >1/2 blood glucose | <1/2 blood glucose |
| Bacteriology | sterile | Causative organism + | sterile | TB bacilli |

Encephalitis

Diffuse parenchymal infection of the brain

- Viral
- Bacterial
- Fungal -Candida, Cryptococcus, Histoplasma, Mucor, Blastomyces
- Protozoal –malaria, toxoplasma, amoeba, cysticercosis

Common in immunocompromized
and in patients with lymphomas
and other cancers

Viral encephalitis

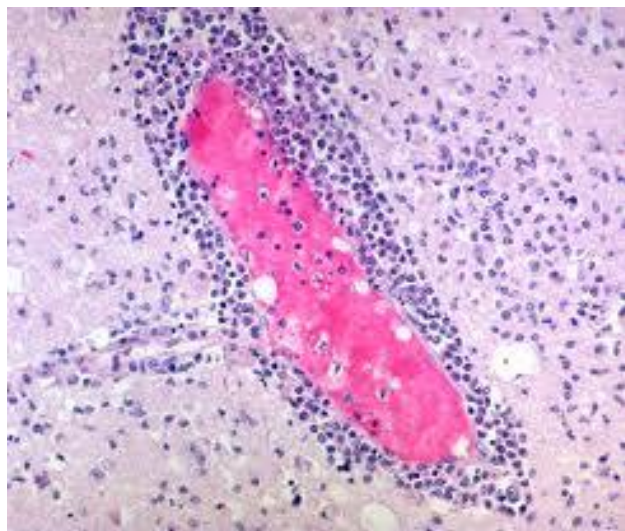
- Most viral infections of CNS are the result of preceding viral proliferation in some other site.

Eg alimentary tract, skin or mucus membranes

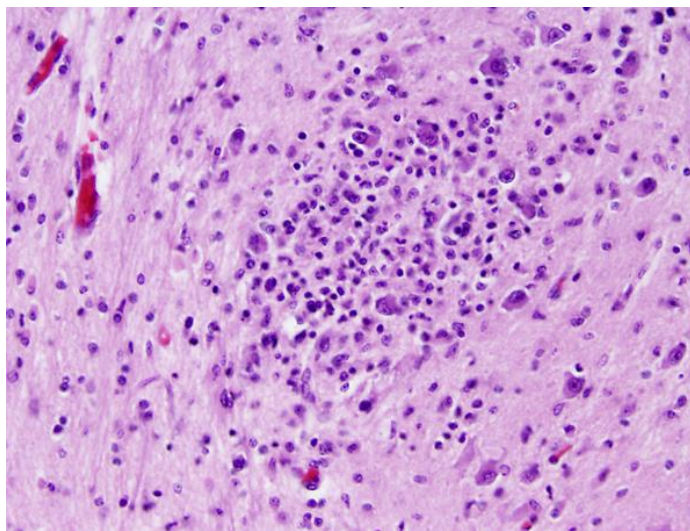
- Viruses enter by different routes
 - Oral –enteroviruses
 - skin -herpes
 - placenta -CMV
 - - body fluids- HIV
- They reach the brain via
 - Blood
 - Peripheral nerves -rabies

Viral encephalitis

- Mononuclear cell infiltrate , mainly around blood vessels (Lymphocytes, plasma cells , macrophages)
- Microscopic clusters of microglia
- Neuronophagia



Perivascular infiltrate



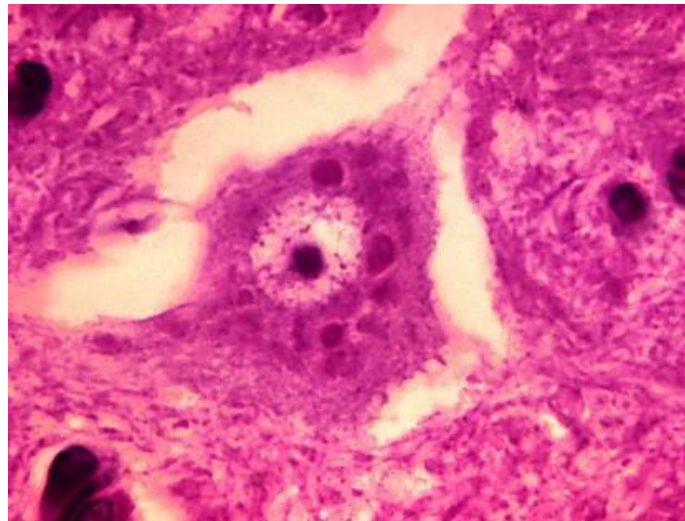
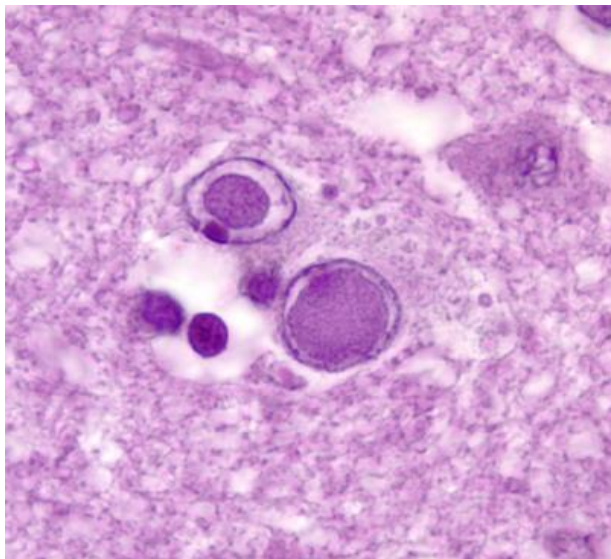
Microglial nodule

Viral encephalitis

Specific cellular changes depending on the causative virus

Negri bodies in purkinje cells- rabies

Intranuclear inclusions - HSV,CMV



Brain abscess

- Acute focal suppurative infection of the brain matter
- Routes of spread
 - Direct implantation of organisms
 - Local extension
 - Haematogenous
- Predisposing factors
 - Acute bacterial endocarditis
 - Cyanotic heart diseases with R-L shunts
 - Chronic pulmonary sepsis

Brain abscess- morphology

- Well defined , focal lesions with central necrosis
- Surrounded by a fibrous capsule
- Cerebral oedema
- Common sites - frontal and parietal lobes, cerebellum
- **Effects of a space occupying lesion- *refer***

Microscopy

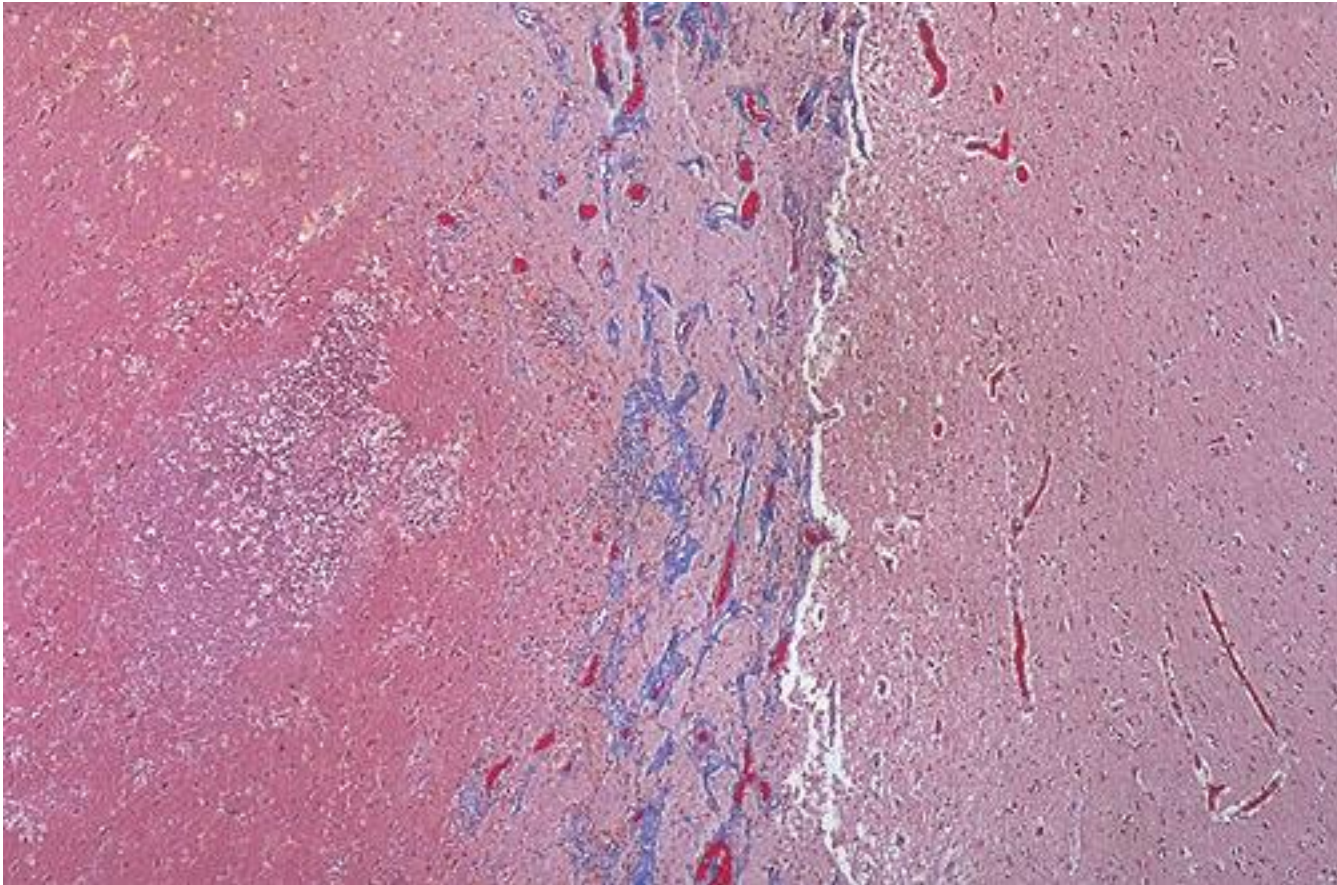
- Central colliquative necrosis
- Neovascularization surrounding the necrotic centre

Brain abscess- morphology



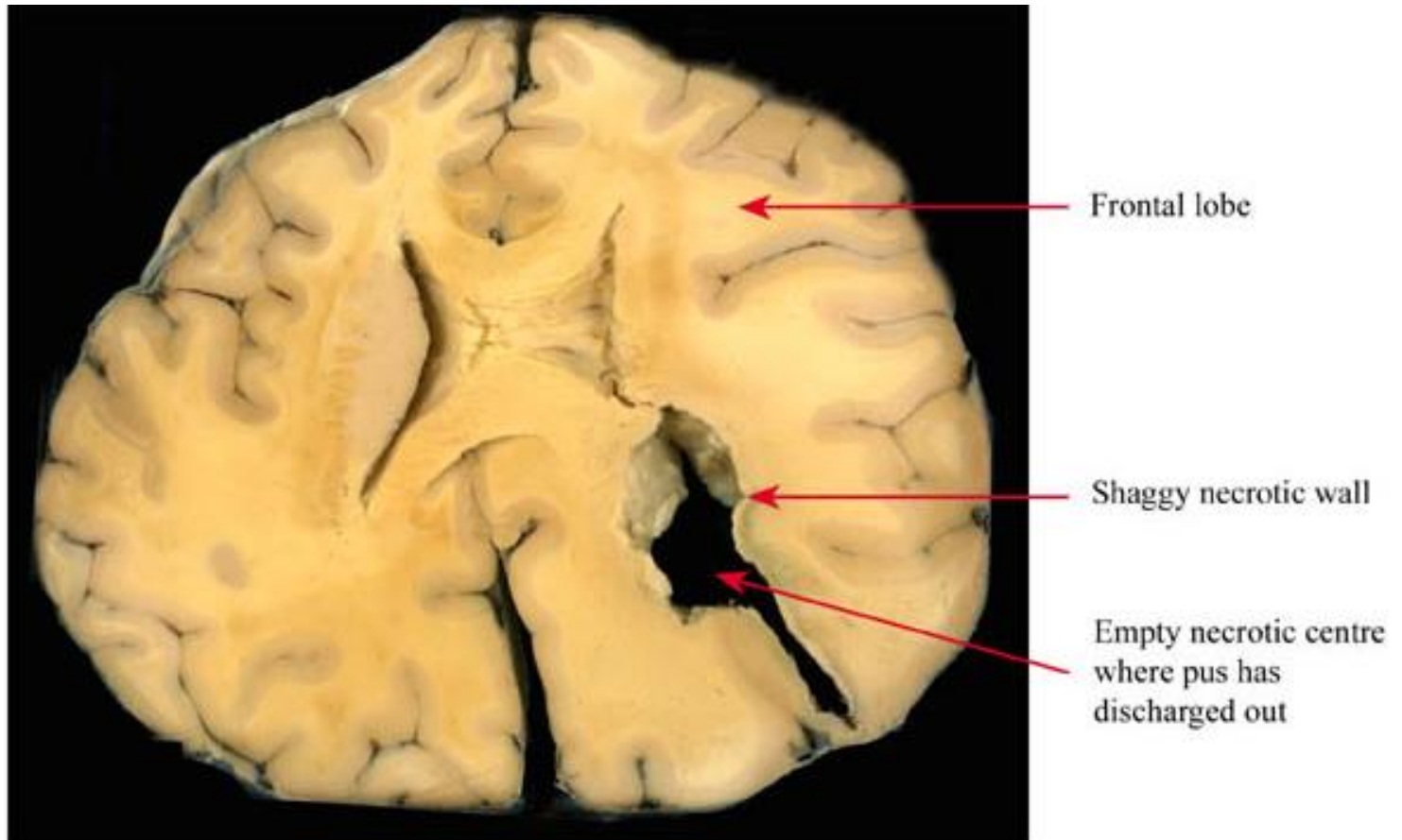
liquefactive center with yellow pus
surrounded by a thin wall

Brain abscess- morphology



Normal brain is at the right and the center of the abscess at the left. Trichrome stain demonstrates the light blue connective tissue in the wall of an organizing cerebral abscess.

Organized/ old abscess



Read on.....

- Arthropode borne (arbo) viral encephalitis
- HSV and CMV encephalitis
- Poliomyelitis
- Rabies
- HIV associated nervous system pathology
- Brain infections in immunocopromized
- Slow virus infections/ Prion diseases

*Reference: Pathologic basis of disease -
Robbins*

Summary.....