

Central Nervous System

SHEET# 4 - PATHOLOGY

LEC. TITLE : INFECTIONS OF CNS (PART 1)

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If you come by any mistake , please
kindly report it to
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INFECTIONS OF CNS

IMPORTANT FACTORS

- **Pathogenesis:**
 - Hematogenous spread (most common)
 - Traumatic implantation (open or penetrating trauma)
 - Local extension from a nearby infection (e.g., frontal sinus, mastoid)
 - Ascent via peripheral nerve (e.g., rabies)
- Bacteria, Viruses, Fungi, Parasites.
- **Normal or immunocompromised host**

Meningitis :

Inflammation of leptomeninges & CSF

- **1- Acute Pyogenic (Bacterial) Meningitis :**
 - **Neonates:** E.coli & Group B Streptococci
 - **Adolescents & young adults :** N. meningitidis
 - **Older adults :** S.pneumonia & L.monocytogenes
 - **Pyogenic (Pus forming).**

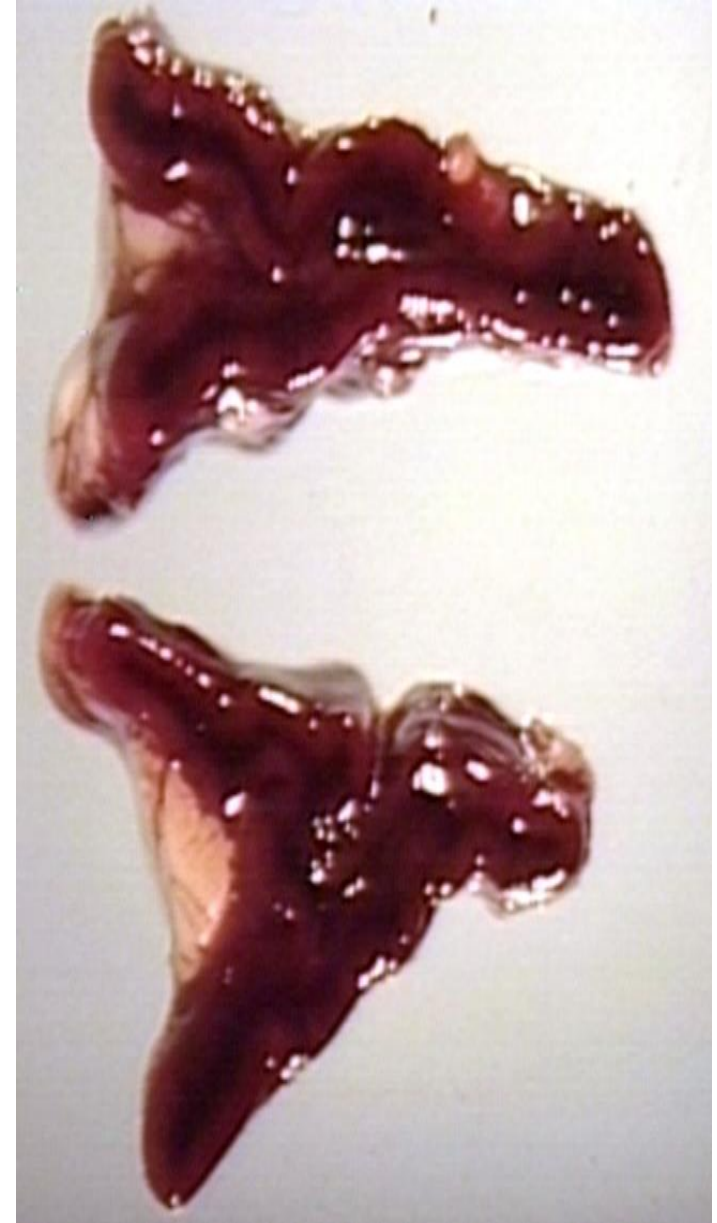
Clinical picture :

- Fever, headache, photophobia, vomiting, neck stiffness
- **Waterhouse Friderichsen Syndrome:**
 - Results from meningitis associated septicemia with **hemorrhagic infarction of the adrenal glands** and cutaneous petechiae.
 - Occurs with meningococcal and pneumococcal meningitis

- **very important slide.**

- حساس للضوء **Photophobia**

- ألم وتشنج بالرقبة **neck stiffness**



C.S.F. findings:

- Cloudy or frankly purulent
- \uparrow P, \uparrow Protein, \downarrow glucose, numerous **neutrophils**
- Bacteria may be seen or cultured

- **Treatment:**
 - Antibiotics
 - Fatal, if untreated.

Sheet# 1

- عشان نعرف نوع المسبب للمرض بنعمل خزعة ونفحصها لأنه ممكن يوجد عنا كذا مرض نفس الأعراض والشكل .

- Cloudy or frankly purulent (thick fluid).

- لو ما كان الطبيب شاطر وشخص صح المرض وعالجه ف رح يموت المريض المصاب.

Morphology :

- Exudate within the leptomeninges
- Meningeal vessels: Severely congested
- May cause cerebritis & ventriculitis
- May show phlebitis → venous occlusion & hemorrhagic infarction of underlying brain.

PURULENT (BACTERIAL) MENINGITIS





Thick exudates over base of brain in pyogenic meningitis

2- Acute Aseptic Meningitis (Viral Meningitis)

Clinical course: Less fulminant, self-limiting.

CSF: moderate ↑ protein, normal glucose ,
↑↑ lymphocytes

Morphology: Brain swelling in some cases.

- مافي حرارة وماله علاج بدھا شوية وقت واعراضها اقل خطورة و
حدة .

- Presence of bacteria lead to ↑ neutrophils.
- Presence of virus lead to ↑ lymphocytes.

3- CHRONIC Meningitis

- **Tuberculous**
- **Spirochetal**
 - Neurosyphilis**
 - Neuroborreliosis**
- **Fungal**
 - May involve the brain parenchyma.

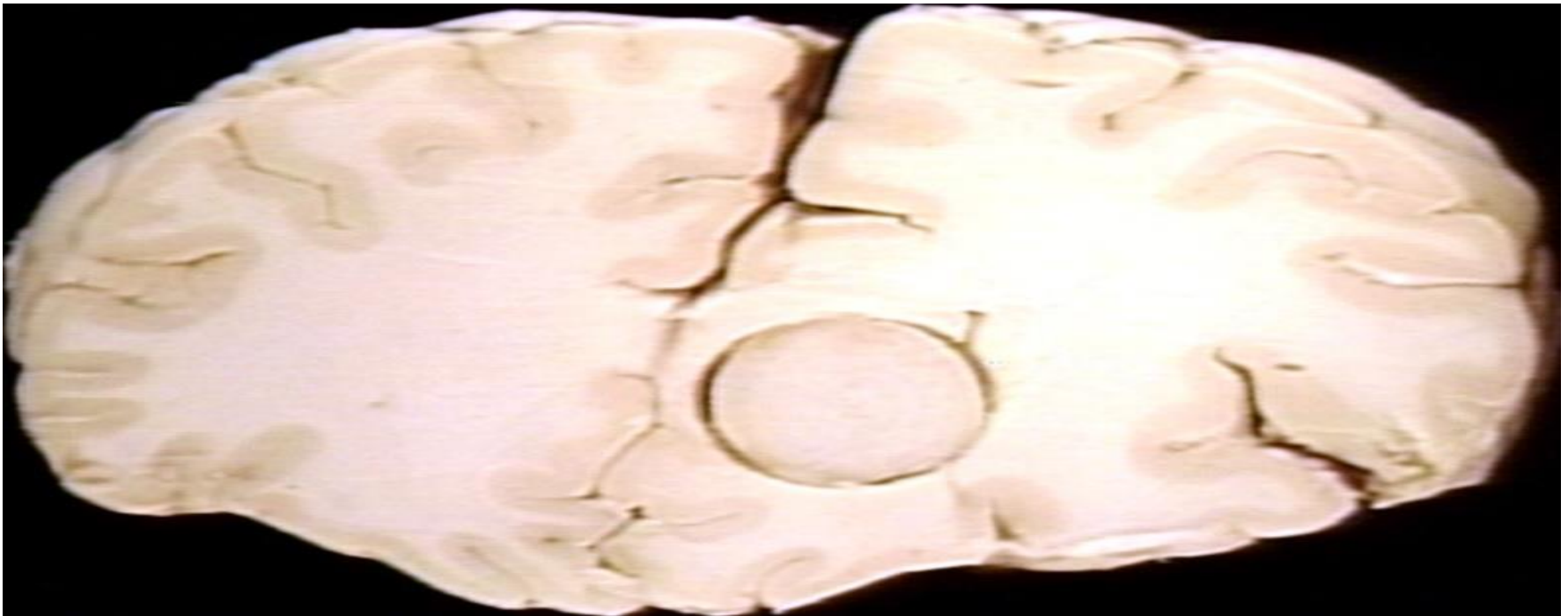
1-Tuberculous Meningitis :

- Hematogenous spread from lung → brain
- Direct spread from Tuberculous vertebra
- Result : Diffuse **meningoencephalitis** or tuberculoma

- **Morphology :**

- Diffuse meningoencephalitis: Gelatinous or fibrinous exudate, mostly at the base, obliterating the cisterns, and encasing cranial nerves.
- Tuberculoma: Single or multiple intraparenchymal mass+/- Meningitis.

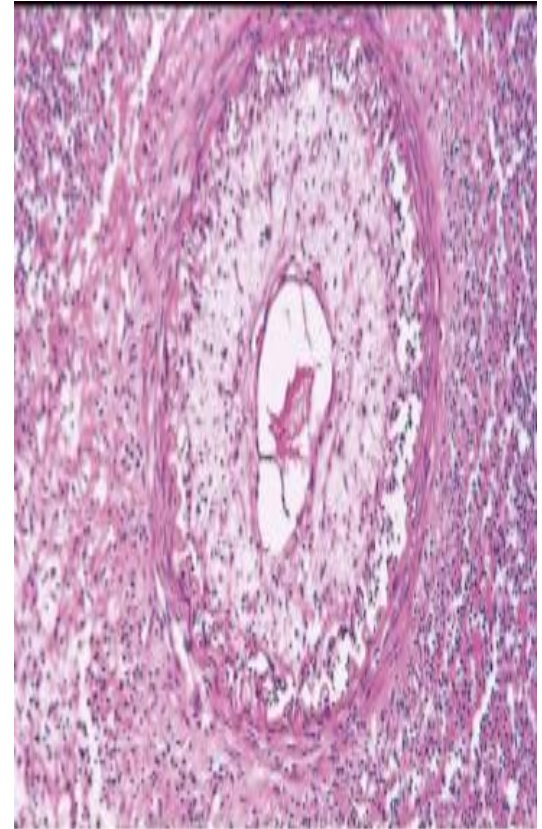
- بسبب وجود كتلة يمكن نفيها ورم بس هي لا مو ورم.



- **Microscopy:**

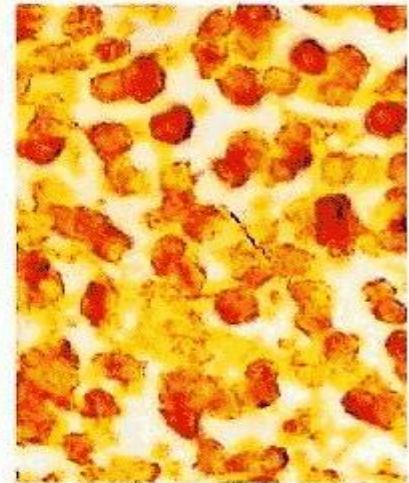
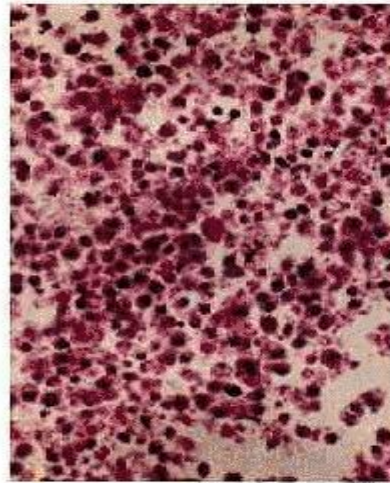
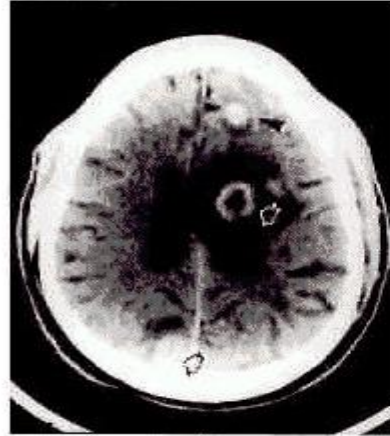
- Mixtures of lymphocytes, plasma cells and macrophages
- Florid cases: Caseating granulomas
- Obliterative endarteritis: inflammation in the wall, marked **intimal** thickening → arterial occlusion → infarction
- Dense fibrous adhesive arachnoiditis → Hydrocephalus.

- **CSF** : Marked ↑ ↑ Protein, , glucose normal or ↓, ↑ lymphocytes and neutrophils.



2- Neurosyphilis : caused by spirochete (T.pallidum) ,Tertiary stage

- **Meningovascular syphilis:**
 - Chronic Meningitis, base of the brain.
 - Obliterative endarteritis (Heubner arteritis): Perivascular plasma cells and lymphocytes
 - Cerebral gummas: Plasma cell-rich mass lesion



- **Paretic neurosyphilis :**
 - Invasion of the **brain**, mainly frontal lobe by T.pallidum
 - Insidious, but progressive mental and physical deficits with mood alteration, and eventually severe dementia → **General paresis of the insane**
 - Inflammation with parenchymal damage: **loss of neurons**, proliferation of microglia (ROD CELLS) & gliosis
 - Spirochetes may be seen in tissue section

- **Tabes Dorsalis :**

- Damage to the sensory nerves in the **dorsal root**
- Loss of axons & myelin → pallor and atrophy of dorsal columns
- Impaired joint position sense and ataxia (locomotor ataxia), loss of pain sensation → skin and joint damage → **Charcot joints**
- Others: lightning pains, absence of deep tendon reflexes



- **Acute syphilitic meningitis :**

- HIV infected patients

Sheet# 2

- المصاب بهاد المرض رح يفقد الاحساس ويصير عنده خلل بالتوازن، ما عنده احساس بالألم ويمكن تصير عنده مشاكل كثيرة لأنه رجله بتضرب بأي شي وتتصاب وهو مو حاسس أو منتبه بس شايفها وهاد بيكون بسبب ال



+ بتصير حركته صعبة

Loss of axons

3- Neuro-Borreliosis (LYME Disease)

- Borrelia burgdorferi
- **Neurologic manifestations:**
 - Meningitis
 - facial nerve palsies
 - polyneuropathies
 - encephalopathy

neuron كان سبب تسميته بسبب اصابته لل neuron + انه بيصيب اكثر من مكان مو مكان واحد بس.

Parenchymal Infections:

- Localized : abscess, tuberculoma, toxoplasmosis, some parasites
 - Diffuse : encephalitis, usually viral
- Not meningeal in general.

Brain Abscess

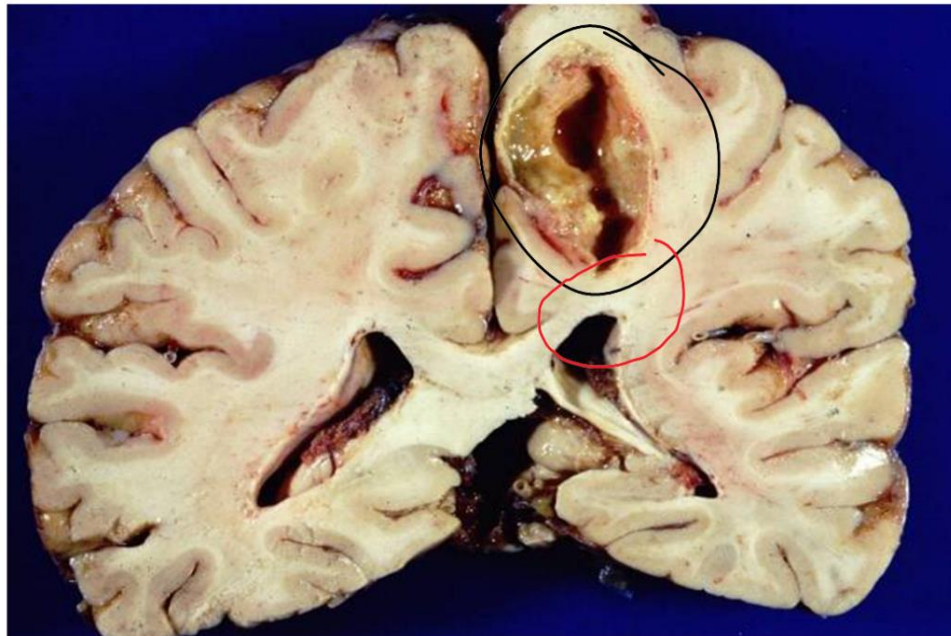
- Usually bacterial
- Direct implantation of organisms, or local extension from adjacent foci (paranasal sinusitis, mastoiditis)
- Hematogenous route from heart, lungs or after tooth extraction.
- **Grossly:** Discrete lesion with central **liquefactive** necrosis

CEREBRAL ABSCESS

- liquefactive necrosis (black) ⓪
- reactive gliosis (red) ⓪

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CEREBRAL ABSCESS



شريحة ٢٠ من ٢٢

- **Microscopic picture :**
 - Localized liquefactive necrosis surrounded by granulation tissue, & severe edema leading to ↑ ICP.
 - Fibrous capsule, outer zone of reactive gliosis
- **CSF :** ↑protein, ↑white cells, normal glucose
- **Clinical presentation:** Progressive focal deficit, and signs of ↑ ICP
- **Complications :**
If rupture → ventriculitis, meningitis, venous sinus thrombosis
- **Treatment:** Surgery and antibiotics.

VIRAL Encephalitis (Meningoencephalitis)

- **ARBO VIRUSES (West Nile, Equines,... etc)**
- **HSV1 & HSV2**
- **Herpes Zoster**
- **CMV**
- **POLIO**
- **RABIES**
- **HIV**
- **JC (Progressive Multifocal Leukoencephalopathy)**
- **Measles (Subacute Sclerosing Panencephalitis)**

VIRAL ENCEPHALITIS

- **Neurotropic** : Polio, Rabies
- **Intrauterine** : CMV, Rubella
- **Immune deficiency** :
HIV, CMV, JC, Herpes Zoster

- يمكن ينتقل من الام للجنين .

- Some viruses have selective sites :
 - HSV :Temporal lobe & orbital frontal area
 - CMV : Subependymal region
 - Polio : Anterior horn cells of spinal cord
 - Herpes Zoster: Sensory neurons of dorsal root ganglia

- **Features common to most viral infections :**

- 1- Perivascular mononuclear infiltrate**

- 2- Neuronophagia**

- 3- Microglial nodules**

- 4- Nuclear or cytoplasmic inclusions**

- **Mononuclear: can be a lymphocyte and macrophage but mainly lymphocyte.**

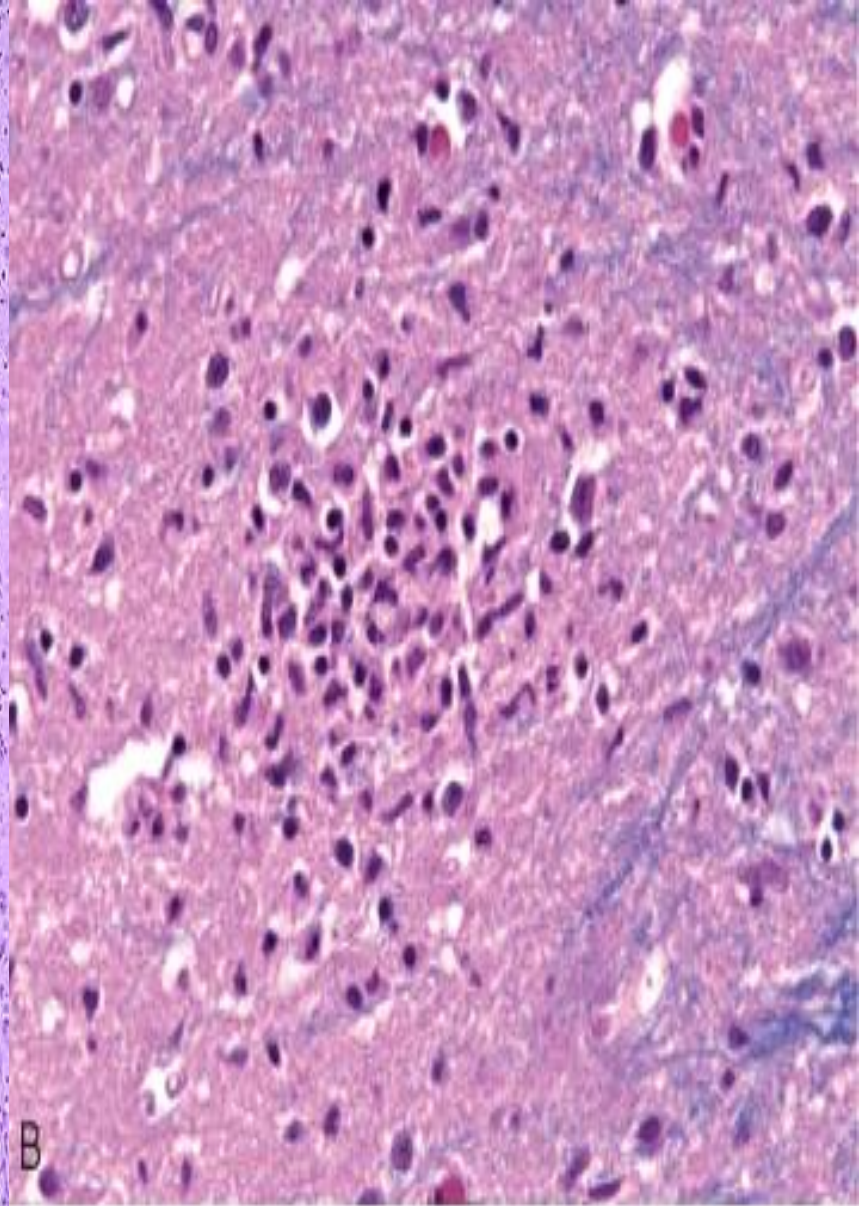
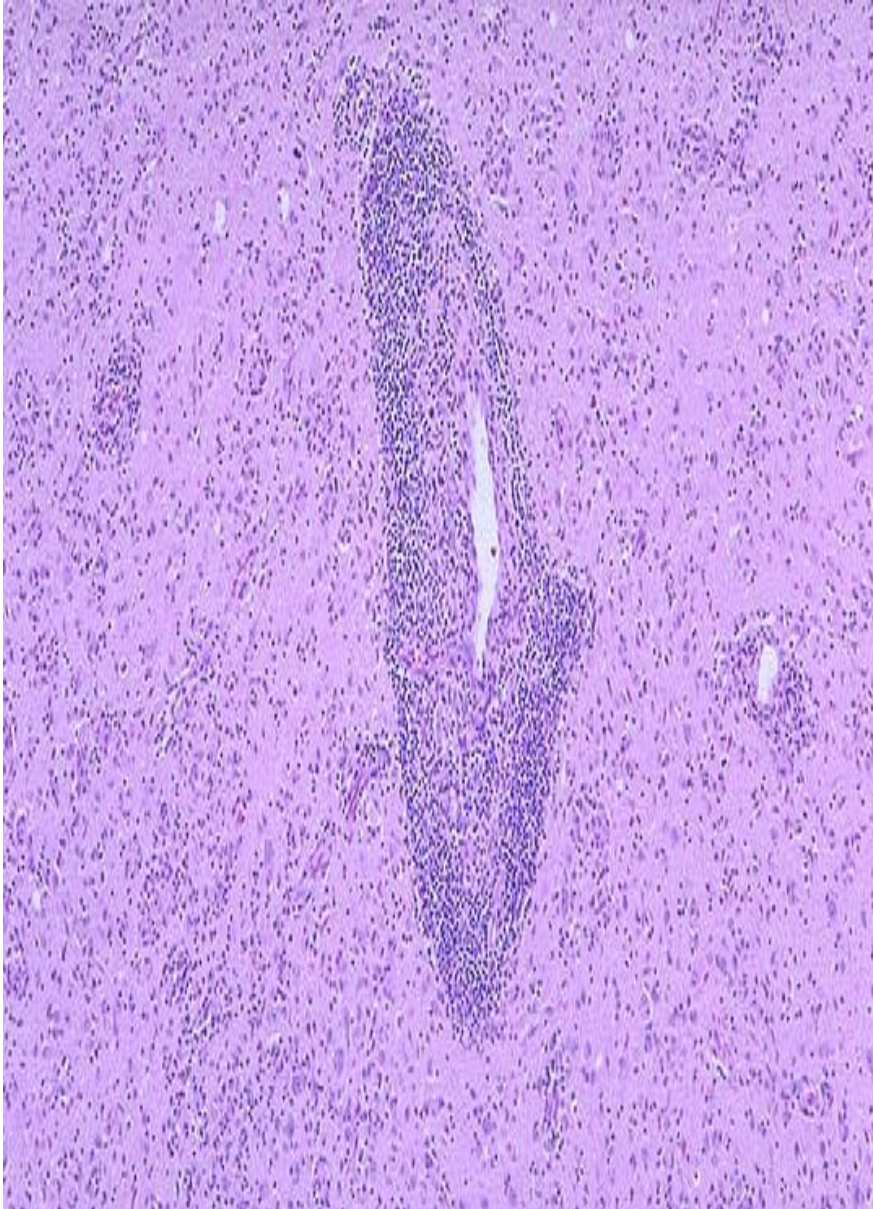
- **Perivascular: lymphocytic infiltrate around the vessel.**

- **Neuronophagia: engulfment of the neuron.**



neuronophagia

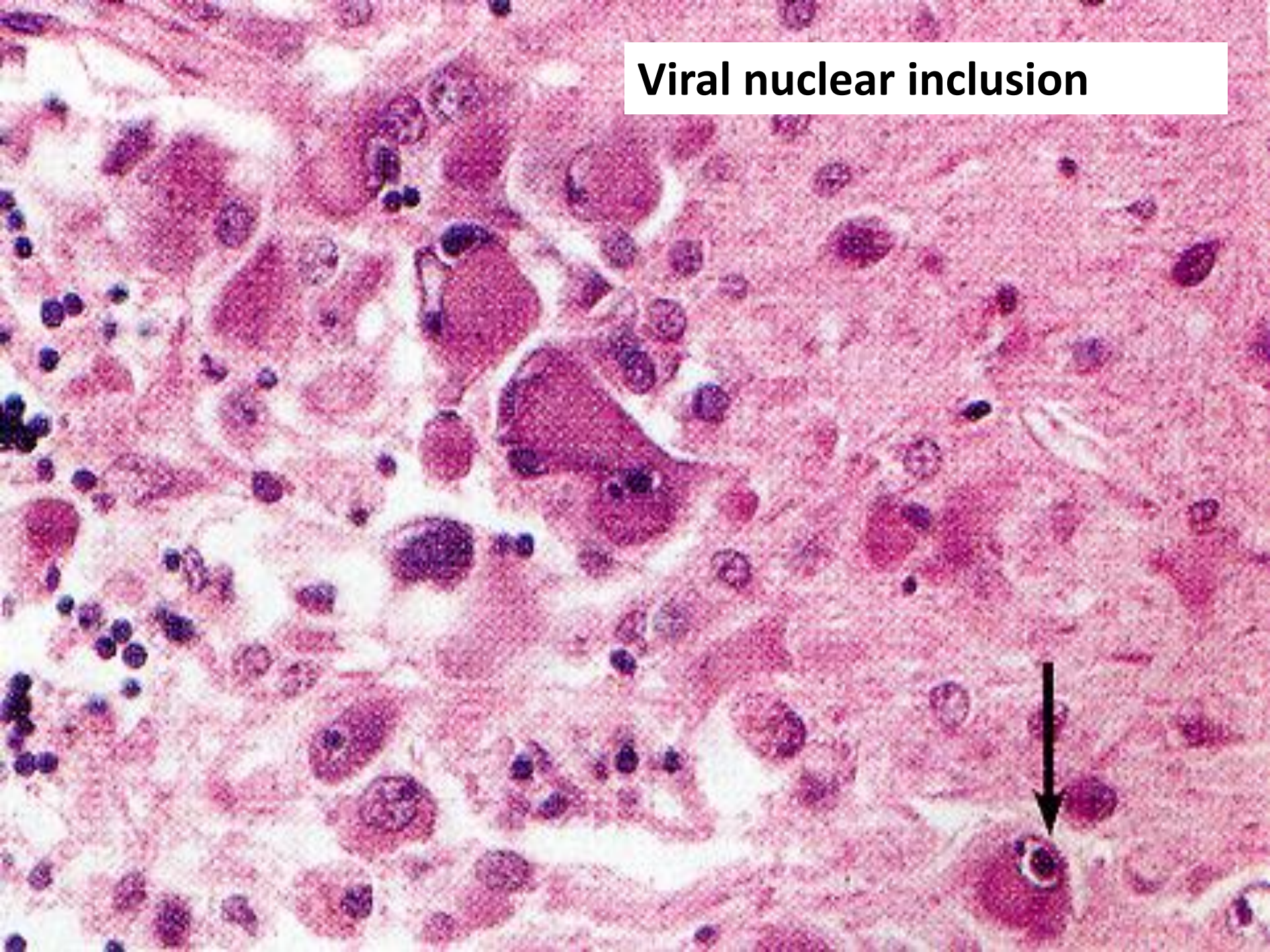
- Lumen of blood vessels.

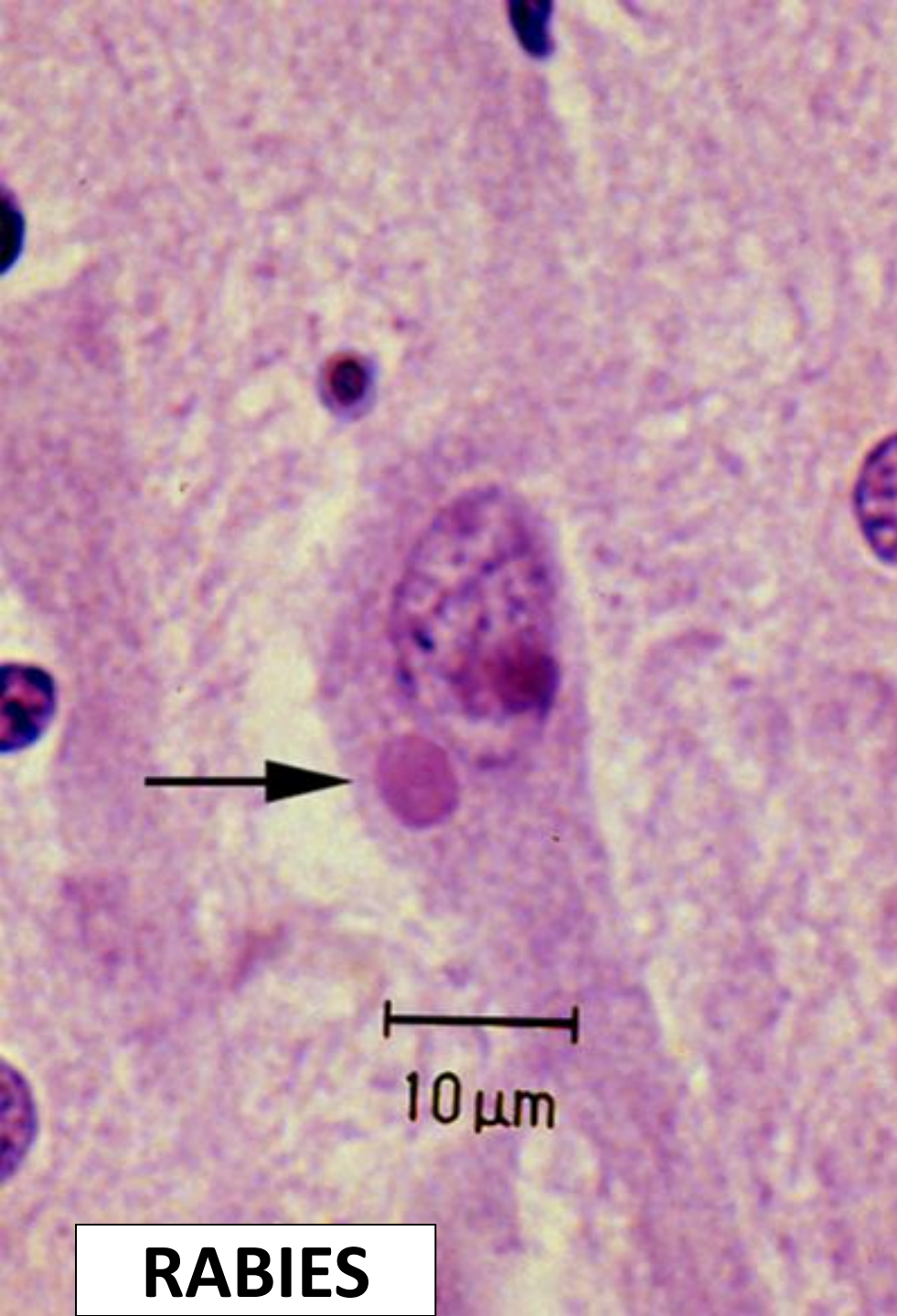


Perivascular cuffs of lymphocytes

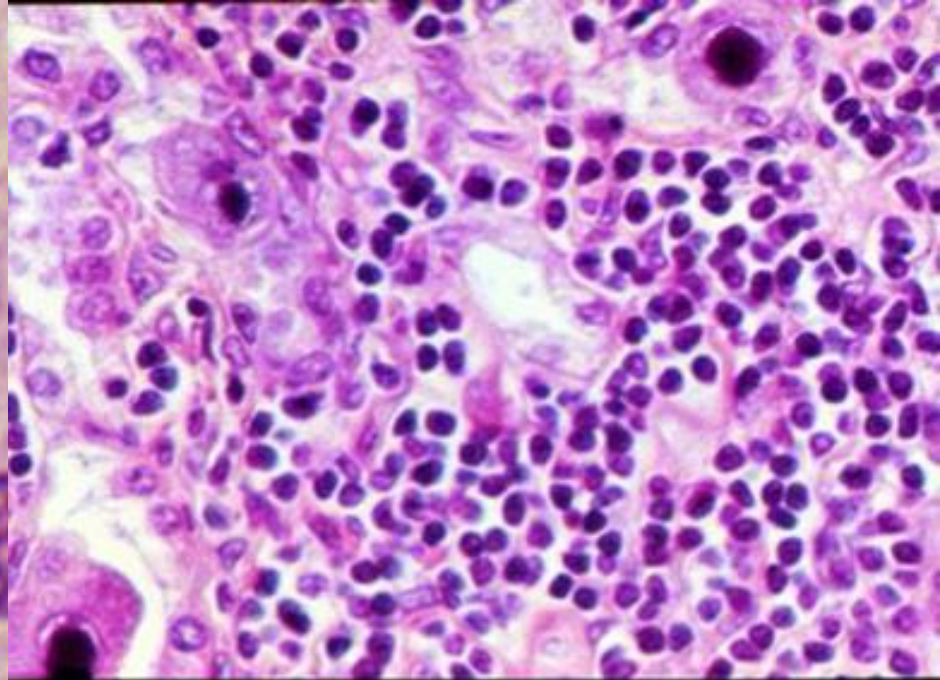
Microglial nodules

Viral nuclear inclusion





RABIES



CMV

1- Herpes Simplex Virus type 1 & 2

- HSV1

- Children or young adults
- Hemorrhagic necrotizing inflammation in temporal lobe & orbital gyri of frontal lobe
- Alteration in mood, memory and behavior
- All common features of viral encephalitis seen +Cowdry type A **intranuclear** viral inclusions in neurons & glial cells

- **HSV-2** in adults may cause meningitis



HERPES ENCEPHALITIS

2- Varicella –Zoster Virus (Herpes-Zoster)

- Causing Chicken pox during primary infection in children.
- latent infection in **dorsal root ganglia**.
- Reactivation in adults (Shingles): painful vesicular skin eruption along a dorsal nerve in one or a few dermatoms, Self limited.
- Lesion is typical of viral infection, inclusions ± granulomatous arteritis & infarction
- In immunosuppressed patients, may show acute encephalitis.

Patient with shingles



Shingles (herpes zoster) rash



Shingles (Herpes Zoster)

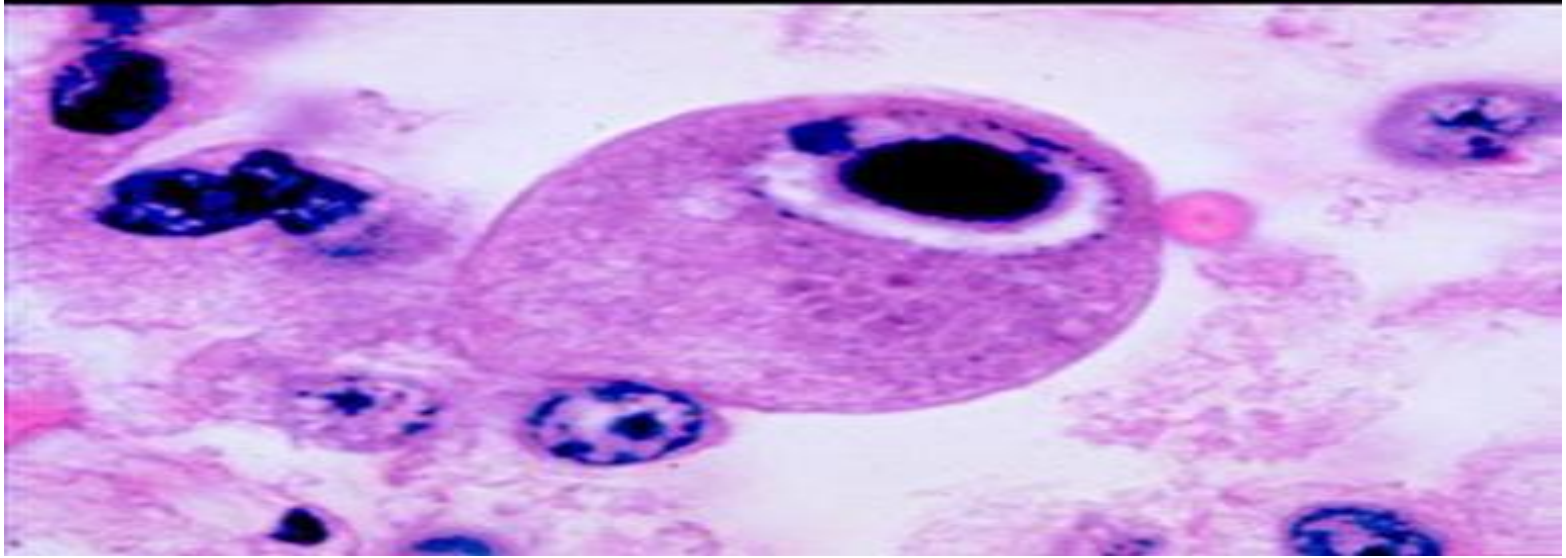
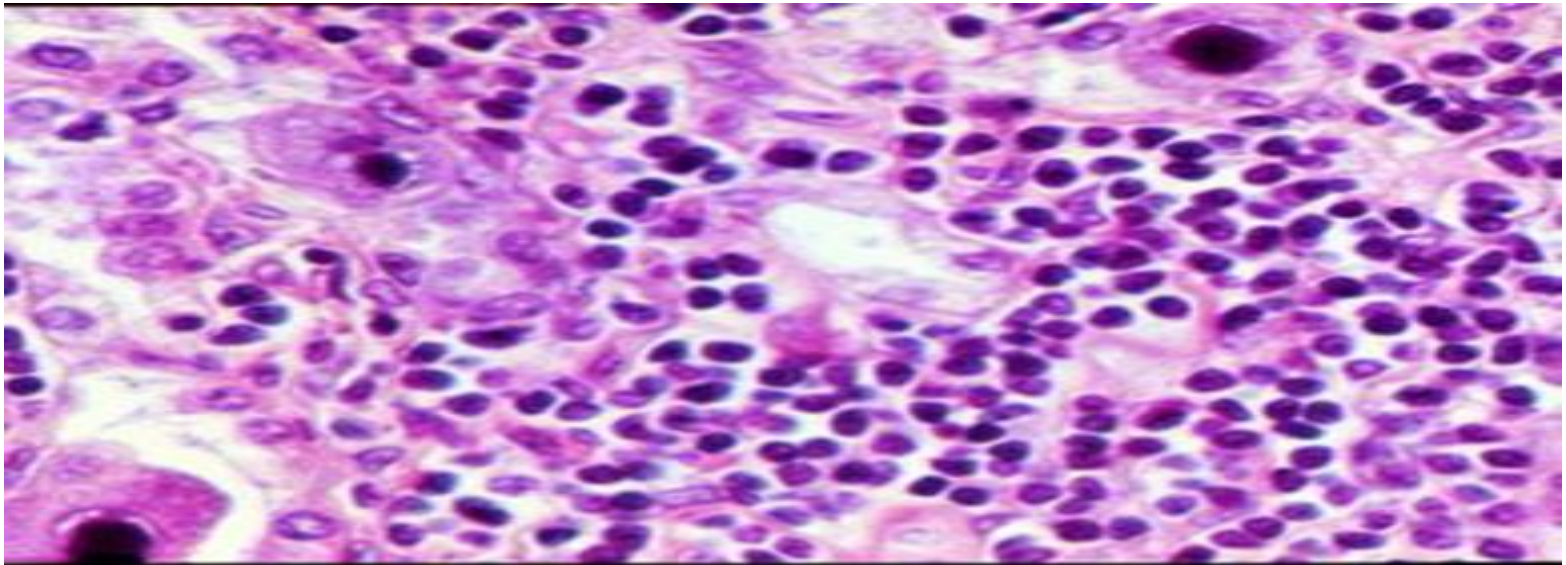


Herpes zoster blisters



3- Cytomegalovirus (CMV)

- **Immunosuppressed** especially AIDS : subacute encephalitis in any region & any cell but mainly **Paraventricular subependymal region** of the brain → **Sever hemorrhagic necrotizing ventriculoencephalitis**
 - hemorrhagic necrosis of ependymal lining with large **cytoplasmic & intranuclear** inclusions
- **Fetus** : intrauterine infection:
 - Periventricular necrosis and brain destruction , microencephaly & calcification



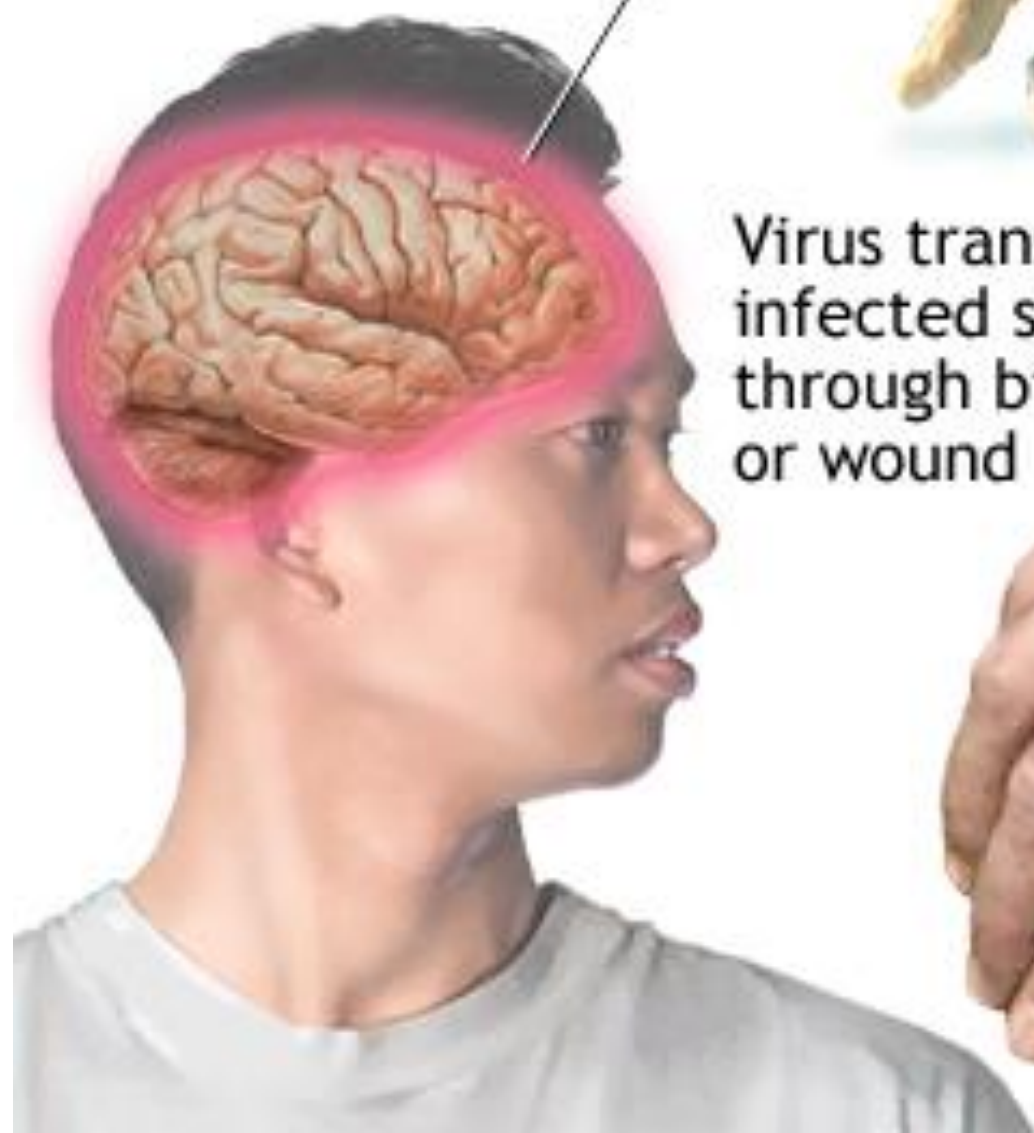
4- Rabies

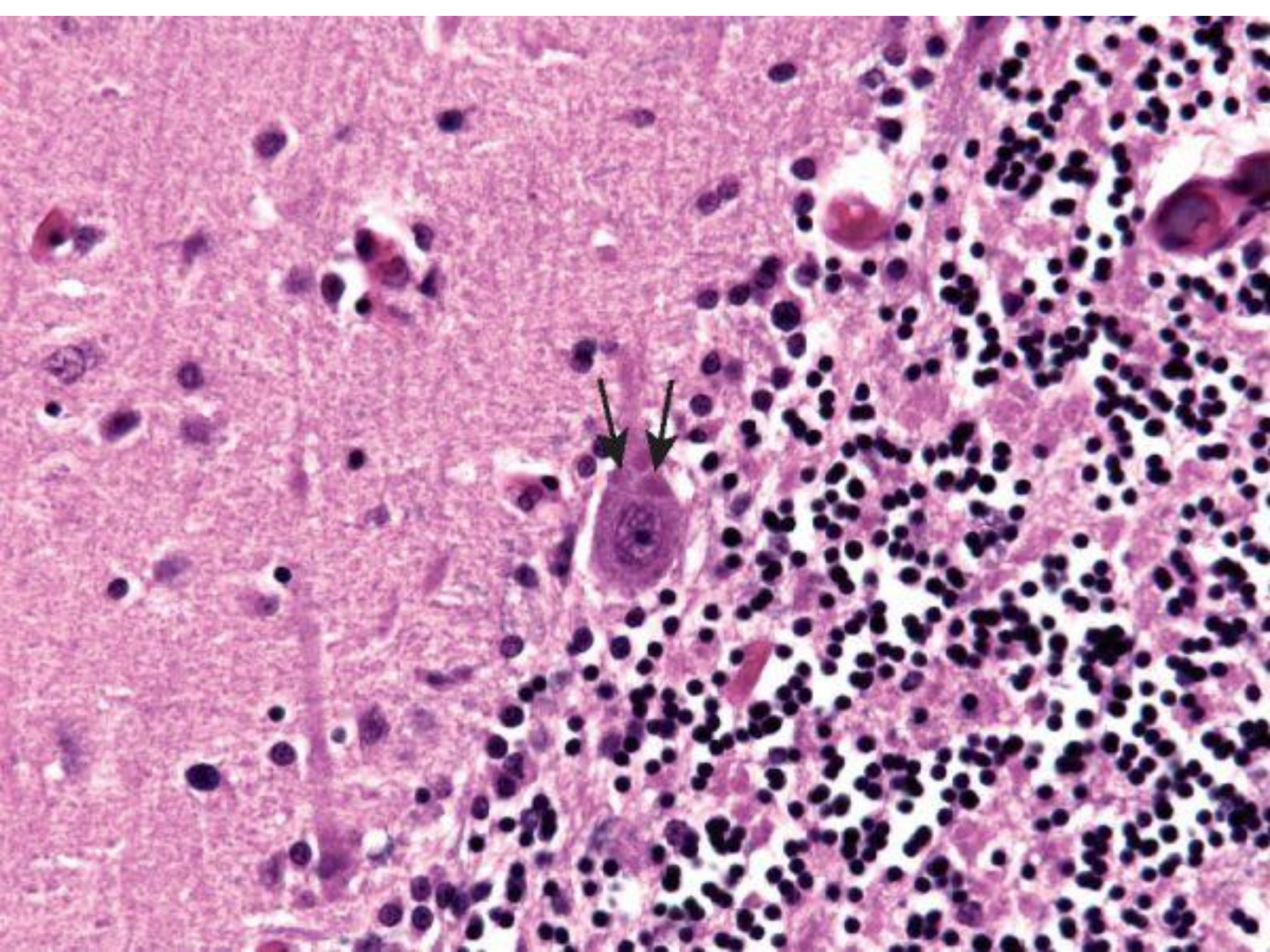
- Severe encephalitis
 - Transmitted to humans by bite of a rabid animal such as dog
 - Ascends along peripheral nerve from bite
- Headache, fever, extraordinary CNS excitability, Periods of mania and stupor.
- Neuronal degeneration and inflammatory reaction , most severe in brain stem
 - also can be in basal ganglia, S.C, dorsal root ganglia
- Presence of **Negri bodies** : **cytoplasmic**, eosinophilic inclusions in pyramidal neurons of the **hippocampus** & **Purkinje cells of cerebellum**, in sites usually devoid of inflammation

Brain inflammation



Virus transmitted by
infected saliva
through bite
or wound





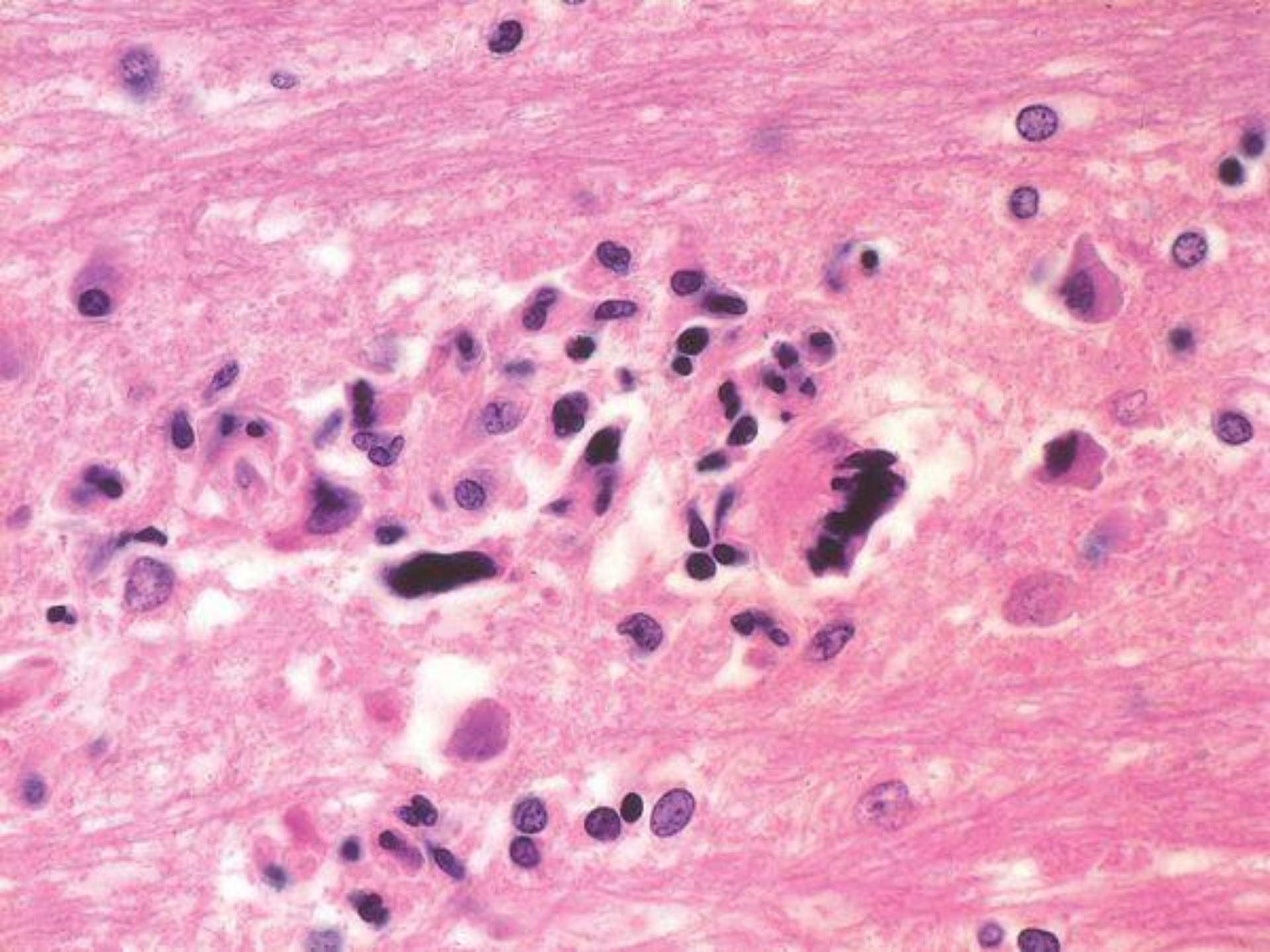
5- Poliovirus

- Enterovirus causing mild gastroenteritis
- Involvement of CNS in the non- immunized
- Acute :
 - mononuclear cell perivascular cuffs and neuronophagia of the **anterior horn motor neurons** of the spinal cord
- Chronic :
 - Loss of neurons and atrophy of the anterior (motor) spinal roots,**and neurogenic atrophy of muscle.
- Clinical presentation:
 - Flaccid paralysis with muscle wasting
 - Death can occur from paralysis of the respiratory muscles in acute phase.



6- Human Immunodeficiency Virus (HIV)

- **Early:** aseptic viral meningitis in 10%
- **Chronic : HIV Encephalitis:** chronic inflammatory reaction with **widely distributed microglial nodules with multinucleated giant cells**
- Can cause disorder of white matter : Multifocal or diffuse area of myelin pallor, axonal swelling and gliosis
- **HIV- associated dementia**



7- JC virus → PML

(Progressive Multifocal Leuko-Encephalopathy)

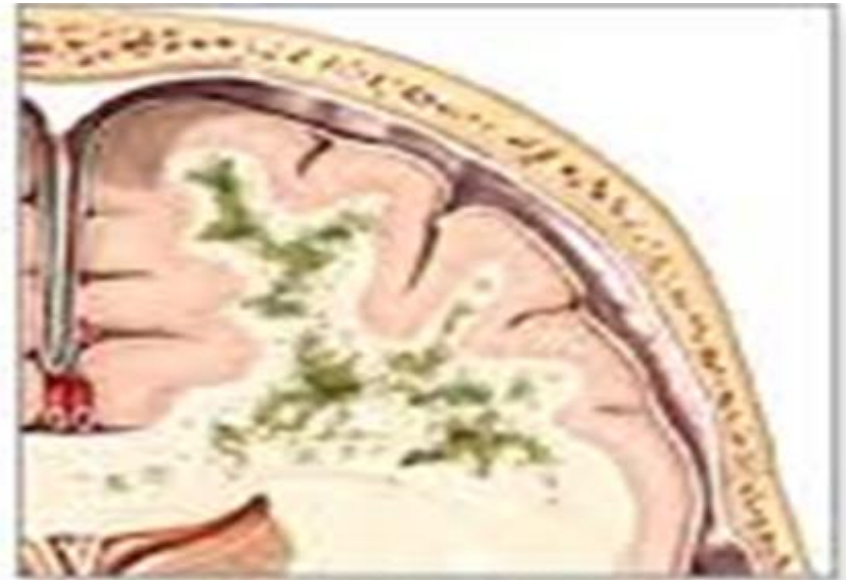
- Caused by **JC polyomavirus** exposure during childhood
- Reactivation mainly in AIDS patients & other immunosuppressed patients
- Infect **oligodendrocytes**

RESULT : Progressive **demyelination** of white matter

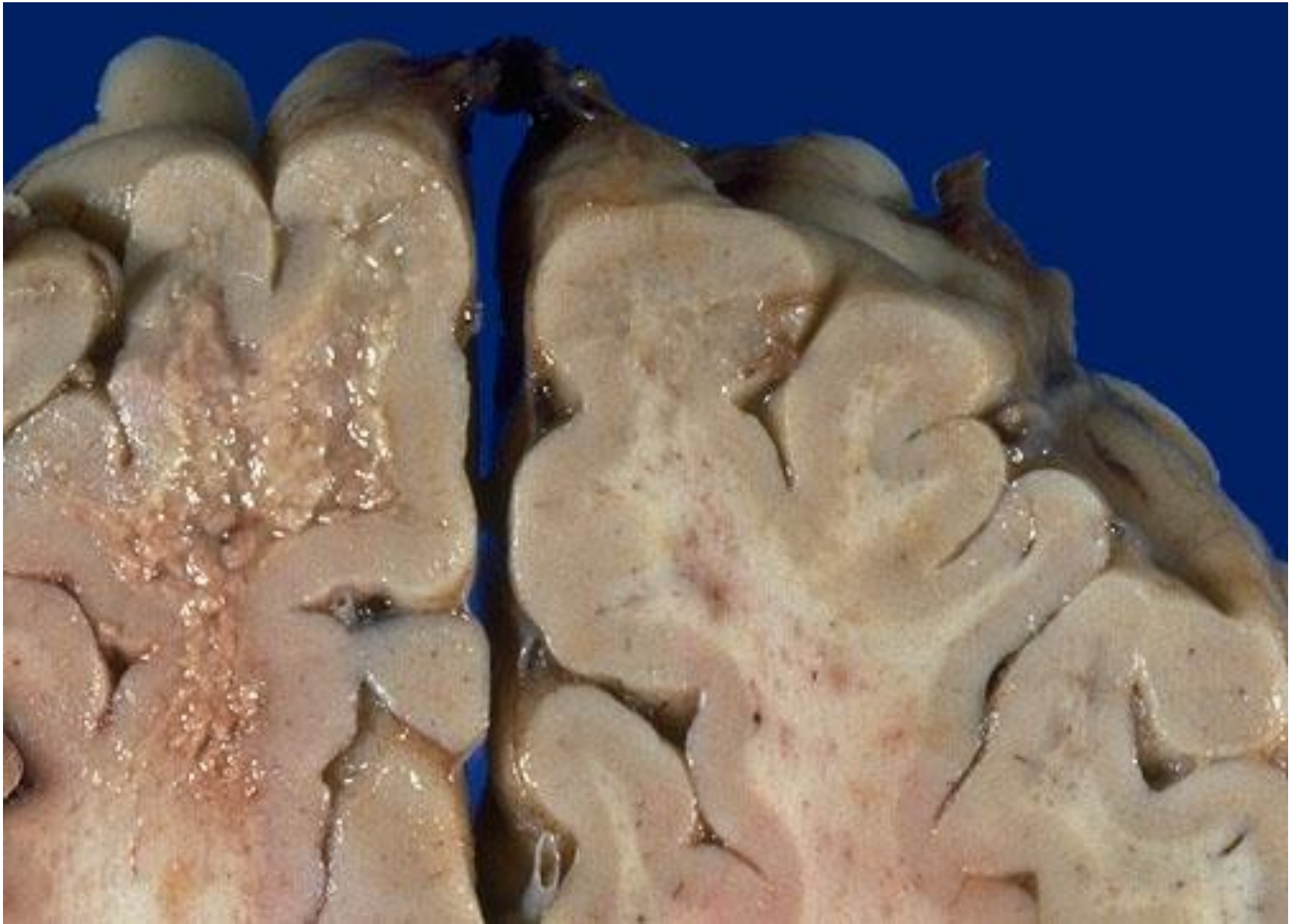
- **Grossly:**
 - Patches of irregular, ill-defined destruction of white matter from mm to extensive involvement of the entire lobe



Normal brain



Brain with lesions



- **Microscopy:**

- Patch of demyelination , with scattered lipid laden macrophages at the center, and reduced number of axons
- Enlarged oligodendrocyte nuclei with viral inclusions
- Large astrocytes are also seen.

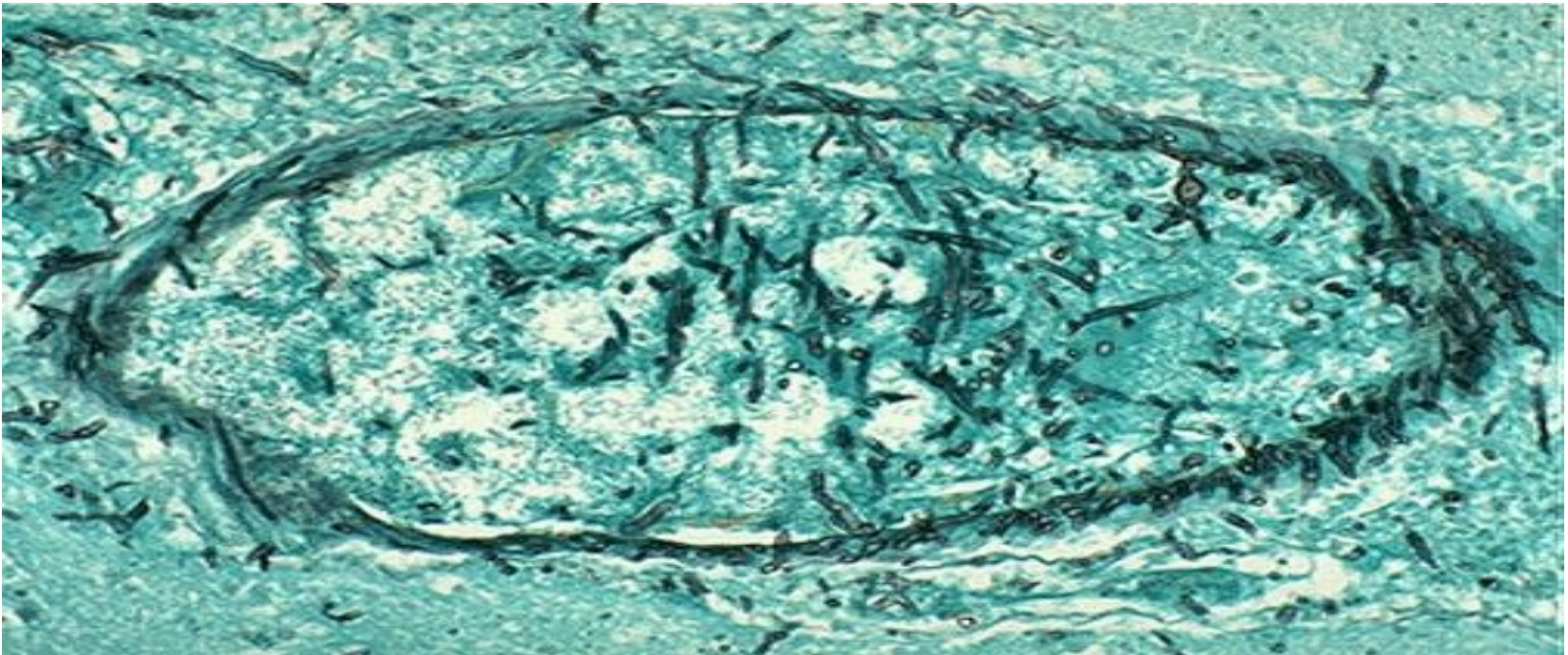
FUNGAL ENCEPHALITIS :

- Candida, Cryptococcus , Aspergillus, & Mucor
- Mainly in Immunocompromised patient
- Hematogenous or direct invasion
- Parenchymal granulomas or abscesses, often associated with meningitis
- AIDS patients are prone to cryptococcal meningoencephalitis

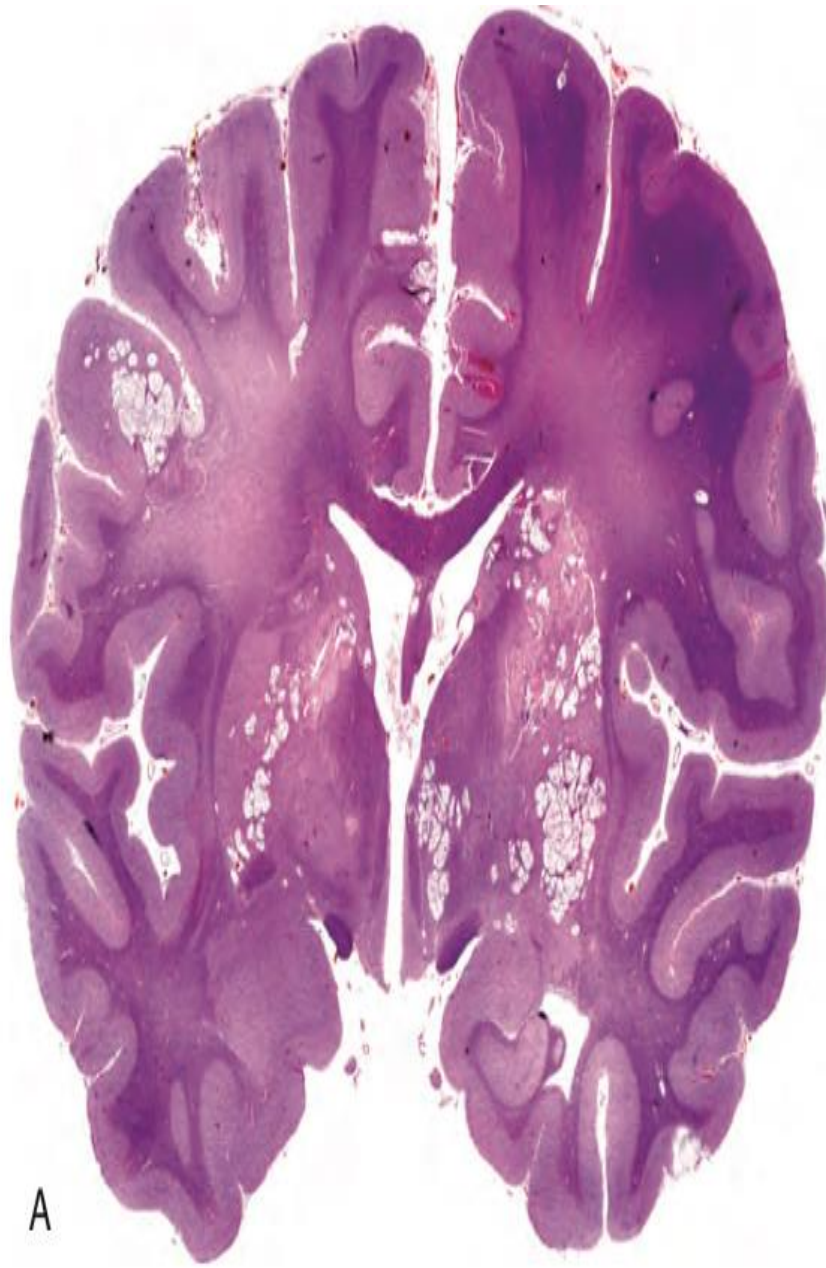
- **Candida albicans** : Multiple microabscesses, with or without granuloma formation.
- **Mucormycosis** :
 - Presents as an infection of the nasal cavity or sinuses of a **diabetic** patient with ketoacidosis.
 - May spread to the brain through vascular invasion or by direct extension through the cribriform plate.

- **Aspergillus fumigatus :**

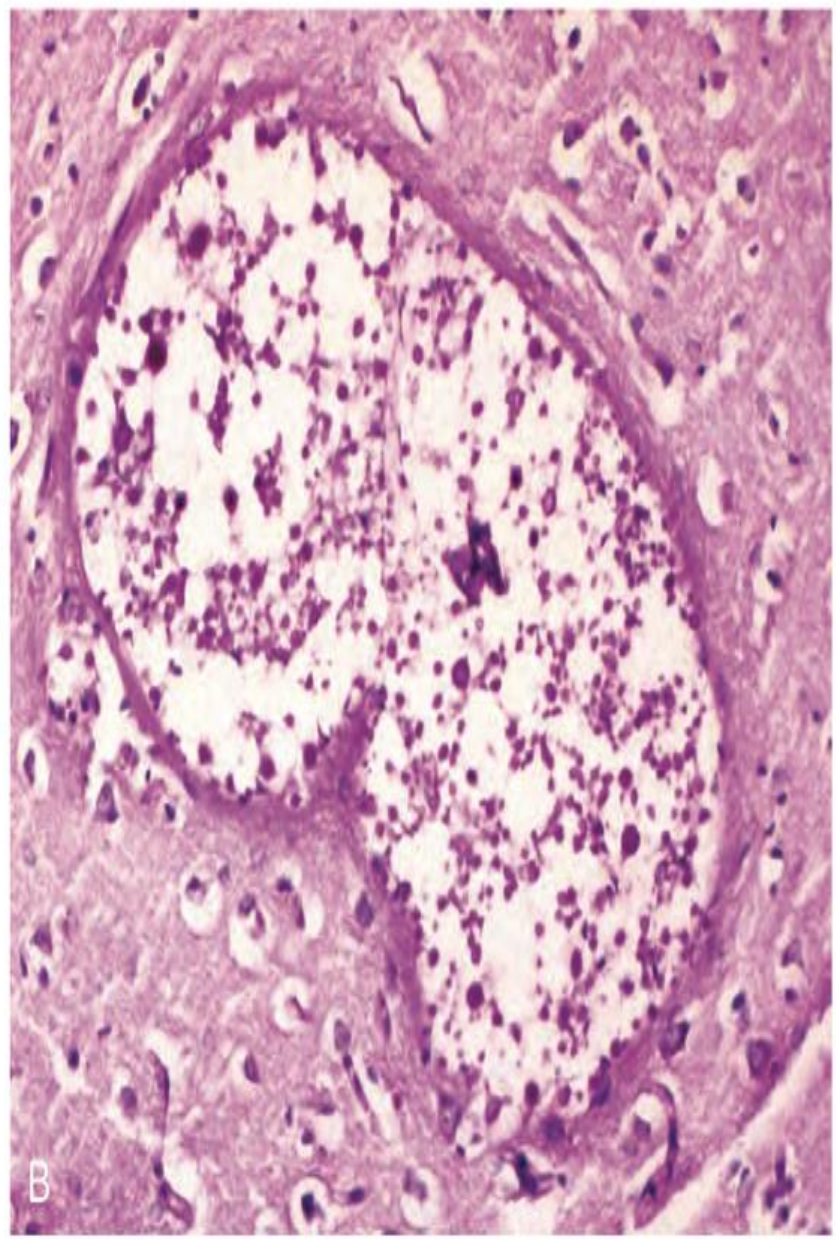
- Widespread septic hemorrhagic infarctions,
Why??



- **Cryptococcus neoformans:**
 - Meningitis or meningoencephalitis
 - Immunosuppressed patients
 - Extension into the brain follows vessels in the Virchow-Robin spaces.
 - As organisms proliferate, these spaces expand, giving rise to a “soap bubble”–like appearance



A

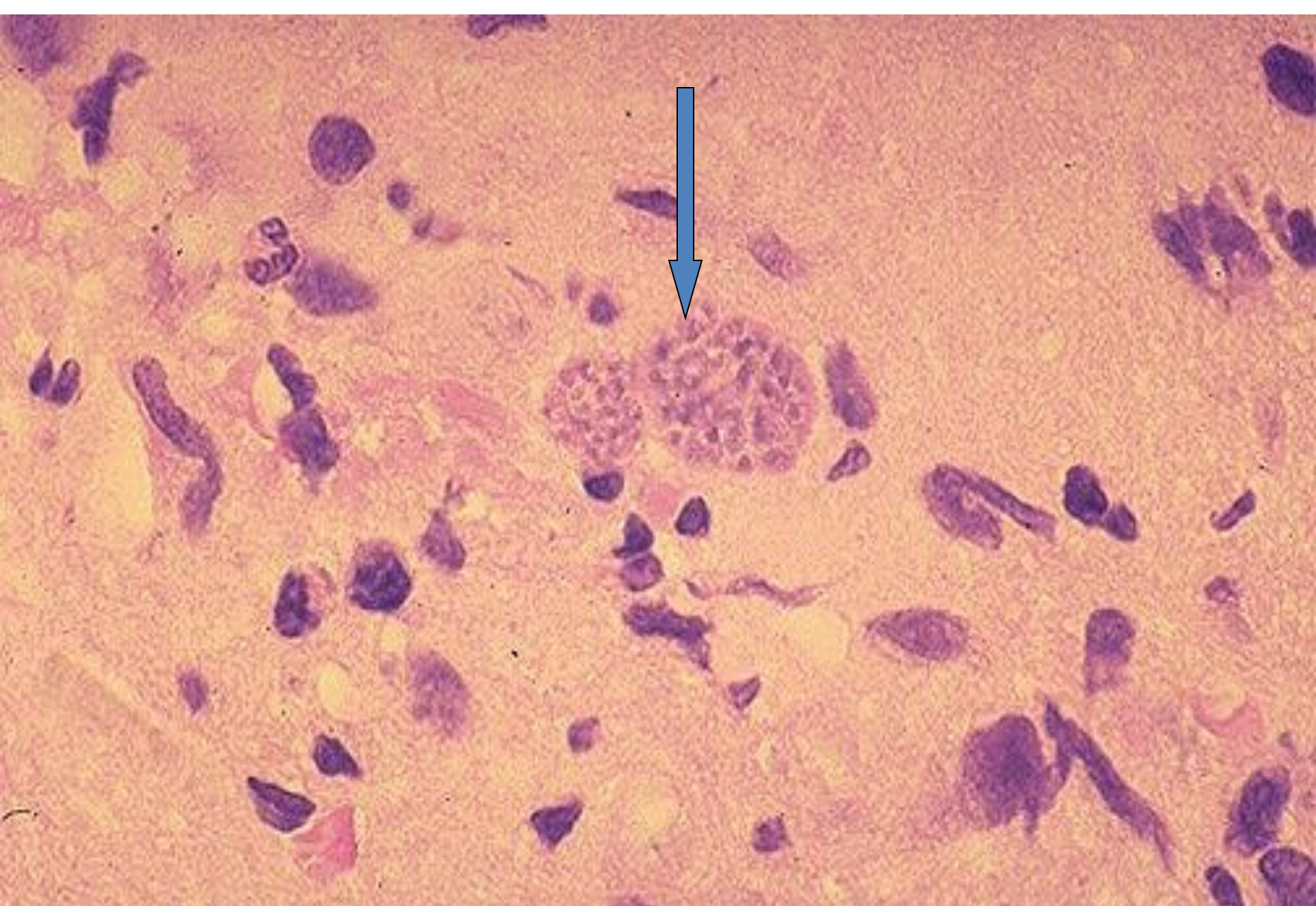


B

Other infections :

- **Cerebral Toxoplasmosis :**
 - Immuno-compromised patients, especially(AIDS)
 - Small, usually multiple abscesses & necrotic foci
 - Both free tachyzoites and encysted bradyzoites may be found at the periphery of the necrotic foci
 - In newborns who are infected in utero: triad of chorioretinitis, hydrocephalus, and intracranial calcifications





Toxoplasma Pseudocyst

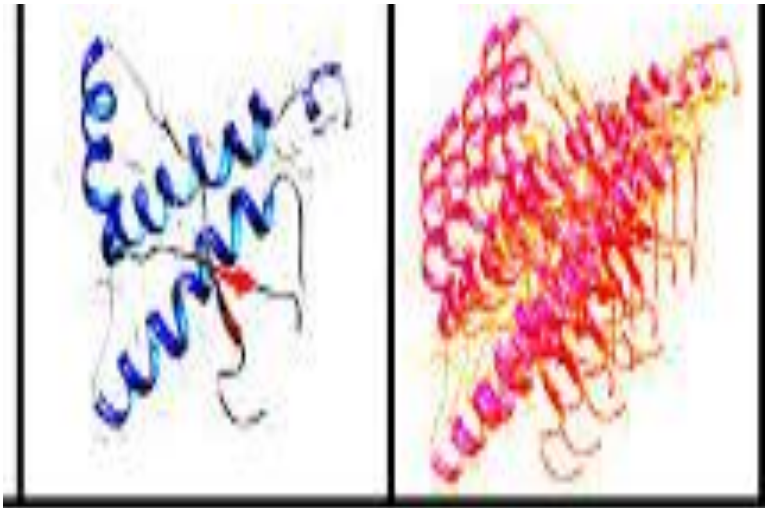
- **Cysticercosis:**

- Infection of a human brain with the larva of the pork tapeworm (*Taenia solium*) .
- Clinically: - Mass lesion, seizures.



PRION DISEASES :

- Normal PrP (prion protein) is a cellular protein present in neurons
- Disease occurs when the PrP undergoes conformational changes from its normal shape (PrP^c) to an abnormal conformation called PrP^{sc}.



Prion protein or PrP
is a protein on the
surface of your cells

A prion is an
infectious particle
made up of
misfolded prion
proteins

Include a variety of conditions :

- Sporadic and familial Creutzfeldt- Jacob Disease
- Scrapie in sheep
- bovine spongiform encephalopathy in cattle (“mad cow disease”)

CJD (Creutzfeldt-Jakob)

- 1 per million incidence, 7th decade
- Sporadic cases 85%
- Familial cases (15%), younger
- **Rapidly progressive dementia**
- Onset of subtle changes in memory and behavior to death is only 7 months
- FATAL, no treatment known, like ALL prion diseases

- **Microscopy:**
 - Multifocal spongiform transformation (Intracellular vacuoles in neurons and glia) of cerebral cortex & deep gray matter.
 - Advanced cases:
 - Neuronal loss
 - Gliosis

