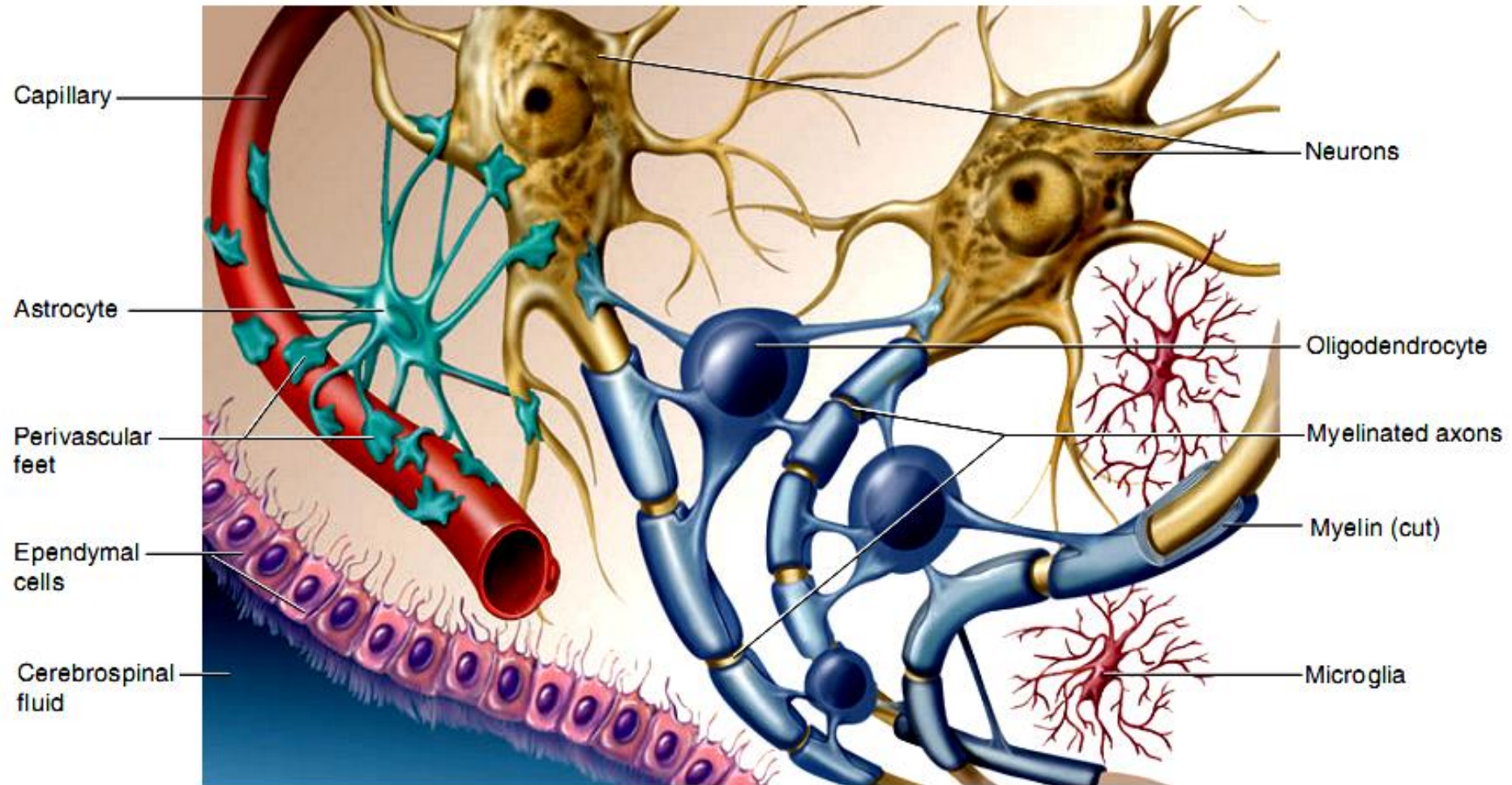




# Pathology of central nervous system

Dr. F. solhjoo M.D.  
Fellowship of molecular pathology  
and cytogenetic

# Neuroglial Cells



# Neurons

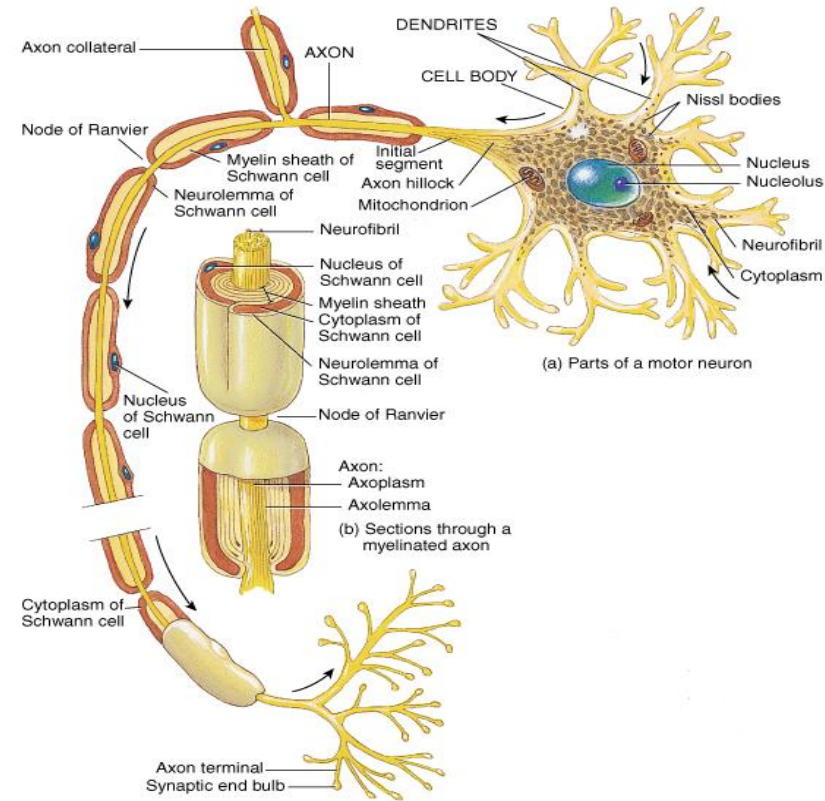
- Functional unit of nervous system

## 1. Cell body

- a) Nissl bodies
- b) Neurofilaments
- c) Microtubules
- d) Lipofuscin pigment clumps

## 2. Cell processes

- a) Dendrites
- b) Axons



# CNS

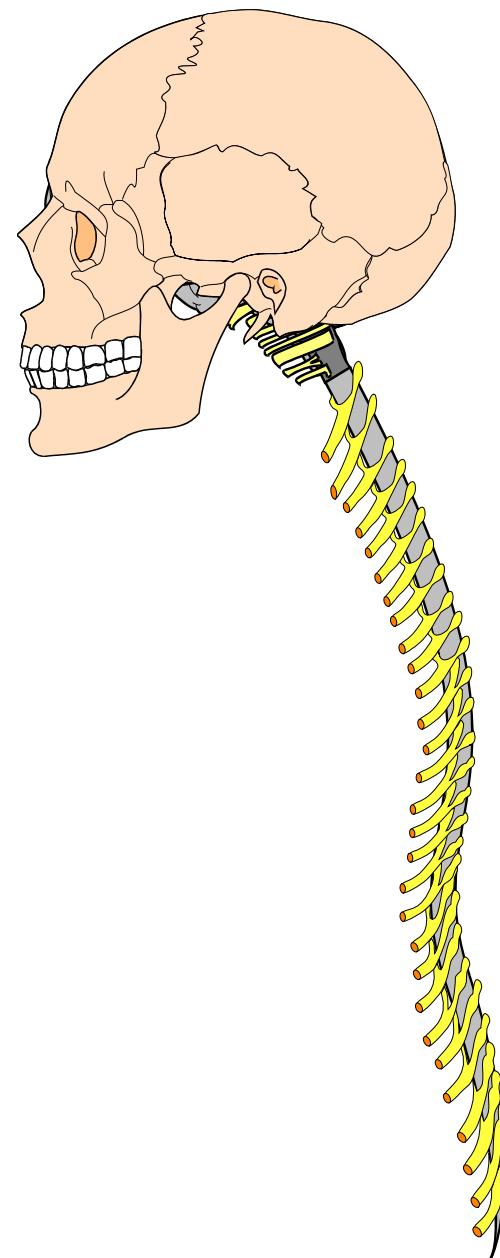
- ویژگی ها 1

محدود بودن در فضای استخوانی

لوکالیزه شدن فانکشن

قدرت ترمیمی محدود به بافت پشتیبان

CSF عدم وجود لنف و وجود مایع



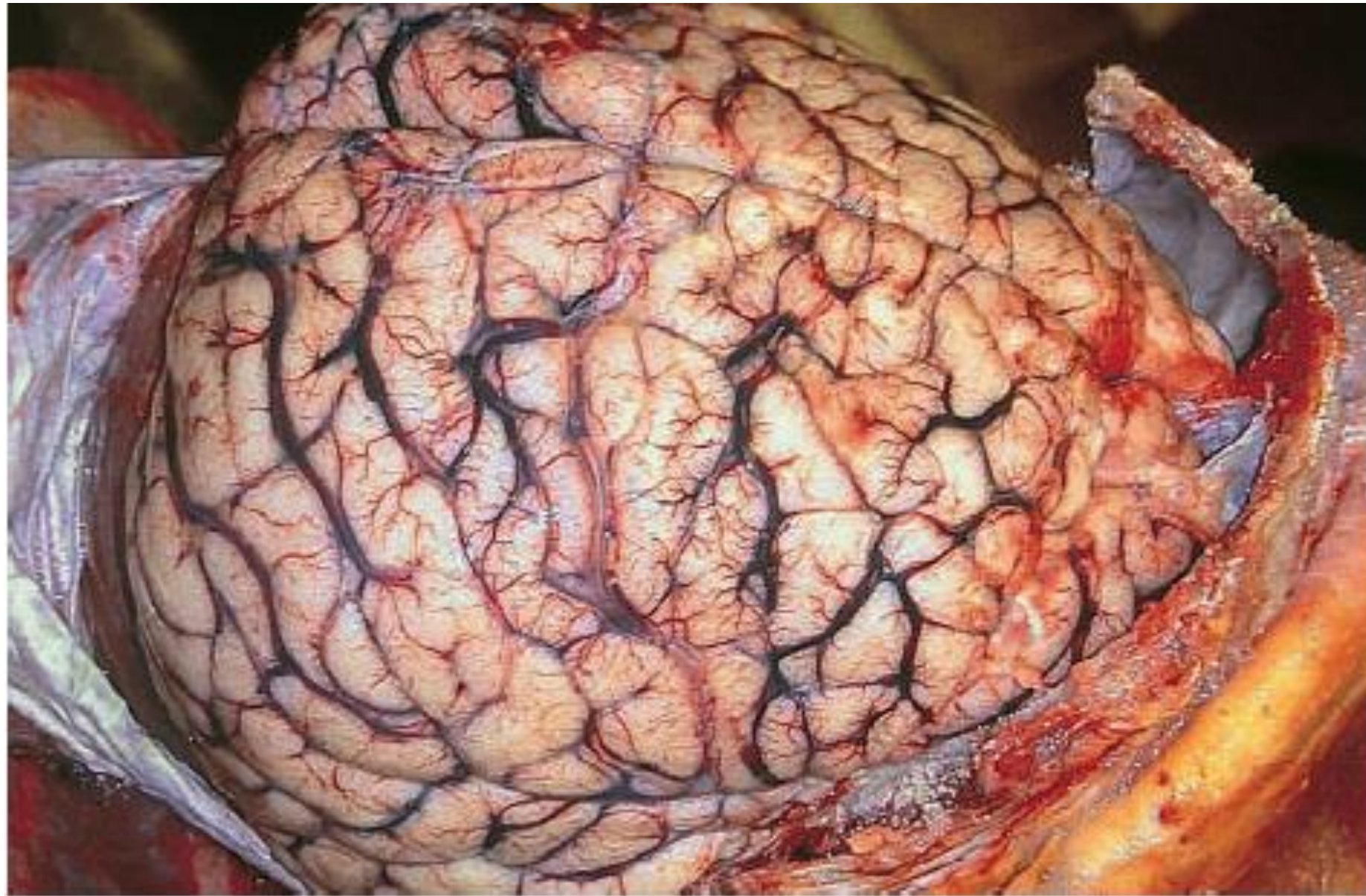
- The brain and spinal cord are encased within the **skull and spinal canal**.
- The advantage of housing the delicate CNS within hard, rigid structures is obvious, but this arrangement provides little room for expansion of the brain in disease states. As a result, virtually any increase in the volume of the skull contents brings with it an increase in intracranial **pressure**.
- Substantial increases in the intracranial pressure compromise the ability of the cardiovascular system to deliver blood to the brain, resulting in decreased brain **perfusion**, with serious or fatal consequences.

- Disorders that may cause dangerous increases in the volume of intracranial contents include :
  - generalized cerebral edema
  - Hydrocephalus
  - Hemorrhages
  - Ischemia
  - mass lesions such as tumors.

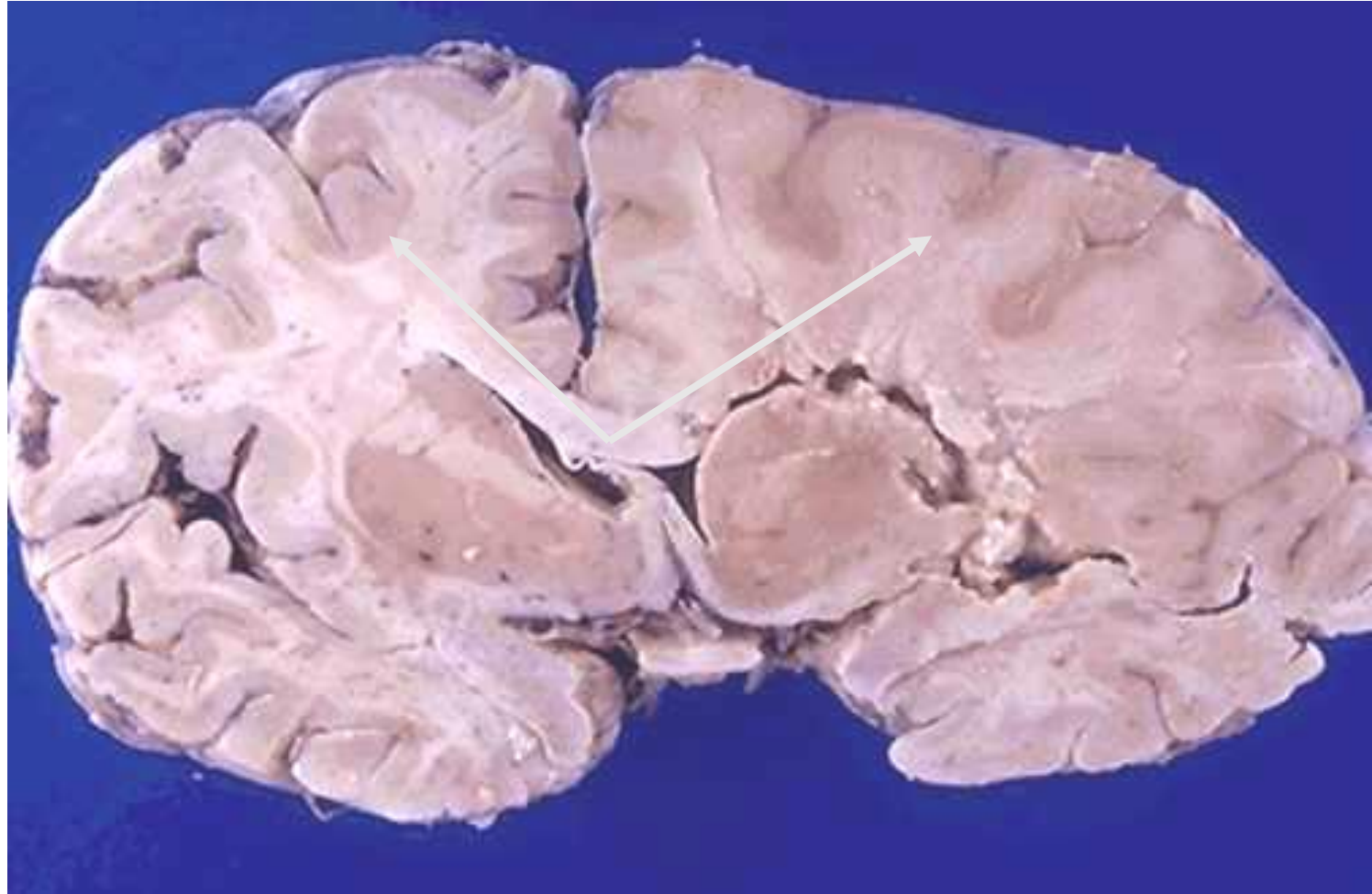
# Cerebral Edema

- Cerebral edema is the accumulation of excess fluid within the brain **parenchyma**:
  - *Vasogenic edema*: an increase in **extracellular fluid** can be **localized** (e.g., the result of increased vascular permeability due to inflammation or in tumors) or **generalized**
  - *Cytotoxic edema*: an increase in **intracellular fluid** secondary to neuronal and glial cell injury, as might follow generalized hypoxic or ischemic insult or exposure to certain toxins.
- This two types, which often **occur together**, particularly after generalized injury

- The edematous brain is **softer** than normal and often appears to “overfill” the cranial vault. In generalized edema, the gyri are **flattened**, the intervening sulci are narrowed, and the ventricular cavities are compressed



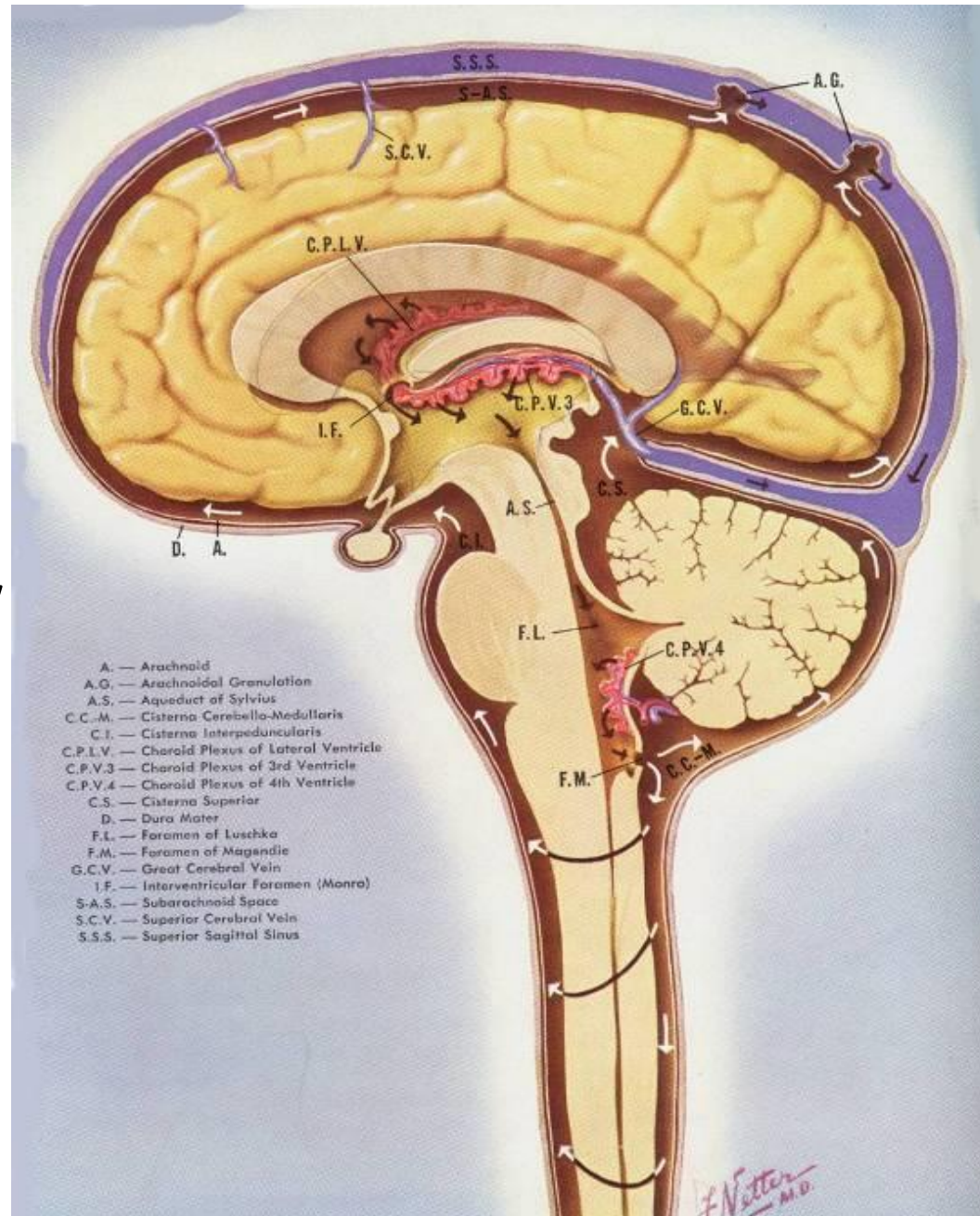
Edema, loss of demarcation:



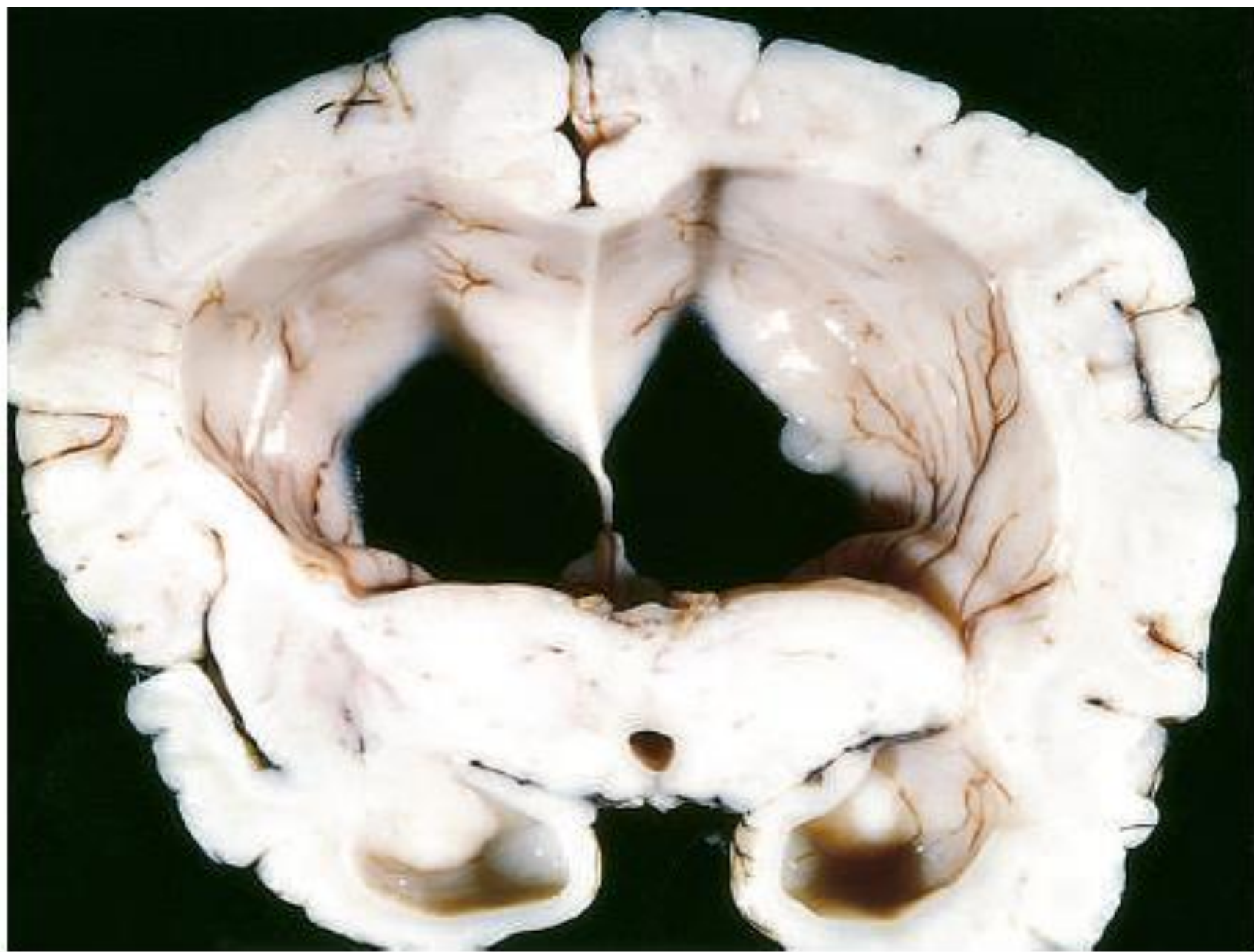
# Hydrocephalus

- After being produced by the **choroid plexus** within the ventricles, CSF circulates through the ventricular system and flows through the foramina of Luschka and Magendie into the subarachnoid space, where it is absorbed by **arachnoid granulations**.

# CSF FLOW



- *noncommunicating hydrocephalus*: there is a localized obstacle to CSF flow within the ventricular system, then a portion of the ventricles enlarges while the remainder does not. Most commonly is caused by **masses** obstructing the foramen of Monro or compressing the cerebral aqueduct
- *Communicating hydrocephalus*: the entire ventricular system is enlarged; it is usually caused by **reduced CSF resorption**
- *Hydrocephalus ex vacuo*: occur secondary to a **loss of brain volume** from any underlying cause (e.g., infarction, neurodegenerative disease)



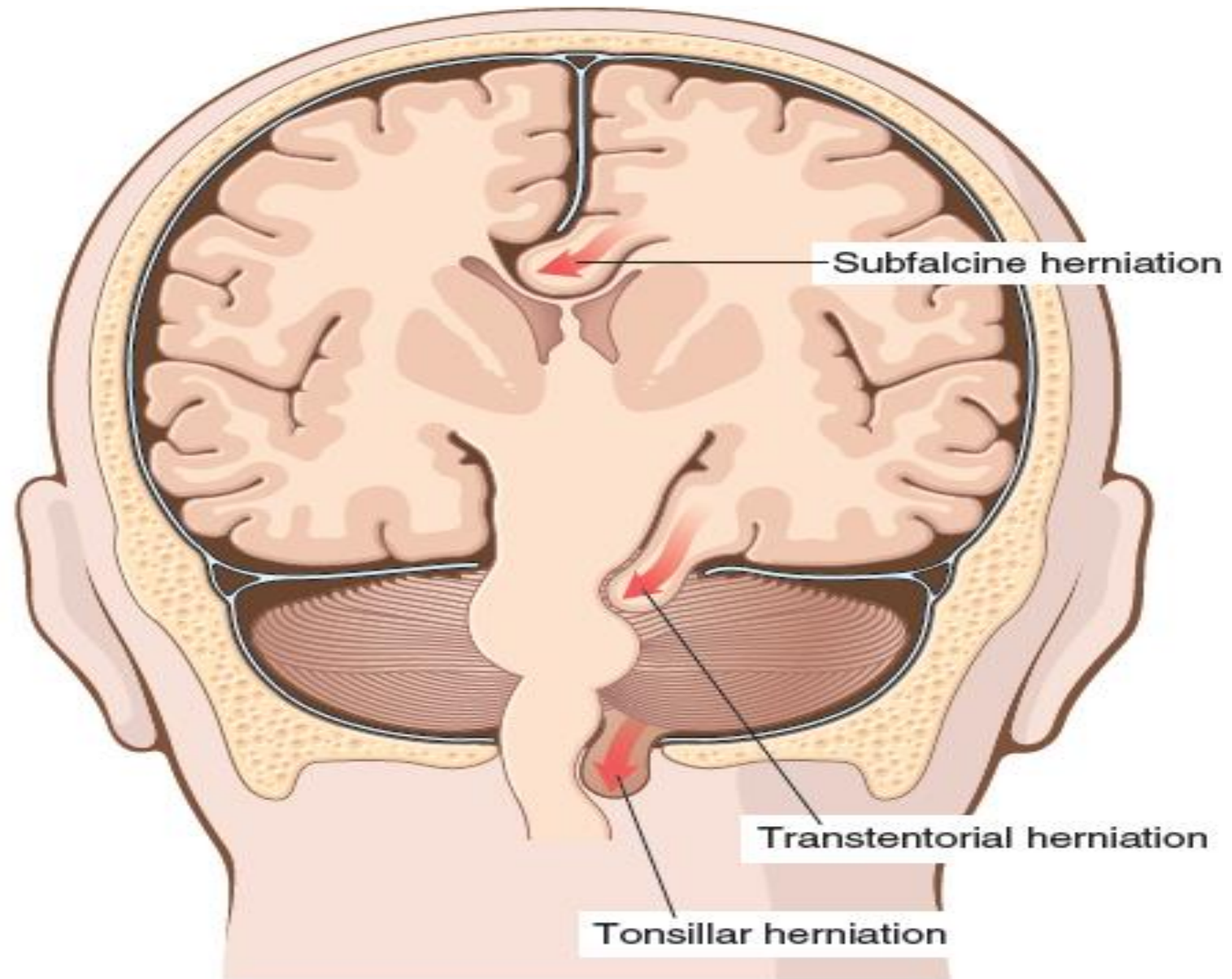
# Herniation

- Herniation is the **displacement** of brain tissue from one compartment to another in response to increased intracranial Pressure
- often leads to compromise of the **blood supply** to compressed tissue, producing infarction, additional swelling, and further herniation.

- *Subfalcine (cingulate) herniation*: occurs when unilateral or asymmetric expansion of a cerebral hemisphere displaces the cingulate gyrus under the edge of the falx.
- This may compress the **anterior cerebral artery**.

- *Transtentorial (uncinate) herniation*: occurs when the medial aspect of the temporal lobe is compressed against the free margin of the tentorium. As the temporal lobe is displaced, the **third cranial nerve** is compromised, resulting in pupillary dilation and impaired ocular movements on the side of the lesion (**"blown pupil"**).
- The **posterior cerebral artery** may also be compressed, resulting in ischemic injury to tissue supplied by that vessel, including the primary visual cortex.
- Progression of transtentorial herniation is often accompanied by linear or flame-shaped hemorrhages in the midbrain and pons, termed **Duret hemorrhages**

- *Tonsillar herniation*: displacement of the cerebellar tonsils through the foramen magnum.
- This type of herniation causes **brain stem compression** and compromises vital respiratory and cardiac centers in the medulla, and is often fatal.



# CEREBROVASCULAR DISEASES

- They are a **major cause of death** in the developed world and are the most prevalent cause of neurologic morbidity

The three main pathogenic mechanisms are

- **(1)** thrombotic occlusion
- **(2)** embolic occlusion
- **(3)** vascular rupture

- Thrombosis and embolism have similar consequences for the brain: loss of oxygen and metabolic substrates, resulting in infarction or **ischemic** injury of regions supplied by the affected vessel.
- Hemorrhage accompanies rupture of vessels and leads to direct **tissue damage** as well as secondary **ischemic** injury.

# Hypoxia, Ischemia, and Infarction

- The brain is a **highly oxygen-dependent** tissue that requires a continual supply of glucose and oxygen from the blood
- it constitutes no more than **2% of body weight**
- the brain receives **15% of the resting cardiac output** and
- is responsible for **20% of total body oxygen consumption**
- Cerebral blood flow normally remains **stable** over a wide range of blood pressure and intracranial pressure because of autoregulation of vascular resistance.

The brain may be deprived of oxygen by two general mechanisms:

- 1) *Functional hypoxia*: low partial pressure of oxygen (e.g., high altitude), impaired oxygen-carrying capacity (e.g., severe anemia, carbon monoxide poisoning), or toxins that interfere with oxygen use (e.g., cyanide poisoning)
- 2) *Ischemia*, either *transient* or *permanent*, due to tissue hypoperfusion, which can be caused by hypotension, vascular obstruction, or both

# *Global Cerebral Ischemia*

- Widespread ischemic-hypoxic injury can occur in the setting of severe systemic hypotension, usually when **systolic** pressures fall below **50 mm Hg**, as in cardiac arrest and shock.
- The **clinical outcome** varies with the severity and duration of the insult

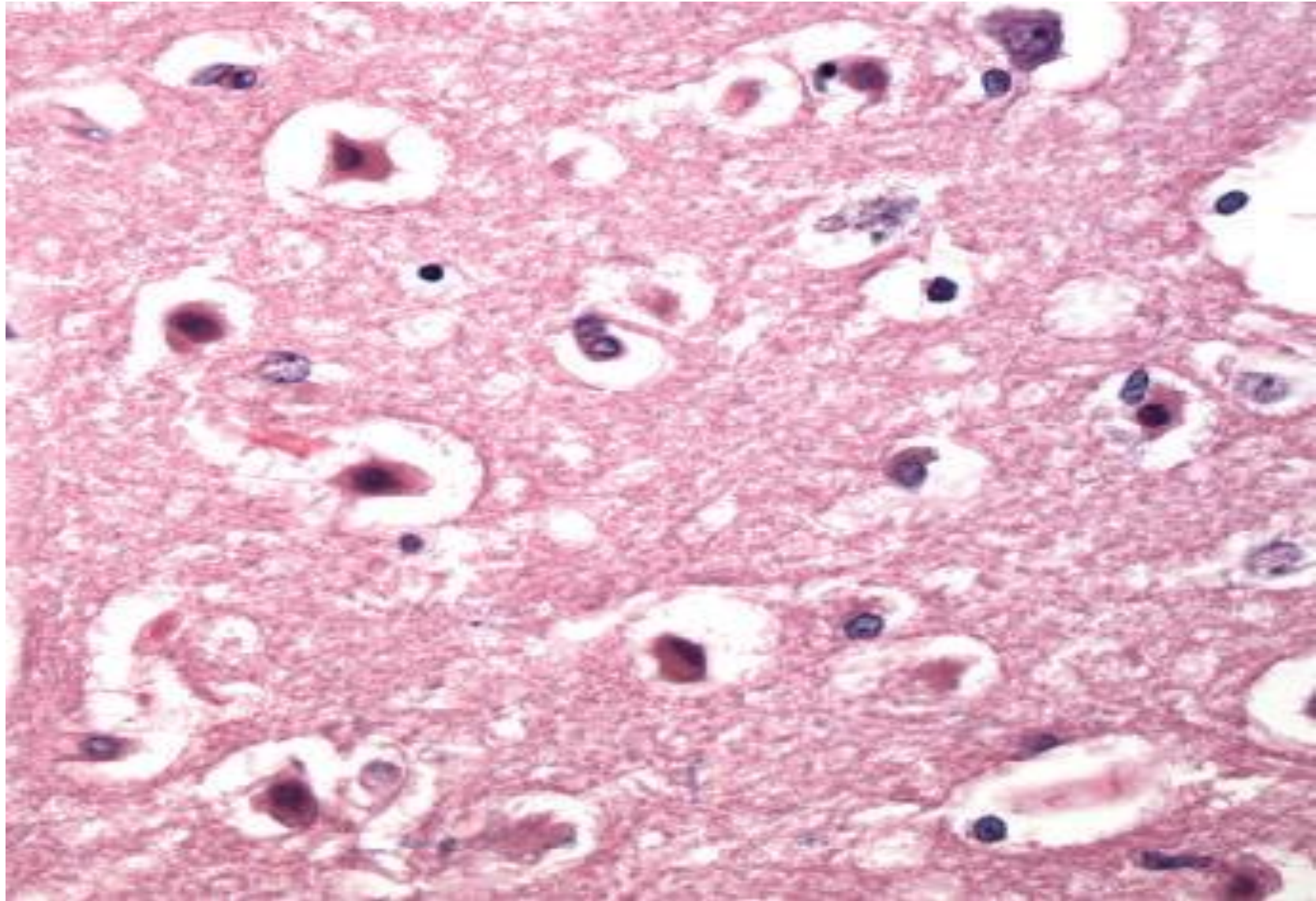
- When the insult is **mild**, there may be only a transient postischemic confusional state, with eventual complete recovery.
- **Neurons** are more susceptible to hypoxic injury than are glial cells, and the most susceptible neurons are the **pyramidal cells** of the hippocampus and neocortex and **Purkinje cells** of the cerebellum

- In **severe global cerebral ischemia**, widespread neuronal death occurs irrespective of regional vulnerability. Patients who survive often remain severely impaired neurologically and in a persistent vegetative state.
- Other patients meet the clinical criteria for so-called “**brain death**,” in which all voluntary and reflex brain and brain stem function is absent, including respiratory drive

# MORPHOLOGY

- **Early changes**, occurring 12 to 24 hours after the insult
- **Subacute changes**, occurring at 24 hours to 2 Weeks
- **Repair**, seen after 2 weeks

- **neuronal injury** becomes evident on routine hematoxylin and eosin (H&E) staining .
- There is shrinkage of the cell body, pyknosis of the nucleus, disappearance of the nucleolus, loss of Nissl substance, and intense eosinophilia of the cytoplasm (“**red neurons**”).



# *Focal Cerebral Ischemia*

- The size, location, and shape of the infarct and the extent of tissue damage that results may be modified by **collateral blood flow**. Specifically, collateral flow through the circle of Willis or can limit damage in some regions
- there is little if any collateral blood flow to structures such as the **thalamus**, **basal ganglia**, and **deep white matter**, which are supplied by deep penetrating vessels.

# *Embolic infarctions*

- **more common** than infarctions due to thrombosis. **Cardiac mural thrombi** are a frequent source of emboli; myocardial dysfunction, valvular disease, and atrial fibrillation are important predisposing factors.
- Thromboemboli also arise in **arteries**, most often from atheromatous plaques in the **carotid arteries** or **aortic arch**.
- Emboli of **venous origin** may cross over to the arterial circulation through a patent foramen ovale and lodge in the brain (**paradoxical embolism**)

- Infarcts can be divided into two broad groups:
- 1- *Nonhemorrhagic infarcts* result from acute vascular occlusions and may evolve into
- 2- *Hemorrhagic or red infarcts* when there is reperfusion of ischemic tissue, either through collaterals or after dissolution of emboli.

- The **macroscopic** appearance of a **nonhemorrhagic infarct** evolves over time.
- **.first 6 hours**, the tissue is unchanged in appearance
- By **48 hours**, the tissue becomes pale, soft, and swollen.
- From **days 2 to 10**, the injured brain turns gelatinous and friable, and the boundary between normal and abnormal tissue becomes more distinct as edema resolves in the adjacent viable tissue.
- From **day 10 to week 3**, the tissue liquefies, eventually leaving a fluid-filled cavity, which gradually expands as dead tissue is resorbed

# Intracranial Hemorrhage

- Primary brain parenchymal hemorrhage
- Subarachnoid hemorrhages most commonly are the result of ruptured aneurysms but also occur with other vascular malformations.
- Subdural or epidural hemorrhages usually are associated with trauma

# *Primary Brain Parenchymal Hemorrhage*

- Hypertensive intraparenchymal hemorrhages typically occur in the **basal ganglia**, **thalamus**, **pons**, and **cerebellum**, with the location and the size of the bleed determining its clinical manifestations.

- Microscopic examination: early lesions consist of **clotted blood** surrounded by edematous brain tissue containing neurons and glia displaying morphologic changes typical of **anoxic injury**.
- Eventually the edema resolves, **pigment- and lipid-laden macrophages** appear, and proliferation of reactive astrocytes becomes visible at the periphery of the lesion.

# *Subarachnoid Hemorrhage and Saccular Aneurysms*

- **The most frequent cause of clinically significant nontraumatic subarachnoid hemorrhage is rupture of a **saccular (berry) aneurysm****
- In about one-third of cases, rupture of a saccular aneurysm occurs at the time of an acute increase in intracranial pressure, such as occurs with straining at **stool** or **sexual orgasm**.
- Blood under arterial pressure is forced into the subarachnoid space, and the patient is stricken with sudden, excruciating headache (known as a **thunderclap headache**, often described as “the worst headache I’ve ever had”) and rapidly loses consciousness

- The aneurysms are **not present at birth** but develop overtime because of underlying defects in the vessel media
- Overall, roughly 1.3% of aneurysms bleed per year, with the probability of rupture increasing with **size**. For example, aneurysms **larger than 1 cm** in diameter have a roughly 50% risk for bleeding per year.

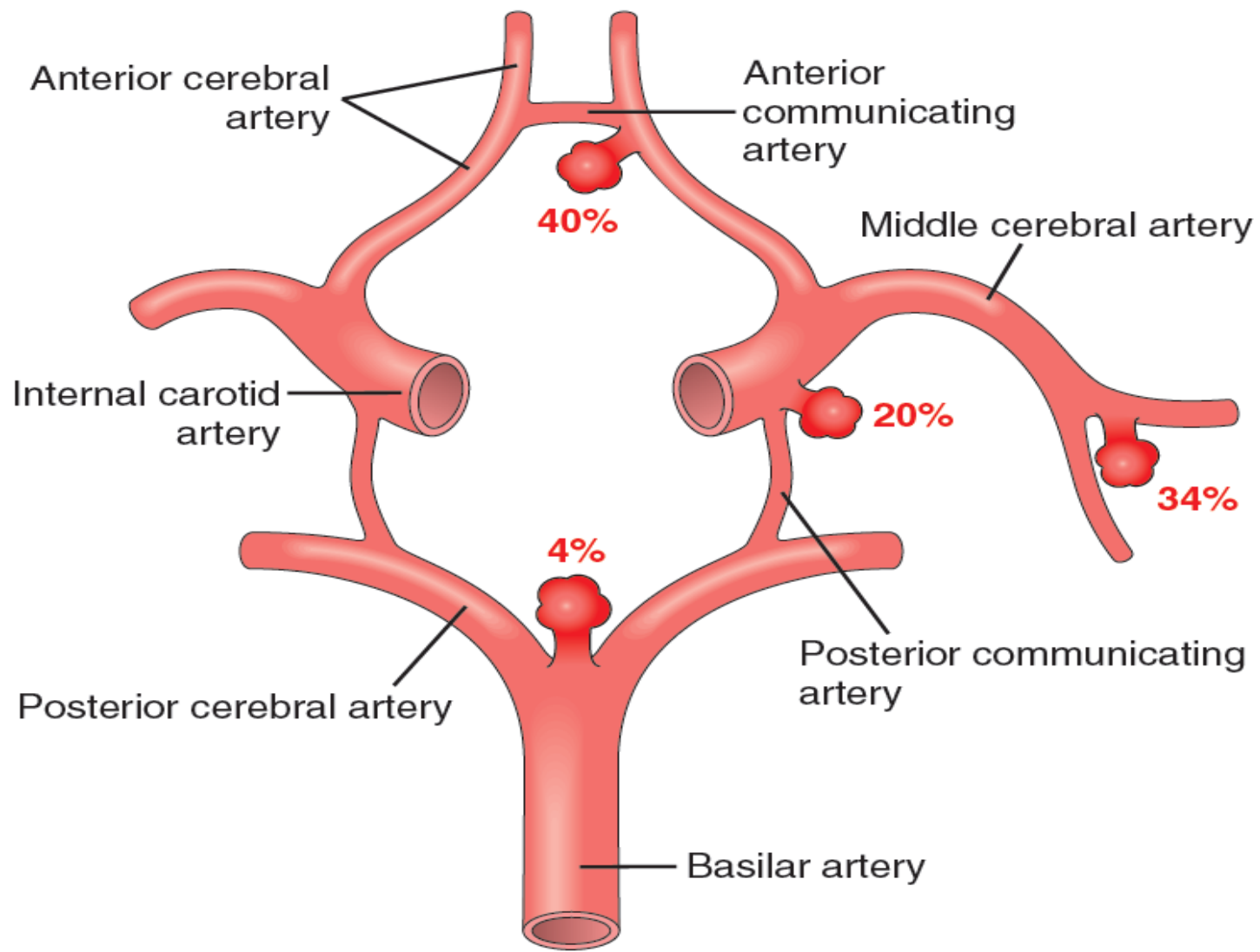
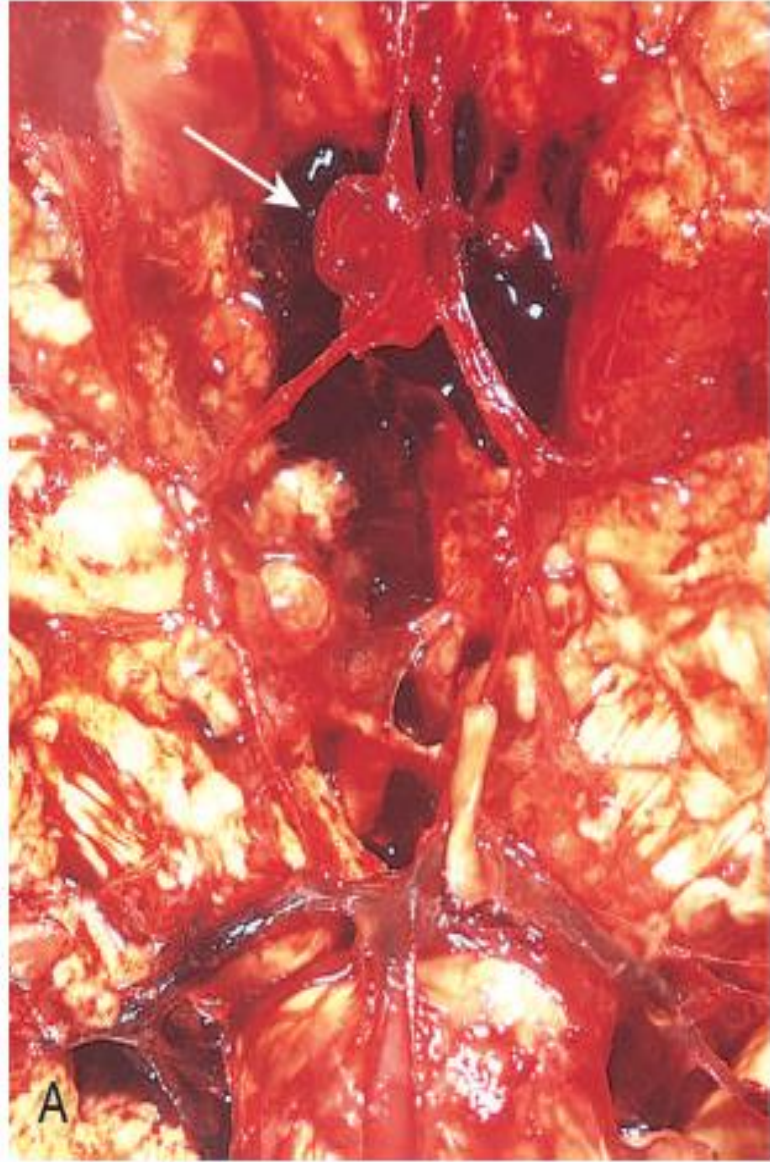


**Fig. 23.9** Common sites of saccular aneurysms.

# Morphology

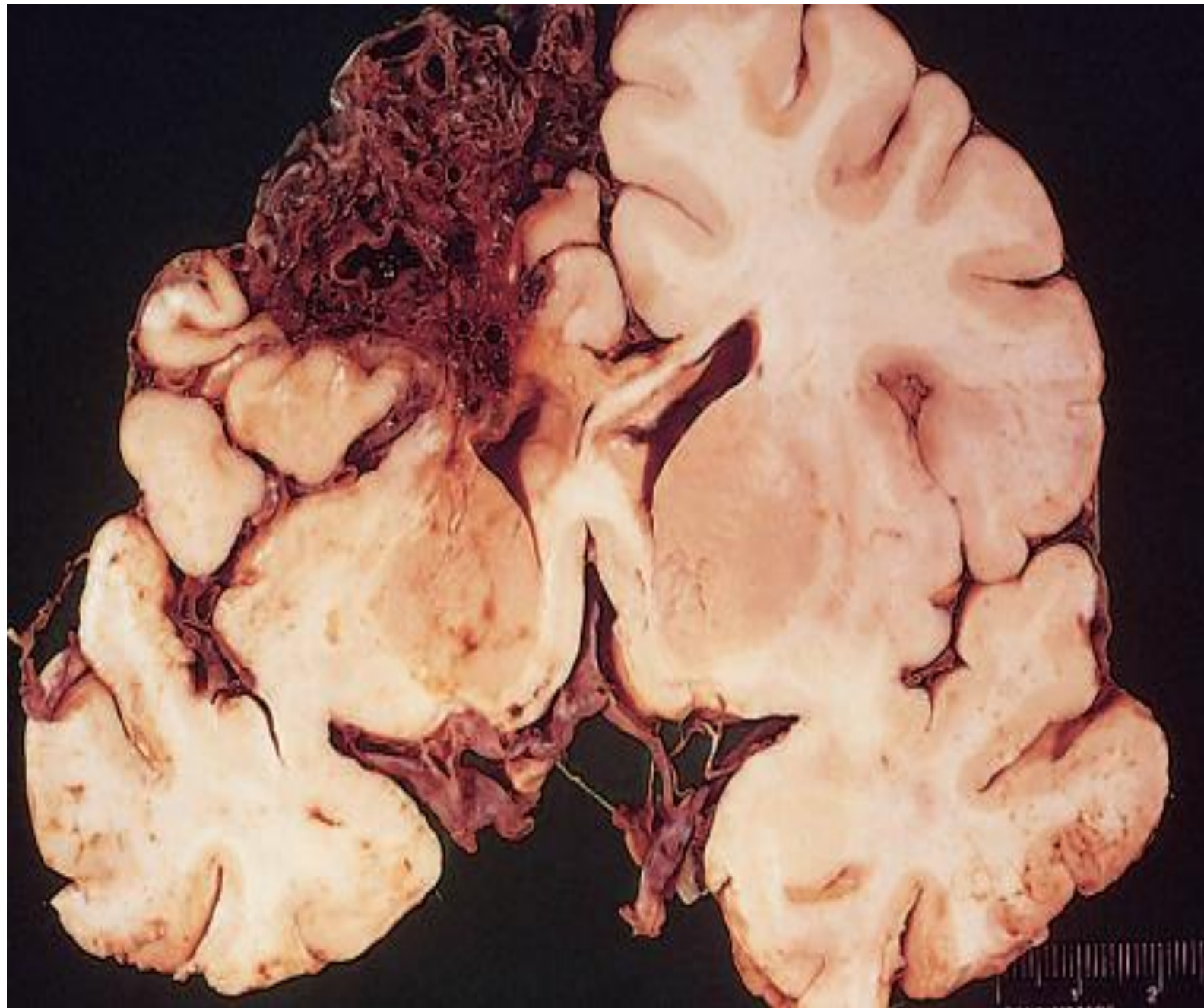
- A saccular aneurysm is a **thin-walled outpouching** of an artery.
- Beyond the neck of the aneurysm, the muscular wall and intimal elastic lamina are absent, such that the aneurysm sac is lined only by **thickened hyalinized intima**.
- The **adventitia** covering the sac is continuous with that of the parent artery.
- Rupture usually occurs at the **apex of the sac**



# *Vascular Malformations*

- **based on the nature of the abnormal vessels:**
  - **arteriovenous malformations (AVMs)**
  - **cavernous malformations**
  - **capillary telangiectasias**
  - **Venous Angiomas**
- AVMs, the **most common** of these, affect **males** twice as frequently as females and most commonly manifest between **10 and 30** years of age with seizures, an intracerebral hemorrhage, or a subarachnoid hemorrhage.

- AVMs: On **gross inspection**, they resemble a tangled network of wormlike vascular channels
- **Microscopic** examination shows enlarged blood vessels separated by **gliotic tissue**, often with evidence of previous hemorrhage.
- Some vessels can be recognized as arteries with duplicated and fragmented internal elastic lamina



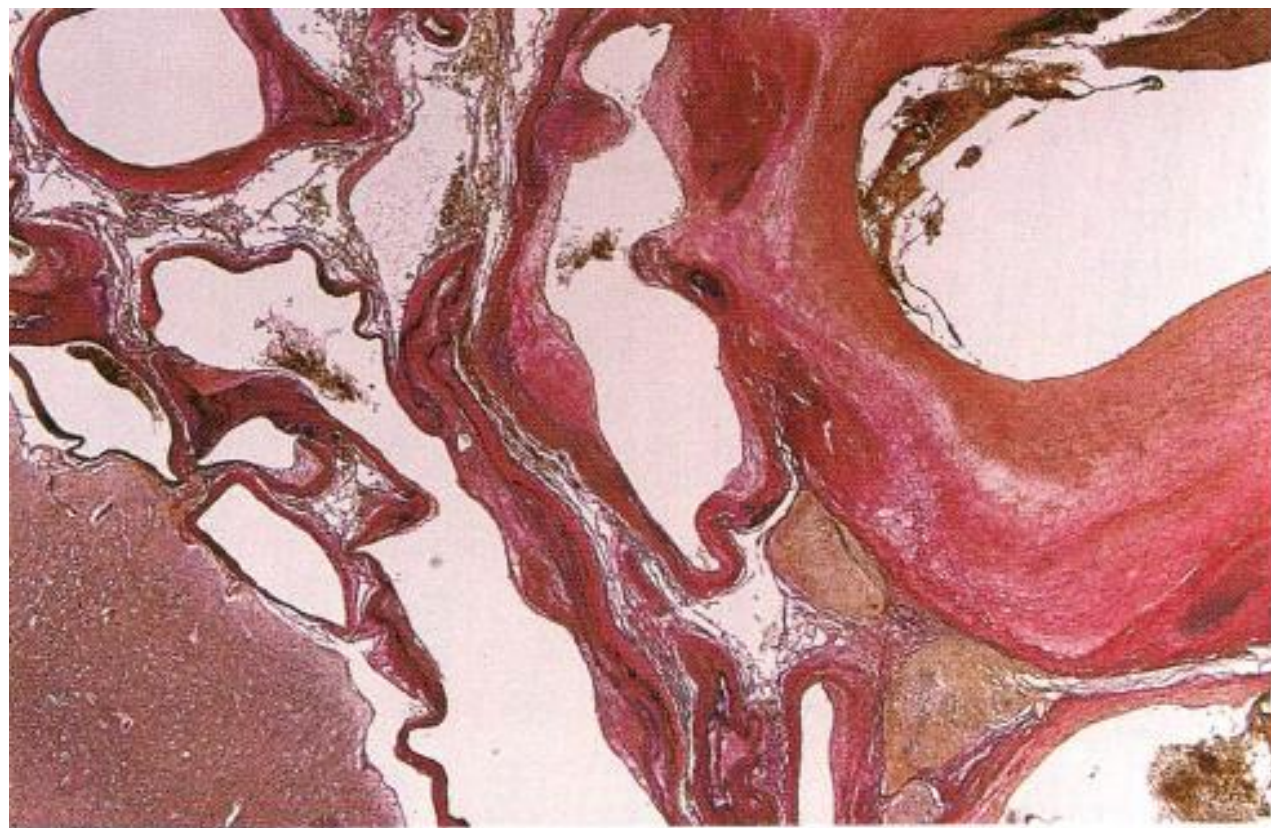


**Fig. 28.7** Arteriovenous malformation. Ectatic, variably muscularized

- **Cavernous malformations** consist of distended, loosely organized vascular channels with thin collagenized walls without intervening nervous tissue.
- They occur most often in the cerebellum, pons, and subcortical regions, and have a low blood flow without significant arteriovenous shunting.
- Foci of **old hemorrhage**, **infarction**, and **calcification** frequently surround the abnormal vessels.

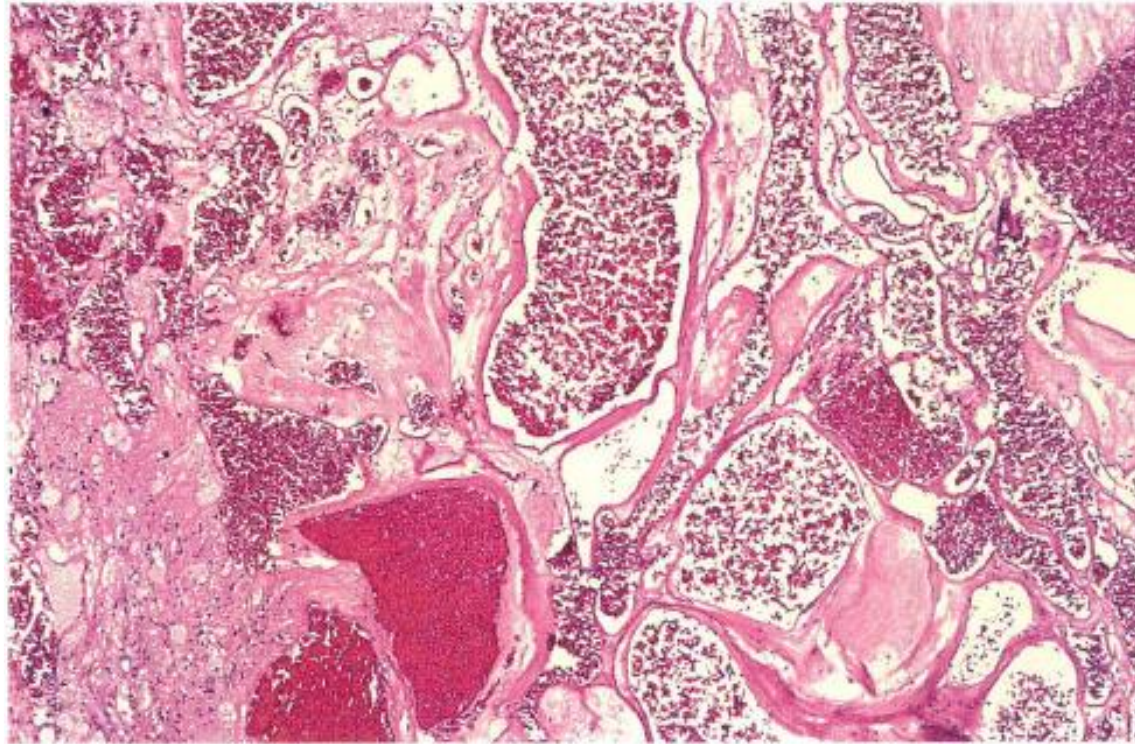


**Fig. 28.6** Cavernous angioma. As illustrated, the cavernous angioma consists of ectatic and fibrous-walled vascular channels devoid of intervening neuroglial tissue. Neighboring brain parenchyma is present

- **Capillary telangiectasias** are microscopic foci of **dilated thin-walled** vascular channels separated by relatively **normal brain parenchyma** that occur most frequently in the **pons**.
- **Venous angiomas** (varices) consist of aggregates of **ectatic venous** channels.
- These latter two types of vascular malformation are unlikely to bleed or to cause symptoms, and most are **incidental findings**

# CENTRAL NERVOUS SYSTEM TRAUMA

- The **severity** and **site** of injury affect the outcome:
  - injury of several cubic centimeters of brain parenchyma may be clinically **silent** (if in the frontal lobe) **severely disabling** (affecting the spinal cord), or **fatal** (involving the brain stem).

# Traumatic Parenchymal Injuries

- **Contusions**: When an object impacts the head, brain injury may occur at the site of impact—a *coup injury*—or opposite the site of impact on the other side of the brain—a *contrecoup injury*. Contusions are common in regions of the brain overlying rough and irregular inner skull surfaces, such as the **orbitofrontal** regions and the **temporal lobe tips**.
- **Laceration**

- *Concussion* describes **reversible altered brain function**, with or without loss of consciousness, from head injury.
- The characteristic transient neurologic dysfunction includes loss of consciousness, temporary respiratory arrest, and loss of reflexes. Neurologic recovery is the norm, although amnesia for the event persists
- **Repeated episodes of concussion** can result in persistent and profound neurologic deficits including cognitive impairment, parkinsonism, and others, and later development of neurodegenerative processes. Initially described in **boxers**. This syndrome is termed **chronic traumatic encephalopathy** and is characterized by accumulation of **tangles in cerebral cortex** and other brain regions

# Traumatic Vascular Injury

- **CNS trauma often directly disrupts vessel walls, leading to hemorrhage**
- Depending on the affected vessel, the hemorrhage may be :
  - epidural*
  - subdural*
  - subarachnoid*
  - intraparenchymal*

# *Epidural Hematoma*

- Dural vessels—especially the **middle meningeal artery**—are vulnerable to traumatic injury.
- In infants, traumatic displacement of the easily deformable skull may tear a vessel, even in the absence of a skull fracture. In children and adults, by contrast, tears involving dural vessels almost always stem from **skull fractures**.
- Once a vessel tears, blood accumulates under arterial producing a hematoma that compresses the brain surface.
- Clinically, patients can be lucid for **several hours** after the traumatic event before neurologic signs appear.

# *Subdural Hematoma*

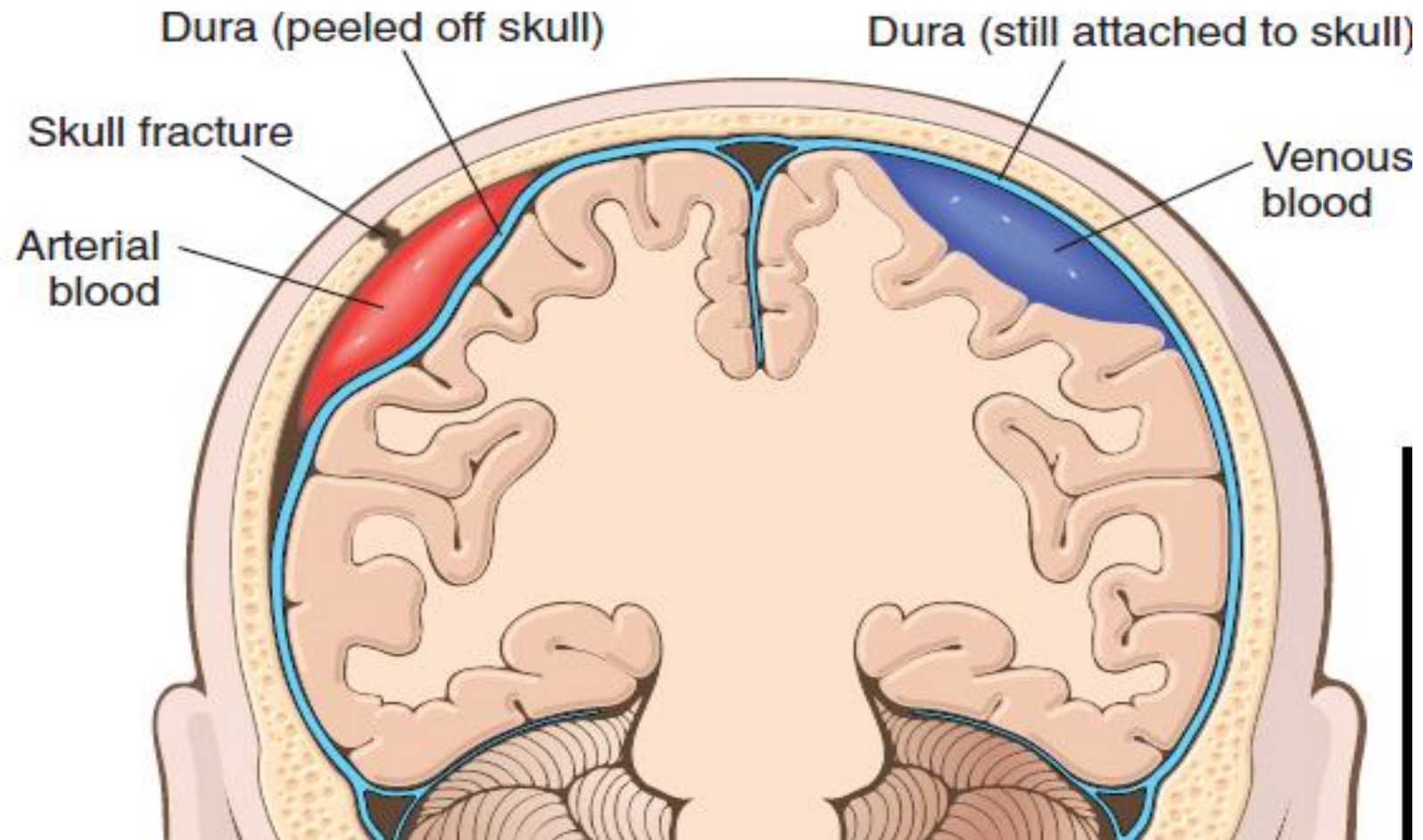
- Rapid movement of the brain during trauma can tear the **bridging veins** that extend from the cerebral hemispheres through the subarachnoid and subdural space to the dural Sinuses
- In patients with brain atrophy, the bridging veins are stretched out and the brain has additional space within which to move, accounting for the higher rate of subdural hematomas in older adults.
- Infants also are susceptible to subdural hematomas because their bridging veins are thin walled.

# *Subdural Hematoma*

- Subdural hematomas typically become manifest within the **first 48** hours after injury.
- They are most common over the lateral aspects of the **cerebral hemispheres** and may be **bilateral**.
- Symptoms are most often nonlocalizing, taking the form of headache, confusion, and slowly progressive neurologic deterioration.

## EPIDURAL HEMATOMA

## SUBDURAL HEMATOMA



- Subdural hematomas organize by **lysis of the clot** (about 1 week), growth of **granulation tissue** from the dural surface into the hematoma (2 weeks), and **fibrosis** (1–3 months)
- Subdural hematomas commonly **rebleed**, presumably from the thin-walled vessels of the granulation tissue, leading to microscopic findings consistent with **hemorrhages of varying ages**



# CONGENITAL MALFORMATIONS AND PERINATAL BRAIN INJURY

- The incidence of CNS malformations, giving rise to mental retardation, cerebral palsy, or neural tube defects, is estimated at **1% to 2%**.
- Malformations of the brain are more common in the setting of **multiple birth defects**.
- During gestation, the **timing** of an injury determines the pattern of malformation, with earlier events typically leading to more severe phenotypes

# *Neural Tube Defects*

- **most frequent** type of CNS malformation
- **Folate deficiency** during the first trimester sharply increases risk through uncertain mechanisms and represents an important opportunity for prevention, as administration of folate to women of child-bearing age reduces the incidence of neural tube defects by up to 70%.

- Neural tube defects include the following:
- spina bifida occulta (asymptomatic bony defects) to spina bifida, a severe malformation consisting of a flat, disorganized segment of spinal cord associated with an overlying meningeal outpouching.
- Myelomeningocele: an extension of CNS tissue through a defect in the vertebral column that occurs most commonly in the lumbosacral region. Patients have motor and sensory deficits in the lower extremities and problems with bowel and bladder control.

- Anencephaly is a malformation of the anterior end of the neural tube that leads to the **absence of the forebrain** and the **top of the skull**.
- encephalocele is a diverticulum of malformed CNS tissue extending through a defect in the cranium. It most often involves the occipital region or the posterior fossa

# Anencephaly MICROENCEPHALY



# Meningoencephaloco



# INFECTIONS OF THE NERVOUS SYSTEM

- Damage to nervous tissue may be the consequence of **direct** injury of neurons or glial cells by the infectious agent or microbial **toxins**, or may be a consequence of the **host immune response**.

- Infectious agents may reach the nervous system through several routes:
  - *Hematogenous spread*: arterial blood supply is the **most common** means of entry
  - *Direct implantation* of microorganisms is almost invariably due to open or penetrating trauma or iatrogenic
  - *Local extension* Sources include air sinuses, most often the mastoid or frontal; infected teeth; cranial or spinal osteomyelitis; and congenital malformations, such as meningocele.
  - *Peripheral nerves* also may serve as paths of entry for a few pathogens—in particular, **viruses** such as rabies and herpes zoster

# Epidural and Subdural Infections

- usually as a consequence of **direct local** spread.
- *Epidural abscesses* arise from an adjacent focus of infection, such as sinusitis or osteomyelitis
- Infections of the skull or air sinuses may also spread to the subdural space, producing *subdural empyema*.
- **arachnoid and subarachnoid spaces usually are unaffected**

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

# Meningitis

- ***Meningitis*** is an inflammatory process involving the leptomeninges within the subarachnoid space
- if the infection spreads into the underlying brain, it is termed ***meningoencephalitis***
- *chemical meningitis*
- *carcinomatous meningitis*

- Infectious meningitis can be broadly divided into
  - acute pyogenic* (usually bacterial)
  - aseptic* (usually viral)
  - chronic* (usually tuberculous, spirochetal, or fungal) subtypes

**Table 23.2 Common Central Nervous System Infections**

| Type of Infection           | Clinical Syndrome         | Common Causative Organisms                                                                                                                                                                   |
|-----------------------------|---------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Bacterial Infections</b> |                           |                                                                                                                                                                                              |
| Meningitis                  | Acute pyogenic meningitis | <i>Escherichia coli</i> or group B streptococci (infants)<br><i>Neisseria meningitidis</i> (young adults)<br><i>Streptococcus pneumoniae</i> or <i>Listeria monocytogenes</i> (older adults) |
|                             | Chronic meningitis        | <i>Mycobacterium tuberculosis</i>                                                                                                                                                            |
| Localized infections        | Abscess                   | Streptococci and staphylococci                                                                                                                                                               |
|                             | Empyema                   | Polymicrobial (staphylococci, anaerobic gram-negative)                                                                                                                                       |

## 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)  
West Nile virus, other  
arboviruses

Arthropod-borne  
encephalitis

Brain stem and  
spinal cord  
syndromes

Rhombencephalitis  
Spinal poliomyelitis

Rabies  
Polio  
West Nile virus

# *Acute Pyogenic Meningitis (Bacterial Meningitis)*

- patients typically show **systemic signs** of infection along with **meningeal irritation** and neurologic impairment, including headache, photophobia, irritability, clouding of consciousness, and neck stiffness.
- Lumbar puncture reveals an **increased pressure**
- examination of the CSF shows abundant **neutrophils** elevated **protein**, and reduced **glucose**.

- In acute meningitis, an **exudate** is evident within the leptomeninges on the surface of the brain. The **meningeal vessels** are engorged and prominent.
- On **microscopic** examination, neutrophils may fill the entire subarachnoid space or, in less severe cases, may be confined to regions adjacent to leptomeningeal blood vessels.
- In untreated meningitis, **Gram stain** reveals varying numbers of the causative organism.
- Severe involvement of leptomeningeal veins (**phlebitis**) may lead to venous occlusion and hemorrhagic infarction of the underlying brain.
- When the meningitis is fulminant, the organisms and the associated inflammatory cells may spread into the substance of the brain (focal **cerebritis**), sometimes leading to the formation of **abscesses**

# *Aseptic Meningitis (Viral Meningitis)*

- *Aseptic meningitis* is a clinical term for acute illness with meningeal signs and symptoms that is believed to be of **viral** origin.
- The clinical course is **less fulminant** than in pyogenic meningitis and is typically self-limiting.
- the CSF often shows **lymphocytosis**, moderate protein elevation, and a normal glucose level, but bacteria cannot be cultured

- There are no distinctive macroscopic findings except for brain **swelling**, which may be seen in only some instances.
- On microscopic examination, there is either no recognizable abnormality or a mild to moderate leptomeningeal lymphocytic infiltrate.

# *Chronic Meningitis*

- Mycobacteria
- spirochetes
- fungi

# Tuberculous Meningitis

- Tuberculous meningitis usually manifests with generalized signs and symptoms of headache, malaise, mental confusion, and vomiting. There is only a **moderate increase in CSF cellularity**, with mononuclear cells or a mixture of polymorphonuclear and mononuclear cells
- protein level is **elevated, often strikingly**
- glucose content typically is **moderately reduced or normal**
- Infection with *Mycobacterium tuberculosis* also may result in a well circumscribed intraparenchymal mass (**tuberculoma**), which may be associated with meningitis.

# Spirochetal Infections

- *Neurosyphilis*, a **tertiary stage** of syphilis, occurs in about 10% of individuals with untreated *Treponema pallidum* Infection with HIV increases the risk
- several patterns of CNS involvement by syphilis:
  - Meningovascular neurosyphilis* is a chronic meningitis
  - Paretic neurosyphilis* stems from **parenchymal involvement** by spirochetes and is associated with neuronal loss and marked proliferation of microglial cells
  - Tabes dorsalis* results from damage to the **sensory nerves in the dorsal roots**. Consequences include impaired joint position sense and ataxia; loss of pain sensation, leading to skin and joint damage (***Charcot joints***)

# Fungal Meningitis

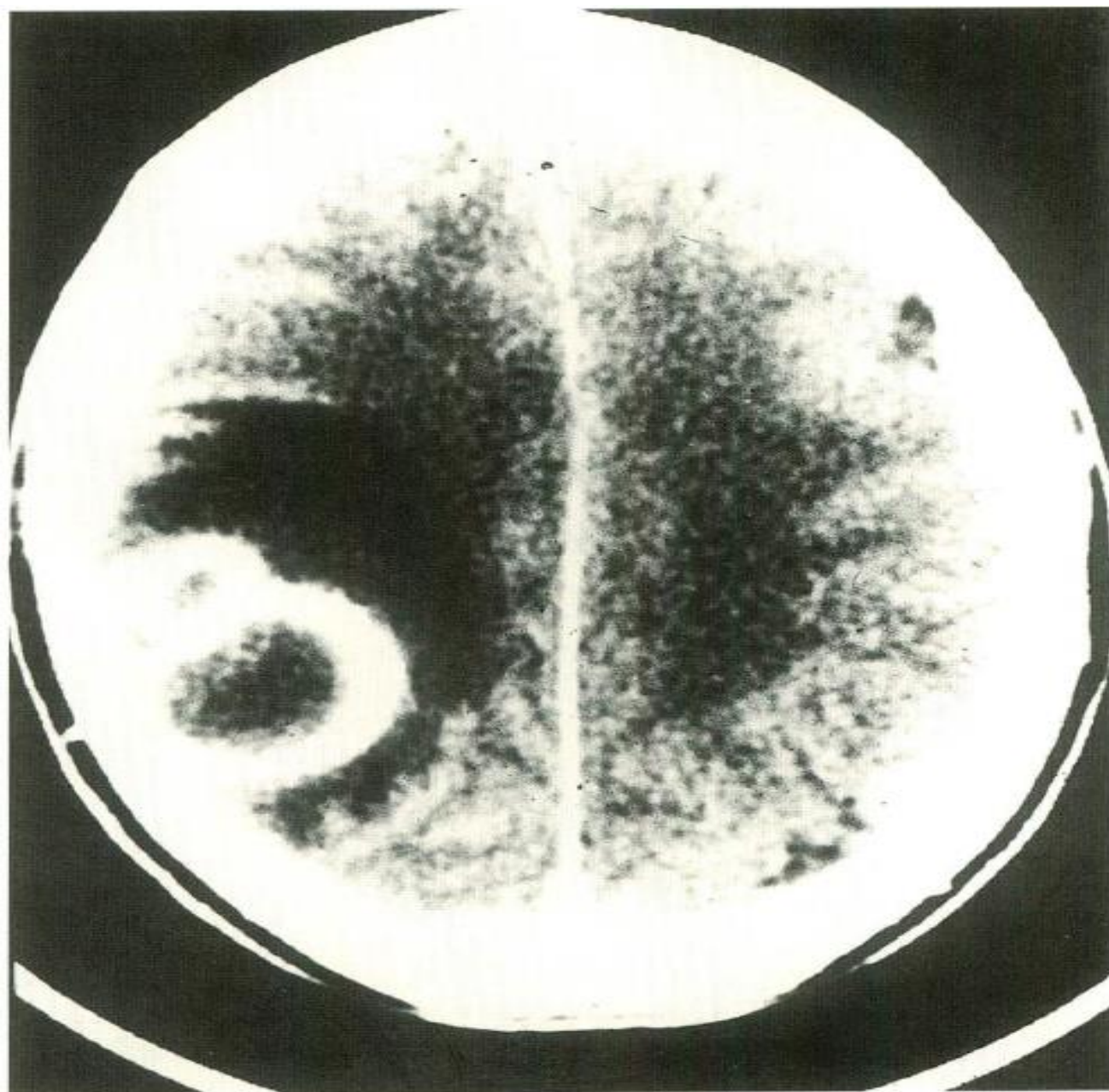
- *Cryptococcus neoformans*: The CSF may have few cells but elevated protein, and the mucoid encapsulated yeasts can be visualized on **India ink** preparations.
- Extension into the brain follows vessels in the Virchow- Robin spaces. As organisms proliferate, these spaces expand, giving rise to a “**soap bubble**”-like appearance

# Parenchymal Infections

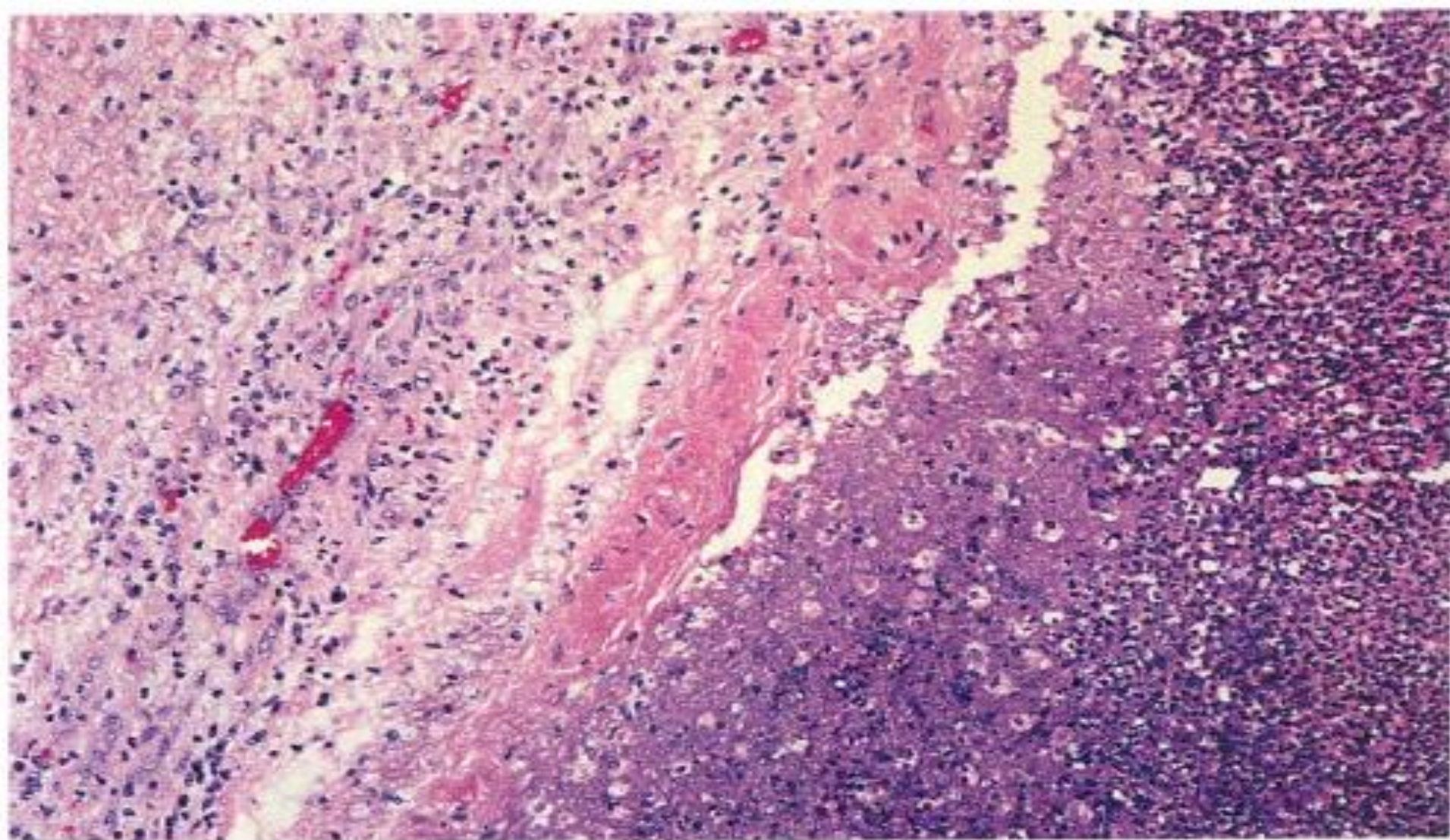
- The entire gamut of infectious pathogens (**viruses to parasites**) can infect the brain, often in characteristic patterns.
- In general, **viral infections are diffuse**, bacterial infections (when not associated with meningitis) are localized, while other organisms produce mixed patterns.
- In immunosuppressed hosts, more **widespread** involvement with any agent is typical.

## -Brain Abscesses

- **Brain abscesses are most often caused by bacterial infections**
  - 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)
- Predisposing conditions :
  - *Acute bacterial endocarditis,*
  - *cyanotic congenital heart disease,*
  - *chronic pulmonary infections, as in bronchiectasis,*

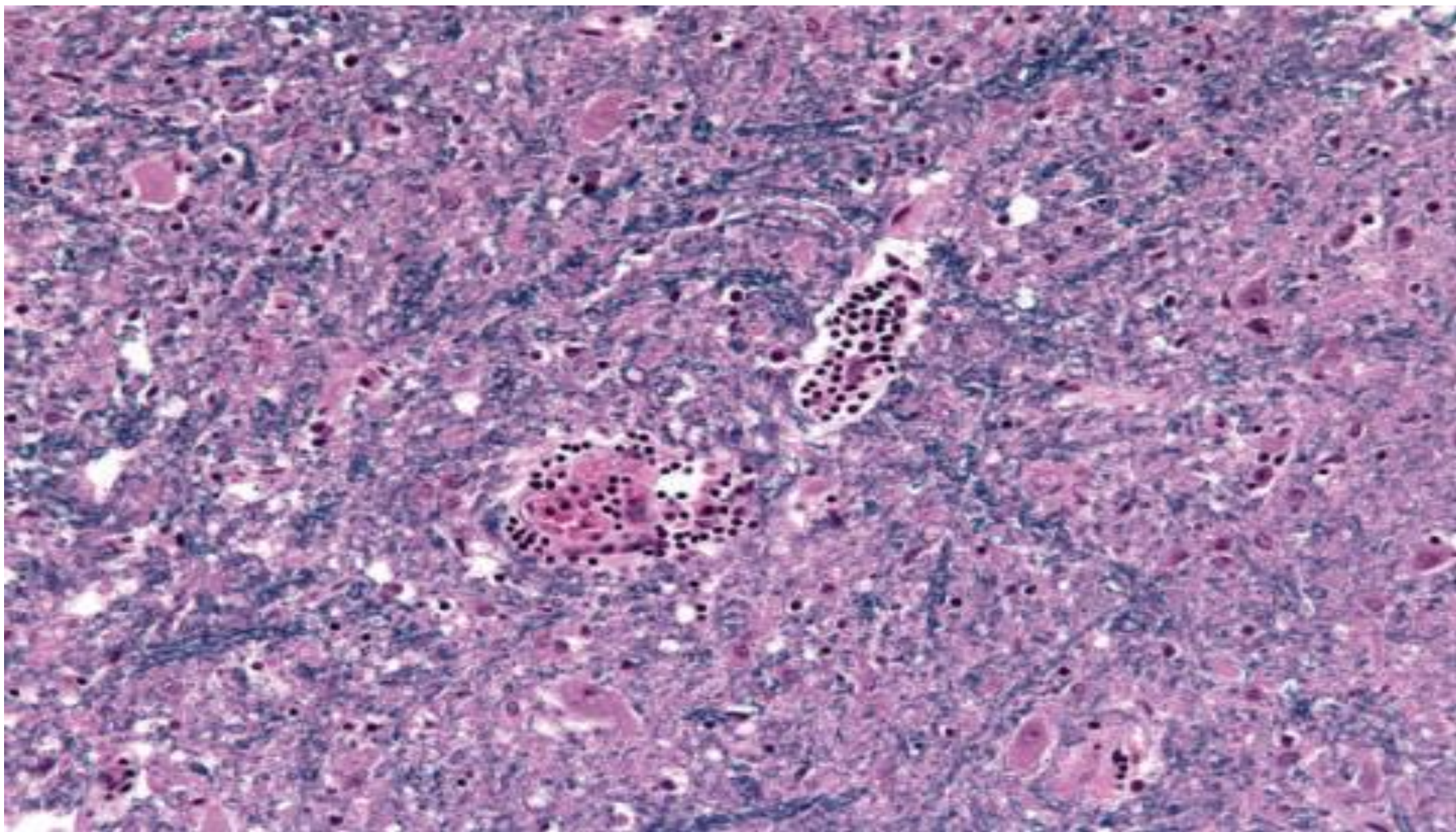


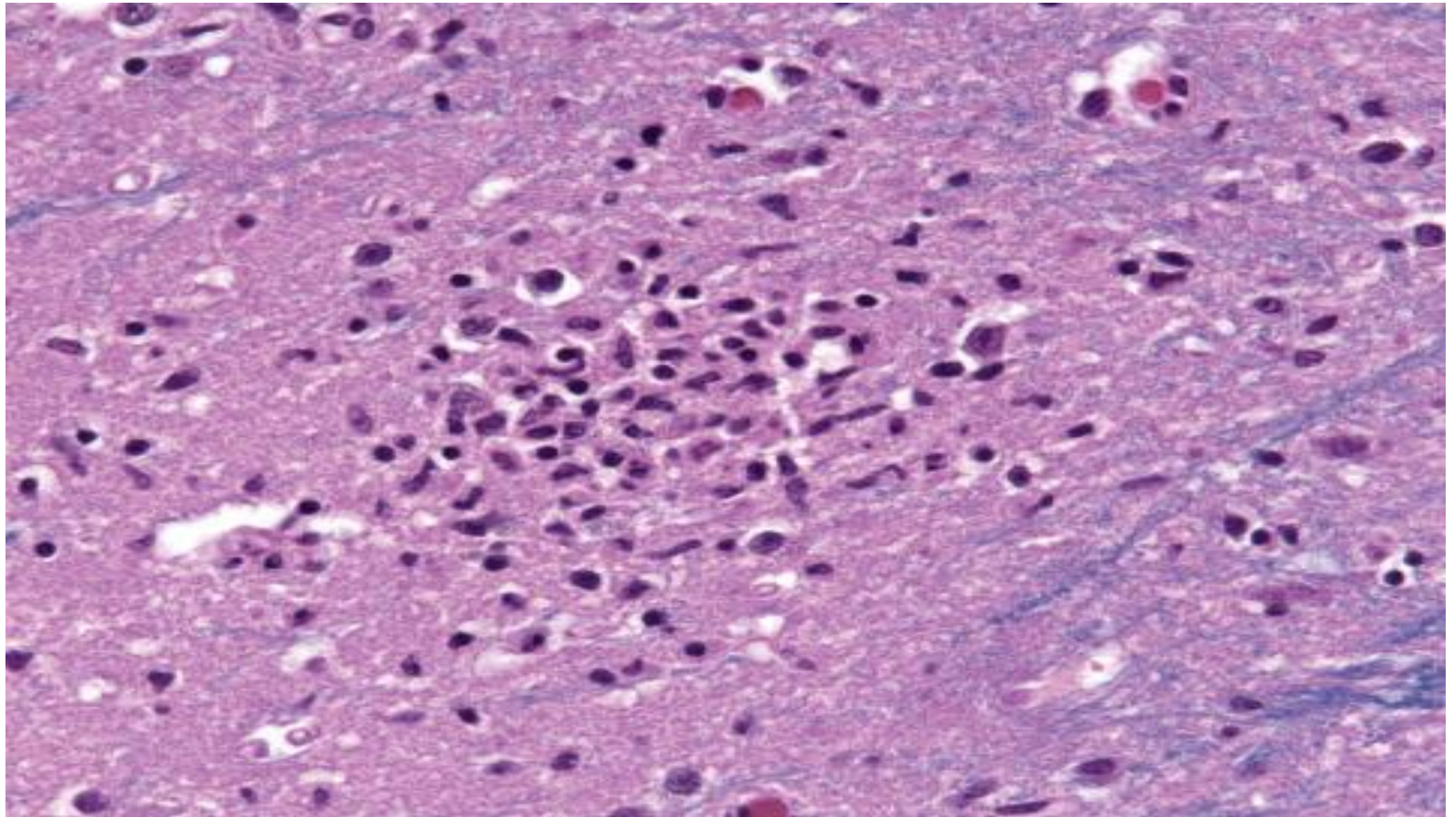
- Abscesses are discrete destructive lesions with central liquefactive **necrosis** surrounded by a rim of vascularized granulation and fibrous tissue.
- Outside the fibrous capsule is a zone of reactive gliosis.
- lumbar puncture has little role in the diagnosis of brain abscess since organisms are more reliably cultured by **draining the abscess directly**



## -*Viral Encephalitis*

- **Viral encephalitis** is a parenchymal infection of the brain that is **almost invariably** associated with meningeal inflammation (meningoencephalitis).
- the most characteristic histologic features are perivascular and parenchymal **mononuclear** cell infiltrates, **microglial nodules**, and neuronophagia. Certain viruses also form characteristic **inclusion** bodies.



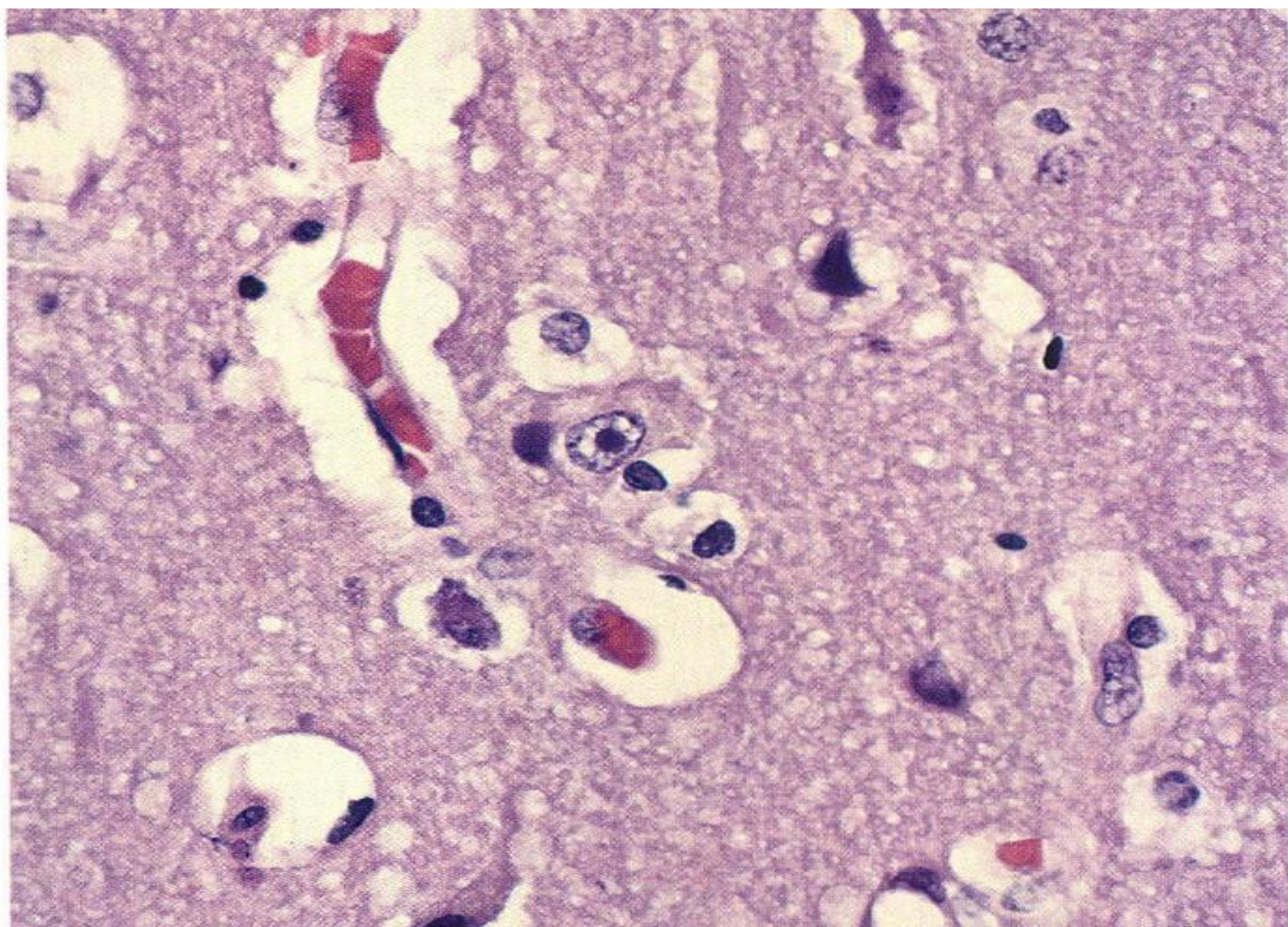


# Herpesviruses

- HSV-1 encephalitis may occur in **any age** group but is most common in children and young adults. It typically
- manifests with alterations in mood, memory, and behavior, reflecting involvement of the frontal and temporal lobes.
- **Recurrent HSV-1** encephalitis is sometimes associated with inherited mutations that interfere with **Toll-like receptor**
- signaling (specifically that of **TLR-3**), which has an important role in anti-viral defense

- HSV-2 also affects the nervous system, usually in the form of meningitis in adults.
- Disseminated severe encephalitis occurs in many neonates born by vaginal delivery to women with active primary HSV genital infections.

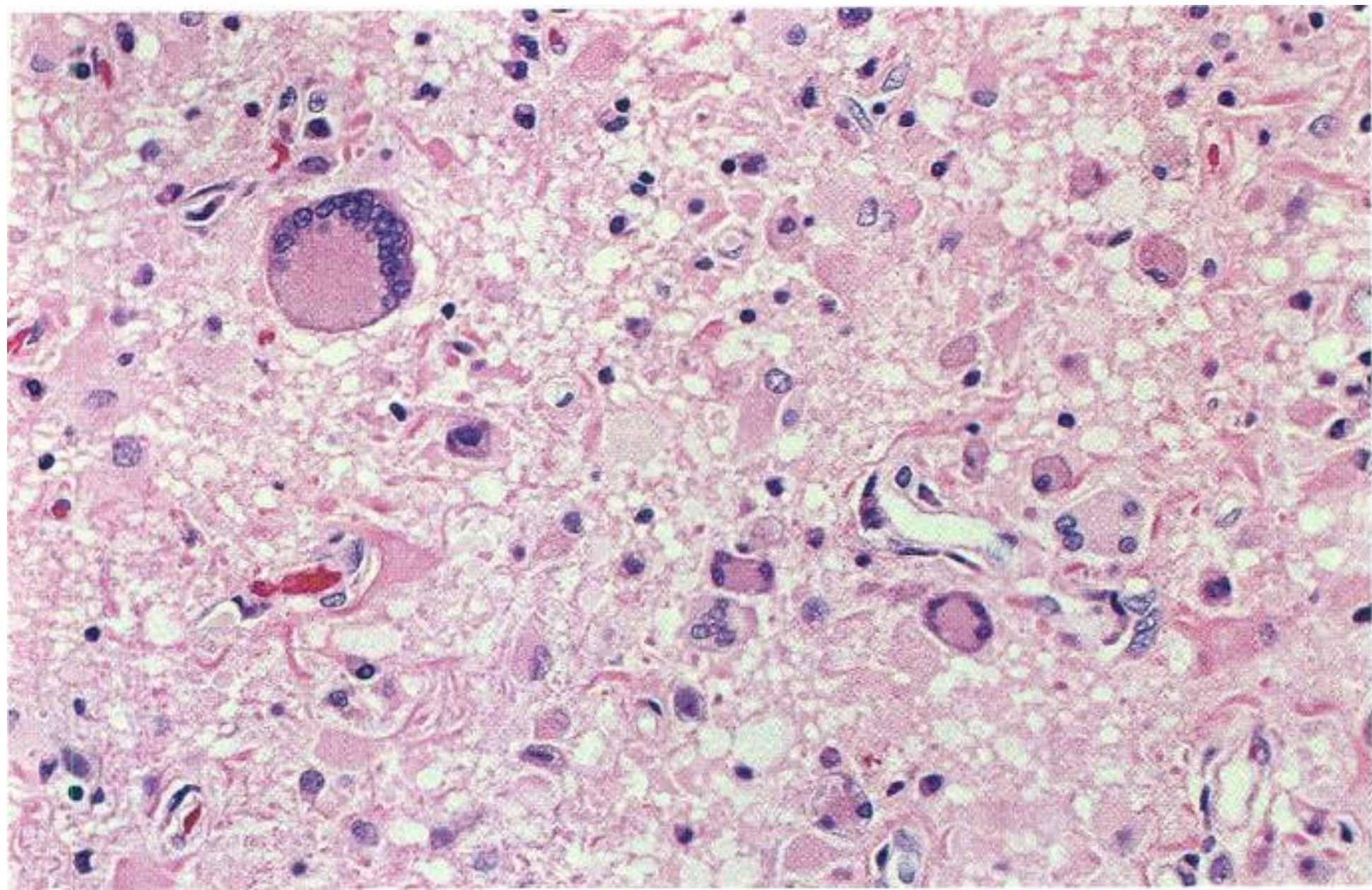
- The infection is necrotizing and often hemorrhagic in severely affected regions.
- Perivascular inflammatory infiltrates usually are present, and large eosinophilic intranuclear viral inclusions (**Cowdry type A bodies**) can be found in both neurons and glial cells.

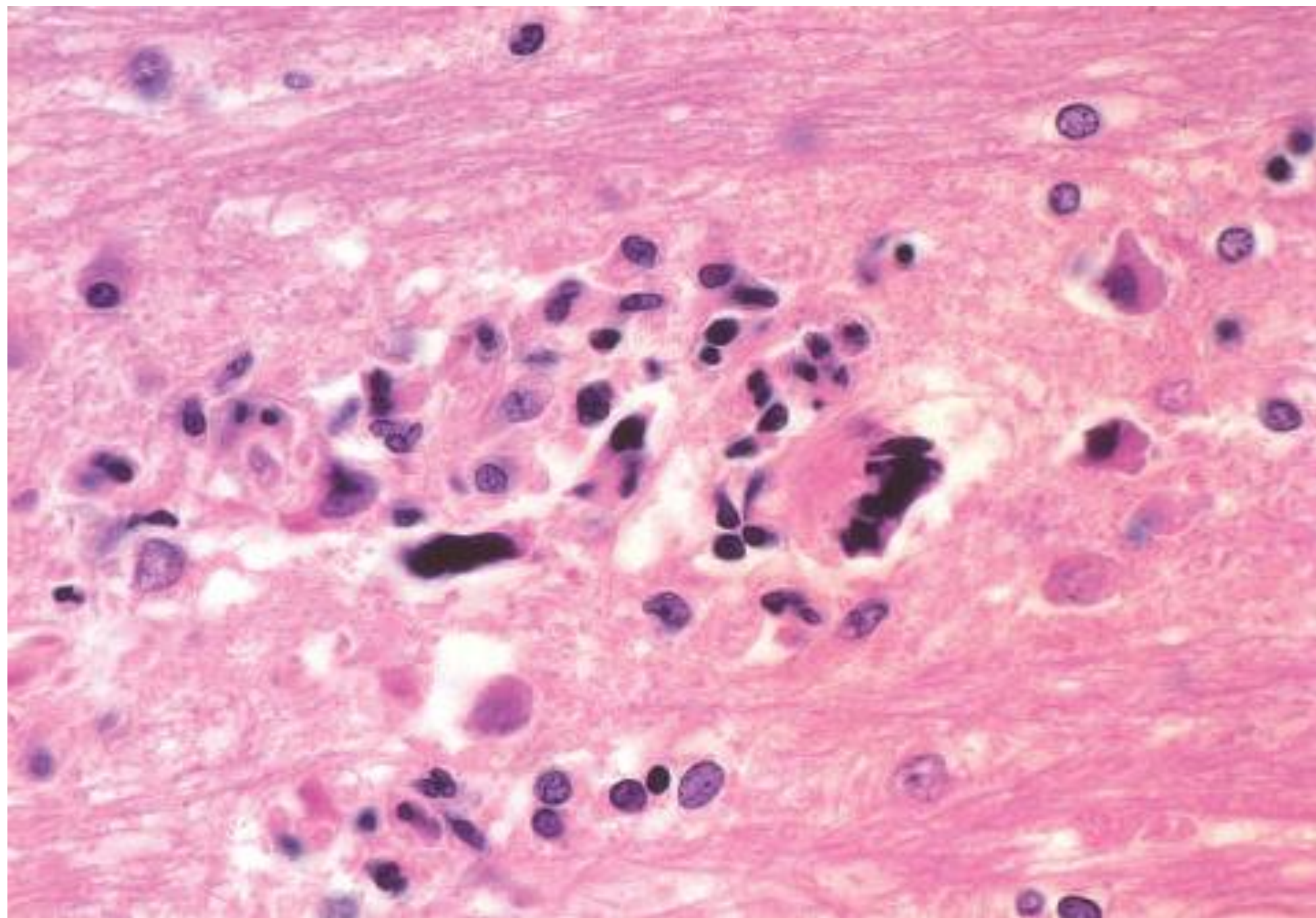


- **CMV** infects the nervous system in fetuses and immunosuppressed individuals. All cells within the CNS (neurons, glial cells, ependyma, and endothelium) are susceptible to infection.
- **Intrauterine infection** causes periventricular necrosis, followed later by **microcephaly** with periventricular calcification.
- Lesions can be hemorrhagic and contain typical **viral inclusion–bearing** cells.

# Human Immunodeficiency Virus

- HIV encephalitis is a chronic inflammatory process with widely distributed **microglial nodules**, sometimes with associated foci of tissue necrosis and reactive gliosis
- An important component of the microglial nodule are macrophage-derived **multinucleate cells**
- **HIV** is present in CD4+ mononuclear and multinucleate macrophages and microglia

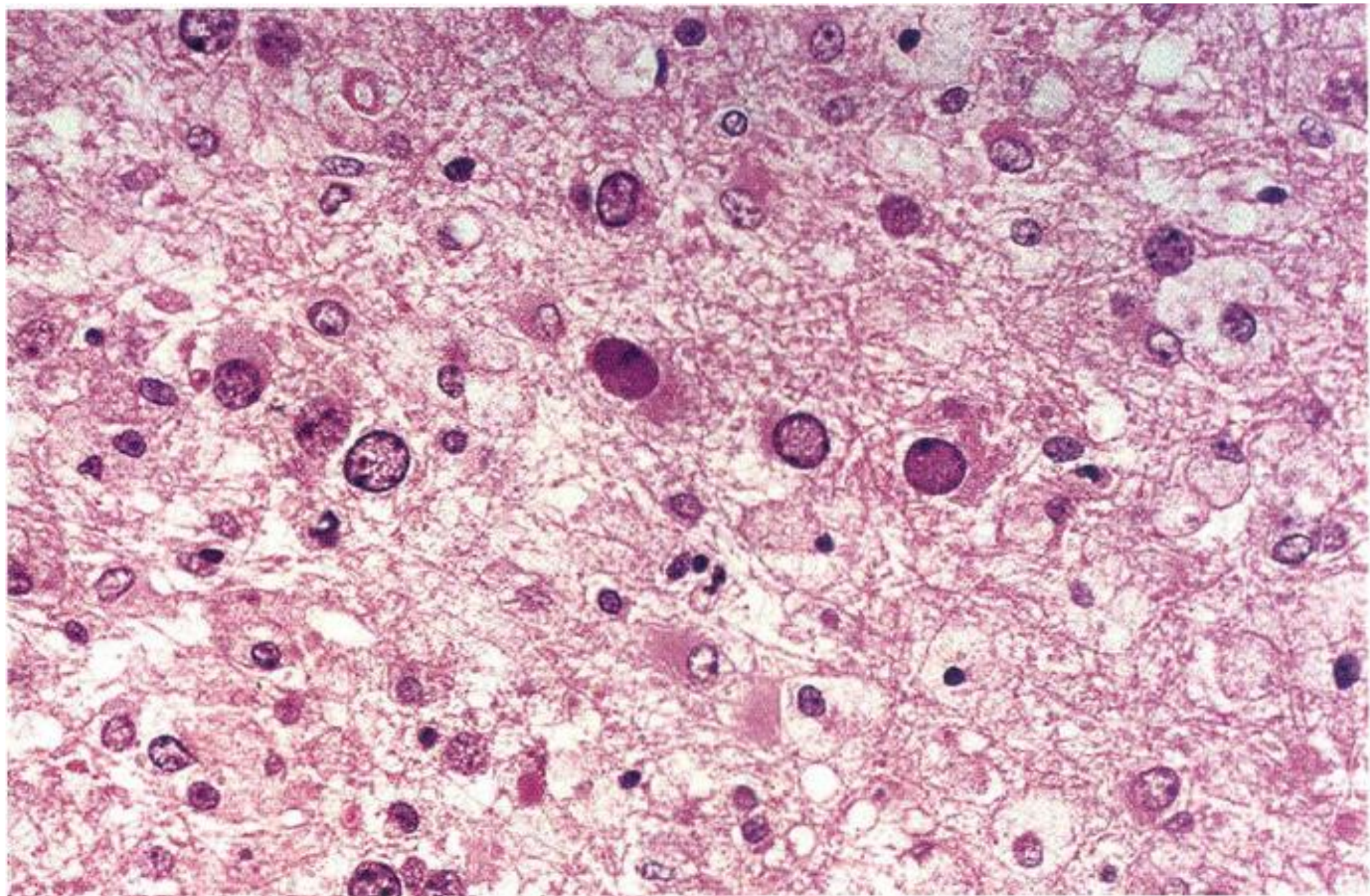


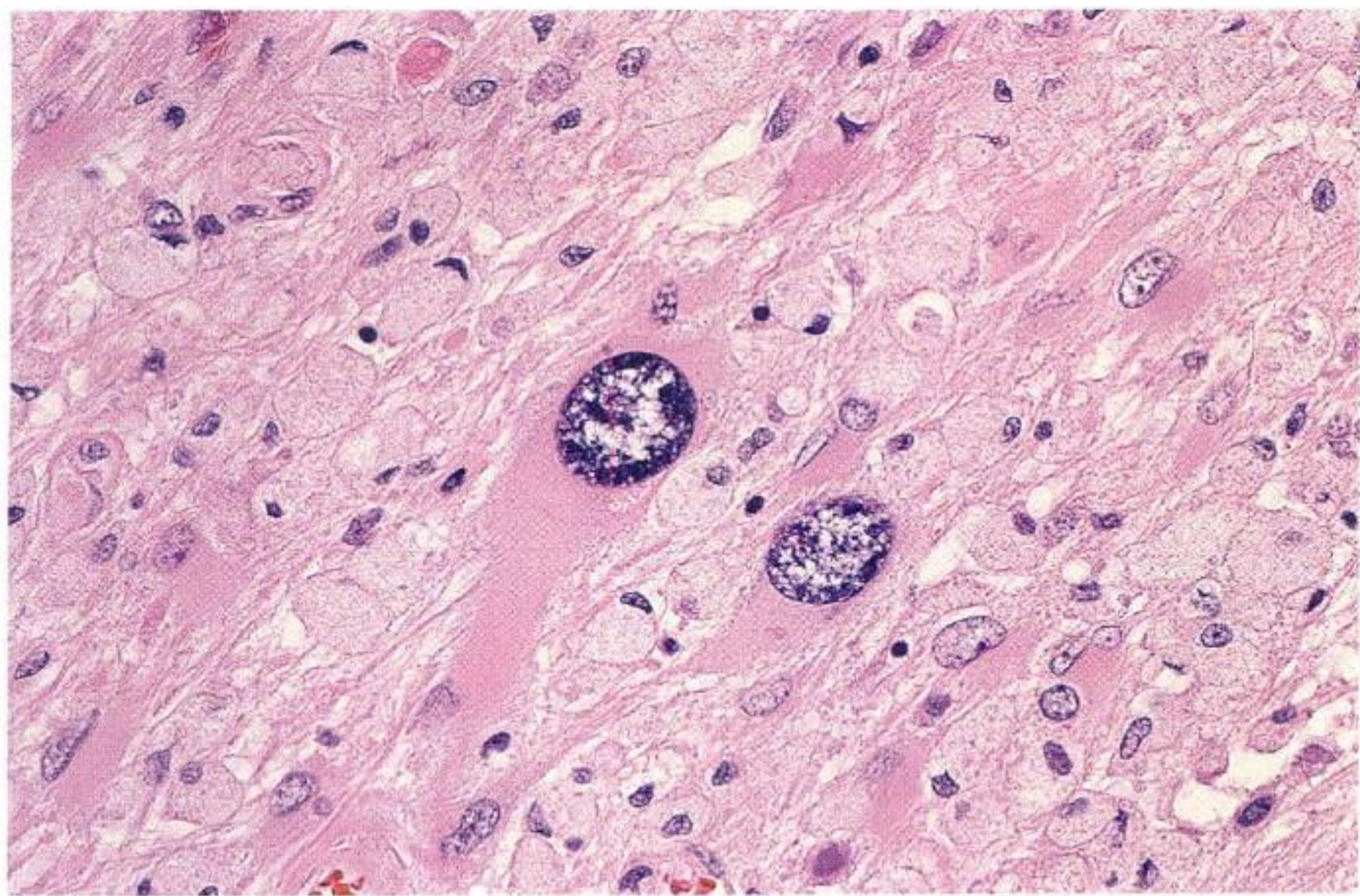


# Polyomavirus and Progressive Multifocal Leukoencephalopathy

- Progressive multifocal leukoencephalopathy (PML) is caused by JC virus, a polyomavirus, which preferentially infects oligodendrocytes, resulting in demyelination as these cells are injured and then die
- it is believed that PML results from virus reactivation, as the disease is restricted to immunosuppressed individuals.

- The lesions are patchy, irregular, ill-defined areas of white matter destruction that enlarge as the disease progresses.
- Each lesion is an area of demyelination, in the center of which are scattered **lipid-laden macrophages** and a reduced number of axons.
- At the edges of the lesion are greatly **enlarged oligodendrocyte nuclei** whose chromatin is replaced by glassy-appearing amphophilic viral **inclusions**.
- The virus also infects **astrocytes**, leading to bizarre giant forms with irregular, hyperchromatic, sometimes multiple nuclei that can be mistaken for a tumor





# *Fungal Encephalitis*

- Fungal infections usually produce parenchymal granulomas or abscesses, often associated with meningitis. The most common fungal infections:
  - *Candida albicans* usually produces multiple microabscesses, with or without granuloma formation
  - *Mucormycosis*: typically presents as an infection of the nasal cavity or sinuses in a diabetic patient with ketoacidosis. It may spread to the brain through vascular invasion or by direct extension through the cribriform plate
  - *Aspergillus fumigatus* tends to cause a distinctive pattern of widespread septic hemorrhagic infarctions because of its marked **predilection for blood vessel wall** invasion with subsequent thrombosis.

