Cerebrovascular disease

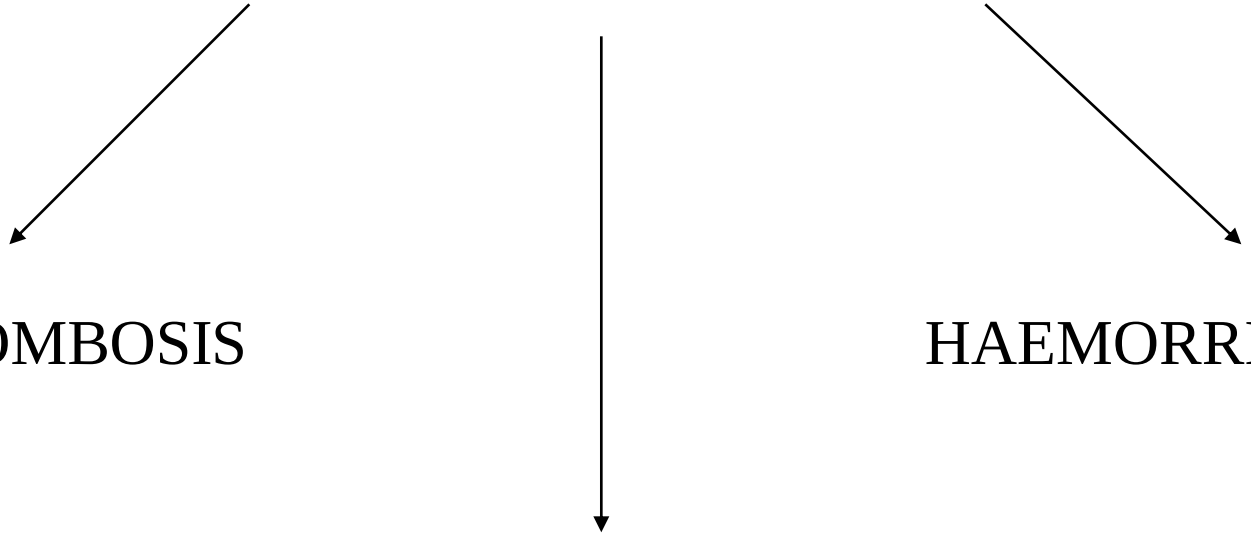
Prof. Janaki Hewavisenthi
Faculty of Medicine
University of Kelaniya

Cererbrovascular disease

- Denotes any abnormality of the brain caused by a pathological process of the blood vessels.

- STROKE
  - Clinical term
  - Denotes a more acute event.

CEREBROVASCULAR DISEASE (Clinical)



CEREBROVASCULAR DISEASE (Pathophysiological basis)

Due to impairment of blood supply and O2

Hypoxia

Ischaemia

Infarction

Haemorrhage resulting from rupture of CNS vessels

Aneurysms

Arteriovenous malformations

Hypertensive vascular disease leads to a combination of both

Cerebral circulation

- Brain accounts for 1 - 2% of the total body weight, but receives 15% of the O_2 concentration
- Cerebral blood flow – 50ml/mt for each 100gm of tissue
- Considerable variation between white and grey matter
- Remains constant over a wide range of blood pressures – autoregulation.

Impairment of O_2 supply - Hypoxia

- Low partial pressure of O_2 – (Hypoxic)
- Imparied O_2 carrying capacity – (Anaemic)
- Inhibition of O_2 use by tissue - (Cytotoxic)
- Ischaemia – interruption of blood flow
  - Transient
  - Permanent

Ischaemia

- Modifying factors
  - Collateral circulation
  - Duration
  - Magnititude
  - Rapidity of the decrease in blood supply
- Two types of ischaemic injury
  - Global ischaemia
  - Focal ischaemia

Global cerebral ischaemia Diffuse hypoxic / ischaemic encephalopathy

- Varies with the severity of the insult
- Mild insult only a transient post ischaemic confusional state may occur – but some times irreversible damage)
- With more severe insult – widespread neuronal injury irrespective of **selective vulnerability**

  Patients who survive are severely impaired neurologically and are deeply comatose (vegetative state)

Global ischaemia

- Selective vulnerability – This is the hierarchy of CNS cells that show preferential susceptibility of hypoxia
  - Eg: Neurons are more susceptible than glial cells
- Based on
  - The regional cerebral blood flow
  - Metabolic requirements.

Global ischaemia - Morphology

- **MACROSCOPY**
- Swollen
- Gyri widened
- Sulci narrowed.
- Cut surface reveals poor demarcation between grey and white matter

Global ischaemia - microscopy

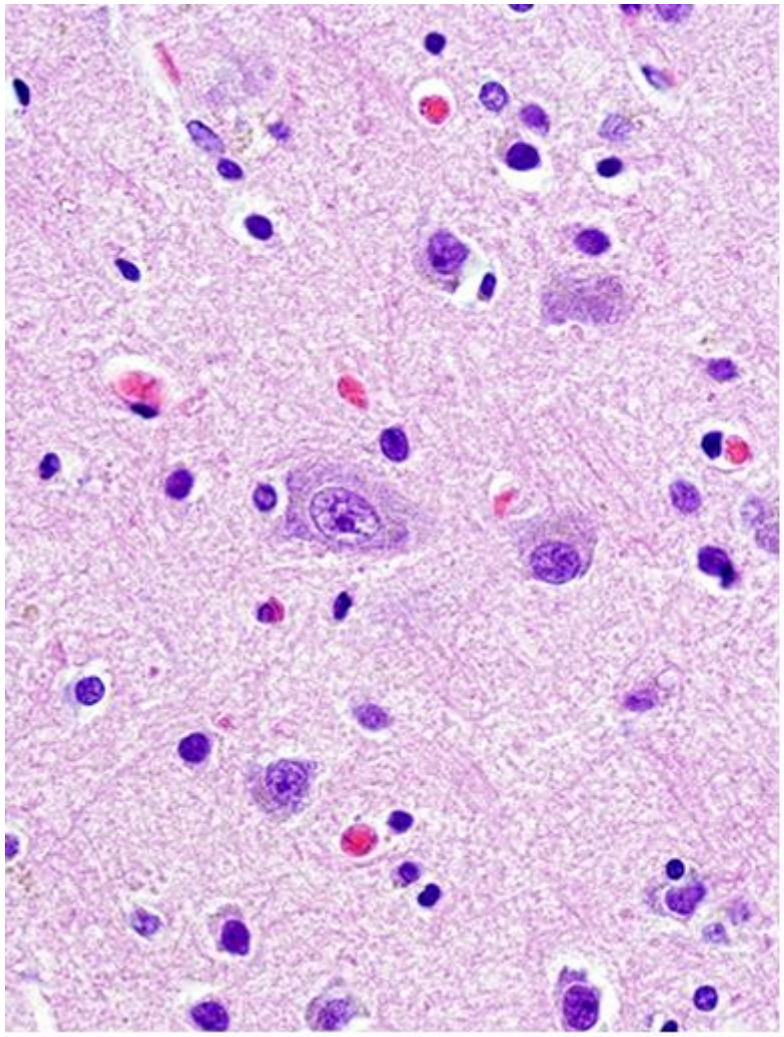
- Early (12 – 24hrs)
  - Acute neuronal cell change (Red neurones)
  - Microvacuolization and eosinophilia of the cytoplasm.
  - Neurones most susceptible in global ischaemia include pyramidal cells of the hippocampus, purkinje cells of the cerebellum and pyramidal neurones in the neocortex
- Subacute (24hrs – 2/52)
  - Necrosis of tissue
  - Influx of macrophages
  - Vascular proliferation
  - Gliosis

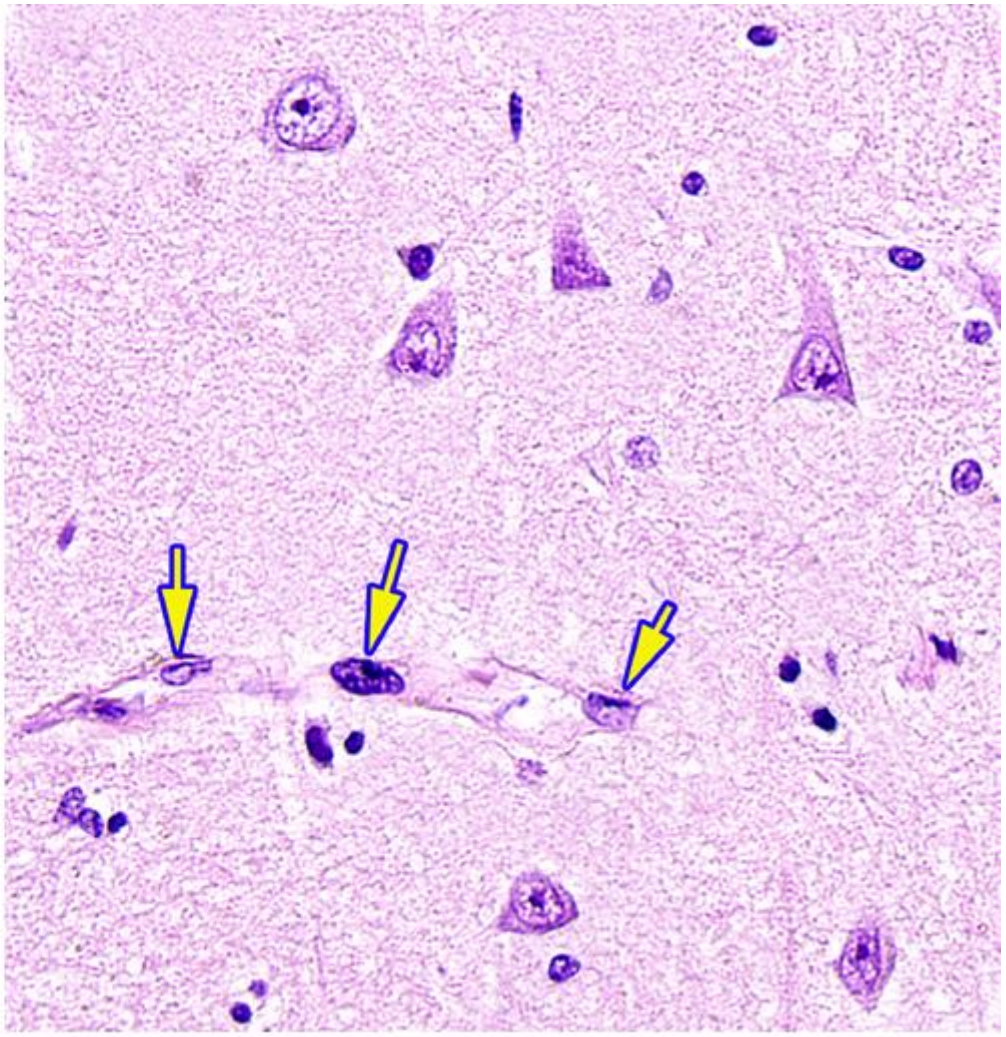
Global ischaemia - microscopy

- Repair (> 2/52)
  - Removal of necrotic tissue
  - Loss of normally organized CNS structures and gliosis which produce and uneven destruction of the neocortex – pseudolaminar necrosis

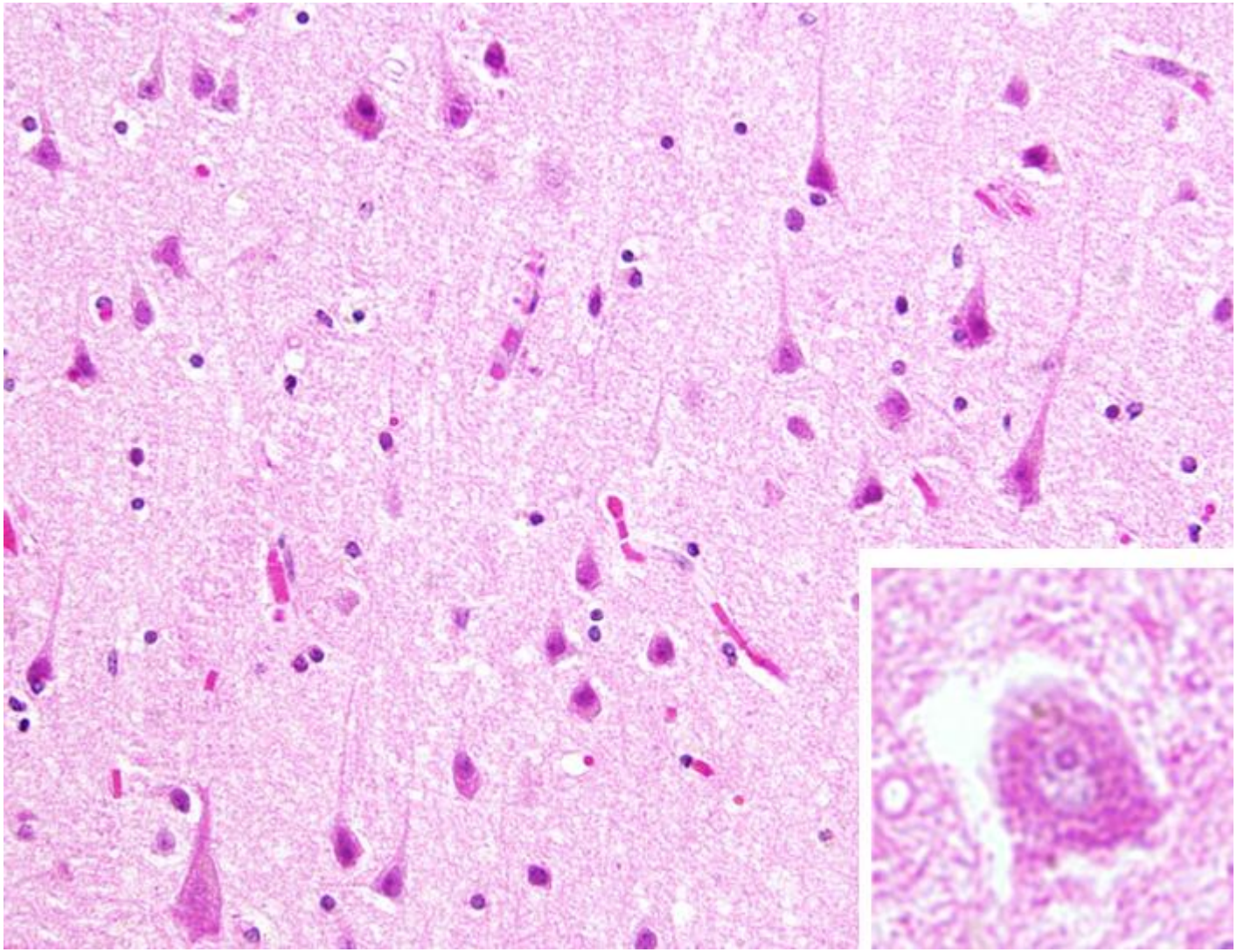
Normal brain tissue

Patient dying within 12 hours of cerebral ischaemia

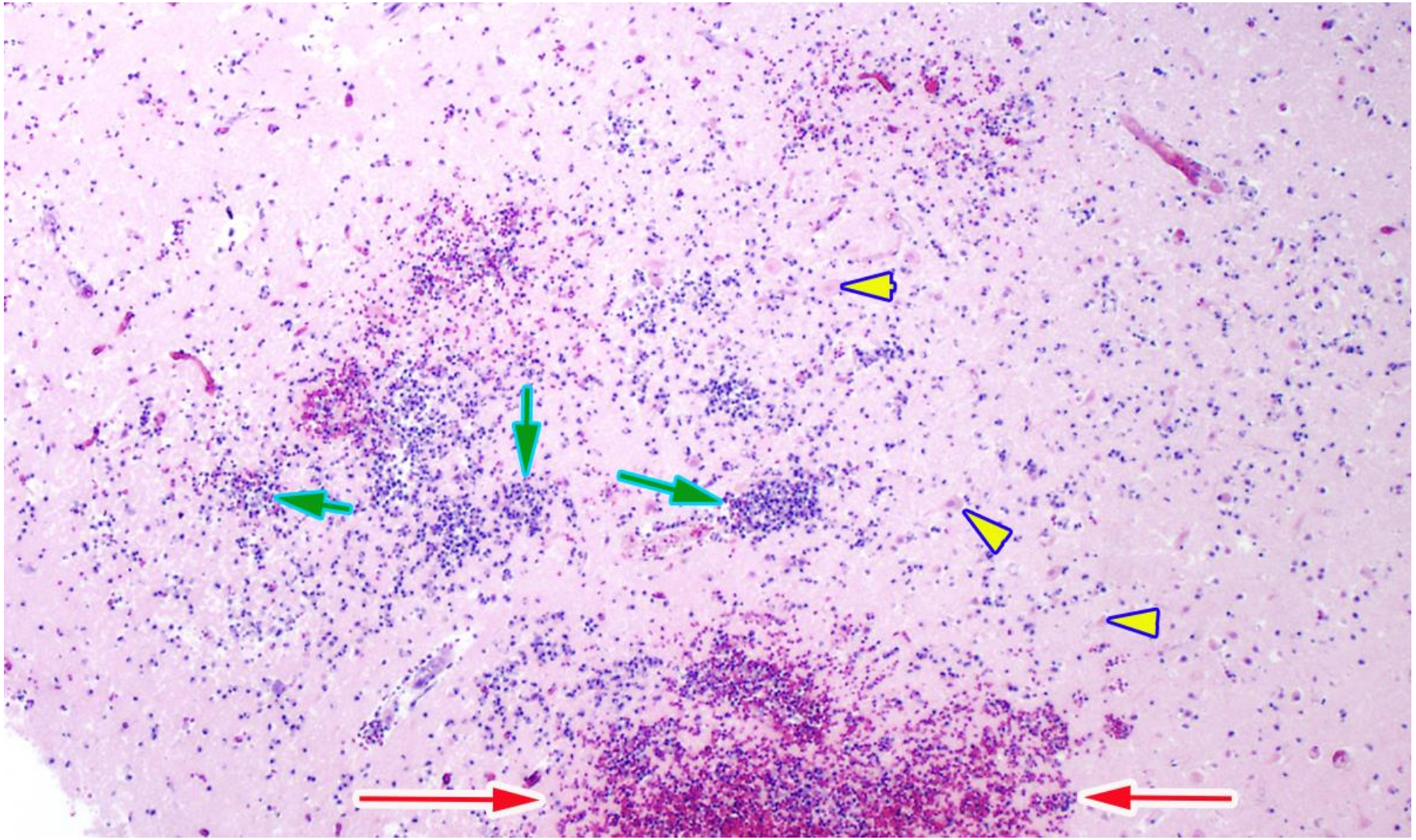




Changes occurring within 12 – 24 hours – Red neurons

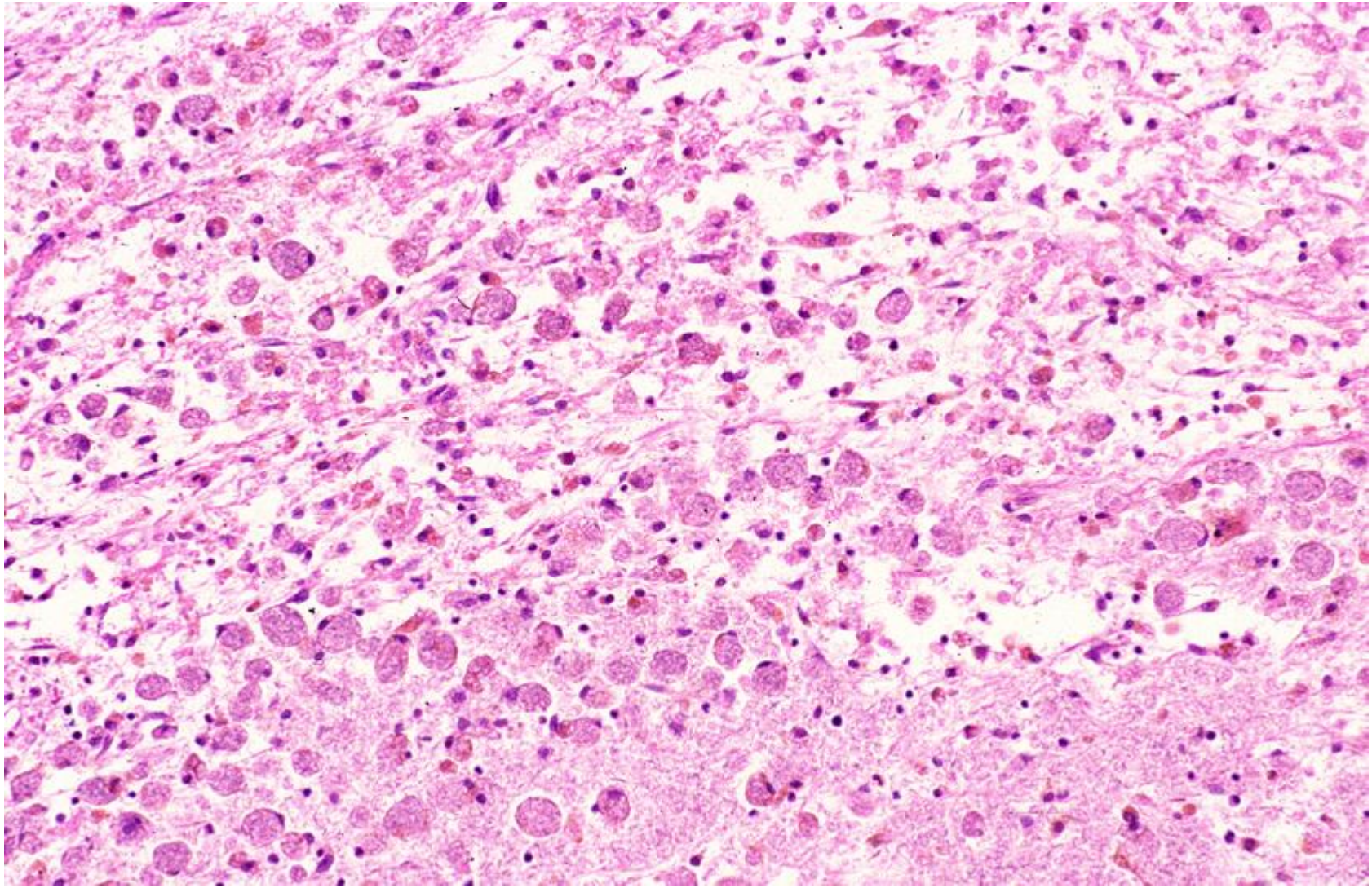


> 24 hours later – infiltration of inflammatory cells

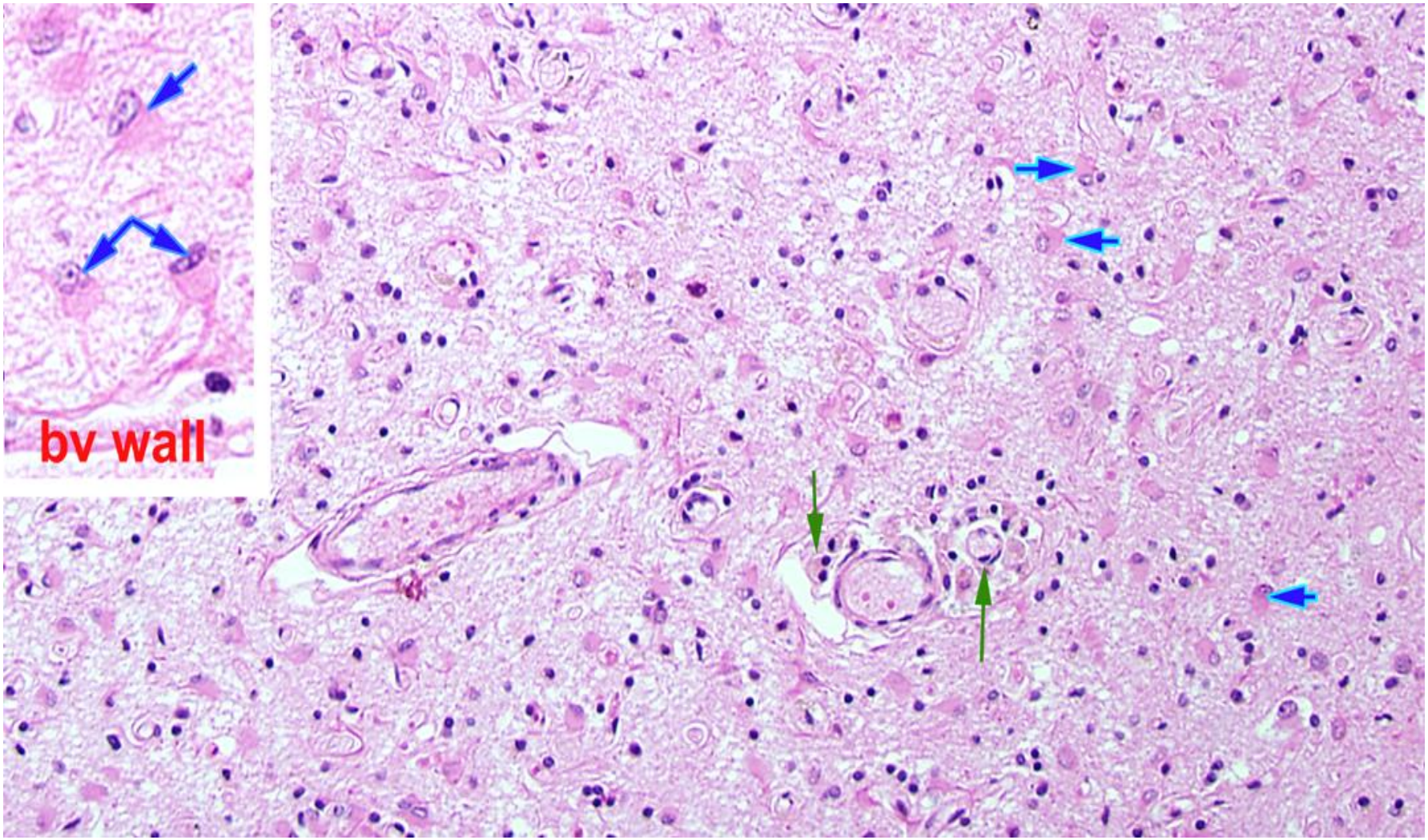


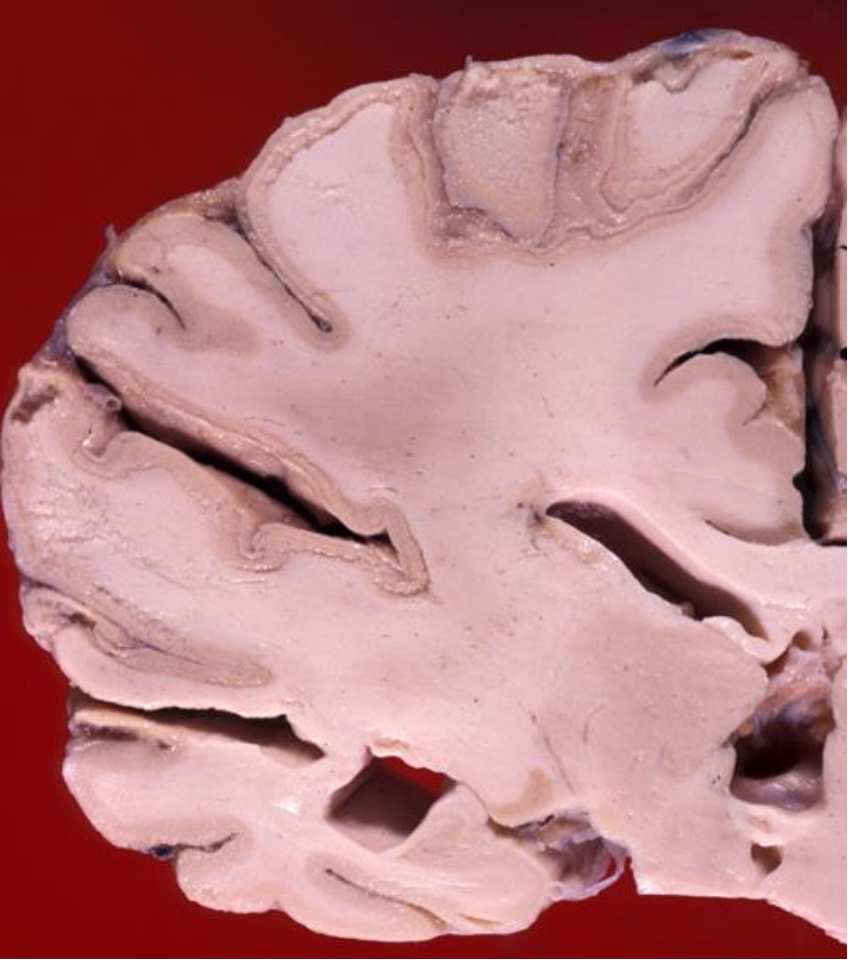
Note also a micro haemorrhage

Liquefactive necrosis and influx of macrophages

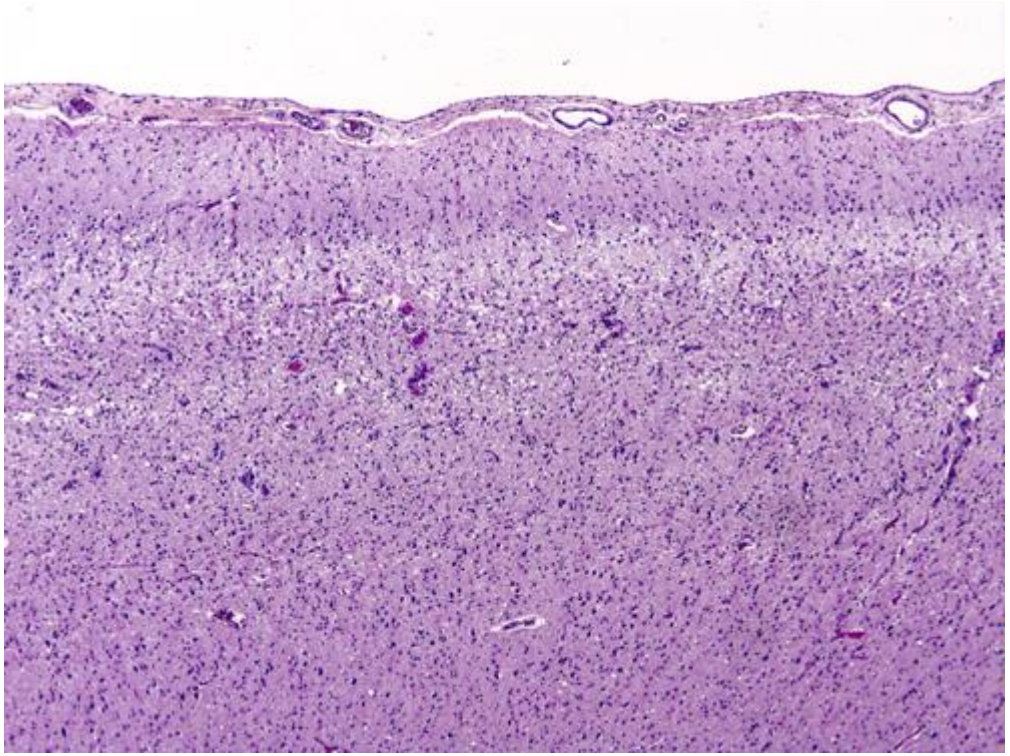


Reactive gliosis, microvascularization occurring in the repair stage





Note: superficial layer of the cortex is almost separated from the deeper ones



Note the light band that marks the loss of neurones and neuropil

Border zone / watershed infarcts

- Occur in the regions of the brain and spinal cord that lie at the most distal field of arterial irrigation
- Wedge shaped
- The border zone between the ACA and MCA is at greatest risk.
- Seen after hypotensive episodes

Water shed infarct – wedge shaped

Focal cerebral ischaemia

- Leads to ***cerebral infarction*** – the site, size and the shape and the extent of tissue damage will depend on the blood vessel affected and the modifying factors
- Modifying factors
  - Collateral circulation
  - Duration
  - Magnititude
  - Rapidity of the decrease in blood supply

Focal cerebral ischaemia - aetiology

- Thrombosis – mainly due to atherosclerosis
- Embolism
  - Myocardial infarct,
  - Valvular disease
  - Atrial fibrillation
  - Originating in atheromatous plaques in carotid arteries
  - Paradoxical embolism in children with cardiac anomalies
- The common sites of embolic infarction include
  - The territory of MCA distribution (the direct extension of the internal carotid artery)

Focal cerebral ischaemia - aetiology

- Arteritis
  - Infections
    - Tuberculosis and syphilis in the past
    - Immunosupression and opportunistic infections (Toxoplasmosis, Aspergillosis and CMV)
  - Collagen vascular disease
    - Polyarteritis nodosa
  - Haematological disease with hypercoagulable states

Focal cerebral ischaemia due to primary CNS disease

- Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy **(CADASIL)**
- Cerebral amyloid angiopathy **(CAA)**
- Primary angiitis of the central nervous system

Cerebral infarcts

Haemorrhagic / Red infarcts

Due to embolic events

Multiple confluent petechial haemorrhages

Haemorrhage is due to secondary reperfusion of damaged vessels and tissue due to collaterals or direct dissolution of the embolus

Venous infarcts

Non haemorrhagic / pale infarct

Usually associated with thombosis

Clinical management is anticoagulation – cf haemorrhagic infarcts

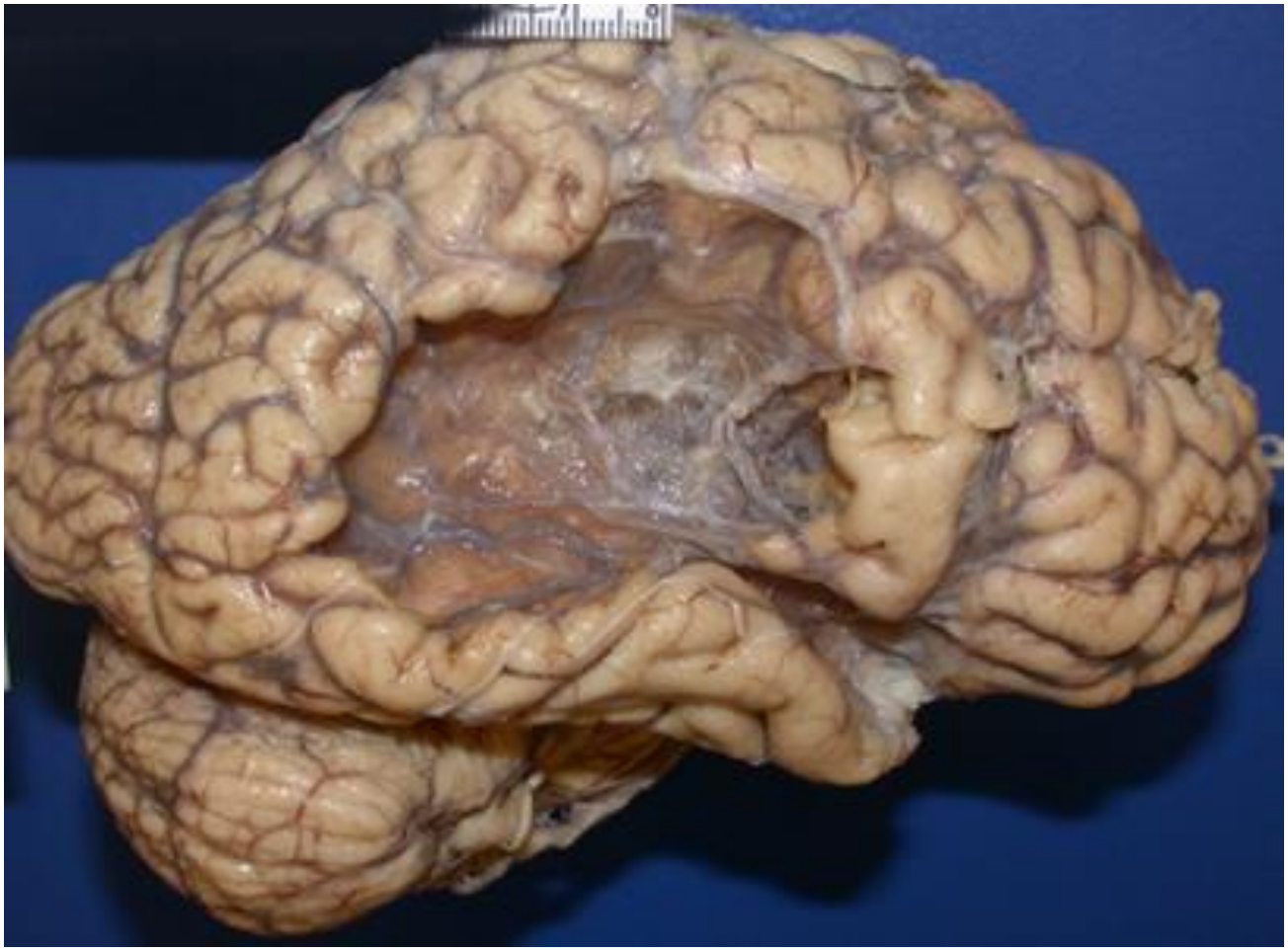
Non haemorrhagic infarct – morphology & evolution

- Morphology changes with time
- First 6 hours
  - Little can be observed
- 48 hours
  - Tissue becomes pale, soft, swollen
  - The boundary between normal and abnormal is indistinct

Acute infarct in the region of the MCA with swelling and disintegration of the infarcted tissue

Non haemorrhagic infarct – morphology & evolution

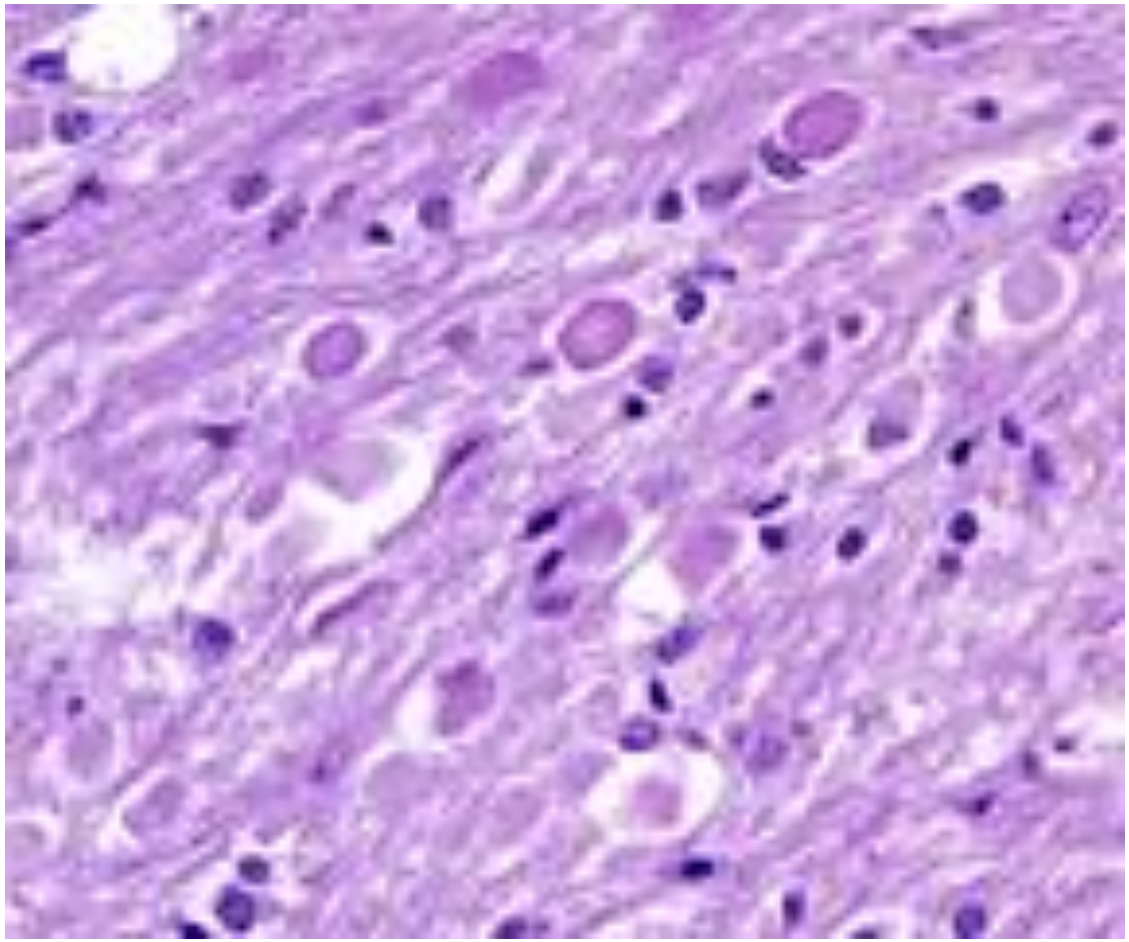
- 2 – 10 days
  - The boundary between the normal and abnormal becomes more distinct as the oedema resolves in the adjacent tissue
- From 10 days onwards (upto 3 weeks)
  - The tissue liquefies, eventually leaving a fluid filled cavity lined by dark gray tissue.



Old infarct in the MCA territory – collapsed cavity

Cerebral infarction - microscopy

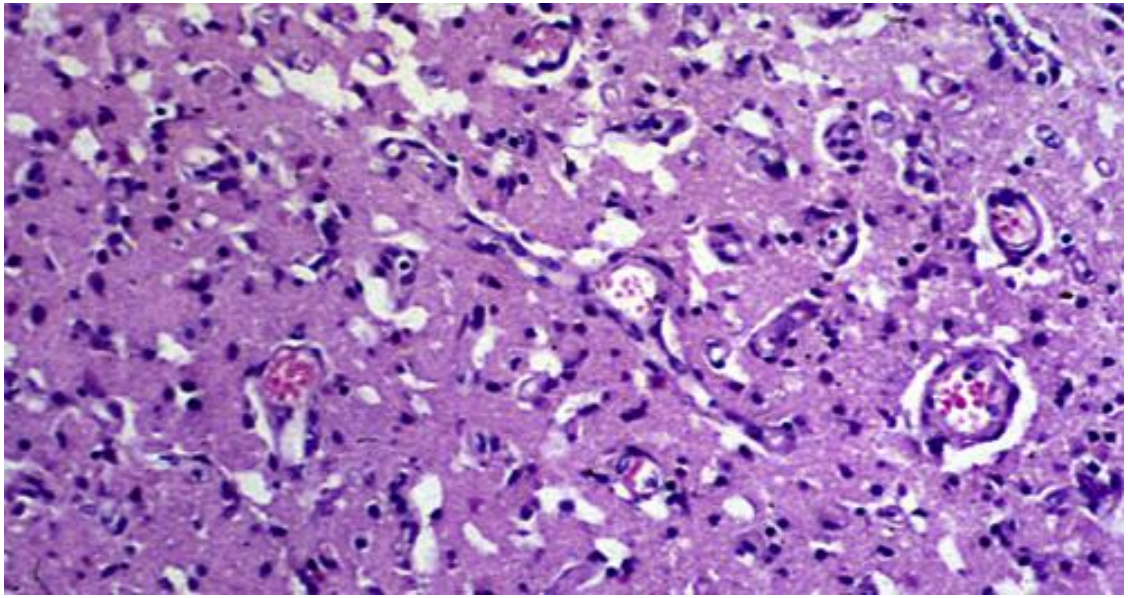
- After first 12 hours
  - Red neurones present
  - Loss of the staining characteristics of the white and gray matter
  - Oedema
  - Myelinated fibres disintegrate
  - Glial cells begin to swell
  - Neutrophilic emigration progressively increases
- At 48 hours
  - Phagocytic cells (monocytes and microglia) become the predominant cell type



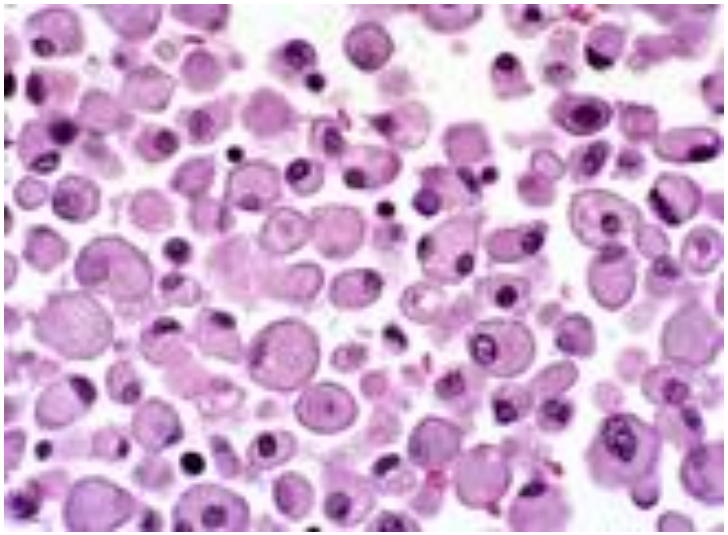
Axonal swelling with red neurones and oedema

Cerebral infarction - microscopy

- Up to 2 – 3 weeks
  - The macrophages / phagocytic cells become stuffed with myelin breakdown products
  - Process of liquefaction and phagocytosis proceeds.
  - The astrocytes at the edge of the lesion divide and enlarge and develop and network of protoplasmic inclusions.



Neovascularization and outpouring of macrophages in a 2 week old infarct



Cerebral infarction - microscopy

- After several months
  - The astrocytic enlargement receeds
  - Astrocyte processes form a dense feltwork of glial fibres admixed with new capillaries.

Haemorrhagic infarcts

- Similar to pale / ischaemic infarcts with more blood extravasation and resorption.
- Venous infarcts are often haemorrhagic.
  - Thrombotic occlusion of the superior saggital sinus
  - Occlusion of the superior saggital sinus
  - Occlusion of deep cerebral veins
  - Hypercoagulable states – Eg: Carcinoma

Intracranial haemorrhages

TRAUMATIC

Epidural

Subdural

SPONTANEOUS

Intracerebral / intraparenchymal

Mainly due to hypertension

Others – coagulation disorders, open heart surgery, fusiform aneurysms, vascular malformations.

Subarachnoid

Saccular (berry) aneurysm

Traumatic / hypertensive haematoma extension

Vascular malformations

Haematological disturbances

Tumours

Intracerebral (intraparenchymal) haemorrhage

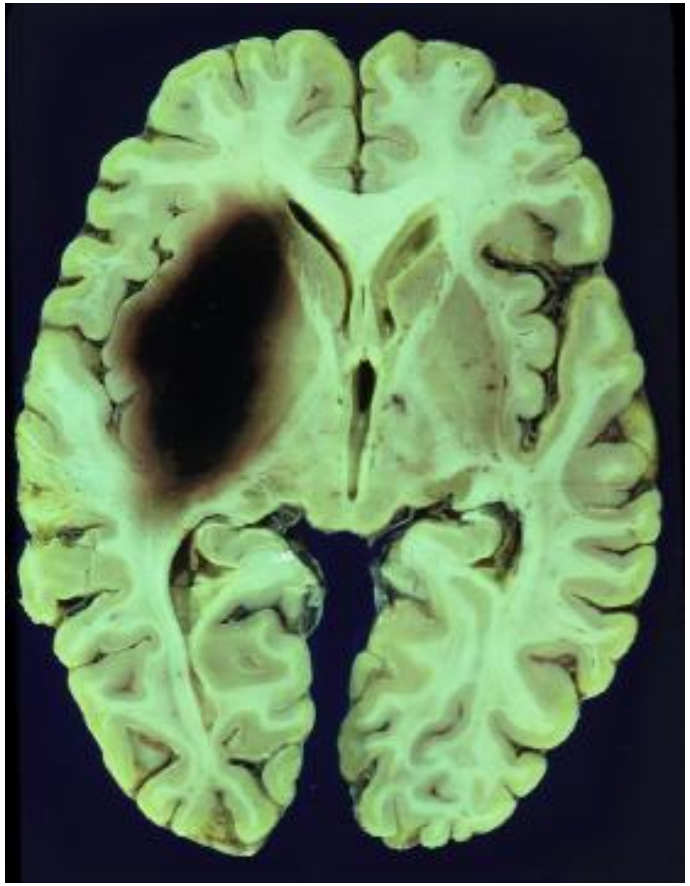
- Mostly in the middle – late life with peak incidence at 60 years.
- Hypertension is the most common cause
  - > 50% of the clinically significant haemorrhage
  - 15% of the deaths of chronic hypertensives
- Hypertension causes many anomalies the vessels
  - Hyaline arteriosclerosis is small vessels
  - Atherosclerosis in larger vessels
  - Charcot – Bouchard microaneurysms in < 300 μm vessels

Intracerebral (intraparenchymal) haemorrhage

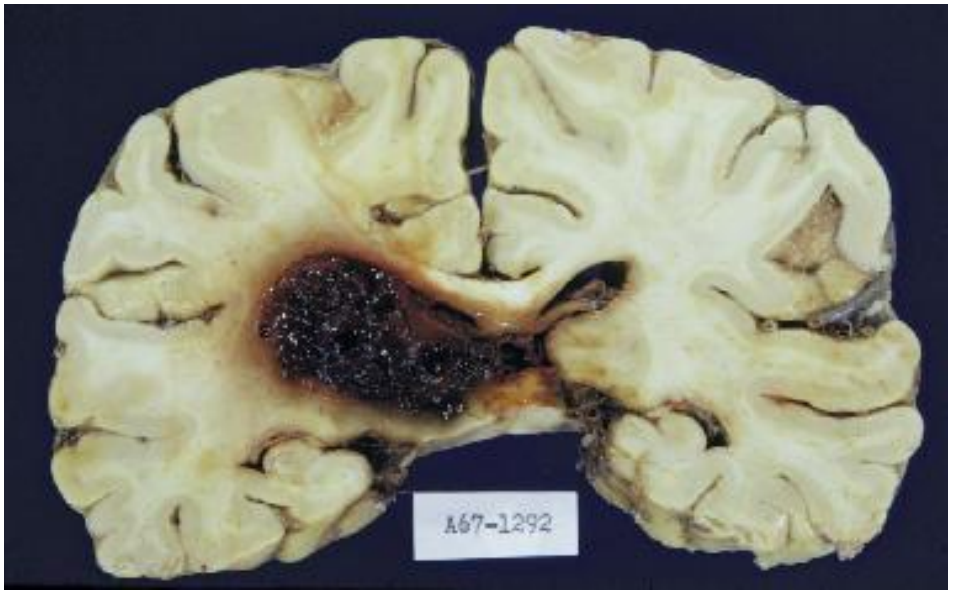
- Origins
  - Putamen (50 - 60%)
  - Thalamus
  - Pons
  - Cerebellar hemisphers (rarely)
- Two types
  - **Ganglionic haemorrhages** – occuring in the basal ganglia and thalamus
  - **Lobar haemorrhages** – occuring in the cerebral hemispheres

Intracerebral (intraparenchymal) haemorrhage

- Early lesion
  - Morphology extravasation of blood with compression of the adjacent parenchyma
  - Central core of clotted blood surrounde by a rim of brain tissue showing anoxic neuronal and glial changes and oedema
- Late lesion
  - Area of cavitatory destruction with a rim of brownish discolouration
  - Oedema resolves and pigment and lipd laden macrophages appear with reactive gliosis



Spontaneous haemorrhage into the left putamen in hypertension



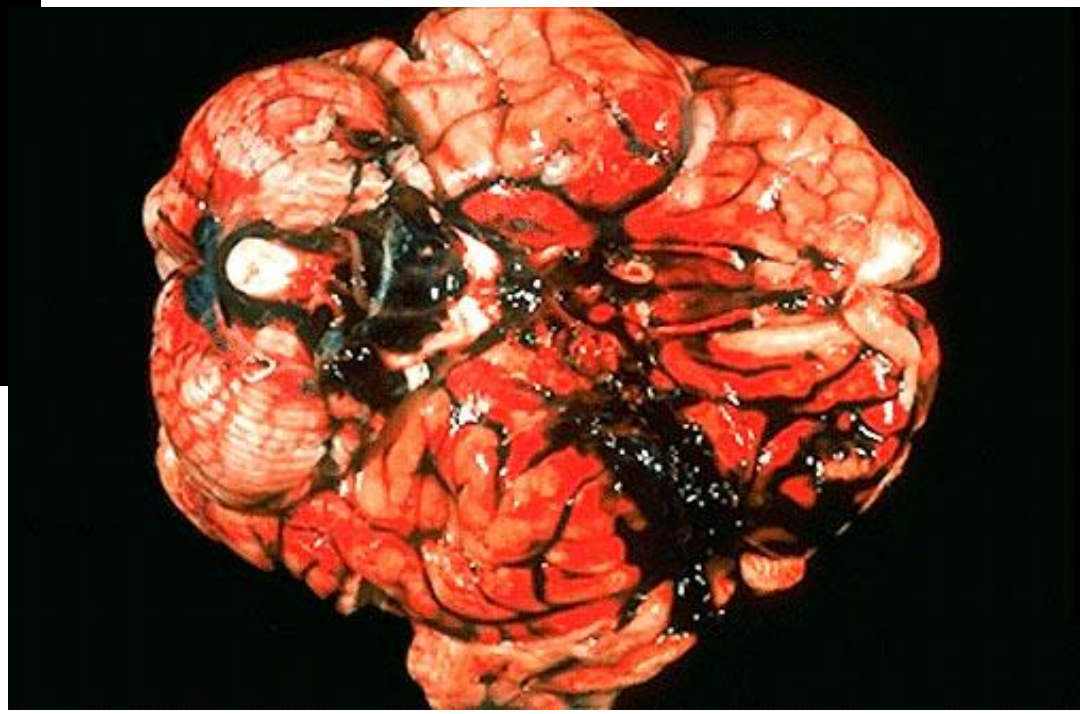
Hypertensive thalamic haemorrhage with intraventricular extension

Aneurysms of the cerebral vessels

- Most common is the saccular / berry / congenital aneurysm
- Atherosclerotic – fusiform, mostly in the basilar artery
- Traumatic, dissecting, mycotic are mostly in the anterior circulation and present with cerebral infarction rather than SAH.

Saccular / Berry aneurysm

- Most common type.
- 2% of post mortem specimens
- 90% occur in the anterior circulation and are near major arterial branch points.
- 20 – 30% are multiple
- ? Congenital
  - Not present at birth and develop owing to defect in the media of the vessels
  - Associated with certain heritable disorders such as neurofibromatosis , polycystic kidney disease, Ehlers Danlos syndrome, fibromuscular dysplasia of extracranial arteries and Coarctation of the aorta.



A ruptured berry aneurysm with SAH.

Clinical features

- Slightly more frequent in females
- Clinically significant haemorrhage is most frequent in the 5th decade.
- Probability of rupture increases with size.
- Typically presents with an excruciating headache and rapidly lose conciousness.
- 20 – 50% of patients die with the 1st rupture.
- Rebleeding is common among those who survive and with each rebleed the prognosis worsens.

Clinical features ctd.

- Acute events
  - Risk of injury with vasospasm involving the other vessels due to vasoconstrictive effects of mediators – eg: endothelin – 1. leading to additional ischaemic injury
- Late events associated with healing
  - Meningeal scarring and fibrosis leading to obstruction of the CSF flow.

Vascular malformations

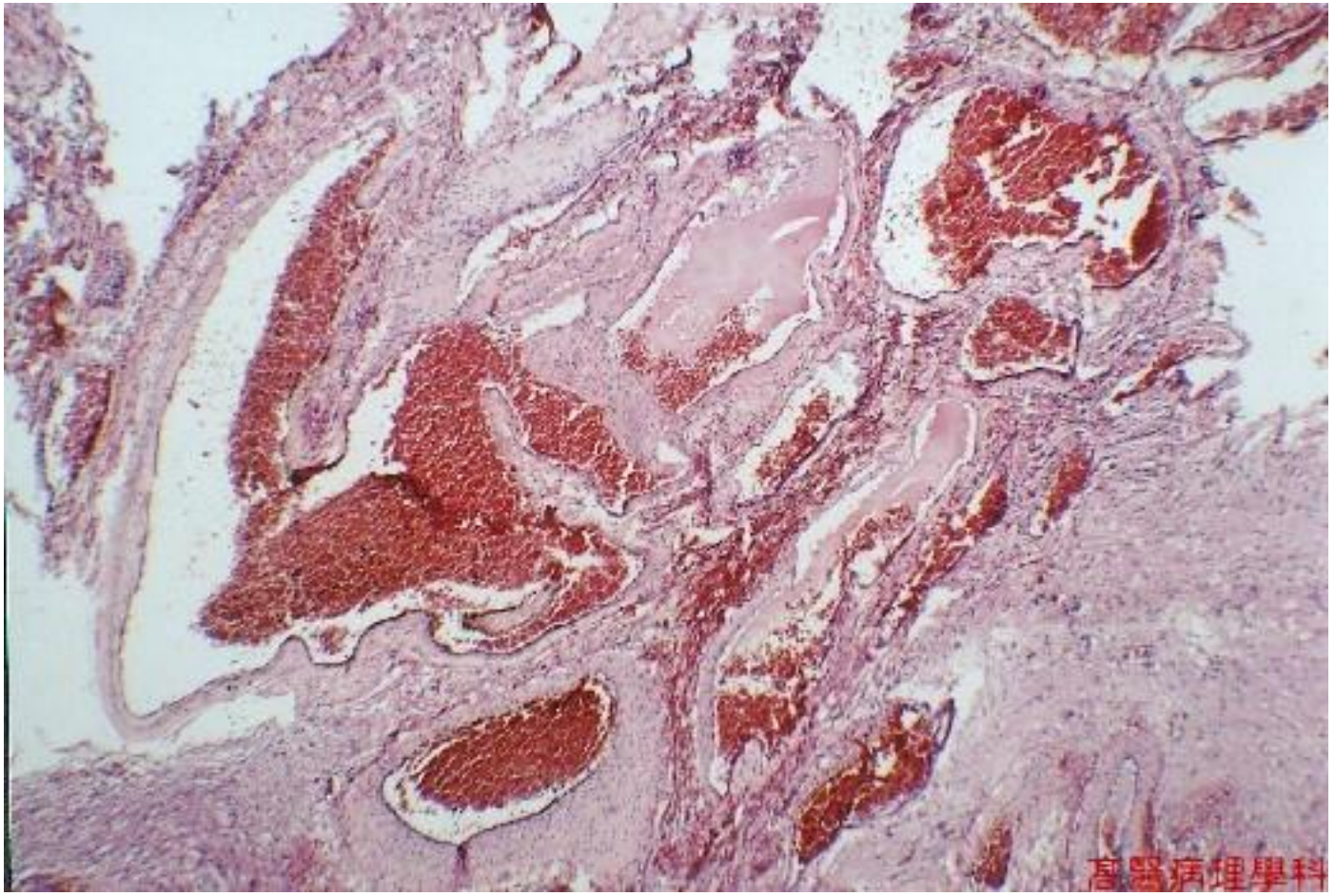
- 4 types
  - **Ateriovenous malformations**
  - **Cavernous haemangioma** – greatly distended, loosely organized vascular channels with thin collaganized walls *devoid of intervening nervous tissue*.

    Most common in the cerebellum, pons and subcortical region (in decreasing order of frequency)
  - **Capillary telangiectasia** – thin walled vascular channels separated by *relatively normal brain tissue*
  - **Venous angioma** – aggregates of venous channels.

Arteriovenous malformation

- Involve vessels of the subarachnoid space extending into the parenchyma or exclusively within the brain.
- Have a prominent pulsatile arterivenous shunt with high blood flow.
- Macroscopy – worm like vascular channels
- Microscopy – enlarge blood vessels separated by gliotic tissue with evidence of prior haemorrhage

  Some vessels can be recognized as arteries tieh duplication and fragmentation of the IEL.



A tangle of thick and thin vessels with some having collagenous walls of veins and others with IEL of the arteries

Clinical features

- Males are twice as frequently affected as females.
- Recognized clinically between ages of 10 – 30 yrs
- Presents with
  - Seizures
  - Intracerebral haemorrhage
  - Subarachnoid haemorrhage

Clinical features

- Most common site is the territory of the MCA particularly the posterior branch.
- Other sites include
  - Mid brain
  - Cerebellum
  - Spinal cord

Hypertensive cerebrovascular disease

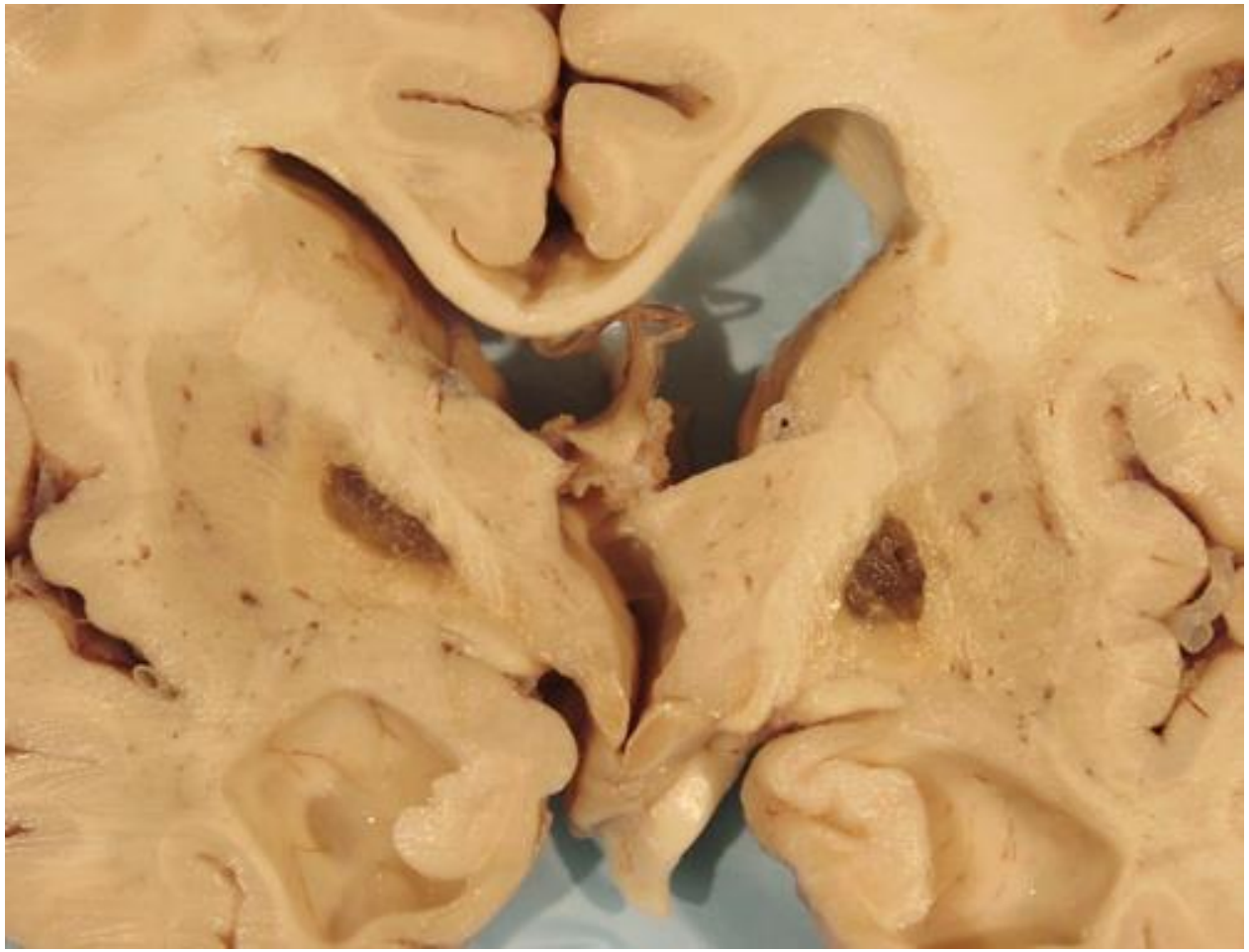
- Hypertensive intracerebral haemorrhage
- Association with atheroclerosis leading to focal cerebral ischaemia / cerebral infarction
- Lacunar infarcts
- Slit haemorrhages
- Hypertensive encephalopathy
  - Acute hypertensive encephalopathy
  - Multi infarct dementia
  - Binswanger disease

Lacunar infarcts

- Deep penetrating arteries and arterioles of the CNS may become occluded.
- Development of lake like spaces less than 15mm wide - lacunae.
- Occurring in (decreasing order of frequency)
  - Lenticular nucleus
  - Thalamus
  - Internal capsule
  - Deep white matter
  - Caudate nucleus
  - Pons

Lacunar infarcts

- Microscopy
  - Cavities of tissue loss with scattered fat laden macrophages and surrounding gliosis.
- Clinical features
  - Depending on their location they may be clinically silent or cause severe neurological impairment.



Bilateral lacunar infarcts in the basal ganglia

Slit haemorrhages

- Rupture of small caliber penetrating vessels and the development of haemorrhages.
- The haemorrhages resorb and leave behind slit like cavities with a surrounding brownish discolouration.
- Microscopy
  - Focal tissue destruction
  - Pigment laden macrophages
  - Gliosis

Slit haemorrhage

Old haemorrhage in the putamen due to hypertension

– Slit haemorrhage

Hypertensive encephalopathy

- **Acute hypertensive encephalopathy**
  - Clinicopathological syndrome in hypertensive patients chaaracterized by
    - Headaches
    - Confusion
    - Vomiting
    - Convulsions
    - Sometimes leading to coma

Acute hypertensive encephalopathy

- Macroscopy
  - Oedematous brain
  - Transtentorial / tonsillar herniation
  - Petichiae in the gray and white matter
- Microscopy
  - Fibrinoid necrosis of the arterioles in the gray and white matter

Vascular / multi infarct dementia

- In patient who over the course of many months or years suffer multiple bilateral, gray and white matter infarcts.
- Clinical syndrome characterized by
  - Dementia,
  - Gait abnormalities
  - Pseudobulbar signs
  - Superimposed focal neurological deficits.

Vascular / multi infarct dementia

- Pathogenesis
  - Cerebral atherosclerosis
  - Vessel thrombosis or embolization from carotid vessels or from heart
  - Cerebral arteriolar sclerosis

Binswanger disease

- When the pattern of injury involves large areas of subcortical white matter

- Large areas of myelin and axon loss.