

## Nervous System 2 Cerebrovascular Disease

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## Cerebrovascular disease (CVD)

- “strokes”
- brain disease due to vascular pathology
  - thrombosis, embolism or hypotension causing ischaemia/hypoxia
  - haemorrhage causing disruption
- major cause of death and disability, especially in more developed countries
- commonly associated with atheroma, diabetes and hypertension

## Two major pathologies

- infarction
  - thrombotic (overall 80%+ of all strokes)
  - embolic
  - hypotensive
  - (venous)
- haemorrhage
  - intracerebral
  - subarachnoid
- but, one can lead to the other!

## Hypoxia and the brain

- brain highly oxygen (and glucose) dependent
- blood flow normally autoregulated
- problems arise from
  - 1) major fall in BP or systemic hypoxia causing diffuse damage or
  - 2) vessel blockage, causing focal damage

## Diffuse hypoxic damage

- depends on severity and duration of hypoxia
- most susceptible neurons in hippocampus, Purkinje cells, cerebral cortex
- affected brain oedematous, raising ICP
- causes anything from mild confusion to PVS to immediate brain death
- in acute hypotension, may also be focal damage
  - “watershed” (border zone) infarcts – most often between anterior cerebral and middle cerebral artery supplies

## Focal hypoxic damage

- results depend on presence of collaterals
  - some exist on surface, e.g. Circle of Willis
  - but not within brain
- focal vascular abnormality due to
  - thrombosis or embolism
- clinical effects ~ site, extent and speed of onset of vascular block

## Thrombotic causes of focal hypoxia

- mostly atheroma - commoner in DM and HT
  - usually thrombosis at carotid bifurcation, origin of middle cerebral artery or in basilar artery
- vasculitis
- infective (more so in immunosuppressed)
  - syphilis, TB, fungi, toxoplasmosis
- autoimmune disease
- hypercoagulable states
- dissecting aortic aneurysms
- drug abusers
- trauma
- cardiac or respiratory arrest

## Embolic causes of focal hypoxia

- commonest are cardiac mural thrombi
  - MI, valvular disease, atrial fibrillation
- arterial thromboemboli - especially from carotid plaques (sometimes include plaque material)
- paradoxical emboli - children with cardiac anomalies
- emboli of other material (tumour, fat, marrow, air)

## Cerebral embolism

- middle cerebral territory most often affected
- emboli lodge at branches or stenoses
- often, occlusion cannot be identified PM
  - ?thromboemboli already lysed
- “shower” embolism of fat may occur after fractures
  - capillary blockages – disturb higher cortical function and consciousness, often with no localizing signs
- widespread haemorrhagic lesions of white matter characteristic of bone marrow embolism after trauma
- tumour emboli more important as source for metastases, then cause of hypoxia

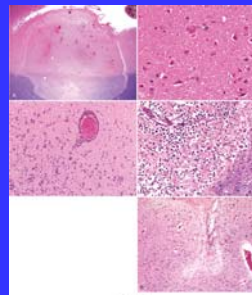
## Cerebral infarcts

- sometimes classified as red or pale
- depends on presence of haemorrhage from infarcted vessels
- (any infarct may show surrounding zone of lesser hypoxic damage and hyperaemic reaction, which may be oedematous)
- venous infarcts – usually beside sinuses – associated with infection, dehydration and drugs (oral contraceptives)

## Natural history of infarcts

- effects depend on site, size and speed of onset
  - in some effect complete from the start, in others clinical picture evolves
- thrombotic infarcts most commonly internal capsule (corticospinal paths), hence hemiplegias etc
- reperfusion (micro)haemorrhages may occur
- if patient survives, infarcted tissue phagocytosed by microglia and monocytes from blood, then gliosis
  - macrophages persist at site for years as lipid-containing “compound granular corpuscles”
  - in red infarct, macrophages also contain iron
  - end result of repair often a cystic cavity with gliotic wall

## Microscopic changes in infarct

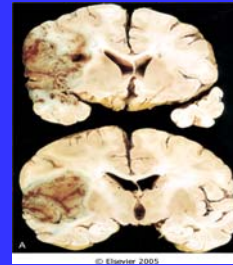


- increased eosinophilia of neurons
- then neuronal death and cell infiltrate
- eventual gliosis

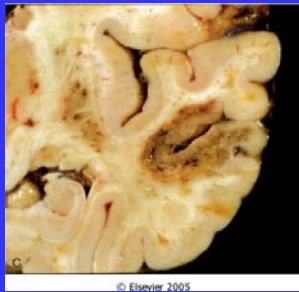
### Atheroma of Circle of Willis



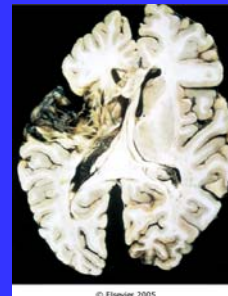
### Haemorrhagic infarct



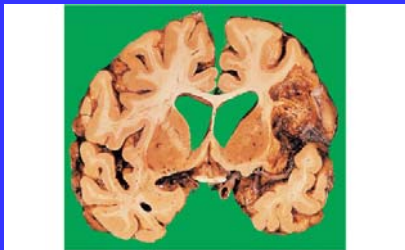
### Infarct with reperfusion haemorrhages



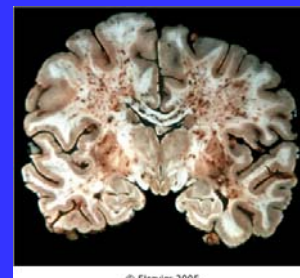
### Old cystic infarct



### Cerebral infarct – cystic change



### Petechial haemorrhages in bone marrow embolism



## Intracranial haemorrhage

- secondary
  - following infarction
- primary
  - extradural and subdural
    - usually traumatic in origin
  - subarachnoid and intraparenchymal (aka intracerebral)
    - usually due to vascular disease

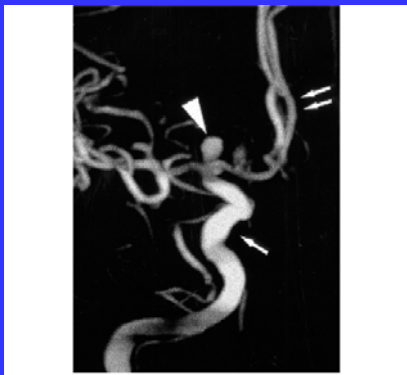
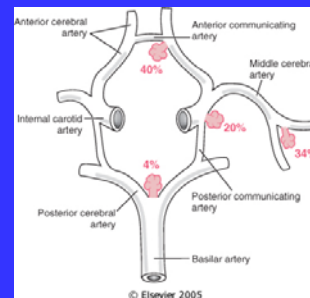
## Subarachnoid haemorrhage

- most often due to cerebral artery berry (saccular) aneurysms
- but also by extension from intracerebral haemorrhages or due to bleeding diseases, trauma, tumour, vasculitis etc

## Berry (saccular) aneurysms

- incidental finding in ~ 2% of post-mortem examinations, multiple in maybe a third
- occur near major branch points on Circle of Willis or just beyond
- more common on anterior part of Circle or its branches

## Berry aneurysms



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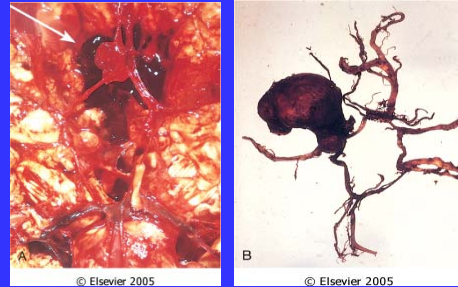
## Aetiology of berry aneurysms

- genetic factors may be important in some cases
  - e.g. increased risk in ADPKD, Ehlers-Danlos syndrome, Marfan's syndrome) etc
- cigarette smoking and hypertension also predisposing factors
- "congenital", but not present at birth, though underlying defect in media may be

## Berry aneurysms

- thin-walled out-pouching
- usually < 1 cm diameter
- wall consists only of intima
- rupture at apex, usually into subarachnoid space, but sometimes into brain or both

## Berry aneurysms



## Berry aneurysm



## Berry aneurysms

- rupture most often in 40- 50s
- may be precipitated by sudden ICP rise
  - also by hypertension
- typically sudden severe headache and rapid loss consciousness
- ~ 10-15% die, but most recover consciousness in minutes
- may show meningism
- rebleeding common and makes prognosis worse

## Subarachnoid haemorrhage

- early effects include
  - increased risk of vasospasm of other vessels
  - can lead to additional ischemic injury, espec. if spasm involves Circle of Willis
  - presumably due to vascular mediator
- late sequelae
  - meningeal fibrosis and scarring
  - possible obstruction of CSF flow/reabsorption.

## CSF in subarachnoid haemorrhage

- initially bright red blood
- later, xanthochromia as red cells degenerate

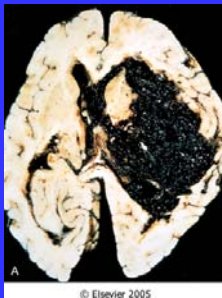
## Intraparenchymal (intracerebral or cerebral) haemorrhage

- 80 % death rate
- sudden onset, causing rapid rise in ICP
- 50%+ associated with hypertension
  - ? microaneurysms (of Charcot-Bouchard)
  - ? just arteriosclerotic branch points
- remainder due to vascular malformations, bleeding disease, vasculitis etc

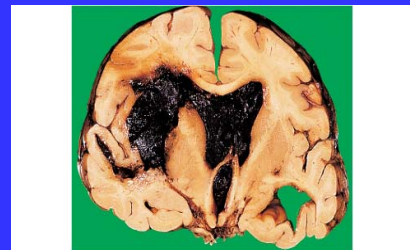
## Intracerebral haemorrhage

- usually affects basal ganglia, brainstem, cerebellum or cerebral cortex
- major tissue disruption and destruction
- may extend into ventricles and/or subarachnoid space
- in survivors, haematoma surrounded – like infarcts - by zone of reaction, then repair with gliosis

## Intracerebral haemorrhage rupturing into ventricle



## Intracerebral haemorrhage with intraventricular extension

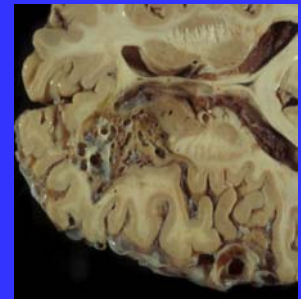


## Pontine haemorrhage rupturing into 4<sup>th</sup> ventricle



## Other causes of haemorrhage

- angiomas, AV malformations etc



## Hypertension and CVD

- common cause of CVD
- frequently associated with atheroma and diabetes
- responsible for -
  - intracerebral haemorrhage
    - and rupture of berry aneurysms, so subarachnoid haemorrhage
  - lacunar infarcts
  - hypertensive encephalopathy
    - acute or chronic

## Hypertension and lacunar infarcts

- arteriosclerosis +/- occlusion of vessels supplying basal ganglia, hemispheres and brainstem
- causes single/multiple small cavitated infarcts (“lacunes”)
  - tissue loss with scattered compound granular corpuscles surrounded by gliosis
- clinical effects depend on location - may be “silent”

## Lacunar infarcts in caudate & putamen



## Acute hypertensive encephalopathy

- syndrome of diffuse cerebral dysfunction
  - headaches, confusion, vomiting and convulsions, sometimes leading to coma
- usually part of “malignant” phase hypertension
- rapid treatment needed to reduce raised ICP
- at PM, oedematous brain +/- tentorial or tonsillar herniation
- arteriolar fibrinoid necrosis and petechiae throughout brain

## Chronic hypertensive encephalopathy

- one cause of vascular (multi-infarct) dementia
  - dementia often with focal neurological defects
- caused by multifocal vascular disease over long time
  - cerebral atheroma
  - thrombosis or embolism from carotids or heart
  - cerebral hypertensive arteriolosclerosis

## Intracranial vascular pathology in summary

- Extradural and subdural haemorrhage
  - trauma
- Subarachnoid haemorrhage
  - berry aneurysms
- Intracerebral haemorrhage
  - hypertension
- Cerebral infarction
  - atheroma/thrombosis/embolism

