CNS lecture 2

Cerebrovascular disease

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Cerebrovascular diseases

→ affect cerebral blood vessels

-a major cause of death . one of the 3 main causes of death worldwide (with CVDs & Cancer)

-most common cause of neurologic morbidity.

-mechanisms: **thrombi**

emboli

vascular rupture → hemorrhage

-**stroke**: clinical term applies to all three when symptoms are acute.

↓ symptoms suddenly occur → due to any

- Thrombi and emboli.. Occlusion.. **Ischemic** damage — if irreversible → infarction
- Vessel rupture: **hemorrhage**.

Hypoxia and ischemia

needs energy continuously

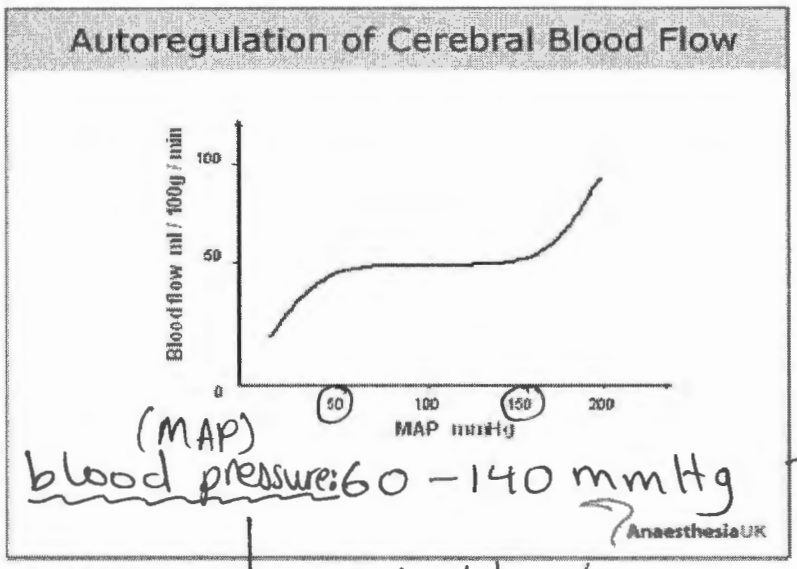
Hypoxia → ↓ O_2 due to any cause

ischemia → ↓ blood supply → so ↓ O_2, nutrients, etc...

O_2 + glucose

- Brain is highly oxygen dependent.
- Brain 2% of body weight but receives 15% of cardic output → continuous blood supply → huge proportion compared to body weight
- 20% of total body oxygen consumption.
- Autoregulation of vascular resistance allows stability of cerebral blood flow over a wide range of blood pressures and intracranial pressure. This allows the brain to get what it needs (constant blood flow) → at different blood pressures (within a limit)

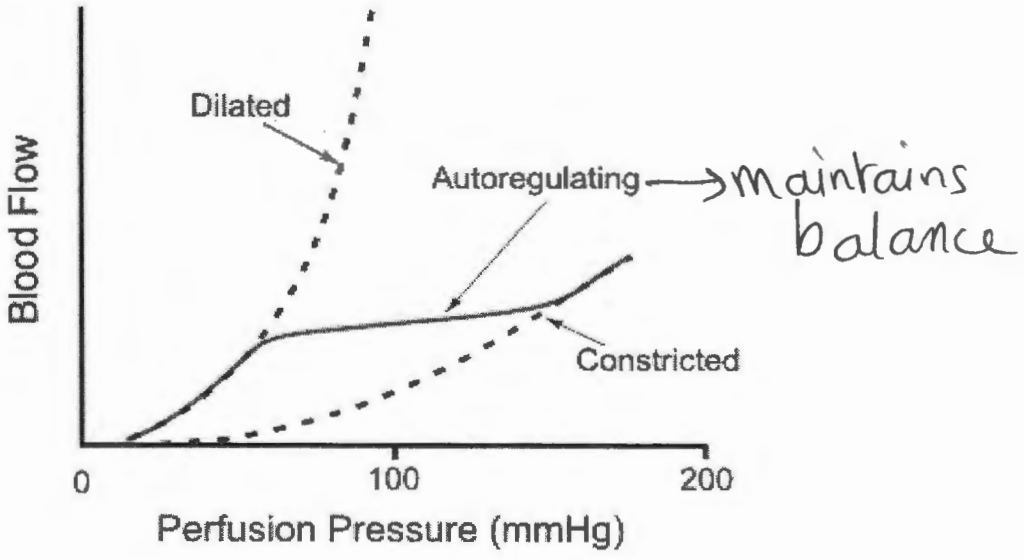
$$F = \frac{\Delta P}{R}$$



→ outside these limits ↓ autoregulation will not work

→ Strable / constant blood flow

→ regulated by arteriolar muscles → constrict } → to after flow
→ dilate }



→ maintains balance

Brain hypoxia

2 forms:

- Functional hypoxia.
- ischemic hypoxia

① Functional hypoxia

→ Non-ischemic hypoxia

a • Low partial pressure of oxygen: high altitude

b • Impaired oxygen carrying capacity: anaemia and CO poisoning

c • Decreased oxygen use by tissues: cyanide poisoning (O_2 available but cannot be used)

② Ischemic hypoxia

a → critical if b.p. is below 60mmHg

- Hypo-perfusion due to hypotension or
b vascular obstruction (↓ blood supply)

- Ischemia can be global or focal
  - global → all brain

* Global cerebral ischemia

→ Problem in vasculature of entire brain

- Occurs due to severe hypotension, systolic below 50mm Hg. (60 mm Hg)

1. Cardiac arrest
2. Shock
3. Severe hypotension

- Outcome depends on severity and duration of insult

This also depends on types of

Global ischemia

- Neurons more susceptible to hypoxic injury than glial cells. → neurons injured before
- Most susceptible neurons: **pyramidal cells** of hippocampus and neocortex + **Purkinje cells** of the cerebellum

ischemia

- If mild: transient confessional state
- severe : neural death, if survive: severely impaired neurologically
- Severest forms result in brain death.

ex: fetal distress (hypoxia/ischemia during delivery) → if occurs for a certain time → death of neurons → cannot be replaced ⇒ neurological deficit.

Brain death → death of humans

- Diffuse cortical injury with flat EEG (isoelectric EEG)
  - flat EEG ↓ criteria
- Brain stem damage: No reflexes and no respiration
- If on mechanical support: autolysis of brain= respirator brain (patient on respirators and his brain becomes autolytic)

Ischemia < reversible / irreversible

✳ Morphology of reversible global ischemia

- Swelling → first manifestation of reversible cell injury due to any cause
- Wide gyri
- Narrow sulci
- Poor grey-white matter demarcation

→ due to fluid + edema

→ resorbed by lymphatics

* Infarction/ irreversible ischemia

↳ death due to ischemia

- Early changes
- Subacute changes
- repair

The brain ⇓ liquefactive necrosis → due to ischemia (the only solid organ)

Injury: Loss of function
Time ↓ Microscopic changes
Macroscopic changes

Early changes → tissue rxn due to injury

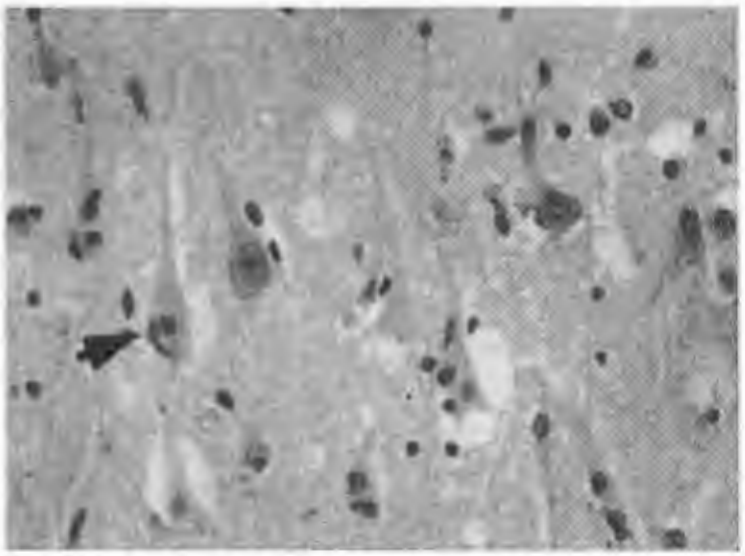
First 12 hours → no morphological changes → only functional loss

- 12-24 hours after insult → evidence of infarction seen
- Acute neuronal cell damage = red neurons =
  ① micro-vaculations followed by ② cytoplasmic eosinophilia then ③ pyknosis and karyorrhexis
  - ① enzymes lyse part of cells
  - ② due to loss of basophilia → loss of DNA, RNA, enzymes (coagulation/denaturation) → give a pinkish colour
  - ③ → loss of nucleus
- Similar changes later on glial cells
- Then: neutrophilic infiltrate.
  → acute inflammation → rxn to cell death

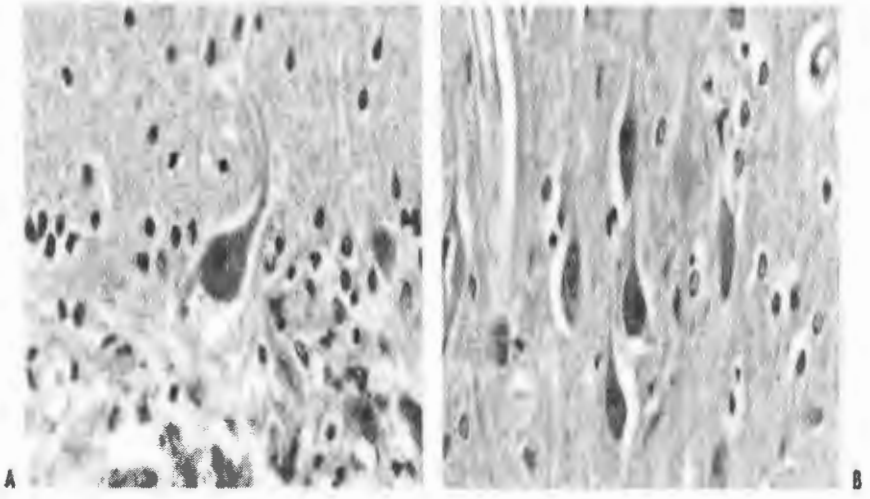
⇒ ① Cell death
② Neutrophils

Red neurones

→ can be seen in any insult which causes death
- Ischemia
- Tumors
- etc...



Red neurones



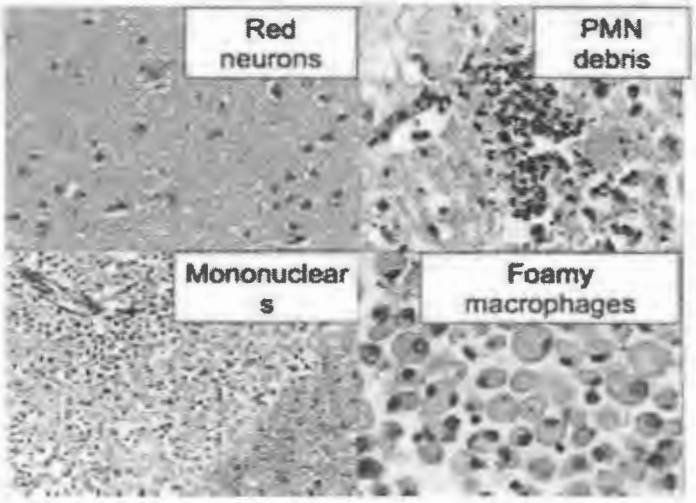
Subacute change

- 24 hours to 2 weeks
- Necrosis (liquefactive) → loss of entire tissue → cannot be replaced
- Macrophages → phagocytosis of dead tissue
- Vascular proliferation (angiogenesis)
- Reactive gliosis

⇓ Cystic space

beginning of repair

proliferation of glial cells ⇒ supportive tissue (similar to fibrosis in other tissues)



repair

- After 2 weeks → becomes evident
- Removal of necrotic tissue (phagocytosis)
- Gliosis
- Loss of organised CNS structure
- Pesudo-laminar necrosis: uneven neuronal loss and gliosis in neocortex → not all cells affected equally with ischemia ⇒ "zonation"

not all areas affected with same rate of injury

repair

- Astrocytes are the main cells responsible for repair and scar formation (gliosis).
- Injury.. Causes 1. hypertrophy and hyperplasia in astrocytes. → ↑ size + number

Changes in astrocytes to ↑ glial tissue + supporting tissue

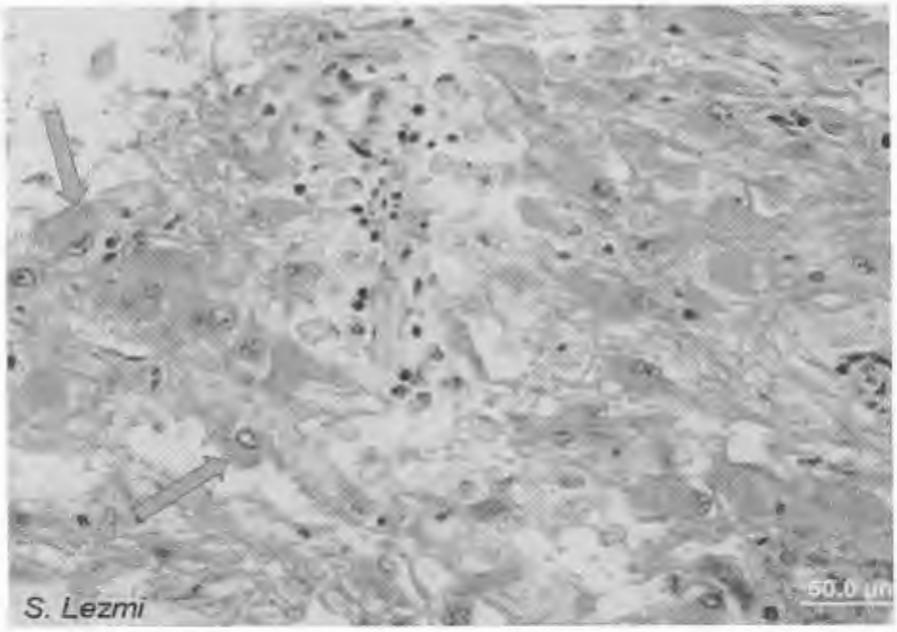
2. enlarged nuclei
3. prominent nucleoli.
4. increased pink cytoplasm.
5. increased, ramifying processes

These changes in astrocytes: gemistocytic astrocyte.

⇒ Also seen in tumors

Change in cell to

gemistocytes



Border zone infarcts

- =Watershed infarcts
- Wedge shaped areas of infarction
- At most distal portions of arterial territories.
- Usually seen after hypotension episodes.
- Border between anterior and middle cerebral artery territories is most vulnerable → little vascularity

✳ Focal cerebral ischemia

- Focal occlusion of a vessel. → ischemia in area supplied by that vessel only
- Occlusion: thrombi or emboli
- Size, location and shape of infarct depend on the vessel occluded and can be modified by collateral blood flow. → damage will be less due to collaterals
- Collateral flow in circle of Willis and cortico-leptomeningeal anastomoses can limit damage
- Little collaterals in : thalamus, basal ganglia, and deep white matter. → severe damage since there are no collaterals to compensate in case of occlusion of vessel

Good collaterals ← ↓ damage to one vessel ↓ others compensate → little damage

⇝ Embolic infarcts

- More common than thrombotic infarcts
- Source: 1. **cardiac mural thrombi**, arise due to myocardial dysfunction, valvular disease, and atrial fibrillation
- 2. **arterial atheroma** in carotid arteries or aortic arch (arterial thrombi → can dislodge)
- 3. **venous** thrombi crossing to arterial circulation through cardiac defects = paradoxical embolism.. DVT, fat emboli

from ... to left

Emboli usually stop when vessels are narrow (mainly at bifurcation + branching)

- Most common site of embolic occlusion : middle cerebral artery, a direct extension of the internal carotid.
- Emboli lodge where vessels **branch** or in **stenotic** areas caused by atherosclerosis

→ Thrombotic occlusions

→ within vessels supplying brain tissue

- Atherosclerosis

Common sites:

1. Carotid bifurcation
2. Origin of middle cerebral artery
3. Ends of basilar artery (upper or lower ends)

infarcts → will occur if it irreversible injury (severe occlusion lasting for a long time)

- **Haemorrhagic or non haemorrhagic**
- Non haemorrhagic : due to acute vascular occlusion.. Treat with thrombolytic therapy
- Haemorrhagic: due to reperfusion through collaterals or after dissolution of emboli.

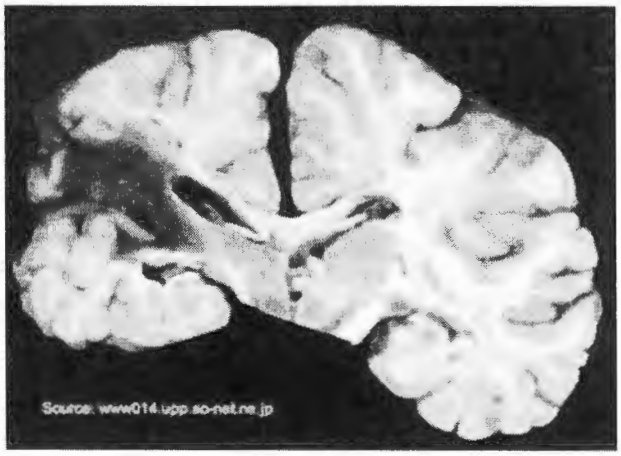
Move blood coming to area → so change for hemorrhage

* Very important to distinguish between both types → we use radiological studies (ex: MRI) → important to know → for treatment

* No antithrombotics if there is any sign of haemorrhage or ↑ risk of hemorrhage due to any cause

Brain infarct

(non-hemorrhage)



• Morphology/ non-hemorrhagic

Gross

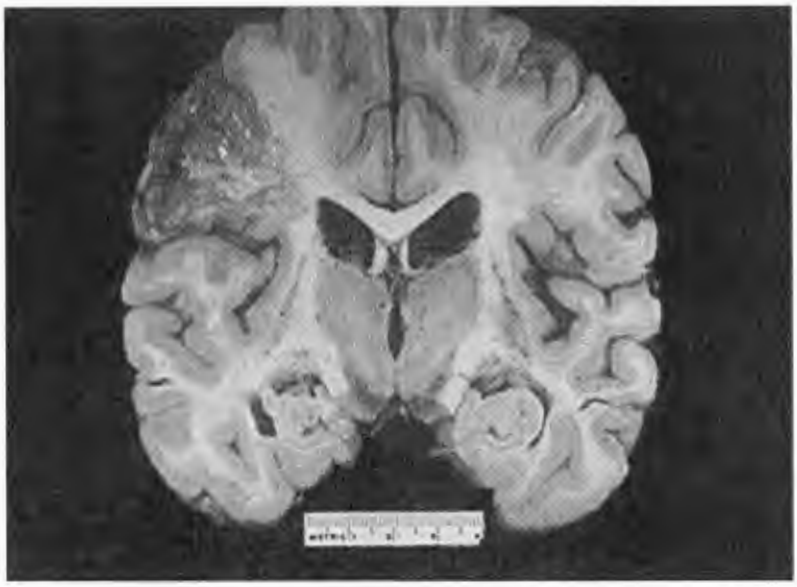
- First macroscopic changes need more than 6 hours to develop.
- By 48 hours: pale, soft swollen area.
- Day 2-10: gelatinous and friable.
- Day 10 to week 3: liquefaction ending in a fluid filled cavity.

Morphology/ nonhemorrhagic

Microscopic

- After 12 hours: red neurons + edema
- Up to 48 hours: neutrophils
- 2-3 weeks: macrophages, gemistocytic astrocytes.
- Months: gemistocytes regress, cavity persists

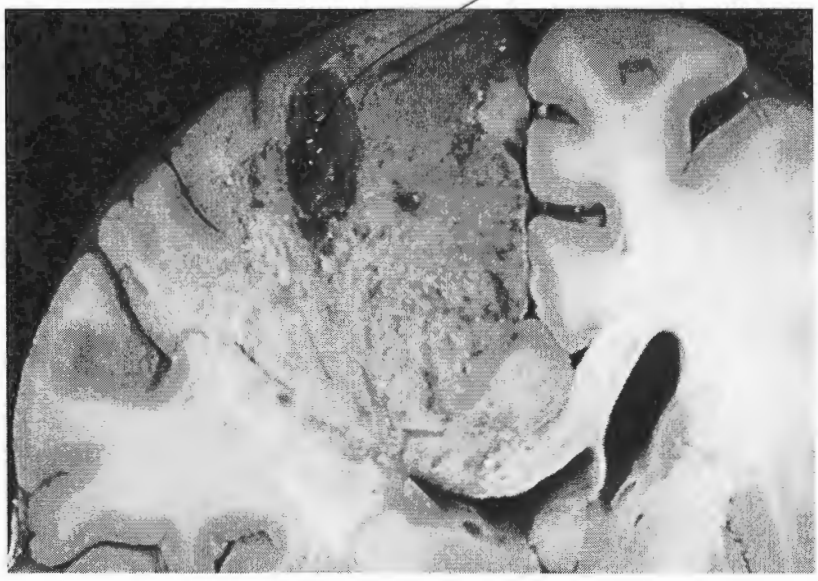
infarct



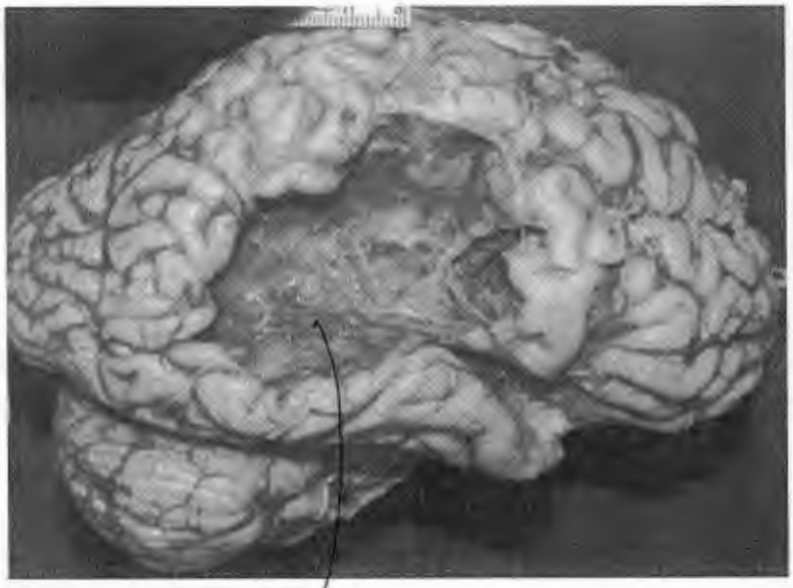
infarct

several weeks

cavity



Old infarct



cavity with nothing inside → no regeneration

hemorrhagic infarct

- Same as non hemorrhagic but with blood extravasation.

Other cerebrovascular diseases

- Intracranial hemorrhage
- Hypertensive cerebrovascular disease
- vasculitis

Hypertensive cerebrovascular disease

Hypertension → will affect brain blood vessels

- Hyaline arteriolar sclerosis.
- Weak arteioles, so.. Can rupture. → hemorrhage
- Minute aneurysms can form (Charcot-Bouchard microaneurysms) → because vessels are weak

SO

Hypertension/ effects

↝ very high b.p → autoregulation no longer functioning → ↑ blood flow

1. Massive intracranial hemorrhage. → severe
2. Lacunar infarcts. → small
3. Rupture of small penetrating vessels
4. Acute hypertensive encephalopathy

① Massive intracranial hemorrhage

- Will be discussed in the next lecture!

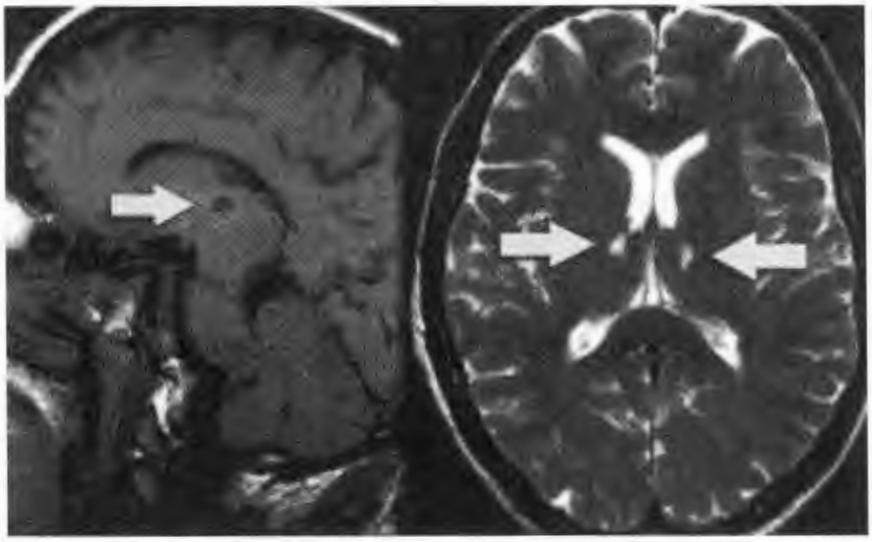
② Lacunar infarcts

→ small vessel rupture → due to HTN
→ affecting a small area → minimal infarction

- Small infarcts, mostly in deep grey matter (basal ganglia and thalamus), internal capsule, deep white matter and pons.
- Caused by occlusion of penetrating branch of a large cerebral artery.
- Effect: depends on site → can have serious effects even if it is very minimal (ex: in respiratory center)

Lacunar infarct

→ minimal



③ Vessel rupture

- Small penetrating vessels may rupture.
- Cause small hemorrhages.

④ Acute hypertensive encephalopathy

- Happen with sudden sustained rise of diastolic more than 130. very severe HTN
- Increased intracranial pressure, global cerebral dysfunction (headache, confusion, vomiting, convulsion, or coma)
  - ↑↑ blood flow
  - → medical emergency
  - (projectile)
- Rapid intervention to decrease intracranial pressure is essential.

Projectile vomiting must be taken seriously (esp. in children)

✳ vasculitis

Infectious arteritis: → weaker wall of vessel → rupture.

- previously seen with syphilis and TB.
- Now in association with: CMV, herpes, aspergillosis..... immunosupression → drugs, HIV, chemotherapy

So mainly opportunistic infections → more common now

Polyarteritis nodosa.

Primary angiitis of CNS cause diffuse encephalopathy with cognitive dysfuction.