CNS Ppathology 2021

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Lecture 5:

Stroke and Increased intracranial pressure.

ILOs

- Define stroke and list its causes.
- List causes and symptoms of increased intracranial pressure.
- Define cerebral edema and know its types and causes.
- Define hydrocephalus and know its types and causes.
- Define herniation and know its types and complications
- Understand auto-regulation of blood flow in the brain
- List causes of brain hypoxia and ischemia

- This lectures covers two topics
- First we will discuss stroke (cerebrovascular accident)
- Then we will discuss the definition and causes on increased intracranial pressure.

Cerebrovascular diseases = CVA= stroke

-CVA is a major cause of death .

-CVA is the most common cause of neurologic morbidity.

-mechanisms: **thrombi**

emboli

vascular rupture

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

Definition

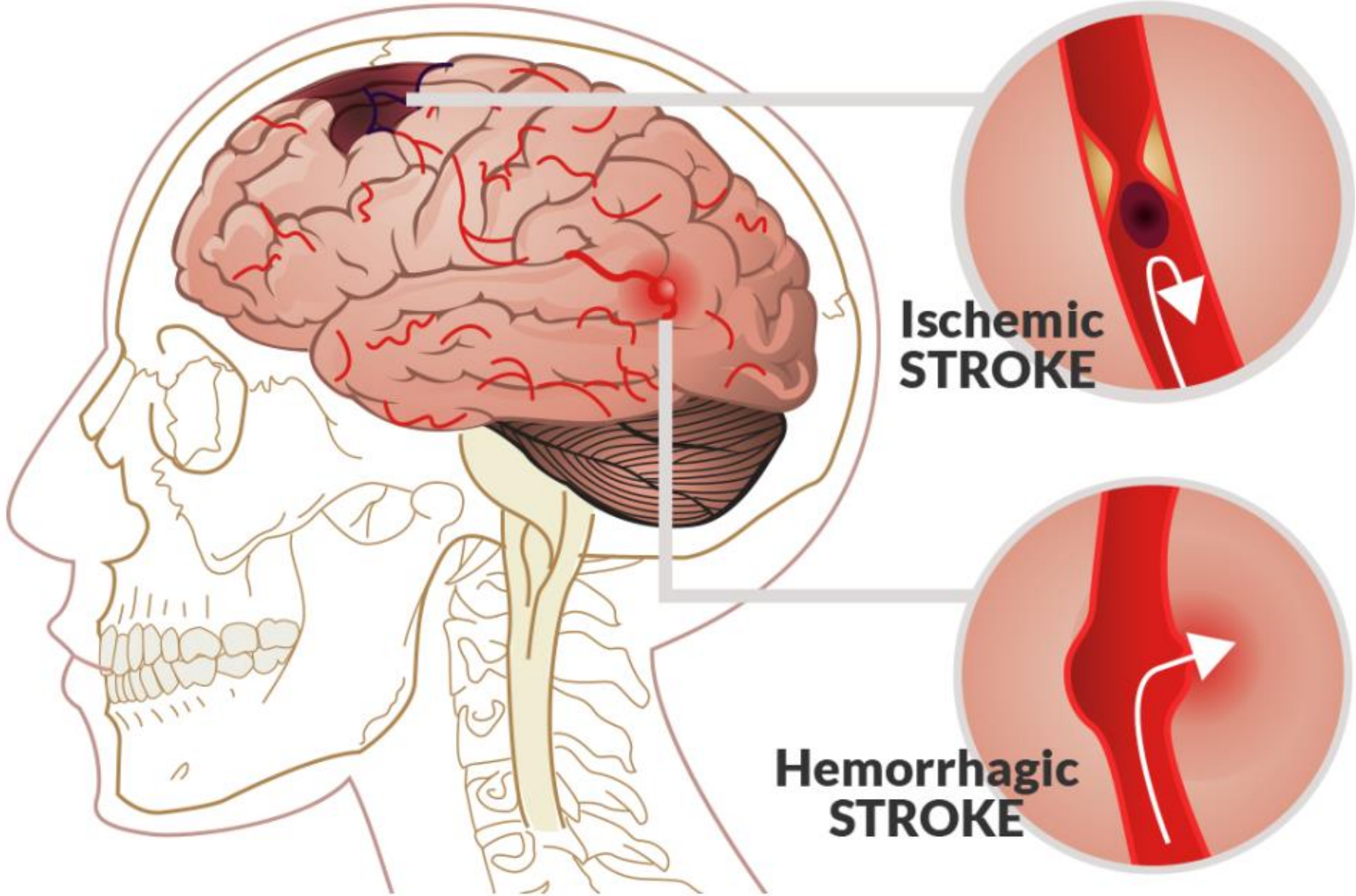
- Stroke: rapidly developing symptoms and signs of loss of focal CNS function lasting for 24 hours or leading to death.
- So: symptoms develop quickly (within seconds or minutes) but they persist for at least 24 hours.
- If the symptoms last for less than 24 hours, it is called: transient ischemic attack.

Types of stroke

- THERE ARE TWO TYPES OF STROKE:
- 1. Ischemic stroke caused by vascular obstruction by a thrombus or an embolus
- 2. Hemorrhagic stroke caused by vessel rupture secondary to several vascular diseases, like hypertension or vasculitis.

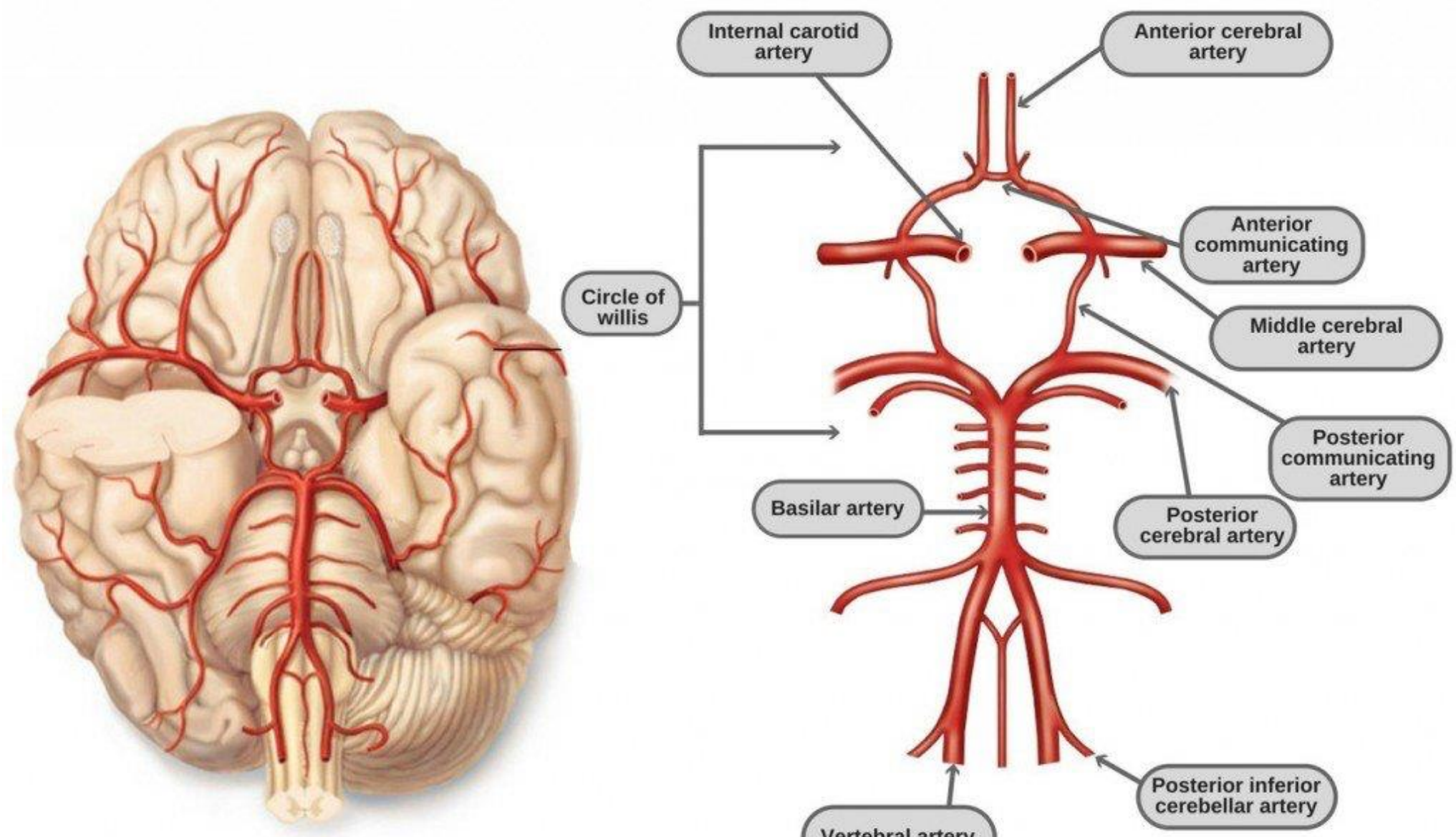
- Ischemic strokes account for 85% of strokes.

- It’s very important to distinguish between the two types because ischemic stroke is treated by anticoagulants, whereas if you use anticoagulants in hemorrhagic stroke you might kill the patient



BRAIN **STROKE**

Brain blood supply



Ischemic stroke : 1. Thrombotic occlusions

- Atherosclerosis of cerebral arteries causing thrombosis.

  <u>Common sites:</u>

1. Carotid bifurcation
2. Origin of middle cerebral artery
3. Ends of basilar artery

Ischemic stroke; 2. 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
- 3. **venous** thrombi crossing to arterial circulation through cardiac defects = paradoxical embolism.. DVT, fat emboli

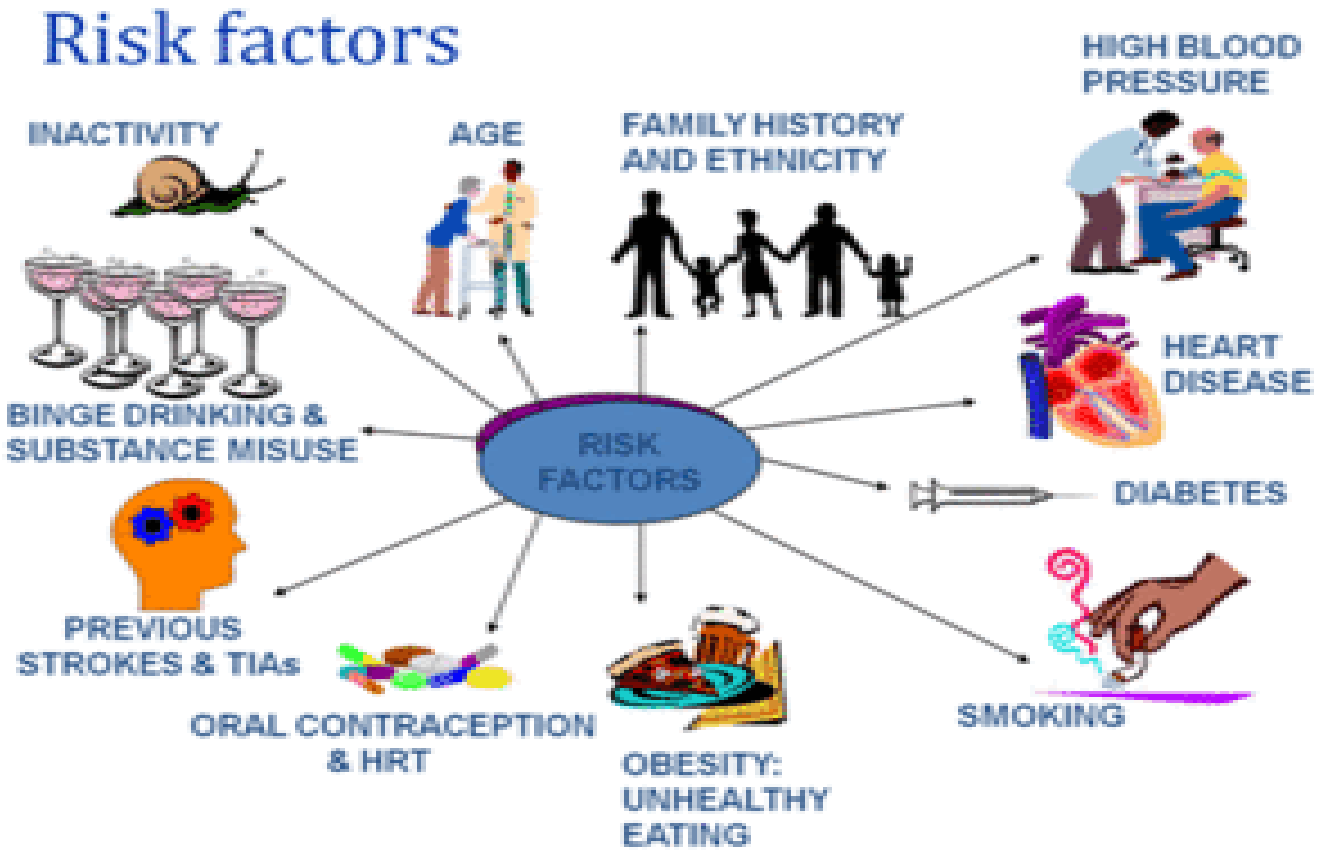
- Most common site of embolic occlusion : middle cerebral artery, a direct extension of the internal carotid.
- Emboli lodge where vessels **branch** or in **stenotic** areas caused by atherosclerosis

Hemorrhagic stroke causes hemorrhagic infarcts

- Can be caused by haemorrhage from a ruptured vessel.
- OR are due to reperfusion through collaterals or after dissolution of emboli.

- Causes of haemorrhage will be discussed in the next lecture.

Stroke: risk factors; basically these are the same risk factors of atherosclerosis



Clinical features of stroke

- **Signs and symptoms= FAST**
- The main symptoms of stroke can be remembered with the word FAST: Face-Arms-Speech-Time.
- **Face** – the face may have dropped on one side, the person may not be able to smile or their mouth or eye may have dropped.
- **Arms** – the person with suspected stroke may not be able to lift both arms and keep them there because of arm weakness or numbness in one arm.
- **Speech** – their speech may be slurred or garbled, or the person may not be able to talk at all despite appearing to be awake.
- **Time** – it is time to dial emergency team immediately if you see any of these signs or symptoms.

Stroke –
there's treatment if you act FAST.

F*ace* Face look uneven?

A*rm* One arm hanging down?

S*peech* Slurred speech?

T*ime* Call 911 NOW!

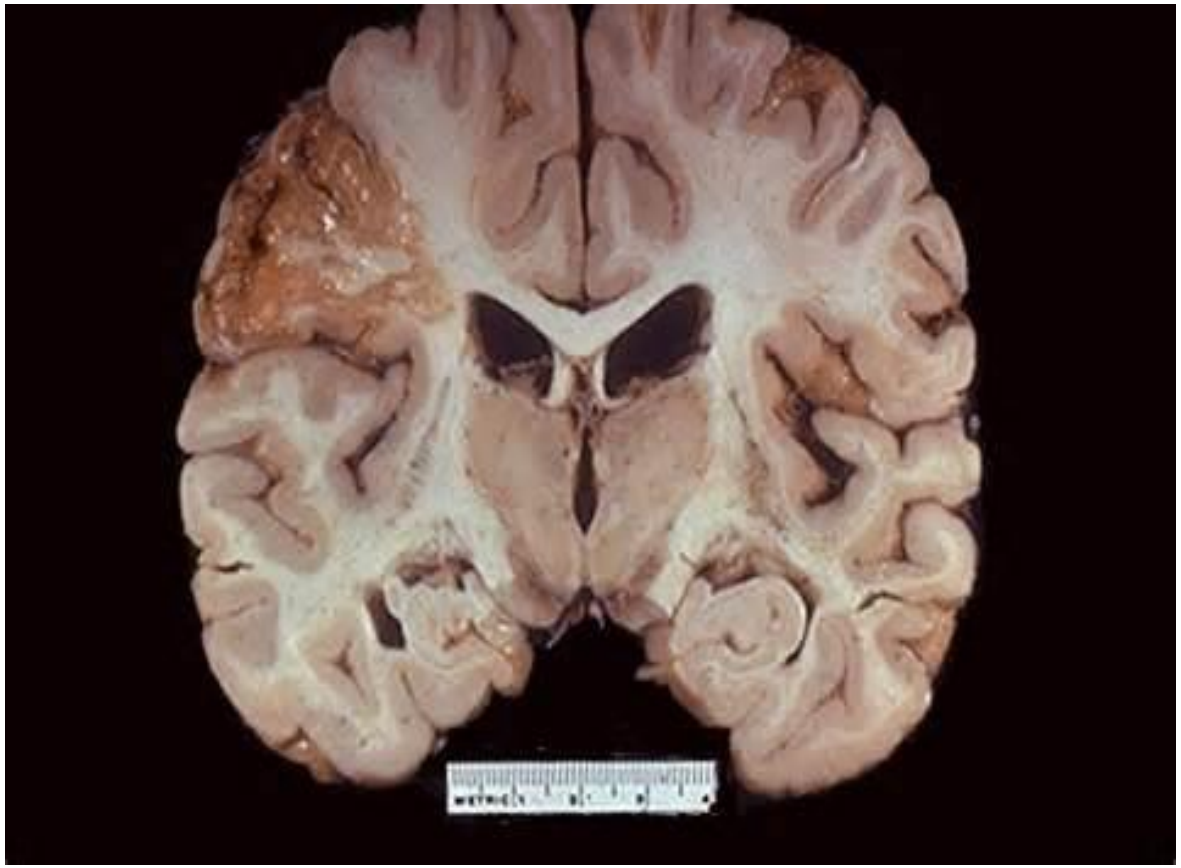
Transient ischemic attack (TIA),

- Sometimes, stroke is preceded by transient ischemic attacks TIA.
- These are important to be recognized clinically because they are a warning sign that a full-blown stroke is imminent
- TIA means that the supply of blood to the brain is temporarily interrupted, causing a "mini-stroke" often lasting between 30 minutes and several hours.
- TIAs should be treated seriously as they are often a warning sign that there is risk of having a full stroke in the near future

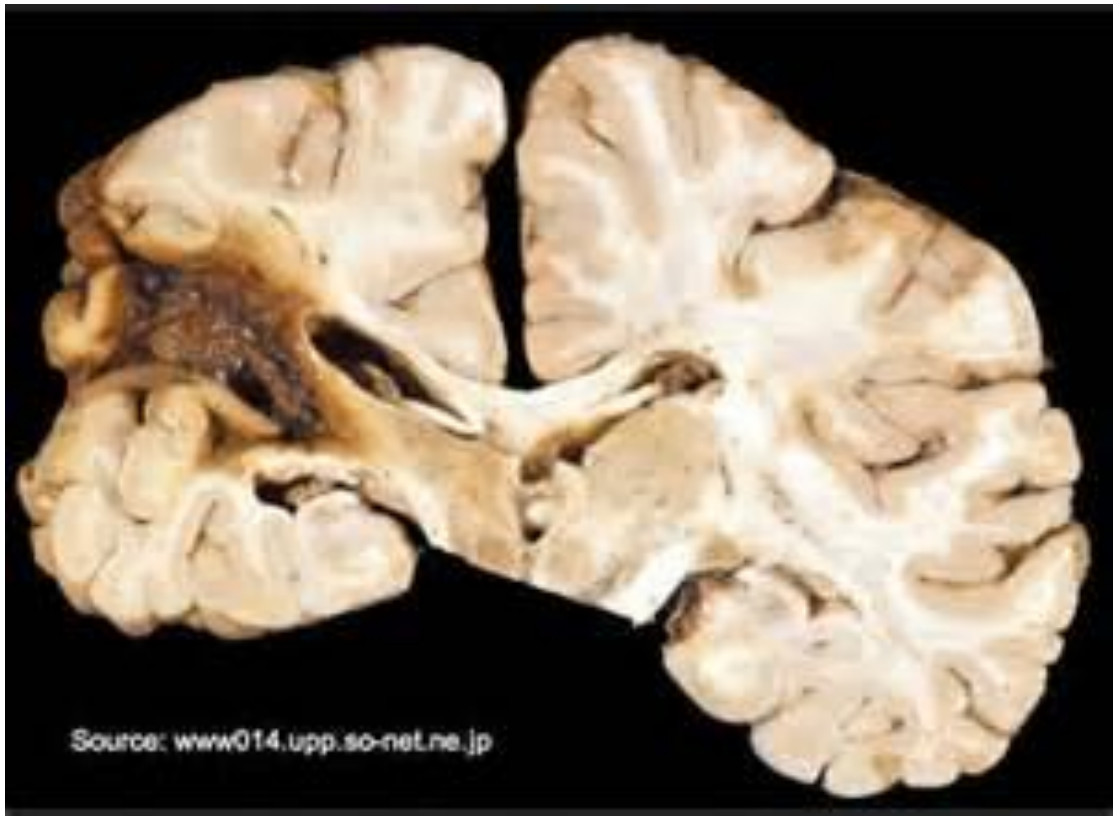
- # Morphology/ non-haemorrhagic infarcts macroscopic appearance

- 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.

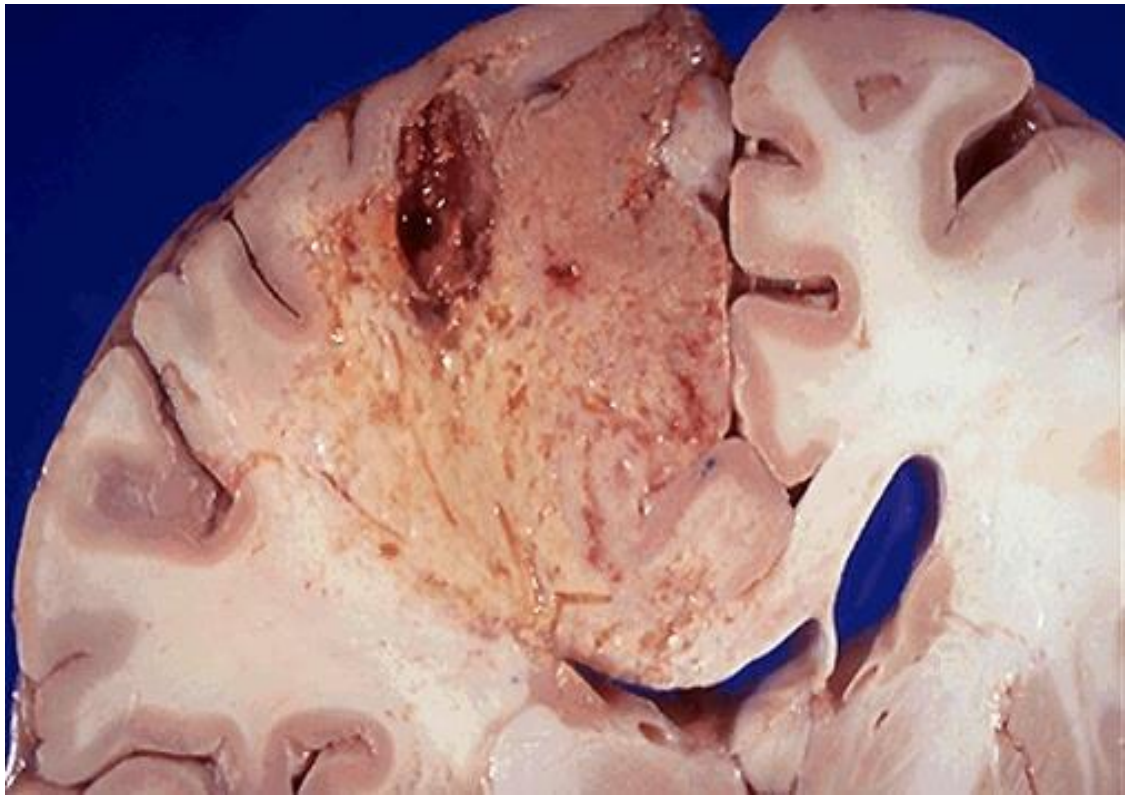
Infarct



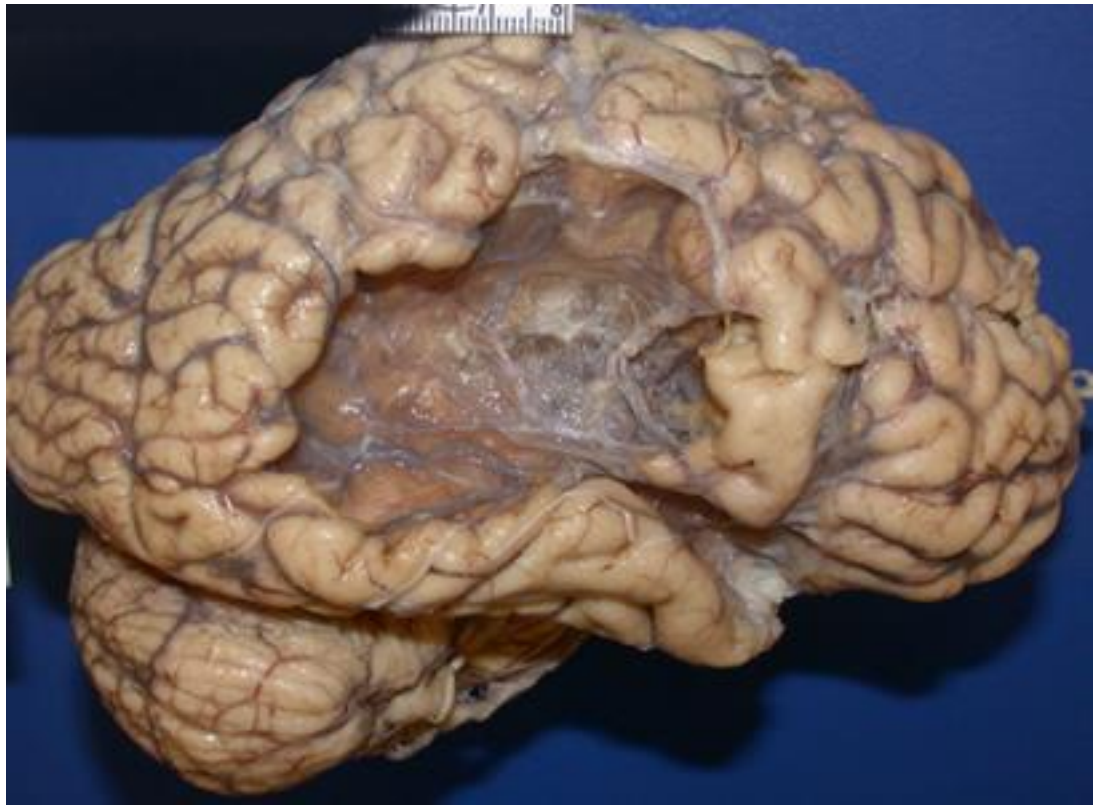
Brain infarct



infarct: note the cavity and liquefaction.
Ischemic damage to the brain causes liquefactive necrosis.



Old infarct: the infarct is resolved leading a cavity.



Morphology / non-hemorrhagic microscopic appearance

- microscopic appearance of brain infarcts is divided into:

- Early changes
- Subacute changes
- repair

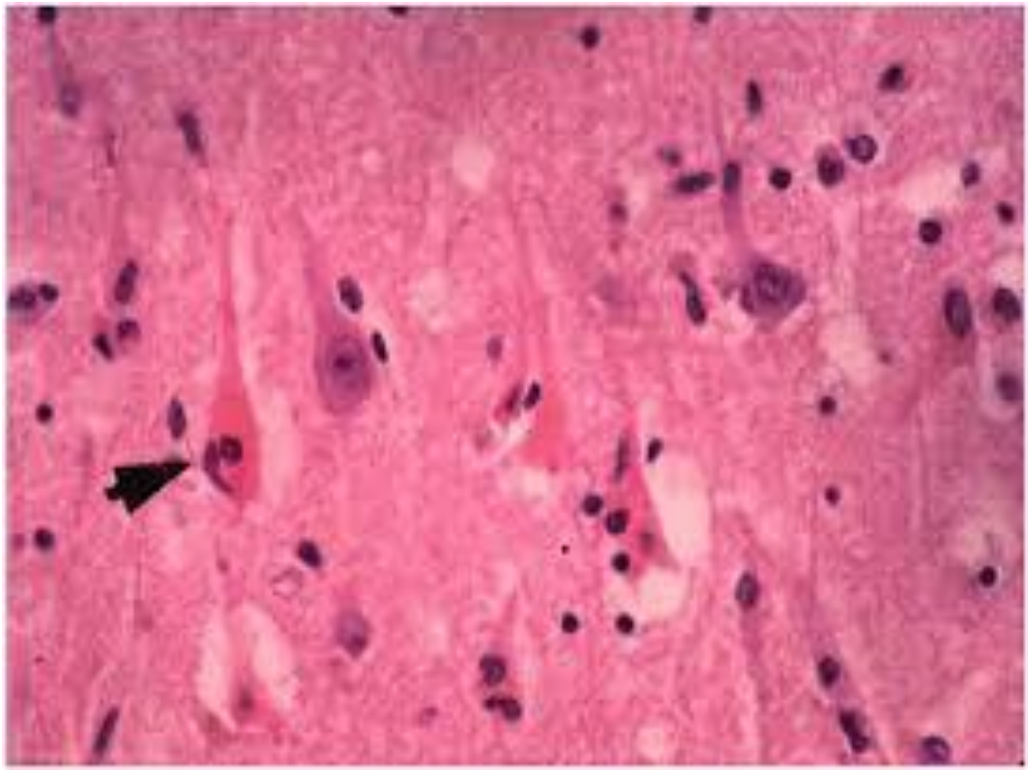
Morphology/ non-hemorrhagic

- early (first 24 hours): red neurons + edema + neutrophils
- subacute (24 hours to 2 weeks): macrophages, gemistocytic astrocytes.
- repair (after 2 weeks): gemistocytes regress, cavity persists

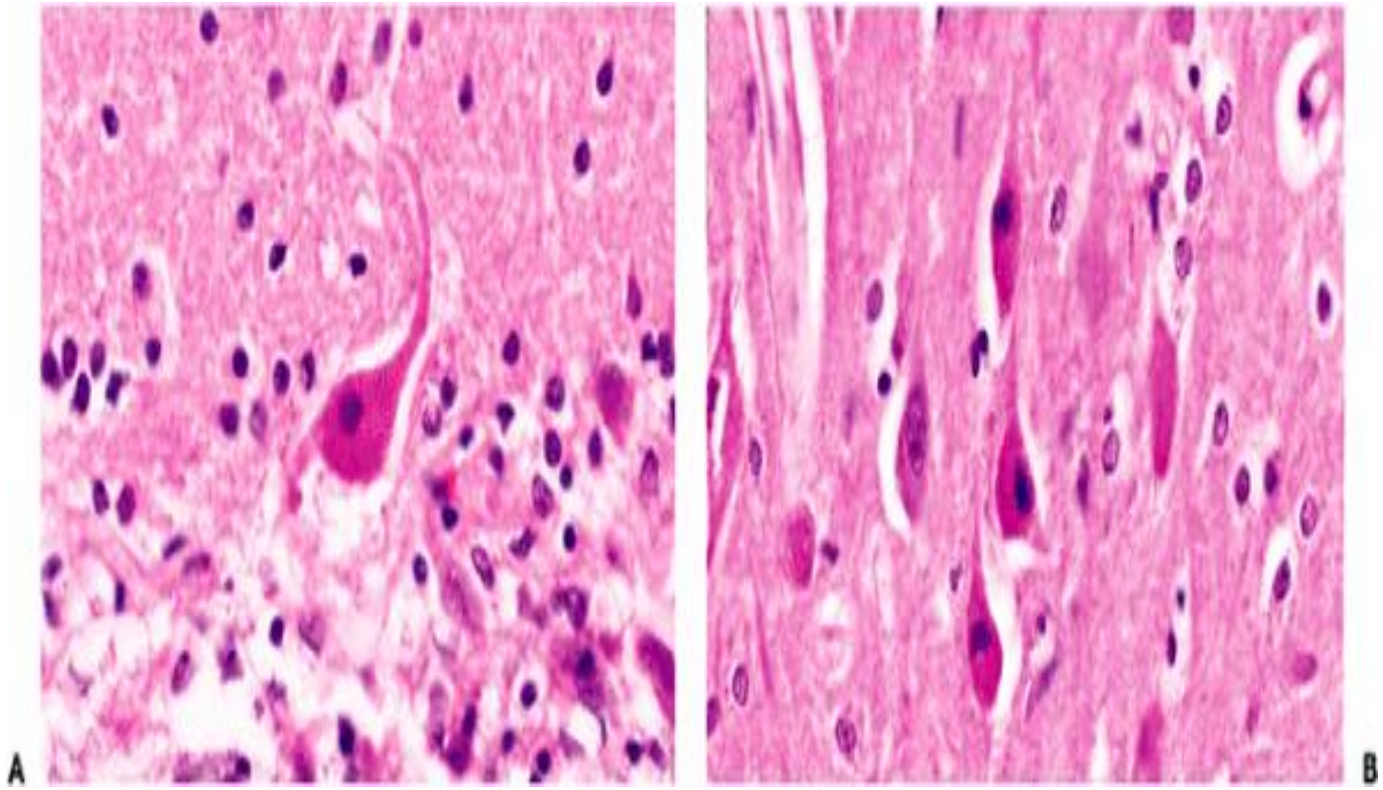
Early changes

- Acute neuronal cell damage= red neurons ,followed by cytoplasmic eosinophilia then pyknosis and karyorrhexis
- Similar changes later on glial cells
- Then: neutrophilic infiltrate.

Red neurones



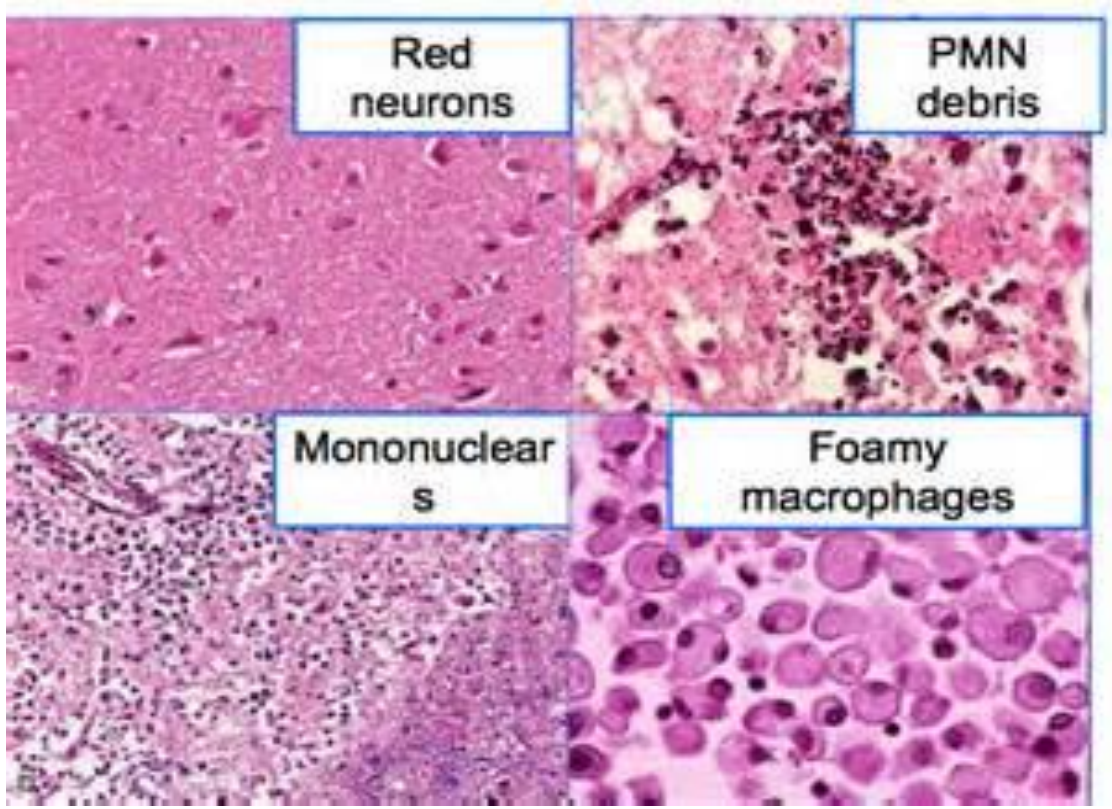
Red neurones



Subacute change

24 hours to 2 weeks

- Necrosis
- Macrophages
- Vascular proliferation
- Reactive gliosis


Red neurons
PMN debris
Mononuclear s
Foamy macrophages

Repair

- After 2 weeks
- Removal of necrotic tissue
- Gliosis
- Loss of organised CNS structure

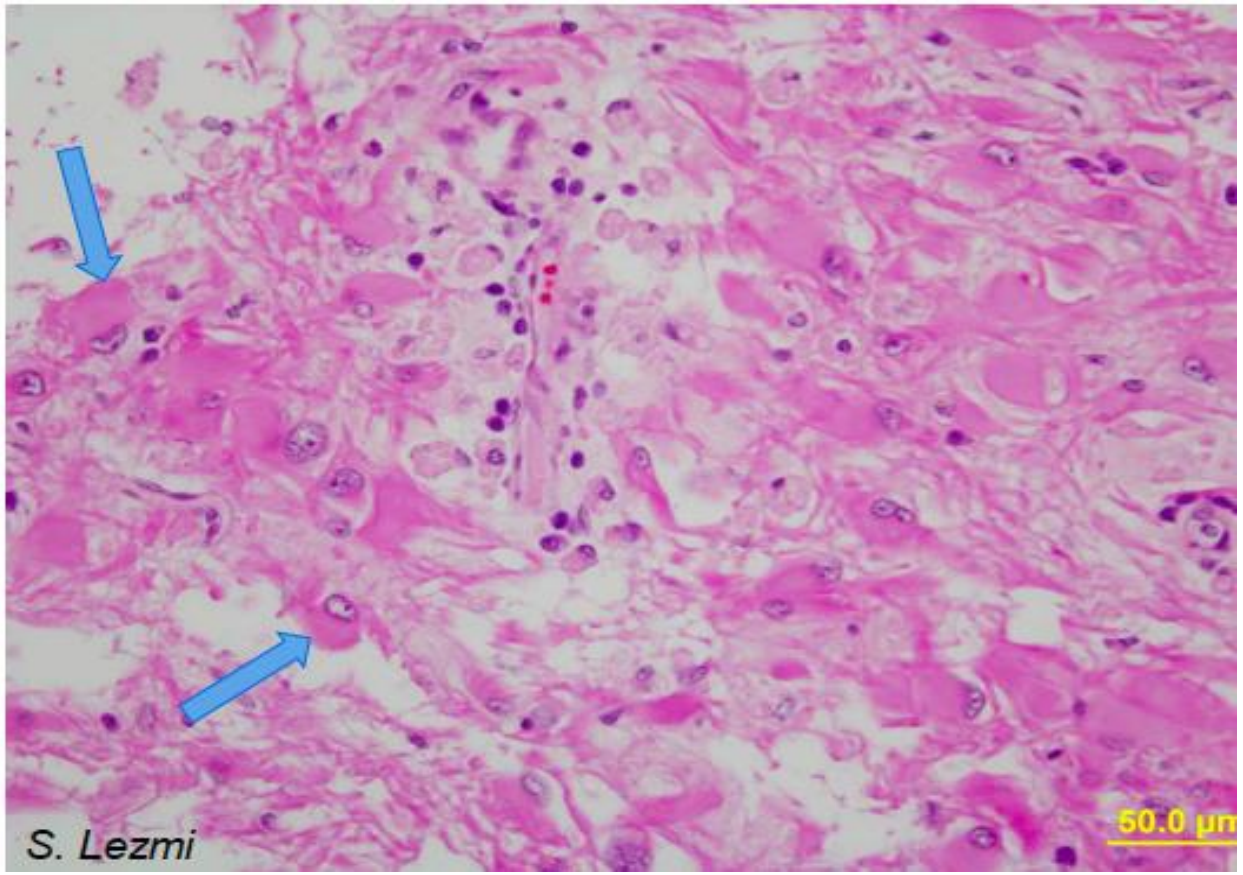
repair

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

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

These changes in astrocytes: gemistocytic astrocyte.

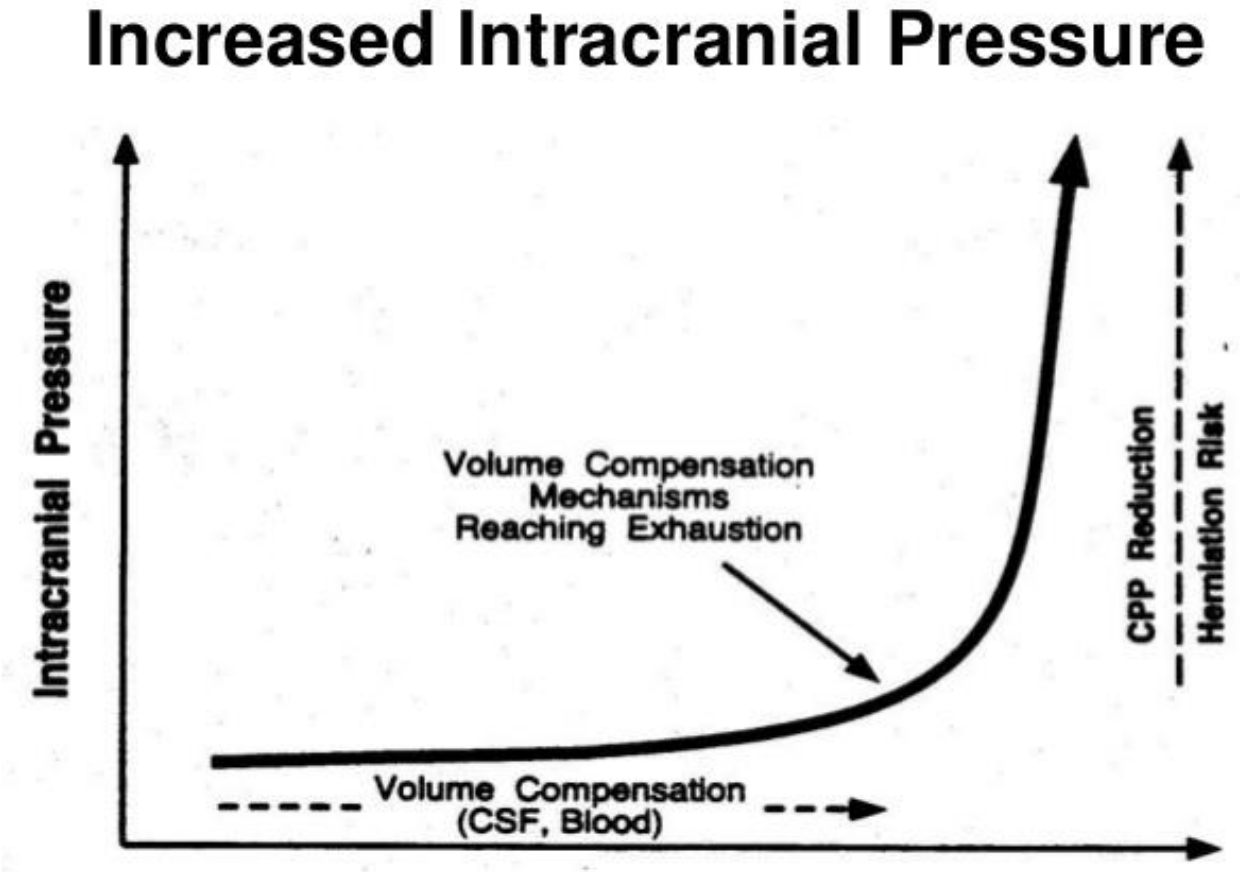
gemistocytes



Summary regarding Stroke.

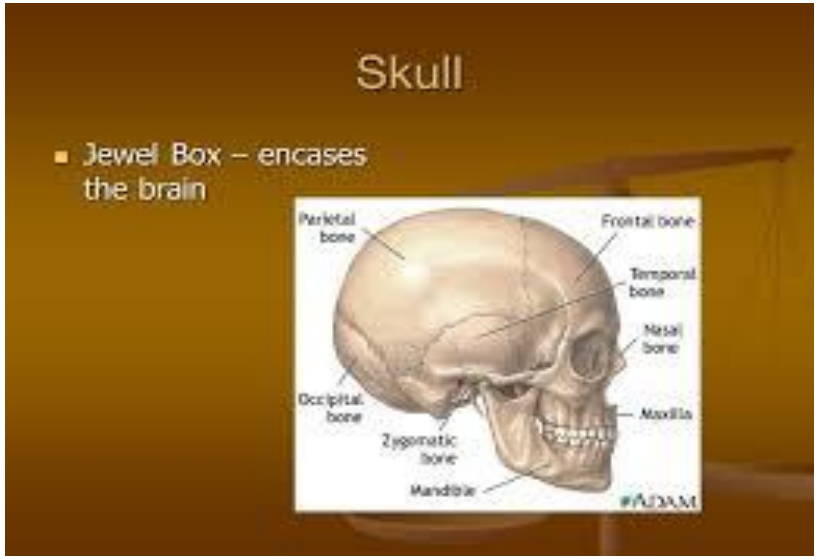
- Stroke = CVA, is a clinical term describing acute neurological symptoms caused by vascular disease.
- stroke can be ischemic or hemorrhagic. Ischemic is commoner
- Ischemic stroke can be embolic or thrombotic. Embolic is commoner.
- Most common site of embolic occlusion is the middle cerebral artery.
- Ischemic strokes might be preceded by TIA= vascular occlusion causing symptoms lasting from minutes to several hours.
- TIAs predict a full stroke and should be treated promptly.
- Ischemic infarcts in the brain cause liquefactive necrosis.
- in the acute stage we see red nuclei and neutrophilic infiltrate
- in subacute stage we see macrophages ,gemistocytes and gliosis.
- in the late stages, gemistocytes disappear leaving a cavity behind.

Intracranial pressure



The cranium..

- The brain is enclosed within the skull, which is a rigid box that protects it.
- In adults, skull bones cannot expand
- So if the material within the cranium increases.. Pressure will increase= increased intracranial pressure



What's inside the cranium?

- ROUGHLY:
- 80% brain tissue (including intracellular and interstitial fluid which is around 75% of brain weight)
- 10% blood
- 10% CSF (cerebrospinal fluid)

If any of these components increases, the intracranial pressure increases.

Monro- Kellie hypothesis

- Monro- Kellie hypothesis: intracranial volume= V_{CNS} +V_{CSF} + V_{Blood} + V_{lesion}
- V= volume.

- This hypothesis indicated that any space occupying lesion in the brain will increase the volume inside the cranium and this will result in increased intracranial pressure.
- Space occupying lesions occur with all major brain diseases (except degenerative diseases). Examples: brain tumours, trauma, stroke, haemorrhage.

OK, so what is intracranial pressure (ICP)???

- It is the pressure inside the skull and is measured in millimetres of mercury
- at rest, it is normally 7–15 mmHg for a supine adult.

- **If pressure in the cranium is higher than this upper limit= increased intracranial pressure (= intracranial hypertension.**

Causes of increased intracranial pressure

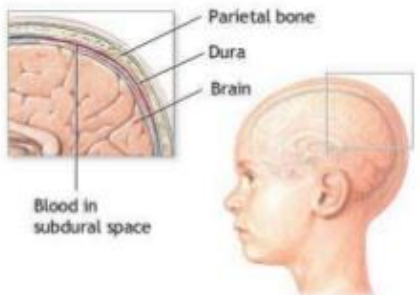
- Mass effect : brain tumor, hematoma, or abscess.
- Generalized brain swelling :ischemia, hypertension
- Increase in venous pressure : heart failure
- Obstruction to CSF flow and/or absorption or increased CSF production: hydrocephalus.
- Idiopathic or unknown

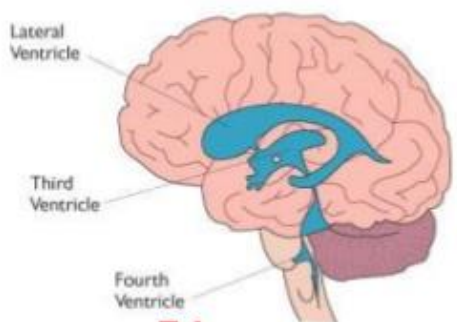
- In this lecture we will discuss two of the causes of increased ICP : ischema and hydrocephalus

Increased Intracranial Pressure

- ✓**Causes**
  - ✓Tumors
  - ✓Accumulation of fluid within the ventricular system
  - ✓Bleeding
  - ✓Edema in cerebral tissues

- ✓**Early signs and symptoms are often subtle and assume many patterns**





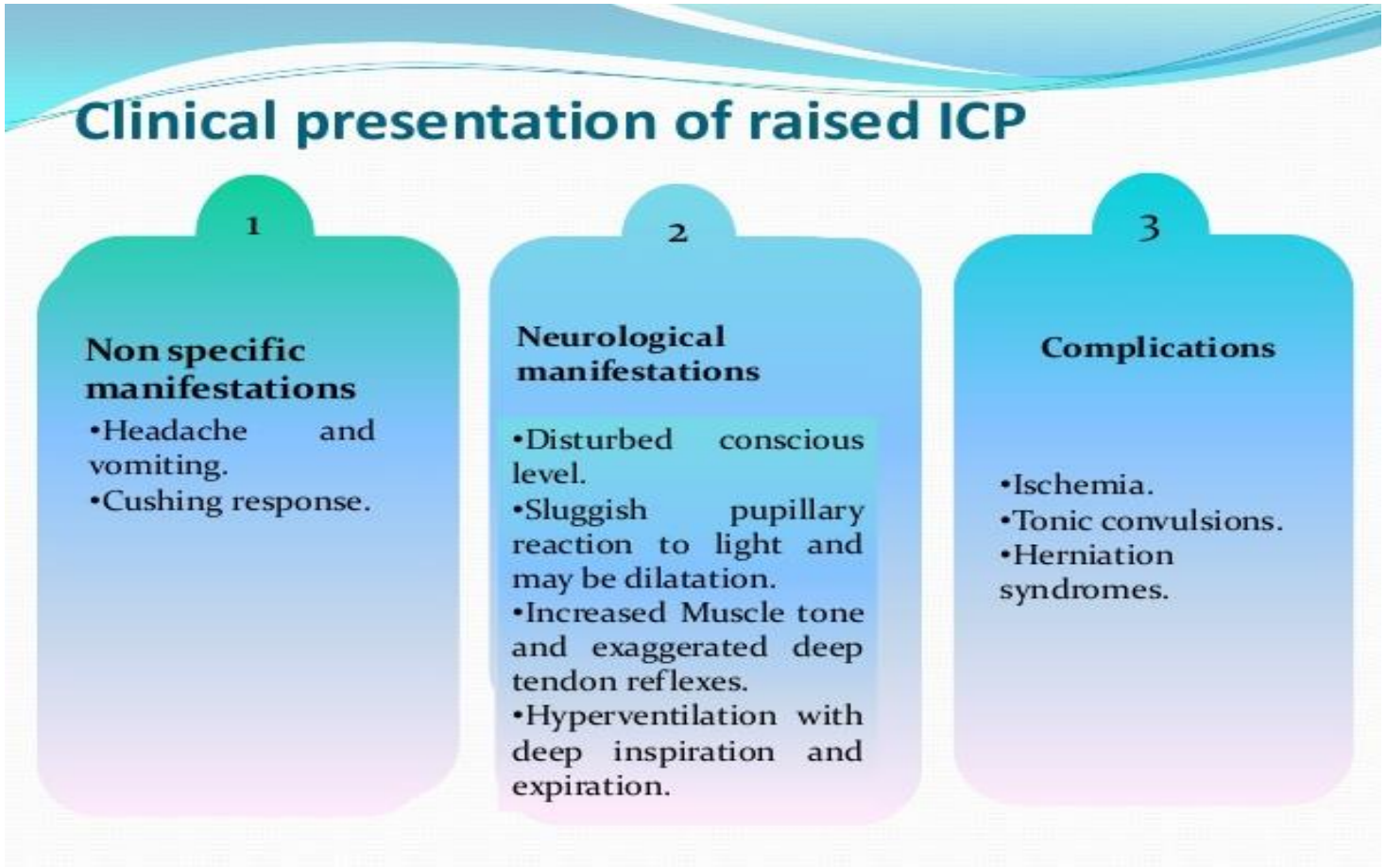
Clinical presentation of increased intracranial pressure.

- In the early stages patients will have non specific symptoms like headache and vomiting.
- Also in the early stages patients might have Cushing reflex (Cushing response or Cushing triad) which manifests by: increased blood pressure, bradycardia and irregular breathing.

- In more advances cases patients have neurological manifestations including disturbed level of consciousness.

- Later, complications can occur, mainly herniation and seizures.

clinical presentation according to severity:



Brain edema= cerebral edema

- = accumulation of excess fluid within the brain parenchyma.
- Two types: vasogenic and cytotoxic edema.. Usually coexist

Vasogenic edema

- Due to disruption of blood brain barrier.
- So: shift of fluids from vessels to brain tissue.
- Lymphatic vessels are rare in the brain.. So there is little or no resorption of excess edema fluid.
- Can be generalised (due to hypoxia) or localised (due to inflammation or tumors)

Cytotoxic edema

- Due to neuronal or glial cell membrane injury.
- Causes: toxins or hypoxia.
- Here fluid moves from cells to interstitial tissue.

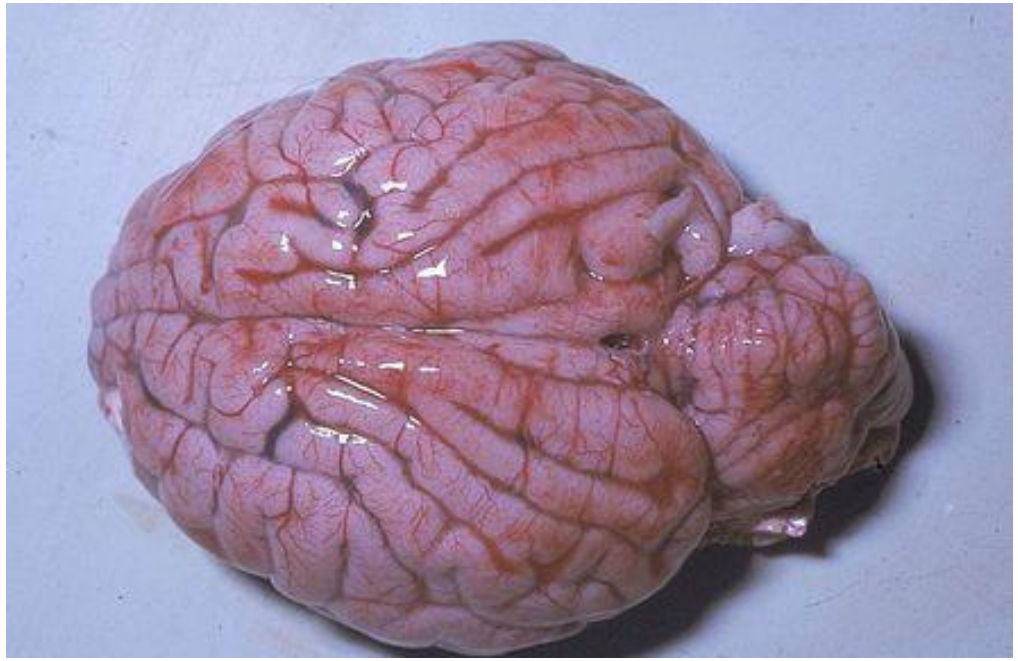
Morphology

- With edema, the brain becomes swollen.. And its weight increases.

- The normal adult human brain weighs on average about **1.2-1.4 kg** ,or about 2% of total body weight, although there is substantial individual variation.

- Edema causes flat gyri and narrow sulci

Brain edema: note that the distinction between gyri and sulci is diminished because the sulci are filled with fluid making them narrow and the gyri are widened by the fluid



hydrocephalus

- Increased CSF within ventricles.
- Caused by overproduction or decreased resorption of CSF.
- Overproduction: rare, due to choroid plexus tumors.
- Decreased resorption.. Can be localised or generalised.

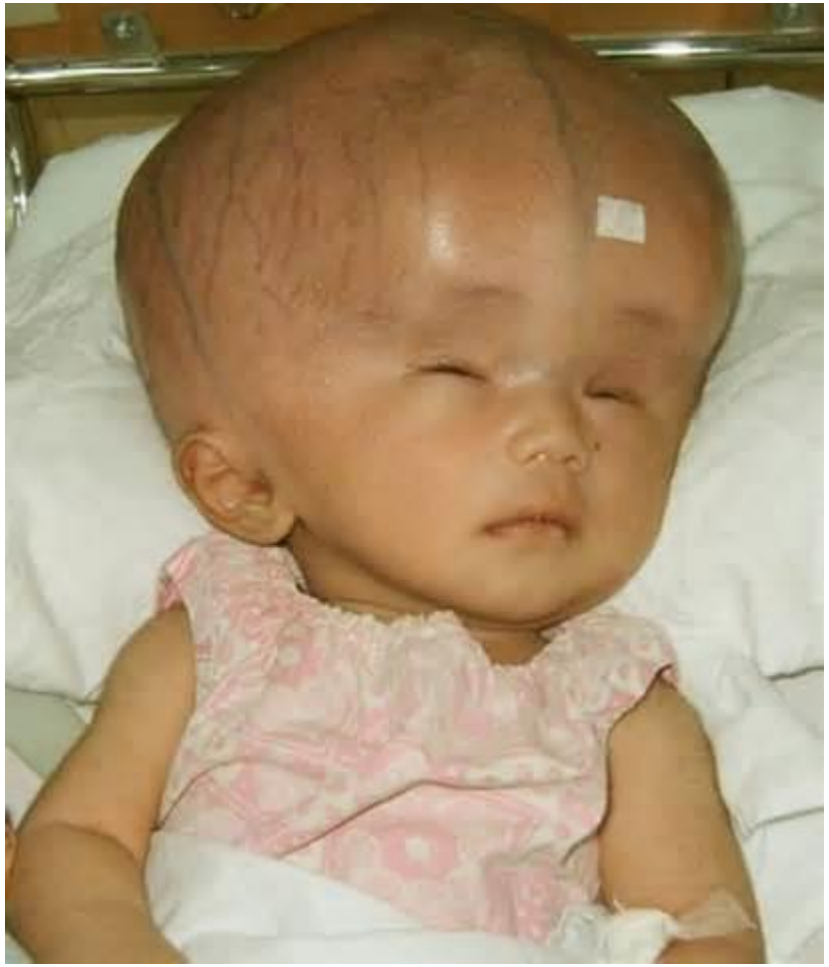
hydrocephalus

- Localised: noncommunicating hydrocephalus.

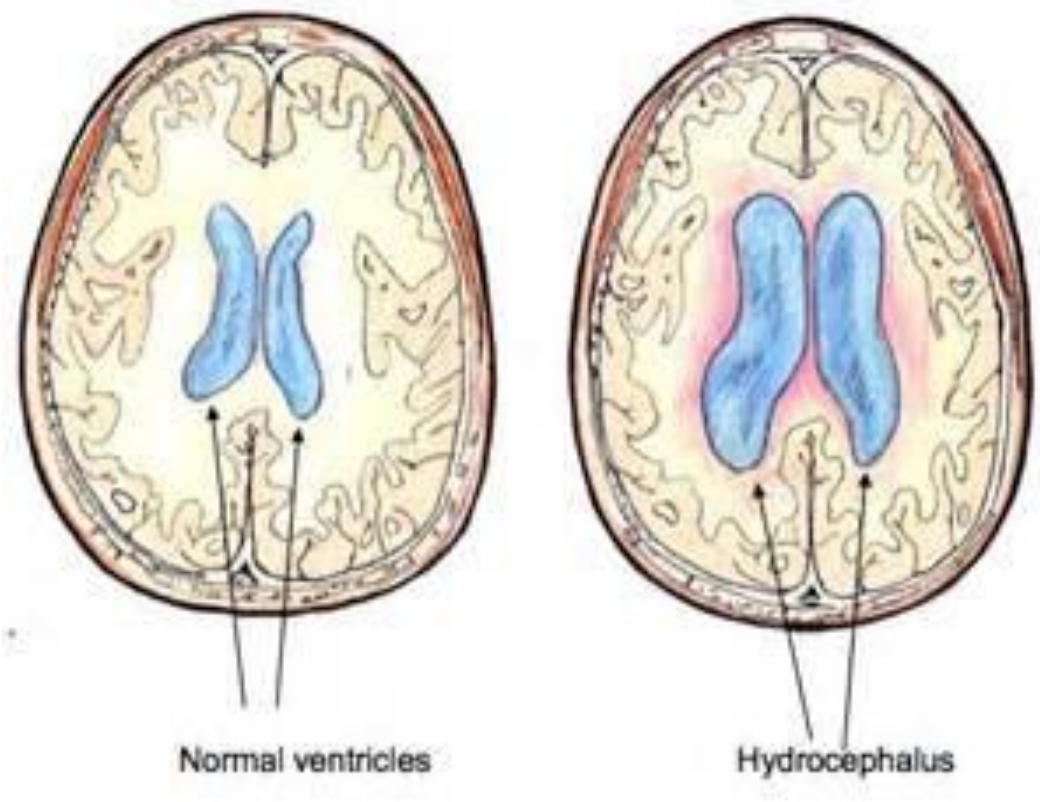
- Generalised: communicating hydrocephalus.

- In infancy, before closure of the cranial sutures , the head can enlarge. Note that complete closure of the skull bones occurs between 18 - 24 months of age.
- After closure of the cranial sutures: increased intracranial pressure occurs. Of course there is no increase in head circumference

hydrocephalus in children: head circumference increases



hydrocephalus: increased CSF within ventricles.



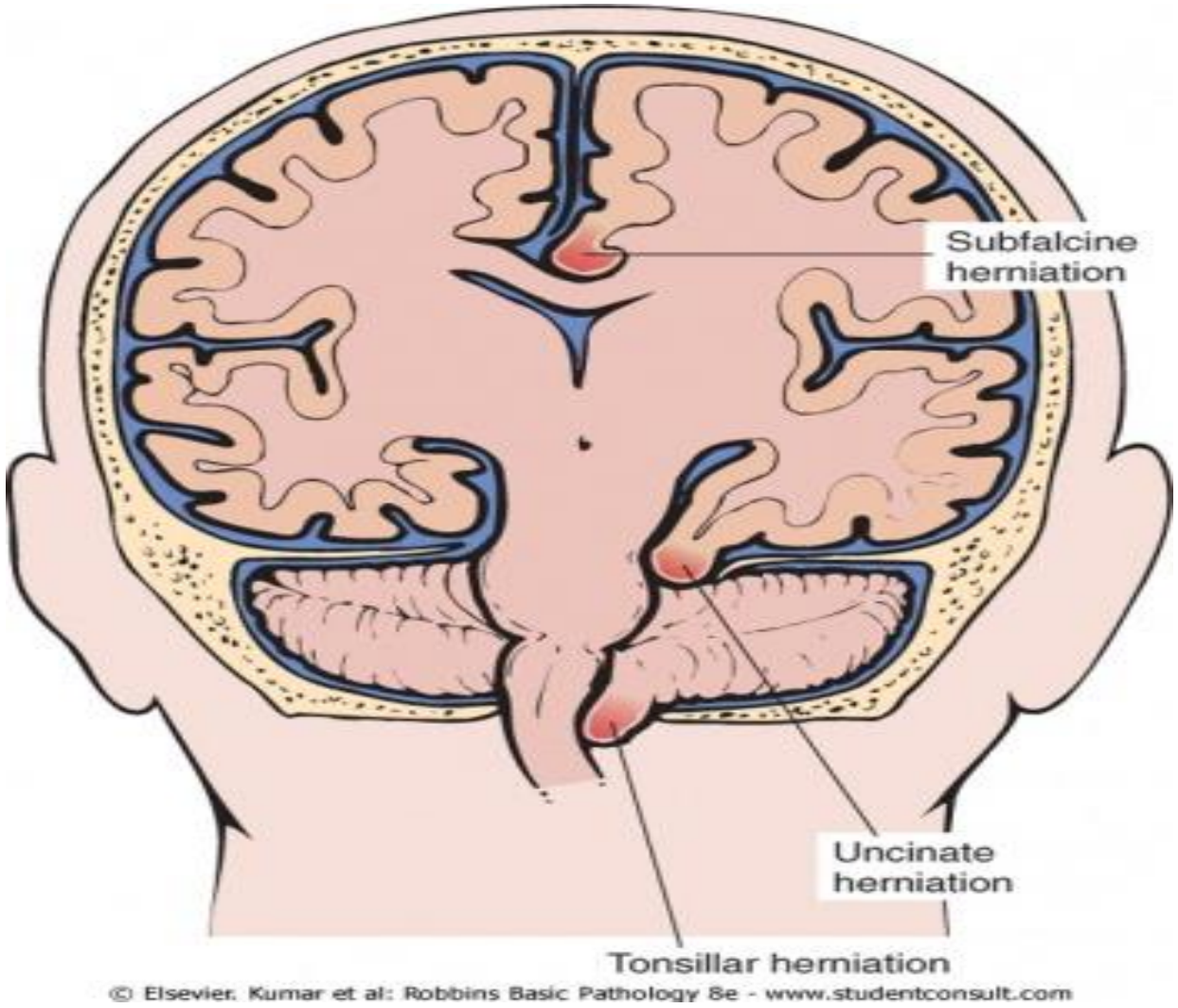
Herniation : a complication of brain edema and hydrocephalus

- Increased volume of tissue inside the skull causes Increased intracranial pressure which causes focal expansion of the brain tissue .
- Because the cranial vault is subdivided by rigid dural folds (falx and tentorium)…. The expanded brain tissue is displaced in relation to these folds.
- Expansion= herniation
- SO: herniation is a complication of increased intracranial pressure and it occurs in relation to margins of the dural folds.

herniation: 3 types

- Subfalcine = cingulate
- Transtentorial = uncinate
- Tonsillar.

herniation


Subfalcine herniation
Uncinate herniation
Tonsillar herniation
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Cingulate herniation

-Cingulate gyrus displaced under edge of falx

-Can cause compression of anterior cerebral artery; so the territory supplied by this artery can suffer ischemic damage and infarction if severe.

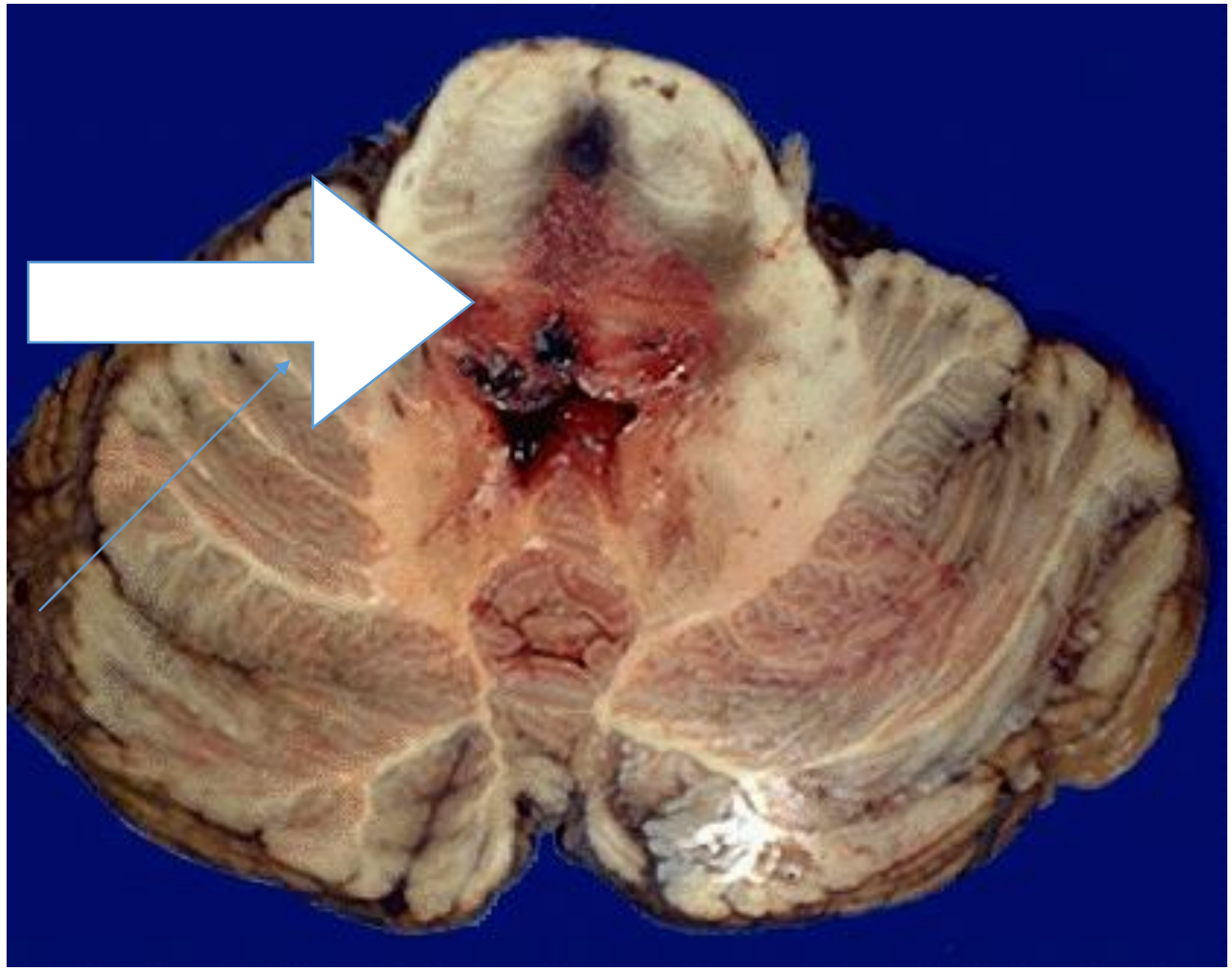
Transtentorial herniation

- Medial aspect of temporal lobe compressed against the free margin of the tentorium.
- so the brain tissue is forced from supra-tentorial towards the infra-tentorial compartment.
- Third cranial nerve compressed.. Dilated pupil, impaired ocular movement on the side of the lesion (ipsilateral side)
- Posterior cerebral artery can be affected.. Ischemic injury to tissues supplied by it including visual cortex.
- **Transtentorial herniation can cause hemorrhage in the midbrain and pons (Duret haemorrhage) which is usually fatal.**

Duret hemorrhage

The end result of temporal medial lobe (transtentorial) herniation is compression of the brainstem (midbrain and pons) and stretching of small arterial branches to cause Duret haemorrhages

Duret haemorrhages are small lineal areas of **bleeding** in the midbrain and upper pons of the brainstem. They are caused by downward displacement of the brainstem. They are named after Henri **Duret**.



Tonsillar herniation

- Displaced cerebellar tonsils through foramen magnum
- Brain stem compression… respiratory and cardiac centres in medulla compromised.
- LIFE THREATENING

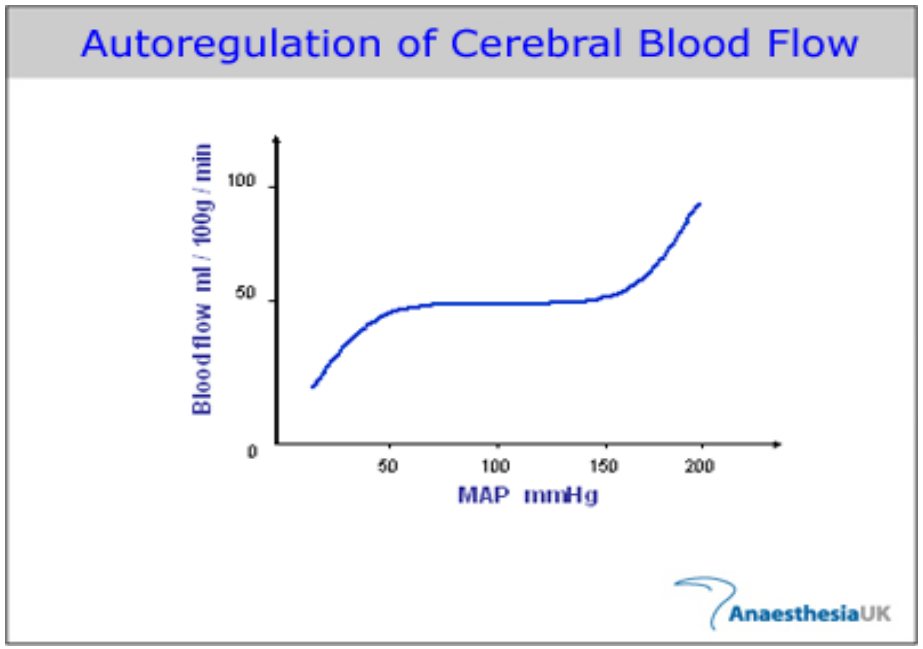
- So far we talked about: edema and hydrocephalus as causes of increased intracranial pressure
- We also discussed herniation as a complication of increased ICP

- The rest of the lecture will discuss hypoxia and ischemia, which are the main cause of generalized cerebral edema.

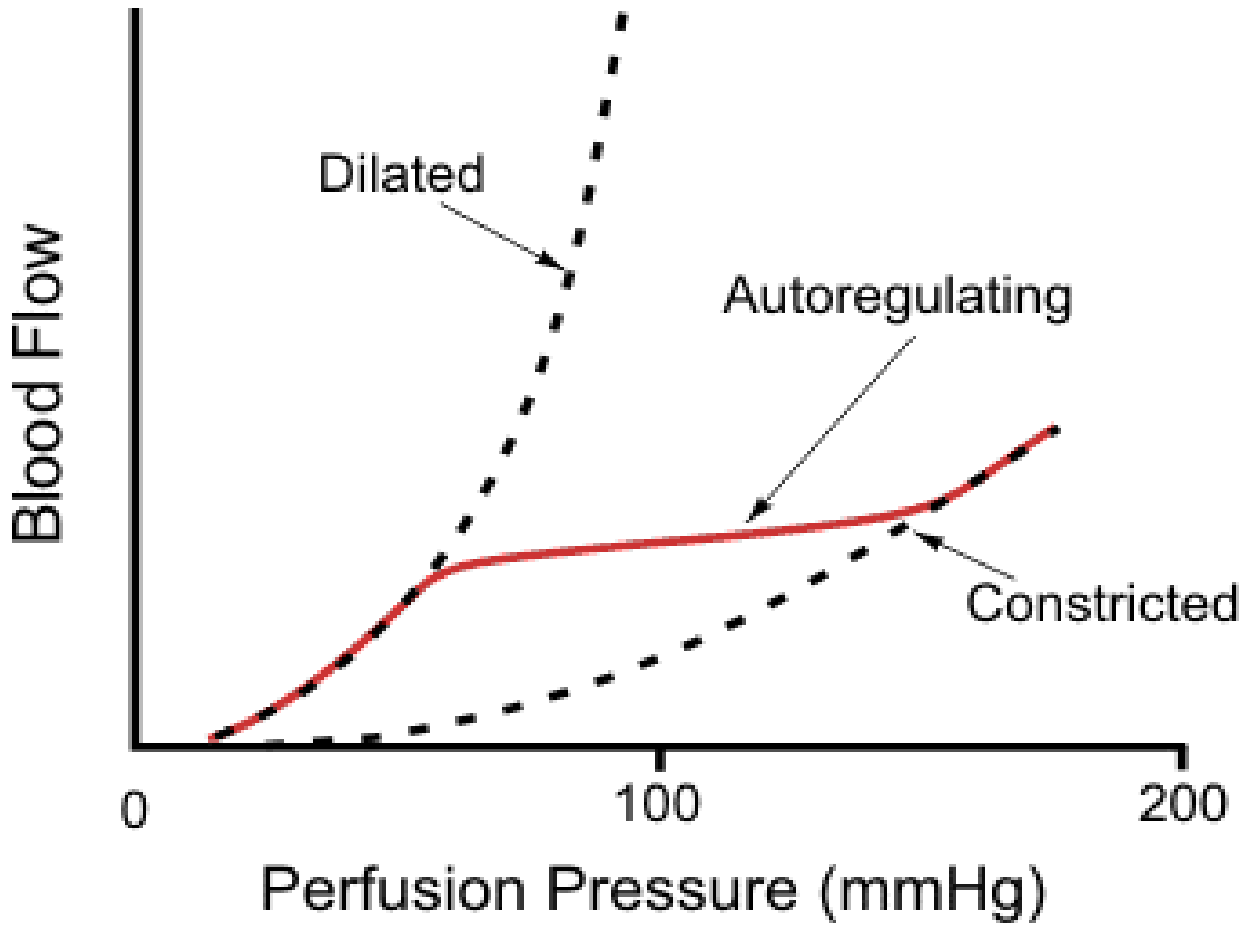
Hypoxia and ischemia

- Brain is highly oxygen dependent.
- Brain weight constitutes 2% of body weight but receives 15% of cardiac output
- 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.
- If blood pressure very low (systolic less than 50)… hypoxia occurs

Auto regulation



- The brain receives the same amount of blood (brain blood flow is constant) if the mean arterial pressure is between 50 - 160 mm Hg.
- If mean arterial pressure is less than 50, the auto regulatory mechanisms fail and the brain blood flow decreases, causing hypoxia.


Blood Flow
Dilated
Autoregulating
Constricted
0
100
200
Perfusion Pressure (mmHg)

Brain hypoxia

- Functional hypoxia.
- Ischemic hypoxia

Functional hypoxia

- Low partial pressure of oxygen: high altitude
- Impaired oxygen carrying capacity: anaemia and CO poisoning
- Decreased oxygen use by tissues: cyanide poisoning

Ischemic hypoxia

- Hypo-perfusion due to hypotension or vascular obstruction
- Ischemia can be global or focal
- Focal ischemia causes infarctions (ischemic stroke)and this will be discussed in another lecture.

Global cerebral ischemia

Occurs due to severe hypotension, systolic below 50mm Hg: this occurs in situations like:

- Cardiac arrest
- Shock
- Severe hypotension

- Outcome depends on **severity** and **duration** of insult

Global ischemia

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

ischemia

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

Morphology of reversible global ischemia= brain edema

- Swelling
- Wide gyri
- Narrow sulci
- Poor grey white matter demarcation

Irreversible global ischemia can cause brain death

- Diffuse cortical injury with flat EEG (isoelectric EEG)
- Brain stem damage: No reflexes and no respiration
- If on mechanical support: autolysis of brain= respirator brain.

/

Brain death

- Brain death is different from coma and vegetative state. The latter two are potentially reversible. Death is irreversible.
- So diagnosing brain death needs very strict criteria.. when you diagnose brain death you can discontinue artificial breathing, you can remove organs for donation…etc
- The most accepted religious opinion in Islam is that brain death is accepted as a definition of death, and all religious and legal aspects regarding death apply. However, **we need very strict criteria to separate brain death from its mimickers.**

UK guidelines to diagnose brain death

1. Evidence for Irreversible Brain Damage of known Aetiology.

2. Exclusion of Reversible Causes of Coma and Apnoea

Examples: hypothermia, drugs and alcohol..

3. Tests for Absence of Brain-Stem Function.

LINK FOR FULL GUIDELINES:

https://ficm.ac.uk/sites/default/files/Form%20for%20the%20Diagnosis%20of%20Death%20using%20Neurological%20Criteria%20-%20Full%20Version%20%282014%29.pdf

UK guidelines regarding doctors performing the neurological examination for brain death

1. The diagnosis of death by neurological criteria should be made by at least two medical practitioners. Both medical practitioners should have been registered with the General Medical Council (or equivalent Professional Body) for more than five years and be competent in the assessment of a patient who may be deceased following the irreversible cessation of brain-stem function and competent in the conduct and interpretation of the brain-stem examination. At least one of the doctors must be a consultant.
2. Those carrying out the tests must not have, or be perceived to have, any clinical conflict of interest and neither doctor should be a member of the transplant team.
3. Testing should be undertaken by the nominated doctors acting together and must always be performed on two occasions. A complete set of tests should be performed on each occasion, i.e., a total of two sets of tests will be performed. Doctor One may perform the tests while Doctor Two observes; this would constitute the first set. Roles may be reversed for the second set. The tests, in particular the apnoea test, are therefore performed only twice in total.

Summary 1/2

- The skull protects the brain, but leaves little space to accommodate for any increase of the cranial contents.
- increased cranial contents cause increased intracranial pressure. This can be due to increased brain tissue (tumours), fluid (edema due to hypoxia or inflammation or other causes), CSF (hydrocephalus) or blood (haemorrhage)
- increased ICP manifests as headache and projectile vomiting, Cushing triad (hypertension, bradycardia, irregular slow breathing)) and can progress to coma.
- Brain edema can be vasogenic or cytotoxic. It manifests as increased brain wight with narrow sulci and flat gyri.
- Hydrocephalus is increased CSF due to increased production by a choroid plexus tumour (rare) or more commonly by decreased resorption.it can be localised (non communicating) or generalised (communicating)

Summary 2/2

- increased ICP can be complicated by herniation; which is a displacement of brain tissue from a compartment to another.
- Subfalcian herniation displaces the cingulate gyrus under edge of falx, it causes compression of anterior cerebral artery
- Transtentorial herniation displaces the medial aspect of temporal lobe against the free margin of the tentorium. This compresses the third cranial nerve, posterior cerebral artery and can cause Duret haemorrhage in the midbrain which is usually fatal.
- Tonsillar herniation displaces the cerebellar tonsils through foramen magnum causing brain stem compression, which is usually fatal.
- Hypoxia and ischemia are the main causes of brain edema.
- Autoregulation maintains blood flow but below 50 systolic pressure, flow decreases.
- Pukinji cells and pyramidal cells are the most susceptible to ischemic damage.
- Irreversible ischemia can cause brain death

Question

- A 54 year old man complained of severe headache and vomiting. imaging studies showed a large subdural hematoma. Two days later he had dilated pupil of the right eye with and his visual acuity decreased. Which of the following is incorrect about his condition?
- A. Can be complicated by haemorrhage in the pons.
- B. His eye symptoms could be related to ischemic injury to the visual cortex
- C.The medial aspect of his temporal lobe is compressed against the free margin of the tentorium
- D. The dilated pupil indicated damage of the left third cranial nerve
- E. He might develop fatal brain stem complications.

Answer

- The scenario describes increased ICP due to hematoma. The complications he had indicate herniation, and the symptoms are those of transtentorial herniation.
- the answer is D: the lesion is related to the ipsilateral nerve (at the same side of the lesion).. so his right third cranial nerve is compressed.
- A is correct, it describes Duret hemorrage . Also E is correct , again it describes Duret haemorrhage.
- C :correct, it simply describes his main complication: transtentorial herniation
- D is correct, note that the decreased visual acuity is due to effect on the visual cortex (ischemic damage due to compression on the posterior cerebral artery) , however, the dilated pupil and impaired ocular movement are effects of compression on the third cranial nerve.


شكراً جزيلاً