Cerebrospinal fluid

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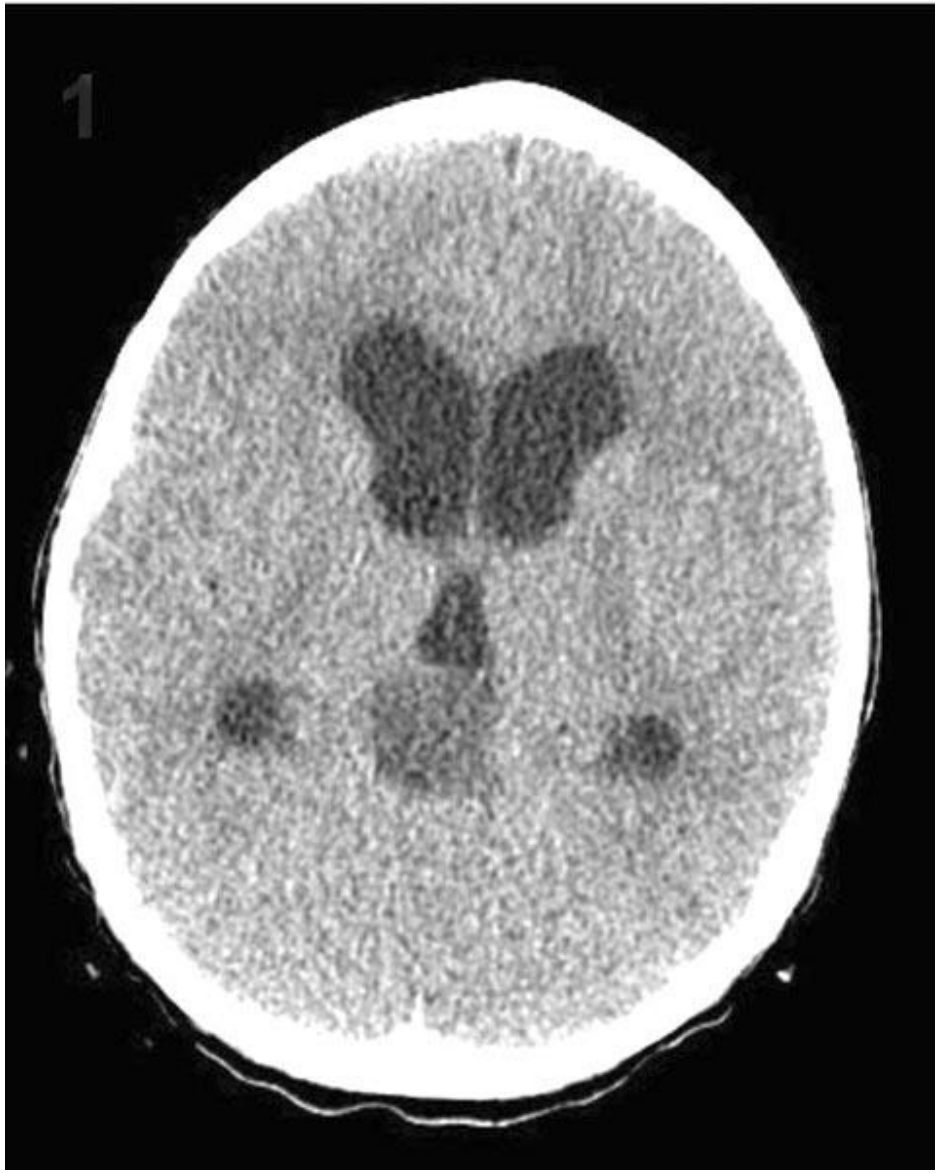
Clinical vignette

- A 6-years-old girl presented with **severe headache** for several days **associated with vomiting, neck stiffness, fever, and unsteady gait.**
- Physical examination was otherwise unremarkable.
- She was recently treated for otitis media approximately one week prior to admission. Mother reported that the patient had frequent headaches and incontinent of bowel and bladder during the past year.

Cont…….

- A lumbar puncture showed **high CSF protein** but no signs of infection.
- Computer Tomography (CT) and Magnetic Resonance Imaging (MRI) of the brain showed obstructive hydrocephalus with a 2.3 cm non-enhancing pineal region mass attached to the tectum.
- MRI of the spinal cord at this time was negative for metastatic disease.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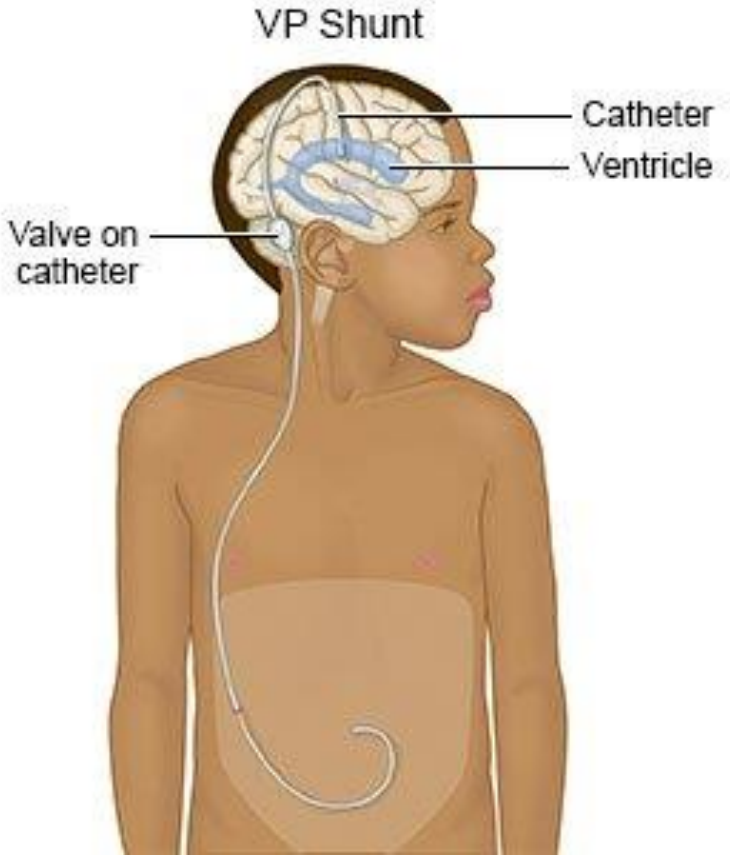

VP Shunt
Catheter
Ventricle
Valve on catheter

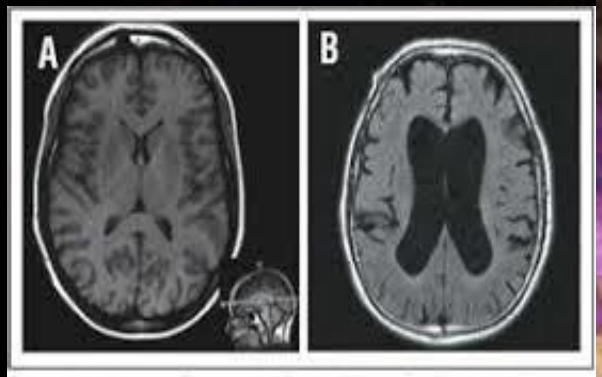


Figure 1. Images of a normal brain (A) and a brain with ventriculomegaly (B).

Learning objectives:

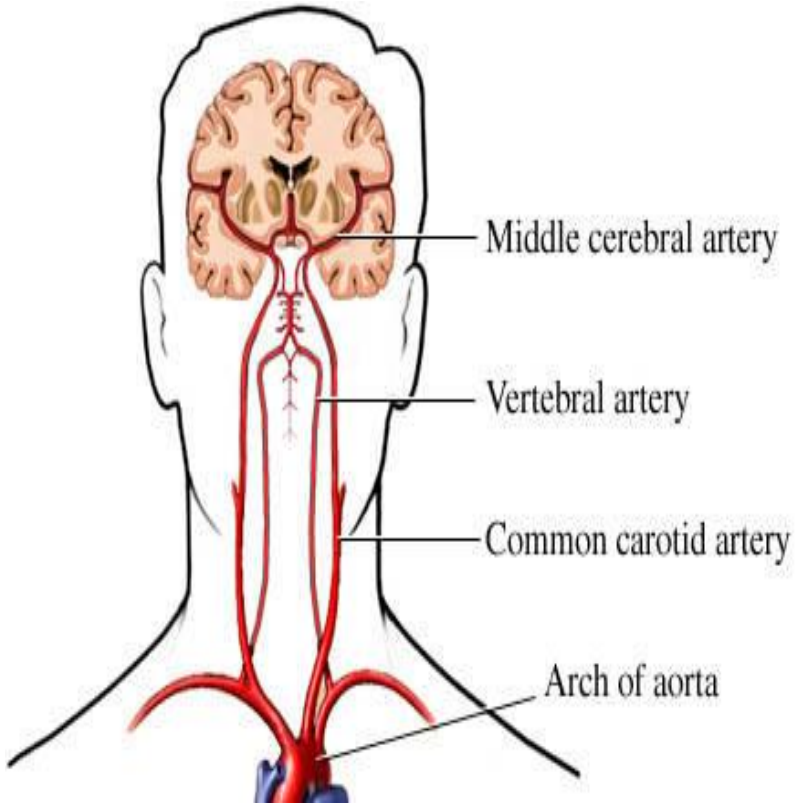
- CSF formation, circulation and functions.
  - Describe regulation of cerebral blood flow.
  - Describe formation, flow, and absorption of cerebrospinal fluid.
  - Describe Blood–Cerebrospinal Fluid and Blood-Brain Barriers.

Blood Flow of Brain

2 Carotid and **Vertebral Arteries** →

CIRCLE OF WILLIS at the base of brain →

Pial arteries → penetrating arteries and arterioles separated from brain by **Virchow Robin Space**



Normal Rate of Cerebral Blood Flow

Normal blood flow in adult brain averages **50 to 65 ml per 100 g of brain tissue per min**

averages to be **750 to 900** ml per min

Brain(2% of body weight**)→** (15% of resting cardiac output)

Regulation of Cerebral Blood Flow

1. ↑ **Carbondioxide** → ↑ blood flow

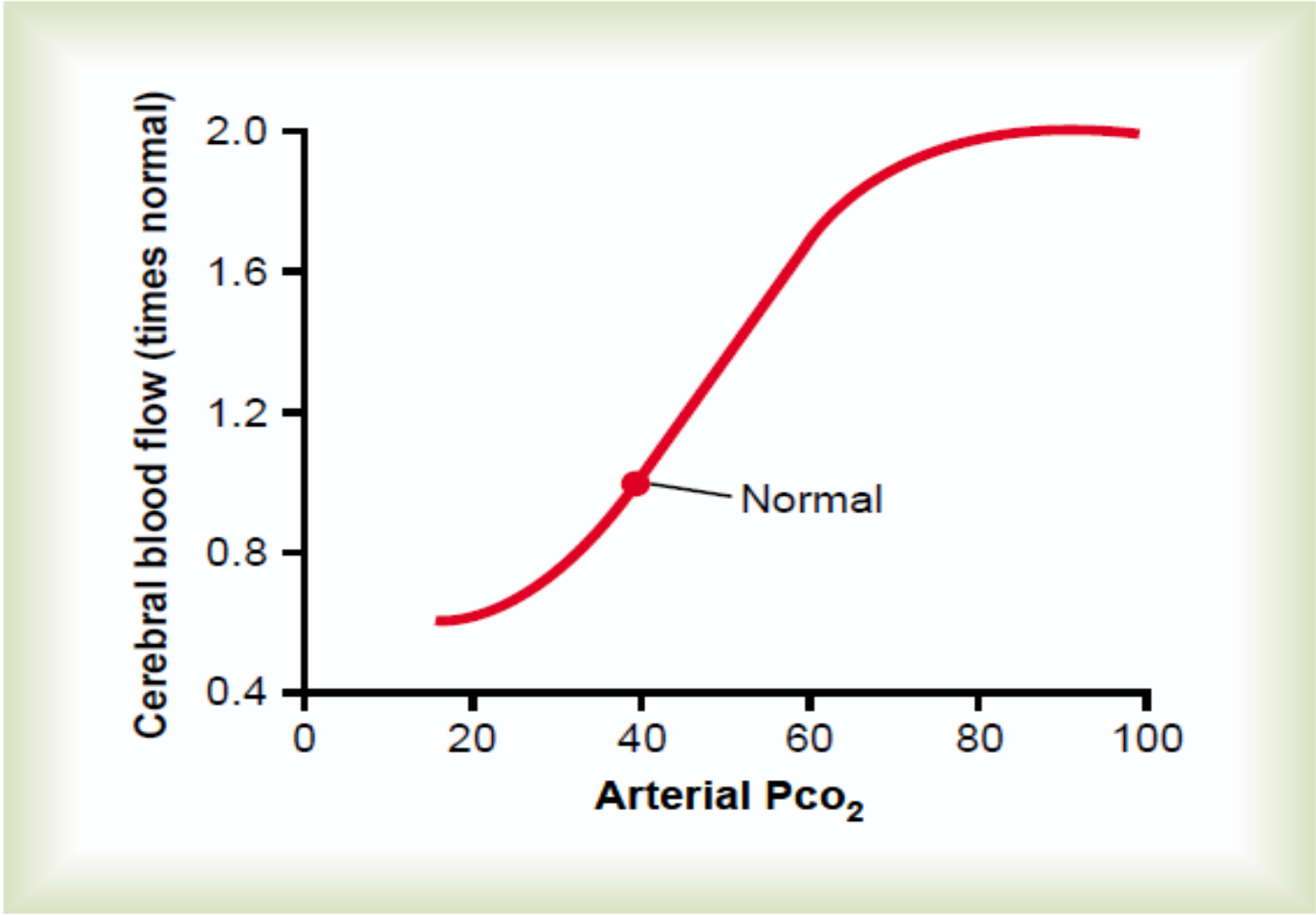
2. ↑ **Hydrogen ion** → ↑ blood flow

3. ↓**Oxygen** levels → ↑ blood flow

Rate of utilization of oxygen is 3.5 ml (± 0.2) per 100 grams of brain tissue per minute

4. Other **Substances released** (Lactic acid, pyruvate acid, any other acidic material & metabolites etc → vasodilation

Relationship Between Arterial PCO2 And Cerebral Blood Flow



Importance Of Blood Flow Control By CO_2 And H^+

Increased H^+ → ↓ Neuronal activity ↑ blood flow → carrying H^+ and CO_2 and other acid forming substances away from brain tissue.

Loss of CO_2 removes Carbonic acid and other acids → H^+ back to normal and thus maintain normal level of Neuronal activity

Effect Of Brain Activity On Blood Flow

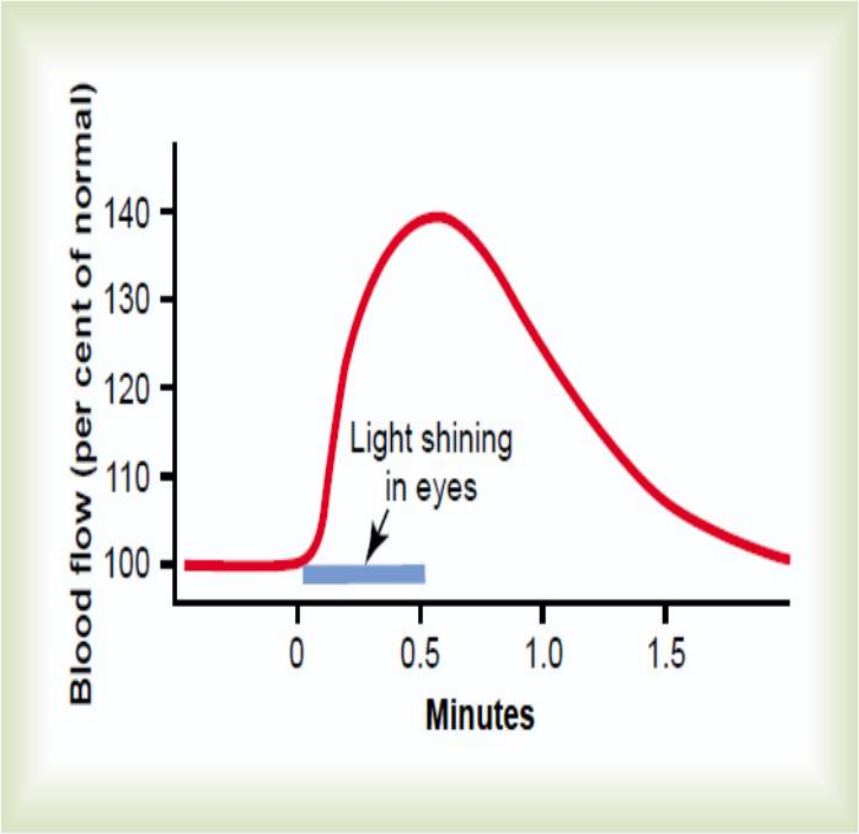
Blood flow increases on increasing local neuronal activity

Simply making a fist

Reading

Epileptic fit

Light Is Shone In A Cat's Eyes



Measurement Of Blood Flow

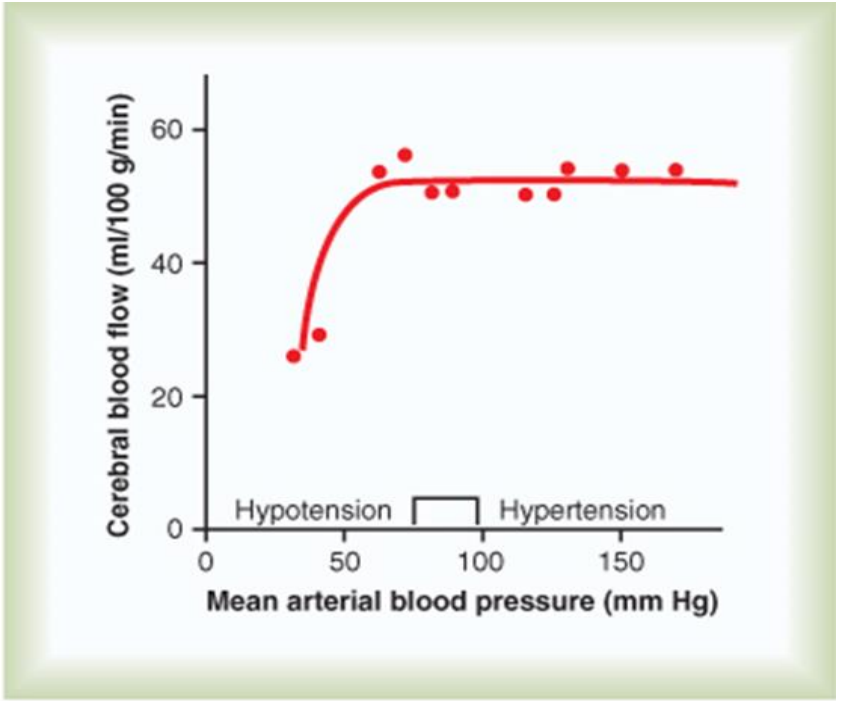
Radioactive Xenon is injected into carotid artery and activity detected by **256 scintillation detectors**

Functional MRI- based on oxyhemoglobin and deoxyhemoglobin

Arterial Spin Labelling – quantitative assay of blood flow

Autoregulation of CBF

- Blood flow is maintained at relatively **constant** level **despite changes** in perfusion pressure → **Autoregulation**
- Well autoregulated between arterial pressure limits of **60 and 140 mmHg**
- **Hypertensives** autoregulation occurs upto **160-180** mmHg



Cerebral Microcirculation

- **Brain gray matter has 4 times the metabolic rate, no of capillaries and cerebral blood flow as white matter**

- **Capillaries** are much less "**Leaky**"

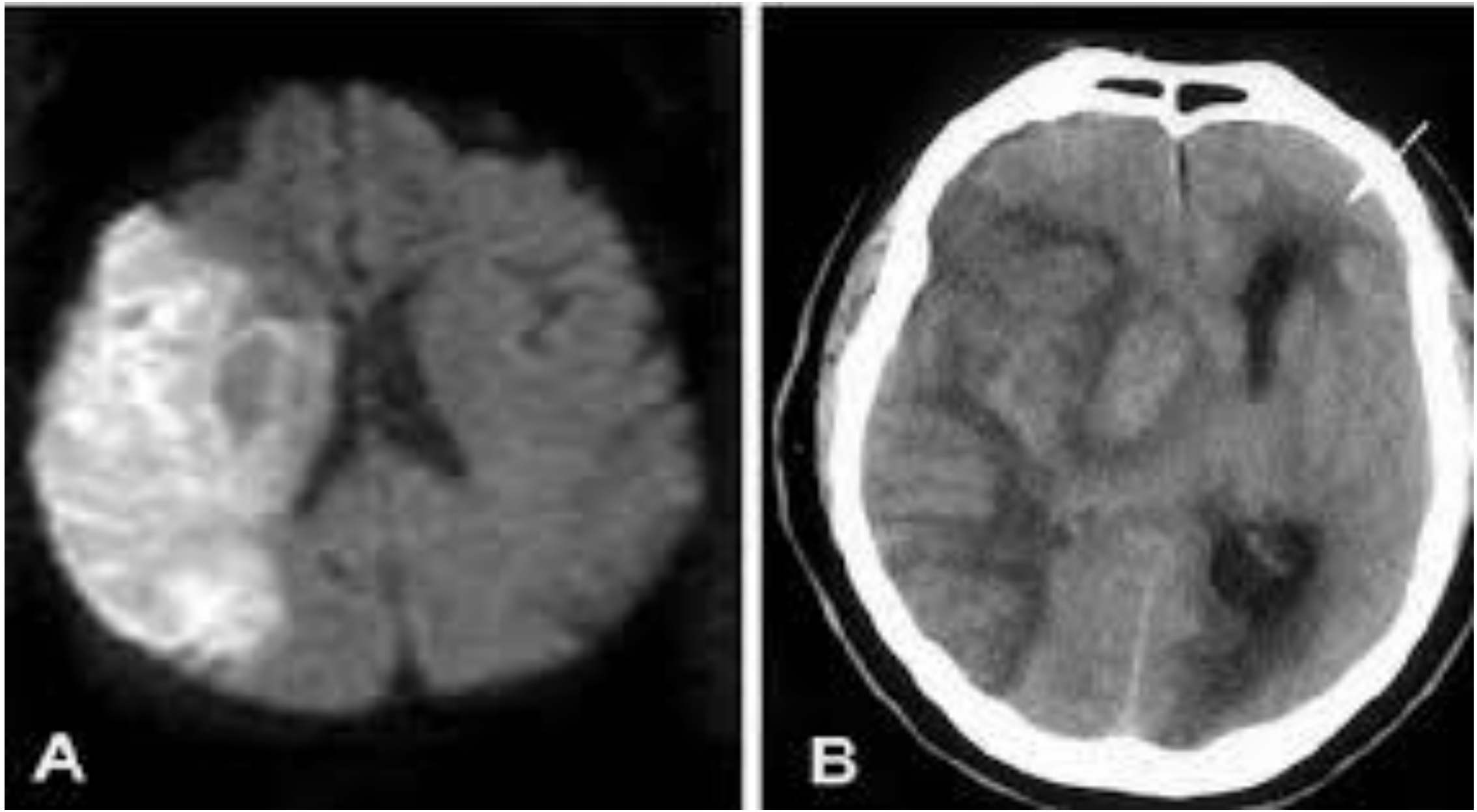
- **Glial feet** from Glial cells provide physical support to prevent overstretching of the capillaries in case of high capillary pressure

Diseases Related To CSF And Cerebral Blood Flow

- Cerebral stroke
- Brain injury
- Brain edema
- ↑CSF Pressure

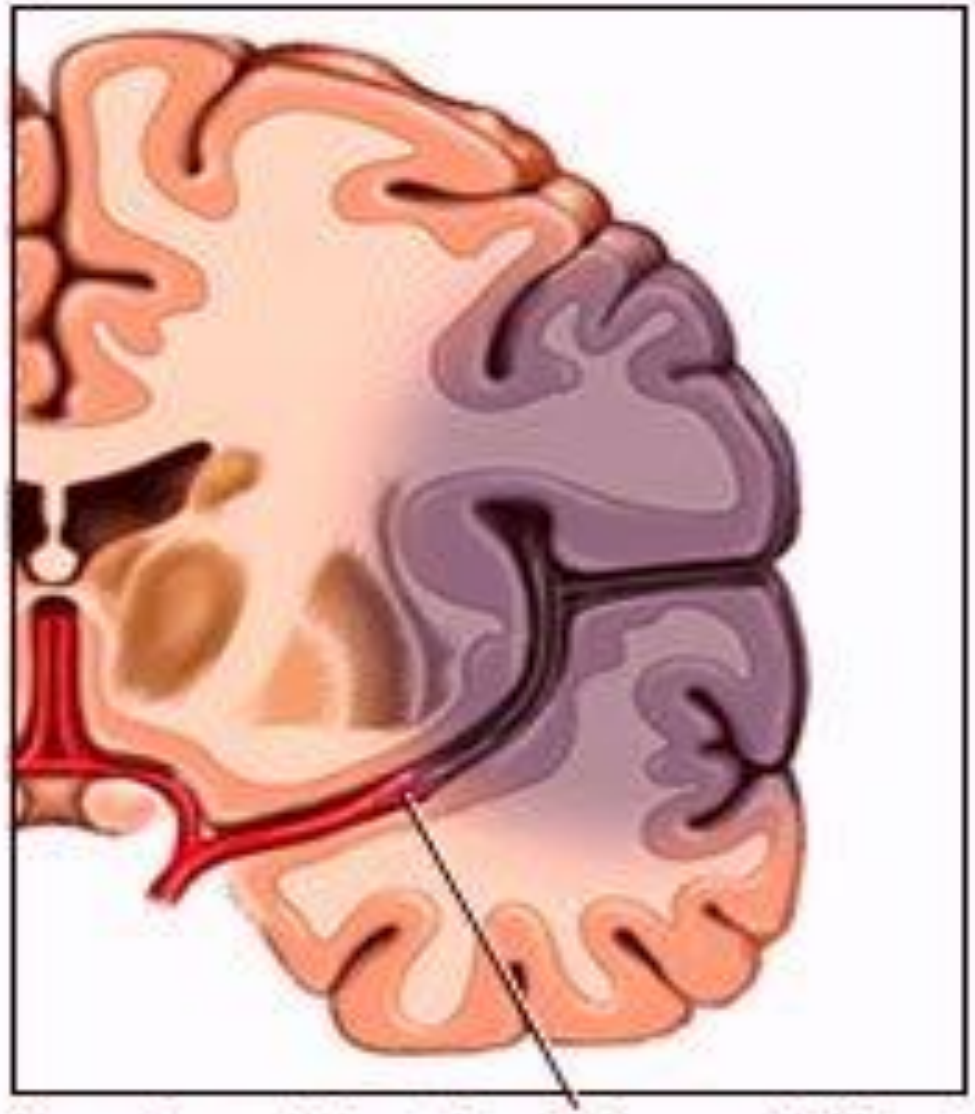
Clinical scenario

- A 70-year-old male was brought to the hospital, with history of personality changes, urinary incontinence, aphasia & right sided weakness.
- On General physical examination Pulse, 82/min irregularly irregular, Bp 150/100 mmHg, rest of GPE normal.
- On systemic examination:
- CVS: S1+S2 with a pansystolic murmur at mitral area.
- CNS: aphasic, with a power of 0/5 on the right side. Rest of systemic examination unremarkable.


A
B

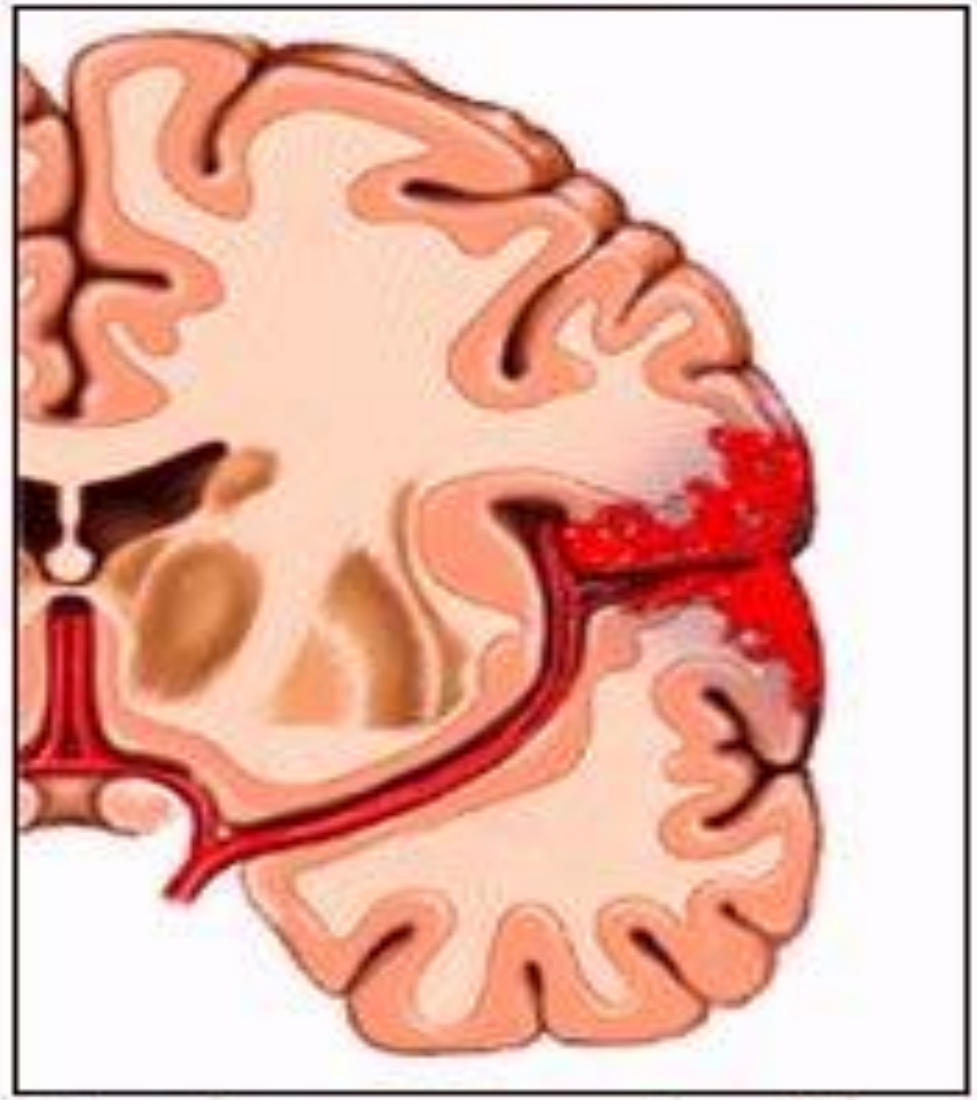
DIAGNOSIS???

Ischemic stroke



A clot blocks blood flow to an area of the brain

Hemorrhagic stroke



Bleeding occurs inside or around brain tissue

Cerebrovascular accident:

The sudden death of some brain cells due to lack of oxygen when the blood flow to the brain is impaired by blockage or rupture of an artery to the brain. A **CVA** is also referred to as a stroke. Symptoms of a stroke depend on the area of the brain affected.

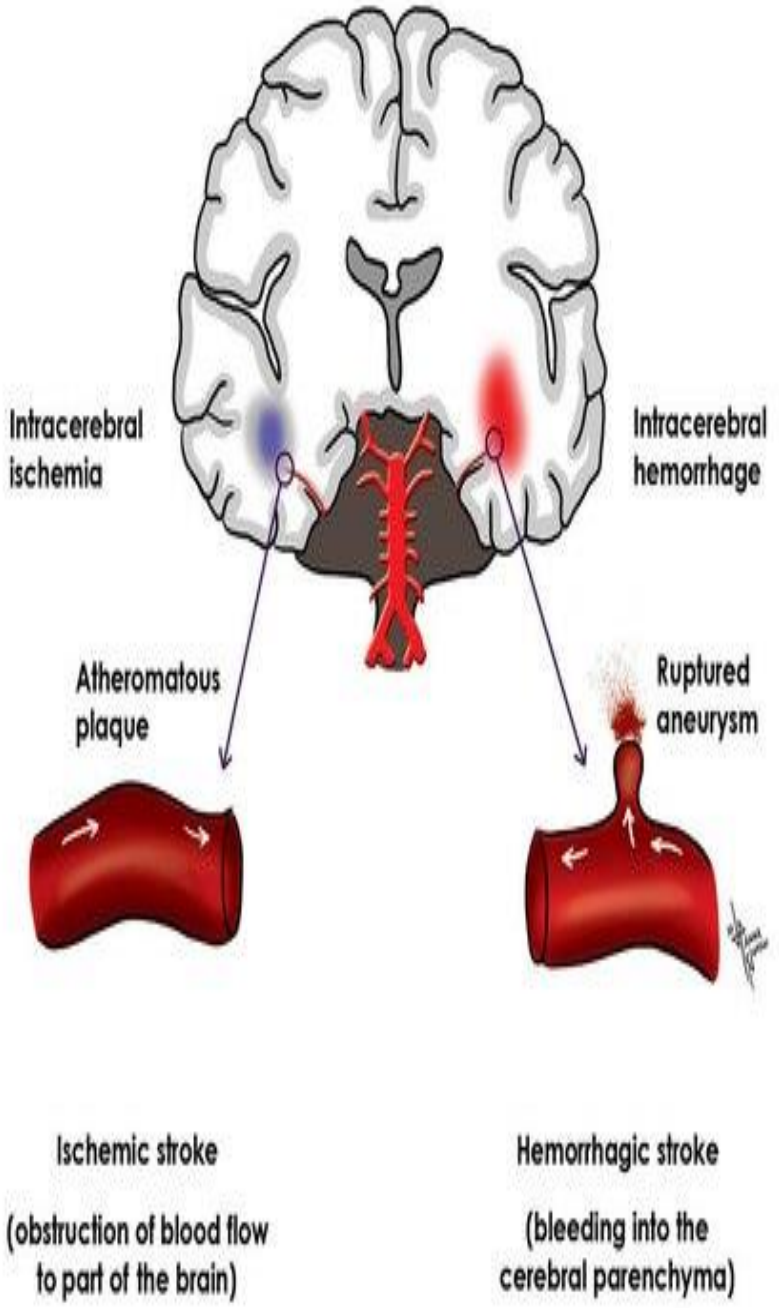
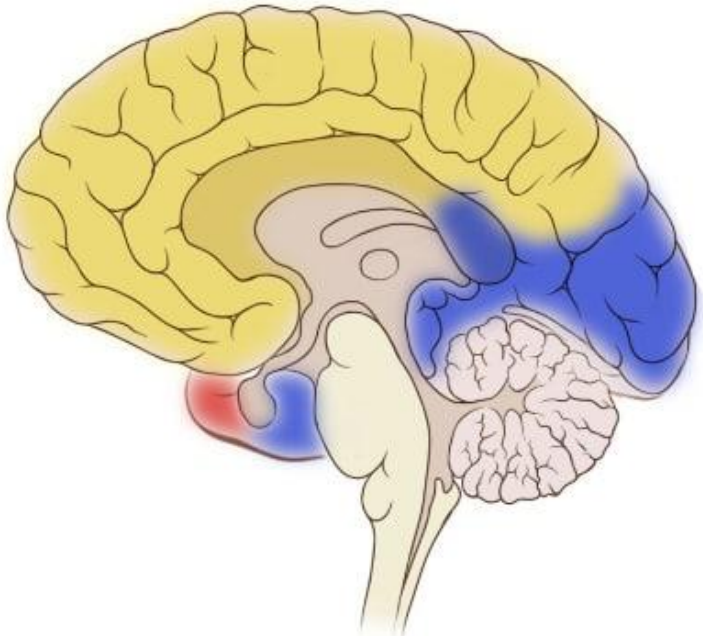


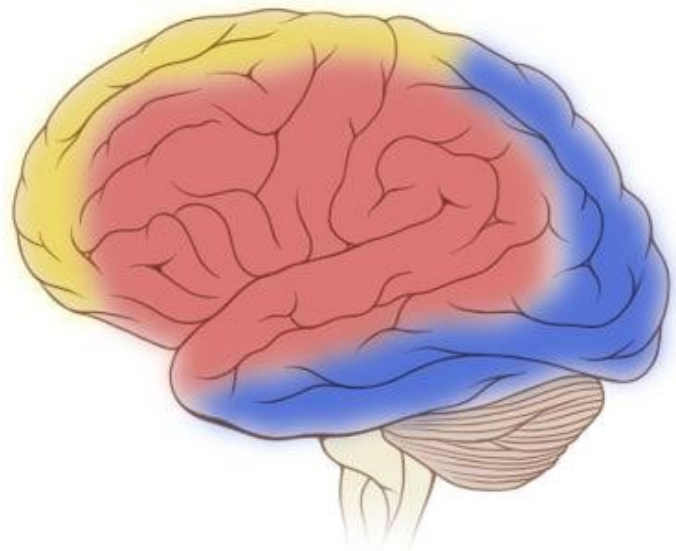
Table 22.14 Clinical deficits associated with problems in vascular supply

Vascular supply	Neurological deficits
Left middle cerebral artery	Right-sided weakness involving face and arm > leg with dysphasia
Right middle cerebral artery	Left-sided weakness involving face and arm > leg, visual and/or sensory neglect, denial of disability
Lateral medulla (posterior inferior cerebral artery and/or parent vertebral artery)	Ipsilateral Horner's syndrome, Xth nerve palsy, facial sensory loss, limb ataxia with contralateral spinothalamic sensory loss. Vertiginous and unable to eat due to failing laryngeal closure and ineffective coughing. Cervical radiculopathies if involvement of radicular branches of the vertebral artery
Posterior cerebral artery	Homonymous hemianopia with varied deficits due to parietal and/or temporal lobe
Internal capsule	Motor, sensory or sensorimotor loss, face = arm = leg. Possible profound dysarthria from involvement of corticobulbar fibres but not dysphasia or other cortical deficits
Bilateral paramedian thalamus	Coma or disturbed vigilance, ophthalmoplegia (internal and/or external), ataxia and memory impairment. Some require ventilation
Carotid artery dissection	Ipsilateral Horner's syndrome from compression of sympathetic plexus around the carotid artery, can also affect lower cranial nerves (Xth and XIIth most clinically obvious). If ipsilateral cerebral infarction follows, clinical picture can mimic brain stem event

Medial view



Lateral view



Posterior cerebral artery

Middle cerebral artery

Anterior cerebral artery

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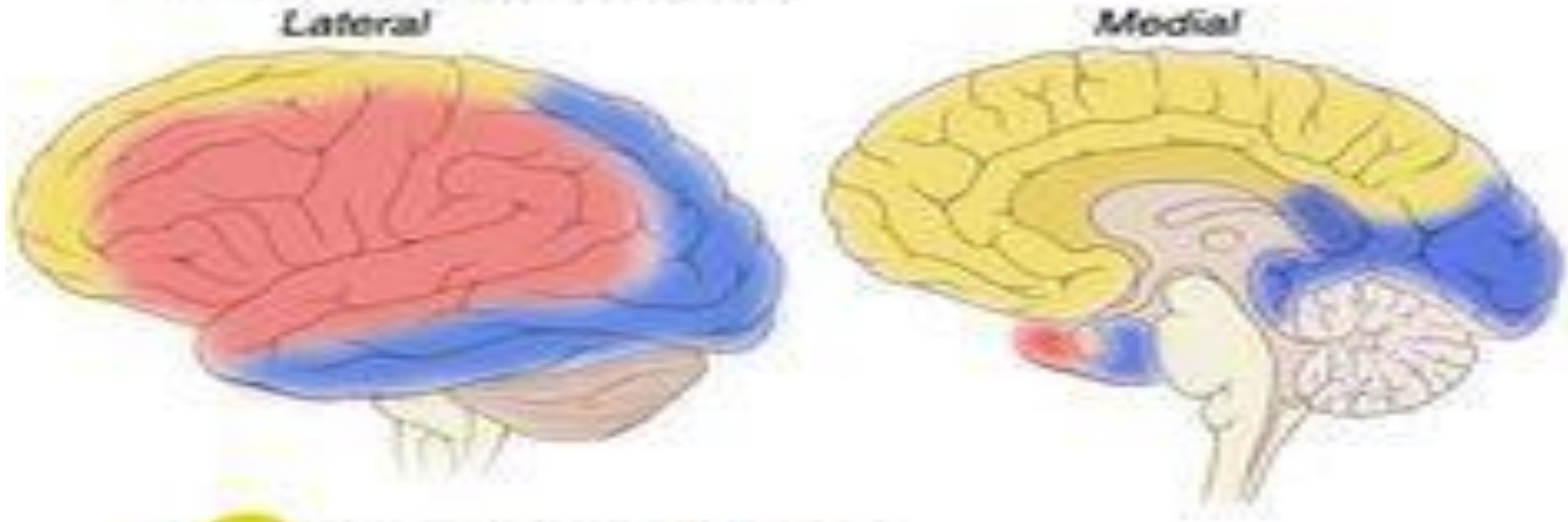
Stroke Distribution

Middle cerebral artery



Anterior cerebral artery

Middle cerebral artery

Posterior cerebral artery

Middle cerebral Artery

- Paralysis of contralateral face, arm and leg
- Sensory impairment over contralateral face, arm, leg
- Homonymous hemi- or quadrantonopia
- Paralysis of gaze to opposite side
- Aphasia, dysarthria

Occlusion of the middle cerebral artery

- *MCA is the largest branch of the ICA. It gives off deep branches (perforating arteries) which supply the anterior limb of the internal capsule and part of the basal nuclei. It then passes out to the lateral surface of the hemisphere and here it gives off cortical branches temporal, frontal, and parietal.*
- **Clinical features** depend on the site of occlusion and whether dominant or non-dominant hemisphere is affected.
- All cortical branches are involved – **contralateral hemiplegia** (leg relatively spared), **contralateral hemianaesthesia and hemianopia**, **aphasia** (dominant), **neglect syndrome** (non-dominant hemisphere).

Symptoms of Occipital Lobe Stroke

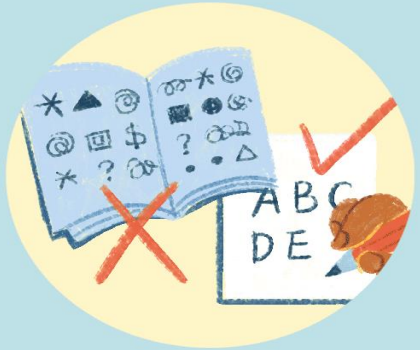
Cortical Blindness

Visual Illusions

Visual Hallucinations

Trouble visually recognizing objects

Face Blindness



Being able to write but not read

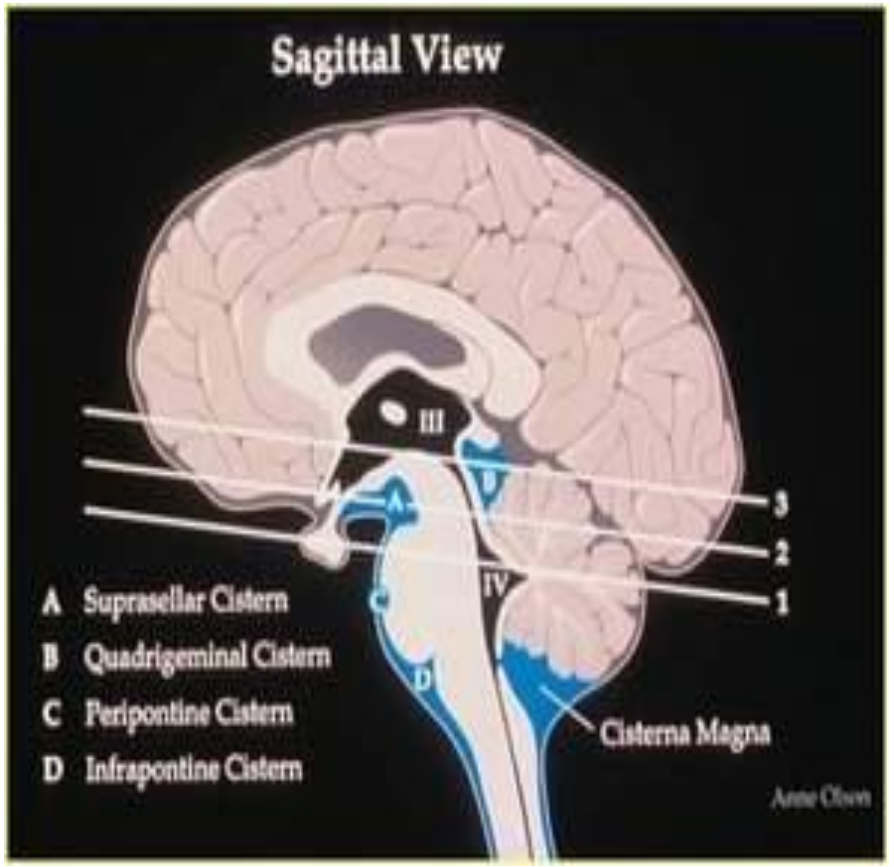
Cerebrospinal Fluid System

- The entire cerebral cavity enclosing brain and spinal cord has 1600 to 1700 ml capacity

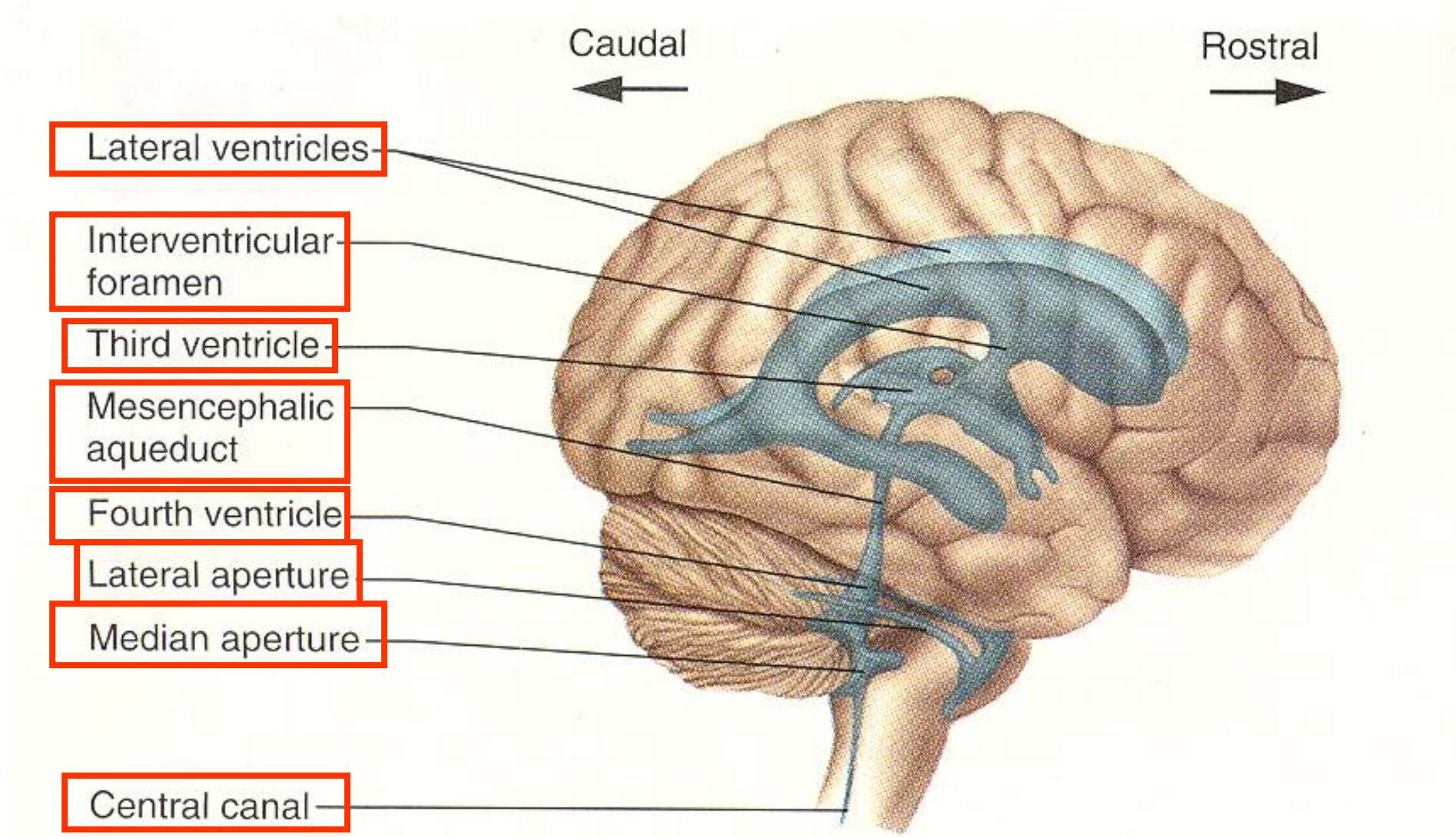
- **150 ml is CSF**

CSF Location

- Ventricles of brain
- Cisterns around outside of brain
- Subarachnoid around
  - Brain
  - Spinal cord
- All these chambers are connected with one another
- Constant pressure of CSF

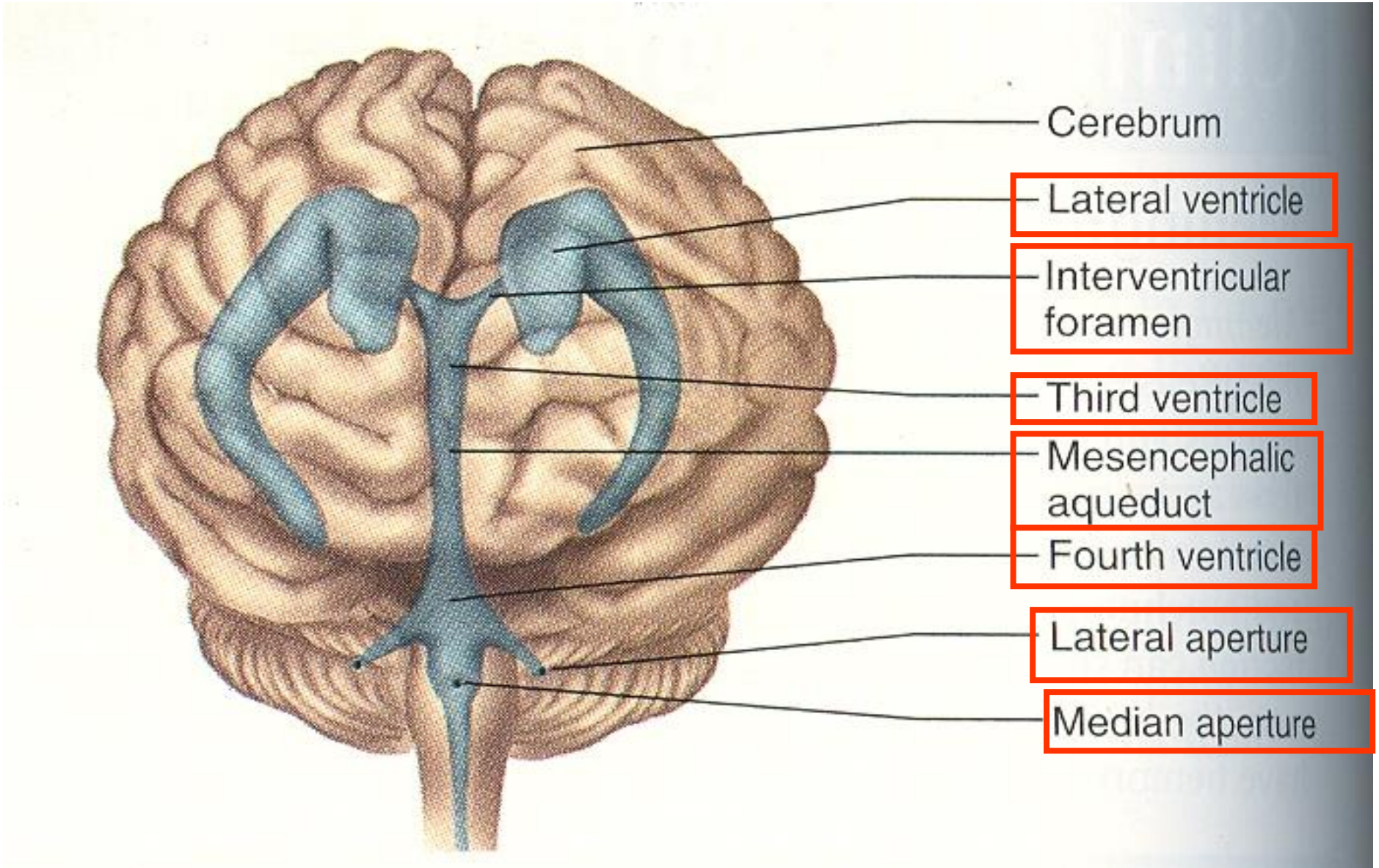


Ventricles of Brain
(Right Lateral aspect)

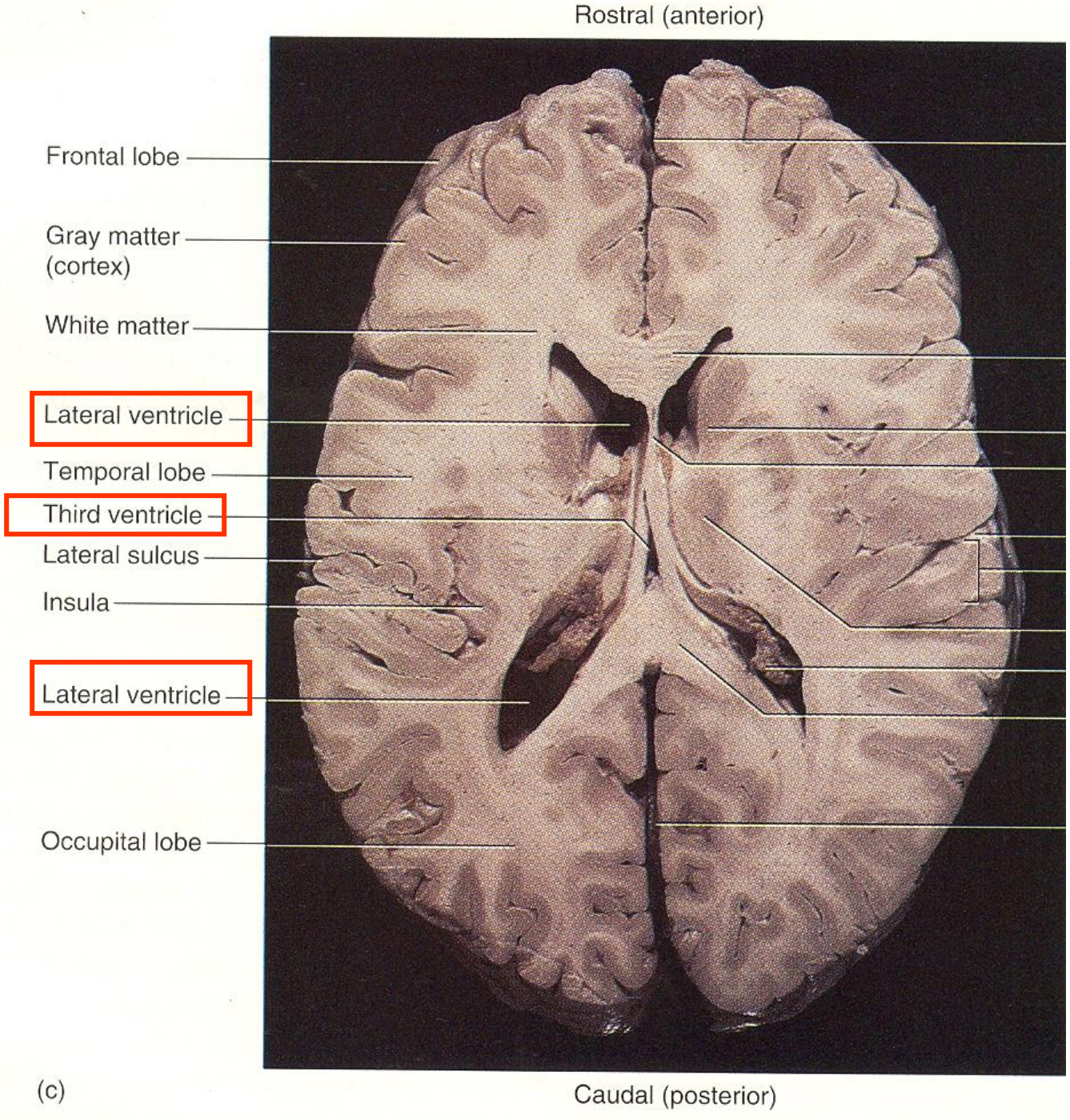


Ventricles of Brain

(Anterior aspect)



Ventricles of Brain (Superior Lateral aspect)



Characteristics of CSF

1. Specific gravity = 1005
2. Clear, colorless, transparent
3. Osmotic pressure is equal to that of plasma
4. Reaction: Alkaline

Composition of CSF

- Water: 99.13%
- Solids: 0.87 %
  - –Organic
  - –Inorganic
  - –Cells

Functions of CSF

Mechanical Support (protective water jacket, shock absorber and buoyancy)

Chemical Protection (optimal chemical environment for nerve impulse conduction)

Removal of waste products

Circulation (exchange of nutrients and wastes)

Pulmonary ventilation and Cerebral blood flow (pH of CSF)

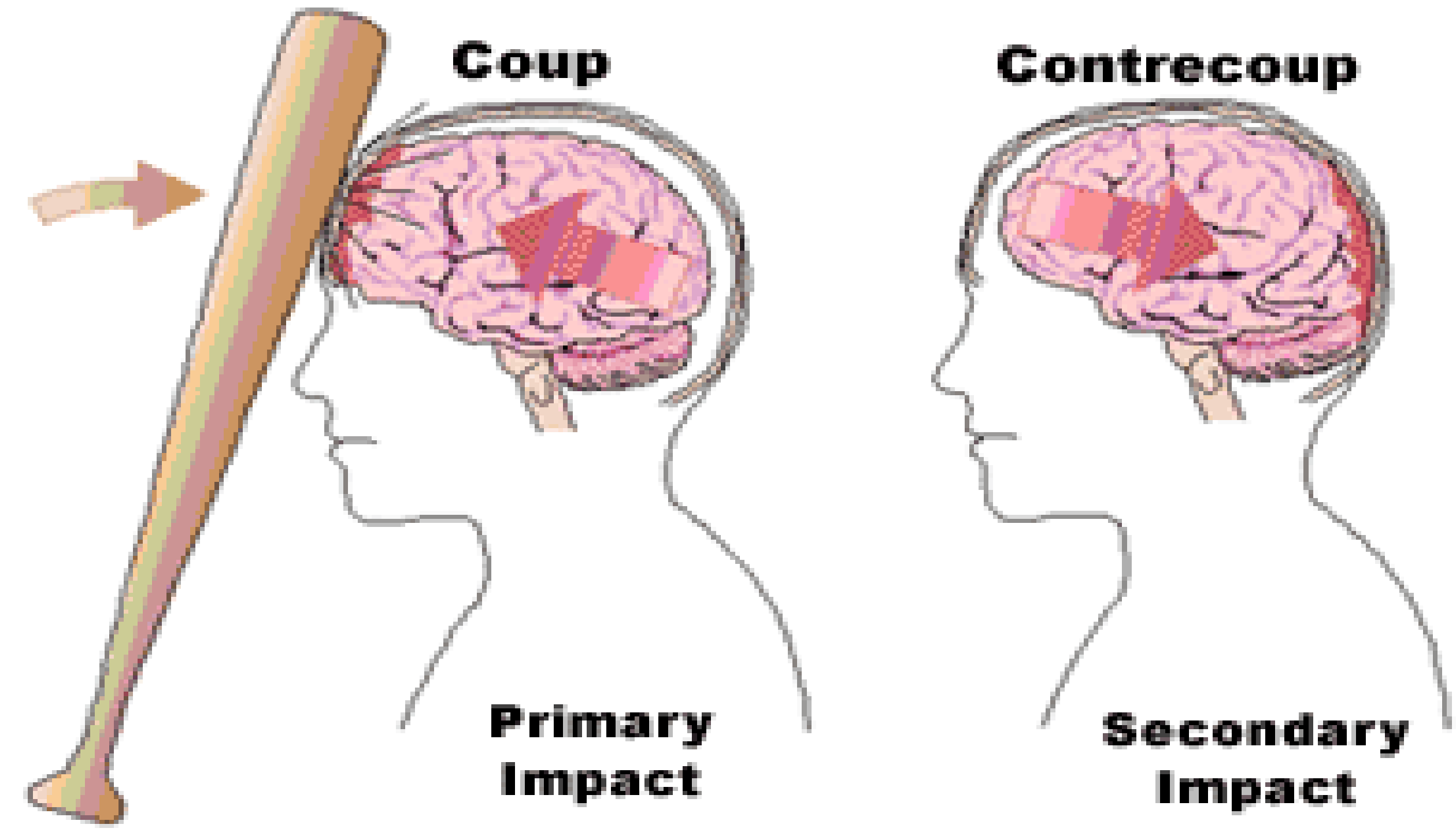
Clinical use (diagnostic and therapeutic)

Cushioning Function of CSF

Specific gravity of brain and CSF is about same
(Only 4% difference)
A blow to head (if not too severe)moves the entire brain simultaneously within skull

- **Coup** same side as impact
- **Contrecoup injury** – opposite side as impact

- Coup and contrecoup injuries are caused by Rapid acceleration and deceleration (shaken baby syndrome)


Coup
Contrecoup
Primary
Impact
Secondary
Impact

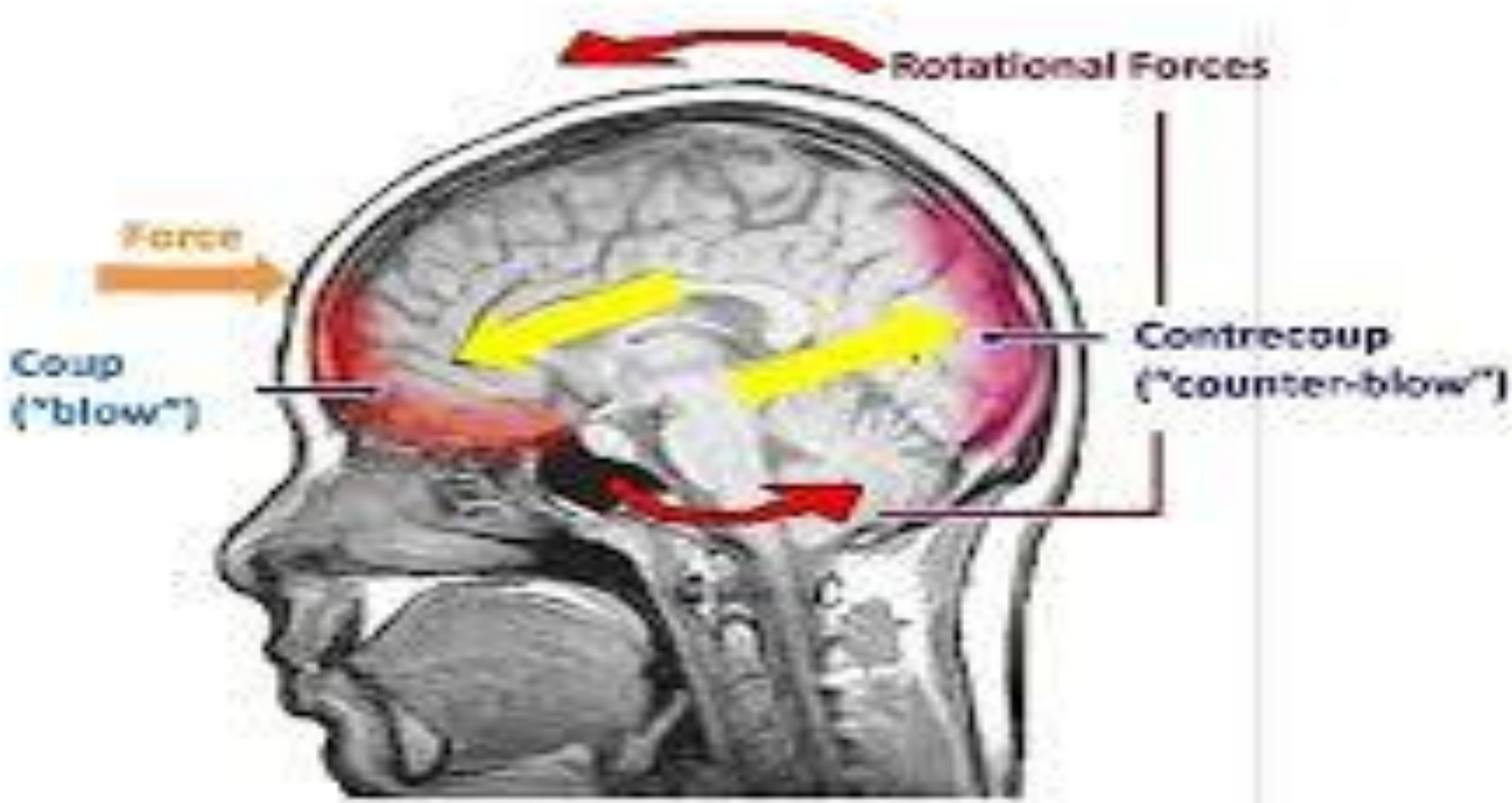


Figure 3. Coup and contrecoup injuries [12].


(Slow motion)
Coup-contrecoup injury
nucleus
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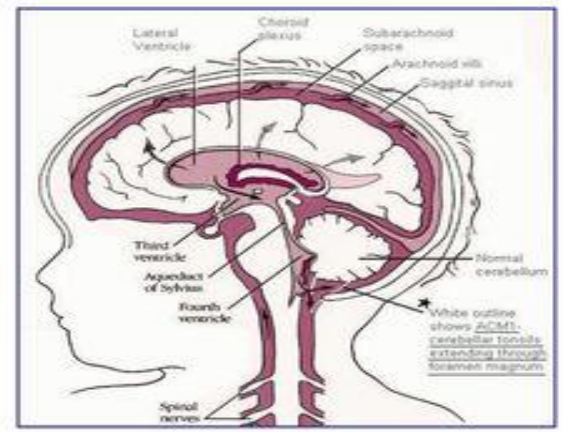
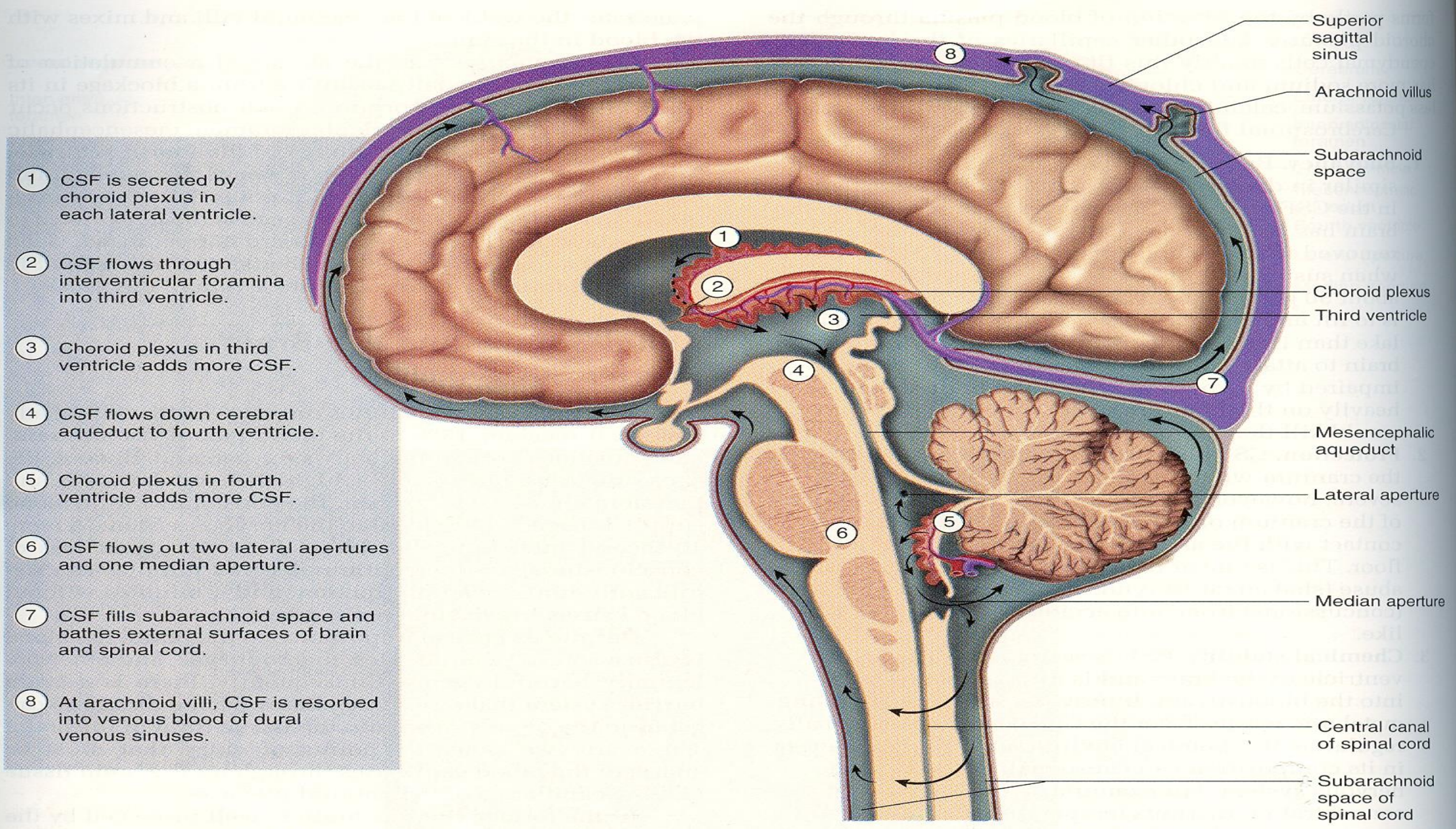
CSF Formation & Circulation

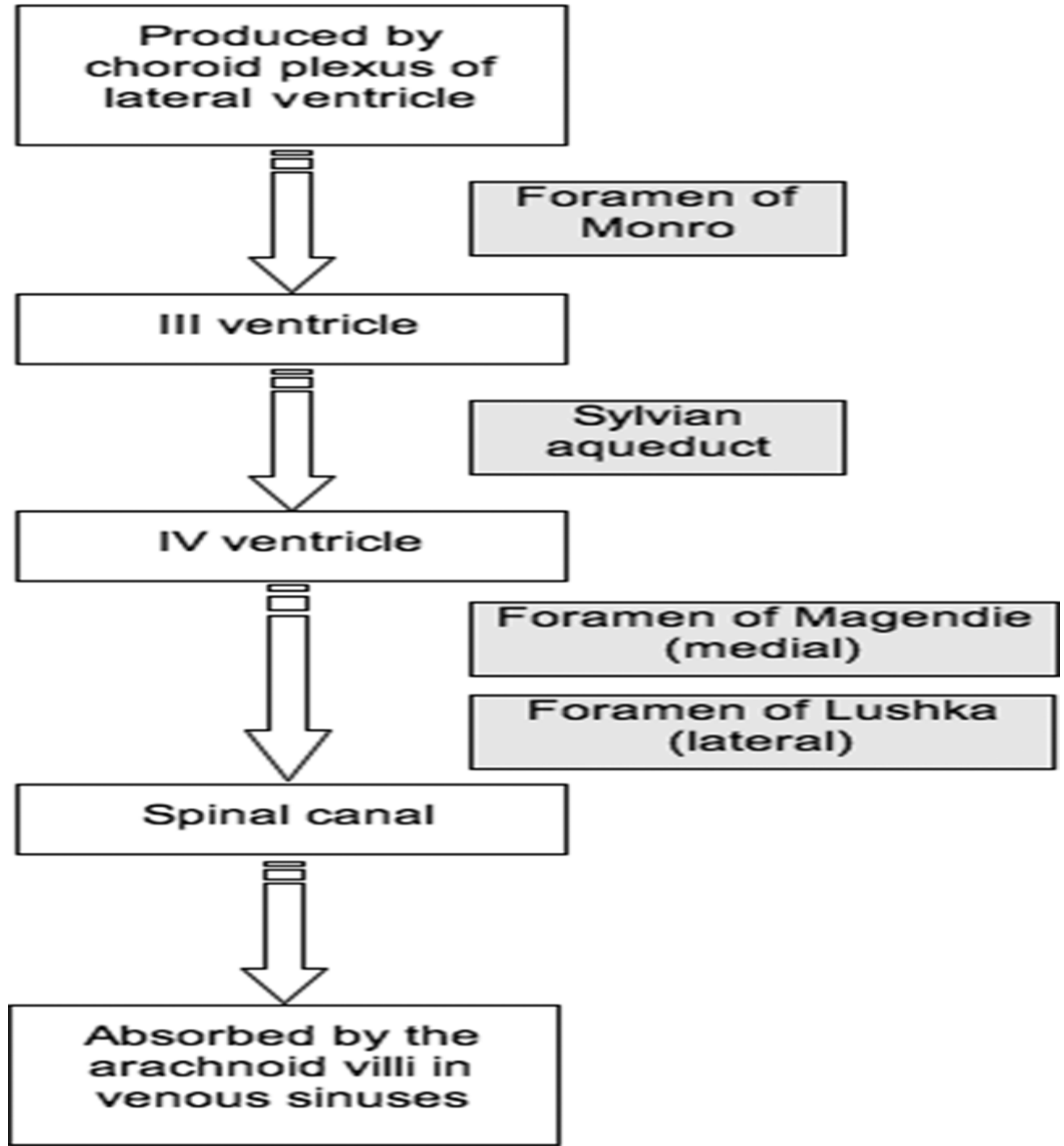
- CSF is formed at the *choroid* plexuses & by the cells lining the *ventricles*.
- Normal blood brain barrier is important for the normal chemistry results of CSF
- Rate of formation:
  - *500 ml/day*
- Mechanism of formation:
  - Selective *ultrafiltration* of plasma
  - *Active secretion* by epithelial membranes
- Mechanism of excretion (absorption):
  - Excretion volume = production volume → constant CSF volume
  - Absorption occurs at the *arachnoid villi* protruding through the dura to the venous sinuses of the brain→ bloodstream



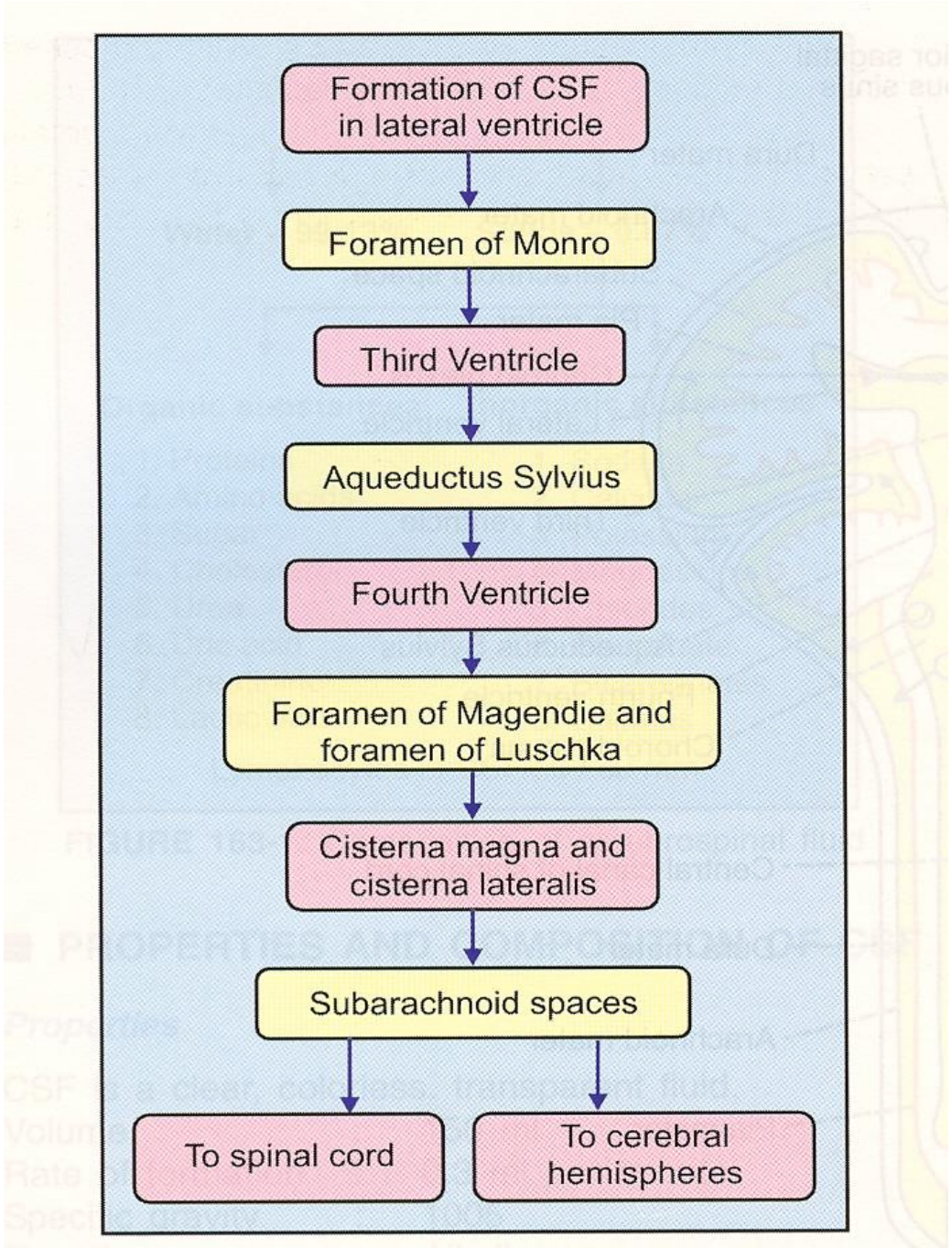
Mechanism Of Secretion Of CSF

- **Active transport of Na+** out of epithelial cells →
- **Passive transport of Cl-** → Osmosis of water into ventricles
- Less important is transport of glucose into CSF,
- Potassium and Bicarbonate ions out of CSF into capillaries


1 CSF is secreted by choroid plexus in each lateral ventricle.
2 CSF flows through interventricular foramina into third ventricle.
3 Choroid plexus in third ventricle adds more CSF.
4 CSF flows down cerebral aqueduct to fourth ventricle.
5 Choroid plexus in fourth ventricle adds more CSF.
6 CSF flows out two lateral apertures and one median aperture.
7 CSF fills subarachnoid space and bathes external surfaces of brain and spinal cord.
8 At arachnoid villi, CSF is resorbed into venous blood of dural venous sinuses.
Superior sagittal sinus
Arachnoid villus
Subarachnoid space
Choroid plexus
Third ventricle
Mesencephalic aqueduct
Lateral aperture
Median aperture
Central canal of spinal cord
Subarachnoid space of spinal cord


Produced by choroid plexus of lateral ventricle
Foramen of Monro
III ventricle
Sylvian aqueduct
IV ventricle
Foramen of Magendie (medial)
Foramen of Lushka (lateral)
Spinal canal
Absorbed by the arachnoid villi in venous sinuses

Flow of CSF


Formation of CSF in lateral ventricle
Foramen of Monro
Third Ventricle
Aqueductus Sylvius
Fourth Ventricle
Foramen of Magendie and foramen of Luschka
Cisterna magna and cisterna lateralis
Subarachnoid spaces
To spinal cord
To cerebral hemispheres

CSF Pressure

- **130 mm H_2O (10 mmHg) in** lateral recumbent position
- Range: **65-195 mm H_2O**
- **200 – 300 mm H_2O in sitting position**
- C.S.F absorption **stops** below 68 mm H_2O
- Arachnoid villi function like **Valves** and allow one-way flow

Regulation of CSF Pressure by Arachnoid Villi

Formation	Reabsorption
Almost constant rate	Due to pressure gradient Normally CSF pressure does not rise more than a few mm of Hg than pressure in venous sinuses due to valve action of villi

→Abnormally high amount of cells or proteins may block the reabsorption

→Diseases of villi result in ↓ reabsorption

- ↓ **Number of villi**
- **Poor Quality of villi**

Protective Mechanisms Of Brain

1. **Skull Bones and CSF**

2. **Autoregulation**

CO_2, H^+, O_2 and substances from astrocytes

3. **Sympathetic nervous system** e.g. in exercise

4. **Tight capillary junctions** to prevent edema

5. **Blood-CSF and Blood- Brain Barriers**

Protection of brain from endogenous and exogenous toxins

Diseases Related To CSF And Cerebral Blood Flow

Cerebral stroke

Brain injury

Brain edema

↑CSF Pressure

- Tumors
- Infections (Meningitis and Encephalitis)
- Hemorrhages
- Developmental defects – Hydrocephalus→↑ fluid in cranium

  Communicating or Non Communicating

Brain Edema

- When systems for protecting against transudation of fluid into the brain break down e.g.
  - **Brain concussion**
    - Blow to head
  - **High blood pressure**
- **Mechanism**
  - ↑Capillary Pressure
  - ↑ Damage to capillary walls

    → Coma and death

Diseases Related To CSF And Cerebral Blood Flow (↑ CSF Pressure)

Causes

1. **↑ Formation** (rare)
2. **↓Reabsorption (Obstruction to outflow)**

↑ number of blood cells or plasma proteins

Hemorrhage, Infection →Blockage of reabsorption

- Fibrosis of villi
- Brain tumors
- Congenital
  - –Hydrocephalus

Papilledema(Edema of Optic Disc)	1. **↑ CSF pressure pushes fluid first →** optic nerve sheath and then along the spaces between the optic nerve fibers to the interior of the eyeball 2. **It ↓ outward fluid flow** in the optic nerves, causing accumulation of excess fluid in the optic disc at the center of the retina 3. **Impedes flow of blood** in the retinal vein 4. Detected by ophthalmoscope and can lead to **Blurred vision and blindness**

Types of Hydrocephalus

Communicating Type or Non Obstructive → decreased absorption

Non Communicating or Obstructive type → outflow obstruction

Congenital below 3 years of age

Acquired high CSF pressure, very painful

Communicating type

This results from blockage distal to the ventricle system, i.e.

In the subarachnoid space like

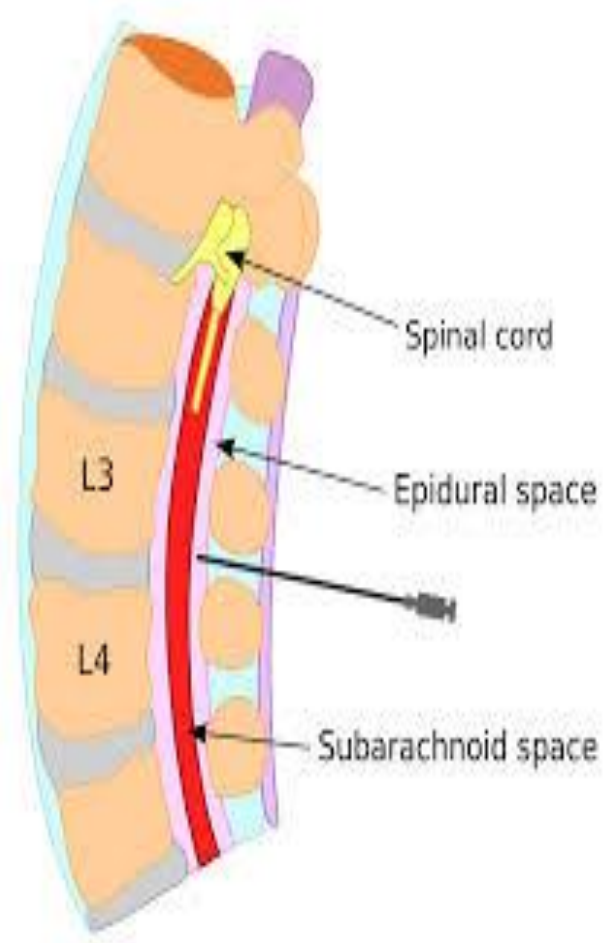
.Adhesion after meningitis

.Subarachnoid hemorrhage

Measurement of CSF Pressure

- Person lying **horizontally** on his/ her side so that pressure in spinal canal = pressure in cranial vault

- Spinal needle is inserted in lumber spinal canal **(Lumbar Puncture)**
- inserted between the Lumbar Vertebrae **L3/L4, L4/L5 or L5/S1**
- Same procedure for composition of CSF

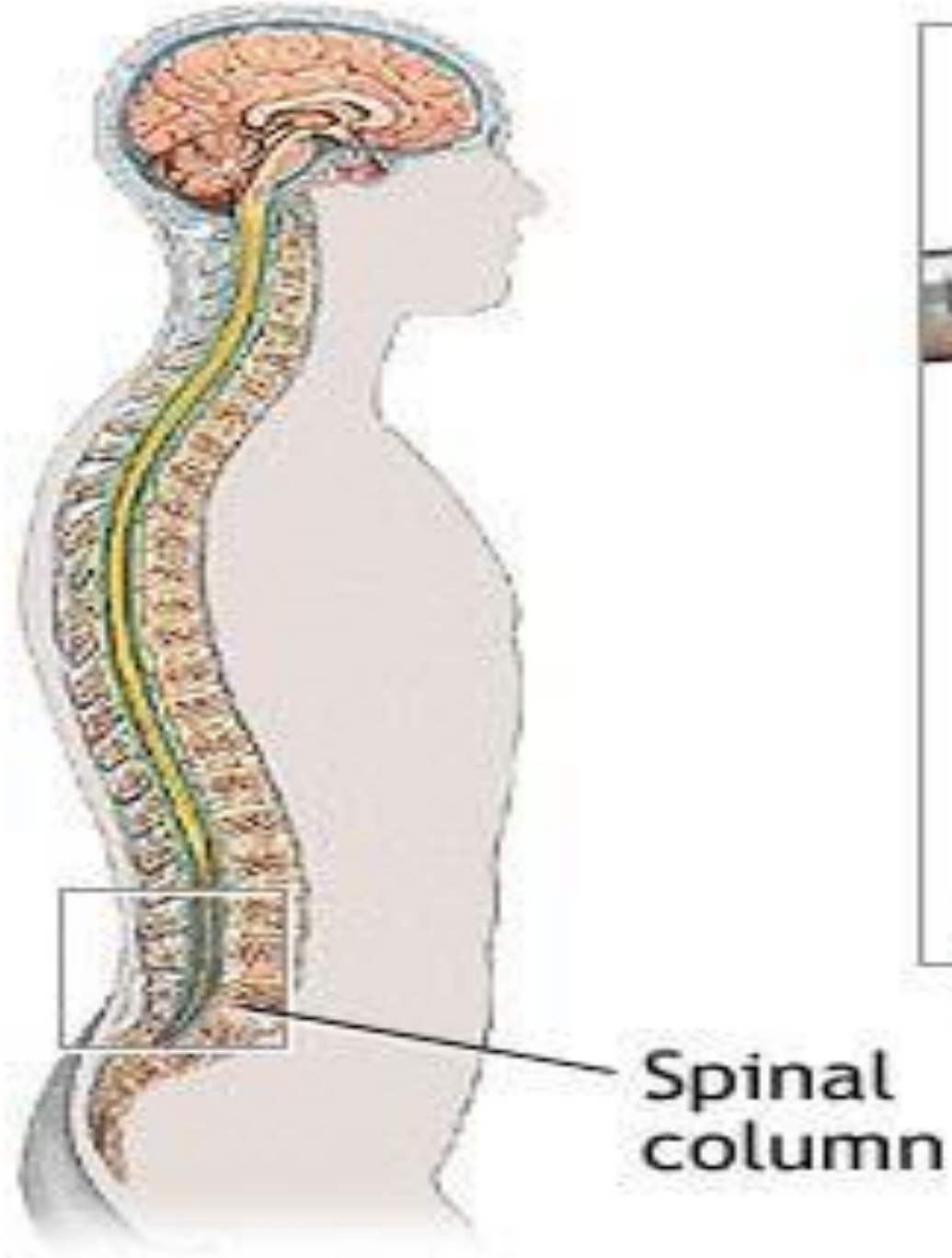


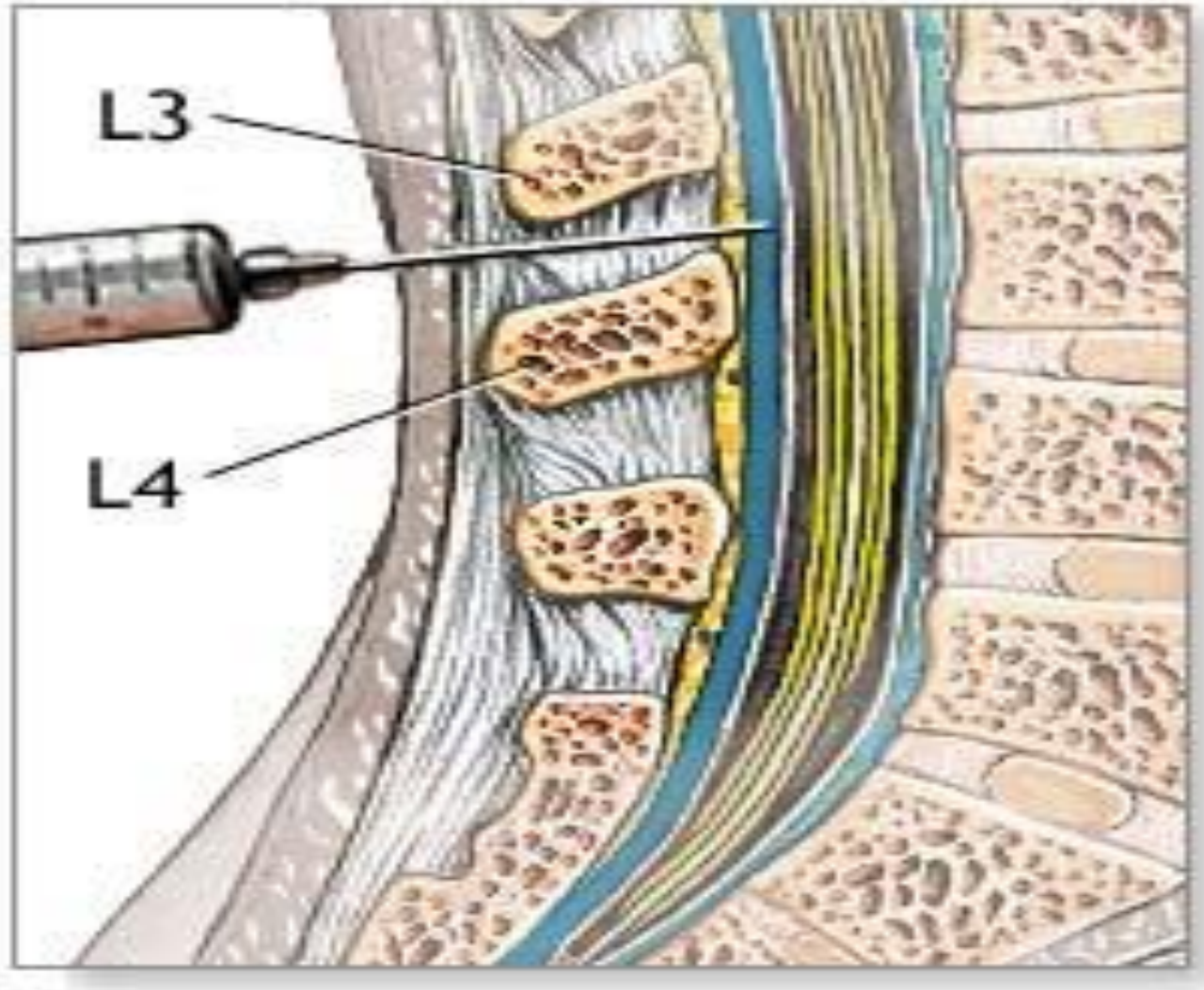
LUMBAR PUNCTURE

A lumbar puncture also called a spinal tap is a procedure where a sample of cerebrospinal fluid is taken for examination.

CSF is mainly used to diagnose meningitis [an infection of the meninges].

It is also used to diagnose some other conditions of the brain and spinal cord.





POSITIONS FOR LUMBAR PUNCTURE

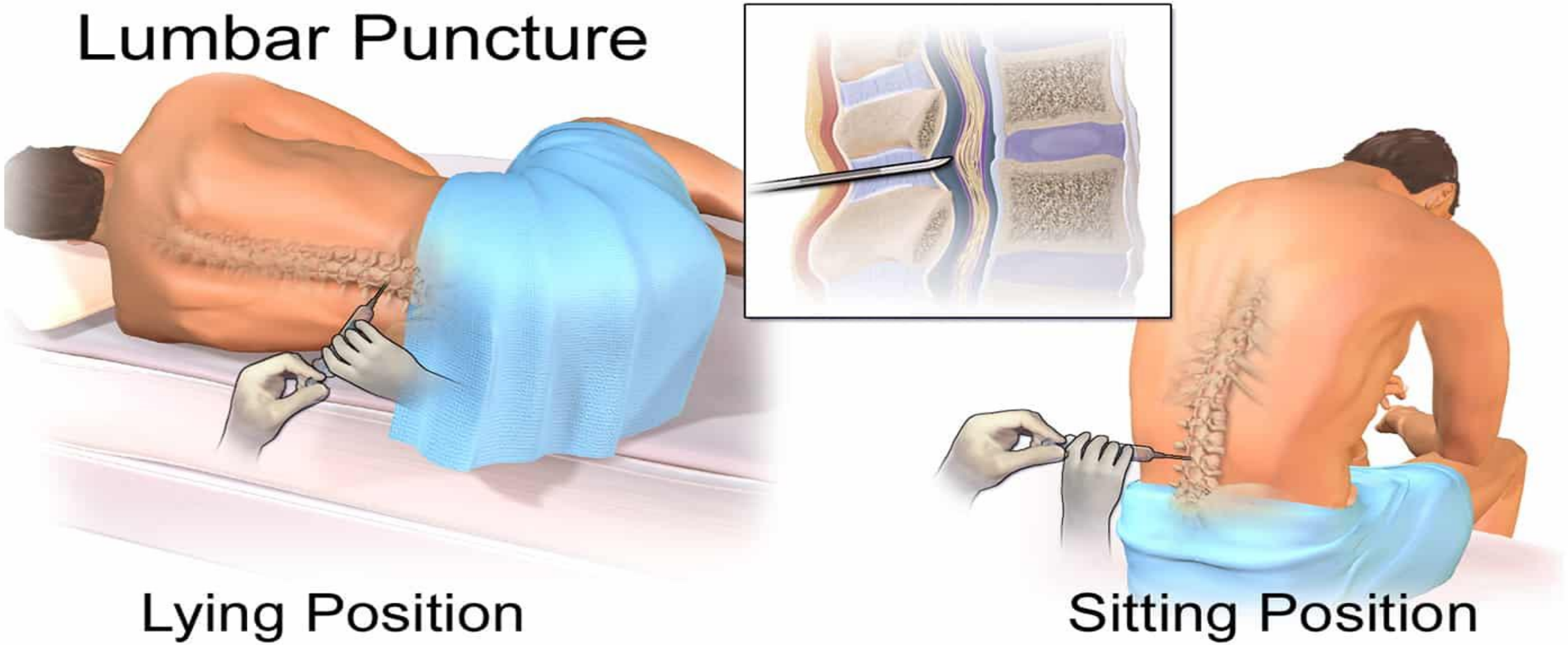


IMAGE SOURCE: WIKIPEDIA

Blood-CSF and Blood- Brain Barriers

- **Blood- Brain Barrier**

  Tight junctions between adjacent **Endothelial cells**

- **Blood-CSF Barrier**

  Tight junctions between adjacent **Choroid Epithelial cells**

- **Highly permeable** to water, CO2, O2 and most lipid soluble substances like alcohol and anaesthetics
- **Slightly permeable** to electrolytes
- **Impermeable** to plasma proteins and lipid insoluble large molecules (organic)

BBB and Blood CSF….

The ease of diffusion is important in these areas as

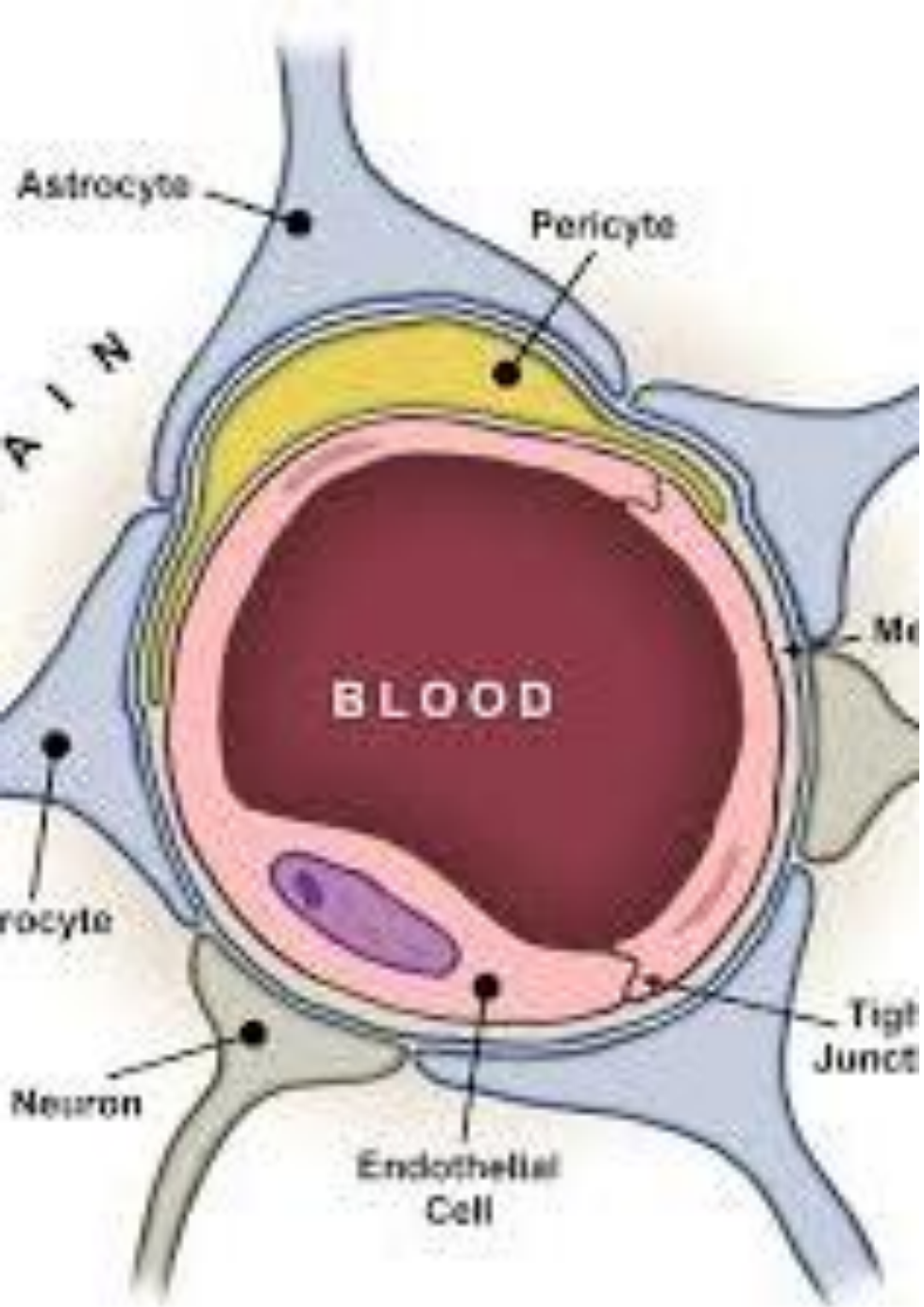
- have **receptors** which detect changes in body fluids like osmolality, glucose concentration
- Have **peptide hormone receptors** (angiotensin II) that regulate thirst
- **Specific carrier molecules** for transport of LEPTIN (controls appetite and sympathetic nervous activity)

Blood- Brain Barrier

- The blood-brain barrier controls the content of brain interstitial fluid.
- It has a 5000-fold greater surface area than the blood-CSF barrier.
- The anatomic basis for the blood-brain barrier is a series of high-resistance, tight junctions between endothelial cells as well as astrocytes with processes that terminate in overlapping fashion on capillary walls.
- Lipid-soluble small molecules with a molecular mass less than 400 to 600 Da are transported readily through the blood-brain barrier. In contrast, many drugs and other small molecules cannot cross this barrier system.

Blood-CSF Barrier

- The blood-CSF barrier controls the composition of the CSF, which, is primarily dependent upon secretion in the choroid plexus. The blood-CSF barrier is formed by tight junctions between choroid epithelial cells.



Functions of Blood- Brain Barrier

1. Maintain **constant environment** of neurons

   Brain neurons highly sensitive to changes in ionic concentration

2. Protection of brain from endogenous and exogenous **toxins**

3. Prevention of escape of **neurotransmitters** into general circulation

Clinical implications of Blood- Brain Barrier

1. Immature at birth → **Kernicterus** (Entry of free bilirubin in brain)

2. Some amines (e.g. dopamine and serotonin do not penetrate brain tissue, so their **precursors** are given, i.e. L-Dopa and 5-Hydroxytryptophane)

3. Breakdown of Blood- Brain Barrier in **infection** or **injury**

4. **Blockage leads to Hydocephalus**

Brain Metabolism

- Brain Mass = **2%** of body Mass
- Brain metabolism= **15%** of body metabolism (resting but awake)
- **Under resting conditions** Brain metabolism per unit mass of tissue is about **7.5 times the** average metabolism in non nervous tissues
- **High level of brain activity**, it can rise to **100 to 150%**

Special requirements of Brain for Oxygen (Lack of Significant Anaerobic metabolism)

Anaerobic metabolism occurs in most tissues of body

at the expense of glucose and glycogen

- Brain is **not** capable of significant anaerobic metabolism → **Reason:**-High metabolic rate of neurons

- Sudden **cessation** of brain blood flow/ or total **lack** of oxygen → **Unconsciousness within 5-10 seconds**

Composition

Substance	CSF	Plasma
Na^+ [meq/L]	147	150
K^+ [meq/L]	2.9	4.6
Ca^{++} [meq/L]	2.3	4.7
Mg^{++} [meq/L]	2.2	1.6
Cl^- [meq/L]	113.0	99.0
HCO_3^- [meq/L]	25.1	24.8
Osmolality [mosm/L]	289.0	289.0
Protein [mg/dl]	20.0	6000
Glucose [mg/dl]	64.0	100.0
Cholesterol	0.2	175

CSF PICTURE IN MENINGITIS

	Appearance	Opening Pressure mmHg	WBC (cell/μL)	Protein (mg/dl)	Glucose (mg/dL)
Normal	Clear	90-180	< 8	15-45	50-80
Bacterial Meningitis	Turbid	Elevated	>1000-2000	>200	<40
Viral Meningitis	Clear	Normal	<300; Lymphocytic predominance	<200	Normal
Fungal Meningitis	Clear	Normal-elevated	<500	>200	Normal - Low


IF YOUR GOALS
DON'T SCARE YOU,
THEY AREN'T BIG ENOUGH.
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Thank you