Autoregulation of the cerebral blood flow

Prof/Faten Zakaria

Ph.D
Professor of physiology
Consultant of neurophysiology
Department of Physiology
College of Medicine, King Saud University

Objectives:

-At the end of this lecture the student would be able to discuss:

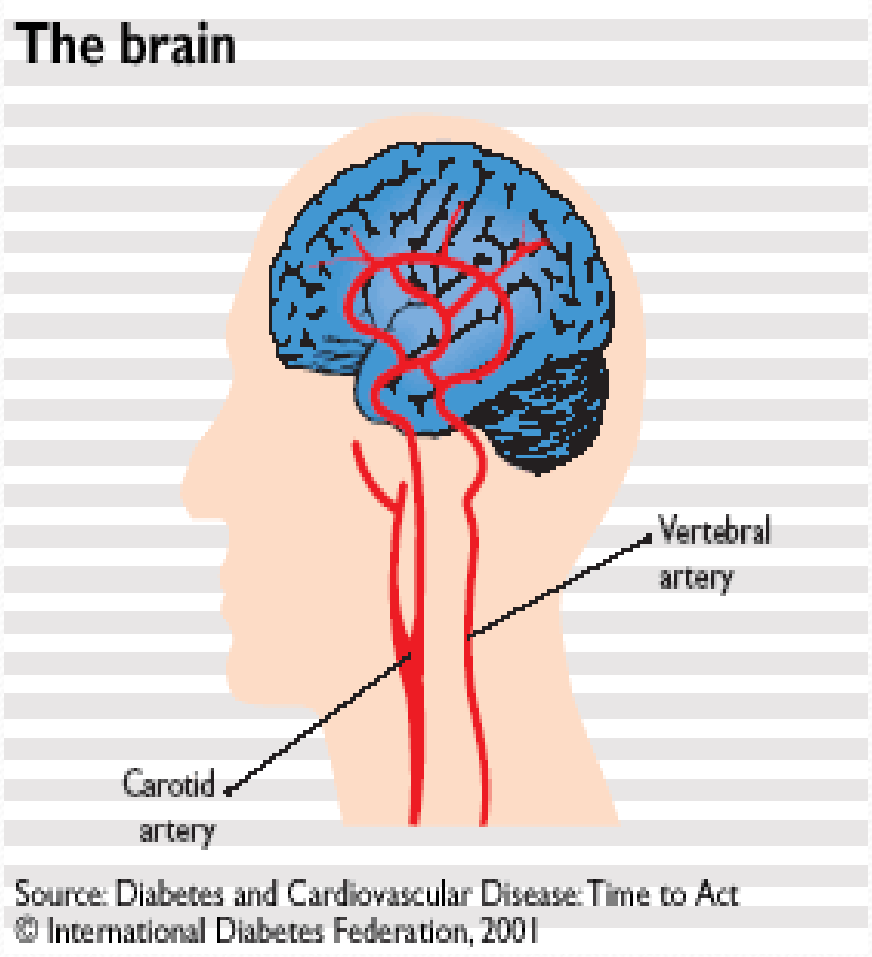
- **Cerebral blood flow**(normal rate & autoregulation).
- - **Cerebral** blood pressure & Intracranial pressure (ICP)
- -Factors affecting cerebral blood flow:
- Blood gases & Neural stimuli,
- - CSF formation & absorption.
- CSF functions.
- Blood brain barrier (BBB)

Brain receive its blood supply from four main arteries:

1- two internal carotid arteries

2- two vertebral arteries.

They form the Circle of Willis: A group of arteries near the base of the brain



Cerebral Circulation

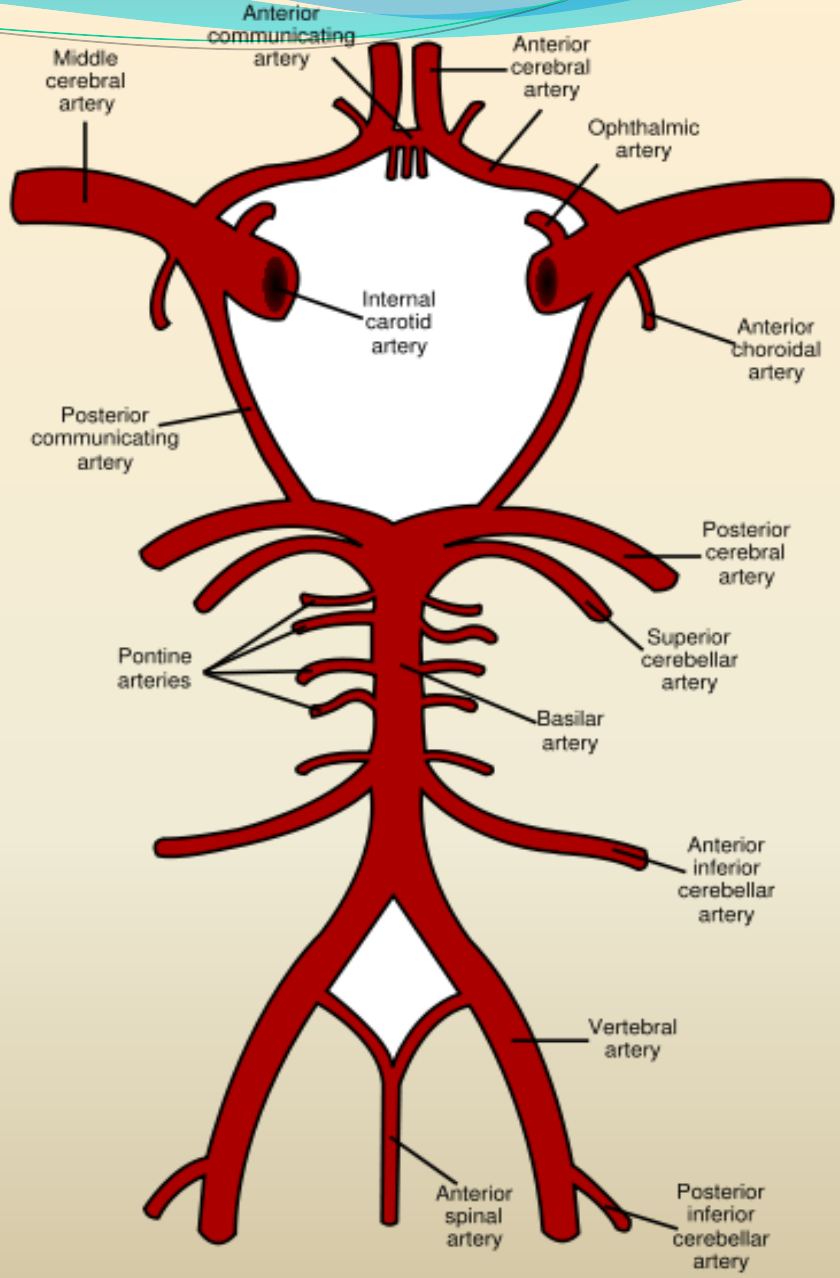
- The vertebral arteries unite to form Basilar artery

-The basilar artery and the carotids form the circle of Willis.

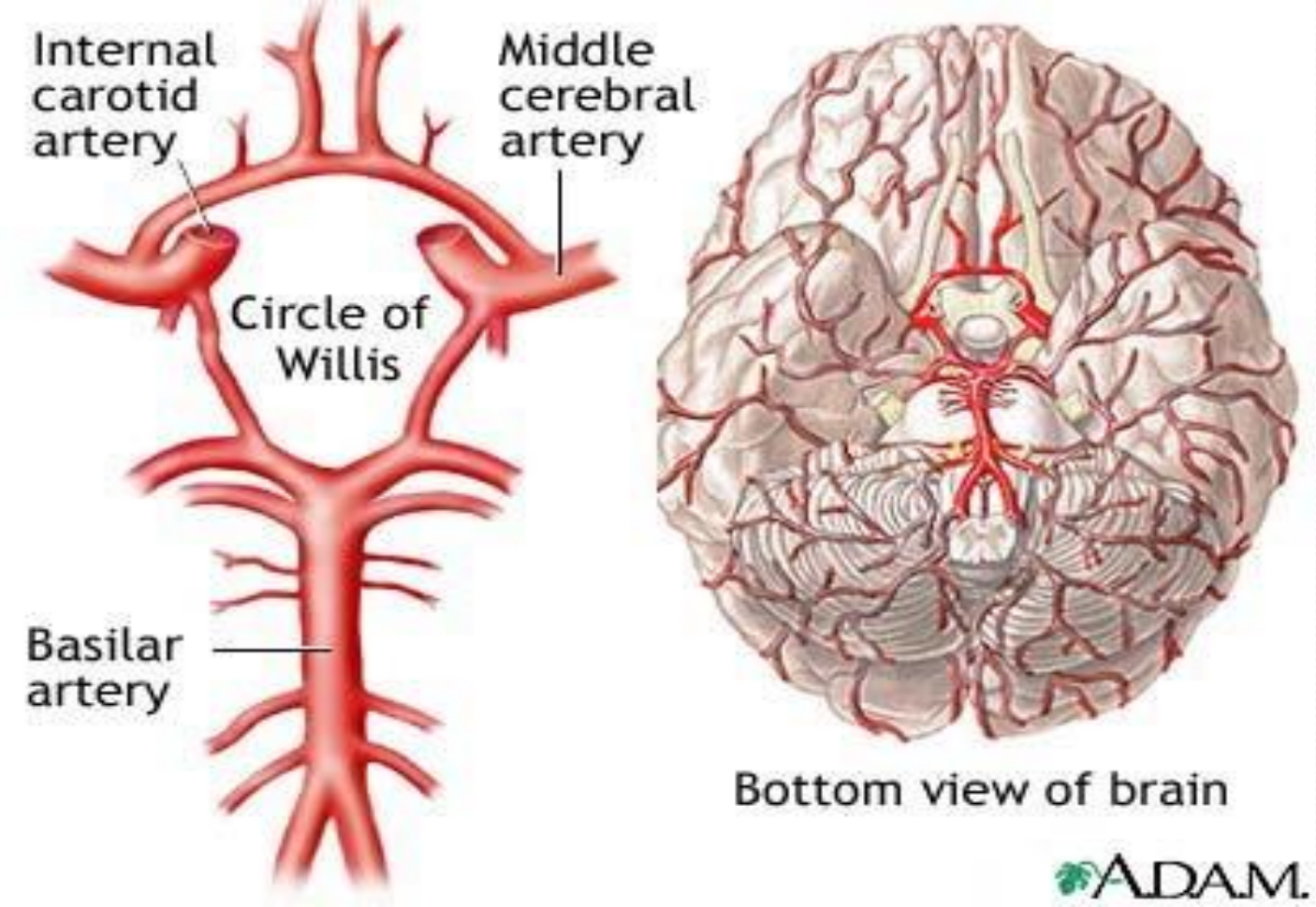
- The circle of Willis consists of six large vessels

1-Anterior cerebral artery (left and right)
Anterior communicating artery
2-Internal carotid artery (left and right)
3-Posterior cerebral artery (left and right)
Posterior communicating artery (left and right)
Basilar artery

-The middle cerebral arteries, supplying the brain, are not considered part of the circle.



CEREBRAL CIRCULATION



Innervation

Three systems of nerves innervate the cerebral blood vessels:

- **1-Sympathetic**: Postganglionic sympathetic neurons have their bodies in the superior cervical ganglia . During acute hypertension it attenuates the increase in CBF.
- **2-Parasympathetic**: Cholinergic neuron originate in sphenopalatine ganglia end on large arteries.
- **3-Sensory nerves**

Cerebral blood flow(CBF)

CBF is tightly regulated to meet the brain's metabolic demands

- **Normal Rate of Cerebral Blood Flow**

Normal blood flow through the brain of the adult person averages

= 50 to 65 ml /100 grams of brain tissue / minute.

For entire brain:

750 to 900 ml/min = 15 % of the resting cardiac output.

It is important to maintain CBF within narrow limits because:-

- Too much blood can raise intracranial pressure (ICP) which can compress and damage delicate brain tissue.

-Too little blood flow causes ischemia.

- **Ischemia results if blood flow to the brain is below:-**
- **18 to 20 ml / 100 gm brain tissue / minute**

- Tissue death occurs if flow drops below 8 to 10 ml / 100 gm brain tissue / minute.

Cerebral perfusion pressure(CPP)

- **Cerebral perfusion pressure (CPP):-**
- The net pressure of blood flow to the brain.
- CPP can be defined as:
- *CPP = MAP – ICP*
- CPP is regulated by **two balanced, opposing forces**:
- **1-Mean arterial pressure(***MAP)* is the force that pushes blood into the brain
- **2-ICP** force that pushes out.
- - CPP is normally between **70 - 90 mmHg in** an adult human

REGULATION OF CEREBRAL BLOOD FLOW

Regulation of Cerebral Blood Flow

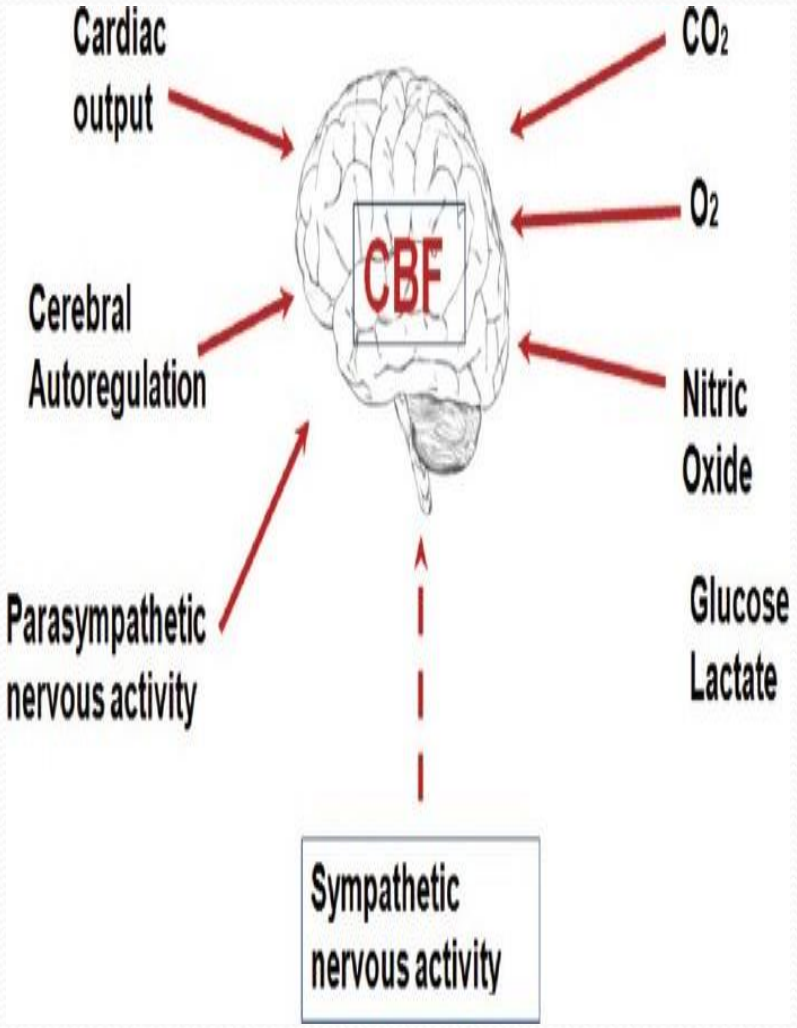
-Three metabolic factors have potent effects in controlling the cerebral blood flow :-

(1) Carbon dioxide concentration,

(2) Hydrogen ion concentration,

(3) Oxygen concentration.

- Neural factors
- Other mediators



REGULATION OF CEREBRAL BLOOD FLOW

1- Increase Cerebral Blood Flow in Response to Excess Carbon Dioxide or Excess Hydrogen Ion Concentration.

-70 % increase in arterial PCO2 approximately doubles the cerebral blood flow.

- Carbon dioxide increase cerebral blood flow by combining first with water in the body fluids to form carbonic acid, with subsequent dissociation of this acid to form hydrogen ions.

- The hydrogen ions cause vasodilation of the cerebral vessels.

The dilation is directly proportional to the increase in hydrogen ion concentration up to a blood flow limit of about **twice normal**.

- Substance that increases **the acidity of the brain tissue** (Such **as lactic acid, pyruvic acid**) & increases hydrogen ion concentration, will increase cerebral blood flow.

Regulation of CBF, cont.,

- **Hypoxia & Hypercapnia:**
- **-Excess carbon dioxide can dilate blood vessels up to 3.5 times their normal size**

  -Blood vessels also dilate in response to low pH (acidity).
- **- when activity in a given region of the brain is heightened, the increase in CO_2 and H^+ concentrations causes cerebral vasodilatation, and deliver more blood to the area to meet the increased demand.**
- **- Hypoxia, or inadequate oxygen, also dilates blood vessels and increases blood flow.**
- **While high levels of oxygen constrict cerebral B.V**

-Nitric oxide & adenosine are autoregulation mediators.

Neural stimuli:

-Under normal conditions sympathetic has little effect, because the blood flow auto-regulation mechanism can override the nervous effects.

-During acute hypertension, sympathetic attenuates increase in CBF.

The sympathetic nervous system normally constricts the large- and intermediate-sized brain arteries enough to prevent the high pressure from reaching the smaller brain blood vessels. This is important in preventing vascular hemorrhages into the brain for preventing the occurrence of "cerebral stroke."

Regulation of CBF, cont.,

- **Increased hydrogen ion concentration greatly depresses neuronal activity.**

- So an **increase in hydrogen** ion concentration causes **an increase in blood flow**, which in turn carries hydrogen ions & carbon dioxide .

-Loss of carbon dioxide removes carbonic acid and other acid forming substances away from the brain tissues ,this **reduces the hydrogen ion** concentration back toward normal to maintain a constant hydrogen ion concentration in the cerebral fluids and thereby helps **to maintain a normal neuronal activity**

Regulation of CBF, cont.,

- **Oxygen Deficiency as a Regulator of Cerebral Blood Flow**.

-The rate of utilization of oxygen by the brain tissue **is :-**

- **3.5 (± 0.2) ml of oxygen / 100 grams of brain tissue/minute.**

- If blood flow to the brain **insufficient** , the oxygen deficiency mechanism causing vasodilation, returning the brain blood flow and transport of oxygen to the cerebral tissues to normal.

- Decrease in cerebral *tissue PO2* ***below about 30 mm Hg (normal value is 35 to 40 mm Hg)*** immediately begins to increase cerebral blood flow.

-brain function becomes deranged at lower values of PO2 especially at PO2 levels **below 20 mm Hg.**

- Oxygen deficiency is a regulator of cerebral blood flow except during periods of intense Brain activity (at this time Co2& H are more important)

Autoregulation

- The brain maintains proper CPP through the process of **autoregulation:**
- **-Cerebral blood flow is "autoregulated"** extremely well between arterial pressure limits of **60 and 140 mm Hg.**
- The response to **lower pressure**, is arteriolar dilation in the brain while when **blood pressure rises** they constrict.
- Thus, changes in the body's overall blood pressure do not normally alter cerebral perfusion pressure drastically.
- At their most constricted condition, blood vessels create a pressure of 150 mmHg, and at their most dilated the pressure is about 60 mmHg.

Auto-Regulation of cerebral circulation, continued,….

- When pressures are outside the range of **60 to 150** mmHg, the blood vessels' ability to autoregulate pressure through dilation and constriction **is lost**, and cerebral perfusion is determined by **blood pressure alone without autoregulation**.

- Thus, hypotension can result in severe cerebral ischemia & hypertension can result in stroke

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Effect of ICP changes on systemic blood pressure;

Cushing reflex:‘Normally, the ICP [Intracranial Pressure] ranges from 1 to 15 mm Hg’, (but other sources give ranges like 8 to 18 mm Hg;)

-If **ICP > 33 mmHg** over a short period of time, CBF will **drop** markedly, leading to hypoxia and hypercapnea of vasomotor area causing blood pressure rises.

Stroke:

Stroke occurs when the blood supply to a part of the brain is blocked resulting in the death of an area.

- if the **middle cerebral artery** is blocked on the left side of the brain, the person is likely to become
- 1- **Totally demented** because of lost function in Wernicke's speech comprehension area in the left cerebral hemisphere
- 2-Unable to speak words because of loss of Broca's motor area for word formation.
- 3-In addition, loss of function of neural motor control areas of the left hemisphere can create spastic paralysis of most muscles on the opposite side of the body.

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- Blockage of a **posterior cerebral artery** will cause infarction of the occipital pole on the same side, which causes loss of vision as (hemianopsia).

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STROKE(con----)

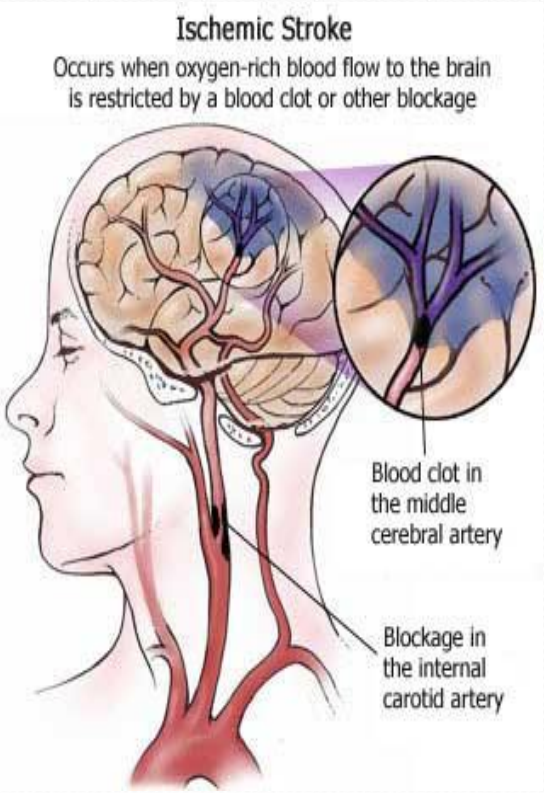
Principal types of stroke:

1-Thrombotic: Stroke due to the blockage of an artery leading to or in the brain by a blood clot.

2-Haemorrhagic: Stroke due to bleeding from a ruptured blood vessel, usually a consequence of hypertension.

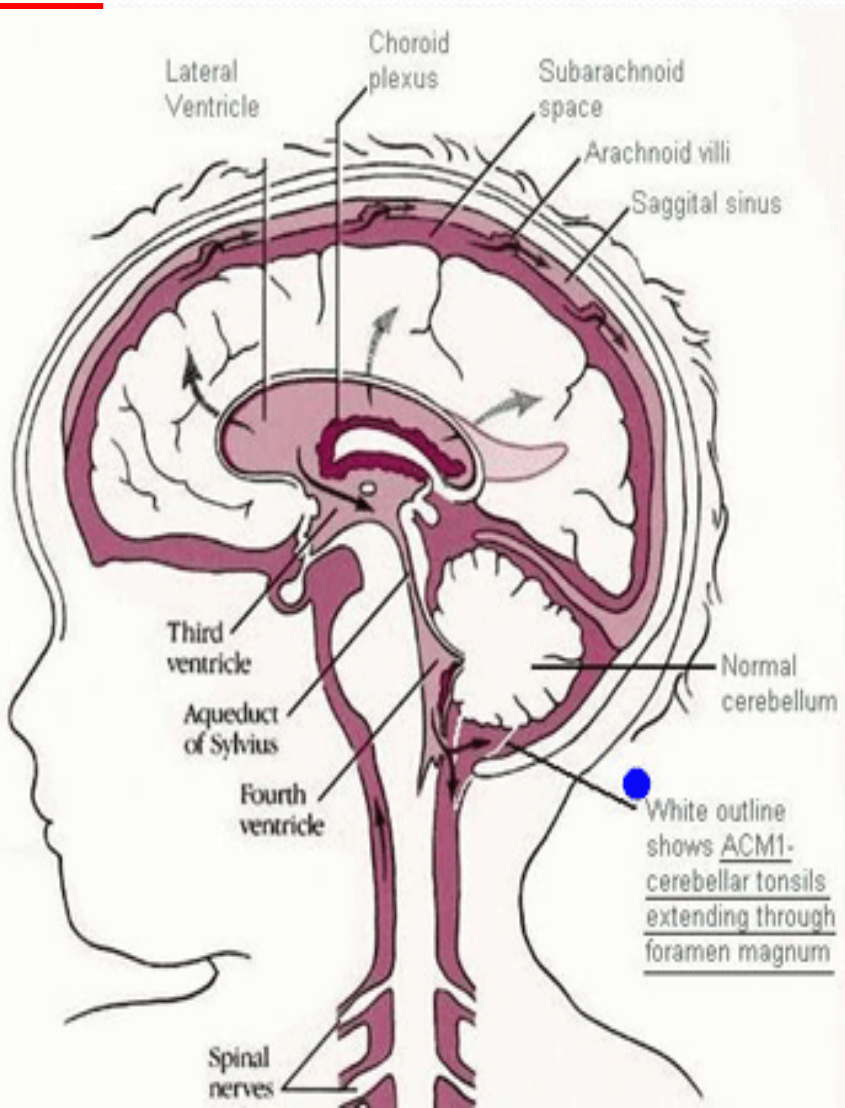
3-Embolic: Stroke due to the formation of a blood clot in a vessel away from the brain. The clot is carried in the bloodstream until it lodges in an artery leading to or in the brain.

The thrombotic and haemorrhagic forms are common,



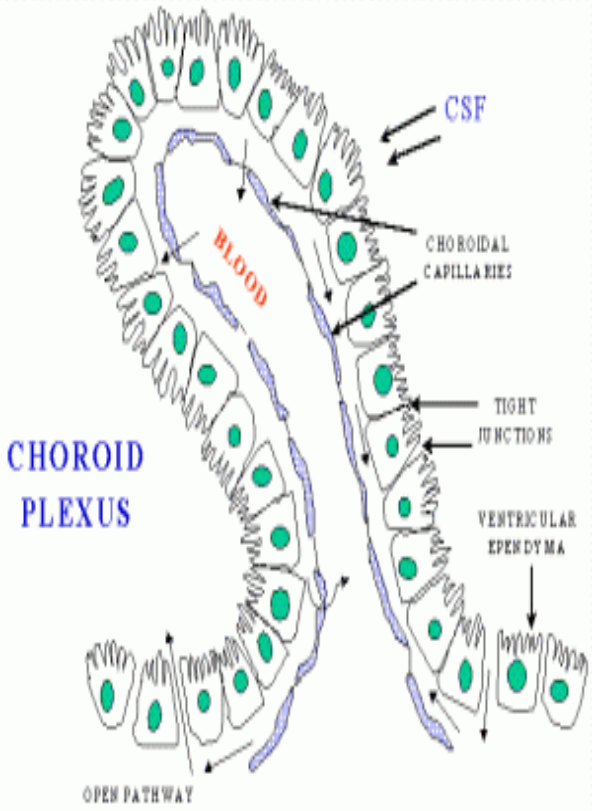
Cerebrospinal fluid

-This fluid is present in the ventricles of the brain, cisterna around brain and in the subarachnoid space around both the brain and the spinal cord. All these chambers are connected with one another, and the pressure of the fluid is maintained at a constant level.



Cerebrospinal Fluid (CSF)

- Volume = 150 ml
- Rate of production = 500 ml/day .
- Lumbar CSF pressure = 70-180 mm hg
- Absorption of CSF is proportionate to CSF pressure
- At pressure of 112 mm (normal average): filtration and absorption are equal.
- Below pressure **of 68** mm CSF, absorption stops.



Composition of the CSF

Substance	CSF	Plasma
Na+	147	150
K+	2.9	4.6
HCO_3-	25	24.8
PCO_2	50	39.5
pH	7.33	7.4
Osmolality Glucose	289 64	289 100

- The composition of CSF is nearly the same as brain ECF
- -osmotic pressure, approximately equal to that of plasma; -
- -sodium ion concentration is approximately equal to that of plasma;
- -chloride ion, about 15 percent greater than in plasma;
- - potassium ion, approximately 40 percent less
- - glucose about 30 percent less.

Functions of the CSF

1-Protective function(cushioning):

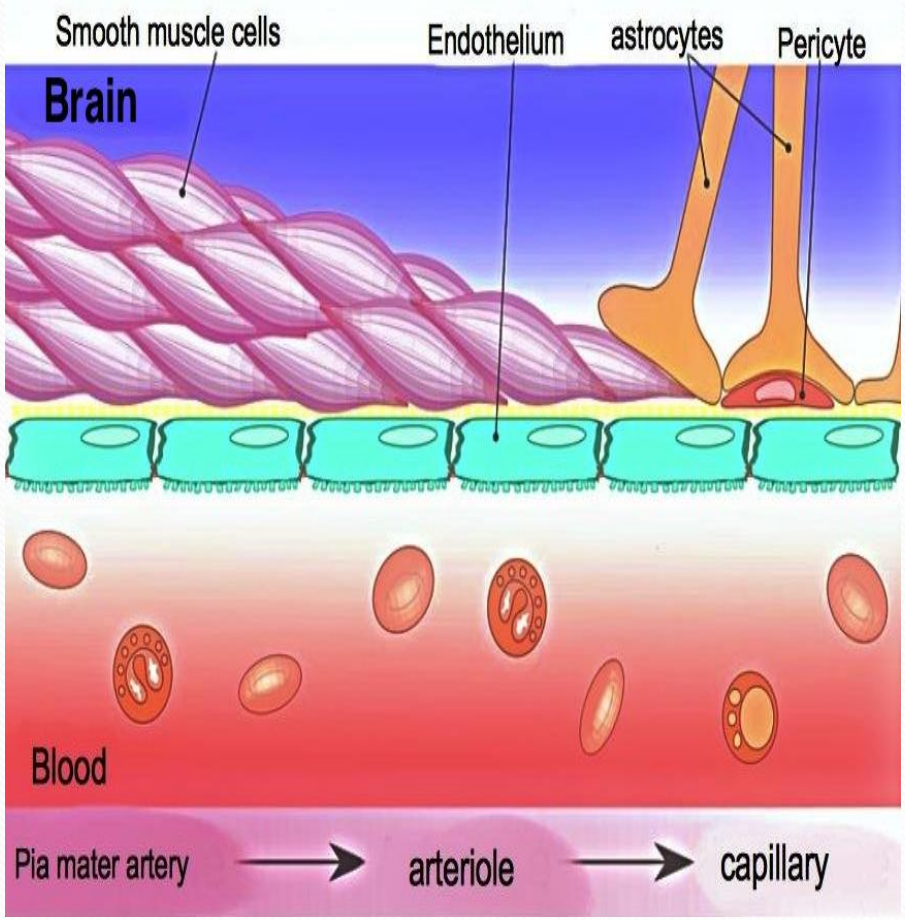
-In air brain weight =1400 gm, but in its water bath of CSF , brain weight = 50 gm, making it suspended and floated effectively.

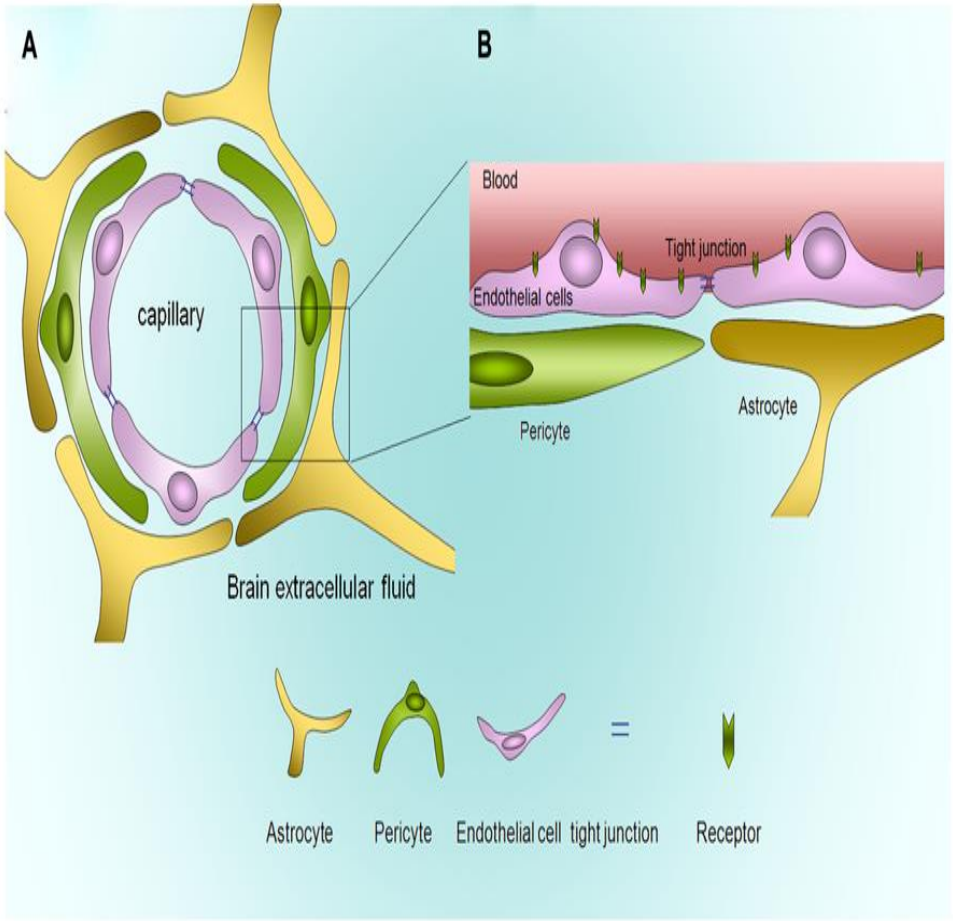
2- Facilitation of pulsatile cerebral blood flow

3- Distribution of peptides, hormones, neuroendocrine factors and other nutrients and essential substances to cells of the body

4- Wash away waste products.

BBB


Smooth muscle cells
Endothelium
astrocytes
Pericyte
Brain
Blood
Pia mater artery
arteriole
capillary


A
B
capillary
Brain extracellular fluid
Blood
Tight junction
Endothelial cells
Pericyte
Astrocyte
=
Astrocyte
Pericyte
Endothelial cell
tight junction
Receptor

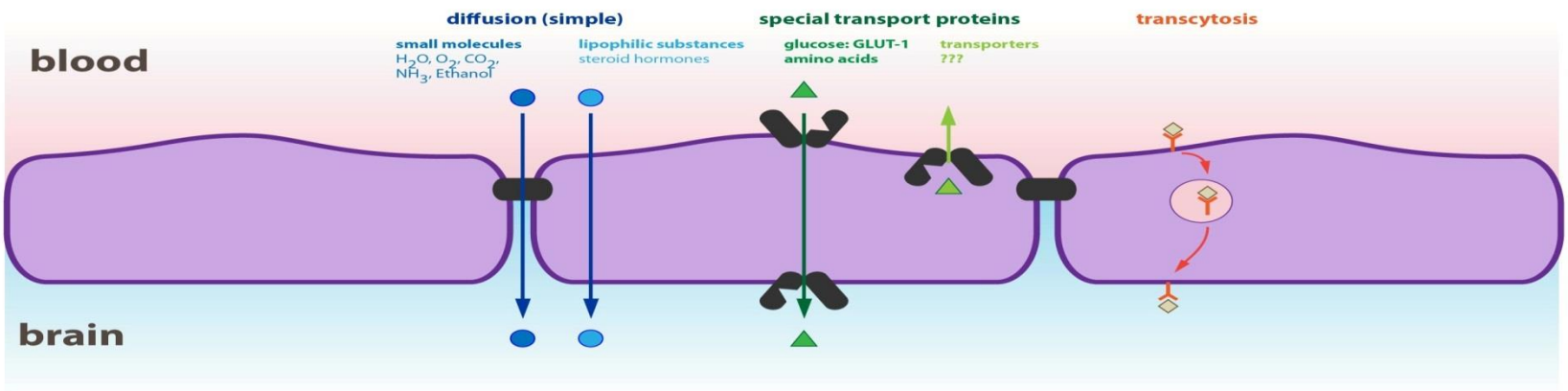
Blood brain Barrier (BBB)

It is between blood & CSF & brain tissue

- It is formed by the tight junctions between :-
- 1-Choroid plexus epithelial cells (astro& pericytes)
- 2- At brain capillary membrane (endothelial cells)

Penetration of substances into the brain

- **Molecules pass easily**:H2O, CO2, O2, lipid-soluble substances(as steroid hormones).
- **Molecules not pass**: proteins, antibodies, non- lipid-soluble large molecules.
- **Slight penetration**: cl, Na, K
- **Glucose** : its passive penetration is slow, but is transported across brain capillaries by GLUT1



Functions of BBB

- 1-Maintanins the constancy of the environment of the neurons in the CNS.
- 2-Protection of the brain from endogenous and exogenous toxins.
- 3-Prevent escape of the neurotransmitters into the general circulation.