Cerebral circulation & CSF formation

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Objectives:

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

-Cerebral circulation & Circle of Willis

- **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 contents & functions.
- Blood brain barrier (BBB), brain oedema

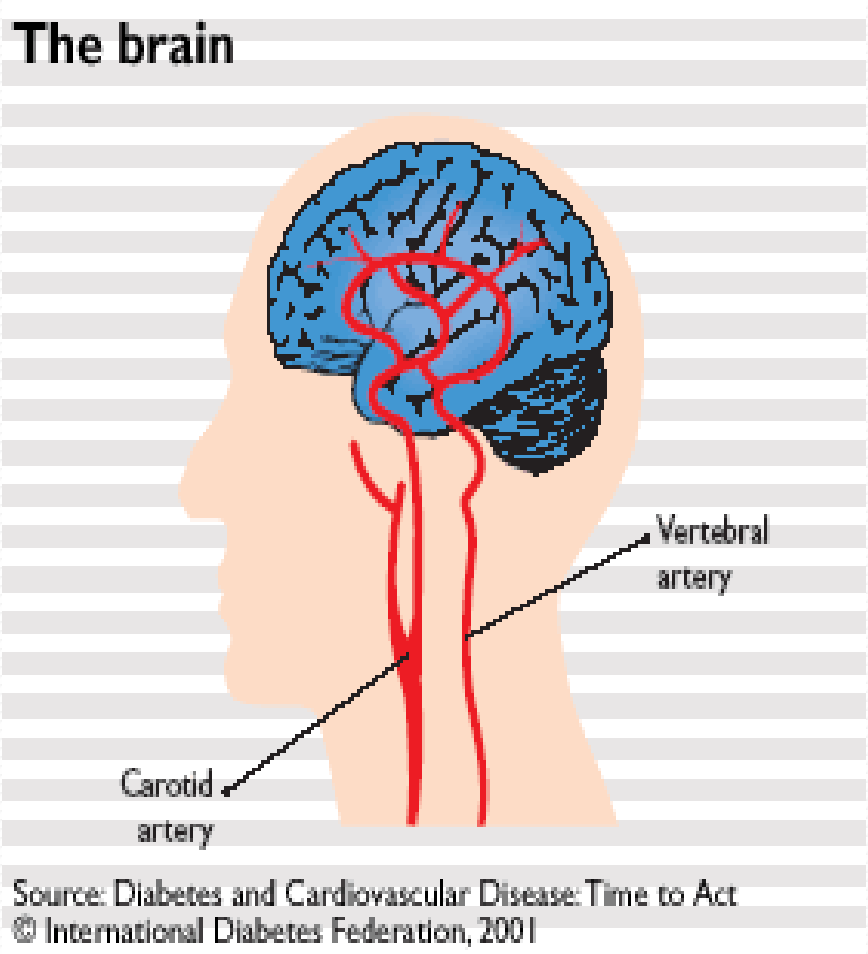
Brain receive its blood supply from four main arteries:

1- **two internal carotid arteries**

2- **two vertebral arteries.**

The Circle of Willis: A group of arteries near the base of the brain

Named after an English physician named Thomas Willis, who discovered it



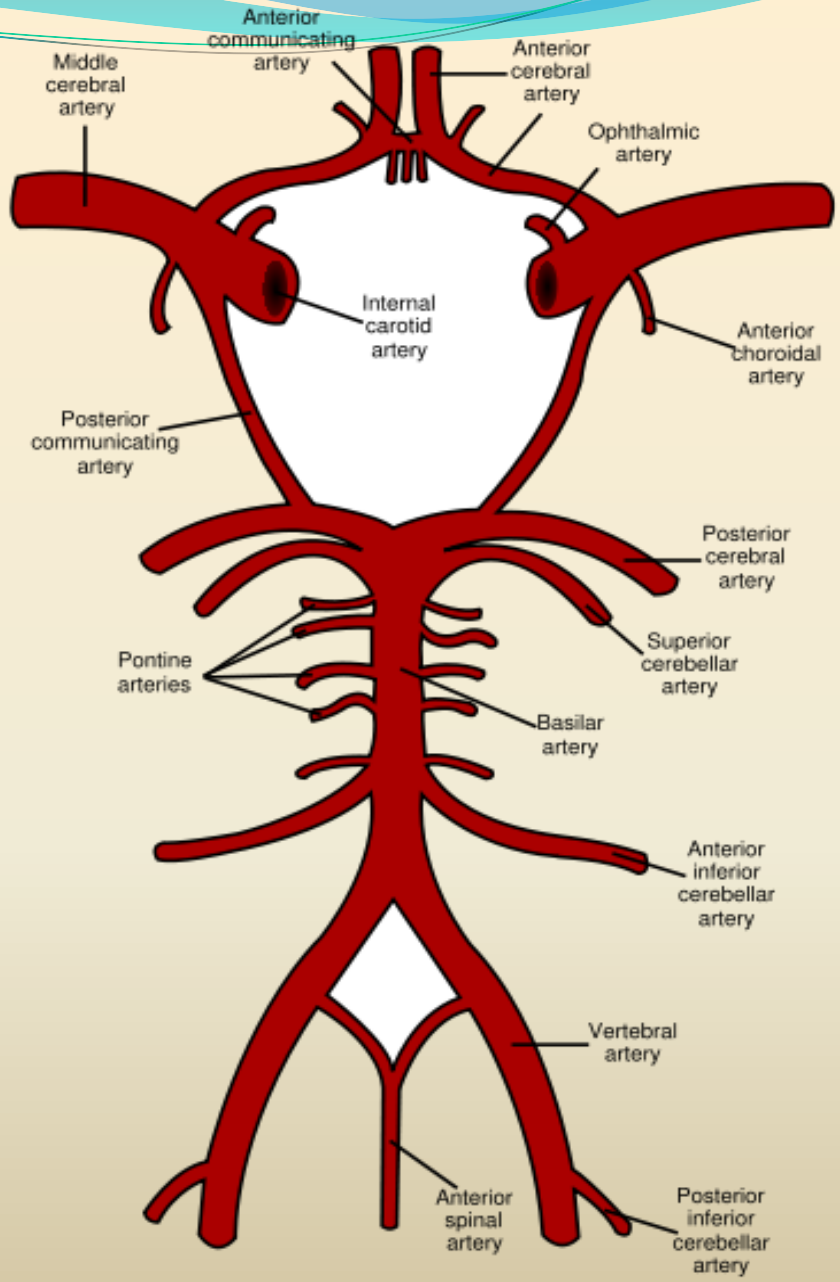
Cerebral Circulation

- The vertebral arteries unite to form Basilar artery

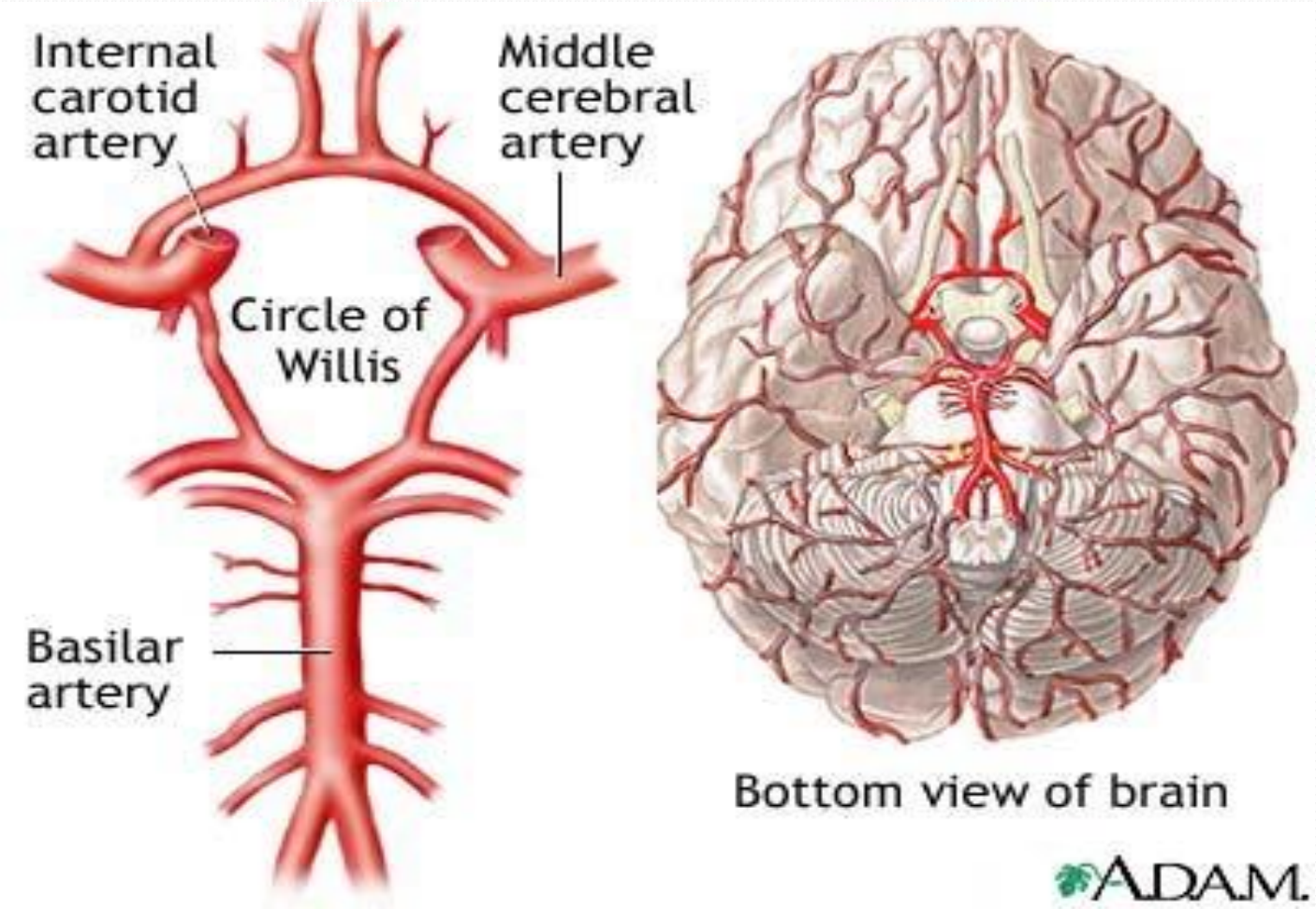
-The basilar artery and the carotids form the circle of Willis.

- The circle of Willis is origin of six large vessels

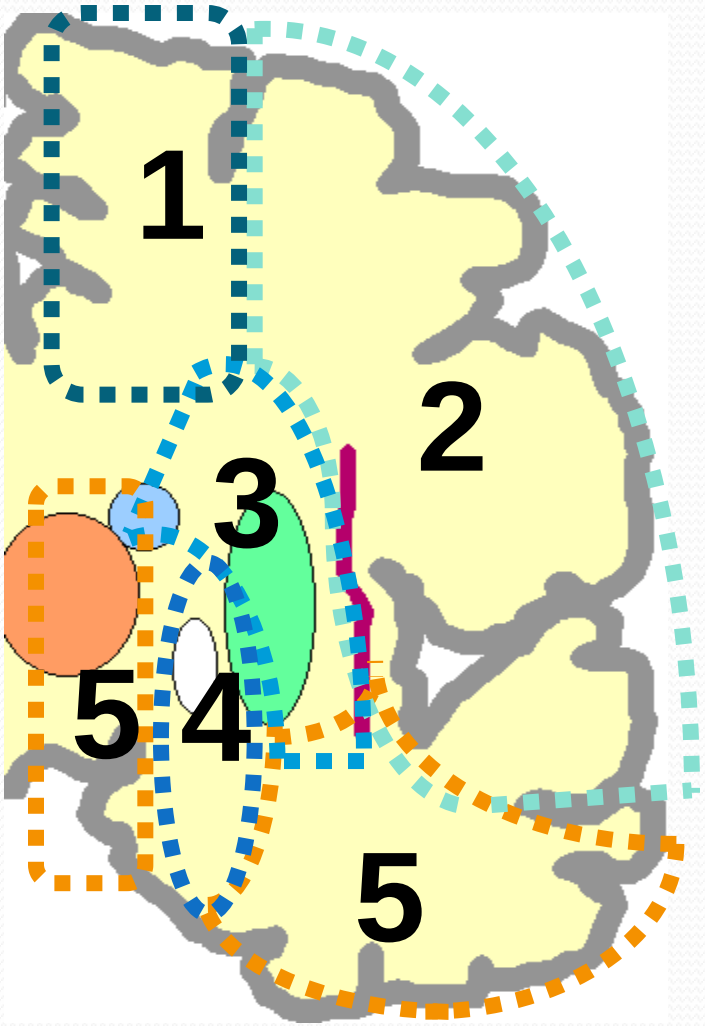
Substances injected into one carotid artery distributed almost completely to the cerebral hemisphere on that side. Normally no crossing over occurs probably because the pressure is equal on both sides



CEREBRAL CIRCULATION



Cerebral Artery Areas



1. anterior cerebral
2. Middle cerebral
3. Penetrating branches of middle cerebral
4. anterior choroidal
5. Posterior cerebral

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 attenuate 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 milliliters /100 grams of brain tissue / minute.**
- **For entire brain: 750 to 900 ml/min, or 15 per cent 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 g / minute, and tissue death occurs if flow drops below 8 to 10 ml / 100 g / 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, 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

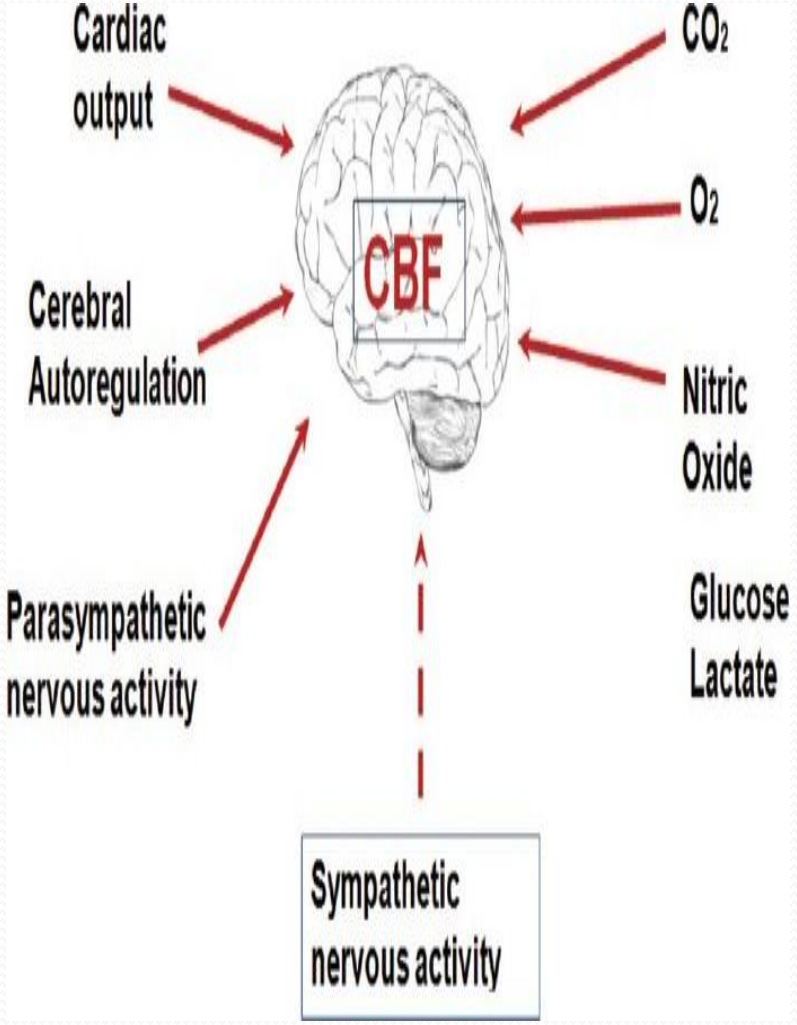
Regulation of Cerebral Blood Flow

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

(1) Carbon dioxide concentration,

(2) Hydrogen ion concentration,

(3) Oxygen concentration.



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 being almost directly proportional to the increase in hydrogen ion concentration up to a blood flow limit of about twice normal.

Any other substance that increases the acidity of the brain tissue, and increases hydrogen ion concentration, will increase cerebral blood flow.

Such substances include **lactic acid, pyruvic acid**,

Regulation of CBF, cont.,

- **Hypoxia & Hypercapnia:**

- -Excess carbon dioxide can dilate blood vessels up to 3.5 times their normal size
- -Hypoxia, or inadequate oxygen, also dilates blood vessels and increases blood flow.

-Blood vessels also dilate in response to low pH.

- - 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.
- -- high levels of oxygen constrict cerebral b.v
- 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."

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- Nitric oxide & adenosine are mediators.

REGULATION OF CEREBRAL BLOOD FLOW

Importance of Cerebral Blood Flow Control by Carbon Dioxide and Hydrogen Ions.

Increased hydrogen ion concentration greatly depresses neuronal activity.

-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 CEREBRAL BLOOD FLOW

Oxygen Deficiency as a Regulator of Cerebral Blood Flow. Except during periods of intense Brain activity:

The rate of utilization of oxygen by the brain tissue is —almost exactly 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.

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.

Regulation of cerebral circulation, continued,….

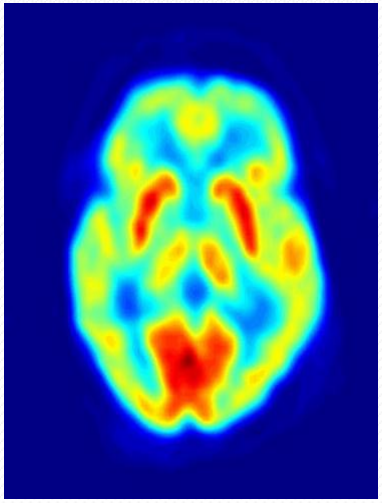
- When pressures are outside the range of **60 to 150** mmHg, the blood vessels' ability to autoregulate pressure through dilation and constriction is lost, and cerebral perfusion is determined by blood pressure alone without autoregulation.
- - Thus, hypotension can result in severe cerebral ischemia

- **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.

Measuring cerebral blood flow

- 1- Functional imaging resonance.
- 2-Positron emission tomography.
- Both be used to measure CBF. These techniques are also used to measure regional CBF (rCBF) within a specific brain region.
- -Radioactive xenon injection into carotid artery, pass into brain tissues show increase radioactivity in areas of increased blood flow due to local neuronal activity(blood flow increase in left motor area by movement of right hand)



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 almost **totally demented** because of lost function in Wernicke's speech comprehension area in the left cerebral hemisphere, and becomes unable to speak words because of loss of Broca's motor area for word formation.
- -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.

- blockage of a *posterior cerebral artery* will cause infarction of the occipital pole on the same side, which causes loss of vision in both eyes in the half of the retina on the same side as the stroke lesion (hemianopsia).
- -strokes that involve the blood supply to the midbrain can block nerve conduction in major pathways between the brain and spinal cord, causing *both sensory and motor abnormalities.*

CEREBRAL CIRCULATION

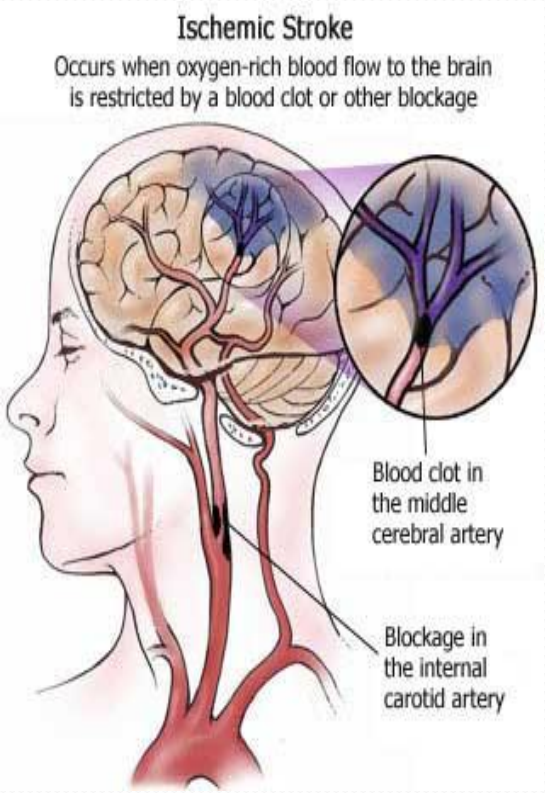
Principal types of stroke:

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,

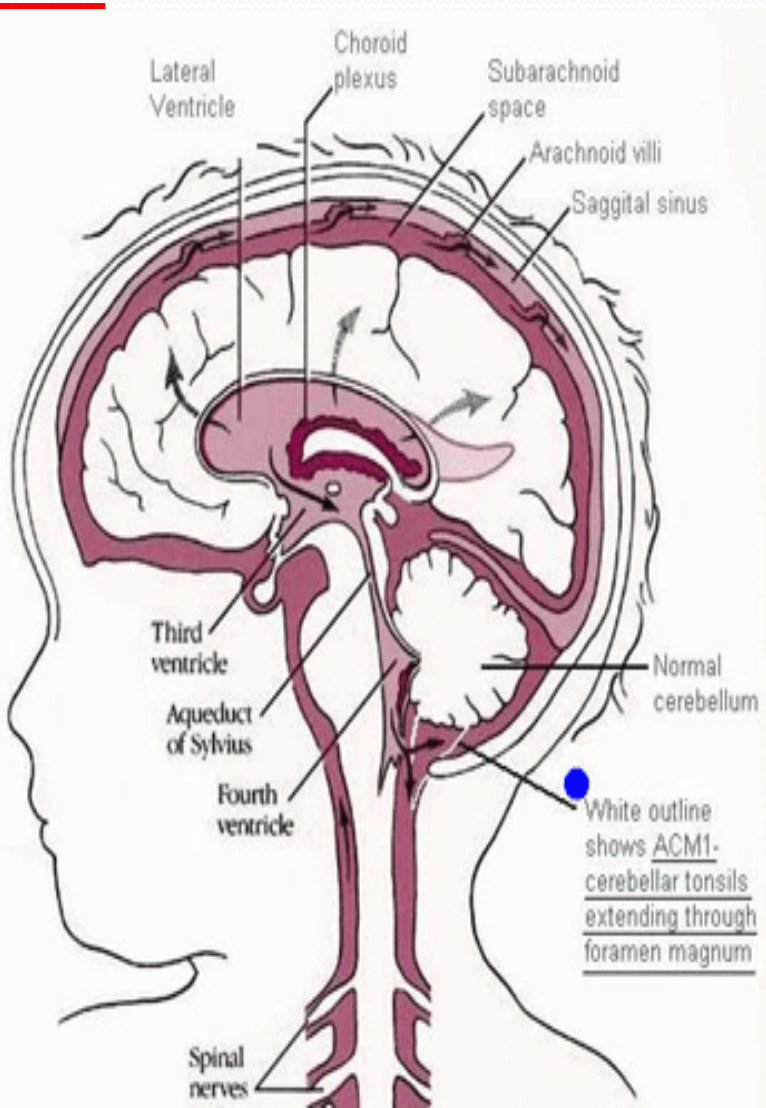


Cerebrospinal fluid

- CSF is formed in:

1. Choroid plexus in the 4 ventricles.

- CSF is absorbed by:Arachnoid villi into venous circulation
- **-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.**



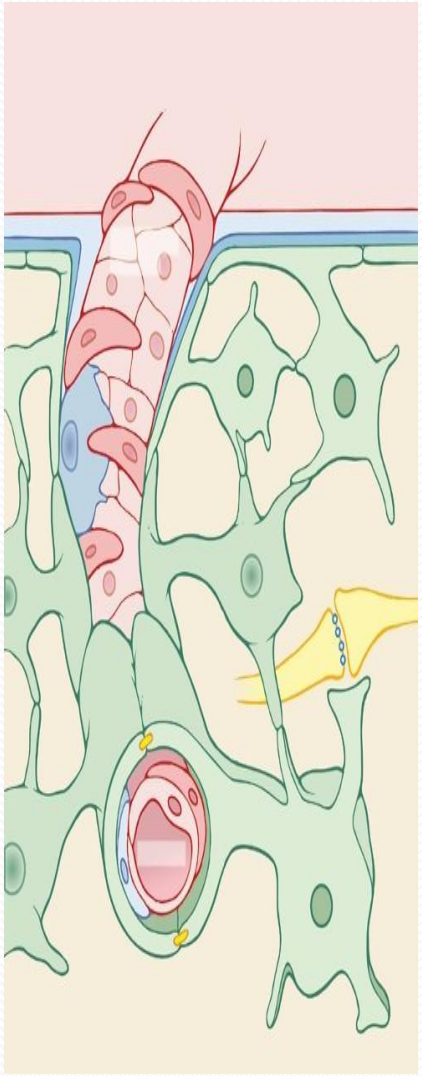
Cerebral Microcirculation

- The metabolic rate of the brain gray matter where the neuronal cell bodies lie is about four times as great as that of white matter; so, the number of capillaries and rate of blood flow are also about four times as great in the gray matter.

An important structural characteristic of the brain capillaries is that :

1-mostly are **much less "leaky"** than the blood capillaries, because they are supported on all sides **by "glial feet,"** which are small projections from glial cells, provide physical support to prevent overstretching of the capillaries in case of high capillary blood pressure.

2-The walls of the small arterioles leading to the brain capillaries **greatly thickened** in people who develop high blood pressure, and these arterioles remain significantly constricted all the time to prevent transmission of the high pressure to the capillaries.

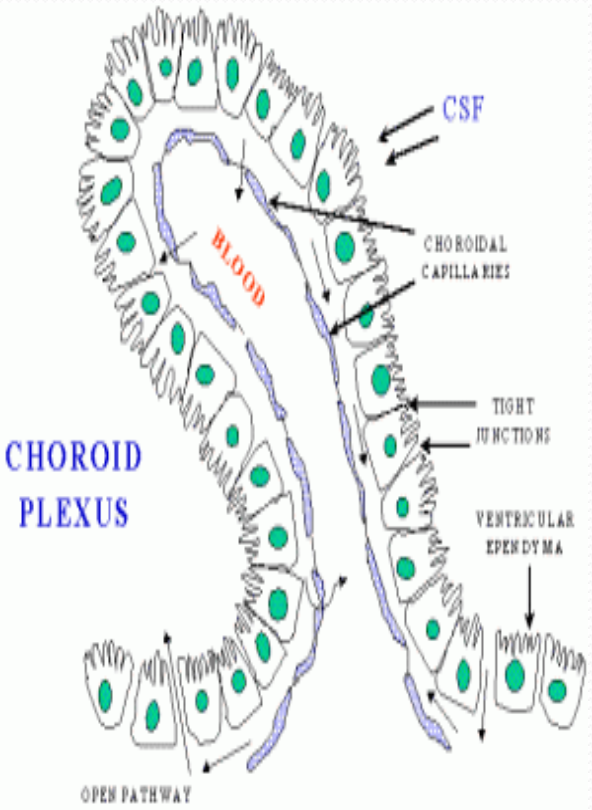


Cerebrospinal Fluid (CSF)

CSF fills ventricles and subarachnoid space.

- Volume = 150 ml
- Rate of production = 500 ml/d .
- 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.
- **Hydrocephallus:**

1. External hydrocephallus: Large amounts of CSF accumulates when the reabsorptive capacity of arachnoid villi decreases.
2. Internal hydrocephallus: occurs when certain foramina are blocked or obstruction within ventricular system, resulting in distention of the ventricles.



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 g, but in its water bath of CSF , brain weight = 50 g, making it suspended and floated effectively.

-When the head receives a blow, the arachnoid slides on the dura and the brain moves, but its motion is gently absorbed by the CSF cushion and by the arachnoid trabiculae.

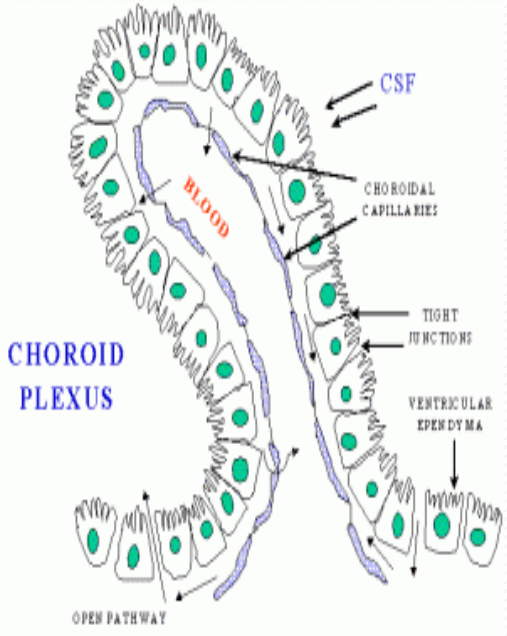
2- Facilitation of pulsatile cerebral blood flow

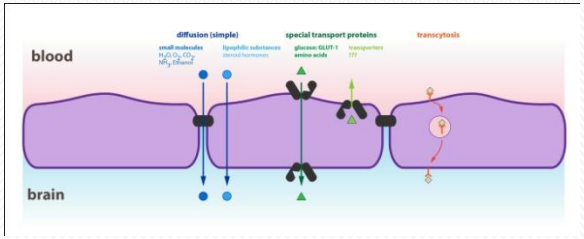
3- Distribution of peptides, hormones, neuroendocrine factors and other nutrients and essential substances to cells of the body

4- Wash away waste products.

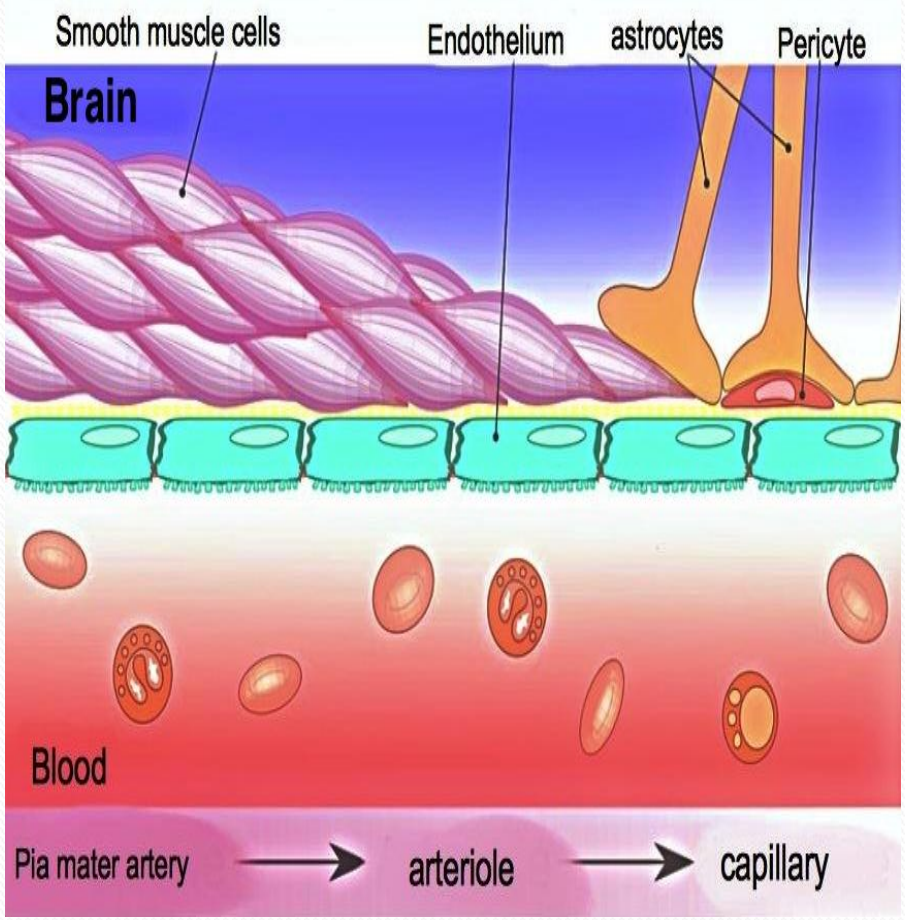
Features of cerebral vessels

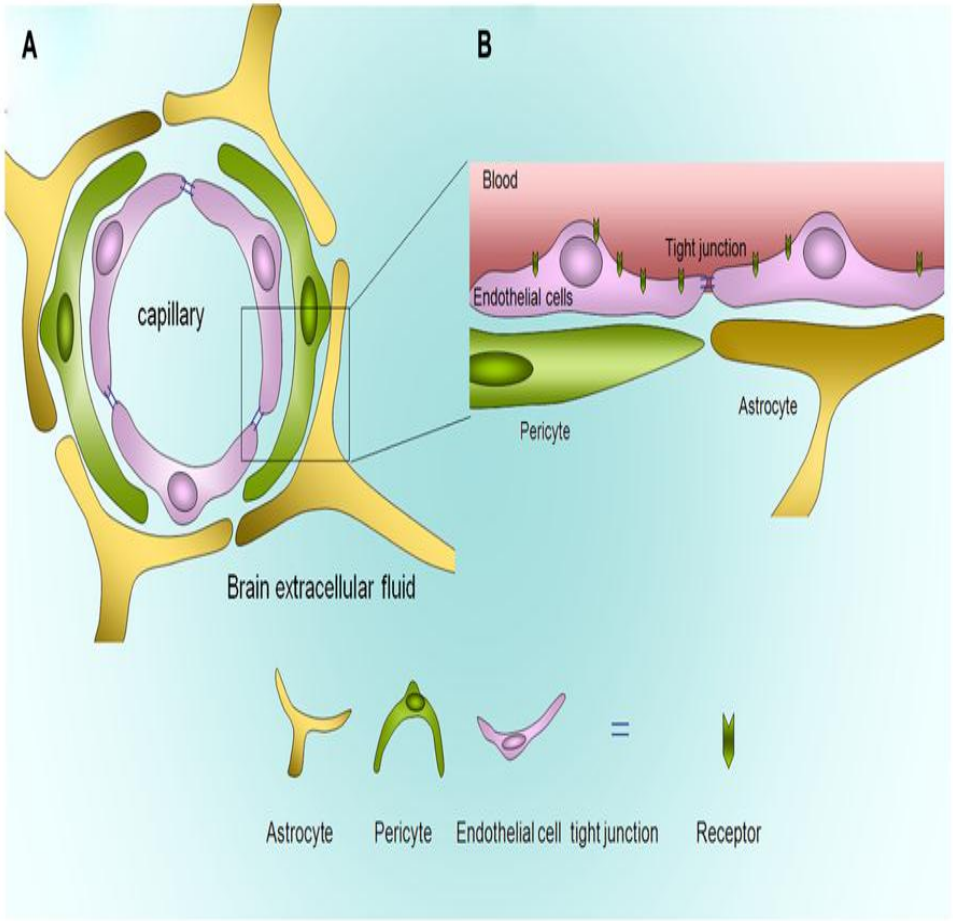
- Choroid plexus:
- There are Gaps between endothelial cells of the capillary wall allow CSF flow& no gaps between epithelial cells which is in direct contact with blood
- Capillaries in the brain substance are non-fenestrated and there are tight junctions between endothelial cells to limit passage of substances through the junctions and supported by glial feets





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

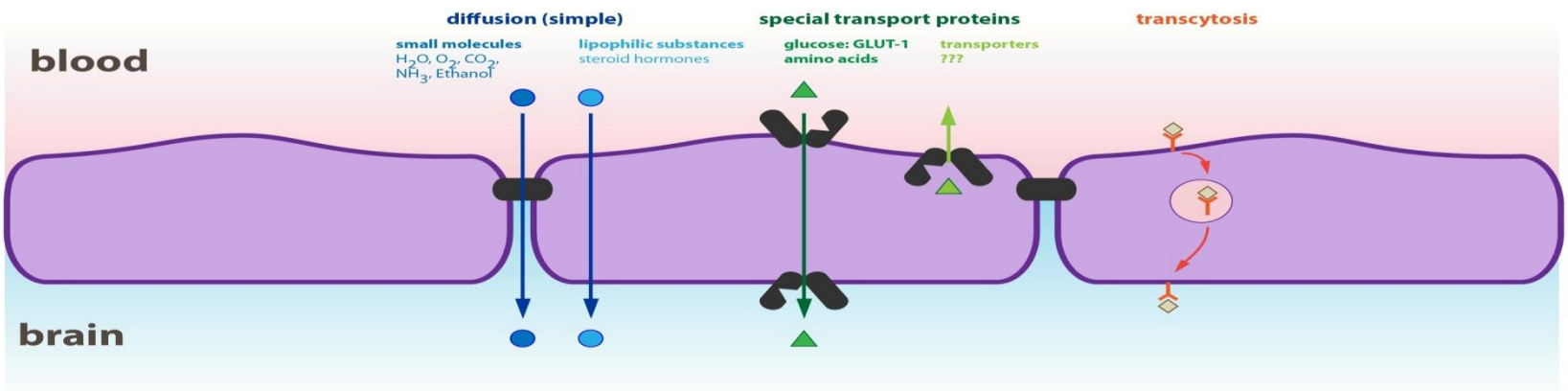
Blood brain Barrier (BBB)

It is between blood &CSF & brain tissue

- It is formed at :-
- 1-choroid plexus epithelial cells and
- 2- at brain tissue capillary membrane (epithelial cells)
- - formed by the tight junctions between capillary endothelial cells of the brain capillaries and between epithelial cells in the choroid plexus. This effectively prevents proteins from entering the brain and slow the penetration of smaller molecules.

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.

Brain Edema

- Accumulation of extra fluid compresses the blood vessels, causing decreased blood flow and destruction of brain tissue.

- - A common cause is a serious blow to the head, leading to *brain concussion,* in which the brain tissues and capillaries are traumatized and capillary fluid leaks into the traumatized tissues.

- Once brain edema begins, it often initiates two vicious circles because of the following positive feedbacks:

- (1) Edema compresses the vasculature. This in turn decreases blood flow and causes brain ischemi causes arteriolar dilation with further increase in capillary pressure, then causes more edema fluid

- (2) The decreased cerebral blood flow also decreases oxygen delivery. This increases the permeability of the capillaries, allowing still more fluid leakage.

- -One such measure is to infuse intravenously a concentrated osmotic substance, such as a concentrated mannitol solution. This pulls fluid by osmosis from the brain tissue. Another procedure is to remove fluid quickly from the lateral ventricles of the brain by means of ventricular needle puncture, thereby relieving the intracerebral pressure.