جامعة الملك سعود
King Saud University

Revised By
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MED437

22th Lecture | The Physiology Team

AUTOREGULATION OF CEREBRAL BLOOD FLOW

Objectives:

- Describe cerebral circulation & circle of Willis
- Explain main arteries that supply blood to brain
- Normal Rate of Cerebral Blood Flow
- Explain auto-regulation of cerebral blood flow
- Explain the factors affecting the cerebral blood flow
- Effects of impaired cerebral blood circulation

Done by:

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Colour index:
- important
- Numbers
- Extra

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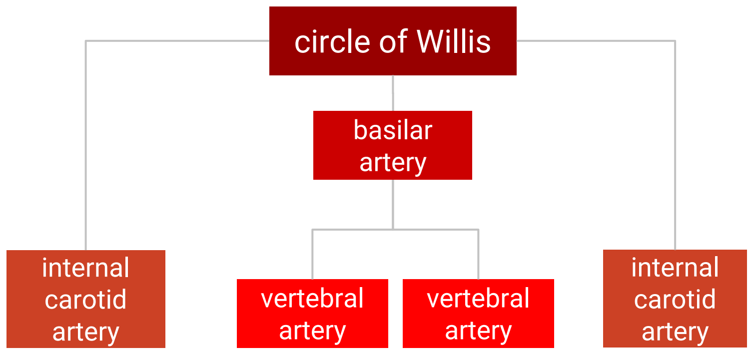
CEREBRAL CIRCULATION

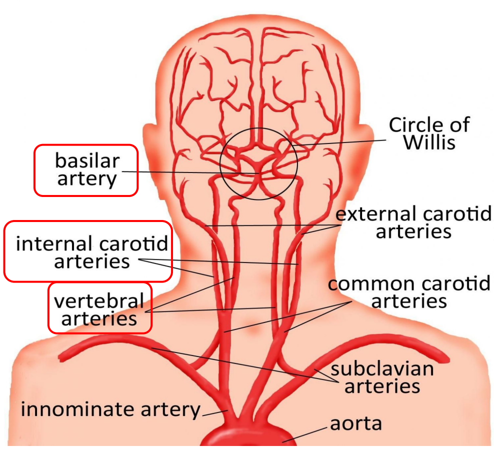
- **Brain receive its blood supply from four <u>main arteries</u>:**
  - Two internal carotid arteries
  - Two vertebral arteries.

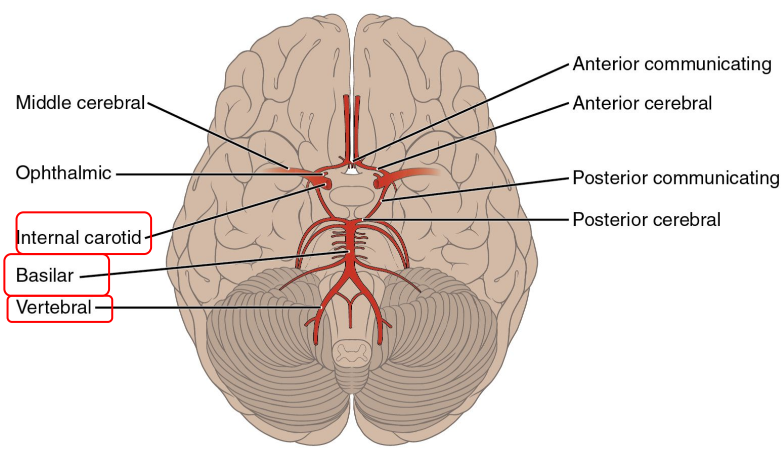
❖ The vertebral arteries unite to form Basilar artery.

❖ The basilar artery and the carotids arteries form the circle of Willis.

❖ The circle of Willis is origin of six large vessels







Carotid artery injection

Substances injected into one carotid artery distributed completely to the cerebral hemisphere on that side. Normally **no crossing over** occurs <u>because of equal pressure on both sides.</u>

Clinical significance

The clinical consequences of vascular disease in the cerebral circulation is depend upon which vessels or combinations of vessels are involved.

CEREBRAL CIRCULATION

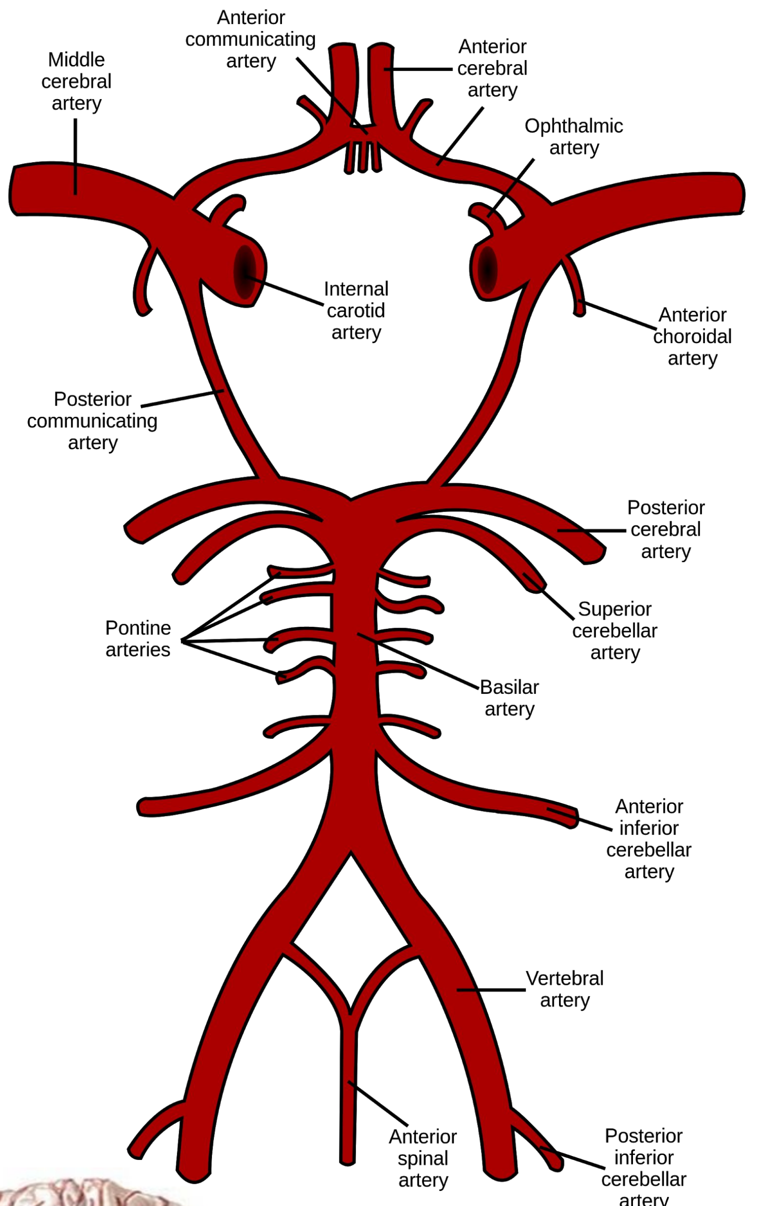
The circle of Willis consists of six large Vessels:

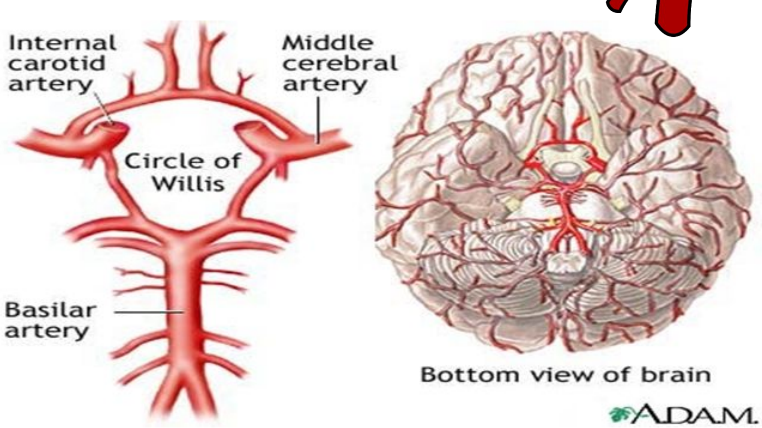
1-Anterior cerebral artery (left and right) Anterior communicating artery

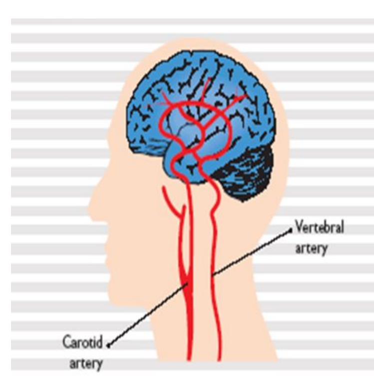
2-Internal carotid artery (left and right)

3-Posterior cerebral artery (left and right) Posterior communicating artery (left and right) Basilar artery

N.B: The middle cerebral arteries, supplying the brain, are **not considered part of the circle.**







Group of arteries near the base of the brain which is called the **Arterial Circle of Willis.** English physician, **Thomas Willis,** who discovered it and then published findings in 1664, on Cerebri anatomi

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.**

Blood Brain Barrier

It is between **blood & CSF & brain tissue**

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).

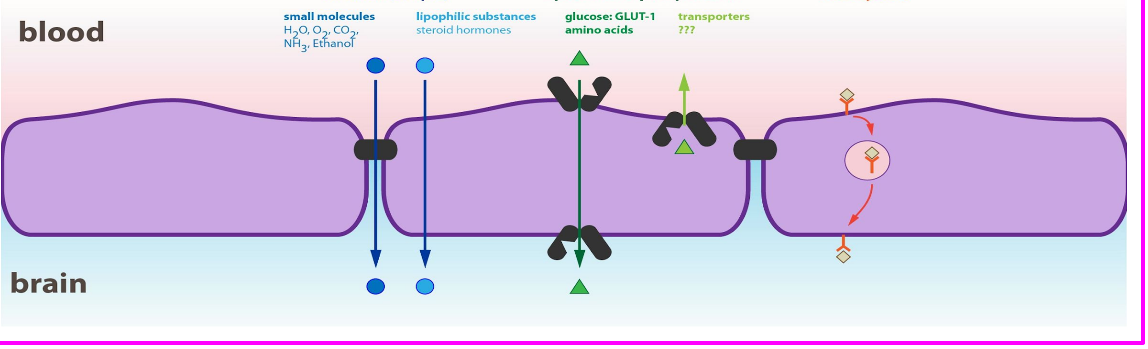
Molecules not pass:
proteins, antibodies, non- lipid soluble large molecules.

Slight penetration: cl, Na, K

Glucose : its passive penetration is slow, but is transported across brain capillaries by GLUT1

Functions of BBB

1. **Maintains** 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.



CEREBRAL BLOOD FLOW

- CBF is tightly regulated to meet the brain's **metabolic demands**
- Normal Rate of Cerebral Blood Flow
  - Brain: 1350 gm; 2% of Total Body Weight
- Normal blood flow through the brain of the adult person average 50 to 65 ml/ per 100 grams of brain tissue per minute.
- For entire brain: 750 to 900 ml/min, **15 percent** of the resting cardiac output.

ischemia

- 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 / min
- **Tissue death** occurs if flow drops below 8 to 10 ml / 100 g / minute.

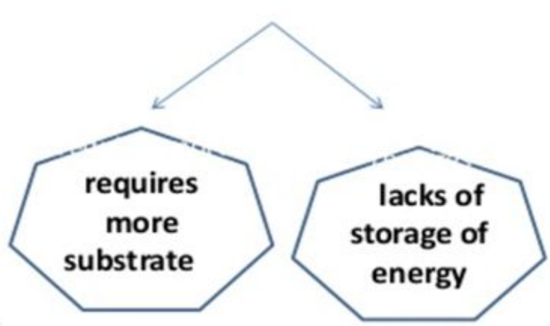
Physiological considerations:

Brain accounts for 2% of body weight yet requires 20% of resting oxygen consumption

O_2 requirement of brain is 3 – 3.5 ml/100gm/min

And in children it goes higher up to 5 ml/100gm/min

Brain has high metabolic rate



That's why brain requires higher blood supply

55ml/100gm/min is the rate of blood supply

Cerebral perfusion pressure(CPP)

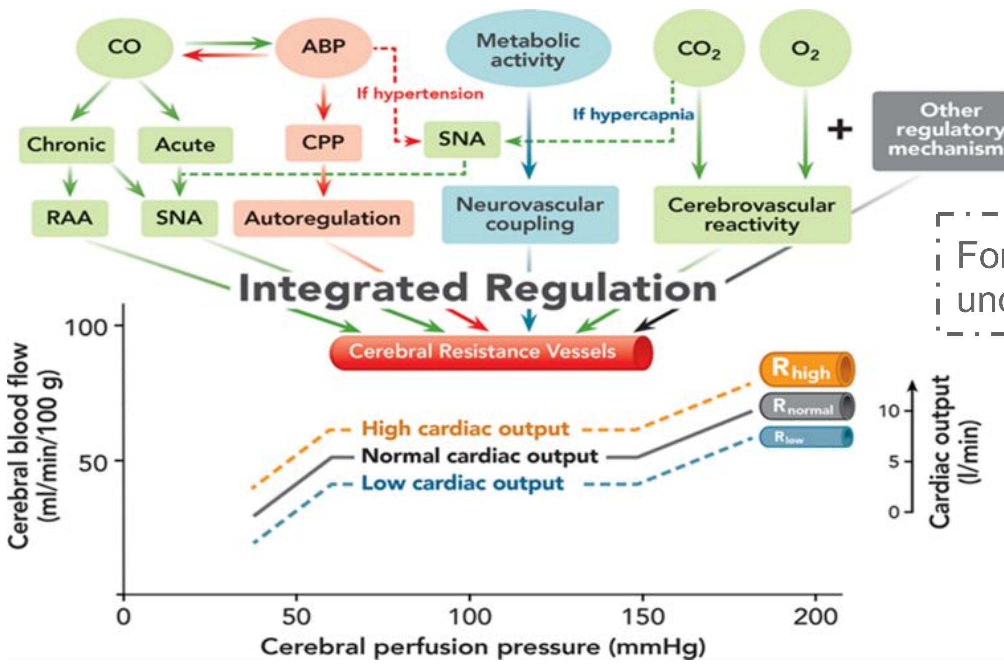
- **Cerebral perfusion pressure (CPP):-**
    - The net pressure of blood flow to the brain. **CPP** can be defined as:

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-intracranial pressure **(ICP)** force that pushes out.

- CPP is normally between **70 - 90 mmHg** in an adult human

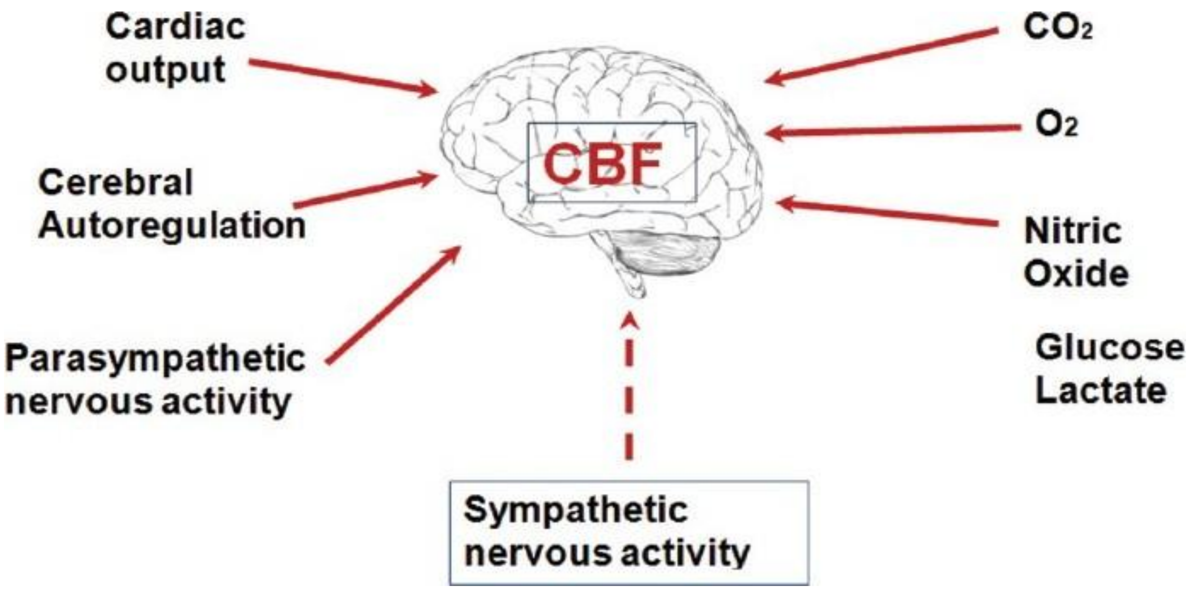
REGULATION OF CEREBRAL BLOOD FLOW

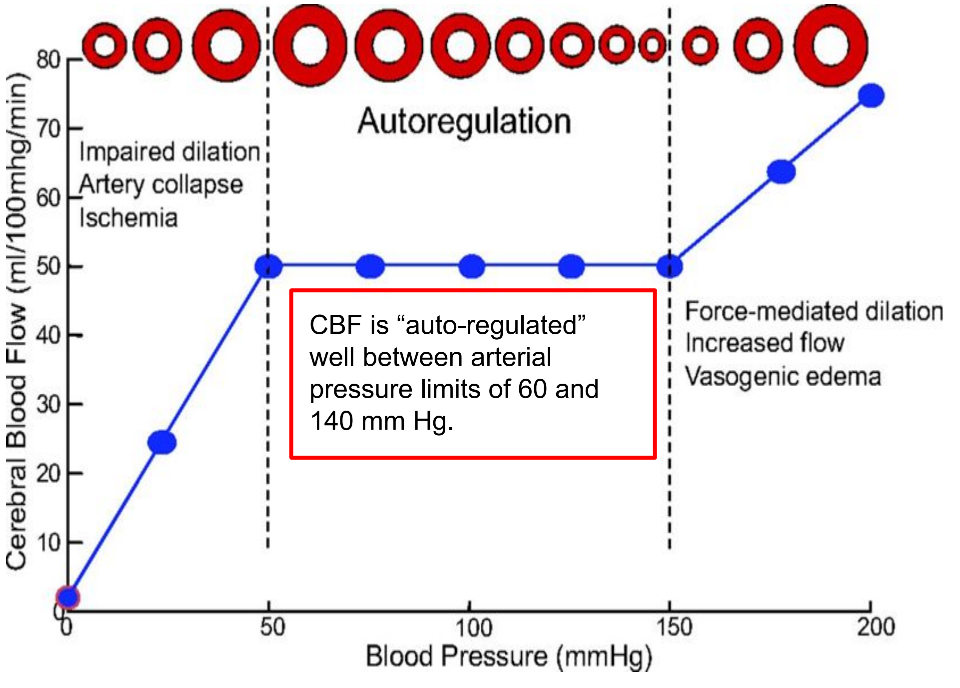


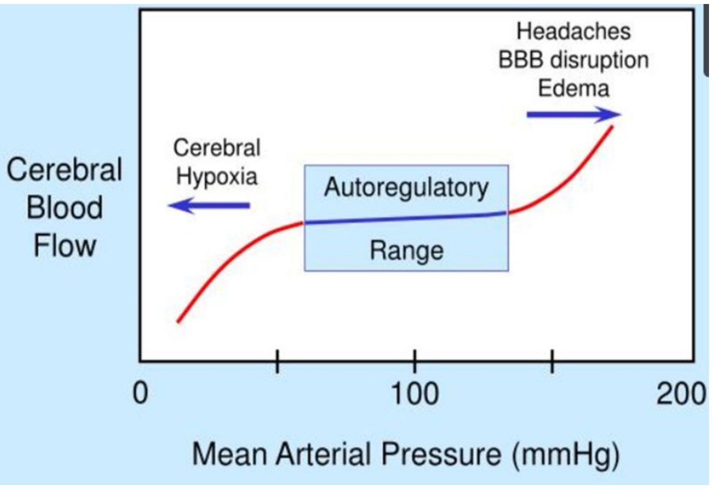
For your understanding

Cardiac output (CO); Sympathetic nervous activity (SNA);Renin–angiotensin–aldosterone (RAA) system; Arterial blood pressure (ABP); Cerebral perfusion pressure (CPP); Carbon dioxide (CO2) and oxygen (O2)
(R) Cerebral resistance vessels at high (Rhigh), normal (Rnorm), and low (Rlow)

REGULATION OF CEREBRAL BLOOD FLOW

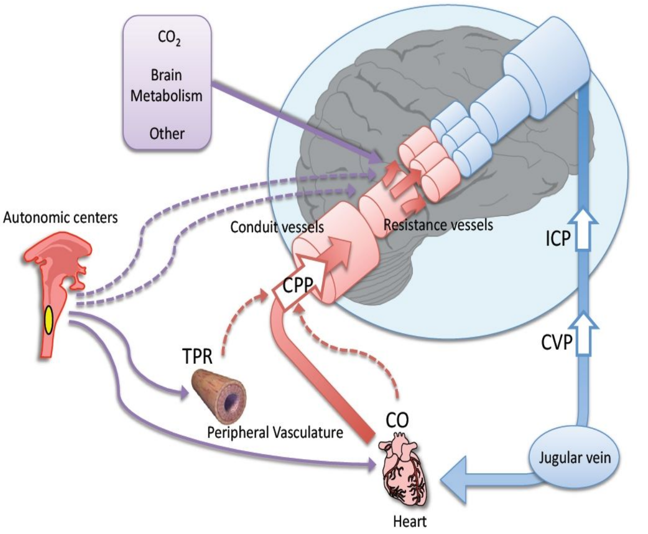






1- Myogenic/Pressure Autoregulation:

- Arterioles dilate or constrict in response to changes in BP and ICP in order to maintain a constant CBF
- Myogenic theory: The vascular smooth muscles are highly responsive to changes in pressure, a process called **myogenic activity,** that contributes to auto-regulation of cerebral blood flow.
- Vascular smooth muscle within cerebral arterioles contract to stretch response, regulating pressure changes. Autoregulation of CBF completely BP-dependent



- **Cerebral blood flow is well extremely "auto-regulated"** between arterial pressure limits of 60 and 140 mm Hg.
- Mean arterial pressure can be decreased acutely to as low as 60 mm Hg or increased to as high as 140 mm Hg without significant change in cerebral blood flow.
- Hypertension, auto-regulation of cerebral blood flow occurs even when the mean arterial pressure rises to as high as 160 to 180 mmHg. If arterial pressure falls below 60 mmHg, cerebral blood flow become severely decreased.

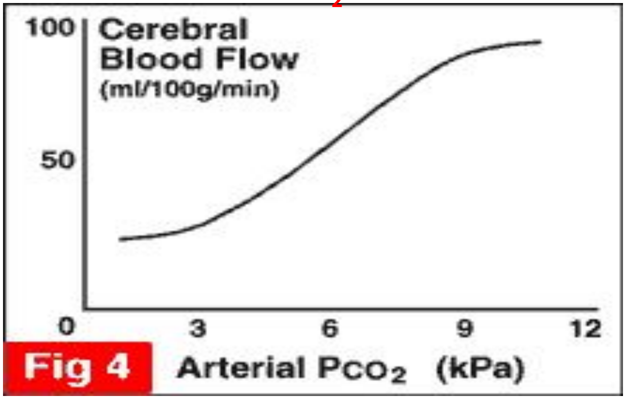
2- Metabolic Autoregulation

- Arterioles **dilate** in response to potent chemicals that are by-products of metabolism such as lactic acid, carbon dioxide and pyruvic acid
- Cerebral blood flow is highly related to metabolism of the tissue. Three metabolic factors have potent effects in controlling the cerebral blood flow. **(1) Carbon dioxide concentration, (2) Hydrogen ion concentration, (3) Oxygen concentration.**

Carbon dioxide concentration

- **CO2** is a potent vasodilator
  - **Increased CO2/decreased BP** →vasodilation
  - **Decreased CO2/increased BP** →vasoconstriction
- Increase Carbon dioxide (Hypercapnia) causes cerebral vasodilation.
- As the arterial tension of CO2 rises, CBV and CBF increases
- When it is decreased vasoconstriction is induced
- 70 % increase in arterial PCO2, approximately **doubles** the cerebral blood flow

CBF and CO_2



Metabolic Autoregulation

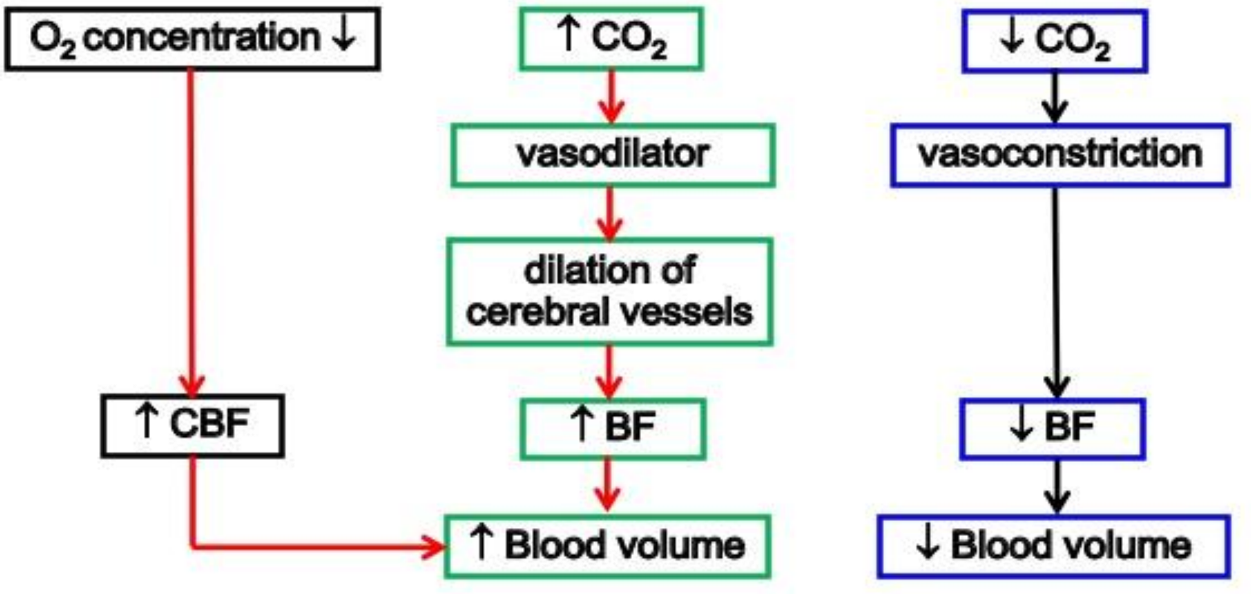
- Increased arterial pCO_2 (hypercapnea) causes cerebral dilation
  - CO_2 diffuses through blood-brain barrier into the CSF to form H^+ (via carbonic acid) which then causes the vasodilation
- Decreased arterial pCO_2 as occurs during hyperventilation causes cerebral vasoconstriction, decreased blood flow, and cerebral hypoxia

Oxygen concentration.

- The rate of utilization of oxygen by the brain tissue remains within narrow limits—almost exactly **3.5 (± 0.2) ml of oxygen per 100 grams** of brain tissue per minute.
- If blood flow to the brain insufficient to supply this needed amount of oxygen, 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 unbalanced at lower values of **PO2**, at PO2 levels below **20 mm Hg**.
- Oxygen mechanism for local regulation of cerebral blood flow is important protective response against diminished cerebral neuronal activity and therefore, against derangement of mental capability.

2- Metabolic Autoregulation

CBF: O2 and CO_2



Hydrogen ion concentration

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

- Increased hydrogen ion depresses neuronal activity. It is fortunate that an **increase in hydrogen** ion concentration also causes an increase in blood flow, which in turn carries hydrogen ions, carbon dioxide, and other acid forming substances away from the brain tissues.
- Loss of **carbon dioxide** removes carbonic acid from the tissues; this, along with removal of other acids, reduces the hydrogen ion concentration back toward normal. Thus, this mechanism helps **maintain a constant hydrogen ion concentration** in the cerebral fluids and thereby helps to maintain a normal, constant level of neuronal activity

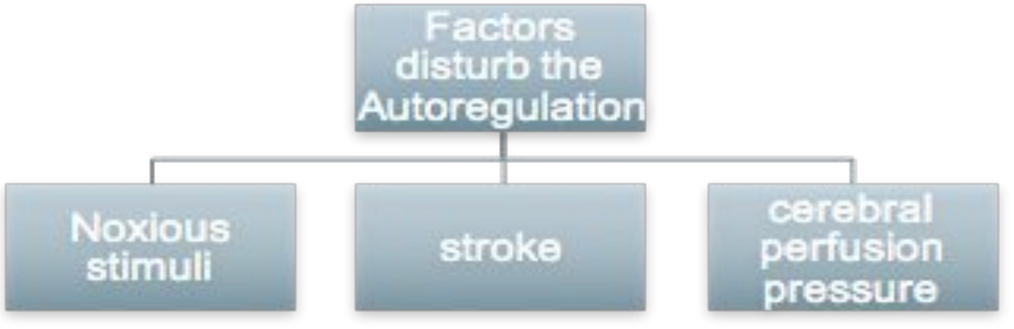
3- Neurogenic Autoregulation

- The cerebral circulatory system has strong sympathetic innervation that passes upward from the **superior cervical sympathetic** ganglia in the neck and then into the brain along with the cerebral arteries.
- **ANS and Neurochemical control has minor role, Pressure and Metabolic Autoregulation is most important**

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, preventing the occurrence of “cerebral stroke.”

Factors disturb the Autoregulation

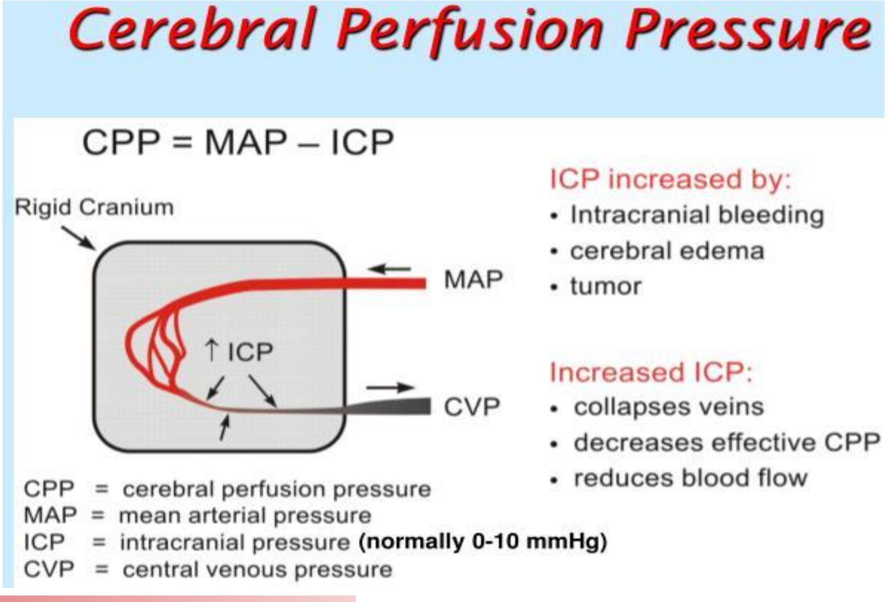


Noxious stimuli such as:

1. Hypoxia due to occlusive cerebro-vascular disease
2. Trauma from head injury
3. Brain compression from tumors, hematoma, cerebral edema. These factors results in the loss of normal cerebral blood flow (CBF) autoregulation

cerebral perfusion pressure

- normal intracranial pressure is 10 mmHg
- if the pressure is over 20 mmHg it is abnormal
- increase in ICP will lead to a decrease in CBF and a decrease in cerebral perfusion

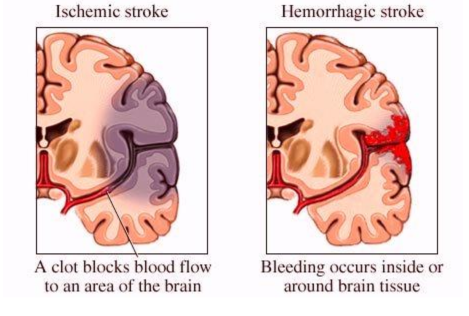


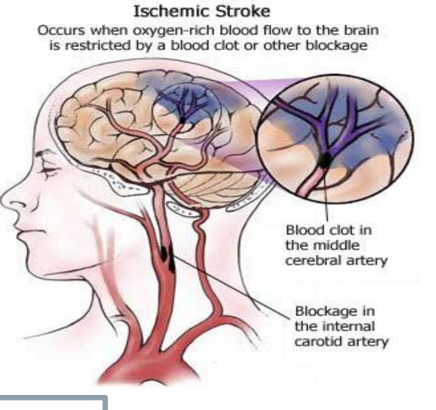
stroke

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

If a large vessel is blocked the outcome may be rapidly fatal or may lead to very severe disability.

The most common types of disability are the loss of functions of one side of the body and speech problems





stroke

Ischemic
- -thrombus formation or embolism
- -vasospasm (ET-1?) associated with subarachnoid hemorrhage

hemorrhagic
- -ruptured aneurism
- -vascular weakening due to chronic hypertension

Fainting

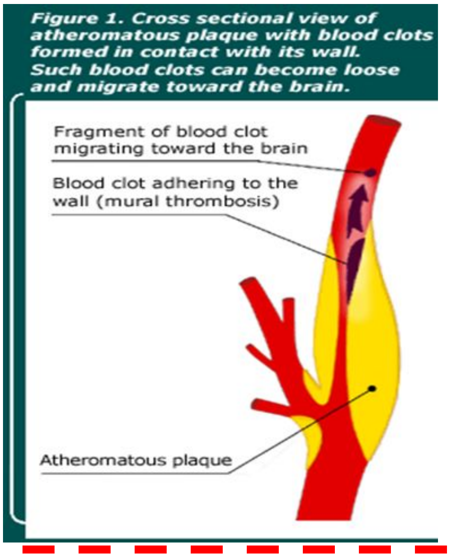
Fainting: Temporary loss of consciousness, weakness of muscles, and inability to stand up, caused by sudden loss of blood flow to the brain, changes in blood pressure.

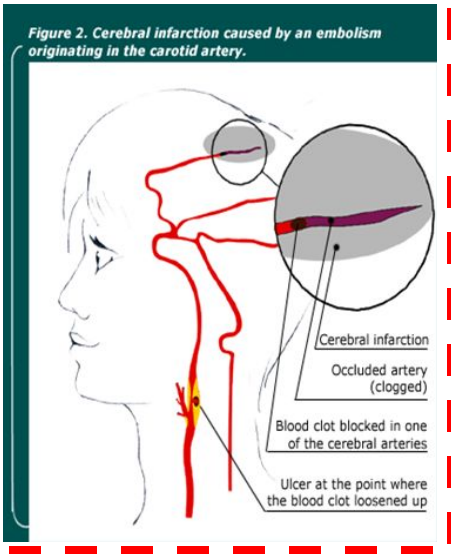
Dementia

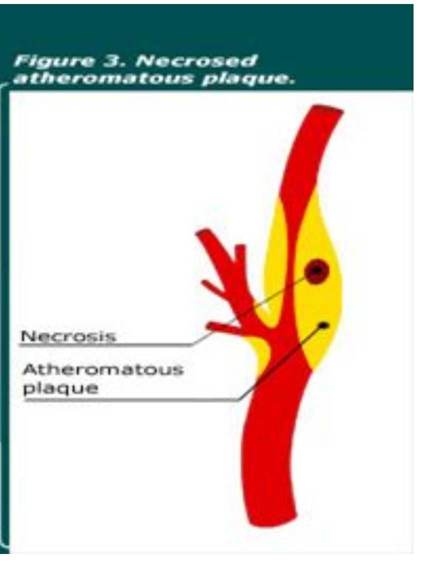
Dementia: Result from repeated episodes of small strokes produce progressive damage to the brain over a period of time.
The main clinical feature of dementia is a gradual loss of memory and intellectual capacity. Loss of motor function in the limbs and incontinence can also occur.

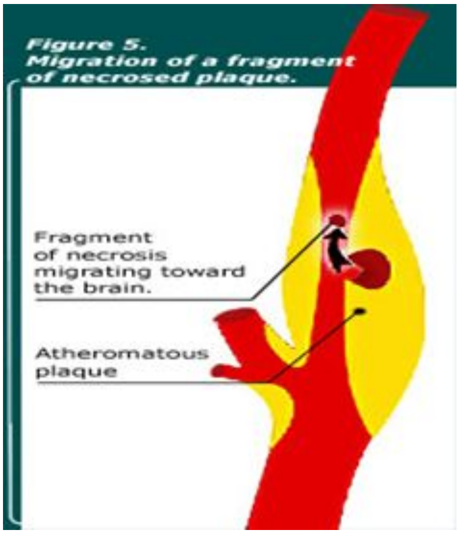
Infarction

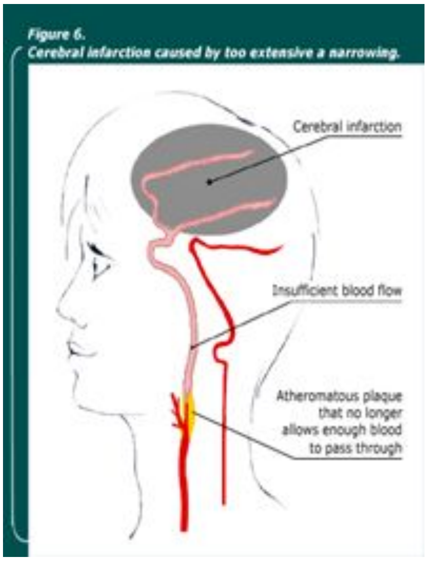
First 2 pictures were in the lecture the other pictures are extra for **illustration**





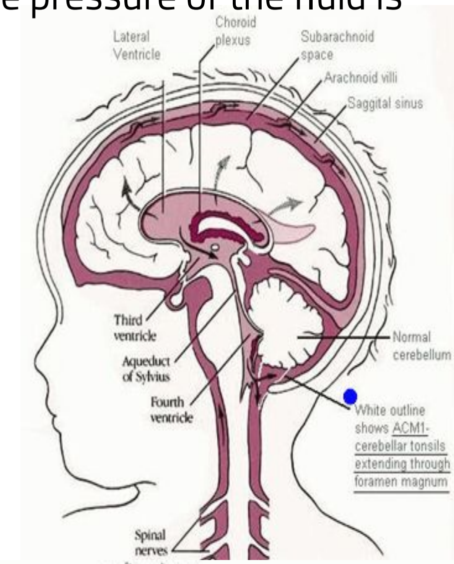




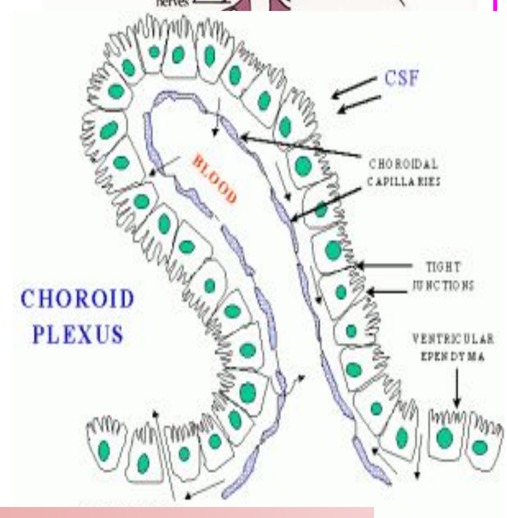


Cerebrospinal fluid

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.



- 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.



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.

Composition of the CSF

- 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.

Substance	CSF	Plasma
Na+	147	150
K+	2.9	4.6
HCO3-	25	24.8
PCO2	50	39.5
pH	7.33	7.4
Osmolality	289	289
Glucose	64	100

Brief Summary

Cerebral blood flow

750ml/min which represents 15% of cardiac output

flow = cerebral perfusion pressure / cerebrovascular resistance

Cerebral perfusion pressure

MAP - (central venous pressure OR intracranial pressure)

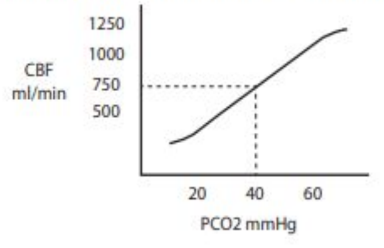
ICP can cause a starling resistor model if it exceeds CVP

normal range is 70-90 mmHg

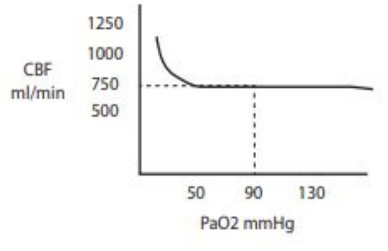
Cerebrovascular resistance

extrinsic factors

pCO_2 demonstrates a near linear relationship with CBF due to changes in resistance



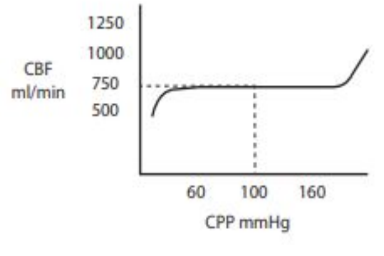
pO_2 only changes the CBF when paO_2 decreases below 50mmHg (steep part of HbO_2 curve)



intrinsic factors

myogenic stretch

demonstrates autoregulation which maintains CBF between a CPP of 60 - 160



metabolic factors

increased metabolic activity will increase flow to the brain

this may be more important from a regional distribution perspective

Christopher Andersen 2012

1-which one of the following does not supply the brain with blood?

A-internal carotid artery.
B-vertebral artery.
C-basilar artery.
D-external carotid artery.

2-The circle of Willis is origin of how many large vessels?

A-6
B-5
C-4
D-7

3- what results if blood flow to the brain is below 18 to 20 ml / 100 g / min

A-h
B-tissue death
C-normal blood flow
D-Ischemia

4-The net pressure of blood flow to the brain is.

A-extracranial pressure
B-Mean Arterial pressure
C-Cerebral perfusion pressure
D-intracranial pressure

5-The vascular smooth muscles are highly responsive to changes in pressure, a process called

A-Neurogenic Autoregulation
B-Metabolic Autoregulation
C-myogenic activity
D-hydrogenic activity

6-)which when of the following is the the primary stimulus that will cause vasodilatation?

a)H
b)CO_2
c)O_2

7-..........increase in arterial PCO2, approximately doubles the cerebral blood flow

a)70%
b)50%
c)75%
d)89%

8-ANS and Neurochemical control have a .... Role and Metabolic Autoregulation has a ....role ?

a)major .. minor
b)minor ...major
c)major ... major
d)miner ... minor

9-..... can dirctly penetrate the blood BBB while ...... cant

a)O_2......CO_2
b)CO_2.....H
c)H.... CO_2

10- an increase in ICP will lead to a ......in CBF and a ....in cerebral perfusion

a)decrease .... decrease
b)increase .... decrease
c)decrease ...increase
d)increase .....increase

Answers:
1-D
2-A
3-D
4-C
5-C
6-A
7-A
8-B
9-B
10-A