

431

CNS System
central Nervous

Block

Physiology Team

Female Side

Male side

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Slide No.(1)

Cerebral circulation & CSF formation

TEXT Book :
Guyton

Team Notes :



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Slide No.(2)

Objectives:

- Innervation of cerebral blood vessels.
- **Cerebral blood flow and factors affecting;**
 - -Autoregulation/metabolic .
 - - blood pressure.
 - - Intracranial pressure (ICP)
 - - Blood gases.
 - - Neural stimuli
 - - Humoral stimuli
- CSF formation / absorption.
- CSF functions.
- Blood brain barrier (BBB).

Team Notes :

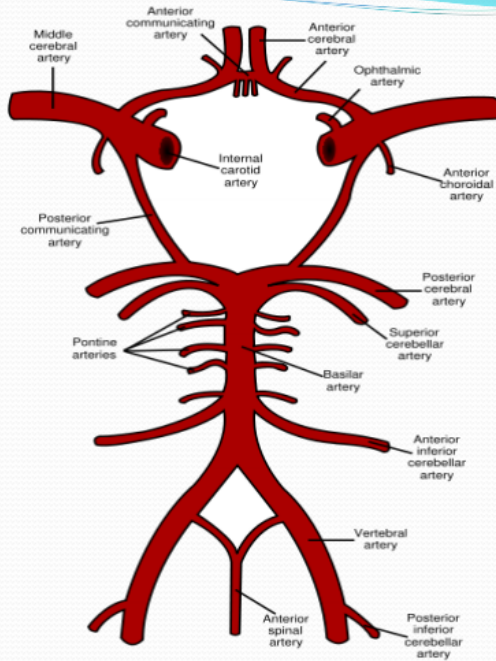
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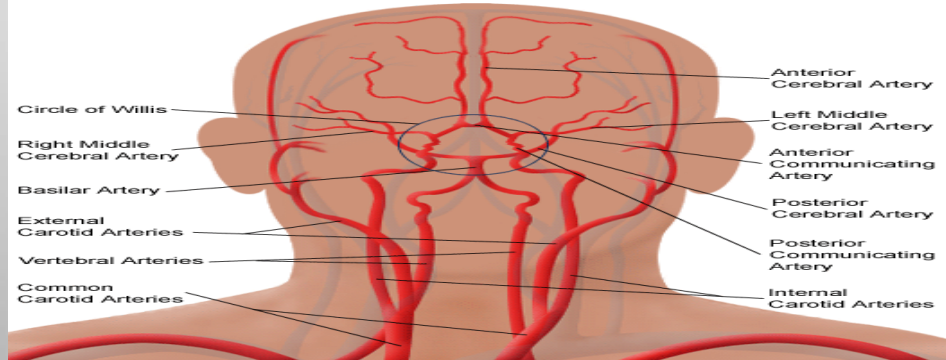
Slide No.(3)

Cerebral Circulation



Team Notes :

Arterial Circulation of the Brain, Including Carotid Arteries



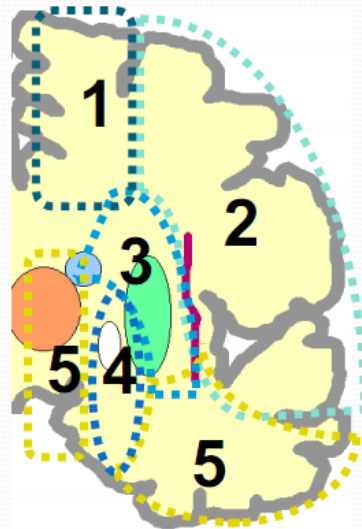
* The brain receives its blood supply from four main arteries: the **two internal carotid arteries** and the **two vertebral arteries**

* The vertebral arteries unite to form **Basilar artery**

The basilar artery and the carotids form the **circle of Willis**

Slide No.(4)

Cerebral Artery Areas



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

Team Notes :

It shows how blood flow to the brain areas through the vessels.

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



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Innervation

Three systems of nerves innervate the cerebral blood vessels:

- **Sympathetic:** Postganglionic sympathetic neurons have their bodies in the superior cervical ganglia (NE & neuropeptide Y). During acute hypertension attenuate increase in CBF.
- **Parasympathetic:** Cholinergic neuron originate in sphenopalatine ganglia (Ach, VIP). End on large arteries.
- **Sensory nerves:** (Substance P, VIP, cause VD, neuropeptide Y causes VC). Contribute to increase in CBF during meningitis.

Team Notes :

The function of sensory nerves is transition of impulses.

* 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.

*This innervation supplies both the large brain arteries and the arteries that penetrate into the substance of the brain

* transection of the sympathetic nerves or mild to moderate stimulation of them usually causes very little change in cerebral blood flow because the blood flow auto-regulation mechanism can override the nervous effects.

*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—that is ,for preventing the occurrence of “cerebral stroke.”

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CBF

- CBF is tightly regulated to meet the brain's **metabolic demands**, and on the average must be maintained at a flow of 50 milliliters of blood per 100 grams of brain tissue per minute in adult humans.
- It is important to maintain CBF within narrow limits because too much blood can raise **ICP**, which can compress and damage delicate brain tissue, and too little blood causes **ischemia**, or inadequate blood supply. Ischemia results if blood flow to the brain is below 18 to 20 ml per 100 g per minute, and tissue death occurs if flow dips below 8 to 10 ml per 100 g per minute.
- Therefore it is important to maintain proper CBF in patients with conditions like **shock** , **stroke** and **traumatic brain injury**.
- Cerebral blood flow in excess of 55 to 60 ml per 100 g per minute, called hyperemia, is more than the brain needs and can contribute to an increase in intracranial pressure.

Team Notes :

*Normal Rate of Cerebral Blood Flow: Normal blood flow through the brain of the adult person averages 50 to 65 milliliters per 100 grams of brain tissue per minute. For the entire brain, this amounts to 750 to 900 ml/min, or 15 per cent of the resting cardiac output.

The brain's metabolic demand in specific or whole brain areas determines the increase or decrease in blood flow. ( **Activity**  **BF**)

INCREASED CBF	DECREASED CBF
INCREASE ICP	
compress+eussit niarb egamad	Ischemia + inadequate blood supply
- Could lead to hyperemia if it reaches 55-60 ml/100 g/min (it is more than the brain needs and can contribute to an increase in ICP)	- Could lead to ischemia if it falls to 18-20 ml/100 g/min -Could lead to tissue death if it falls below 8-20 ml/100 g/min

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Slide No.(7)

Cerebral perfusion pressure

- **Cerebral perfusion pressure**, or **CPP**, is 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**: **Mean arterial pressure**, is the force that pushes blood into the brain, and
- **intracranial pressure** is the force that keeps it out.
- Thus raising MAP raises CPP and raising ICP lowers it (this is one reason that increasing ICP in traumatic brain injury is potentially deadly). CPP, or MAP minus ICP, is normally between 70 and 90 mmHg in an adult human, and cannot go below 70 mmHg for a sustained period without causing ischemic brain damage. Children require pressures of at least 60 mmHg.

Team Notes :

- The CPP in adult is normally between (70-90 mmHg).
- CPP in children = 60 mmHg.
- Raising MAP → Raises CPP
- Raising ICP → lowers CPP
- ↑ ICP causes ↓ CCP that's why it is very dangerous in traumatic brain injury and is potentially deadly.
- CPP is important to maintain CBF if the range of MAP 50-150 mmHg.
- But if it is over or below the MAP limit, arterial blood pressure controls CBF
- **Extreme** changes in mean arterial pressure (below 40 or over 160) affect the cerebral blood flow. (Normal 50-150mmHg).
- Regulation of ABP is important to maintain blood flow to the brain because the brain is vulnerable to ischemic changes.



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Slide No.(8)

Regulation of cerebral blood flow:

- Autoregulation.
- Humoral stimuli.
- Neural stimuli
- Hypoxia/hypercapnia.
- Endothelium mediated vasodilation

Team Notes :

Nothing mentioned.



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Slide No.(9)

Autoregulation

- The brain maintains proper CPP through the process of **autoregulation**:
- **The response to** lower pressure, is arteriolar dilation in the brain creating more room for the blood, while when blood pressure rises, they constrict, or narrow. Thus, changes in the body's overall blood pressure **do not** normally alter cerebral perfusion pressure drastically. At their most constricted, blood vessels create a pressure of 150 mmHg, and at their most dilated the pressure is about 60 mmHg. When pressures are outside the range of **50 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. Thus, hypotension can result in severe cerebral ischemia in patients with conditions like **brain injury**, leading to a damaging process called the ischemic cascade.
- Brain changes its blood flow according to its metabolic activities.
- Nitric oxide & adenosine are mediators.

Team Notes :

- Autoregulation: ability of tissues to regulate their own blood flow according to their needs.
- The most common mediator for autoregulation in brain is Nitric Oxide (NO), vasodilator secreted from endothelium.
- Some people take Nitroglycerin tablets sublingual and complain of headache which is due to vasodilatation because NO can cross BBB.
- Adenosine and K channels are also mediators that can increase CBF in process of autoregulation only.

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Regulation of CBF, cont.,

- **Hypoxia & Hypercapnia:** Alterations in blood gas content. Amounts of carbon dioxide and oxygen in the blood affect constriction and dilation even in the absence of autoregulation: excess carbon dioxide can dilate blood vessels up to 3.5 times their normal size, while high levels of oxygen constrict them. Hypoxia, or inadequate oxygen, also dilates blood vessels and increases blood flow.
- Blood vessels also dilate in response to **low pH**. Thus, when activity in a given region of the brain is heightened, the increase in CO_2 and H^+ concentrations causes cerebral blood vessels to dilate and deliver more blood to the area to meet the increased demand.
- **Neural stimuli:** Under normal conditions sympathetic has little effect. During acute hypertension, a decrease in CBF occurs.
- **Endothelium-mediated dilation:** is impaired by hypertension.

Team Notes :

- Hypoxia: low O_2 .
- Hypercapnia: high CO_2 .
- CO_2 passes faster than O_2 through BBB.
- $\downarrow \text{pH} \rightarrow \text{CBF} \uparrow$
- Neural stimuli: autonomic (sympathetic, parasympathetic) and sensory nerves.
- During acute hypertension, sympathetic stimulation may cause strong vasoconstriction of cerebral blood vessels. Sometimes causes ischemia, numbness in face or half of the body).
- It's important to gradually lower the BP not sharply to prevent complications.
- Endothelium is actually an endocrine organ because it secretes lots of mediators.
- Endothelium of blood vessels covers the smooth muscles.
- Endothelium either secretes:
 - 1- Vasodilator substance (NO) \rightarrow relaxation of smooth muscles.
 - 2- Vasoconstrictor substance (thromboxane) \rightarrow contraction of smooth muscles.
- If there is loss of endothelium-mediated dilation leads to loss of endothelium function (no nitric oxide) \rightarrow hypertension and low CBF.
- Recently defective endothelium is found in hypertensive patients. That's why when they are given NO locally there will be no response. By time lead to ischemia and stroke.
- Treatment of hypertension will lead to improvement to some extent of endothelium dysfunctions.



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Slide No.(11)

Regulation of cerebral circulation, continued,....

- Effect of ICP changes on systemic blood pressure;

Cushing reflex:

If ICP > 33 mmHg over a short period of time, CBF will drop markedly, leading to ischemia of vasomotor area. Then blood pressure rises.

Team Notes :

- CPP depends on MAP and ICP.
- Excess increase in ICP → compression of vessels entering the brain → blood flow to brain will be compromised.

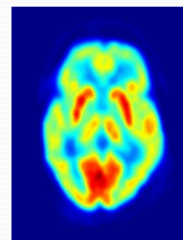
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Slide No.(12)

Measuring cerebral blood flow

Average cerebral blood flow = 756 ml/min

- Functional imaging resonance.
- Positron emission tomography.
- Both be used to measure CBF. These techniques are also used to measure regional CBF (rCBF) within a specific brain region.



Team Notes :

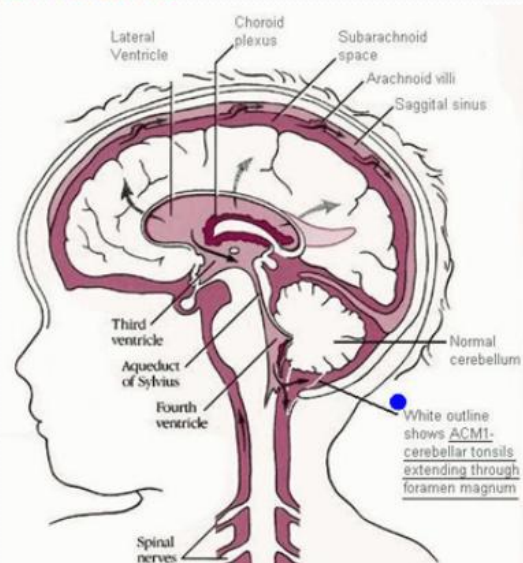
- Positron emission tomography (PET).
- Also measure changes in activity and diseases.

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Slide No.(13)

Cerebrospinal fluid

- This is an illustration (midline view) showing the anatomical structures involved in the production and flow of cerebrospinal fluid through the ventricular system, brain and spinal cord, and finally absorption into the bloodstream. You'll also see the difference between a "normal" cerebellum and the cerebellum of an ACM patient with the cerebellar tonsils protruding through the foramen magnum.



Team Notes :

- CSF passes through lateral, 3rd, 4th ventricles and spinal cord space.

Slide No.(14)

Cerebrospinal Fluid (CSF)

CSF fills ventricles and subarachnoid space.

- Volume = 150 ml
- Rate of production = 550 ml/d, so it turns 3.7 times/day.
- Lumbar CSF pressure = 70-180 mm CSF
- Absorption of CSF occurs by bulk flow 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 foramina of Luschka & Magendie are blocked or obstruction within ventricular system, resulting in distention of the ventricles.

Team Notes :

- Circle of CSF: **continuously formed and absorbed (important to maintain ICP).**
- If CSF is continuously formed without drainage:
 - 1- Increase ICP
 - 2- Obstruction of CSF circulation and accumulation in ventricles and subarachnoid space.
- Volume: amount of CSF present at any time you measure= 150ml.
- Hydrocephalus: patient has large head and sunset eyes appearance.



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- CSF is formed in:
 1. Choroid plexus.
 2. Around blood vessels.
 3. Along ventricular walls.
- CSF is absorbed by:
 - Arachnoid villi

Team Notes :

Nothing mentioned.

Slide No.(16)

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	289	289
Glucose	64	100

- The composition of CSF is essentially the same as brain ECF

Team Notes :

- What is the most discriminative point between the composition of CSF and plasma?



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Slide No.(17)

Functions of the CSF

1. Protective function: The brain is supported within the arachnoid by the blood vessels , nerve roots and the arachnoid trabeculae. In air brain weight =1400 g, but in its water bath of CSF , brain weight = 50 g, making it suspended effectively. When the head receives a blow, the arachnoid slides on the dura and the brain moves, but its motion is gently checked by the CSF cushion and by the arachnoid trabeculae. Removal of CSF during lumbar puncture can cause severe headache


Team Notes :

- Protective function:

1-The brain weight in air=1400g, however in water bath of CSF weight=50g. So we don't feel the heaviness of the head.

2- When there is a car accident, the head and brain moves forward and backward and CSF protects the brain from being damage, this is called cushion effect.

- Cushion: pillow.



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Functions of CSF, continued,...

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.
5. Cardiovascular dynamics are also affected by CSF pressure, as the flow of blood must be tightly regulated within the brain to assure consistent brain oxygenation .

Team Notes :

2- Blood flow of brain cannot have a steady line. It has to be pulsatile (increases with systole and decreases with diastole for the proper function of cerebral tissues).

If it is steady it causes tissue damage and release free radicals.

3- Brain (hypothalamus, pituitary gland) secret hormones distributed by CSF. Also it distributes nutrition.

Slide No.(19)

Features of cerebral vessels

- Choroid plexus:
- Gaps are present between endothelial cells of the capillary wall, while choroid epithelial cells that separate them from CSF are connected by tight junctions.
- Capillaries in the brain substance are non-fenestrated and there are tight junctions between endothelial cells to limit passage of substances through the junctions.

Team Notes :

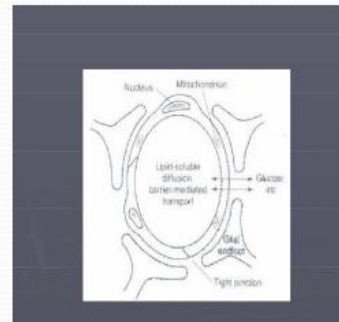
Nothing mentioned.

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Slide No.(20)

- Few vesicles in endothelial cytoplasm and so little vesicular transport.
- Brain capillaries are surrounded by the end-feet of the astrocytes. There are gaps of 20 nm between the end-feet.



Team Notes :

Nothing mentioned.



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Slide No.(21)

Blood brain Barrier (BBB)

It is formed by the tight junctions between capillary endothelial cells of the brain and between epithelial cells in the choroid plexus. This effectively prevents proteins from entering the brain in adults and slow the penetration of smaller molecules.

Team Notes :

- The development of BBB is early, few months after birth.


Slide No.(22)

Penetration of substances into the brain

- Molecules pass easily: H₂O, CO₂, O₂, lipid-soluble free forms of steroid hormones.
- Molecules not pass: proteins, polypeptides.
- Slow penetration: H⁺, HCO₃⁻
- Glucose : its passive penetration is slow, but is transported across brain capillaries by GLUT1

Team Notes :

- People take cortisone (steroid hormone) for long period can cause depression because it crosses BBB.
- Proteins (antigens) don't pass BBB, thus systemic infections don't affect the brain, except in meningitis and encephalitis.



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Slide No.(23)

Functions of BBB

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

Team Notes :

- BBB has protective function:
 - 1- Allow passage of substances and prevent passage of others.
 - 2- prevent passage of toxins (bilirubin, ammonia).
- Continues formation of neurotransmitters exhaust the brain.


Slide No.(24)

Development of BBB

- Premature infants with hyperbilirubinemia, free bilirubin pass BBB, and may stain basal ganglia causing damage (Kernicterus).

Team Notes :

- The development of BBB is early, few months after birth.
- In adult bilirubin doesn't cross BBB.
- Normal level of bilirubin(0.5-1 mg/dL).
- Kernicterus (severe jaundice) in newborn: level of bilirubin (11-20 mg/dL):
In newborn, bilirubin crosses the unwell developed BBB causing toxicity or mental retardation.



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Slide No.(25)

Clinical implications

- Some drugs penetrate BBB with difficulty e.g. antibiotics and dopamine.
- BBB breaks down in areas of infection, injury, tumors, sudden increase in blood pressure, and I.V injection of hypertonic fluids.
- Injection of radiolabeled materials help diagnose tumors as BBB is broken down at tumor site because of increased vascularity by abnormal vessels.

Team Notes :

Nothing mentioned.



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

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

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

If smaller blood vessels are blocked the outcome is less severe and recovery may be good.

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

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

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)

***Transient ischaemic attack:** When blood supply to a part of the brain is temporarily interrupted without producing permanent damage. Recovery may occur within 24 hours.

***Dementia:** This may result from repeated episodes of small strokes which produce progressive damage to the brain over a period of time.

Questions

- If MAP of a person raised from 110 to 140 mmHg, cerebral blood flow will:

1- Increase.

2- Decrease.

3- No effect.

- If MAP is 190 mmHg, what controls the CBF:

1- ABP.

2- CPP.

3- ICP.

- Low PH leads to:

1- Decrease CBF.

2- No effect.

3- Increase CBF.

- Development of BBB is :

1- Before birth.

2- After birth.

- the most important vasodilator in autoregulation of brain is:

1- Nitric oxide.

Answers:

3

1

3

2

1