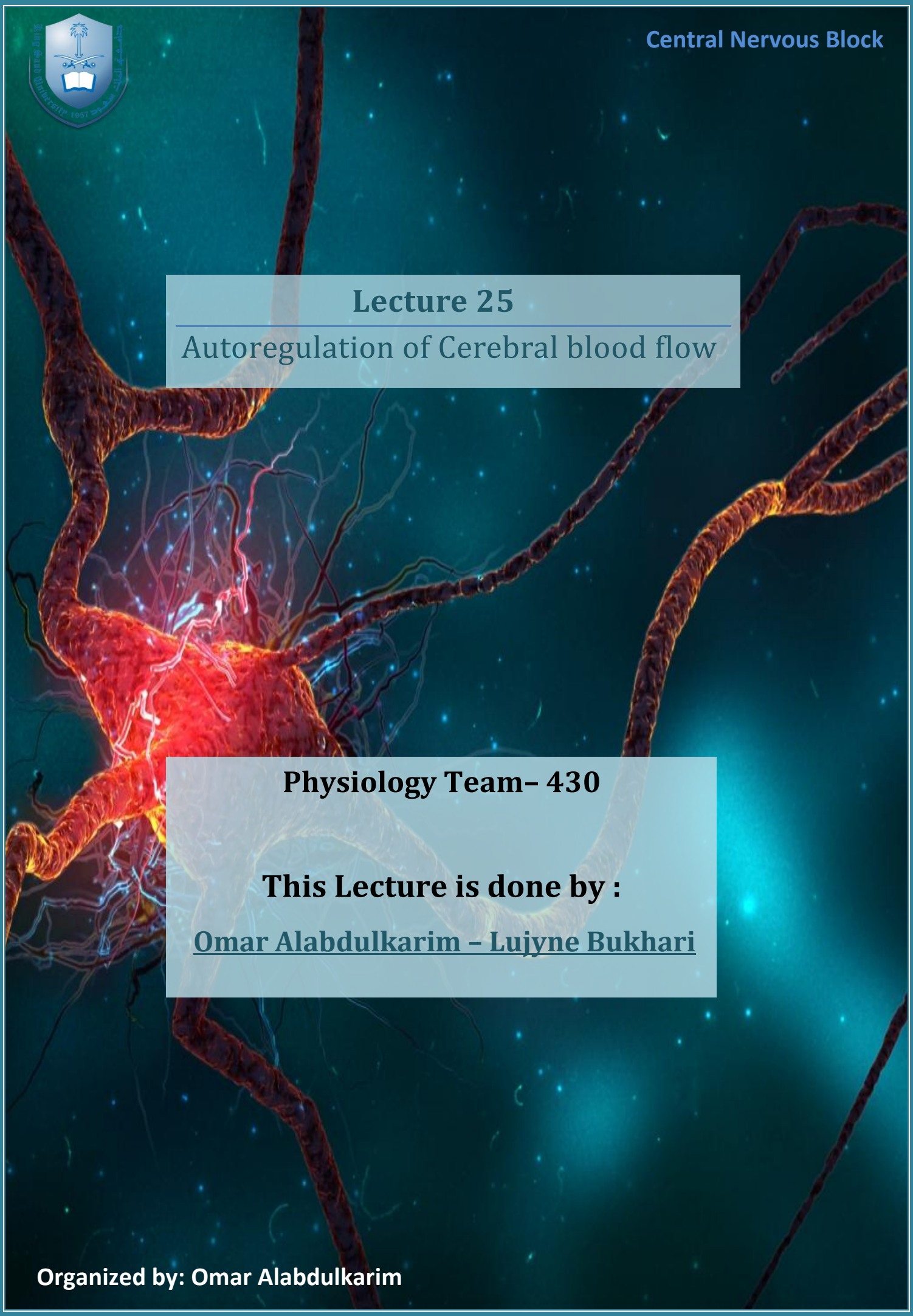

Lecture 25

Autoregulation of Cerebral blood flow

Physiology Team– 430

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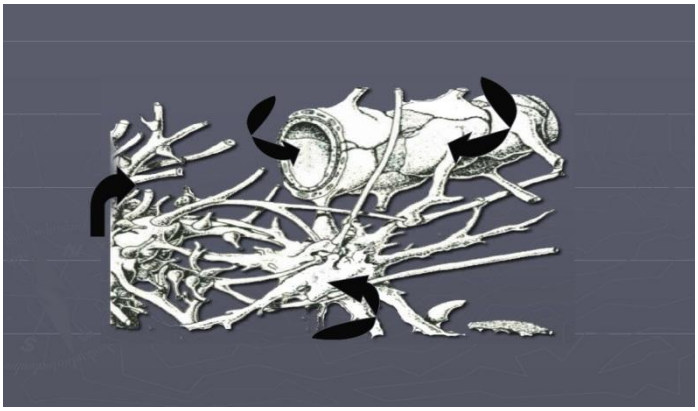
* Cerebral Circulation

Features of cerebral vessels

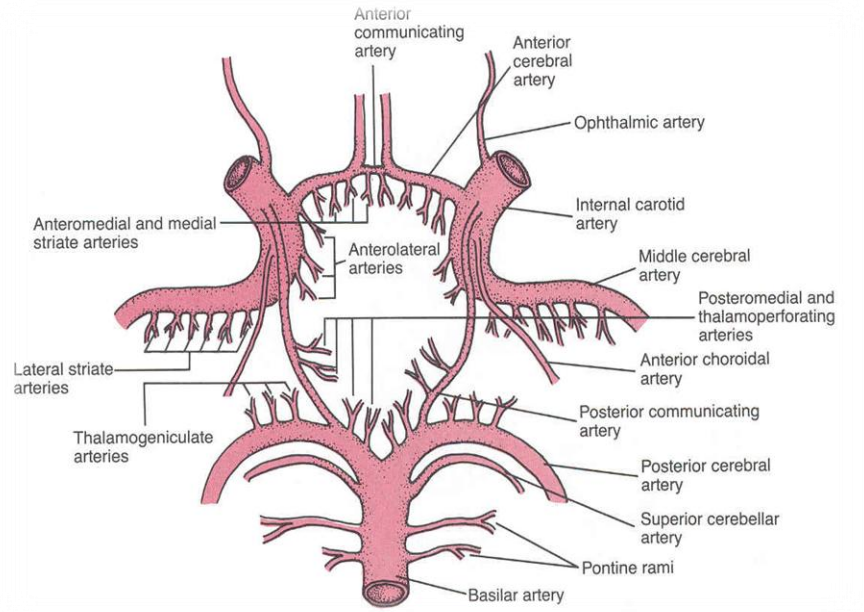
- **Choroid plexus**
  1) Endothelial cells of the capillary wall are separated with gaps
  2) Choroid epithelial cells that separate them from CSF are connected by tight junction.

- **Brain Capillaries**
  1) capillaries in the brain are *non-fenestrated*
  2) There are tight junction between the epithelial cells to limit the passage of substances through the junctions
  3) Surrounded by endfeets of astrocytes and there are gaps of 20 nm between the endfeet.



Circle of Willis

- Is the joining area of several arteries at the bottom (inferior) side of the brain.
- At the Circle of Willis the internal carotid artery branch into smaller arteries that supply oxygenated blood.
- It is named after an English physician named *Thomas Willis*.



- **The brain receives its blood from four main arteries:**
  1. Two internal Carotid arteries
  2. Two vertebral arteries

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

- Vertebral Arteries unite to form Basilar artery
- Basilar and the Carotid arteries form the circle of Willis.

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

* Innervations

Three systems of nerves innervate the cerebral blood vessels:

Postganglionic sympathetic neurons	Cholinergic neurons	Sensory nerves
✓ their bodies are in the superior cervical ganglia ✓ NE/ neuropeptide Y	✓ originate in the sphenopalatine ganglia ✓ Ach/ VIP ✓ end on large arteries	✓ substance P/ VIP cause vasodilation ✓ neuropeptide Y causes

		vasoconstriction

⁎ Cerebral blood flow

- **Normal rate** of cerebral blood flow is 50 milliliters per 100 grams of brain tissue per minute (50 ml/100 g/min).
- For the entire brain this amount to 750 to 900 ml/min OR %15 of the resting cardiac output.
- CBF is tightly regulated to meet the brain's metabolic demands and must be maintained at 50 ml/100 g/min.
- It is important to maintain CBF within narrow limits.

Increased CBF	Decreased CBF
Increased ICP	
Compress + damage brain tissue	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

Therefore, it is important to maintain proper CBF in patients with conditions like shock, stroke and traumatic brain injury.

- **CBF can be measured by:**
  1) functional imaging resonance
  2) positron emission tomography

These techniques are also used to measure regional CBF (rCBF) within a specific brain region.

∗ Cerebral perfusion pressure (CPP)

- the cerebral perfusion pressure is the net pressure of blood flow to the brain

Cerebral blood flow = mean arterial blood flow – intracranial pressure

CCP = MAP – ICP

- **CPP is regulated by two balanced opposing forces:**
  1) mean arterial pressure: the force that pushes the blood into the brain
  2) intracranial pressure: the force that keeps it out

✓ CPP in adults = between 70 to 90 mmHg

✓ CPP in children = 60 mmHg

If CPP falls below 70 mmHg for a sustained period, it could cause ischemic brain damage

Raising MAP → Raises CPP

Raising ICP → Lowers CPP

⬆ **ICP** cause ⬇**CCP** that's why it is very dangerous in traumatic brain injury and is potentially deadly

* Autoregulation

Autoregulation occurs in response to

1) Changes in blood pressure

Low blood pressure	High blood pressure
Leads to arteriolar dilation in the brain to create more space for the blood	Leads to arteriolar constriction in the brain

- This process of autoregulation due to changes in blood pressure prevents the cerebral perfusion pressure from being altered (changes in the body's overall blood pressure do ***NOT*** normally alter cerebral)
- At their most constricted state: blood vessels create a pressure of 150 mmHg
- At their most dilated state: blood vessels create a pressure of 60 mmHg
- **Pressure passive flow:**

Pressure passive flow happens when the pressure is *outside* the range of 50-150 mmHg and 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***

2) Free radicals

3) Alterations in blood gas content

- Cerebral blood flow is highly related to metabolism of the tissue.
- **There are three metabolic factors have effects in controlling the CCF**
  1) Carbon dioxide concentration.
  2) Hydrogen ion concentration.
  3) Oxygen concentration.

- Cerebral blood flow is increased by excess Carbon dioxide or excess Hydrogen ion concentration.
  Note: 70 percent increase in arterial PCO2 approximately doubles cerebral blood flow.

Example of low pH

- Substance that increases the *acidity* of the brain tissue, and therefore increases hydrogen ion concentration, will likewise increase cerebral blood flow.

⇧ **Increase Acidity** → ⇧ **Hydrogen Concentration** →⇧ **CCF**

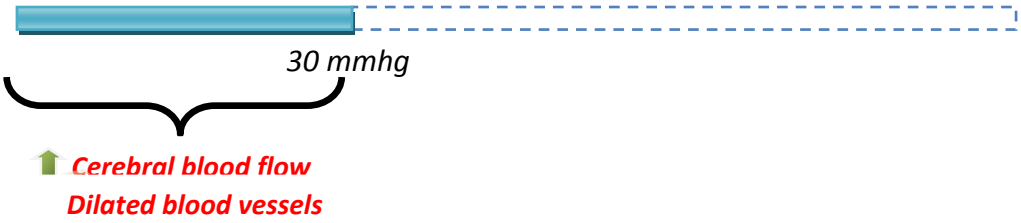
- Substance that increase the acidity such as lactic acid, pyruvic acid, and any other acidic material.

- ***Increase Hydrogen*** ions greatly ***depress the neuronal activity***.
- ***Loss of Carbon dioxide*** removes ***carbonic acid from the tissue***. Thus reduces hydrogen ion concentration to normal. This mechanism helps to maintain constant hydrogen.

- The amount of carbon dioxide and oxygen in the blood affect constriction and dilation even in the absence of autoregulation

Excess amount of carbon dioxide	→	Dilate blood vessels up to 3.5 times their normal size
High levels of oxygen	→	Constrict blood vessels
Inadequate oxygen (hypoxia)	→	Dilate blood vessels and increase blood flow

- **Oxygen deficiency** works as a regulator of cerebral blood flow except during periods of intense brain activity.
- Decreased cerebral tissue PO2 below about *30 mmhg* immediately begins to increase cerebral blood flow.



4) Response to low pH.

- Blood vessels dilated 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.

5) Sympathetic nervous system

- Stimulation of Sympathetic nervous system raises blood pressure and blocking it lowers the pressure

- **Effects of ICP changes on systemic blood pressure**

Cushing reflex: if ICP is more than 33 mmHg over a short period of time, cerebral blood flow will drop markedly leading to ischemia of vasomotor area and then the blood pressure will rise

* Abnormalities of Cerebral Circulation

1) Fainting

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

2) Stroke

- Stroke occurs when the blood supply to part of the brain is blocked resulting in death of area within the brain.
- If a *large vessel* is blocked the outcome may be rapidly fatal.
- If a *small vessel* is blocked the outcome is less severe.
- The ***most common*** disability is the loss of functions on <u>one side of the body and speech problems</u>.

- **Principal types of Stroke**
  - ***a) Thrombotic*:** due to blockage of an artery by blood clot
  - ***b) Hemorrhagic*:** due to bleeding from a ruptured blood vessel
  - ***c) Embolic***
    - Due to formation of blood clot away from the brain.
    - Carried with the bloodstream until it lodges in an artery in the brain.
  - ***d) Transient ischemic attack***
    - When blood supply to a part of the brain is temporarily interrupted <u>without producing permanent damage</u>.
    - Recovery may occurs within 24 hours
  - ***e) Dementia***
    - Repeated episodes of <u>small strokes</u>
    - Main clinical features is gradual ***loss of memory*** and ***intellectual capacity***