Regulation of Respiration

8- Chemical & Non-Chemical Control Of Respiration

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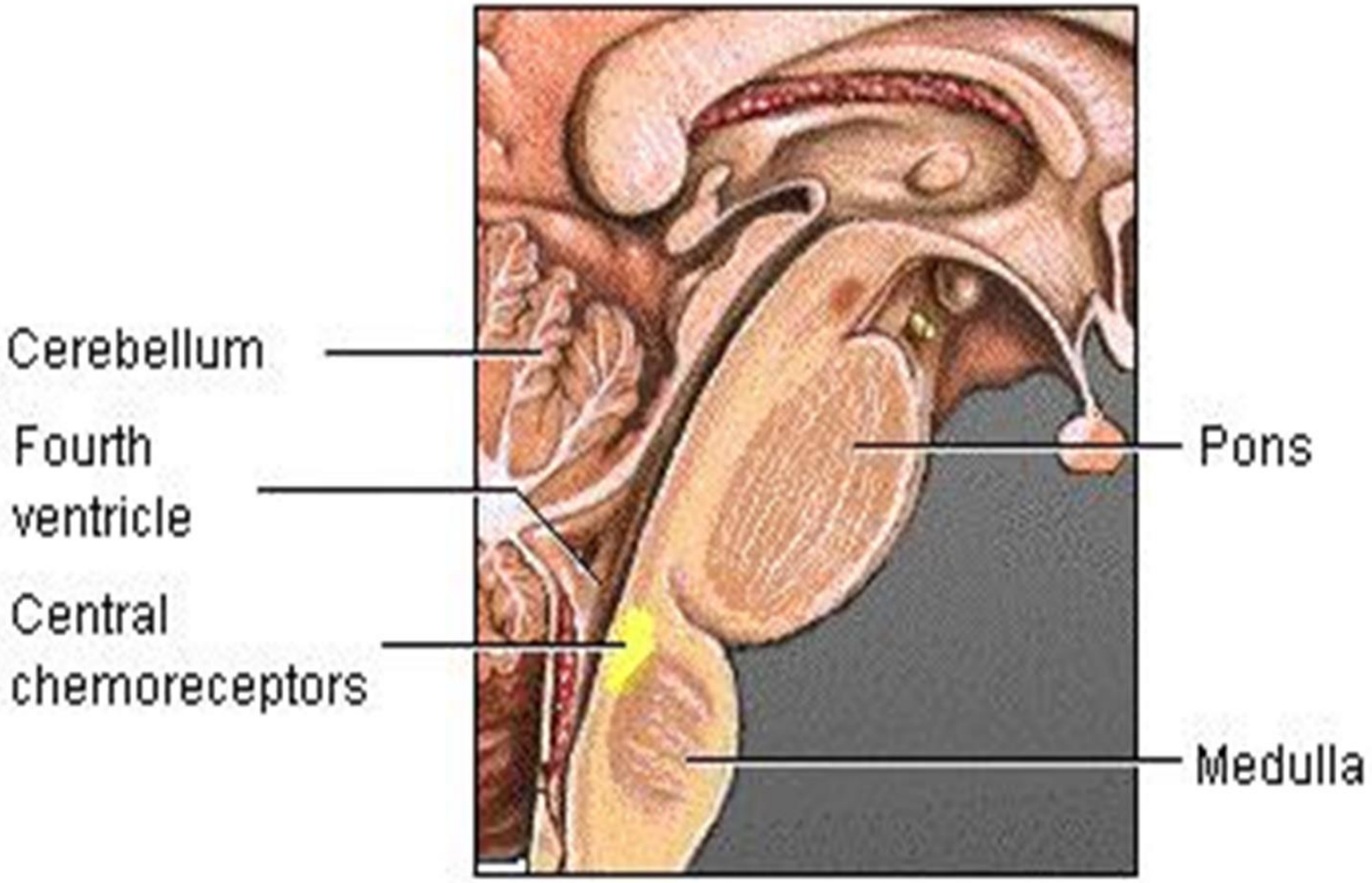
[B] Chemical regulation of respiration

-Respiration is stimulated by: ↑ Co2 tension , ↓ O2 tension and ↑ H+ ion concentration in the arterial blood.

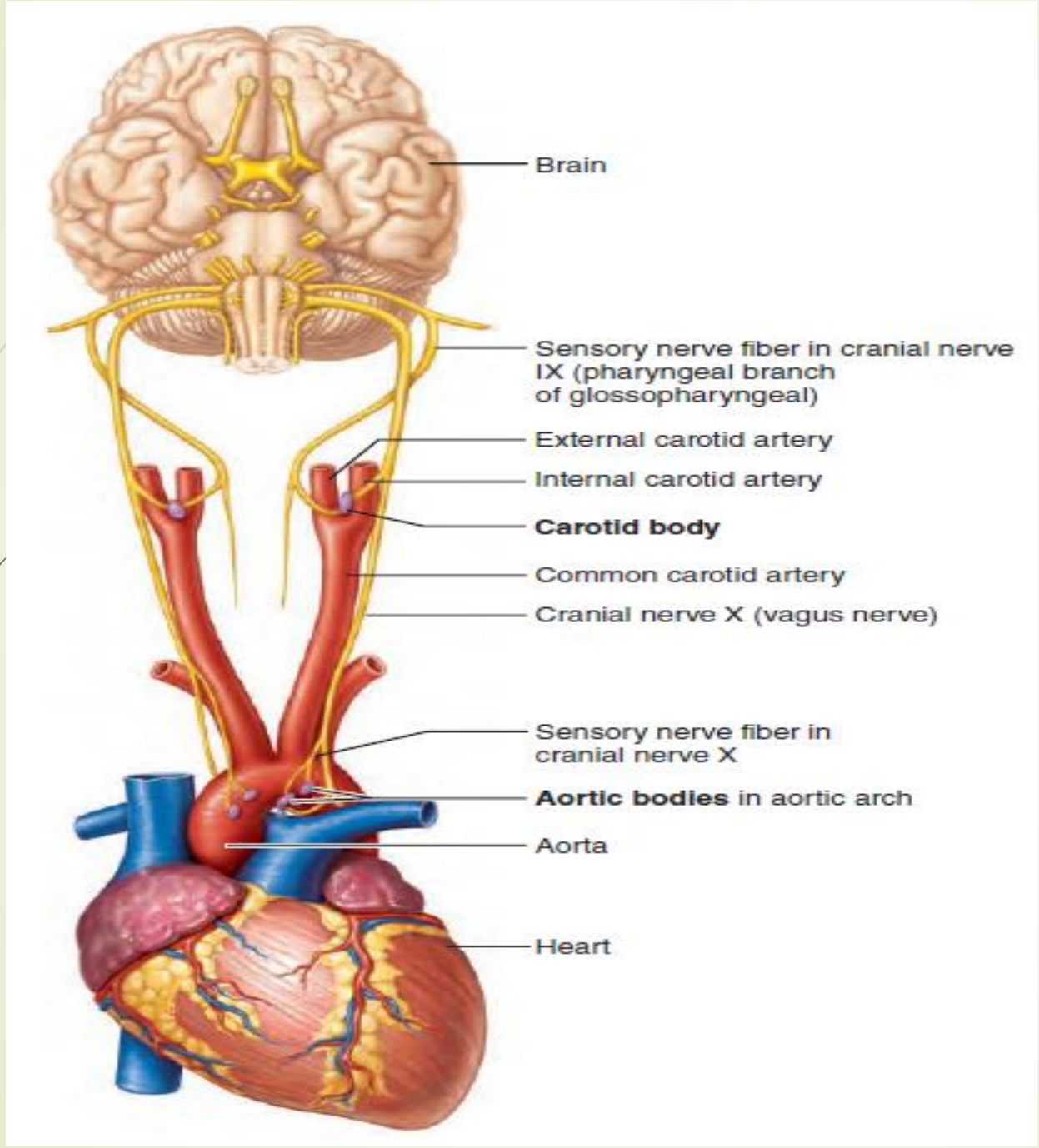
- These changes are associated with increase the metabolic activity

-This effect occurs via the peripheral and central receptors.

The central chemoreceptors in the medulla monitor the pH associated with CO_2 levels in the **CSF** in the fourth ventricle. The chemoreceptors synapse directly with the respiratory centers



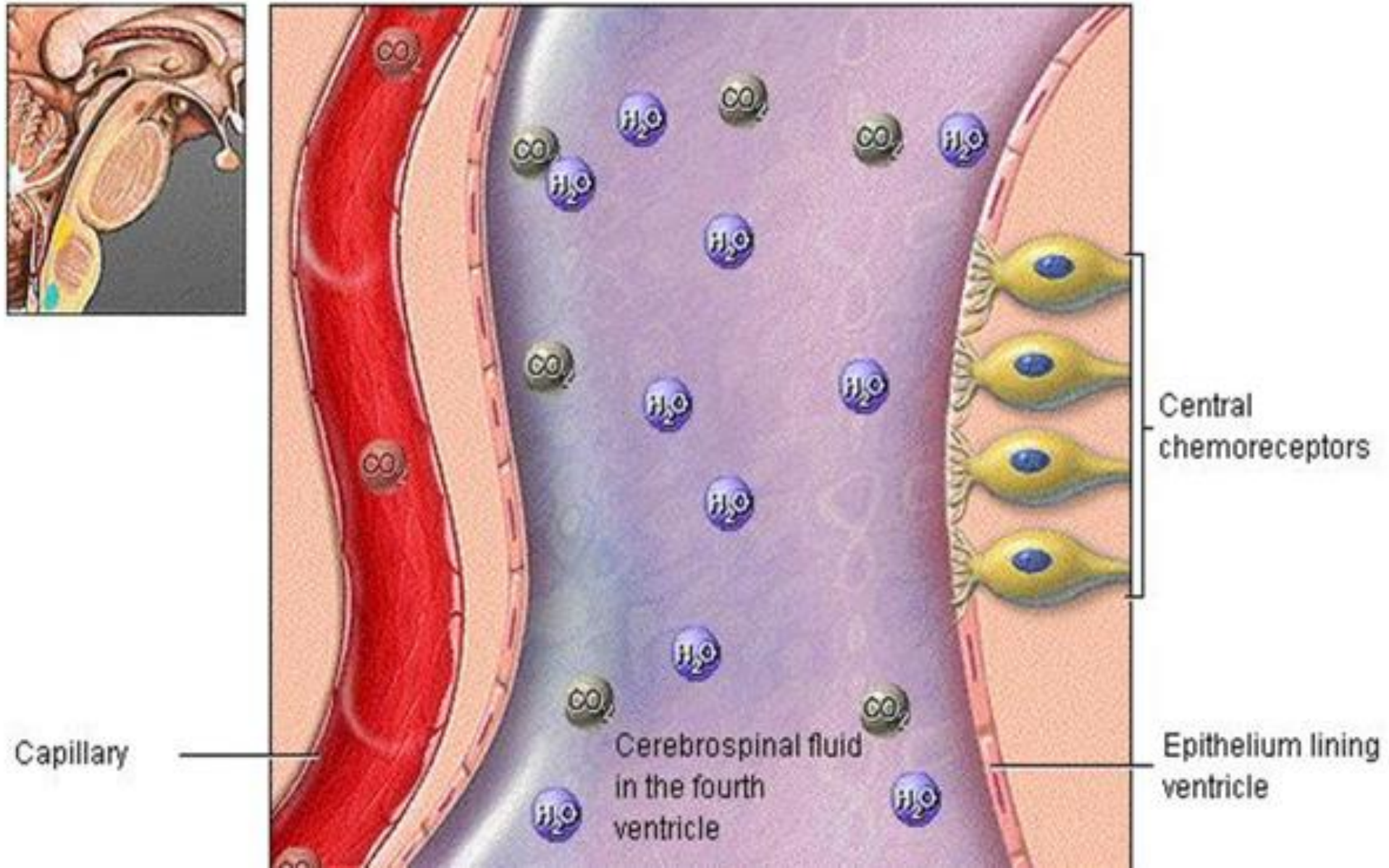
Location & innervation of the peripheral chemoreceptors in the carotid and aortic bodies



Types of chemoreceptors

	Peripheral chemoreceptors	Central chemoreceptors
Site	1) Aortic body: in the aortic arch. 2) Carotid body: at bifurcation of common carotid artery.	- Bilaterally in medulla - Near to respiratory center. **But**, separate from it. - Direct contact with (CSF) **But**, separated from the blood by the blood brain barrier (BBB).
Afferent	1) Aortic body via: Vagus nerve. (X) 2) Carotid body via: glossopharyngeal(IX) BOTH are called: the **buffer nerves**.	
Stimulus	1. **Hypoxia** (⇩ O_2 tension to 60mmHg) the **main** stimulus. So, they are called O_2 **lack** receptors. 2. **Hypercapnia** (⇧ CO_2 tension) with less effect (30% of effect). 3. **Acidosis** (⇧ H^+ concentration). 4. **⇧ K^+ & ⇧ Nicotine.** These conditions occur by: **H**ypotension & **H**yperactive tissue **H**emorrhage & at **H**igh altitude. - The blood flow to these receptors is **very high** = 2000ml/100 gm tissue. - So, these receptors depend only on the dissolved O_2 and stimulated by very low PO_2. - Not stimulated by ⇩Oxyhemoglobin content as in anemia or CO poisoning. - **Histotoxic hypoxia** (⇩ O_2 utilization of tissue) is more powerful stimulant.	- These receptors are **ONLY** stimulated by ⇧ PCO_2 in **arterial** blood. - CO_2 penetrate the BBB because CO_2 is lipid soluble. - **In CSF**: By carbonic anhydrase enzyme: - $CO_2 + H_2O \Leftrightarrow H_2CO_3$ $H_2CO_3 \Leftrightarrow H^+ + HCO_3$. **$H^+$** in CSF stimulates the chemoreceptors which in turn stimulate the respiratory center. **H^+** is not buffered by CSF as it has low protein content. ⇧ **H^+** in arterial blood not stimulate these receptors as H^+ not penetrate the blood brain barrier.

Central Chemoreceptors: Effect of PCO_2



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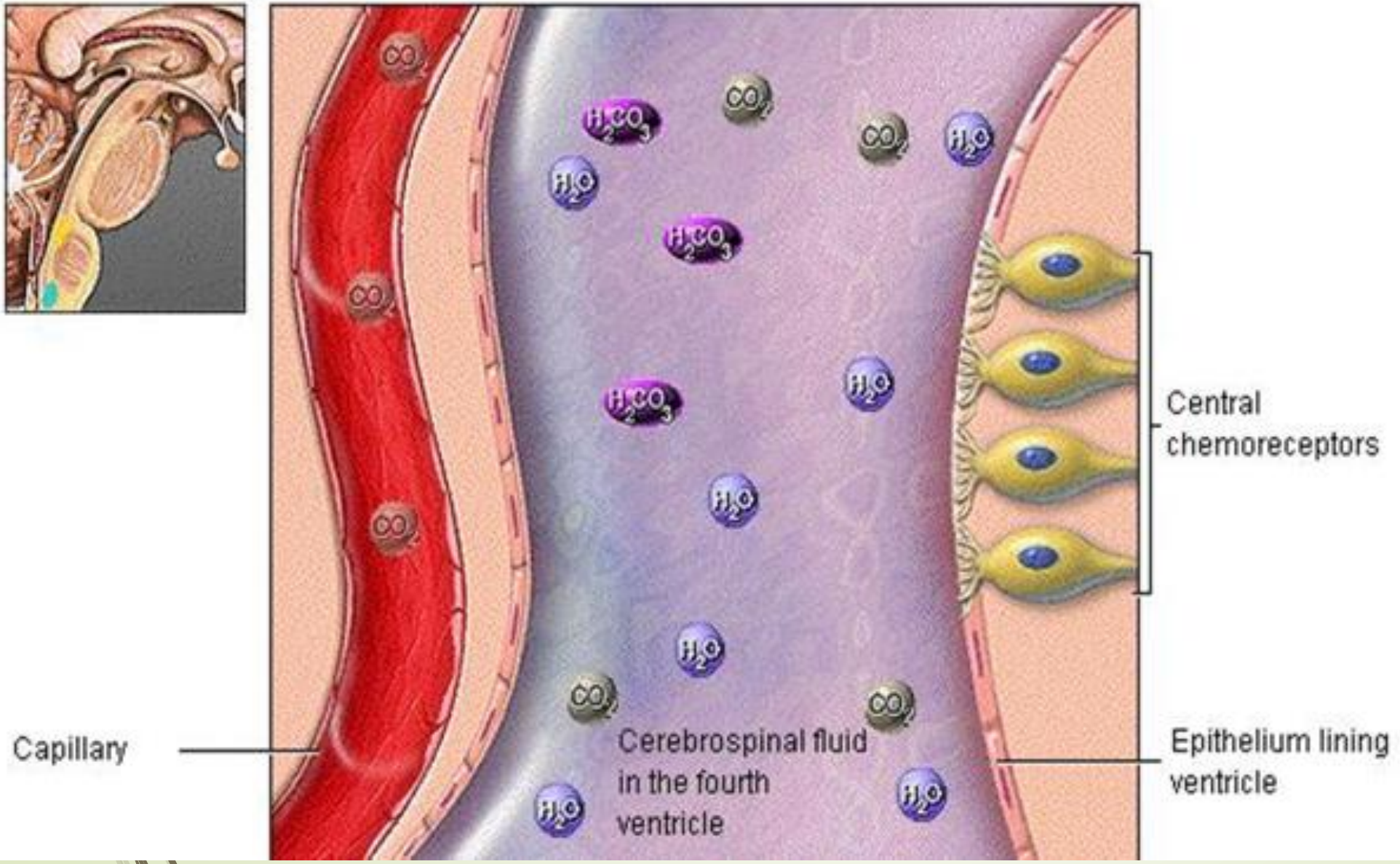
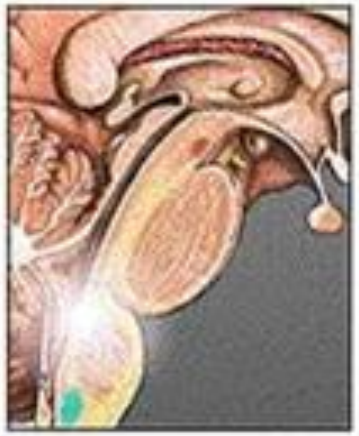
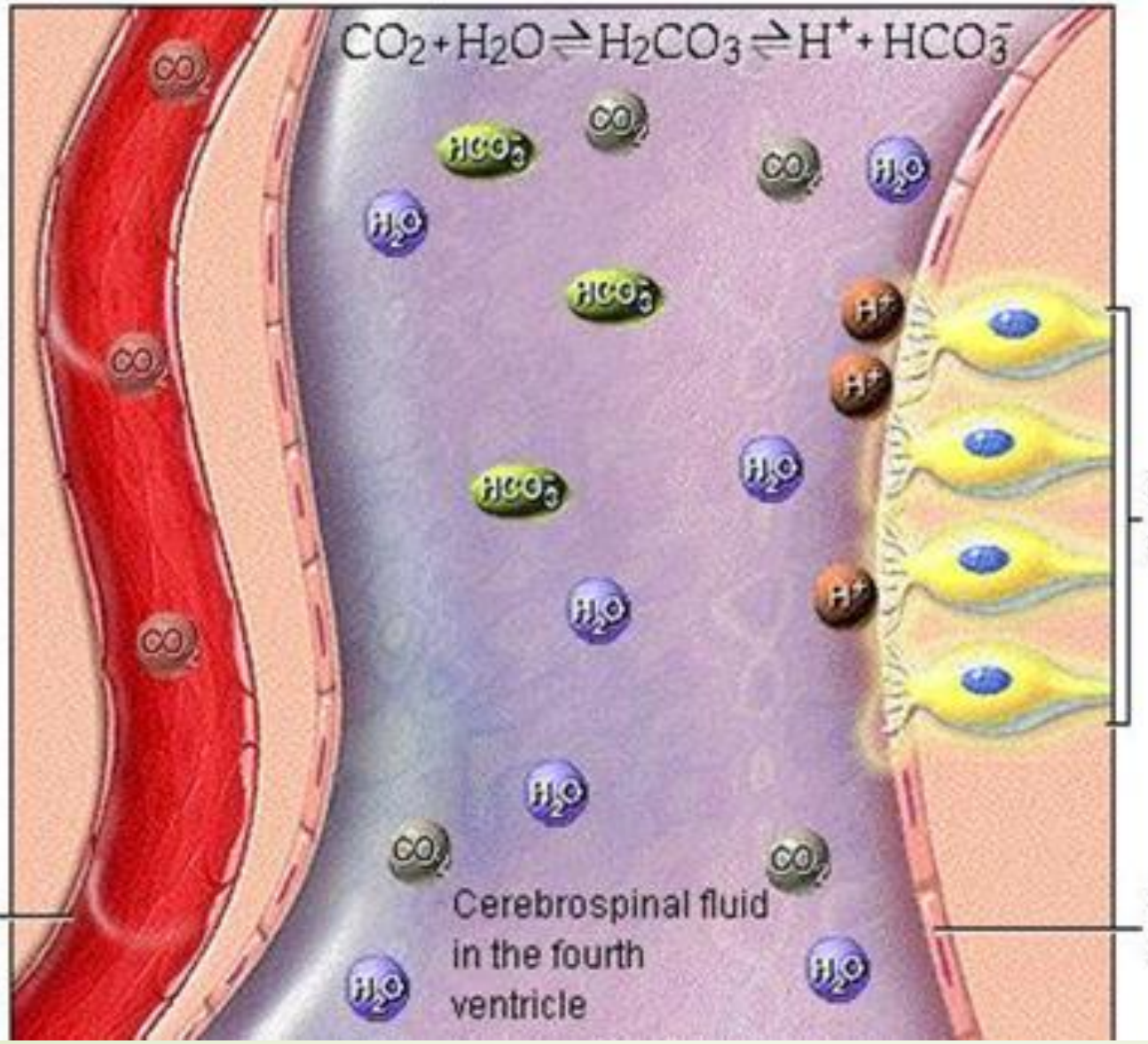


Central Chemoreceptors: Effect of P_{CO_2}

The hydrogen ions stimulate the central chemoreceptors, which send nerve impulses to the respiratory centers in the medulla.





Ventilatory response to O2 lack

O2 lack is a weaker stimulus for the respiration than the Co2 excess, and act only via the peripheral receptors

This weak stimulatory effect (2-4 folds only) is due to:

1- Decrease O2 ⇨ more reduced hemoglobin, which is weak acid and buffer H+ leading to inhibition of respiration.

2- Decrease O2 ⇨ slight stimulation of respiration ⇨ wash of Co2 and H+ ⇨ decrease Co2 ⇨ strong inhibitory effect on respiration which oppose the stimulatory effect of decrease O2 leading to inhibition of respiration.

But **the O2 lack effect increased in cases of:**

1- Overdose of Anesthesia as it depresses the **central chemoreceptors** with no response to Co2 and respiration in these cases is maintained only by **O2 lack** ,So, **100% O2** during anesthesia ⇨ inhibit respiration and may be fatal

Ventilatory response to CO2 excess

⇧ PCO2 is **more** stimulants for respiration than O2 lack

⇧ PCO2 act on **both** central receptors (70%) & peripheral receptors (30%).

Effect of CO2 excess

CO_2 excess	Effect
⇧ CO_2 in inspired air to **5%** ⇨ ⇧ PCO_2 in arterial blood.	**2 folds** increase in respiration To get rid of this excess CO_2.
⇧ CO_2 in inspired air to **10%** ⇨ ⇧ PCO_2 in arterial blood to 50mmHg	**10 folds** increase in respiration To get rid of this excess CO_2.
⇧ CO_2 in inspired air to **>10%**	**CO_2 narcosis:** Inhibition of respiratory center ⇨ more accumulation of CO_2 (hypercapnea) & headache & coma & death from CO_2 narcosis.

Carbogen: Mixture of 5% CO2 + O2 is used to stimulate respiration.

Ventilatory response to H+

Increased H^+ caused by

1)*Respiratory acidosis* in which hypoventilation which isn't secondary to fall in H^+ concentration $\rightarrow$ accumulation of Co_2 & $H^+ \rightarrow$ acidemia ($\downarrow$ pH less 7.4)

2) Metabolic acidosis as in diabetes mellitus with ketoacidosis $\rightarrow$ acidemia.

This led to hyperventilation (rapid and deep **kussmoul** respiration) via stimulation of the peripheral receptor.

C – Non-chemical regulation
1. Afferents from the respiratory system

A. From the lung

	Lung stretch receptor (Herring Breuer inflation reflex)	Lung irritant receptors	J-receptors (Pulmonary chemoreflex)
Receptors	Stretch receptors in the bronchi.	Bronchi & Bronchioles.	Close to alveoli (Juxta capillary)
Stimulus	Overinflation By 1500 ml.	Irritants as: Cigarette.	Pulmonary **E**dema & **E**mboli.
Afferent	Vagus.	Vagus.	Vagus.
Response	a) Inhibit DRG & inhibit apneustic center. b) Bronchodilatation.	a) Cough. b) Bronchoconstriction.	a) Apnea. b) Hypotension. c) Bradycardia.

B. From the upper respiratory passages

	Sneezing	Cough	Swallowing
Stimulus	Irritation of nose.	Irritation of bronchi.	Irritation of pharynx.
Afferent	Trigeminal. (V)	Vagus. (X)	Glossopharyngeal. (IX)
Response	Deep inspiration Followed by forced expiration Against opened glottis.	Deep inspiration Followed by forced expiration Against closed glottis with sudden opening.	Swallowing apnea (stoppage of respiration) and closure of glottis.

2. Afferent from the cardiovascular system

	Arterial baroreceptors	Atrial baroreceptors
Stimulus	⇧ ABP & ⇧ pulse pressure.	⇧ VR.
Afferent	Vagus & glossopharyngeal.	Vagus.
Response	Inhibit respiration.	Stimulate respiration.

✓ ***Adrenaline apnea:*** Injection of large dose of adrenaline ⇨ VC ⇨ ⇧ABP ⇨ stimulate arterial baroreceptors ⇨ reflex apnea

3. Afferents from higher centers

- **A. Limbic cortex & Hypothalamus:**

- Mild pain & emotions: ⇨ tachypnea via sympathetic

- Severe pain & emotions: ⇨ inhibition of respiration

- Hot as fever: ⇨ stimulation of respiratory center

- Panting: shallow rapid breathing in dogs (no sweat glands) ⇨ heat loss

- **B. Cerebral cortex: (Voluntary control)**

I. Voluntary apnea (breath holding)

- Temporary stoppage of breathing till the breaking point.

- Voluntary apnea ⇨ ⇧CO_2 & ⇧H^+ & ⇩O_2 ⇨ stimulate respiration

- Breaking point is delayed by:

a) Previous hyperventilation ⇨ ⇩ CO_2

b) Breathing 100% O_2 before apnea ⇨ ⇧ O_2

c) Holding the breath in full inspiration ⇨ inhibition of respiration

d) Swallowing (deglutition) ⇨ inhibition of respiration

Types of apnea

1)Voluntary apnea may occur during speech, blowing, suckling, childbirth, micturition and defecation

2) Apnea follows the voluntary hyperventilation

3) Adrenaline apnea

4) Swallowing apnea

5) Chyne-stokes respiration

I I . Voluntary hyperventilation

Increase in depth and rate of respiration → ↓ PCo_2 from 40 to 15 mmHg (hypocapnia), ↑ PO_2 from 95 to 130 mmHg and ↓ H^+ (alkalosis) → inhibition of respiration → apnea → ↓O_2 & ↑ Co_2 → stimulate respiration → hyperventilation and the cycle is repeated, then PCo_2 return to normal level and breathing becomes normal. This alternate hyperventilation and apnea is called (**periodic breathing) or (chyne-stokes respiration)**

Causes of chyne-stokes respiration (Periodic respiration)

1. After voluntary **H**yperventilation.
2. **H**igh altitude (hypoxia).
3. **H**eart failure ⇨ prolongation of lung-brain circulation, so changes in arterial gas tension at lung takes longer time to affect the brain center.
4. **Live failure & kidney failure** ⇨ inhibition of DRG by toxic substances.
5. **Narcotics & morphine** ⇨ ⇧ sensitivity of chemoreceptors to CO_2.

4- Afferents from skeletal muscles, joints and skin

(a)From muscle spindle of the intercostal muscle and the diaphragm to regulate the depth of respiration.

(b) From the proprioceptors: During muscle movements, afferent from tendons, ligaments and joints to stimulate the respiratory center → Exercise hyperventilation.

(c) From the skin: Exposure to cold leading to initial apnea followed by deep inspiration

5) Respiratory components of the other visceral reflexes

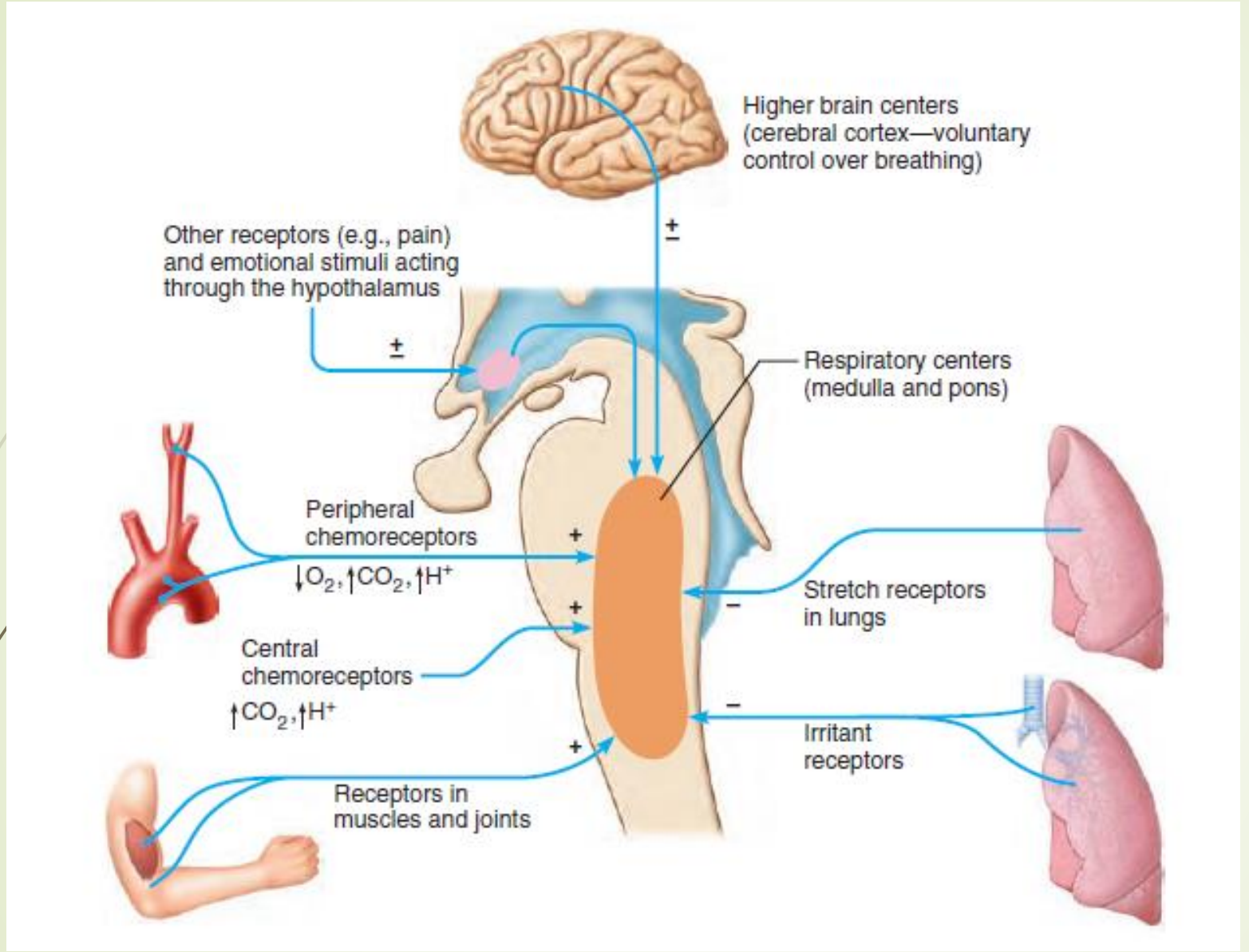
A. **Swallowing and vomiting:** **Apnea** to prevent aspiration of food of vomitus

B. **Hiccup:** Sudden contraction of diaphragm ⇨ sudden inspiration with sudden closure of the glottis → producing characteristic sound

- It occurs due to irritation of diaphragm or upper abdominal viscera
- It is treated by inhalation of CO2 gas mixture or tranquilizer drugs

C. **Yawning:** is infectious respiratory act characterized by deep inspiration to:

a) Open alveoli to prevent collapse b) ↑ venous return



Neural and chemical influences on brain stem respiratory centers


Thank
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