CHEMICAL REGULATION OF RESPIRATION

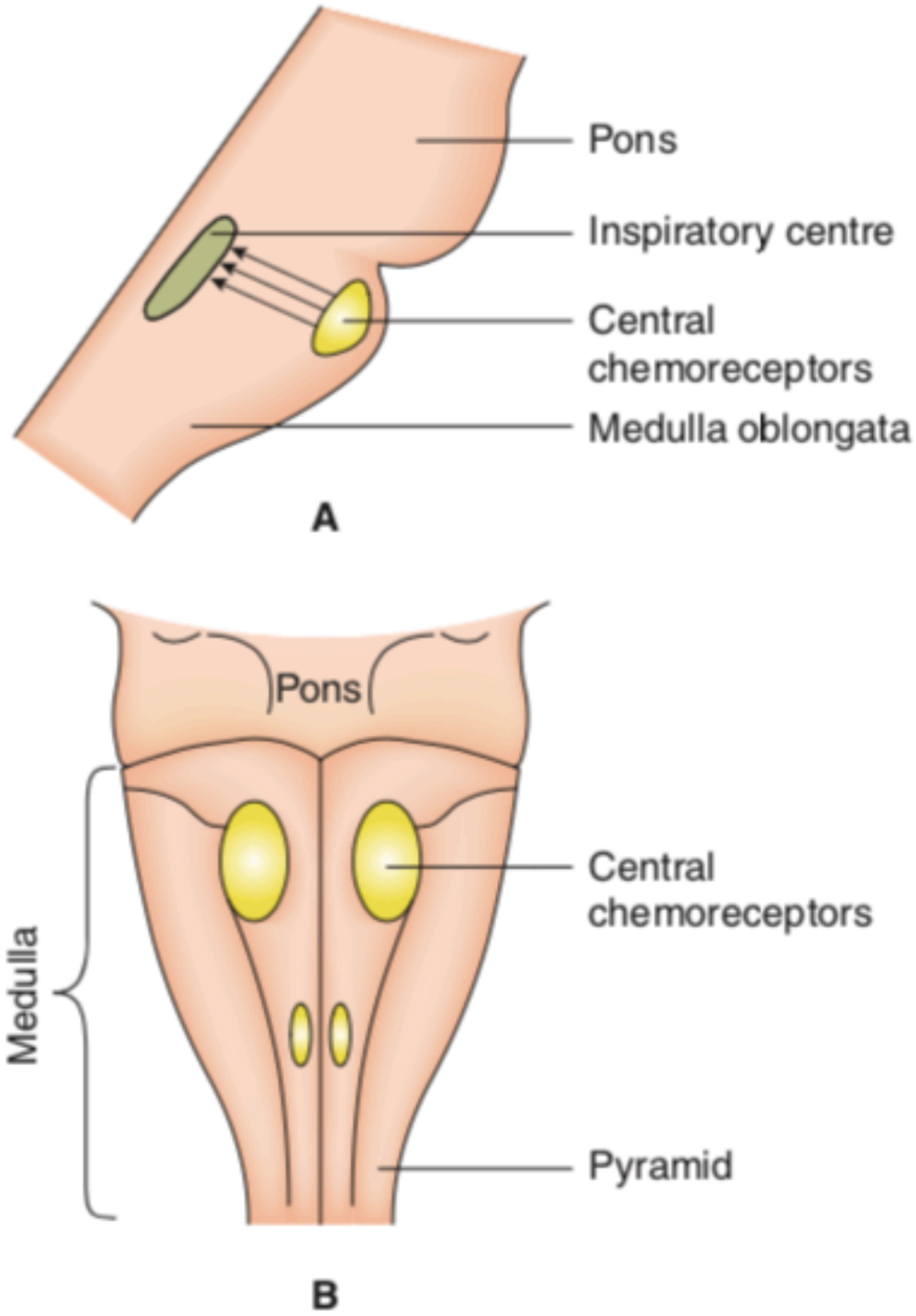
- Blood levels of PO_2, PCO_2 & pH : effect on respiratory mechanism so that blood levels are kept constant.
- Changes in these blood levels : sensed by CHEMORECEPTORS.

CHEMORECEPTORS

- Sensory nerve endings - highly sensitive to changes in blood pH, PO_2 & PCO_2.
- CLASSIFICATION :
    - CENTRAL
    - PERIPHERAL
    - PULMONARY & MYOCARDIAL.

CENTRAL CHEMORECEPORS

- **<u>MEDULLARY RECEPTORS</u>** : ventral surface of medulla.
- Sensitive to : H^+ concentration of brain ISF.
- Blood brain barrier selectively permeable to CO_2, but not H^+.


Pons
Inspiratory centre
Central chemoreceptors
Medulla oblongata
A
Pons
Medulla
Central chemoreceptors
Pyramid
B

- <u>Mechanism of stimulation</u> :
  - HYPERCAPNIA (increase in blood PCO_2) —>
  - Increase in CO_2 in CSF & brain ISF
  - $CO^2 + H_2O$ —> H_2CO_3 —> $H^+ + HCO_3^-$.
  - This H^+ now stimulates medullary chemoreceptors.

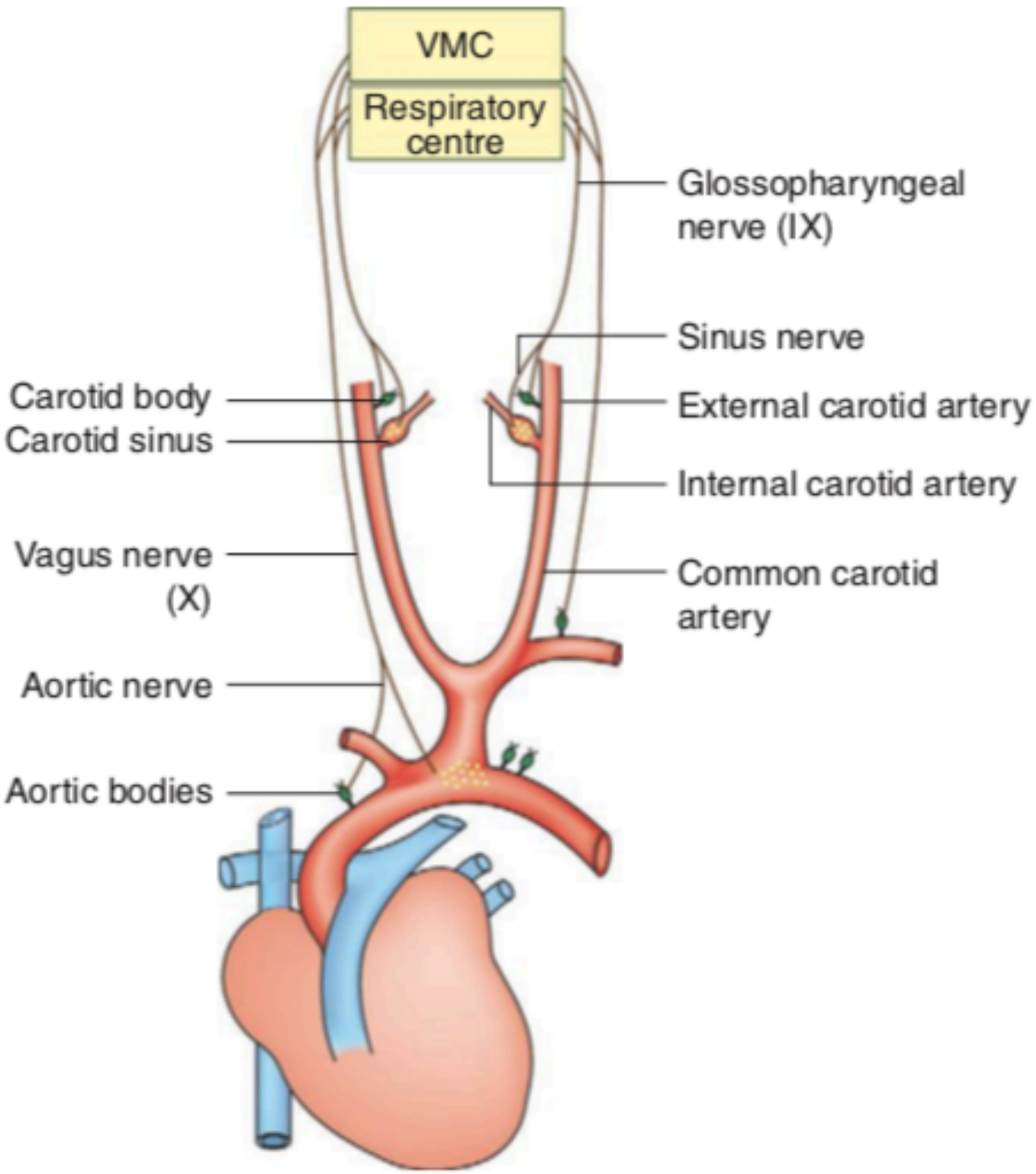
- Effect of stimulation :
    - Increase in rate & depth of ventilation —> CO_2 washout.
    - Responsible for 80-85% of the resting respiratory drive.

- Stimulation of CENTRAL CHEMORECEPTORS:
  - PCO_2 - Indirect action.
  - H^+ - direct action.
  - PO_2 - no stimulation (HYPOXIA - inhibitory action).

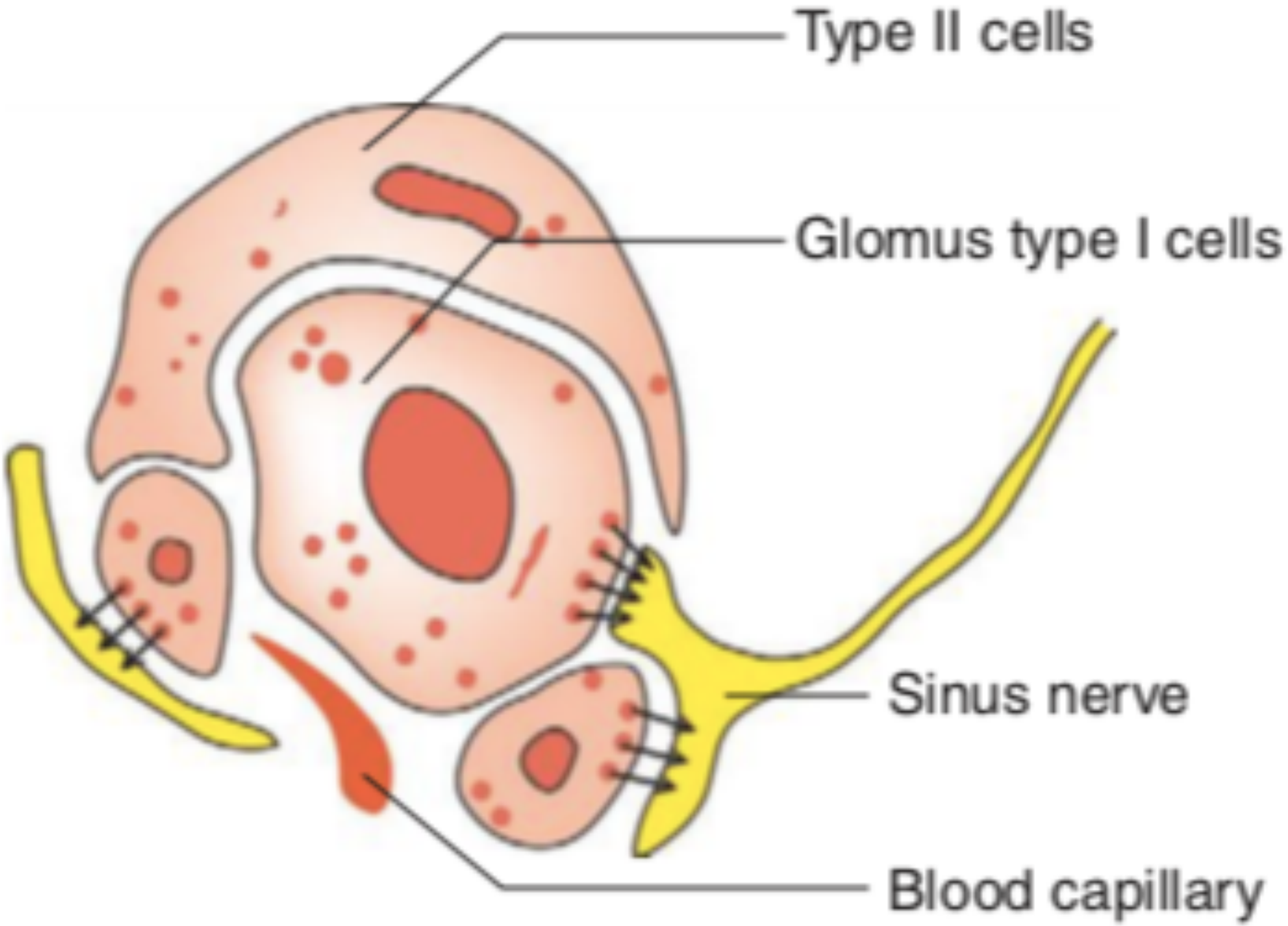
- Inhibition of CENTRAL CHEMORECEPTORS :
    - Anaesthesia
    - Cyanide poisoning
    - Deep sleep.

PERIPHERAL CHEMORECEPTORS

- **CAROTID BODY & AORTIC BODY.**
- Location:
  - Carotid body - bifurcation of common carotid artery.
  - Aortic body - near the arch of aorta.


VMC
Respiratory centre
Glossopharyngeal nerve (IX)
Sinus nerve
Carotid body
Carotid sinus
External carotid artery
Internal carotid artery
Vagus nerve (X)
Common carotid artery
Aortic nerve
Aortic bodies

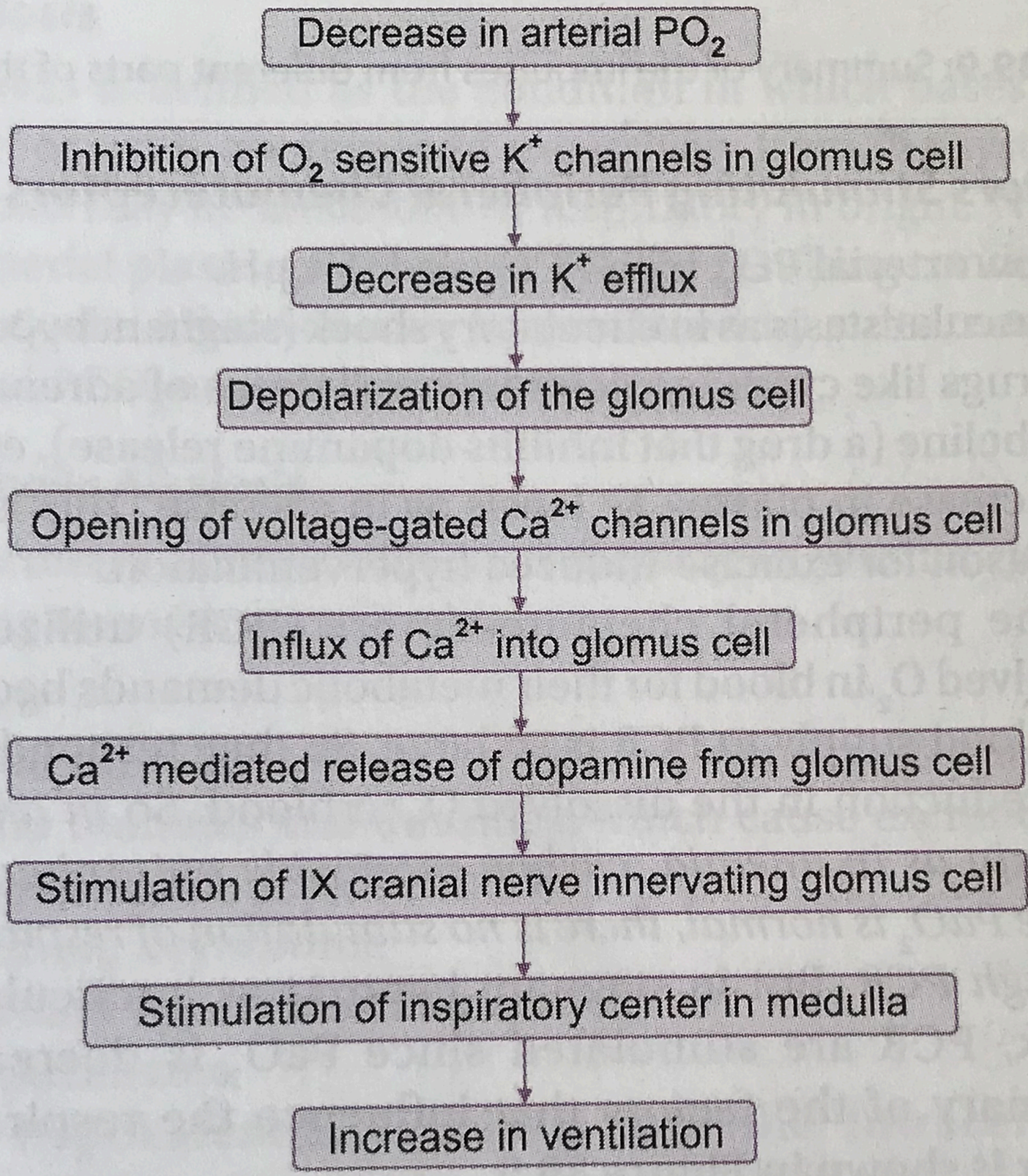
- Structure :
    - capsule with surrounding sinusoidal capillaries.
    - Epithelial cells :
        - **<u>Type I or GLOMUS cells</u>** - dense core granules:- dopamine.
            - innervated by unmyelinated cup shaped nerve endings with D2 receptors.
        - Carotid body - **sinus nerve**, branch of glossopharyngeal or IX cranial nerve.
        - Aortic body - **aortic** branch of vagus or X cranial nerve.
        - **<u>Type II or GLIAL cells</u>** - supporting or sustentacular cells.



. 5.6-9 Histological structure of carotid body.

- Blood flow : highest in the body - 2000ml/100g/min.
- STIMULI :
  - Hypoxia (reduction in arterial PO_2) - most potent stimuli.
  - Respond to high PCO_2 & low pH.

Flowchart 39.1: Mechanism of increase in ventilation by stimulation of peripheral chemoreceptors.



- Effect of stimulation:
    - Increase rate & depth of respiration.
    - Increase in blood pressure & heart rate.
    - Responsible for 15-20% of resting respiratory drive.

Table 39.1: Differences between carotid body and aortic body.

Carotid body	*Aortic body*
Located near the bifurcation of the common carotid artery	Located in the arch of aorta
Supplied by the IX cranial nerve	Supplied by the X cranial nerve
Seven times more effective than aortic bodies in stimulating respiration	Less effective
Increases both rate and depth of respiration	Increases only the rate of respiration

- <u>Factors stimulating peripheral chemoreceptor action:</u>
  - Low arterial PO_2, high PCO_2 & low pH.
  - Vascular stasis - blood flow reduced.
  - Drugs - Cyanide, Nicotine, Lobeline.
  - Increase in plasma K^+ (exercise).

PULMONARY & MYOCARDIAL RECEPTORS

- Location : pulmonary & coronary blood vessels.
- Innervated : Vagus (X) cranial nerve.

- PULMONARY CHEMORECEPTORS :
    - Stimuli : VERATRIDINE /NICOTINE injection into pulmonary circulation.
    - Effect : ***pulmonary chemoreceptor reflex.***
    - Features : Bradycardia, hypotension & apnoea followed by tachypnoea (rapid shallow breathing).
    - Seen in PULMONARY CONGESTION or EMBOLISM.

- MYOCARDIAL CHEMORECEPTORS :
    - Stimuli : VERATRIDINE /NICOTINE injection into coronary circulation.
    - Effect : ***coronary chemoreceptor reflex/ BEZOLD JARISCH reflex.***
    - Features : similar.
    - After MYOCARDIAL INFARCTION.

Effect of HYPOXIA

- Normal arterial PO2 - 100mm Hg.
- **PO2 between <u>100 - 60 mm Hg</u>** : not much effect on ventilation.
- Reason : 1. Breaking effect of CO2.

HYPOXIA -> increased ventilation (peripheral)

-> CO2 washout

-> reduced arterial CO2

-> Inhibition of central chemoreceptors.

2. Decrease in arterial H+ concentration.

HYPOXIA -> deoxyhemoglobin content is higher

-> binds more to H^+ to form HHb

-> decrease in H^+ concentration

-> inhibits respiration.

- PO2 below 60 mm Hg -> marked increase in ventilation.

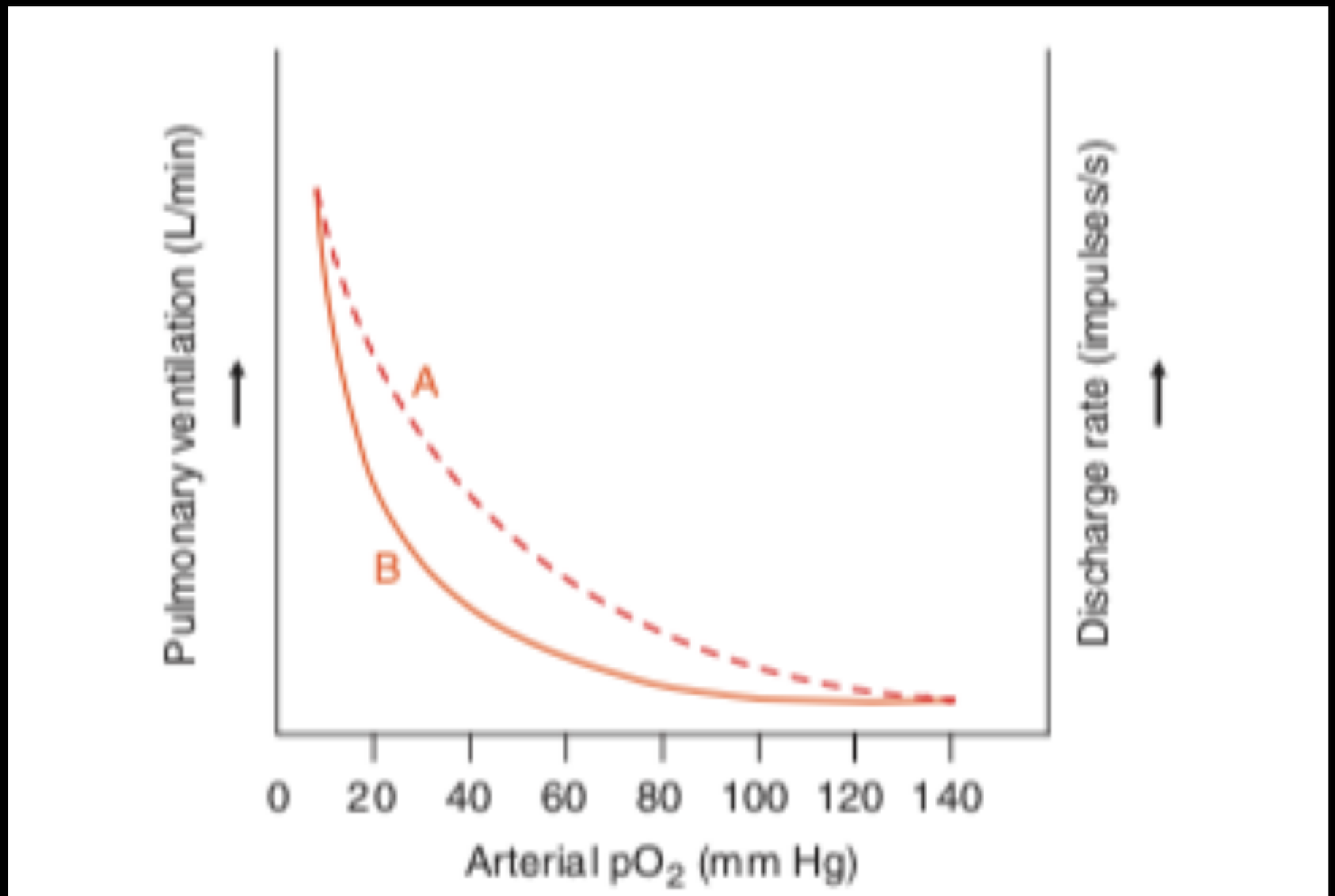


Fig. 5.6-11 Relationship of arterial pO_2 with sinus nerve discharge rate (A) and pulmonary ventilation (B).

Effect of HYPERCAPNIA

- Normal arterial pCO_2 - 40mm Hg.
- Hypercapnia : stimulation of central chemoreceptors mainly; can also act on peripheral.
- Effect : increase in ventilation —> CO_2 washout.
- Linear relation between arterial PCO_2 & pulmonary ventilation.

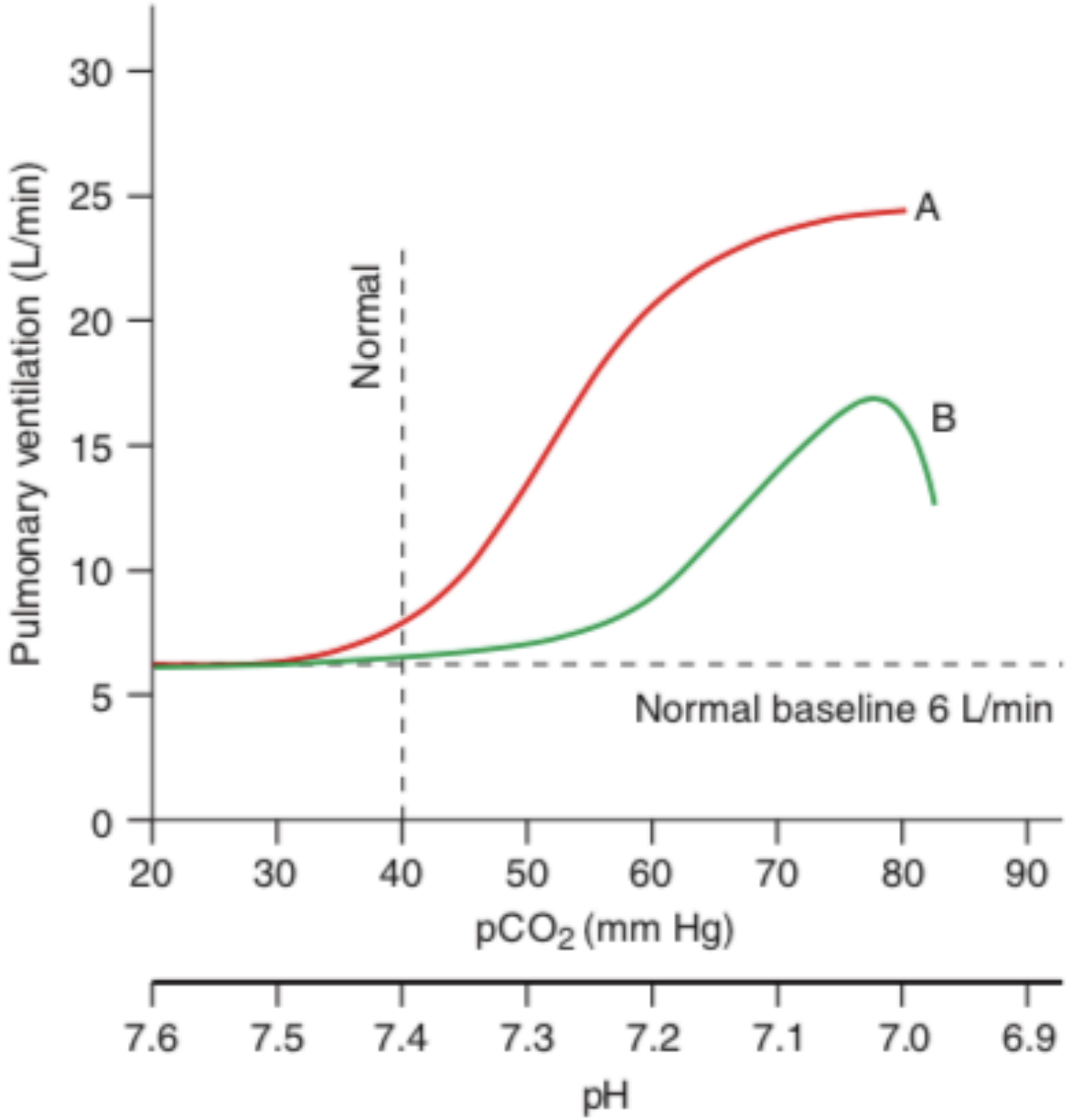


Fig. 5.6-12 Effect of increase in arterial pCO_2 (A), and decreased pH; (B), on pulmonary ventilation.

- CARBON DIOXIDE NARCOSIS:
    - Chronic Emphysema; accidental CO_2 Inhalation.
    - Inspired air $PiCO_2$ = Alveolar PCO_2.
    - CO_2 elimination difficult; rise in arterial PCO_2 >50mm Hg.
    - Headache, confusion, tremor, coma.

Effect of arterial pH

- **<u>METABOLIC ACIDOSIS</u>** : increase in H^+ concentration.
  - Causes : diabetic ketoacidosis, renal failure, lactic acidosis (severe exercise) , diarrhoea.
  - Effect : stimulation of PERIPHERAL chemoreceptors

    -> stimulation of ventilation

    -> decrease in arterial CO_2

    -> fall in blood H^+.

- METABOLIC ALKALOSIS : decrease in H^+ concentration.
  - Causes : excessive vomiting (loss of HCl).
  - Effect : inhibition of PERIPHERAL chemoreceptors

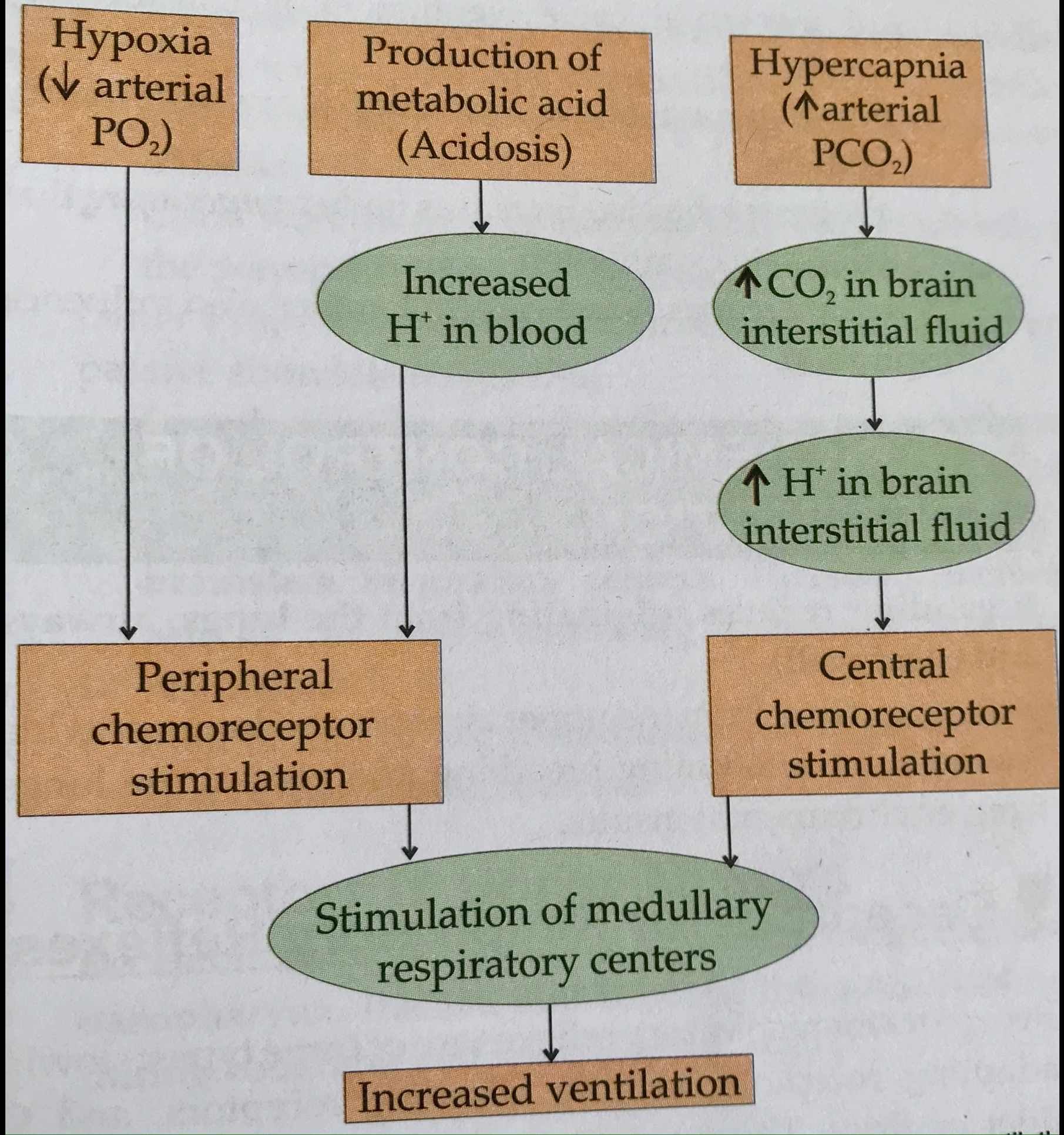
-> depression of ventilation

-> CO_2 retention

-> increase in arterial CO_2

-> rise in blood H^+.

INTEGRATED RESPONSES TO HYPOXIA, HYPERCAPNIA & ACIDOSIS


Hypoxia (↓ arterial PO_2)
Production of metabolic acid (Acidosis)
Hypercapnia (↑arterial PCO_2)
Increased H^+ in blood
↑CO_2 in brain interstitial fluid
↑ H^+ in brain interstitial fluid
Peripheral chemoreceptor stimulation
Central chemoreceptor stimulation
Stimulation of medullary respiratory centers
Increased ventilation