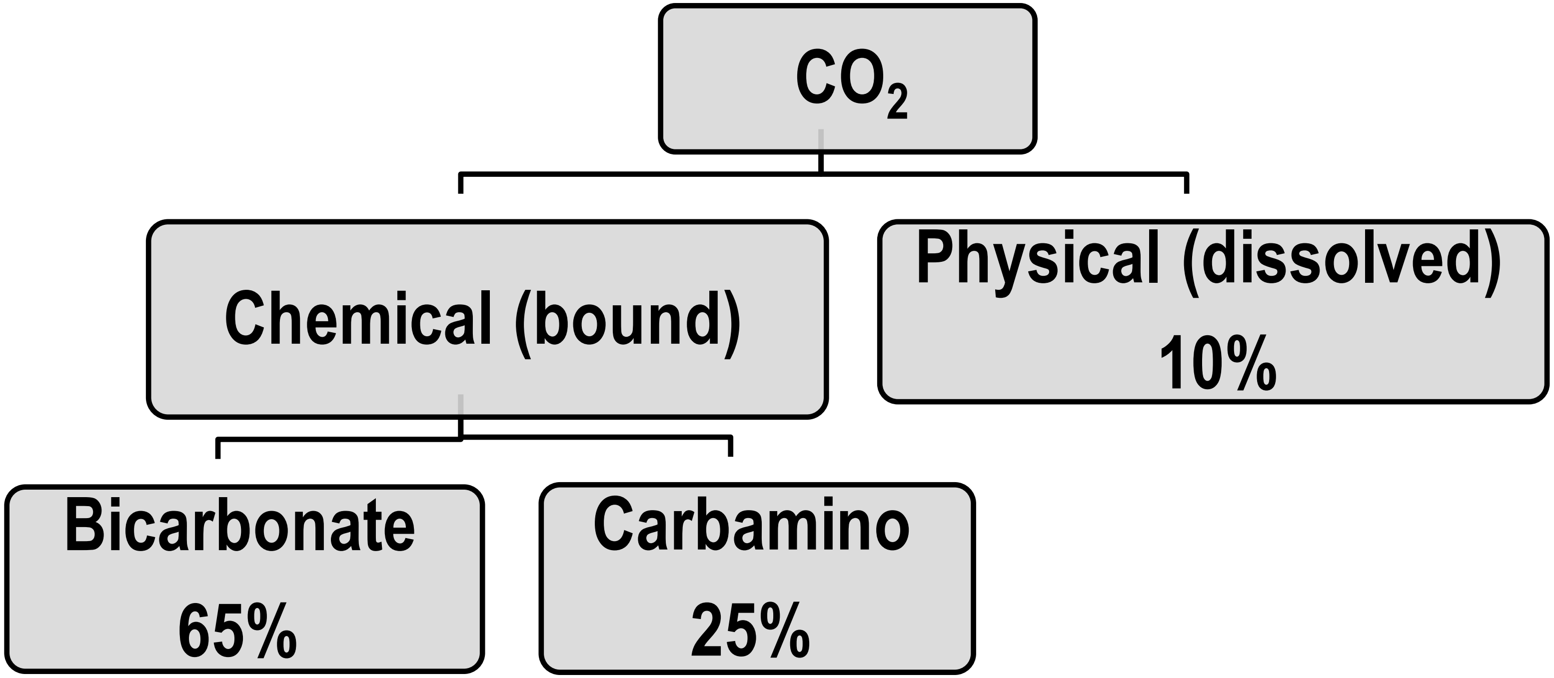
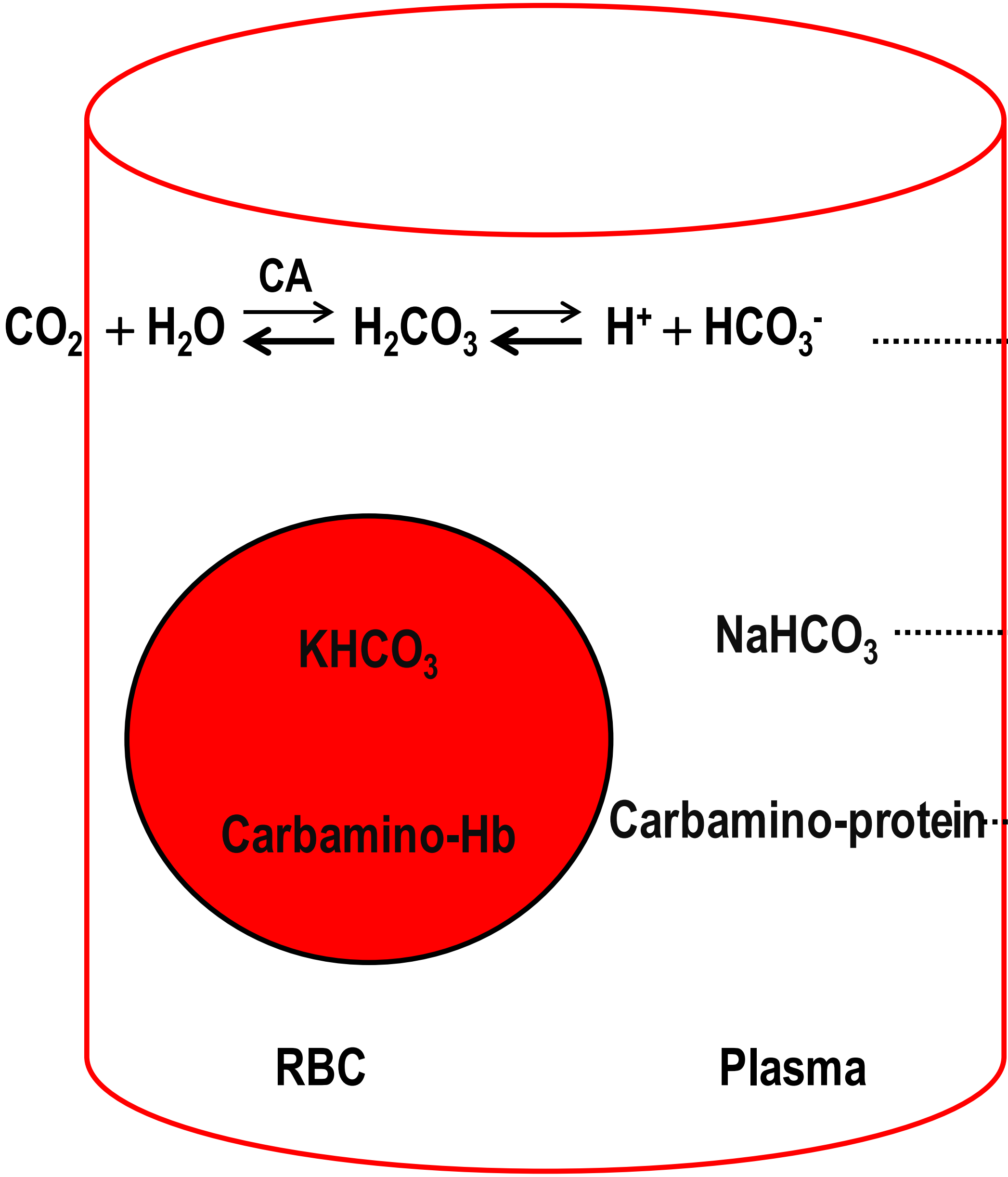
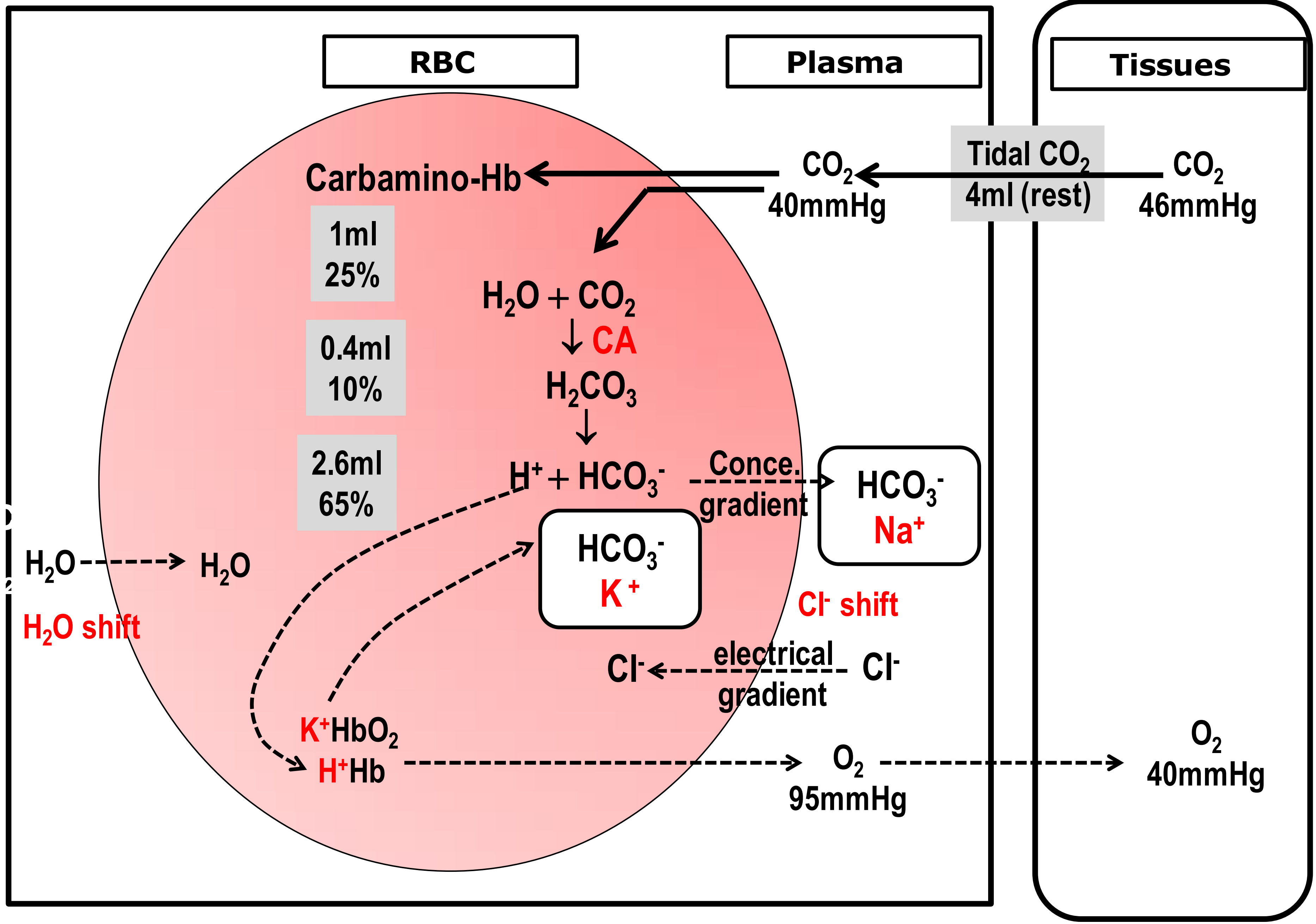
CO_2 transport by blood



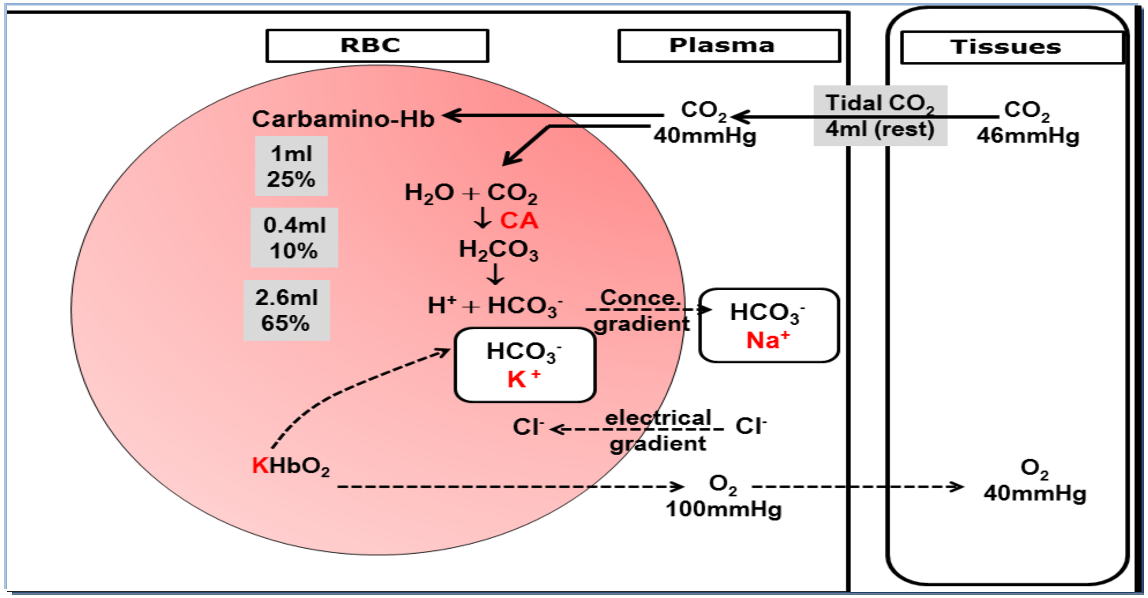


Total CO_2 Arterial 48ml/dL	Tidal CO_2 Tissue 4ml	Venous 52ml/dL
3	0.4ml (10%)	
42	2.6ml (65%)	
3	1ml (25%)	

CO_2 transport at tissues (chloride shift)

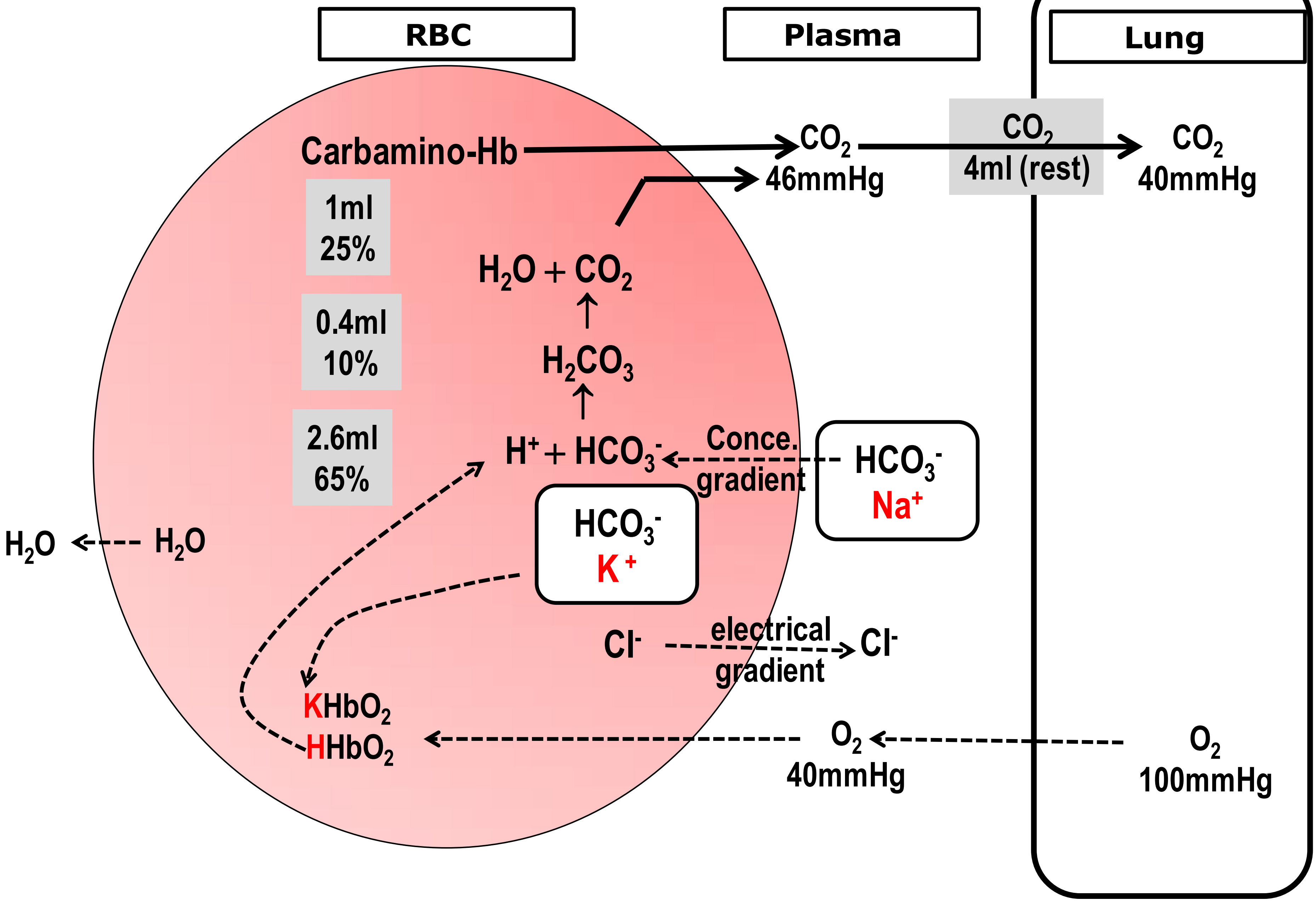


Results of chloride shift at tissues



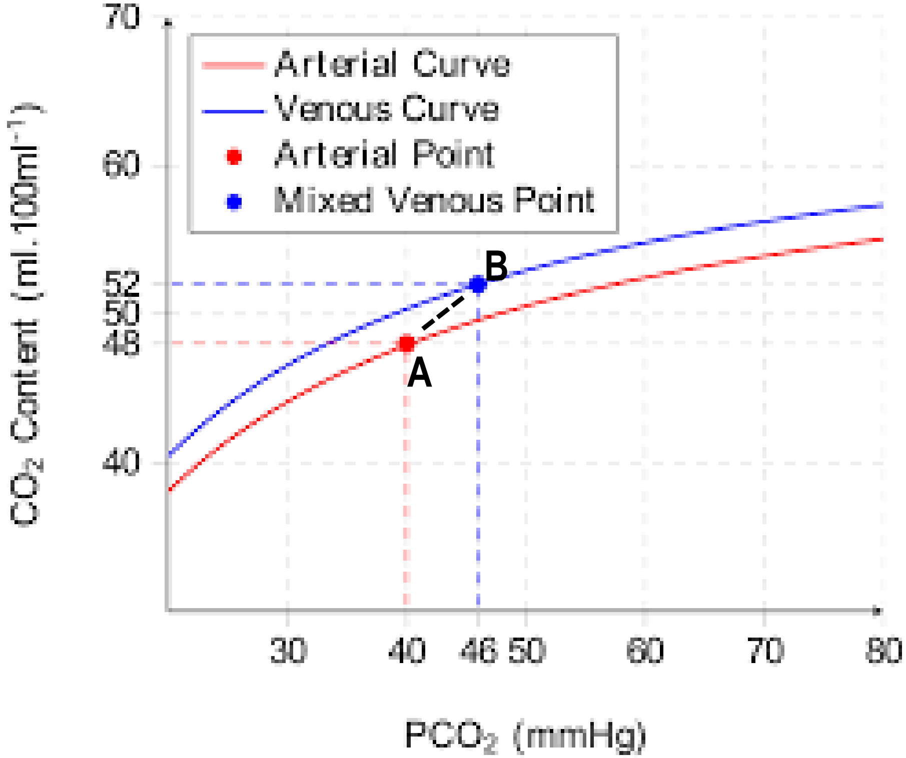
		RBC	Plasma
1	HCO_3^-	+	+
2	Cl^- (Shift)	+	−
3	Cations	±	±
4	Osmotic pressure	++	±
5	H_2O (shift)	←	←
6	PCV	+	
7	pH of blood	Slightly acidic	

CO_2 transport at lung (reverse chloride shift)



CO_2 dissociation curve (CDC)

- A graph is plotted with PCO_2 on the X-axis and CO_2 content on the Y-axis for venous and arterial blood.
  - CO_2 dissociation curve will be at a higher level for venous blood than for arterial blood.
  - Point A, arterial blood (PCO_2 40 mm Hg)→ CO_2 (48 ml/dL of blood)
  - Point B, venous blood (PCO_2 46 mm Hg)→CO_2 (52ml/dLof blood)
  - The line joining A and B is called physiological dissociation curve for CO_2
  - Haldane effect: ↑O_2 content of blood decreases its affinity to CO_2



Lecture 9

Regulation of Respiration

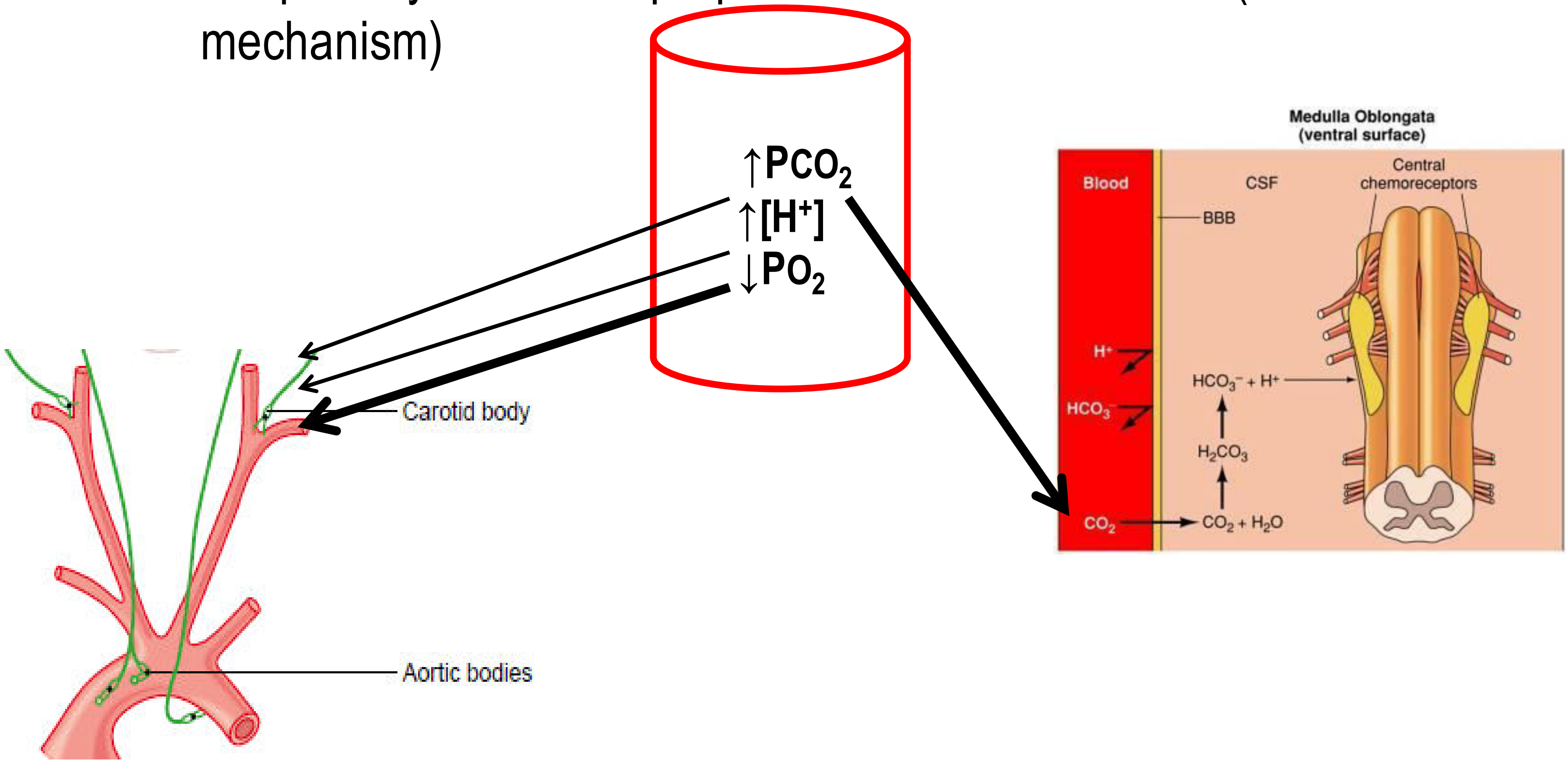
Objectives

- To understand the role of pre-Botzinger complex in producing spontaneous respiration
- To identify the location and probable functions of the dorsal and ventral groups of respiratory neurons, the pneumotaxic center, and the apneustic center in the brain stem
- To understand the ventilatory responses to increased and decreased CO_2 concentrations in the inspired air
- To understand the ventilatory responses to oxygen lack in the inspired air

Chemical control of breathing (basic mechanism)

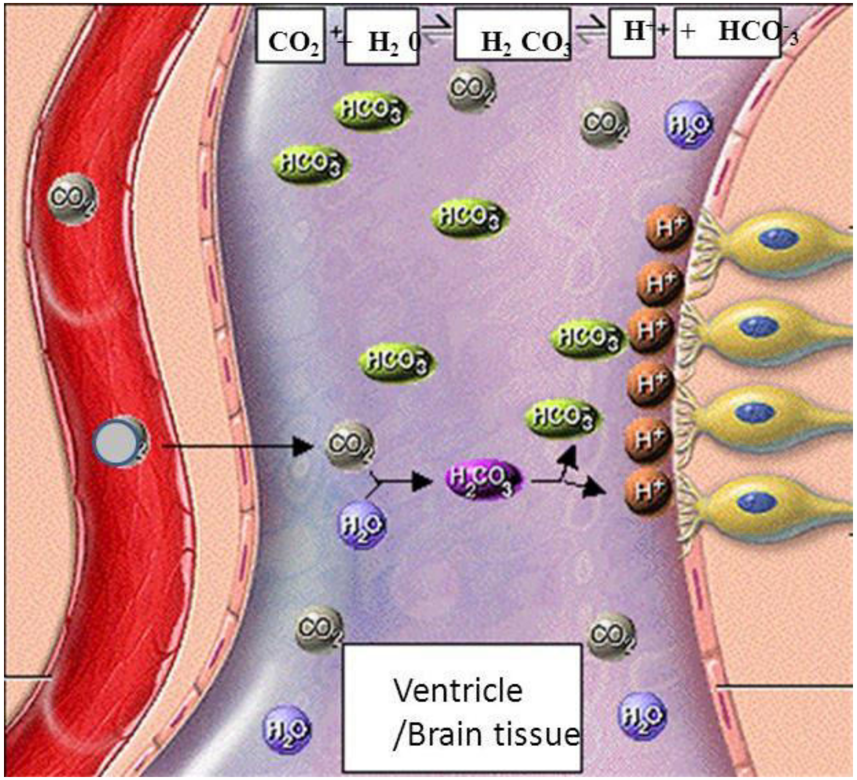
1)

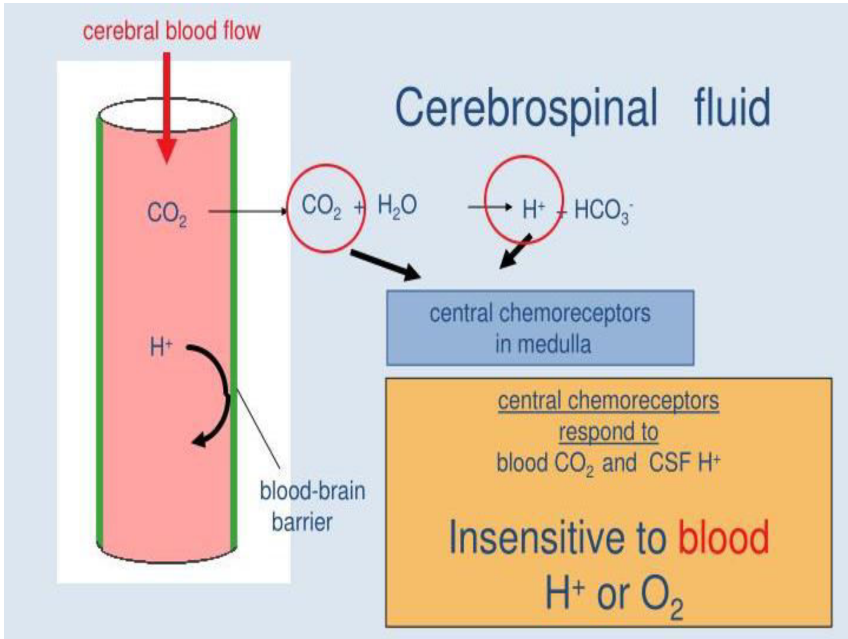
- ⊙ ↑P_{CO_2}, ↑$[H^+]$, ↓P_{O_2} ⇨ stimulation of respiration,
- ⊙ ↓ P_{CO_2}, ↓$[H^+]$, ↑ P_{O_2} (opposite changes) ⇨ slight inhibition
- ⊙ Respiratory rate made proportional to metabolic rate (basic mechanism)



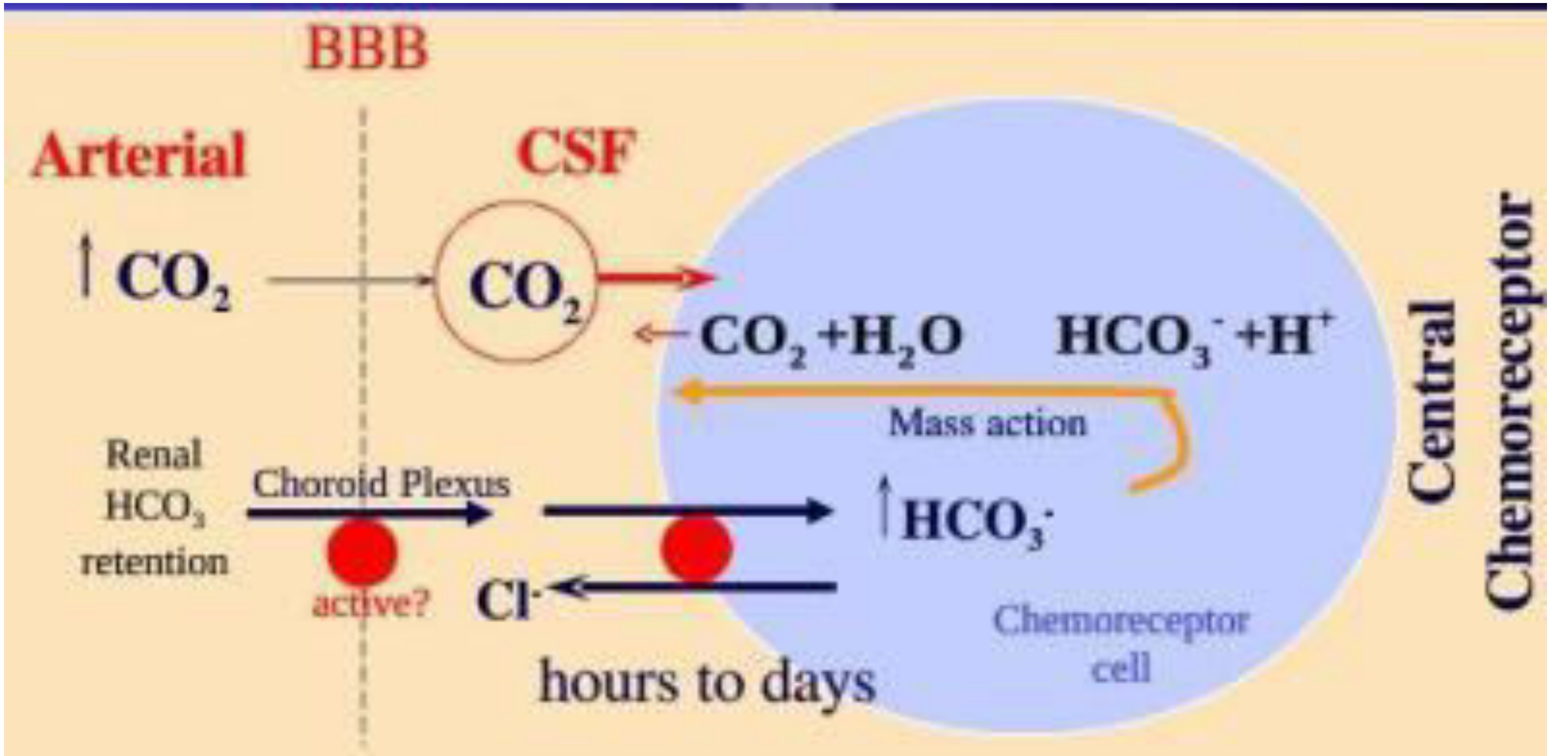
Central chemoreceptors (CCR)

- **Site**: upper part of medulla oblongata, beneath ventral surface
- **Stimulus:** ↑P_{CO_2} (85% respiratory drive)
- **Mechanism:** indirect via H^+
  - Reason: The BBB and blood-CSF barrier impermeable to H^+
  - Proteins in CSF are low (20mg/100ml CSF), do not buffer H^+





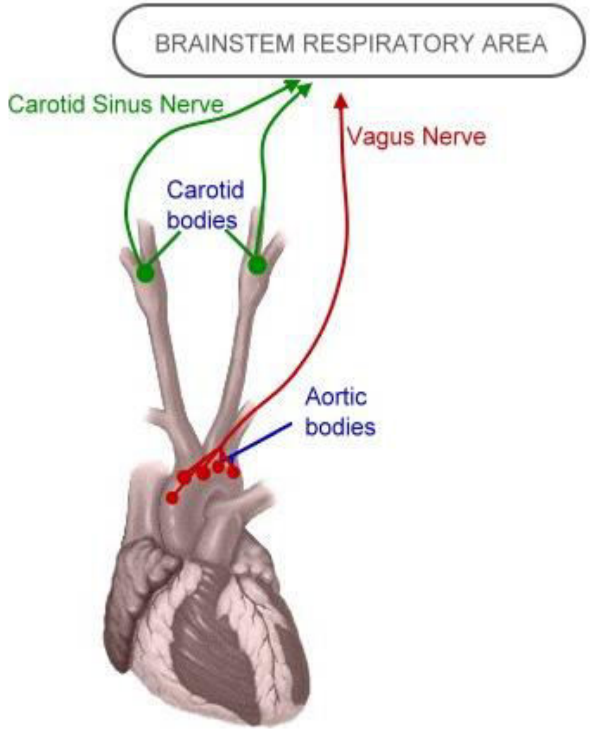
- CCR are inhibited by anesthesia, cyanide, during deep sleep
- Change in blood P_{CO_2} has only a potent acute effect on controlling ventilation and only a weak chronic effect
  - In prolonged hypercapnia, the HCO_3^- diffuses into CSF and neutralizes the H^+



Peripheral chemoreceptors (PCR)

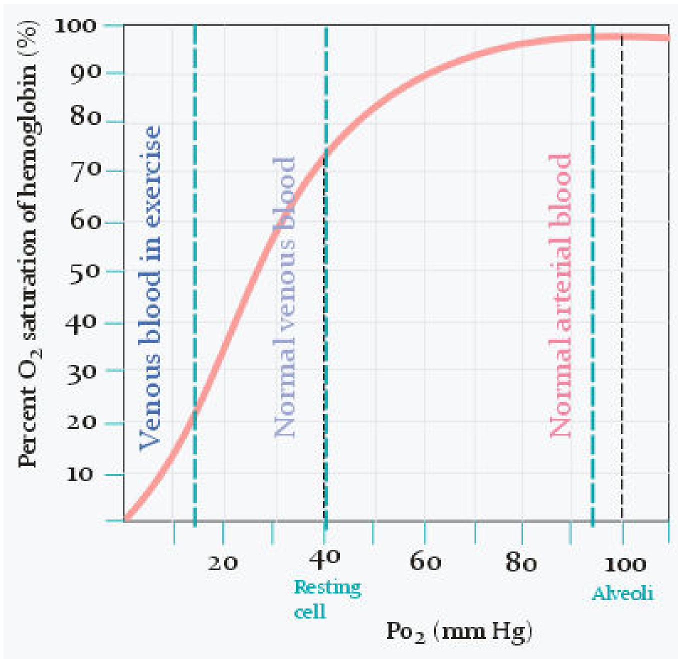
(Neurovascular structures)

- **Site:** carotid bodies (2) bifurcation of common carotid artery, aortic bodies (2 or more) aortic arch
- **Stimulus:** mainly **↓ PO_2 < 60mmHg (15% resp. drive)**, also by ↑PCO_2, ↑$[H^+]$,
- **Mechanism:** by buffer nerves--------

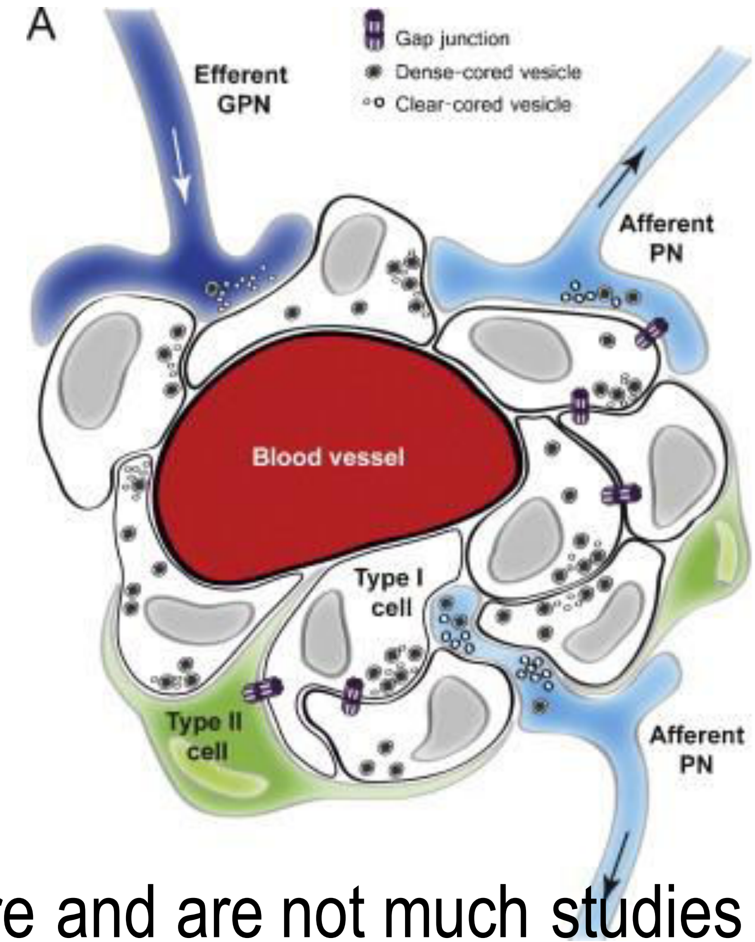


Carotid body

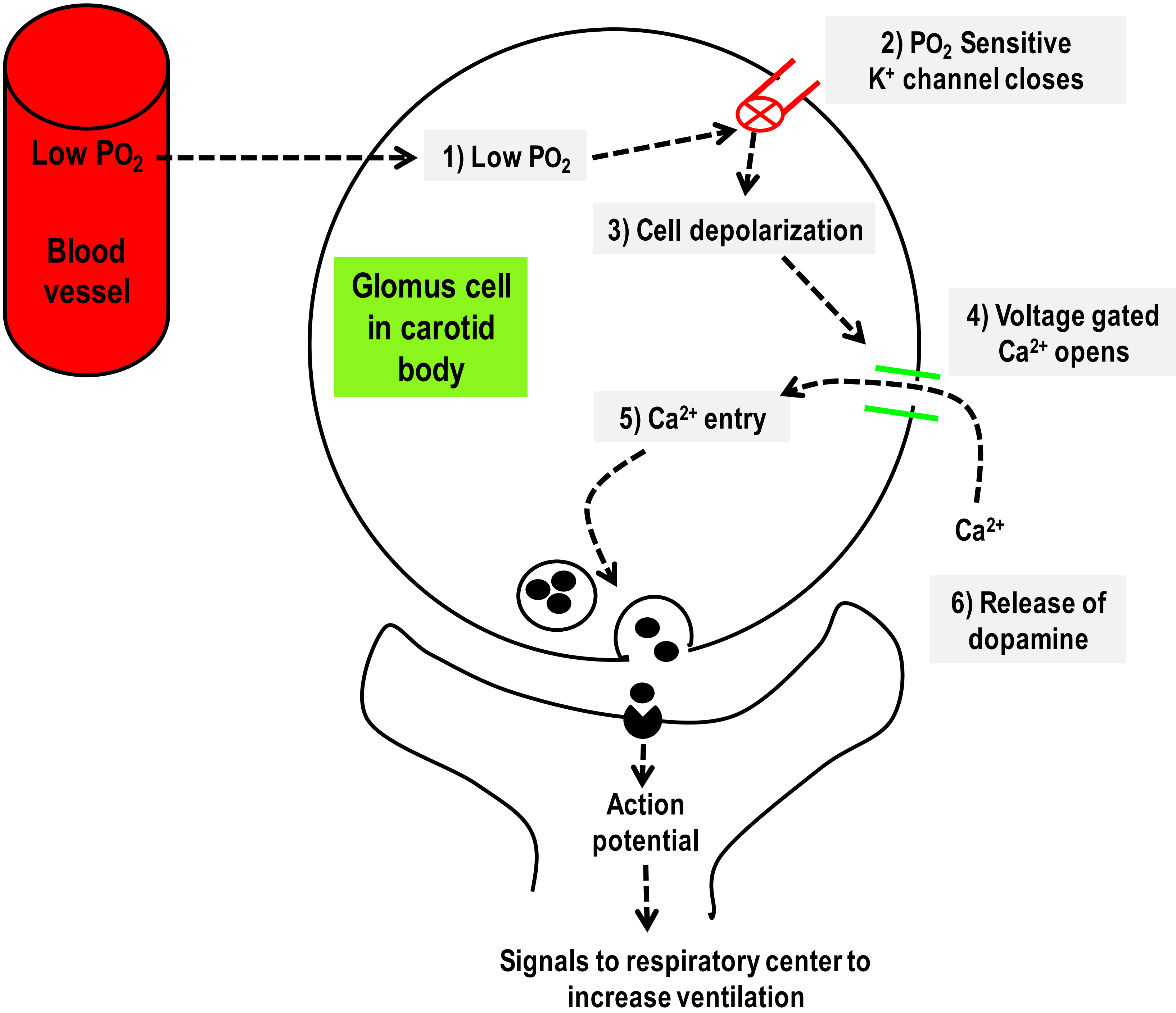
- Weight : 2mg in weight
- High blood flow ≈ 2000ml /100gm tissue/min (40 times that of the brain and 4 times that of kidney)
- Innervation:
  - Carotid body ⇨ carotid sinus nerve (IX)
  - Aortic body ⇨ aortic nerve (chest) ⇨ X



Structure of carotid body



- 2 types of cells surrounded by fenestrated sinusoidal capillaries
  - Type I (glomus) cell
    - Dense core granules (dopamine)
    - Cuplike ending of afferent nerve fibers
  - Type II (glial) cells
    - Supporting cells
    - Each surround 4-6 glomus cells
- Aortic bodies have a similar structure and are not much studies because of their anatomical location.
- Mechanism of stimulation
- ↓ PO_2 is the most potent stimulus for PCR
- PCR also sensitive to ↑ PCO_2 and $[H^+]$to a lesser extent



Low PO_2
Blood vessel
1) Low PO_2
2) PO_2 Sensitive K^+ channel closes
3) Cell depolarization
Glomus cell in carotid body
4) Voltage gated Ca^{2+} opens
5) Ca^{2+} entry
Ca^{2+}
6) Release of dopamine
Action potential
Signals to respiratory center to increase ventilation

- Smooth muscle of pulmonary arteries contain similar O_2 sensitive K^+ channels (Hypoxia →vasoconstriction)
- Systemic arteries contains ATP-dependent K^+ channels (Hypoxia →vasodilatation)

Factors stimulating peripheral chemoreceptors:

1) ↓ PO_2
2) Vascular stasis (↓ The amount of O_2 delivered to the receptors/ time)
3) Cyanide (prevent O_2 utilization at the tissue level)
4) Sufficient doses of nicotine and lobeline
5) ↑ Plasma K^+ (exercise induced hyperpnea)

- The PCR utilize the dissolved O_2 in blood for their metabolic demands because the blood supply is so large (stimulated by ↓ in dissolved O_2)
  - In anemic hypoxia as in anemia and CO poisoning there is no stimulation of respiration through PCR

O_2 lack is weaker stimulus than → 15% respiratory drive		CO_2 excess 85% respiratory drive	
Peripheral chemoreceptors		Central chemorecptors	
70 mmHg	No effect	3%	Ventilation double
60 mmHg	Ventilation double	10%	Ventilation 10 times
30 mmHg	Ventilation 6 times		
20 mmHg	Ventilation inhibited		

⊙ PaO_2 from100 to 60 mm Hg ⇨ no much stimulation of respiration due to counterbalancing inhibitory effect:

1) ↓ Arterial [H^+]:
- ↓PaO_2 ⇨ Hb less saturated with O_2 (de-oxygenated Hb is weak acid and a strong buffer) ⇨ (Hb bind H^+) ⇨ ↓ [H^+]⇨ inhibits respiration

2) ↓ Arterial PCO_2:
- Hypoxia ⇨ ↑ventilation ⇨ wash off CO_2 ⇨ ↓$PaCO_2$ ⇨ inhibits respiration.

Acid base disturbances

	Acidosis (PH < 7.35)			Alkalosis (PH >7.45)		
		Respiratory Hypoventilation	Metabolic		Respiratory Hyperventilation	Metabolic
Cause	↑H^+	↑PCO_2 ------------ HCO_3^-	PCO_2 ------------ ↓HCO_3^-	↓H^+	↓PCO_2 ------------ HCO_3^-	PCO_2 ------------ ↑HCO_3^-
Compensatory	↓↑H^+	↑PCO_2 ------------ ↑HCO_3^- Renal	↓PCO_2 ------------ ↓HCO_3^- Hypervent	↑↓H^+	↓PCO_2 ------------ ↓HCO_3^- Renal	↑PCO_2 ------------ ↑HCO_3^- Hypovent