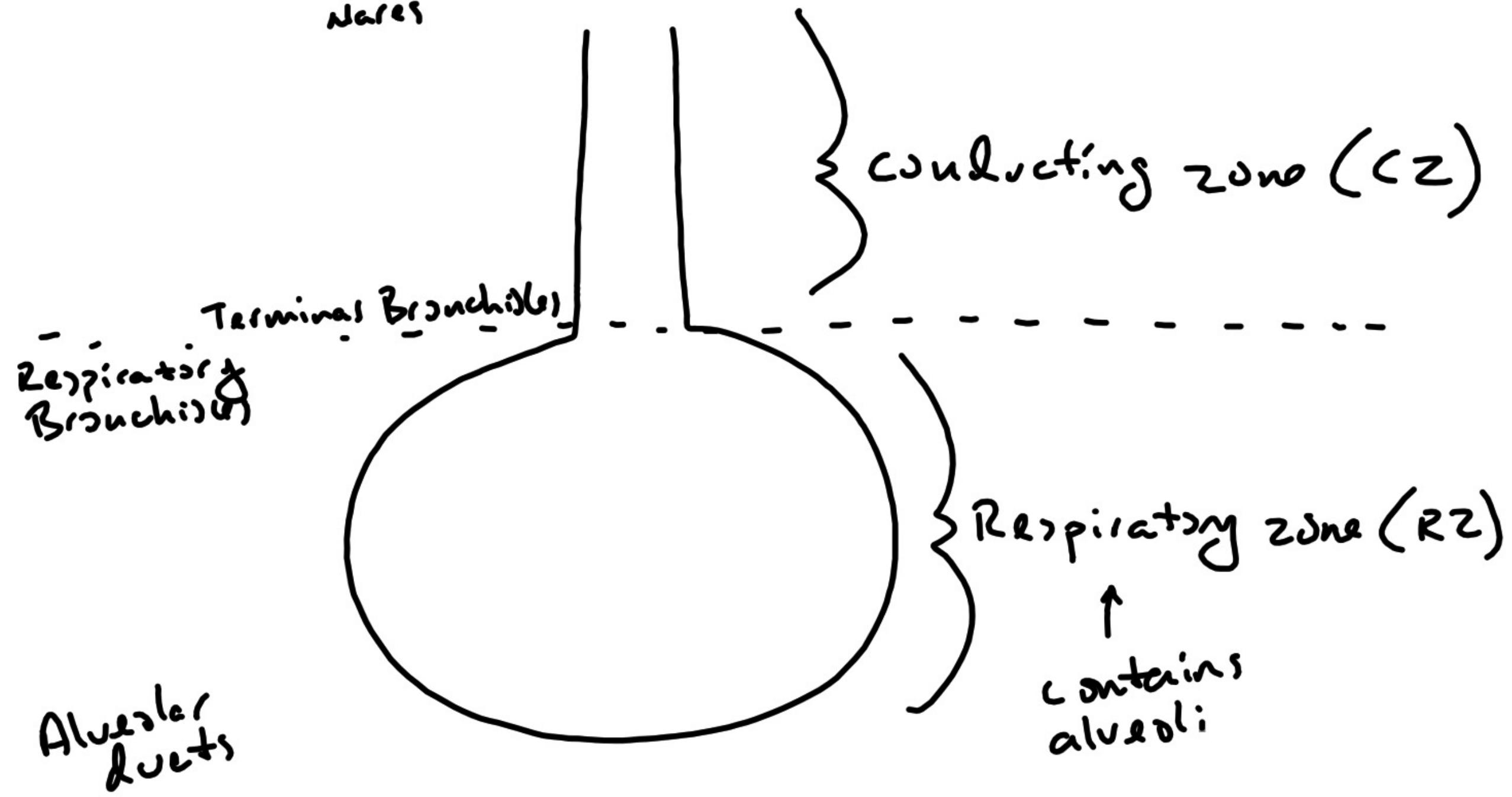


# Definitions

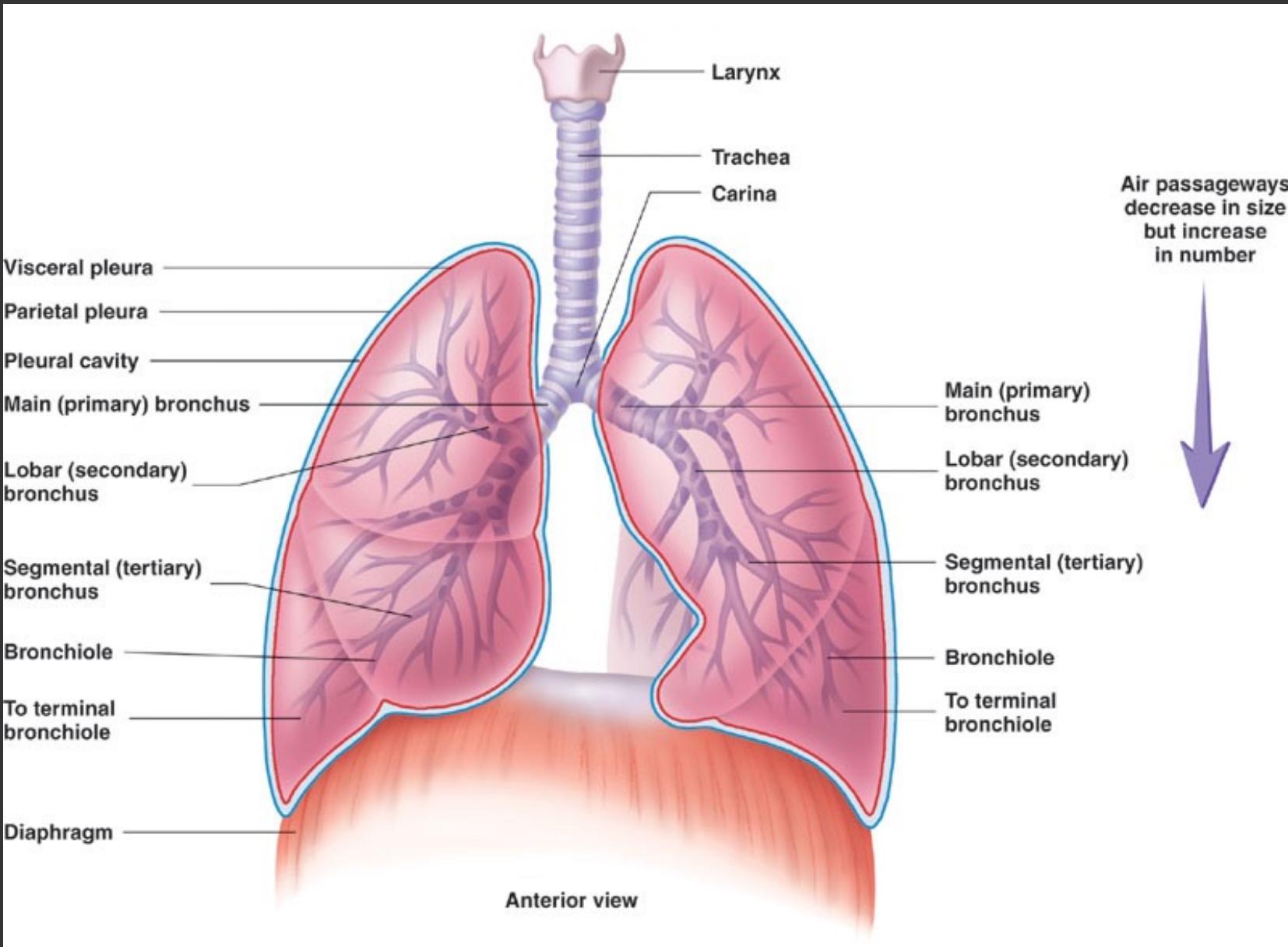
- Eupnea = normal quiet breathing at rest
  - ( breathing rate of 12 – 20 breaths per minute )
- Hyperventilate = increased ventilation that exceeds metabolic needs
  - Increased breathing rate ( ie , tachypnea ) and / or overly deep breaths
  - eg , during anxiety attack
- Hypoventilate = decreased ventilation that is associated with abnormalities
  - Decreased respiratory rate ( ie , bradypnea ) and / or shallow breaths
  - eg , pulmonary diseases , hypoventilation syndrome

# Respiratory System – Airways





# Respiratory System – Airways – Conducting Zone



# Respiratory System – Airways – Conducting Zone

## ➤ Functions :

1. Controls the volume of air into and out of the respiratory tract
  - Controlled by airway smooth muscle tone
    - eg ,  $\beta$ -2 receptors
      - Relax airway smooth muscle
        - Bronchodilation
      - eg , Muscarinic receptors
        - Contract airway smooth muscle
          - Bronchoconstriction
  - 2. Brings inhaled air to body temperature and fully humidifies it
    - Done by rich supply of blood vessels in mucous membrane

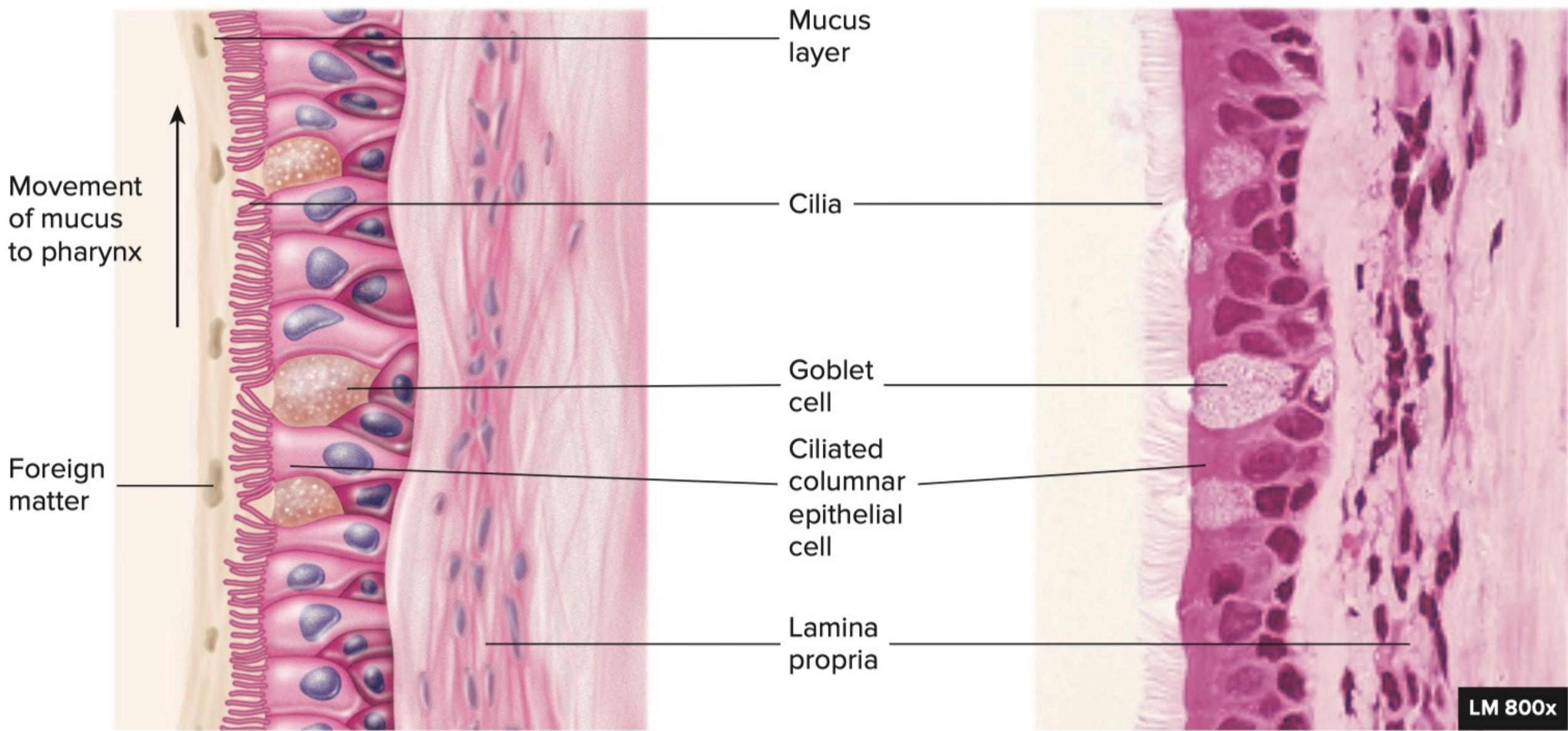
# Respiratory System – Airways – Conducting Zone

## ➤ Functions :

### 3. Filters and protects the respiratory tract from particulates

- Nose hairs and mucus trap larger particles
- Bronchoconstriction when polluted air is breathed
- Mucociliary Escalator
  - Goblet cells produce mucus
    - Traps finer particles
  - Ciliated epithelial cells
    - Propel debris trapped in mucus to pharynx
  - Cilia slowed by cold , dry air
  - Cilia damaged by cigarette smoke
  - Mucus thickened in those with cystic fibrosis
    - Difficult for cilia to propel mucus

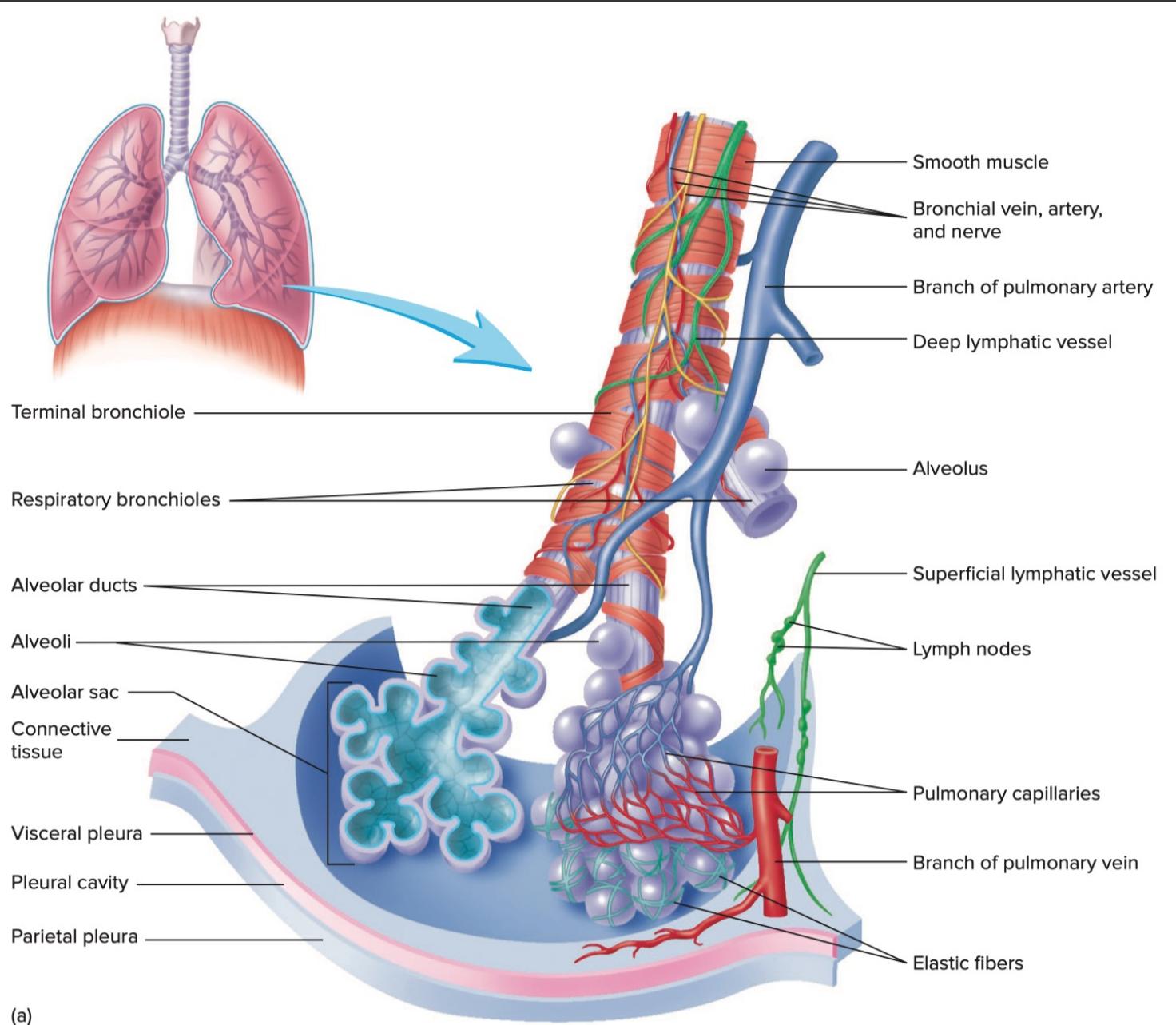
# Respiratory System – Airways – Mucociliary Escalator



# Respiratory System – Airways – Respiratory Zone

- Respiratory bronchioles
- Alveolar Ducts
- Alveolar Sacs
  
- Sole site of gas exchange ( there is no gas exchange in the conducting zone )
  - Occurs in the alveoli which are present solely in respiratory zone

# Respiratory System – Airways – Respiratory Zone



# terminal bronchioles

"polluted" air



bronchoconstrict



via  
mucociliary  
scrapers

↓ air flow

e.g. exercise



bronchodilate

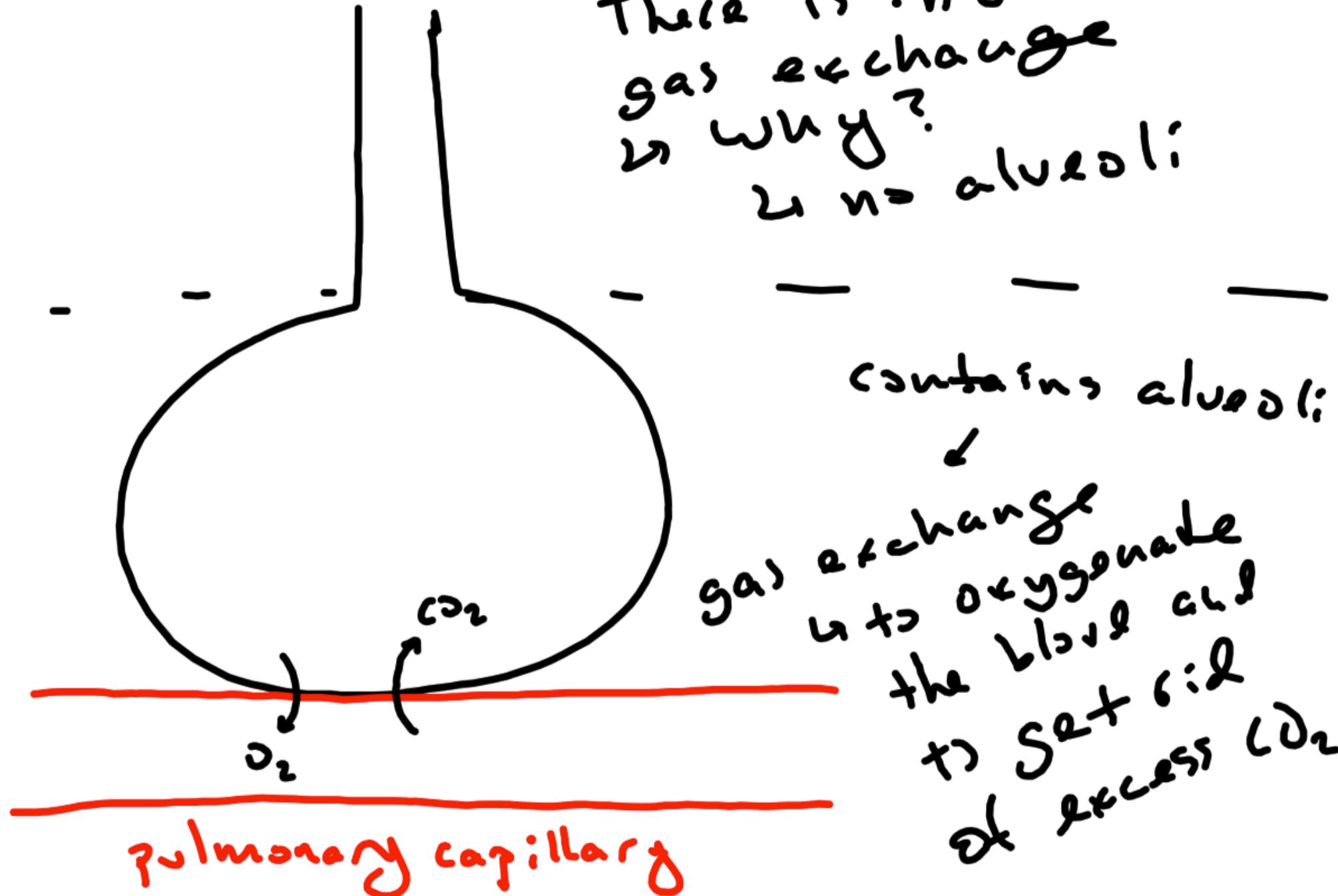


via  $\beta_2$   
receptors

↑ air flow

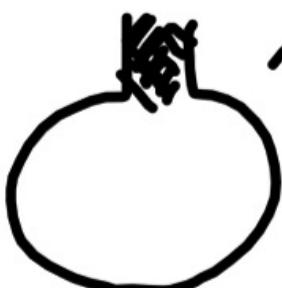
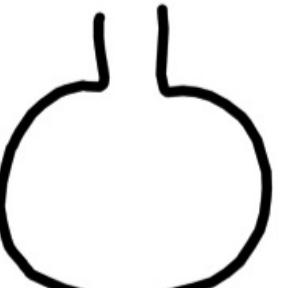
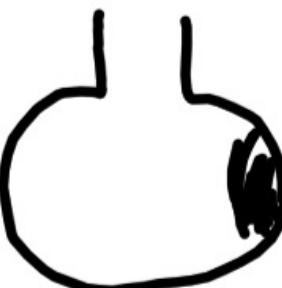
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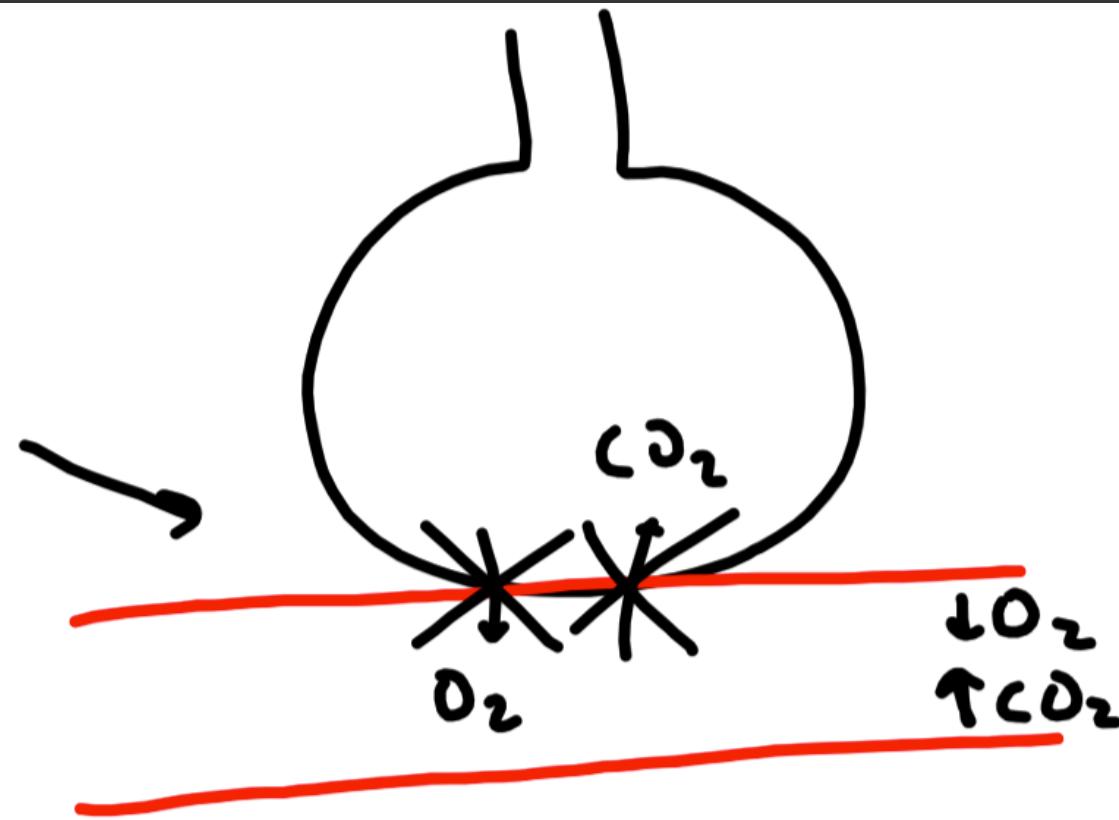


# Respiratory System – Airways – Dead Space

- No Gas Exchange
- Anatomic Dead Space
  - Volume of the conducting zone
    - Averages approximately 150 mL ( varies with height )
  - Contains no alveoli
    - Therefore , there is no gas exchange
- Alveolar Dead Space
  - Alveoli that are not perfused
    - Therefore , there is no gas exchange
  - Volume is "zero" in healthy individuals
- Physiological Dead Space
  - Combination of anatomic and alveolar dead spaces

	Normal (healthy)	Abnormal
Anatomic	 ~150ml	 ~150ml
Alveolar	 $\varnothing$	 ~110ml
Physiologic	 ~150ml	 ~260ml

Aleurial  
Dead  
Space



↑ Physiologic D.S. → ↓ blood O<sub>2</sub>  
↑ blood CO<sub>2</sub> } BAD

# Respiratory System – Lungs

- Elastic
  - Elastin fibers contained in the interstitium
  - Allows lungs to stretch and recoil
- Pleura
  - Visceral Pleura
    - Covers the lungs
  - Parietal Pleura
    - Lines thoracic cavity and is attached to the diaphragm
  - Pleural Space
    - Fluid-filled potential space between the pleural layers
    - Pressure in the space is less than pressure in the alveoli
      - Allows lung to remain inflated
  - Structure of pleura allows lungs to move along with thorax

# Respiratory System – Lungs

- Compliance
  - Measure of the ease with which a structure expands when exposed to pressure
  - In other words : measure of the stretchiness / stiffness of a structure

# Respiratory System – Lungs

- Normal Compliance is directly related to two main things :

## 1. Elastic Properties of the lung

- Elastin fibers give lungs their elastic properties
  - Loss of elastin fibers would make the lungs MORE stretchy

## 2. Surfactant

- Lipoprotein produced and secreted by type 2 pneumocytes
- Lines the inner surface of alveoli
- Laplace's Law :

$$P = \frac{2 * T}{r}$$

P = Pressure

T = Surface Tension

r = radius ( of alveoli )

P : pressure needed to keep alveoli from collapse

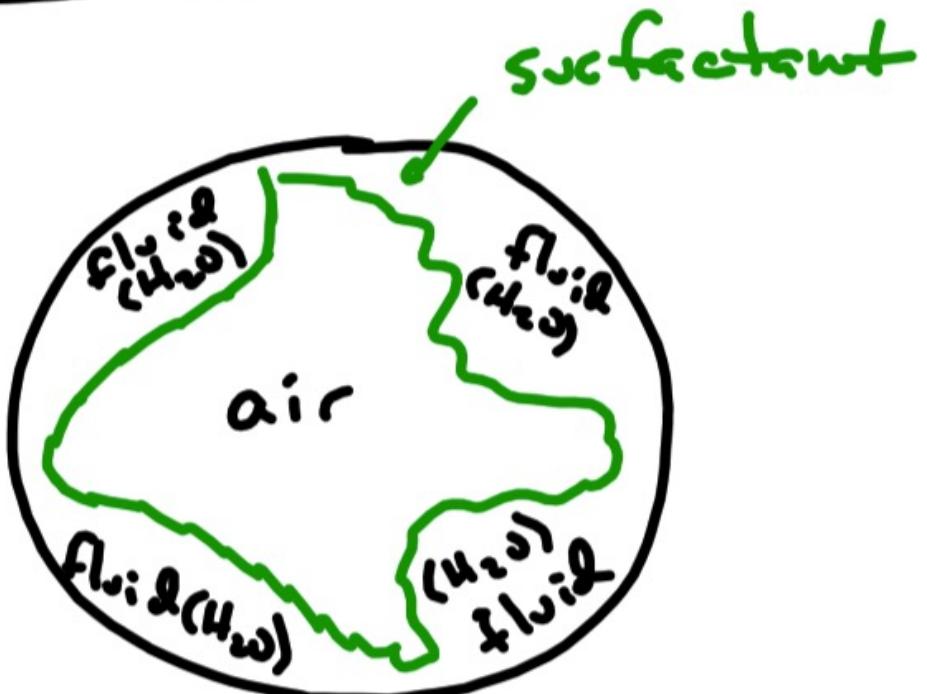
T : force that favors collapse of alveoli

Surfactant reduces surface tension

Reduces the pressure needed to keep alveoli from collapsing

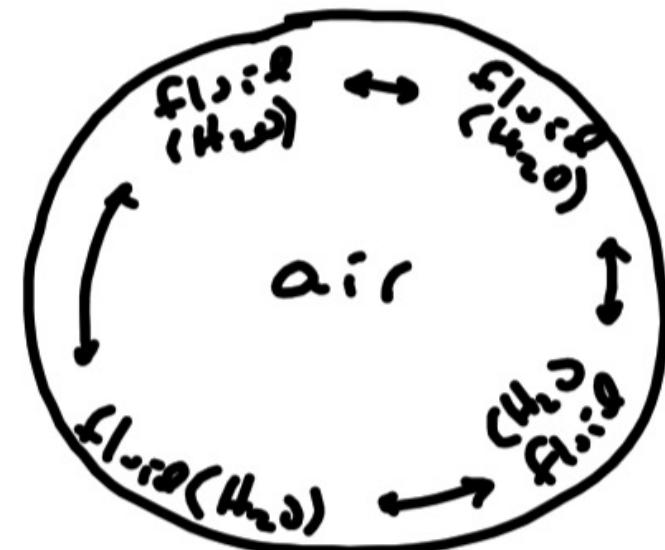
Helps prevent alveoli from collapse

## with surfactant



- H<sub>2</sub>O molecules "hidden" from each other
  - ↳ low surface tension
  - ↳ low collapsing pressure
  - ↳ alveoli remain inflated

## w/o surfactant



- H<sub>2</sub>O molecules "mingle"
  - ↳ ↑↑↑ surface tension
  - ↳ ↑↑↑ collapsing pressure
  - ↳ alveoli collapse
  - ↳ stiff lung

# Respiratory System – Lungs

- An increase in compliance indicates the lung is too “stretchy”
  - Caused by damage / loss of elastin fibers
  - eg , emphysema where there is destruction of elastin fibers
- A decrease in compliance indicates the lung is too “stiff”
  - eg , *interstitial lung disease* where interstitium becomes fibrous
  - eg , *surfactant deficiency disorder* where there is a lack of surfactant
    - Alveoli without surfactant causes surface tension to be high
      - Pressure to keep alveoli from collapsing is now high
        - Alveoli vulnerable to collapse ( atelectasis )
    - When alveoli are collapsed the lung becomes very stiff

## \* Normal Compliance of Lungs

① Healthy elastin fibers

② Presence of surfactant

↳ phospholipid + protein

↳ produced by type II pneumocytes of alveoli

---

## \* Abnormal Compliance

↑ compliance → lungs are too stretchy and  
there is a decrease in recoil

↓ compliance → lungs are too stiff

2.9. emphysema

\* ↑ compliance

↳ loss / destruction of elastin fibers



thin rubber band



thick rubber band

\* ↓ compliance

e.g. interstitial lung disease

↳ damage and scarring of elastin fibers,

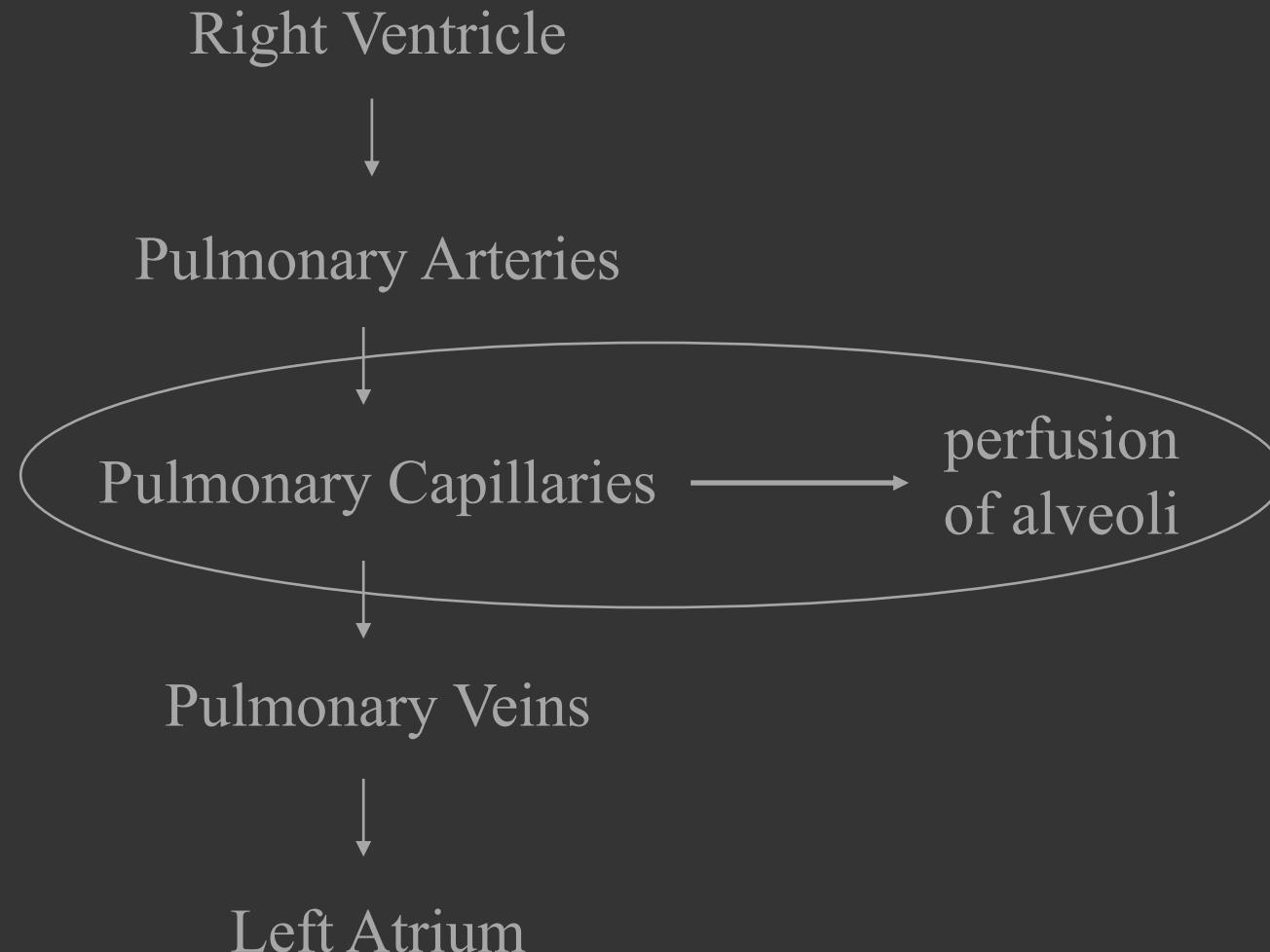
↳ loss of surfactant

↳ alveoli will collapse (atelectasis) ← <sup>surfactant</sup> deficiency disorder

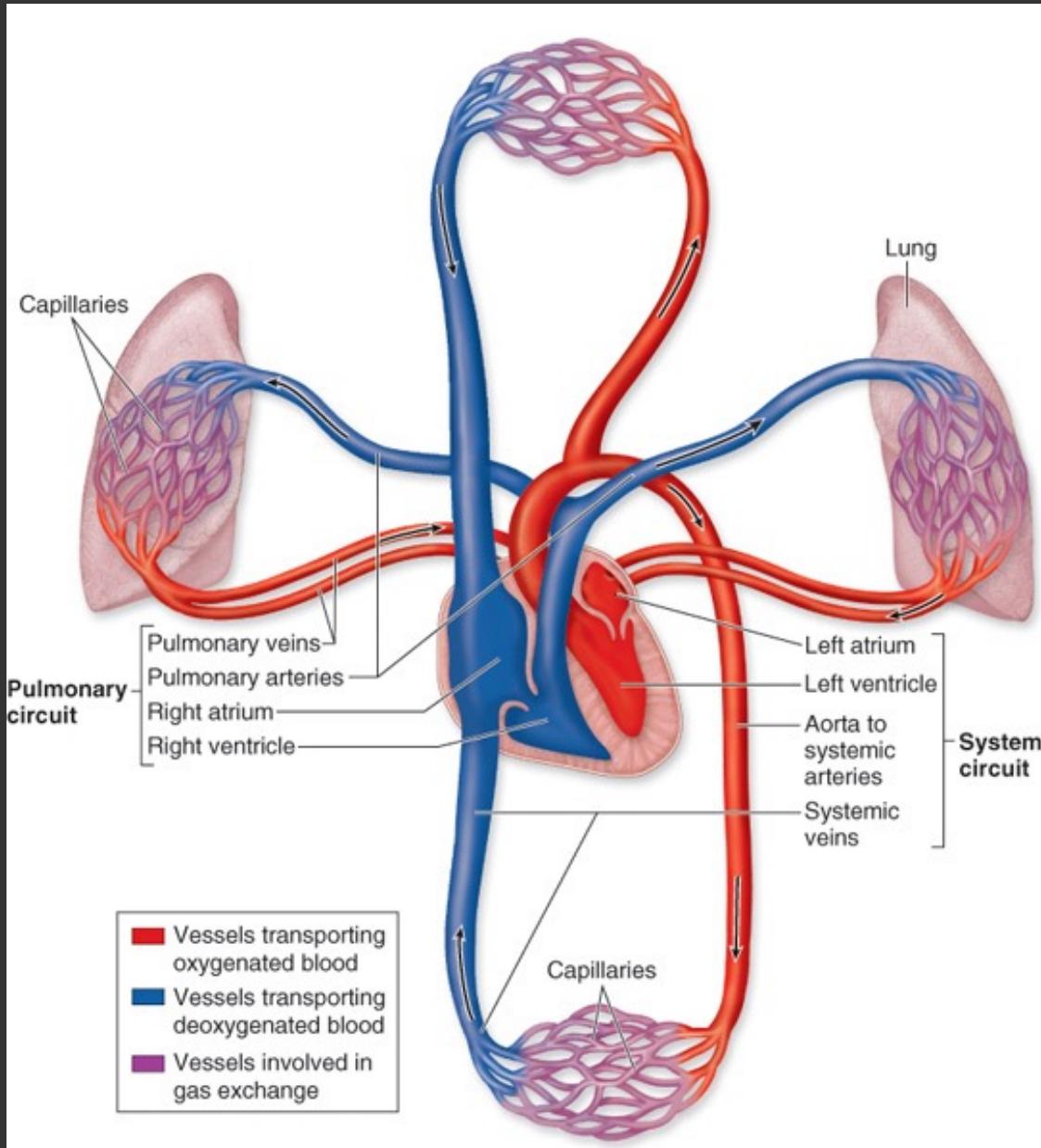
# Respiratory System – Circulation

- Perfusion (  $\dot{Q}$  ) of the lungs ( ie , alveoli ) ... pulmonary circulation
  - Deoxygenated blood is carried to the lungs via the pulmonary arteries
  - and then to pulmonary capillaries where blood is oxygenated at the alveoli
  - Oxygenated blood is then carried back to the heart via the pulmonary veins

# Respiratory System – Perfusion ( $\dot{Q}$ ) of the Lungs

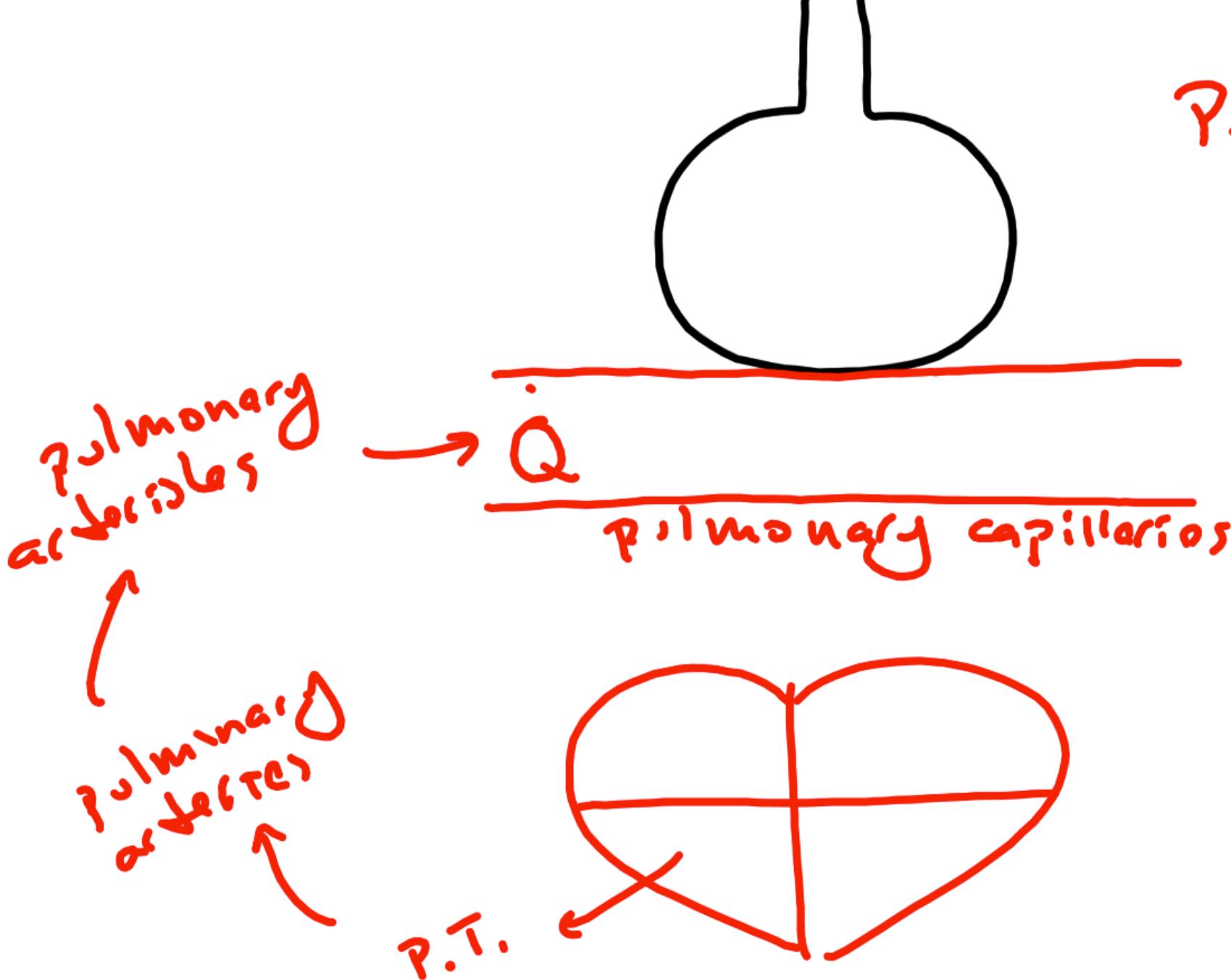


# Respiratory System – Perfusion ( $\dot{Q}$ ) of the Lungs



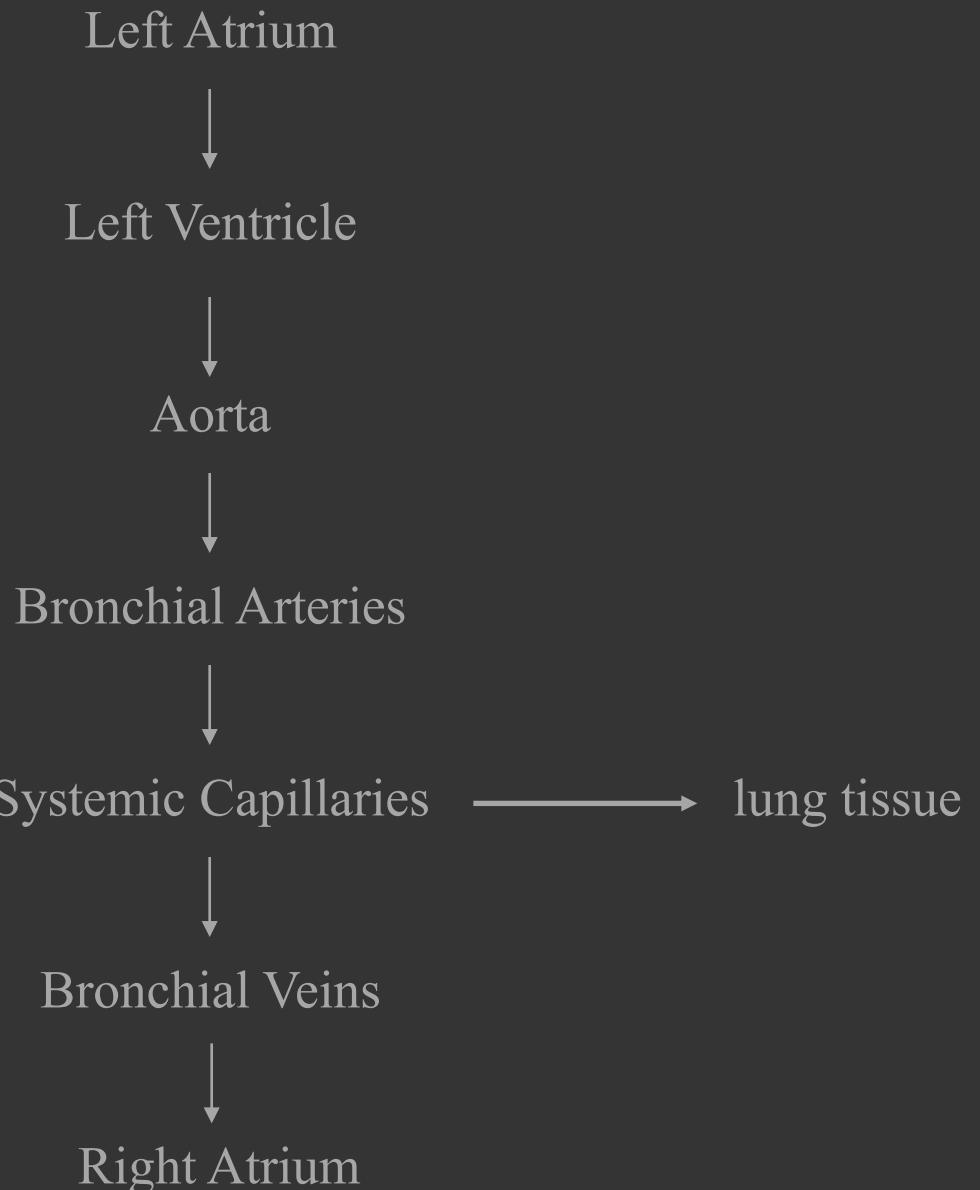
Perfusion ( $\dot{Q}$ )

↑  
cardiac  
output of  
the right  
ventricle



# Respiratory System – Bronchial Circulation

- Oxygenated blood is carried to lung tissue via the bronchial arteries
- Deoxygenated blood is returned to the right atrium via the bronchial veins



# Spirometry

- Measurement of Lung Volumes and Lung Capacities



# Spirometry

➤ Measurement of lung volumes and capacities with the use of a spirometer

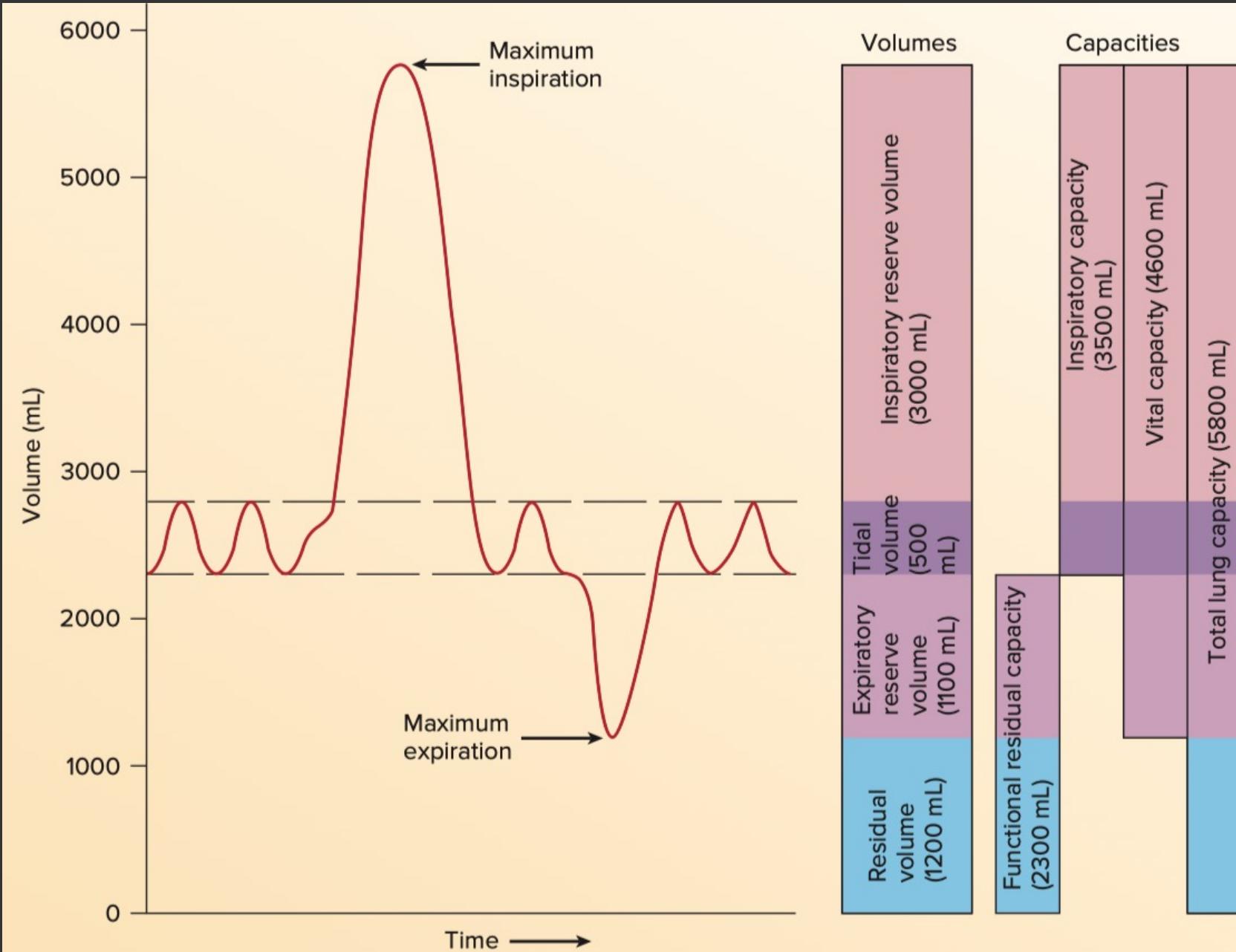
## ➤ Lung Volumes

- ( average values are for average size adult male ... ~10% less for female )
- Tidal Volume (  $V_T$  ) = approximately 500 mL
  - Volume of air inspired or expired during normal , quiet breathing
- Inspiratory Reserve Volume ( IRV ) = approximately 3,000 to 3,300 mL
  - Maximum amount of air that can be inspired at end of a normal inspiration
- Expiratory Reserve Volume ( ERV ) = approximately 1,000 to 1,200 mL
  - Maximum amount of air that can be expired at end of a normal expiration
- Residual Volume ( RV ) = cannot be measured with a spirometer ( ~ 1,200 mL )
  - Volume of air remaining in the lungs after a forced expiration
  - Residual volume cannot be measured by normal spirometry

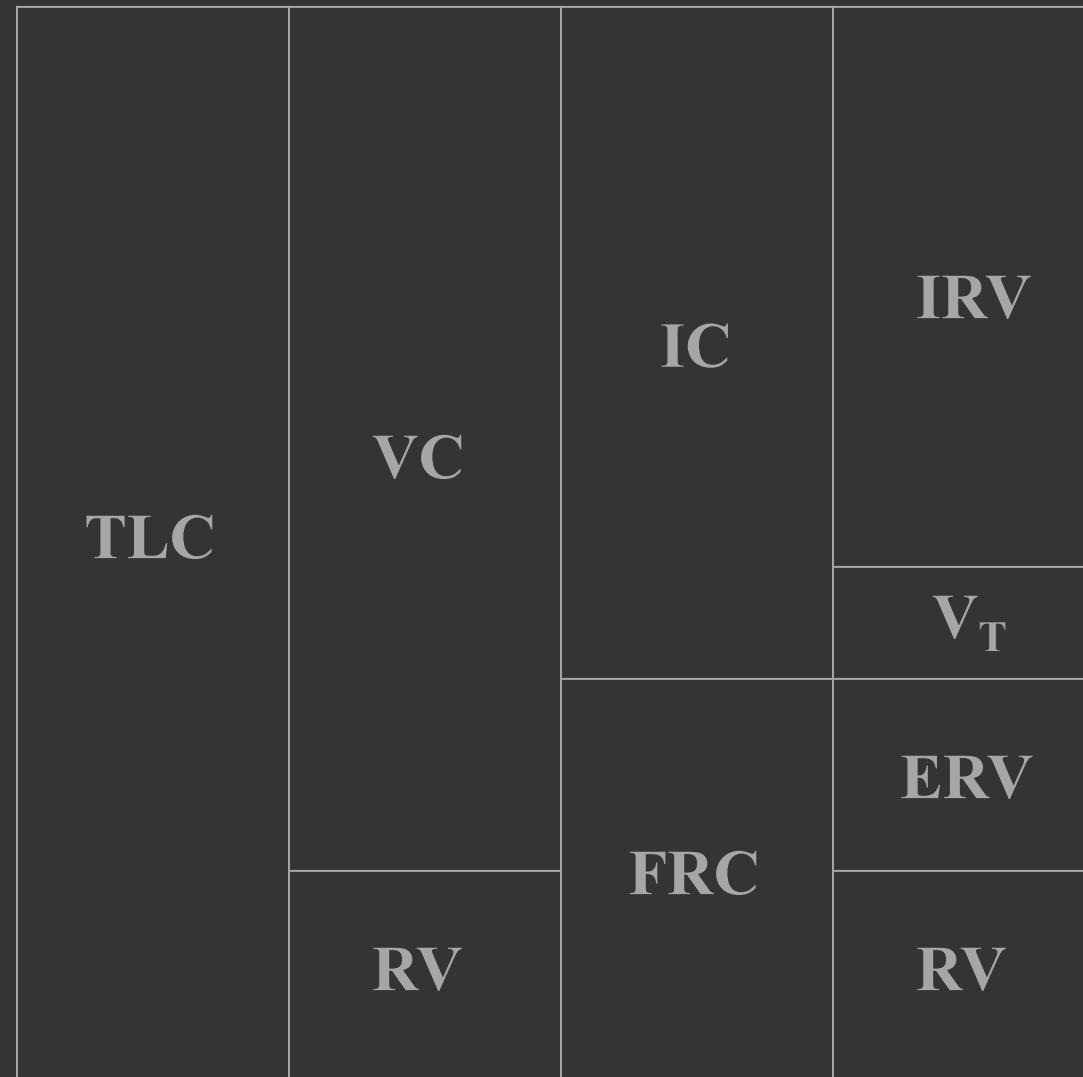
## ➤ Lung Capacities

- ( average values are for average size adult male ... ~10% less for female )
- Inspiratory Capacity ( IC ) = approximately 3,500 to 3,800 mL
  - Volume of air that can be inspired after a normal expiration
  - $IC = VT + IRV$
- Vital Capacity ( VC ) = approximately 4,500 to 5,000 mL
  - Volume of air expired from lungs after a maximal inspiration
  - $VC = VT + IRV + ERV$
- Functional Residual Capacity ( FRC ) = approximately 2,200 to 2,400 mL
  - Volume of air remaining in the lungs after a normal expiration
  - $FRC = ERV + RV$
- Total Lung Capacity ( TLC ) = approximately 5,700 to 6,200 mL
  - Volume of air in the lungs after a maximal inspiration
  - $TLC = VT + IRV + ERV + RV$

# Lung Volumes and Capacities



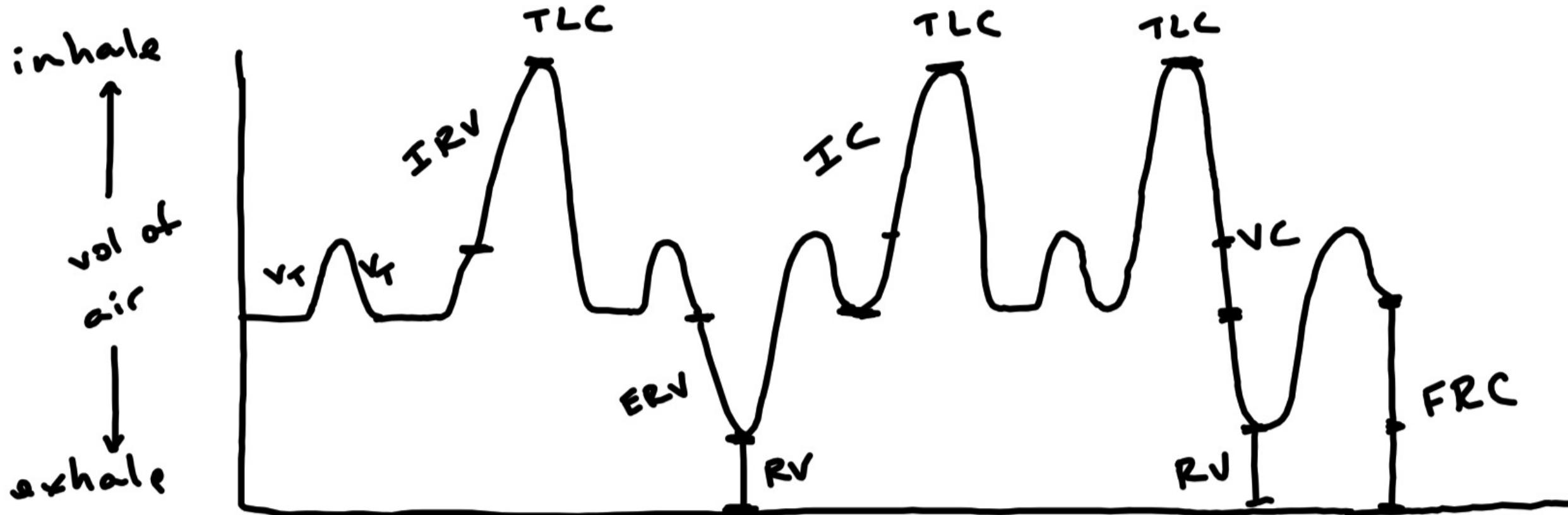
# Lung Volumes and Capacities



$$IC = VT + IRV$$

$$VC = IRV + VT + ERV$$

$$= IC + ERV$$



$$TLC = IRV + VT + ERV + RV$$

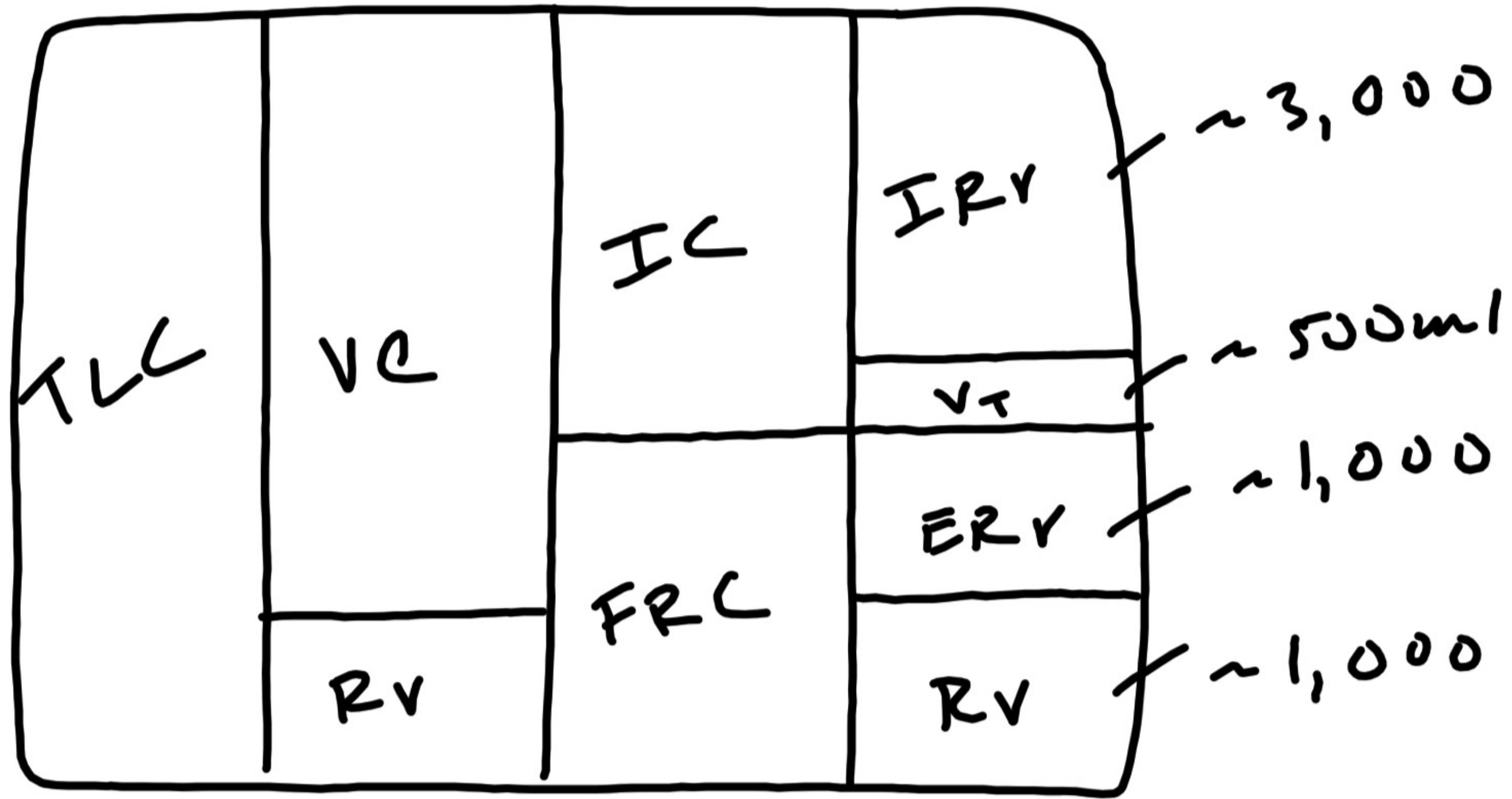
$$= VC + RV$$

$$= IC + FRC$$

time

$$FRC = ERV + RV$$

\* RV cannot be measured by simple spirometry  
↳ and therefore :  
FRC and TLC cannot be measured  
by simple spirometry



VC = 6,200

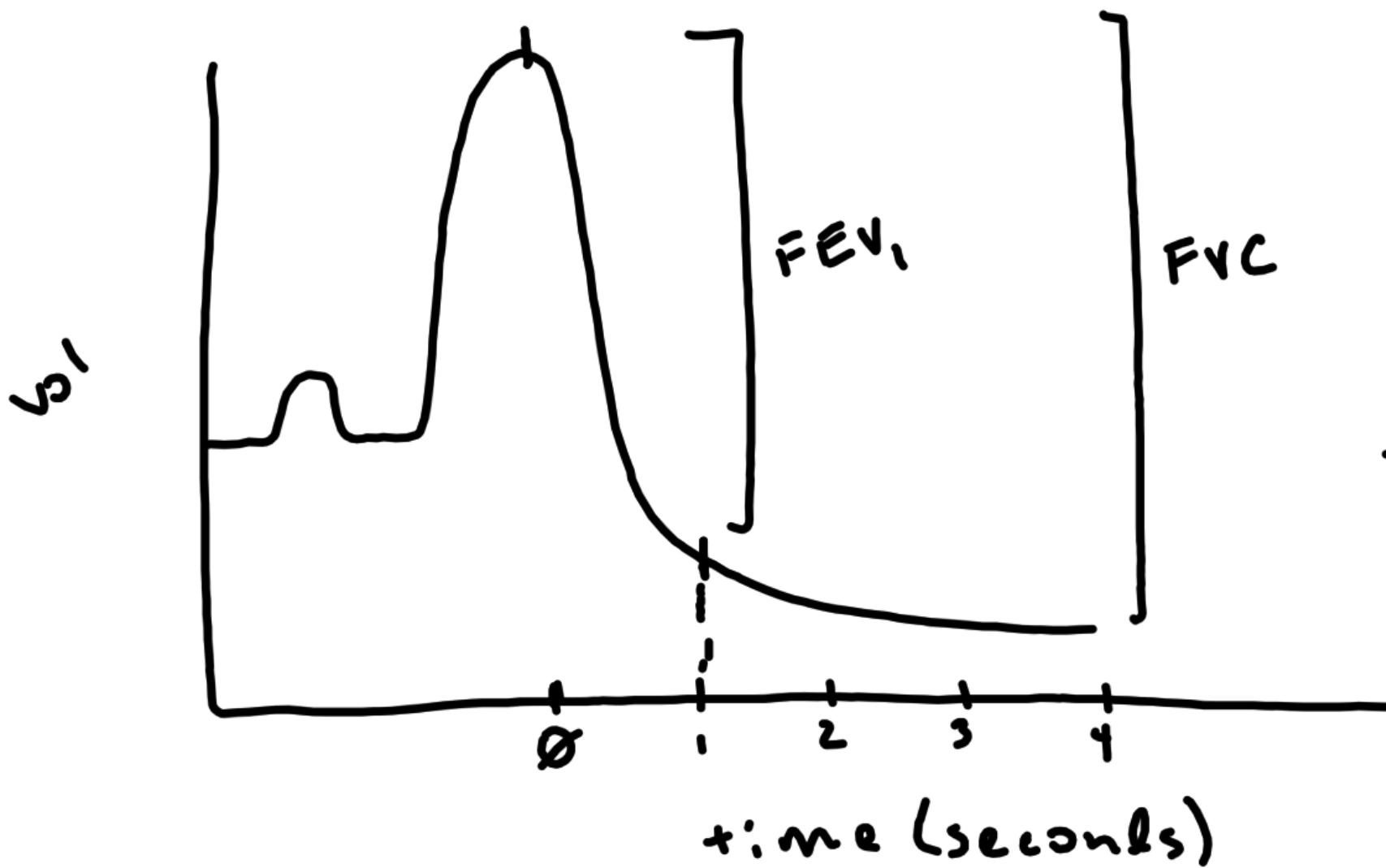
FRC = 2,500 }  
IC = 3,200 } 5,700

RX? = 500

# Forced Vital Capacity ( FVC ) Maneuver ( assesses the health of the respiratory system )

- FVC :
  - Volume of air forcefully expired after a maximal inspiration
  - Normal FVC ≈ 5,000 mL
  
- FEV<sub>1</sub>
  - Volume of air forcefully expired during the first second
  - Normal FEV<sub>1</sub> ≈ 3,500 to 4,000 mL
  
- $\frac{FEV_1}{FVC} * 100 \%$
  
- Normal FEV<sub>1</sub> / FVC ≈ 70 to 80%
  - Therefore , under normal conditions , 70 to 80% of air is forcefully expired from the lungs in the first second

# FVC Test

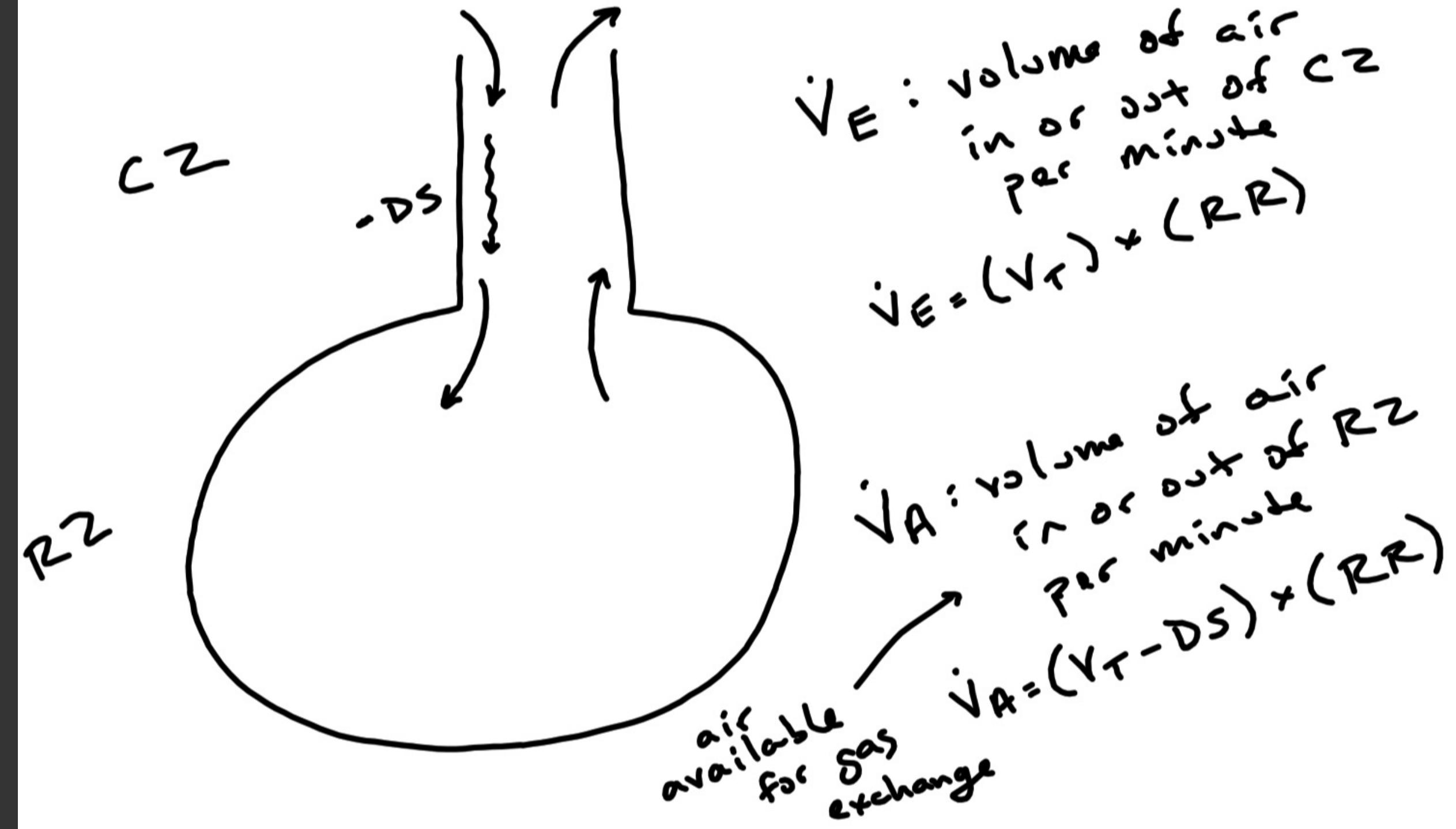


$$\frac{FEV_1}{FVC} \cdot 100 = 70\text{ to }80\%$$

$$\frac{4,000 \text{ ml}}{5,000 \text{ ml}} \cdot 100 = 80\%$$

# Pulmonary Ventilation

- Minute Ventilation (  $\dot{V}_E$  ) = volume of air in or out of the conducting zone per minute
  - $\dot{V}_E = \text{Tidal Volume} * \text{Respiratory Rate}$
  - $$\frac{500 \text{ mL}}{1 \text{ breath}} * \frac{12 \text{ breaths}}{1 \text{ minute}} = \frac{6,000 \text{ mL}}{1 \text{ minute}}$$
- Alveolar Ventilation (  $\dot{V}_A$  ) = volume of air in or out of the respiratory zone per minute
  - This air is available for gas exchange
  - $\dot{V}_A = (\text{Tidal Volume} - \text{Dead Space}) * \text{Respiratory Rate}$
  - $$\left( 500 \text{ mL} - \frac{150 \text{ mL}}{1 \text{ breath}} \right) * \frac{12 \text{ breaths}}{1 \text{ minute}} = \frac{4,200 \text{ mL}}{1 \text{ minute}}$$
  - More efficient to increase tidal volume as opposed to respiratory rate



# Breathing

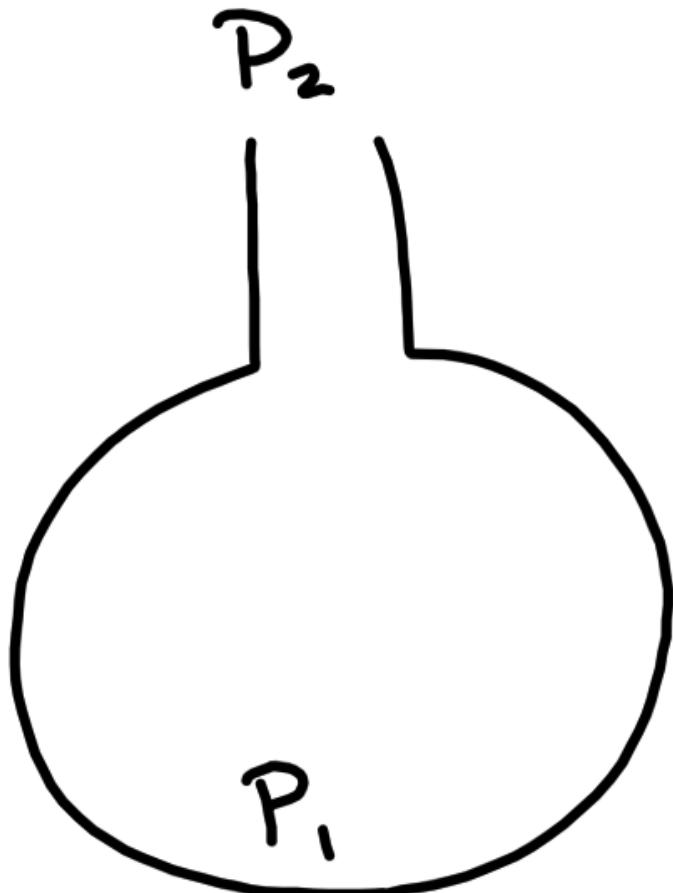
- Movement of air into and out of the lung ( requires pressure gradients )
- Air Flow ( Poiseuille's Law )

$$\text{Flow} = \frac{(P_1 - P_2) * \pi * r^4}{8 * l}$$

P<sub>1</sub> = pressure at point 1 ( inside the lung )  
P<sub>2</sub> = pressure at point 2 ( outside the lung )  
r = radius of airway

- ( P<sub>1</sub> – P<sub>2</sub> ) is equal to pressure gradient
- If P<sub>1</sub> = P<sub>2</sub> , there is no pressure gradient for air to flow
- If P<sub>1</sub> ≠ P<sub>2</sub> , there is a pressure gradient for air to flow
  - The greater the difference , the greater the air flow
- Changing radius will have the greatest effect on air flow
  - Decreasing airway radius increases airway resistance
    - Therefore , air flow decreases
  - Increasing airway radius decreases airway resistance
    - Therefore , air flow increases

$$\text{Air Flow} = \frac{P_1 - P_2}{R} \leftarrow$$



$$P_1 = P_2$$

no air flow



$$P_1 < P_2$$

inhale



$$P_1 > P_2$$

exhale

# Air Flow , Pressure , and Resistance

$P_2$

$P_1$

$$P_1 = P_2$$

$P_2$

$P_1$

$$P_1 < P_2$$

$P_2$

$P_1$

$$P_1 > P_2$$

$P_2$

$P_1$

$$P_1 > P_2$$

$\uparrow r$

$P_2$

$P_1$

$$P_1 > P_2$$

$\downarrow r$

# Breathing

- Ideal Gas Law
- $P = \frac{n * R * T}{V}$
- P = pressure     V = volume     nRT = constant
- ∴ Pressure gradients created by changes in volumes
  - Increase in volume causes a decrease in pressure
  - Decrease in volume causes an increase in pressure

\* Ideal Gas Law

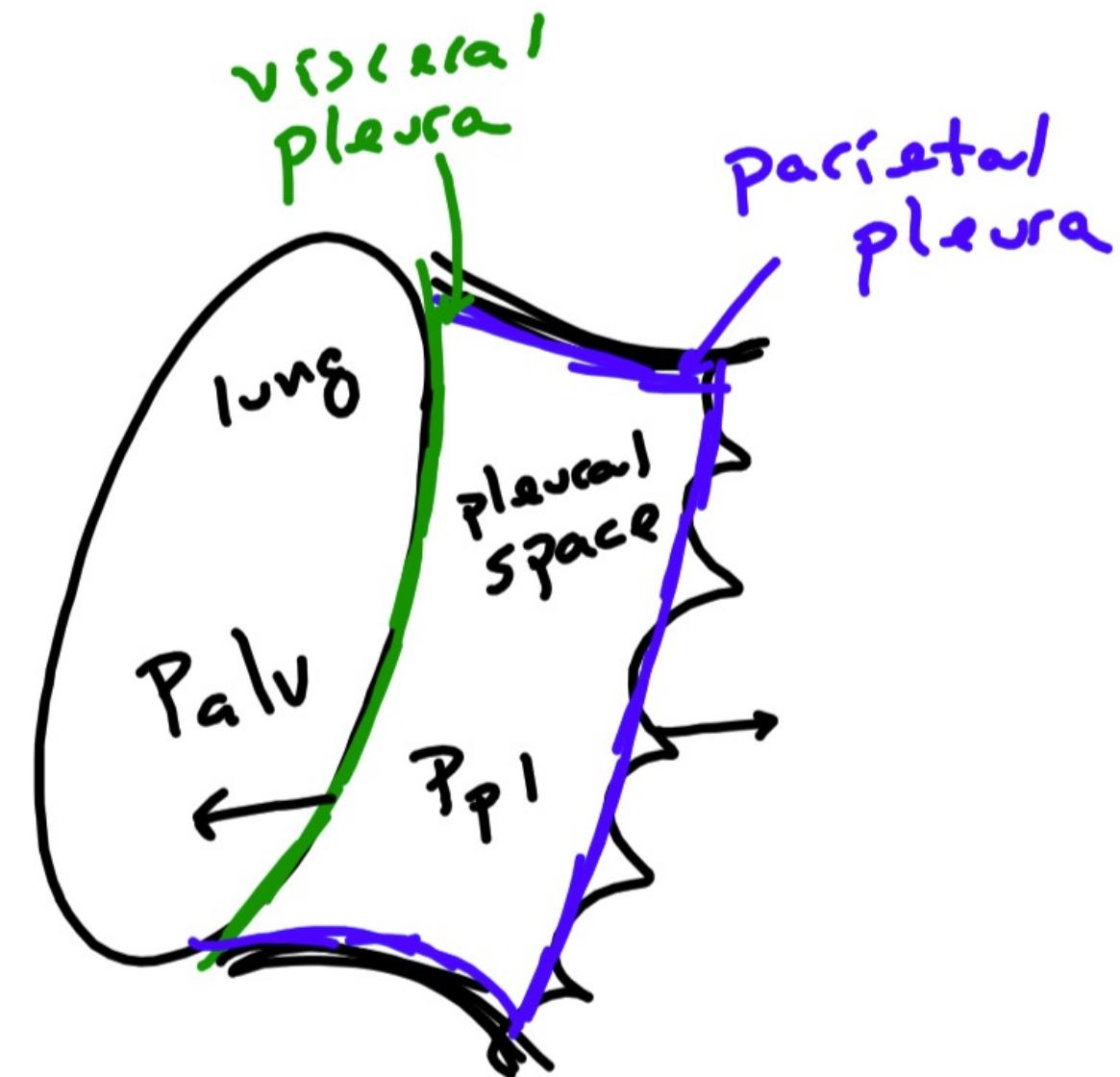
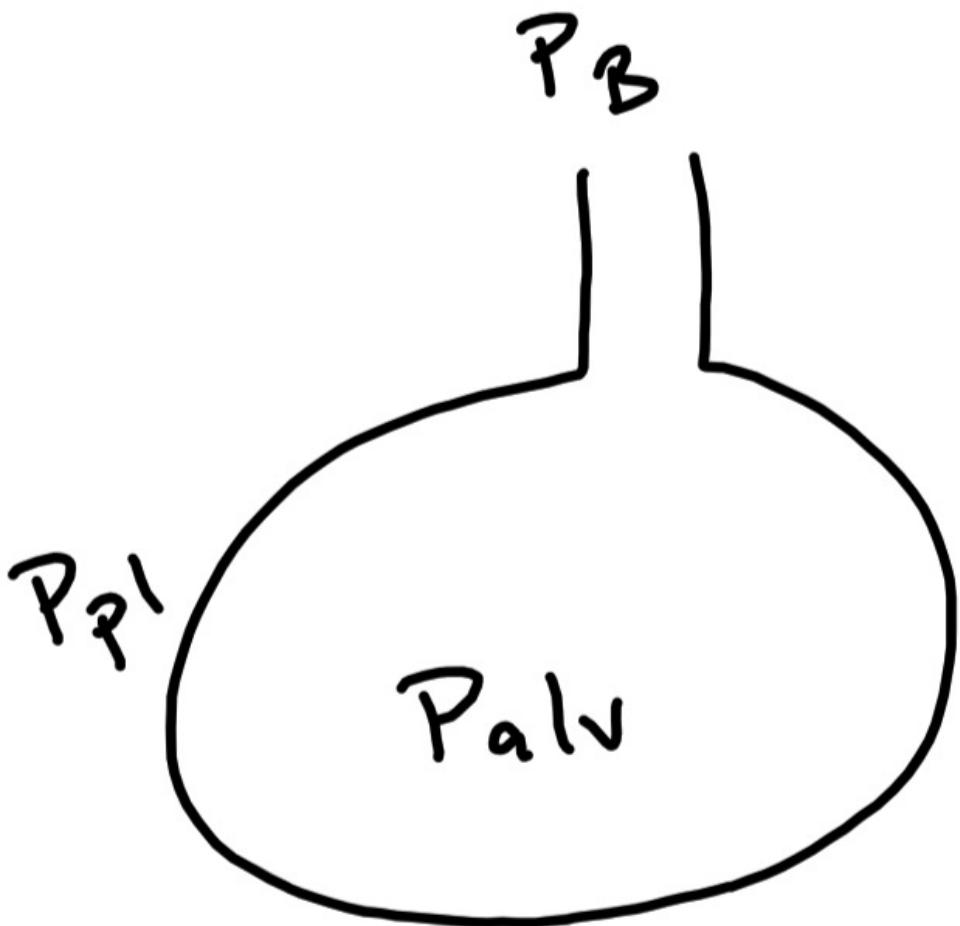
$$P = \frac{nRT}{V}$$

$$\uparrow V \rightarrow \downarrow P$$

$$\downarrow V \rightarrow \uparrow P$$

# Breathing

- Pressures involved in breathing :
  - Barometric Air Pressure (  $P_B$  )
    - Atmospheric air pressure outside the body ( regardless of proximity )
  - Alveolar Pressure (  $P_{alv}$  )
    - Pressure inside of an alveolus
  - Pleural Pressure (  $P_{pl}$  )
    - Pressure in the pleural cavity ( ie , pressure outside of an alveolus )
    - Always less than  $P_{alv}$  ( ensures lungs do not collapse )
      - Due to recoil of lung and recoil of thorax



# Breathing Cycle

## ➤ End of Expiration

- $P_B$  and  $P_{alv}$  are both equal
  - ( ie ,  $\sim 1,000 \text{ cm H}_2\text{O}$  )
  - No pressure gradient
    - No air flow
- $P_{pl}$  is less than  $P_{alv}$ 
  - $P_{pl}$  is 5  $\text{cm H}_2\text{O}$  less than  $P_{alv}$  ( ie , 995  $\text{cm H}_2\text{O}$  )

## ➤ During Inspiration

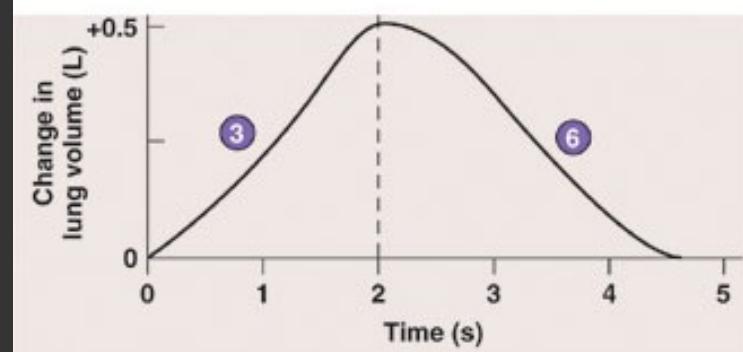
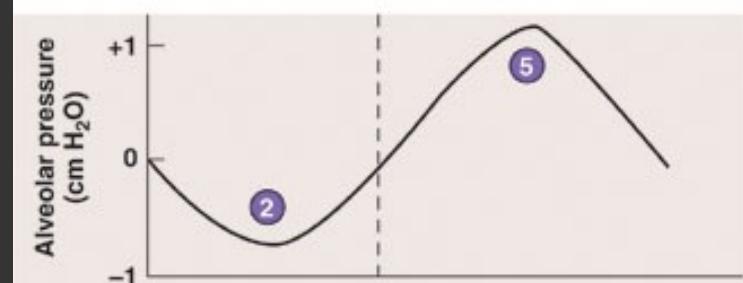
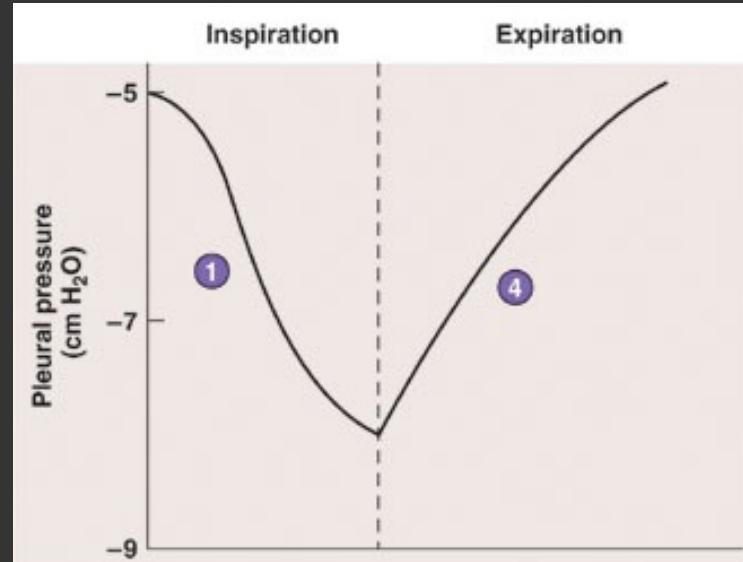
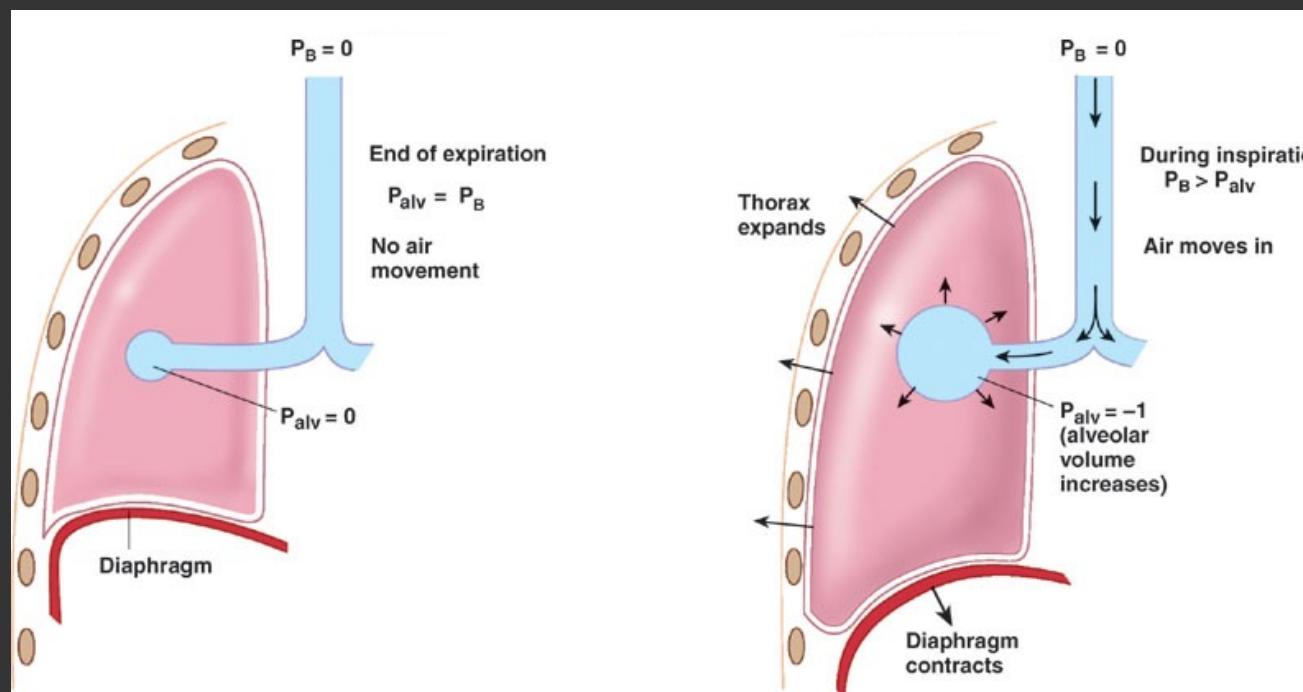
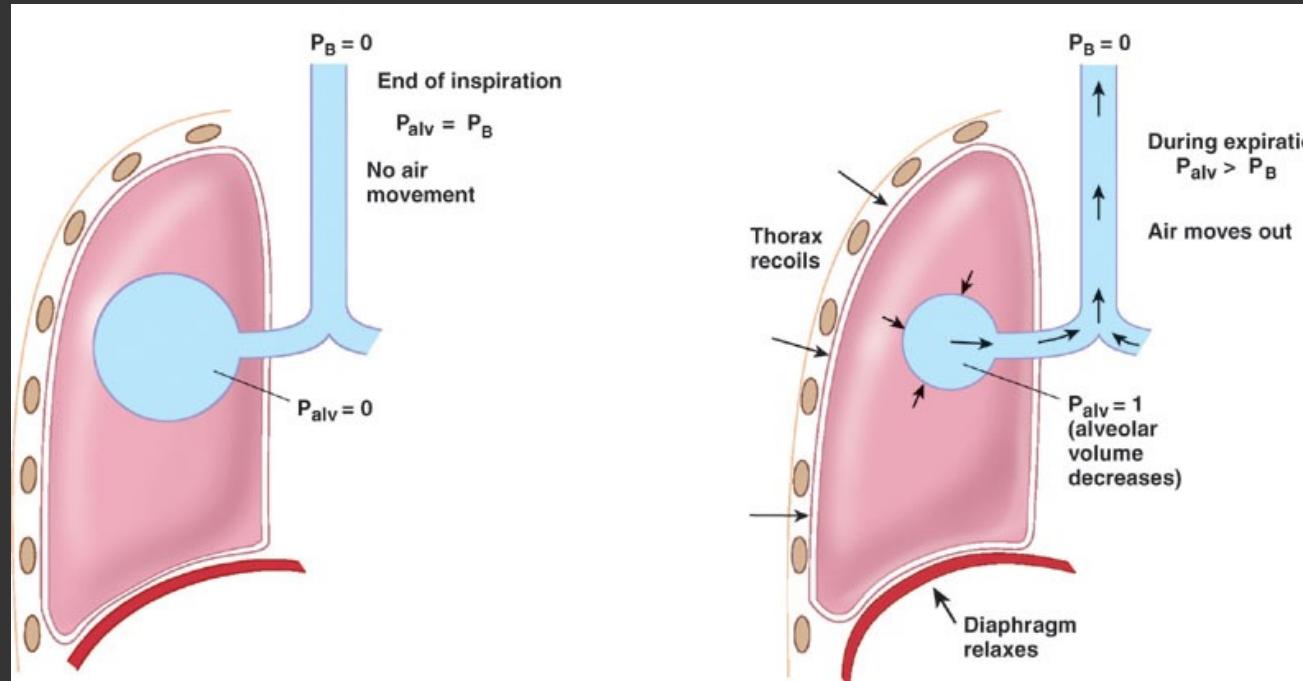
1. Contraction of respiratory muscles
2. Increases thoracic cavity volume , which then increases pleural space volume
3.  $P_{pl}$  decreases towards 992  $\text{cm H}_2\text{O}$  causing alveoli to inflate
4. Increases alveolar volume
5.  $P_{alv}$  decreases towards 999  $\text{cm H}_2\text{O}$
6.  $P_{alv}$  is less than  $P_B$  now
7. Air into lung down pressure gradient
8. Air filling the alveoli causes  $P_{alv}$  to increase back towards 1,000  $\text{cm H}_2\text{O}$

## ➤ End of Inspiration

1. Thoracic cavity has stopped expanding ( thoracic cavity at its greatest volume )
2.  $P_{pl}$  is 992  $\text{cm H}_2\text{O}$  ( lowest level during breathing )
3. Alveoli have stopped inflating ( alveoli at their greatest volume )
4. Air into lungs during inspiration has filled the larger alveoli
5.  $P_{alv}$  is 1,000  $\text{cm H}_2\text{O}$
6.  $P_{alv}$  now equal to  $P_B$
7. No air flow

## ➤ During Expiration

1. Relaxation of respiratory muscles
2. Decreases thoracic cavity volume , which then decreases pleural space volume
3.  $P_{pl}$  increases toward 995  $\text{cm H}_2\text{O}$
4. Decreases alveolar volume toward resting levels
5.  $P_{alv}$  increases above  $P_B$  towards 1,001  $\text{cm H}_2\text{O}$
6.  $P_{alv}$  is greater than  $P_B$  now
7. Air out of lung down pressure gradient
8. Air leaving the alveoli causes  $P_{alv}$  to decrease back towards 1,000  $\text{cm H}_2\text{O}$



$$P_{pl} < P_{alv}$$

→ help keep the alveoli inflated

$P_{pl}$



$\uparrow P_{pl}$



↓ alveolar volume



$\uparrow P_{alv}$

$\downarrow P_{pl}$

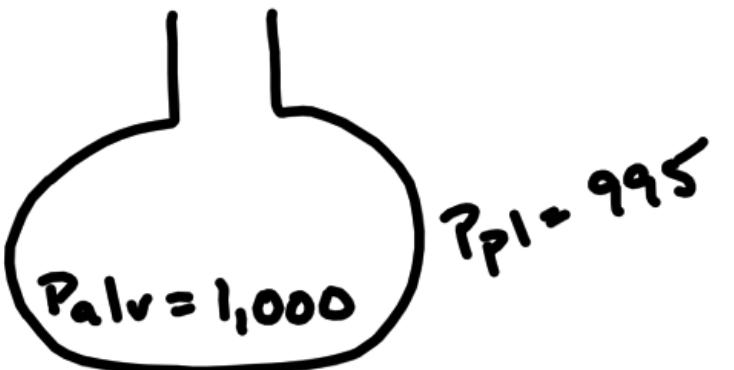


↑ alveolar volume



$\downarrow P_{alv}$

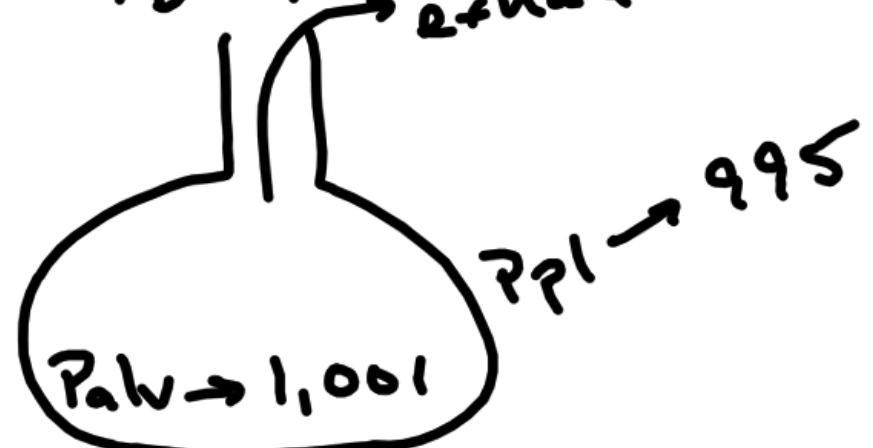
$$P_B = 1,000 \text{ cmH}_2\text{O}$$



End of Exp



$$P_B = 1,000$$



During Exp



$$P_B = 1,000$$

inhale

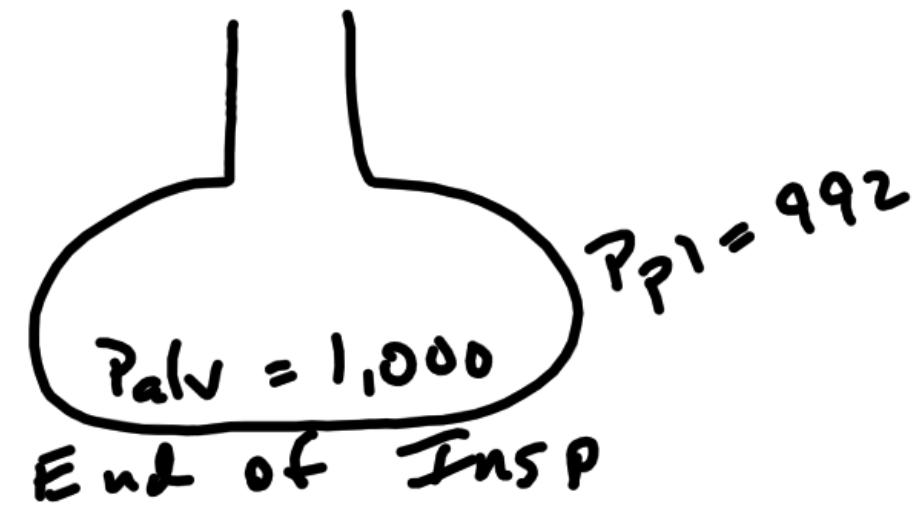
$$P_{alv} \rightarrow 999$$

$$P_{pl} \rightarrow 992$$

During Insp



$$P_B = 1,000$$



End of Insp

## During Insp

Respiratory muscles contract  
↓

↑ Thoracic Cavity Volume



↑ Pleural Space Volume



↓ P<sub>pl</sub>



↑ Alveolar volume



↓ P<sub>alv</sub>



inhale

## During Exp

Respiratory muscles relax  
↓

↓ Thoracic Cavity Volume



↓ Pleural Space Volume



↑ P<sub>pl</sub>



↓ Alveolar volume



↑ P<sub>alv</sub>

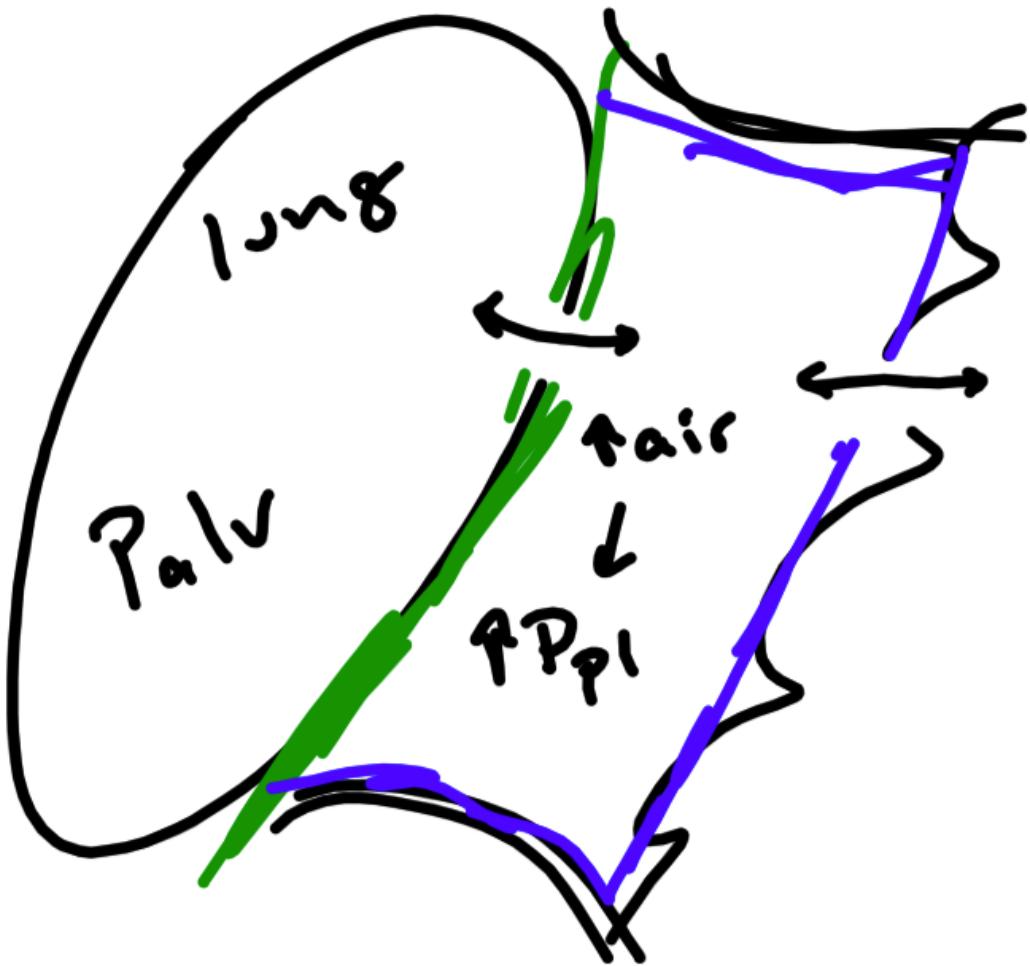


exhale

# Pneumothorax

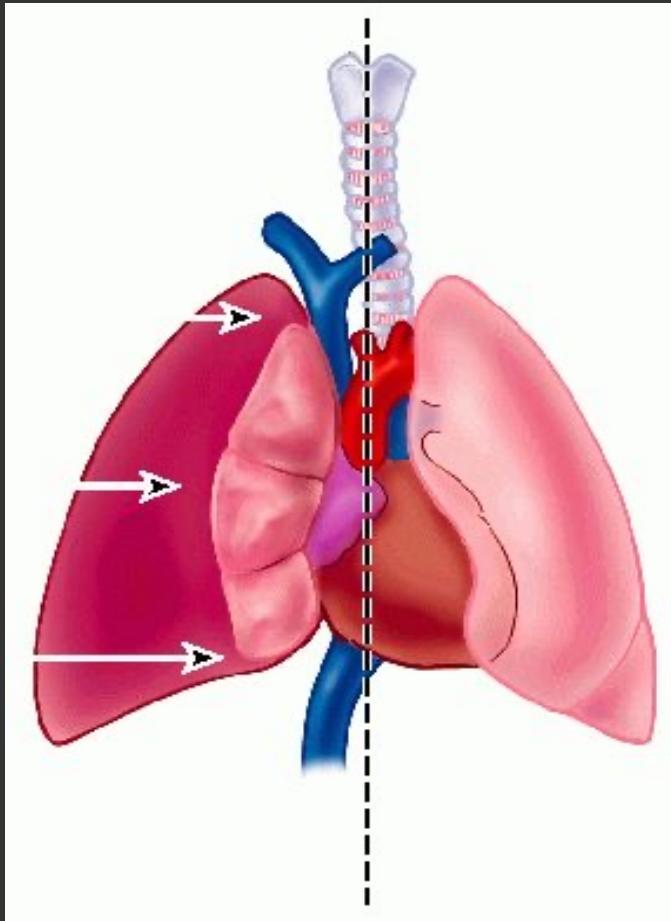
- Presence of excess air in the pleural space leading to an increase in  $P_{pl}$ 
  - $P_{pl}$  is no longer less than  $P_{alv}$
  - Causes the lung to collapse
- Simple pneumothorax
  - $P_{pl}$  and  $P_{alv}$  are equal
  - Surface tension will force alveoli to collapse
- Tension pneumothorax
  - $P_{pl}$  is more positive than  $P_{alv}$
  - Pushes structures on opposite side of thoracic cavity ( ie , the heart )
    - Can lead to dangerous decrease in cardiac output and blood pressure

# Simple Pneum



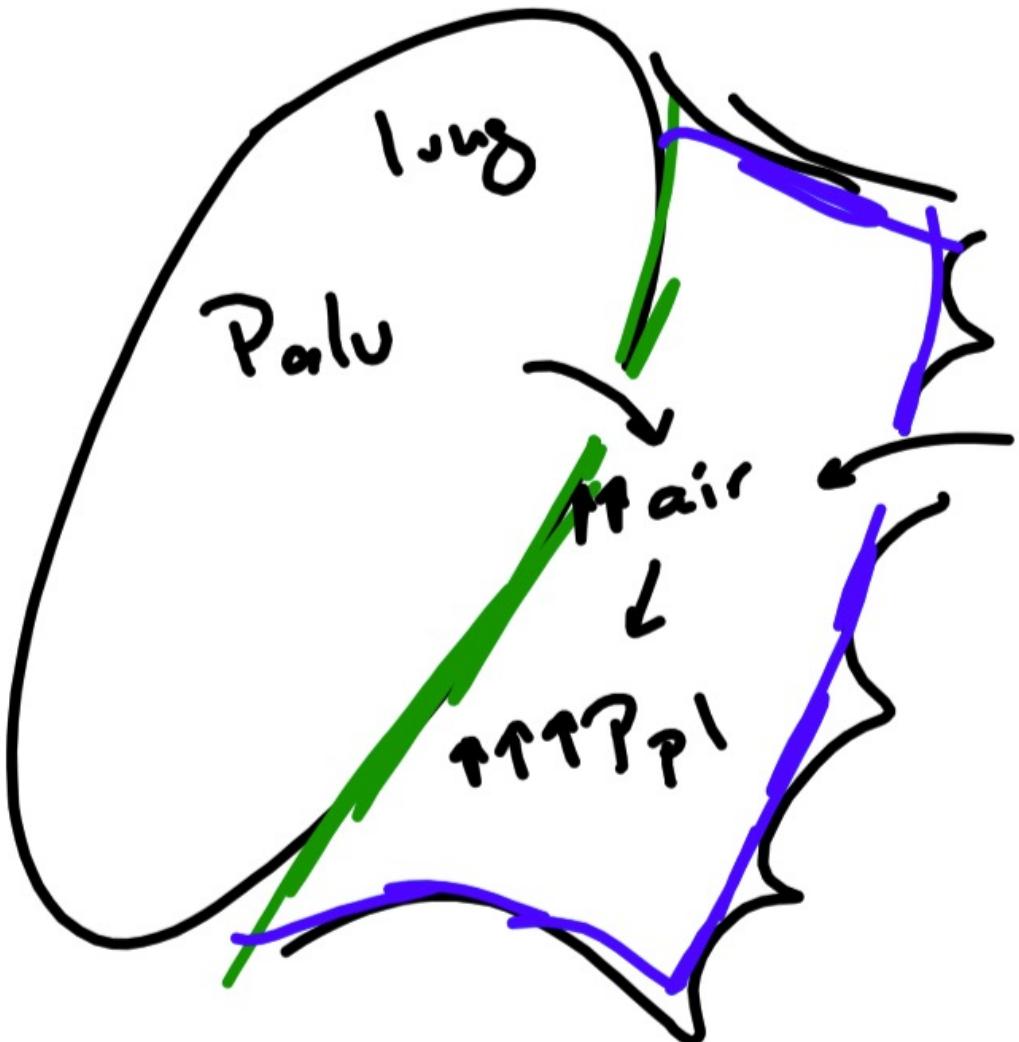
$$P_{pl} = P_{alv}$$

# Tension Pneumothorax



Right-sided tension pneumothorax

# Tension Pneumothorax



$$P_{pl} > P_{alv}$$

# Severe Tension Pneumos

$$MAP = (CO)^+ (TPR)$$

"Squeeze" Heart

↓  
↓ heart contractility

↓  
LLL SV

↓ ← ↑ HR

↓ LCO

↓  
↓ LBP

↓  
↓ blood flow

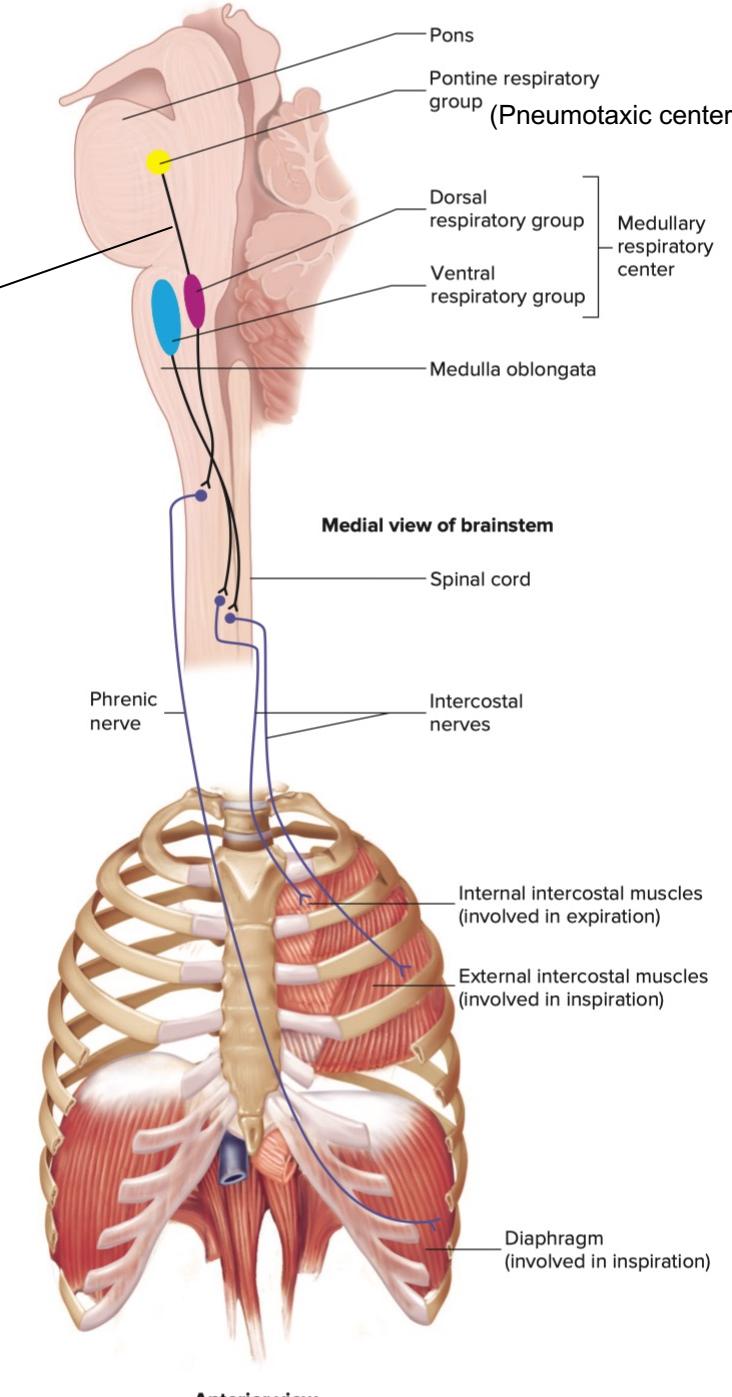
↓  
organ failure → death

# Regulation of Breathing

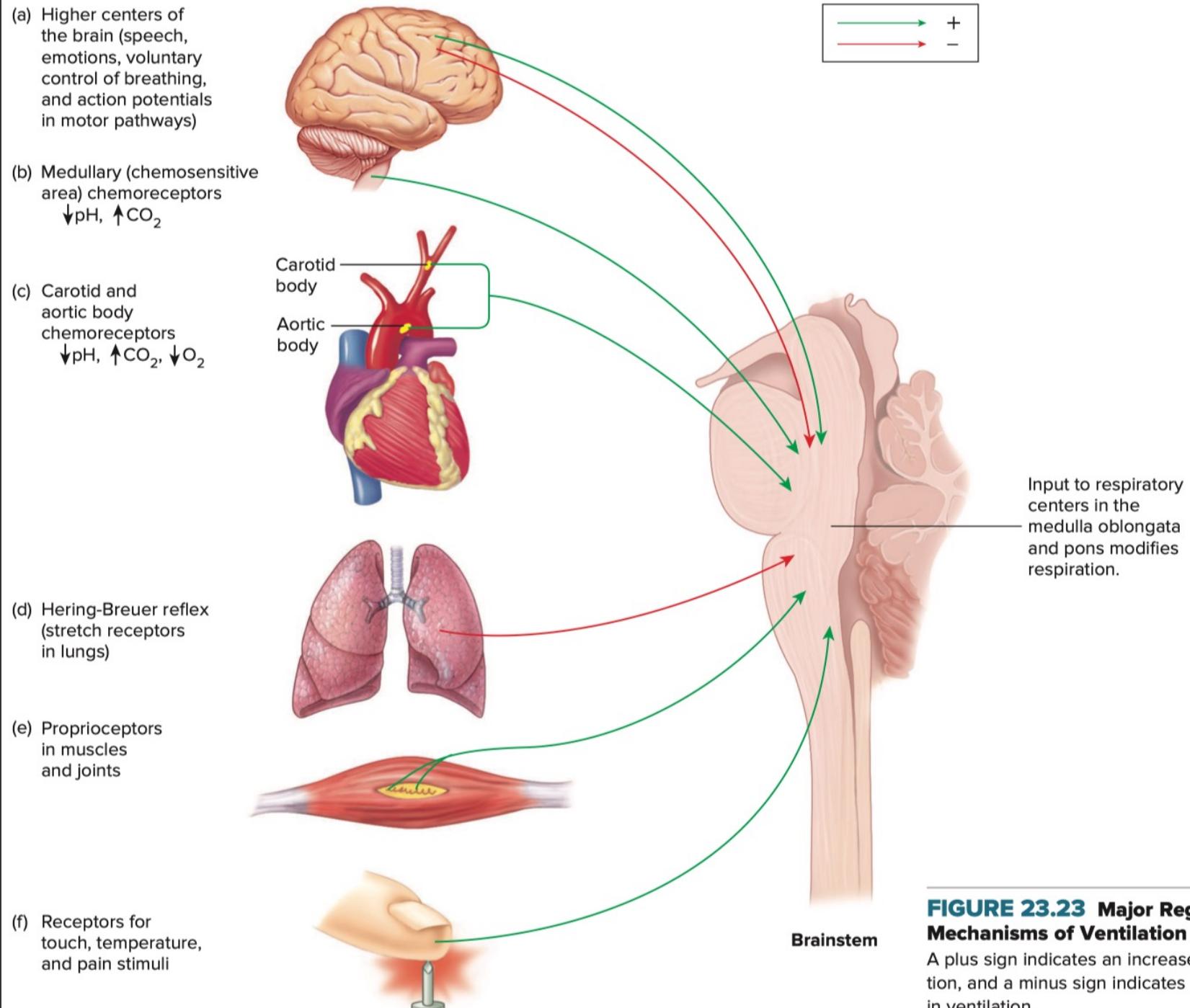
- Respiratory Center
  - Bilateral network of neurons with pacemaker-like activity in the medulla
    - Dorsal respiratory group
      - Innervate and drive the respiratory muscles
    - Ventral respiratory group
      - Innervate and drive the respiratory muscles
      - Contain pacemaker neurons ( pre-Bötzinger complex )
- Respiratory center affected by a number of inputs from the body
  - Cerebrum
  - Hypothalamus
  - Pontine respiratory group / Pneumotaxic center
  - Apneustic center
  - Chemoreceptors
  - Pulmonary stretch receptors
  - Proprioceptors and exteroceptors

# Regulation of Breathing

Apneustic center



# Inputs to Respiratory Centers

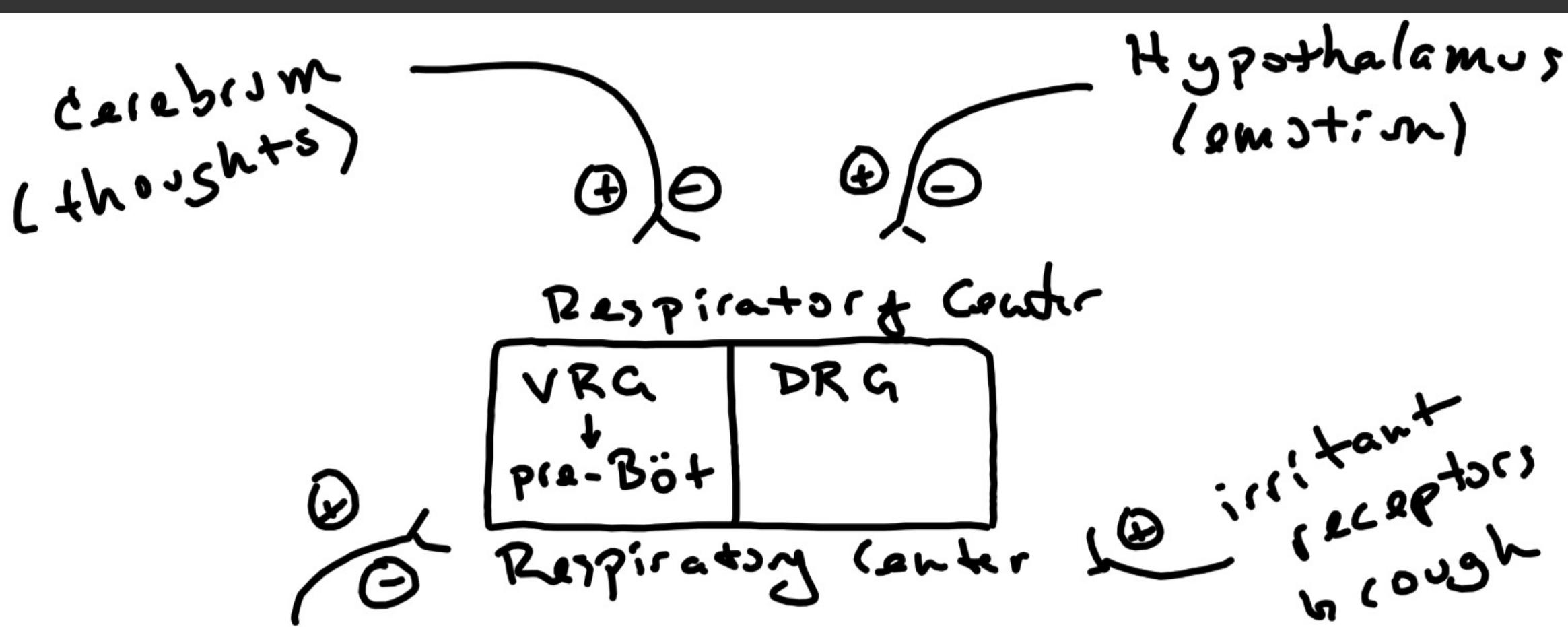


# Inputs to Respiratory Centers

- Cerebrum = voluntary aspect of breathing
  - Breathing is involuntary but can be voluntarily overridden by the cortex
    - eg , you can choose to breath faster or hold your breath
- Hypothalamus = emotional aspect of breathing
  - eg , increase ventilation with excitement : decrease ventilation with stress
- Pulmonary Irritant Receptors
  - Located through-out the airways and alveoli
  - Detect irritants in the lung
    - Stimulate the respiratory centers to cause coughing

# Inputs to Respiratory Centers – Chemoreceptors

- Central Chemoreceptors
  - Neurons located in multiple areas of the medulla and pons
- Peripheral Chemoreceptors
  - Glomus cells located at the bifurcation of the carotid arteries
- Monitor arterial CO<sub>2</sub> levels ( mainly central chemoreceptors )
  - CO<sub>2</sub> is the main stimulus to breathing
- Monitor arterial O<sub>2</sub> levels ( mainly peripheral chemoreceptors )
  - O<sub>2</sub> stimulates breathing only in extreme instances ( PO<sub>2</sub> < 60 mm Hg )



Chemoreceptors (central & peripheral)

detect level of CO<sub>2</sub> and O<sub>2</sub> in the blood

← main drive to breathe  
 is the level of CO<sub>2</sub>  
 ↑ CO<sub>2</sub> → stim      ↓ CO<sub>2</sub> → inhibit

# Gas Exchange

- Partial pressure as defined by Dalton's Law
- Pressure exerted by each gas in a mixture of gases
- Partial Pressure = ( total pressure ) \* ( % of gas in a mixture of gases )
- eg , atmospheric dry air ( at sea level ) = 760 mm Hg
  - Nitrogen ≈ 79% of dry air
  - Oxygen ≈ 21% of dry air
  - ∴ partial of pressure of oxygen (  $P_{O_2}$  ) = ( 760 mm Hg ) \* ( 0.21 ) ≈ 160 mm Hg
  - ∴ partial of pressure of nitrogen (  $P_{N_2}$  ) = ( 760 mm Hg ) \* ( 0.79 ) ≈ 600 mm Hg
- Changing Partial Pressure :
  - Change atmospheric pressure
    - Atmospheric pressure decreases with higher altitudes
  - Change percentage of gases in the mixture of gases

$$P_B = 630$$

Denver, CO  
(1 mile)

$$P_{O_2} = (630) \times (0.21)$$
$$= 130 \text{ mm Hg}$$

sea  
level

$$P_{O_2} = 160 \text{ mm Hg}$$

$$P_B = 760 \text{ mm Hg}$$

# Partial Pressures

- Partial pressures in dry air at sea level
  - $P_{O_2} = (760 \text{ mm Hg}) * 0.21 = 160 \text{ mm Hg}$
  - $P_{CO_2}$  = negligible
- Partial pressures in conducting zone
  - $P_{O_2} = (760 \text{ mm Hg} - 47 \text{ mm Hg}) * 0.21 = 150 \text{ mm Hg}$
  - $P_{CO_2}$  = ~ 30 mm Hg during expiration .... ~ 0 mm Hg during inspiration
- Partial pressures in alveoli
  - $PA_{O_2}$  ~ 100 mm Hg ( normal range : 85 to 130 mm Hg )
  - $PA_{CO_2}$  ~ 40 mm Hg ( normal range : 35 to 45 mm Hg )
- Partial pressures in arterial blood ( arterial blood gas values )
  - $Pa_{O_2}$  ~ 90 mm Hg ( normal range : 80 to 100 mm Hg )
  - $Pa_{CO_2}$  ~ 40 mm Hg ( normal range : 35 to 45 mm Hg )
- Partial pressures in venous blood
  - $PV_{O_2}$  ~ 40 mm Hg ( normal range : 35 to 45 mm Hg )
  - $PV_{CO_2}$  ~ 45 mm Hg ( normal range : 40 to 50 mm Hg )
- Partial pressures in interstitial space
  - $P_{O_2}$  ~ 40 mm Hg ( normal range : 35 to 45 mm Hg )
  - $P_{CO_2}$  ~ 45 mm Hg ( normal range : 40 to 50 mm Hg )
- Partial pressures in cells
  - $P_{O_2}$  ~ 20 mm Hg
  - $P_{CO_2}$  ~ 50 mm Hg

# Oxygen Diffusion Gradients

- $O_2$  diffuses from alveolus to arterial end of pulmonary capillary
  - $P_{O_2}$  in alveolus is approximately 100 mm Hg
  - $P_{O_2}$  at arterial end of pulmonary capillary is approximately 40 mm Hg
  - ∴ gradient for  $O_2$  to diffuse from alveolus into blood
- $P_{O_2}$  at venous end of pulmonary capillary equilibrates to approximately 100 mm Hg
- Blood from pulmonary vein mixes with blood from bronchial veins
  - This is part of the anatomic shunt
- Blood to left atrium .. Left ventricle .. aorta .. arteries .. systemic capillaries of cells
  - Because of anatomic shunt ,  $P_{O_2}$  is 90 mm Hg
- $O_2$  diffuses from arterial end of systemic capillary to interstitial space
  - $P_{O_2}$  in arterial blood is approximately 90 mm Hg
  - $P_{O_2}$  in interstitial space is approximately 40 mm Hg
  - ∴ gradient for  $O_2$  to diffuse from blood into interstitial space
- $O_2$  diffuses from interstitial space into cells
  - $P_{O_2}$  in interstitial space is approximately 40 mm Hg
  - $P_{O_2}$  in cells is approximately 20 mm Hg
    - Low  $P_{O_2}$  because cells consume  $O_2$  during aerobic cellular respiration
  - ∴ gradient for  $O_2$  to diffuse from interstitial space into cells

\* Room Air : 21% O<sub>2</sub>

\* Supplemental Oxygen

$$30\% : P_{O_2} = (760) \times (0.3)$$

$$40\% : P_{O_2} = (760) \times (0.4)$$

$$50\% : P_{O_2} = (760) \times (0.5) = 380 \text{ mm Hg}$$

$$100\% : P_{O_2} = (760) \times (1) = 760 \text{ mm Hg}$$

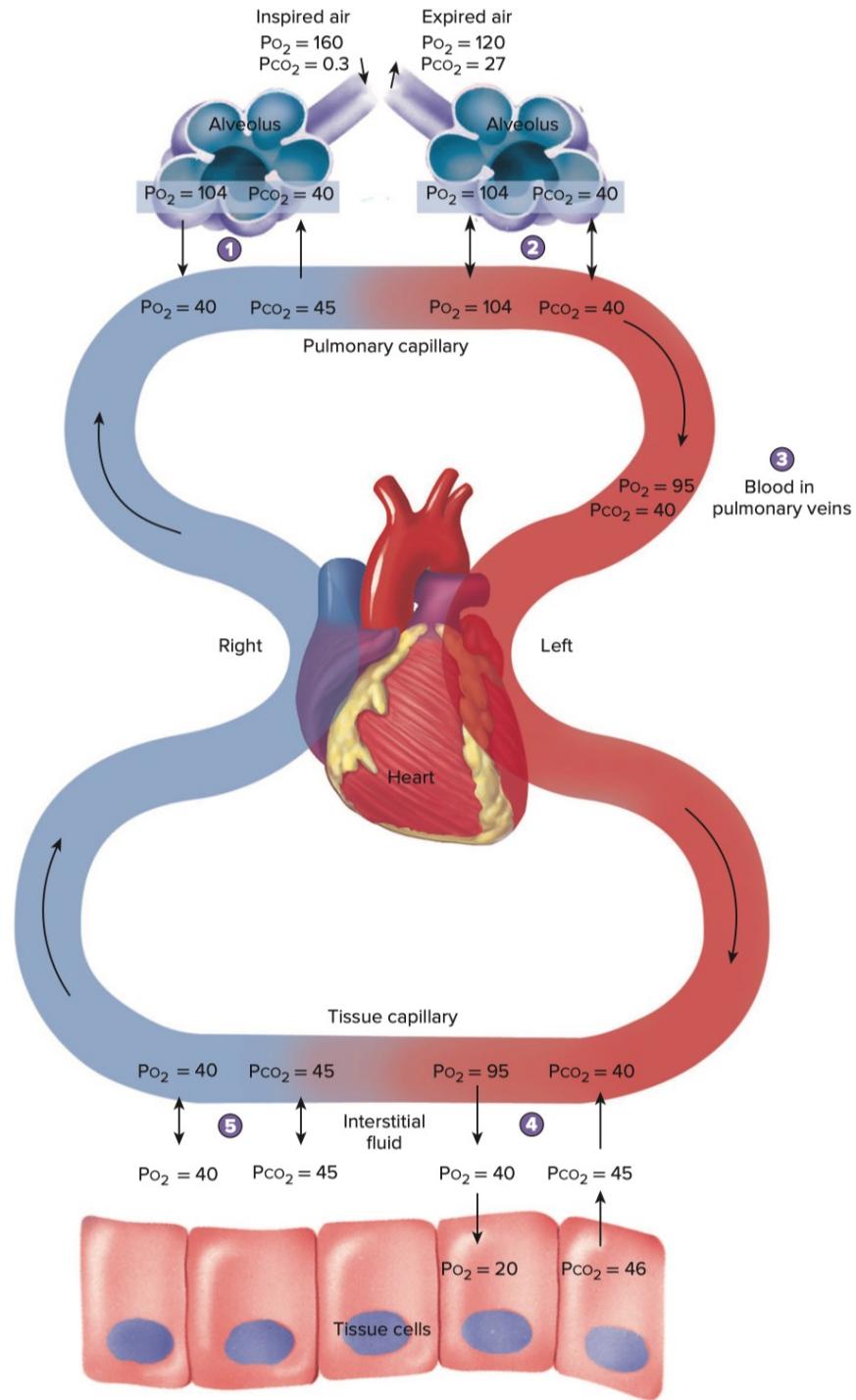
① Oxygen diffuses into the arterial ends of pulmonary capillaries, and CO<sub>2</sub> diffuses into the alveoli because of differences in partial pressures.

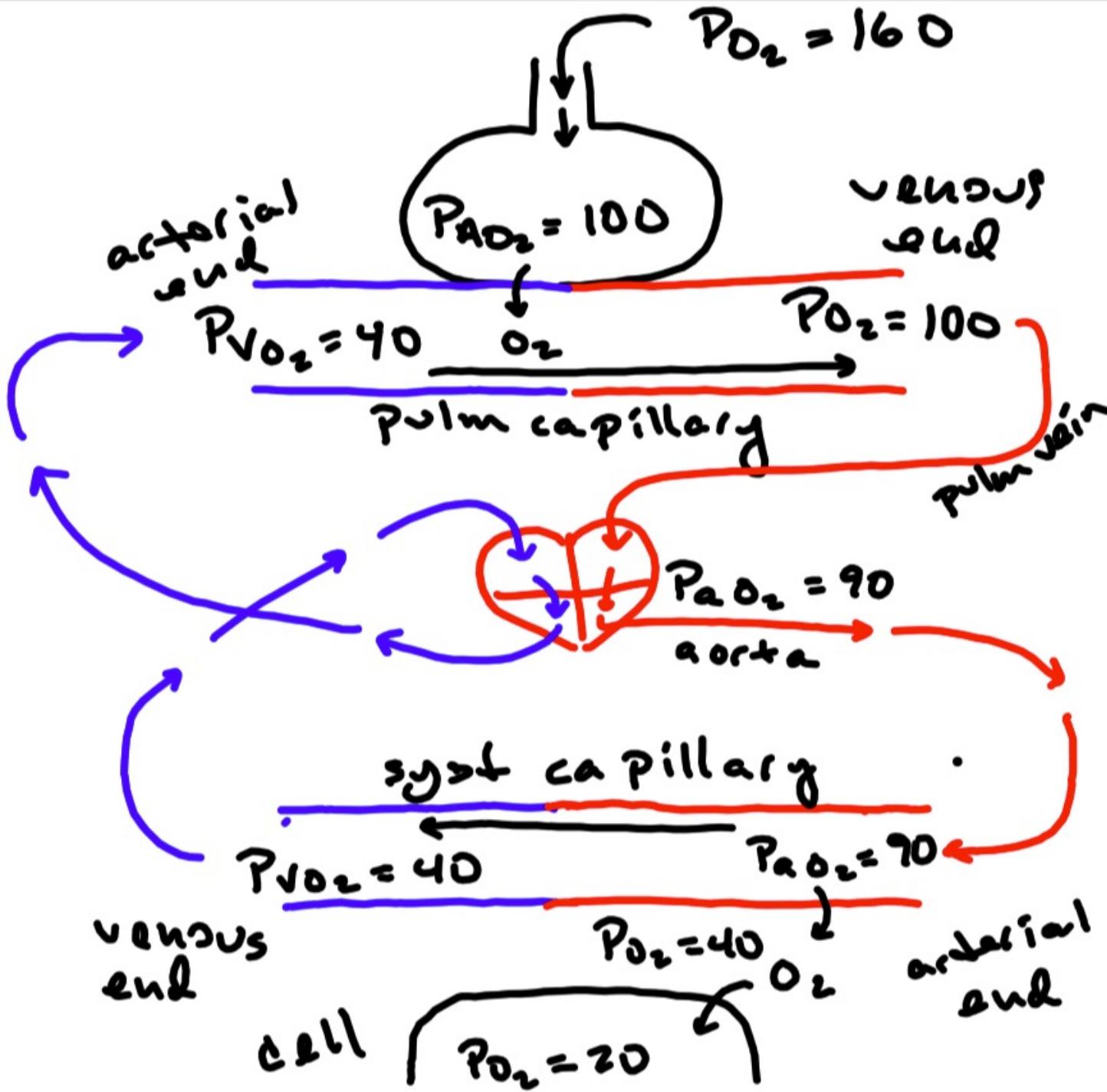
② As a result of diffusion at the venous ends of pulmonary capillaries, the Po<sub>2</sub> in the blood is equal to the Po<sub>2</sub> in the alveoli, and the Pco<sub>2</sub> in the blood is equal to the Pco<sub>2</sub> in the alveoli.

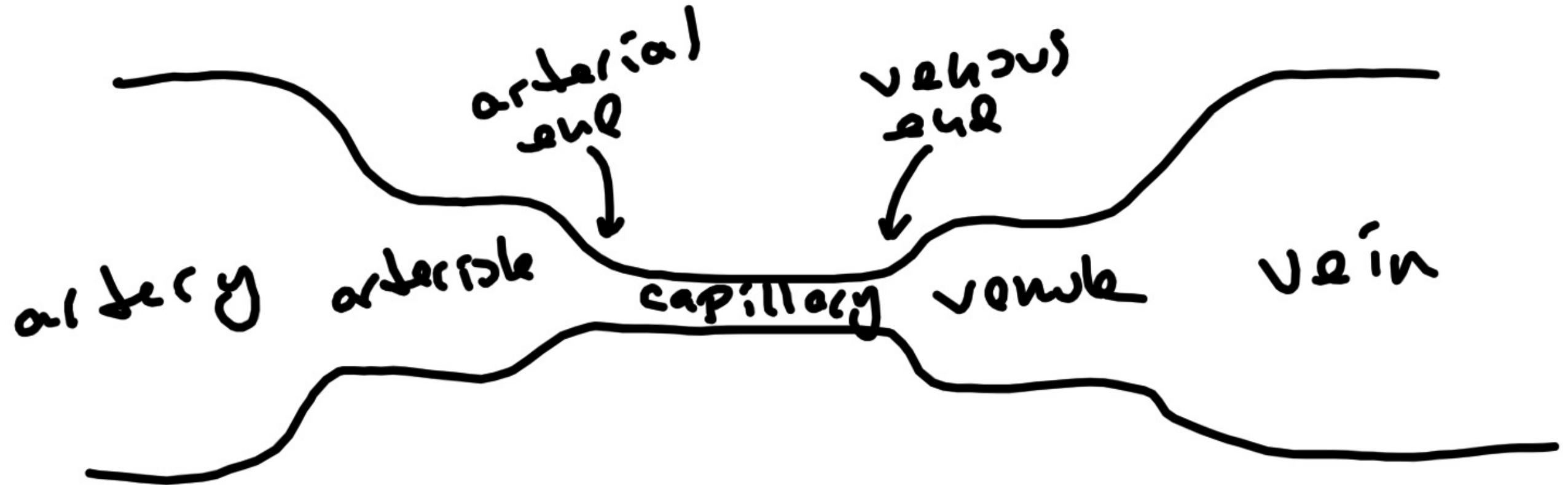
③ The Po<sub>2</sub> of blood in the pulmonary veins is less than in the pulmonary capillaries because of mixing with deoxygenated blood from veins draining the bronchi and bronchioles.

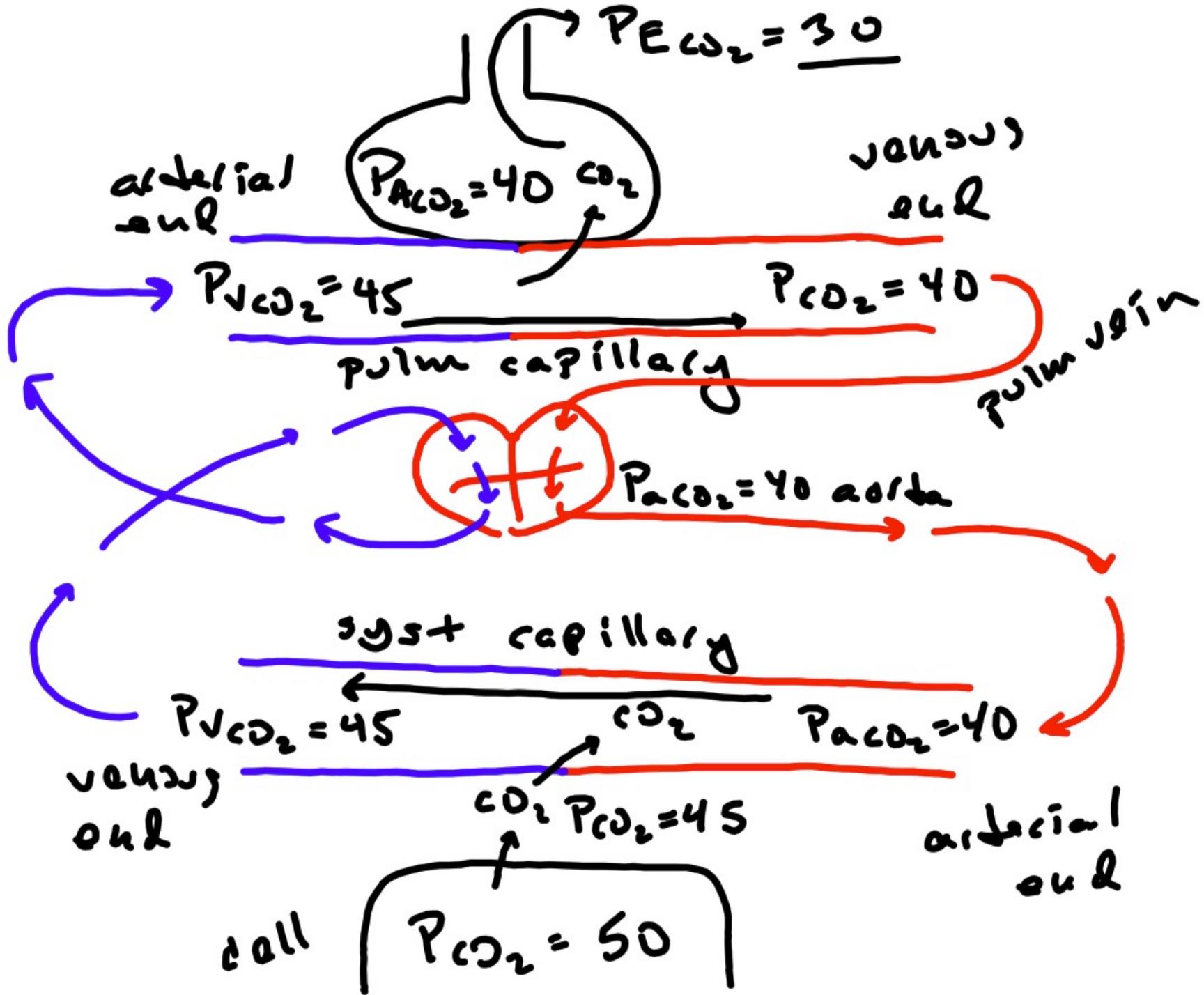
④ Oxygen diffuses out of the arterial ends of tissue capillaries, and CO<sub>2</sub> diffuses out of the tissue because of differences in partial pressures.

⑤ As a result of diffusion at the venous ends of tissue capillaries, the Po<sub>2</sub> in the blood is equal to the Po<sub>2</sub> in the tissue, and the Pco<sub>2</sub> in the blood is equal to the Pco<sub>2</sub> in the tissue.  
Go back to step 1.









# Carbon Dioxide Diffusion Gradients

- $CO_2$  diffuses from cells to interstitial space
  - $P_{CO_2}$  in cells is approximately 50 mm Hg
    - $P_{CO_2}$  produced in cells during aerobic cellular respiration
  - $P_{CO_2}$  in interstitial space is approximately 45 mm Hg
  - ∴ gradient for  $CO_2$  to diffuse from cells to interstitial space
- $CO_2$  diffuses from interstitial space to arterial end of systemic capillary
  - $P_{CO_2}$  in interstitial space is approximately 45 mm Hg
  - $P_{CO_2}$  in arterial end of systemic capillary is approximately 40 mm Hg
  - ∴ gradient for  $CO_2$  to diffuse from interstitial space to blood
- $P_{CO_2}$  at venous end of systemic capillary equilibrates to approximately 45 mm Hg
- Blood to right atrium ... right ventricle ... pulmonary artery ... pulmonary capillaries
- $CO_2$  diffuses from arterial end of pulmonary capillary to alveolus
  - $P_{CO_2}$  at arterial end of pulmonary capillary is approximately 45 mm Hg
  - $P_{CO_2}$  in alveoli is approximately 40 mm Hg
  - ∴ gradient for  $CO_2$  to diffuse from blood to alveolus
- $P_{CO_2}$  equilibrates to approximately 40 mm Hg at venous end of pulmonary capillary

$$[\text{Dissolved gas}] \sim P_{\text{gas}}$$

- \* If  $\uparrow$  dissolved gas then  $\uparrow P_{\text{gas}}$
- \* If  $\uparrow P_{\text{gas}}$  that means there is more dissolved gas
- \* If  $\downarrow$  dissolved gas then  $\downarrow P_{\text{gas}}$
- \* If  $\downarrow P_{\text{gas}}$  that means there is less dissolved

# Gas Transport

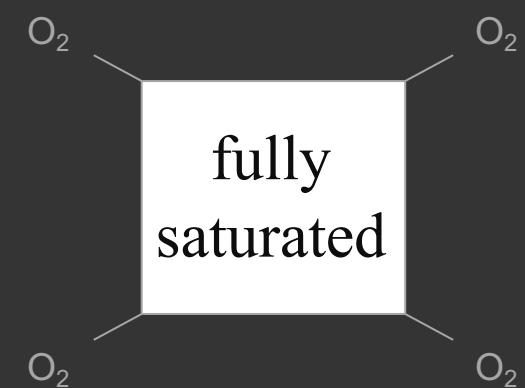
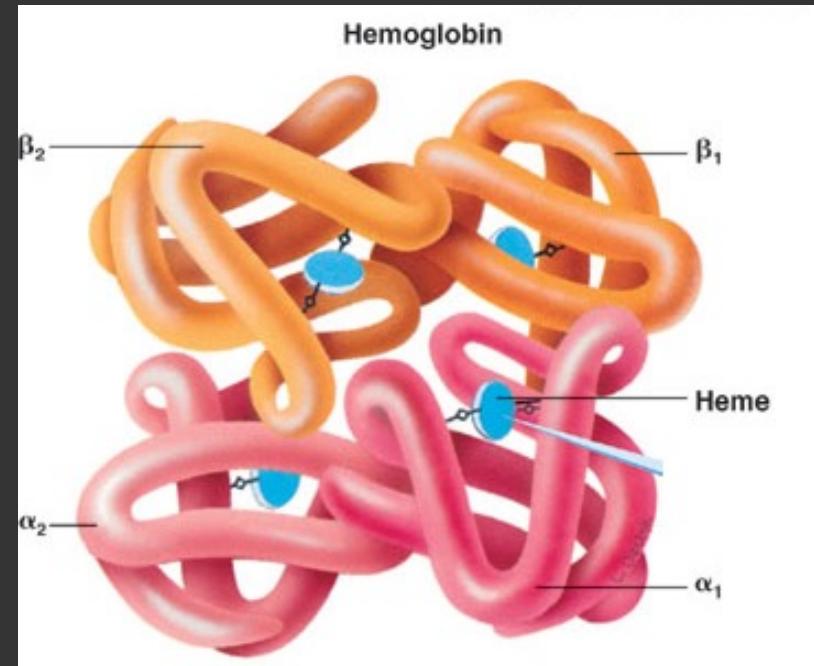
- Oxygen is transported in two different ways :
  - Dissolved ( ~ 1.5 % )
  - Hemoglobin ( ~ 98.5 % )
- Carbon dioxide is transported in three different ways
  - Dissolved ( ~ 5 to 30 % )
  - Hemoglobin ( ~ 5 to 10 % )
  - Bicarbonate ( ~ 60 to 90 % )

# Gas Transport

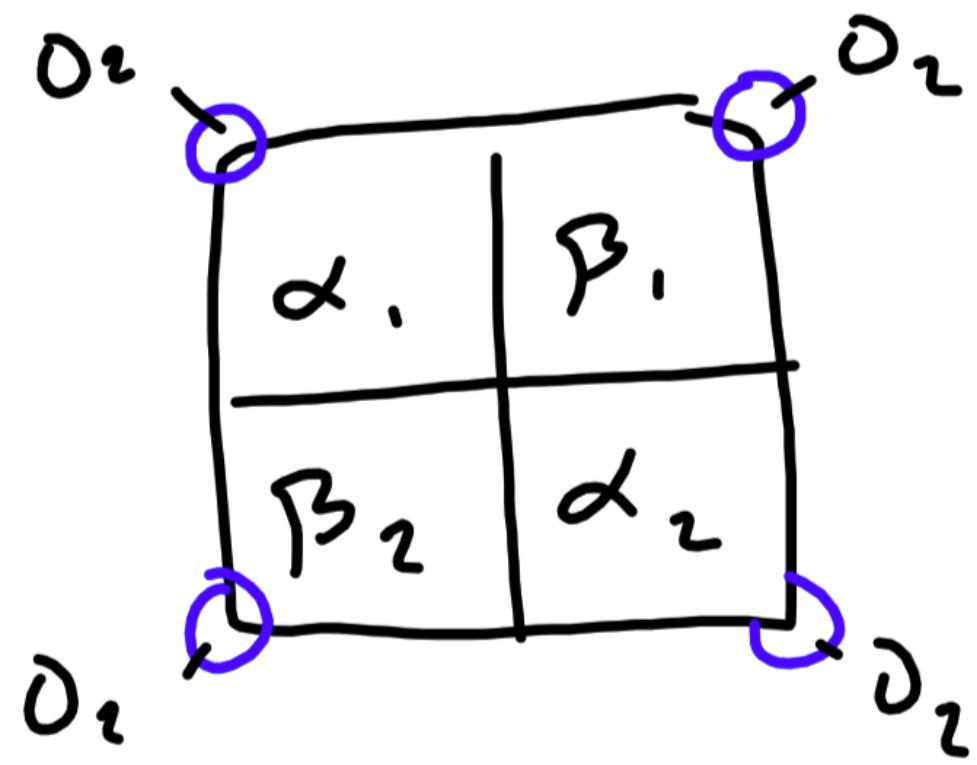
- Oxygen Transport
  - ~ 1.5 % dissolved in the plasma
    - Low because oxygen is not very soluble in water
- Henry's Law
  - $( \text{Dissolved Gas} ) = ( P_{gas} ) * ( \text{Solubility Coefficient of that Gas} )$
- Dissolved oxygen is responsible for its partial pressures in body fluids

# Gas Transport

- Transported by Hemoglobin : ~ 98.5 %
- Hemoglobin has the ability to bind up to 4 oxygen molecules
- When hemoglobin has 4 oxygen molecules bound , it is fully saturated
- $SaO_2$  = percent of Hb molecules fully saturated with oxygen
- $SaO_2$  of arterial blood is measured with a pulse oximeter
- Normal pulse ox range = 95 to 100 %
- Pulse ox under 90 % is considered abnormal



14b

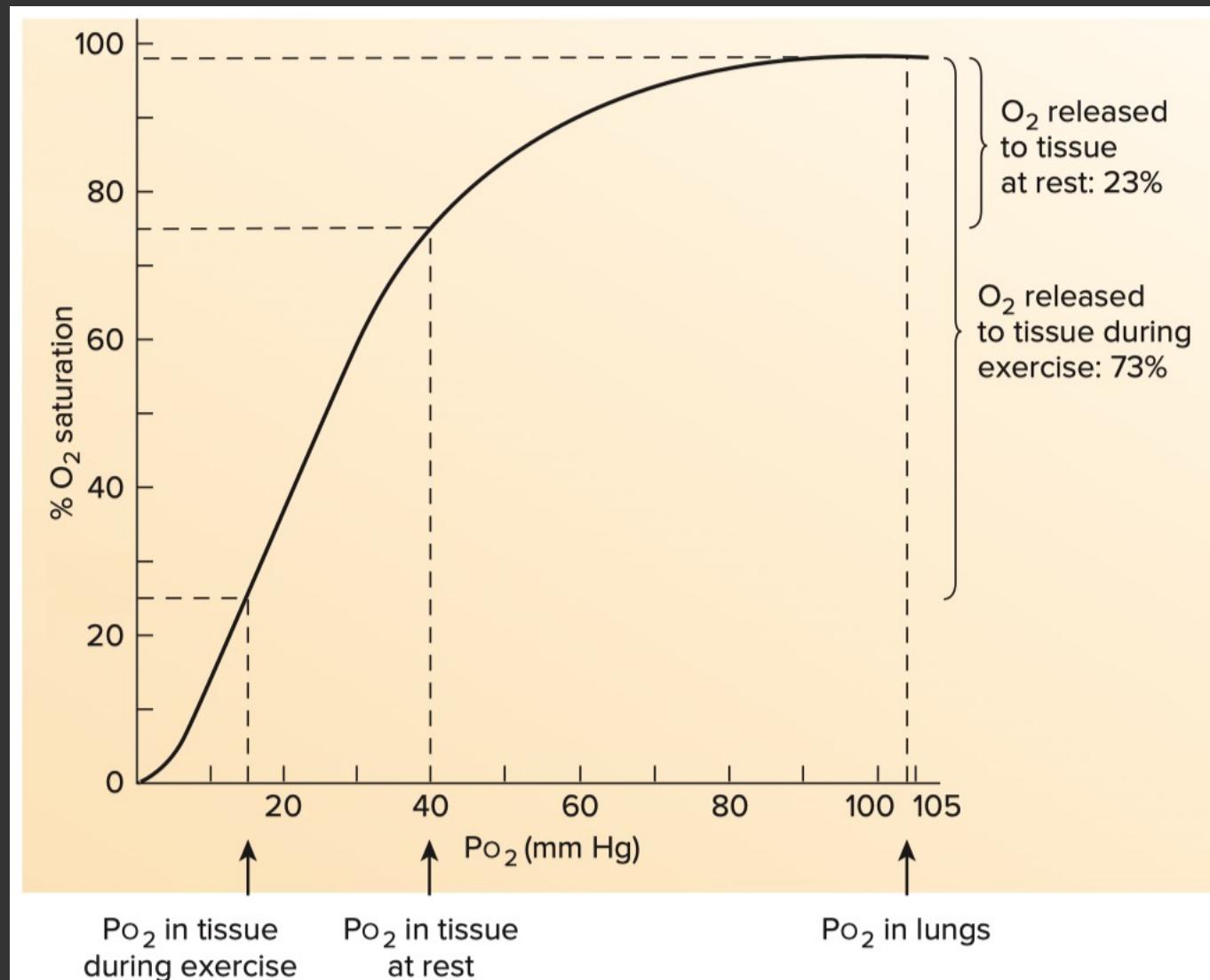


fully saturated

- \*  $SaO_2$  is a measure of the percent of Hb that are fully saturated
- \* Pulse oximeter measures  $SaO_2$  in arterial blood  
normal: 95-100?

# Hemoglobin-Oxygen Binding

- As  $P_{O_2}$  increases , the oxygen bound to Hb increases
- Arterial = At a  $P_{O_2}$  of 90 mm Hg :
  - $SaO_2$  is approximately 100 %
- Venous = At a  $P_{O_2}$  of 40 mm Hg :
  - $SaO_2$  is approximately 75 %



# Oxygen–Hemoglobin Binding

- Affected By :
  - CO<sub>2</sub> / pH
  - Temperature
  - 2,3-biphosphoglycerate
  - Carbon monoxide

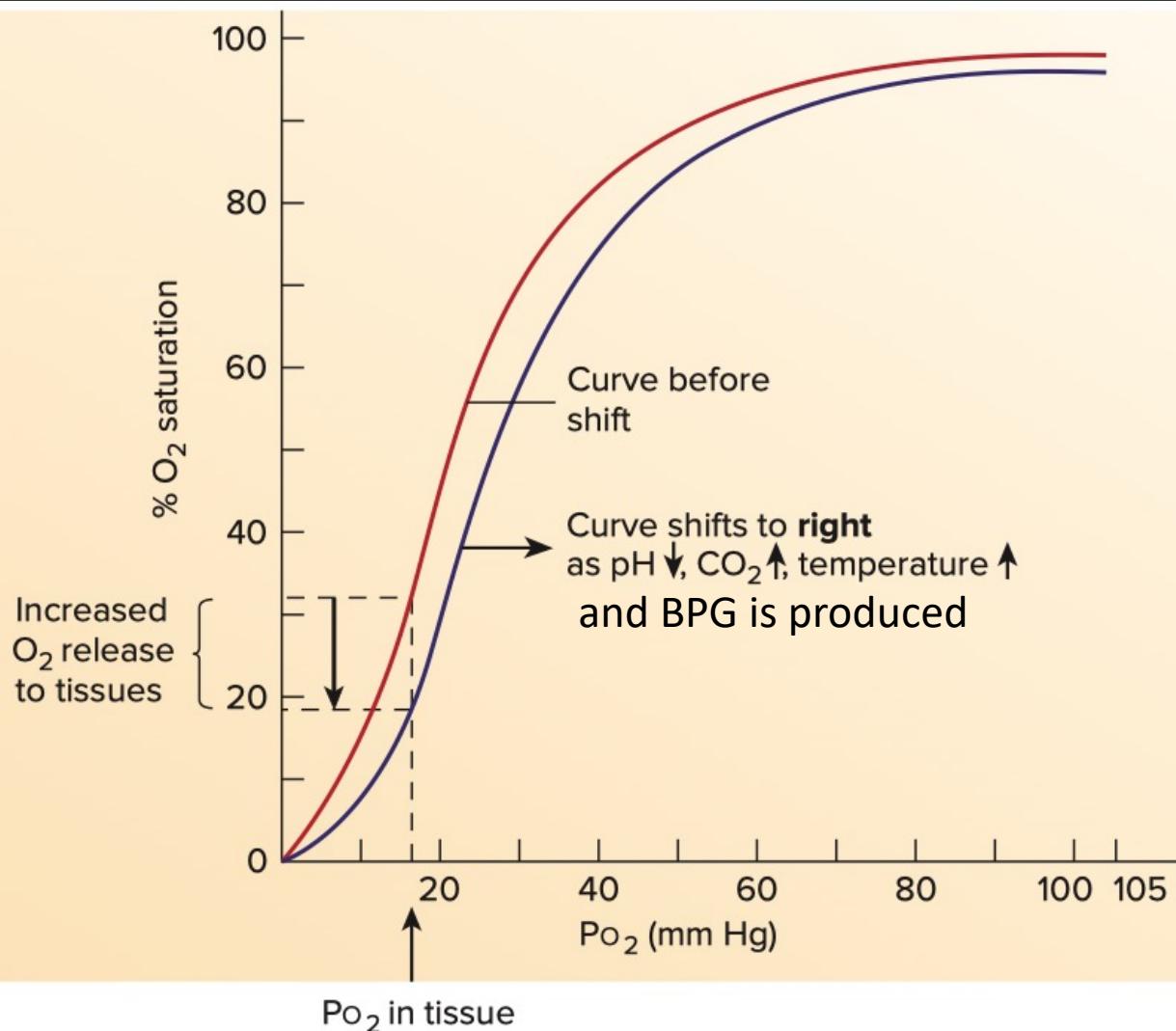
# Altering Oxygen–Hemoglobin Binding

- Changes in  $CO_2$  / pH
  - Increase in  $CO_2$  / decrease in pH decreases binding
    - Decrease in the affinity of Hb for oxygen
    - Occurs at the body tissues
      - More oxygen released from Hb
    - “Right shift” of the oxygen-Hb binding curve
      - ie , affinity of Hb for  $O_2$  is decreased
  - Decrease in  $CO_2$  / increase in pH increases binding
    - Increase in the affinity of Hb for oxygen
    - Occurs at the lungs
      - More oxygen binds to Hb
    - “Left shift” of the oxygen-Hb binding curve
      - ie , affinity for Hb for  $O_2$  is increased
- Changes in Temperature
  - Increase in temperature decreases binding
    - Occurs at the body tissues
    - Right shift
  - Decrease in temperature increases binding
    - Occurs at the lungs
    - Left shift

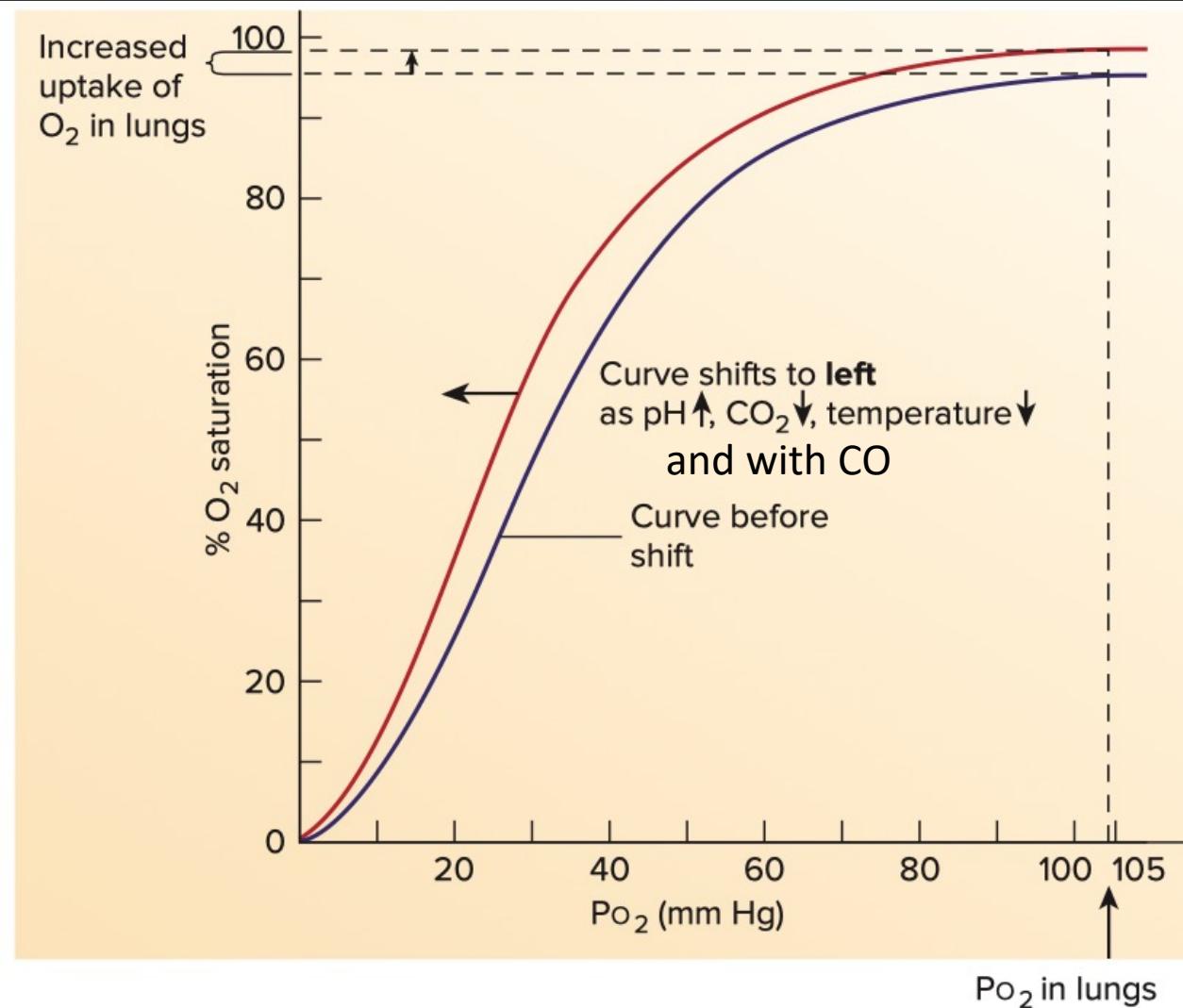
# Altering Oxygen–Hemoglobin Binding

- Carbon Monoxide ( CO )
  - CO displaces oxygen from hemoglobin
    - Hb has 250 times greater affinity for CO
    - $P_{O_2}$  is unchanged
  - Whatever oxygen is bound , is tightly bound
    - CO increases affinity of Hb for oxygen
      - Left shift

# Altering Oxygen–Hemoglobin Binding



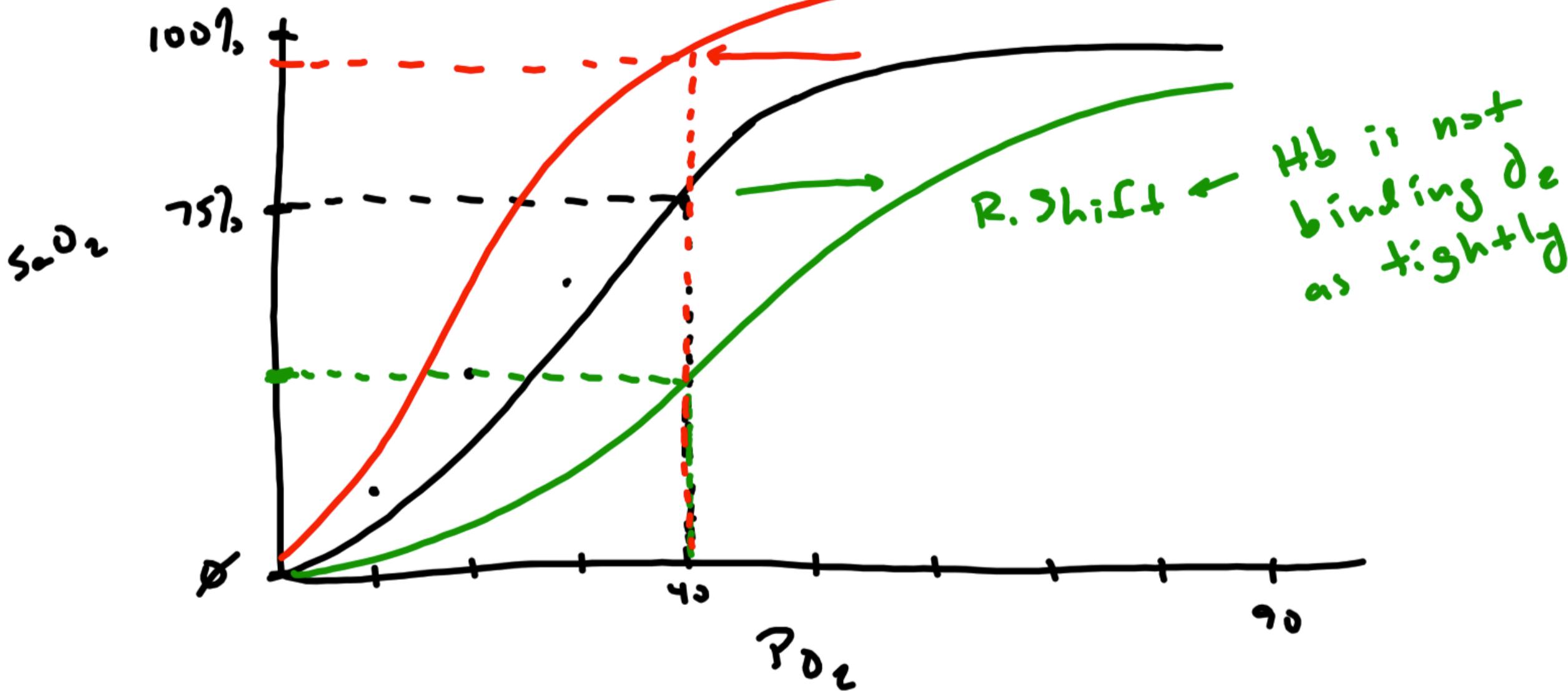
(a) In the tissues, the oxygen–hemoglobin dissociation curve shifts to the right. As pH decreases, P<sub>CO<sub>2</sub></sub> increases, or temperature increases, the curve (red) shifts to the right (blue), resulting in an increased release of O<sub>2</sub>.

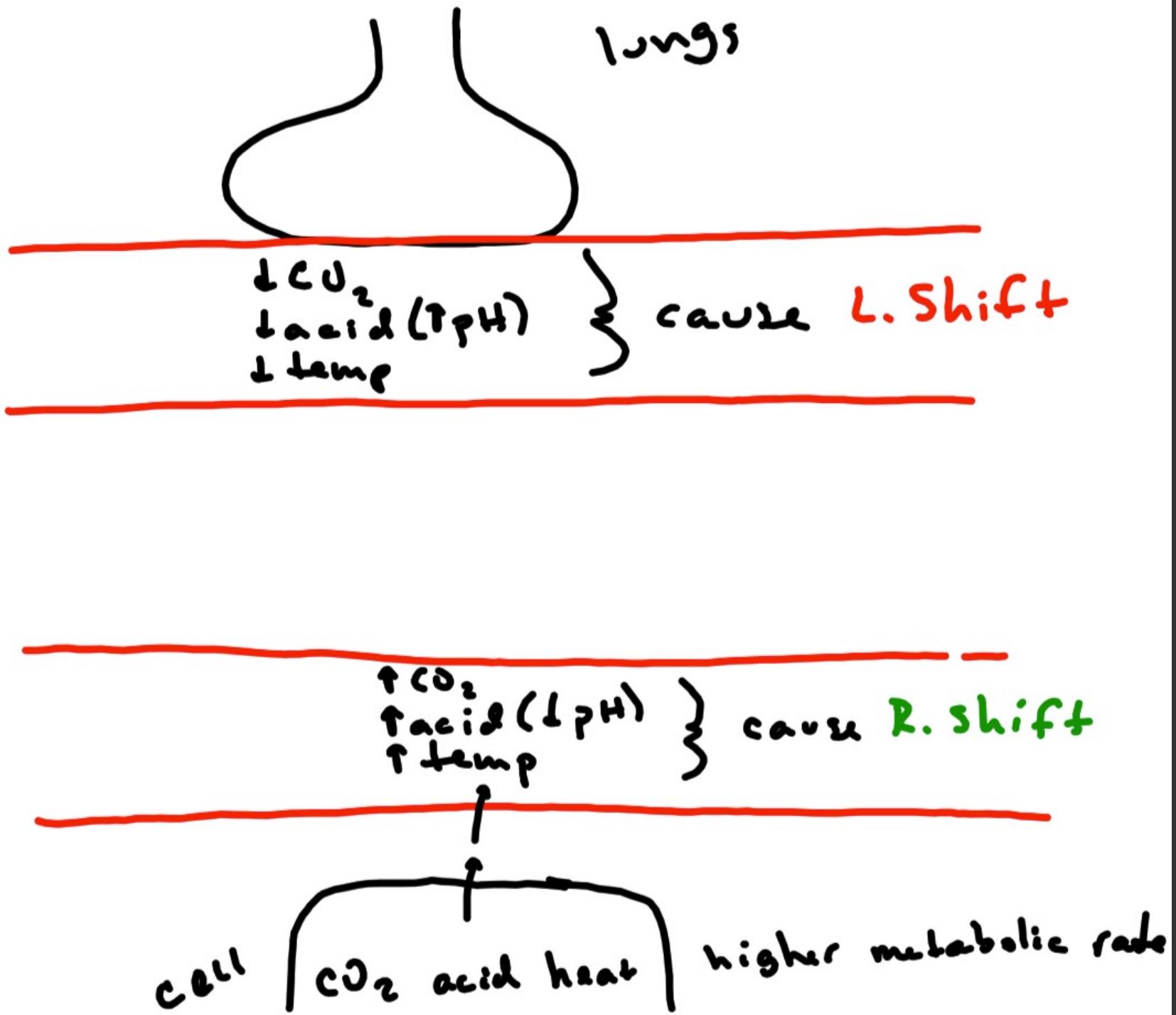


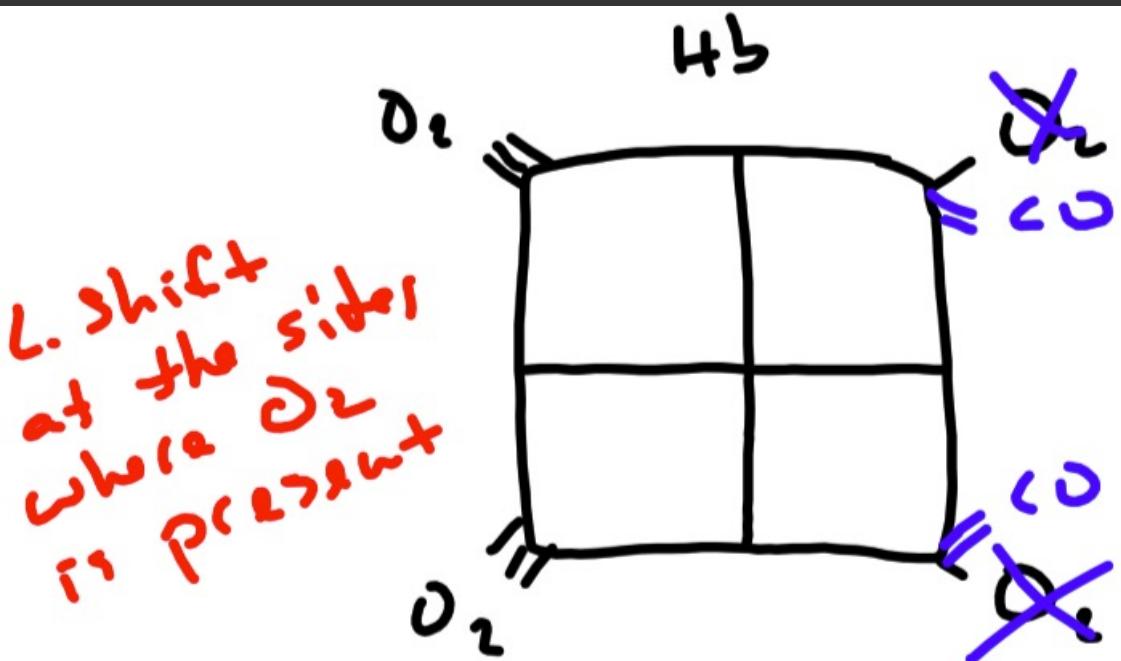
(b) In the lungs, the oxygen–hemoglobin dissociation curve shifts to the left. As pH increases, P<sub>CO<sub>2</sub></sub> decreases, or temperature decreases, the curve (blue) shifts to the left (red), resulting in an increased ability of hemoglobin to pick up O<sub>2</sub>.

$P_{O_2}$  affects  $SaO_2$  but  
 $SaO_2$  does not affect  $P_{O_2}$

L. Shift ← Hb is binding O<sub>2</sub> more tightly







- \* 2 - big problems
    - ①  $\downarrow SaO_2$
    - ② Hb does not "let go" of  $O_2$
- LLL  $O_2$  to cells

- \* CO bound Hb is carboxyhemoglobin
  - Normal: 1%
  - Smokers: 5 - 10%
  - CO poisoning
    - ↳ 20% : headache, nausea
    - ↳ 50% : coma, death

- \* Treatment
  - supplemental  $O_2$
  - hyperbaric chamber

# Altering Oxygen–Hemoglobin Binding

Decrease the Affinity of Hb for O<sub>2</sub>

( i.e. cause a right shift in the O<sub>2</sub> – Hb binding curve )

↓ pH

↑ CO<sub>2</sub>

↑ temperature

Increase the Affinity of Hb for O<sub>2</sub>

( i.e. cause a left shift in the O<sub>2</sub> – Hb binding curve )

↑ pH

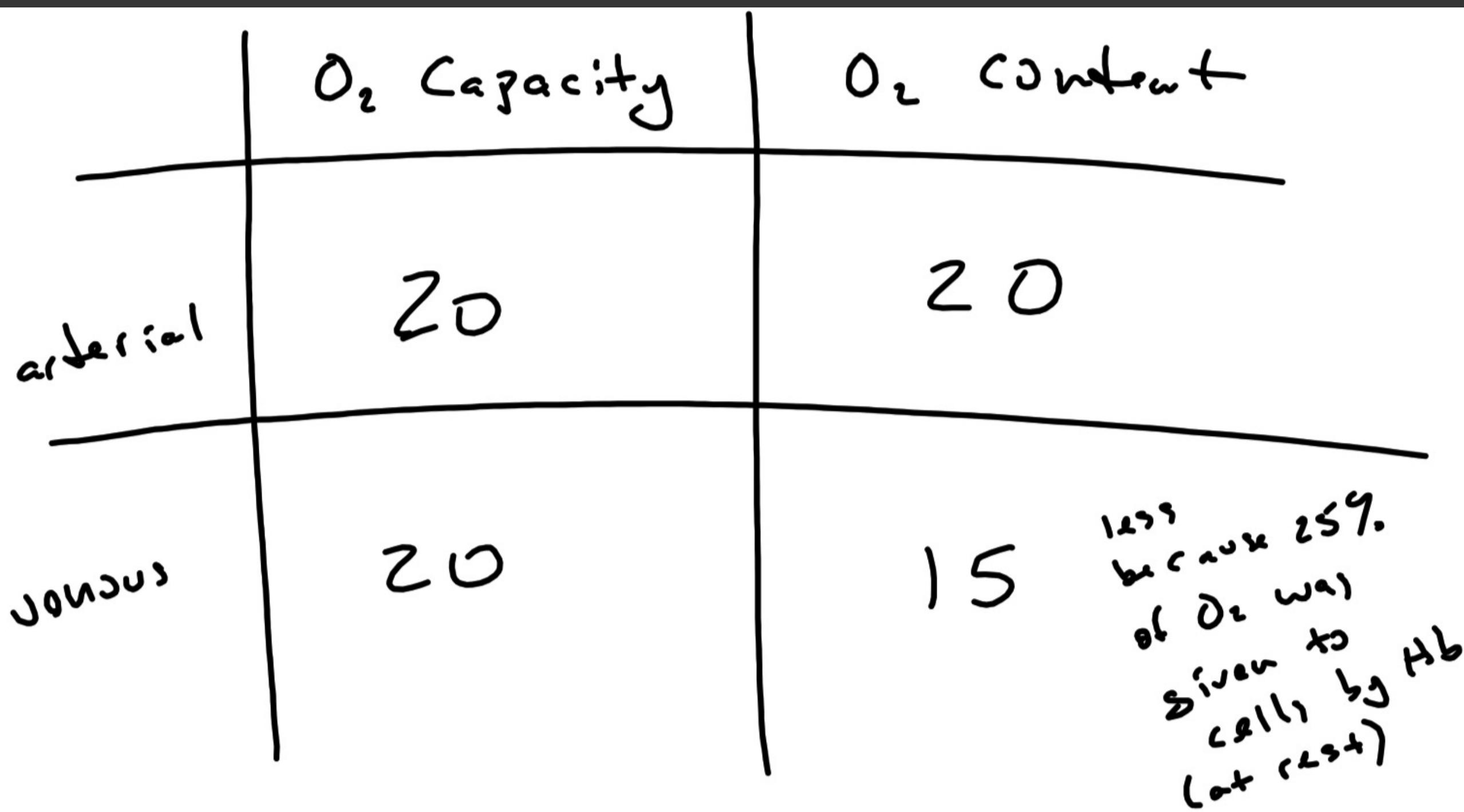
↓ CO<sub>2</sub>

↓ temperature

CO

# $O_2$ Saturation ( $SaO_2$ ), $O_2$ Capacity and $O_2$ Content

- $O_2$  saturation (  $SaO_2$  ) = percent of Hb fully saturated with oxygen
- $O_2$  capacity = greatest amount of  $O_2$  that can be carried in the blood
- $O_2$  content = amount of  $O_2$  that is actually carried in the blood

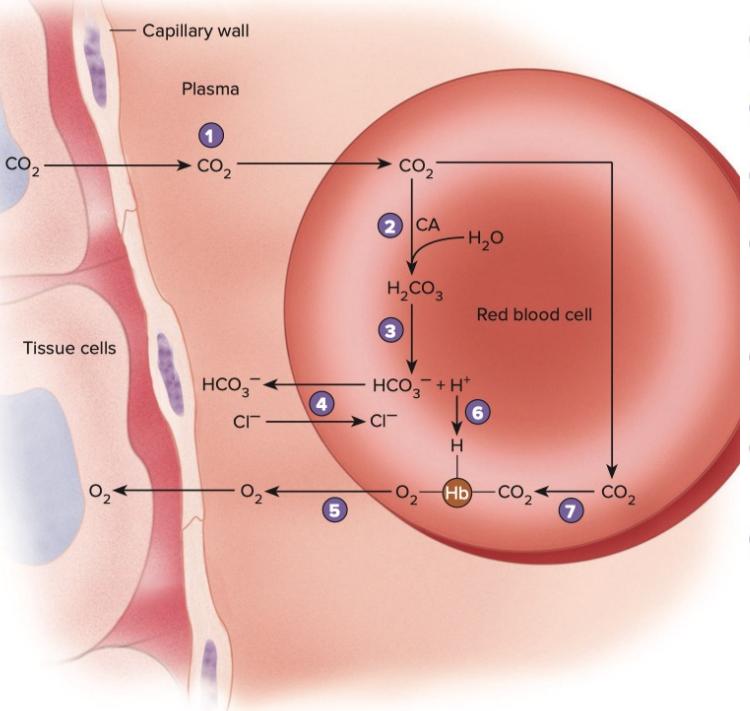


# Carbon Dioxide Transport

- Transported by hemoglobin : ~ 5% in arterial blood ... ~ 10% in venous blood
- Carbaminohemoglobin (  $\text{CO}_2$  bound to hemoglobin )
- Transported as  $\text{HCO}_3^-$  : ~ 90% in arterial blood ... ~ 60% in venous blood
  - $\text{CO}_2 + \text{H}_2\text{O} = \text{HCO}_3^-$  ( “hydration” of  $\text{CO}_2$  )

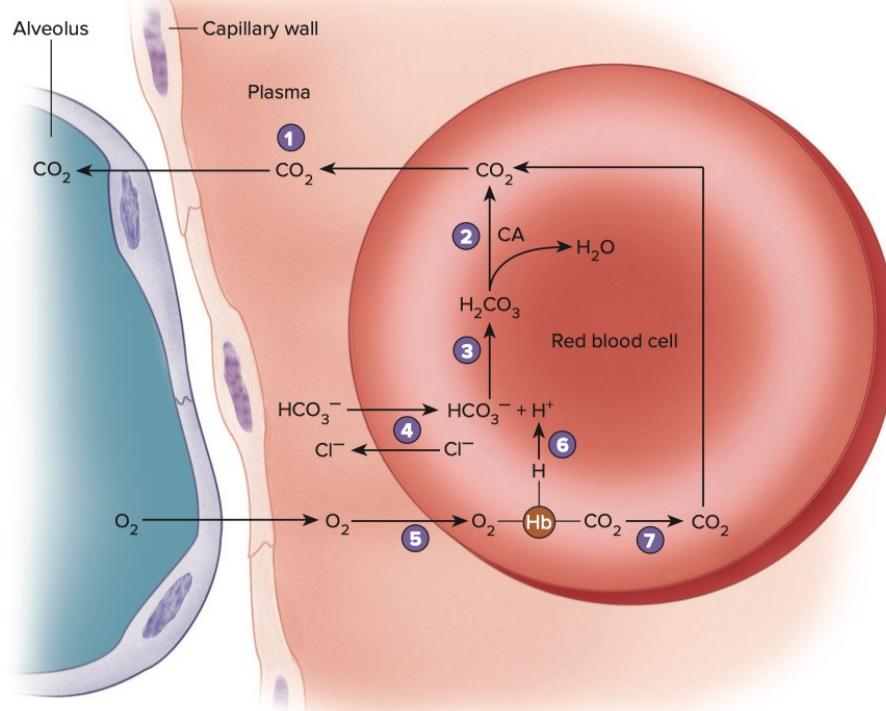
# $CO_2$ Carried as $HCO_3^-$

- 1 In the tissues,  $CO_2$  diffuses into the plasma and into red blood cells. Some of the  $CO_2$  remains in the plasma.
- 2 In red blood cells,  $CO_2$  reacts with water ( $H_2O$ ) to form carbonic acid ( $H_2CO_3$ ) in a reaction catalyzed by the enzyme carbonic anhydrase (CA).
- 3 Carbonic acid dissociates to form bicarbonate ions ( $HCO_3^-$ ) and hydrogen ions ( $H^+$ ).
- 4 In the chloride shift, as  $HCO_3^-$  diffuse out of the red blood cells, electrical neutrality is maintained by the diffusion of chloride ions ( $Cl^-$ ) into them.
- 5 Oxygen is released from hemoglobin (Hb). Oxygen diffuses out of red blood cells and plasma into the tissue.
- 6 Hydrogen ions combine with hemoglobin, which promotes the release of  $O_2$  from hemoglobin (Bohr effect).
- 7 Carbon dioxide combines with hemoglobin. Hemoglobin that has released  $O_2$  readily combines with  $CO_2$  (Haldane effect).



(a) Gas exchange in the tissues

- 1 In the lungs,  $CO_2$  diffuses from red blood cells and plasma into the alveoli.
- 2 Carbonic anhydrase catalyzes the formation of  $CO_2$  and  $H_2O$  from  $H_2CO_3$ .
- 3 Bicarbonate ions and  $H^+$  combine to replace  $H_2CO_3$ .
- 4 In the chloride shift, as  $HCO_3^-$  diffuse into red blood cells, electrical neutrality is maintained by the diffusion of chloride ions ( $Cl^-$ ) out of them.
- 5 Oxygen diffuses into the plasma and into red blood cells. Some of the  $O_2$  remains in the plasma. Oxygen binds to hemoglobin.
- 6 Hydrogen ions are released from hemoglobin, which promotes the uptake of  $O_2$  by hemoglobin (Bohr effect).
- 7 Carbon dioxide is released from hemoglobin. Hemoglobin that is bound to  $O_2$  readily releases  $CO_2$  (Haldane effect).



(b) Gas exchange in the lungs

# Ventilation ( $\dot{V}_A$ ) / Perfusion ( $\dot{Q}$ ) Relationship

- When Upright :
  - Regional differences in ventilation and perfusion exist ( due to the effects of gravity )
    - Perfusion and ventilation are both lower at the apex of the lung
    - Perfusion and ventilation are both higher at the base of the lung
- When Supine or Prone :
  - Even perfusion and ventilation throughout the lung

\* Alveolar Ventilation ( $\dot{V}_A$ )

\*  $\uparrow \dot{V}_A \longrightarrow \uparrow P_{AO_2}$  and  $\downarrow P_{ACO_2}$

$\downarrow$

$\uparrow P_{aO_2}$  and  $\downarrow P_{aCO_2}$

---

\*  $\downarrow \dot{V}_A \longrightarrow \downarrow P_{AO_2}$  and  $\uparrow P_{ACO_2}$

$\downarrow$

$\downarrow P_{aO_2}$  and  $\uparrow P_{aCO_2}$

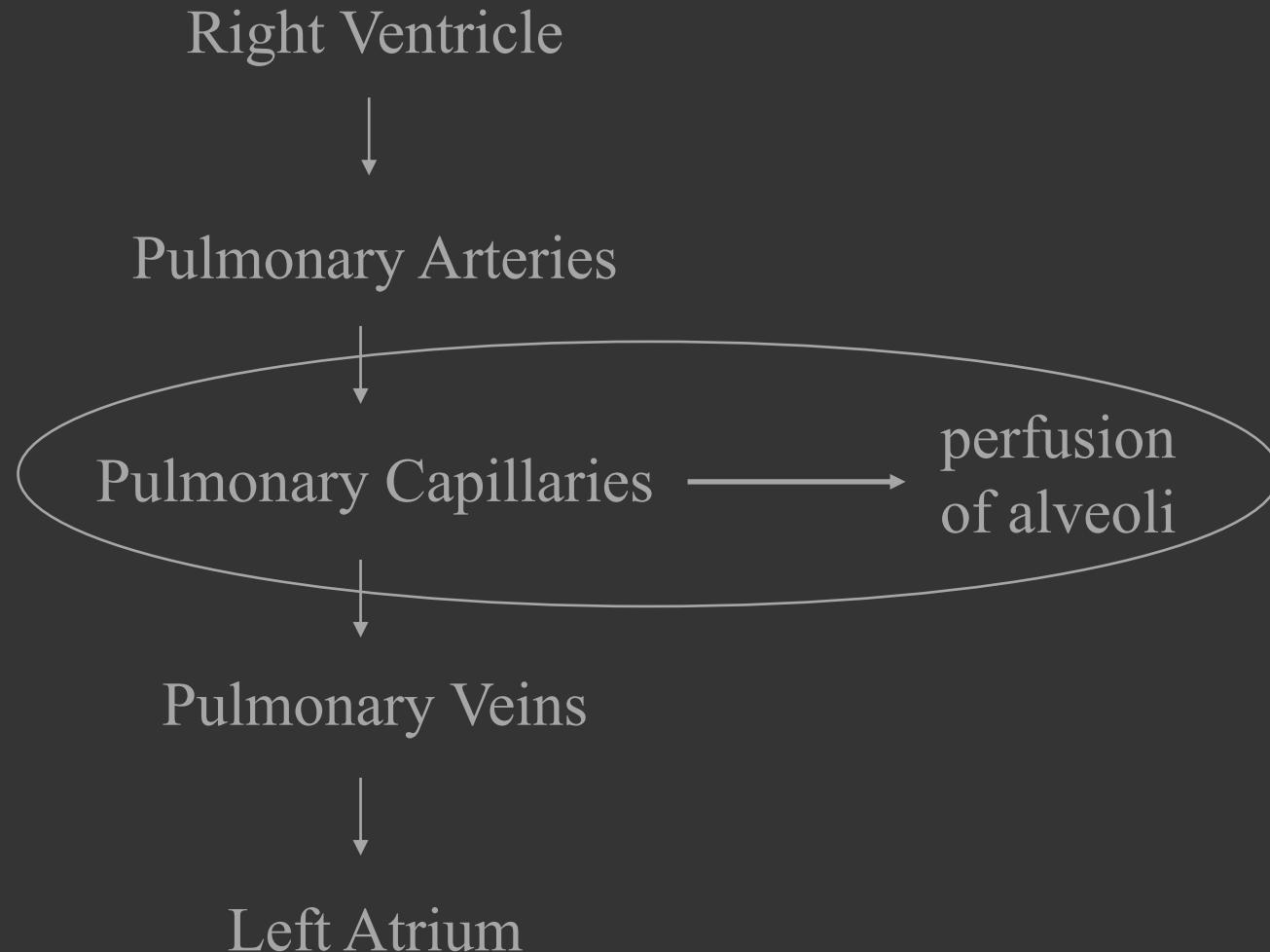
# Pulmonary Ventilation

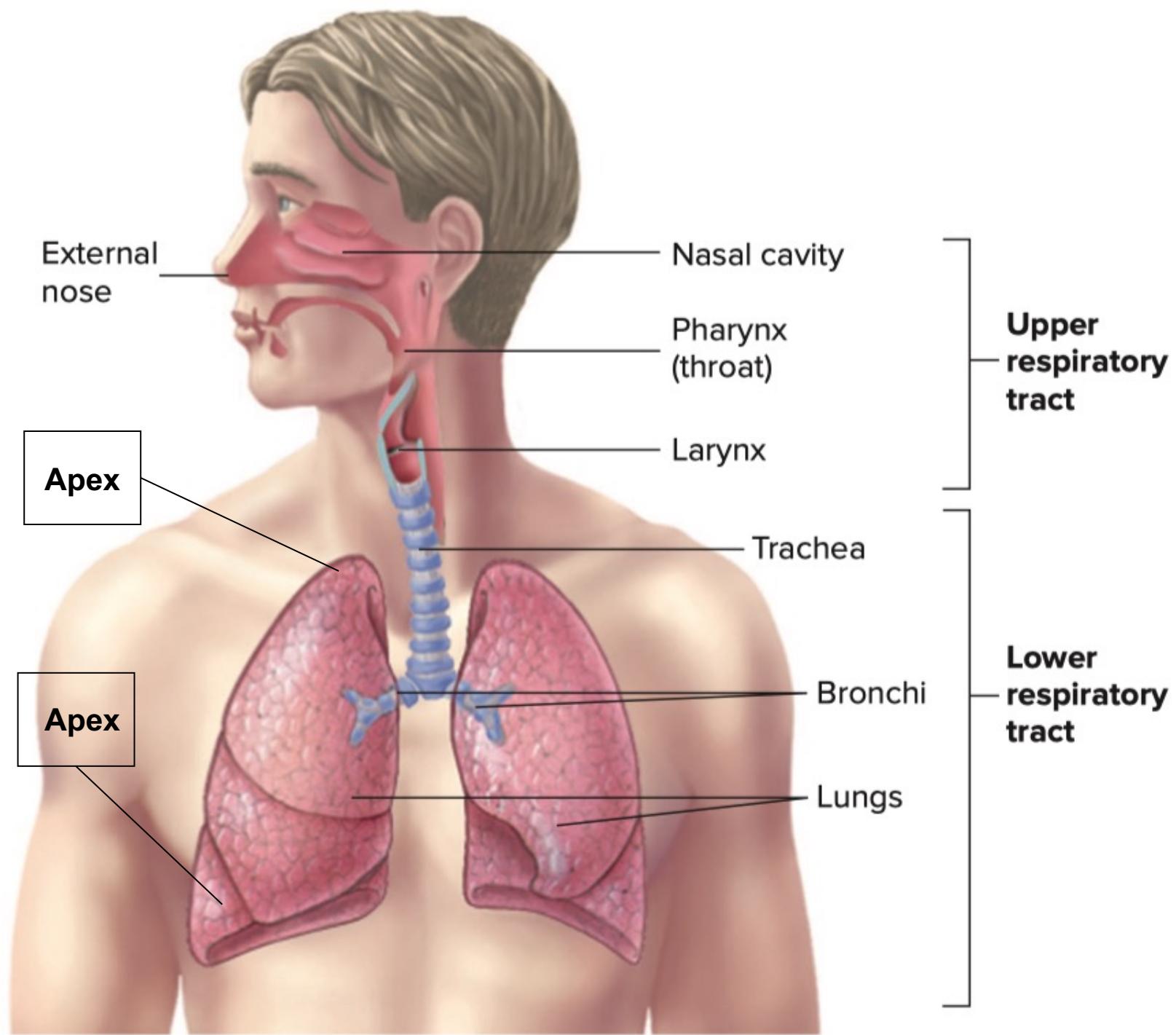
- Minute Ventilation (  $\dot{V}_E$  ) = volume of air moved into the lungs per minute
  - $\dot{V}_E = \text{Tidal Volume} * \text{Respiratory Rate}$
  - $\frac{500 \text{ mL}}{1 \text{ breath}} * \frac{12 \text{ breaths}}{1 \text{ minute}} = \frac{6,000 \text{ mL}}{1 \text{ minute}}$
- Alveolar Ventilation (  $\dot{V}_A$  ) = amount of air available for gas exchange per minute
  - $\dot{V}_A = (\text{Tidal Volume} - \text{Dead Space}) * \text{Respiratory Rate}$
  - $\frac{500 \text{ mL} - 150 \text{ mL}}{1 \text{ breath}} * \frac{12 \text{ breaths}}{1 \text{ minute}} = \frac{4,200 \text{ mL}}{1 \text{ minute}}$
  - More efficient to increase tidal volume as opposed to respiratory rate

# Circulation of the Respiratory System

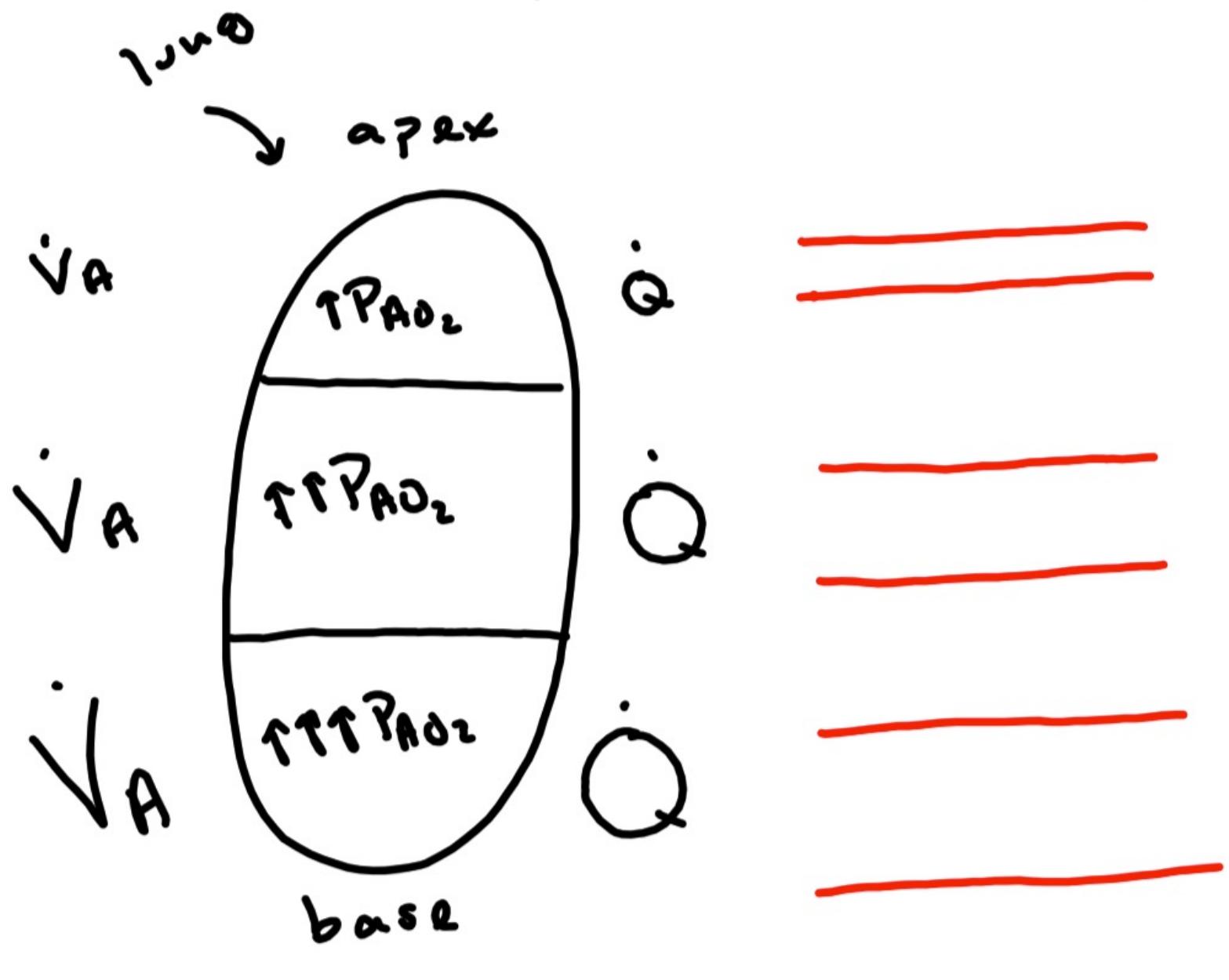
- Perfusion (  $\dot{Q}$  ) of the Lungs
  - Deoxygenated blood is carried to the lungs via the pulmonary arteries
  - and then to pulmonary capillaries where blood is oxygenated at the alveoli
  - Oxygenated blood is then carried back to the heart via the pulmonary veins

# Perfusion ( $\dot{Q}$ ) of the lung ( ie , alveoli )

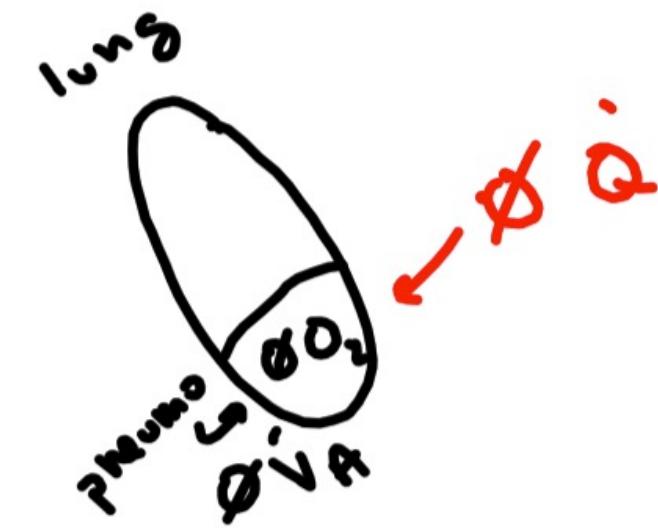




# Upright Lung

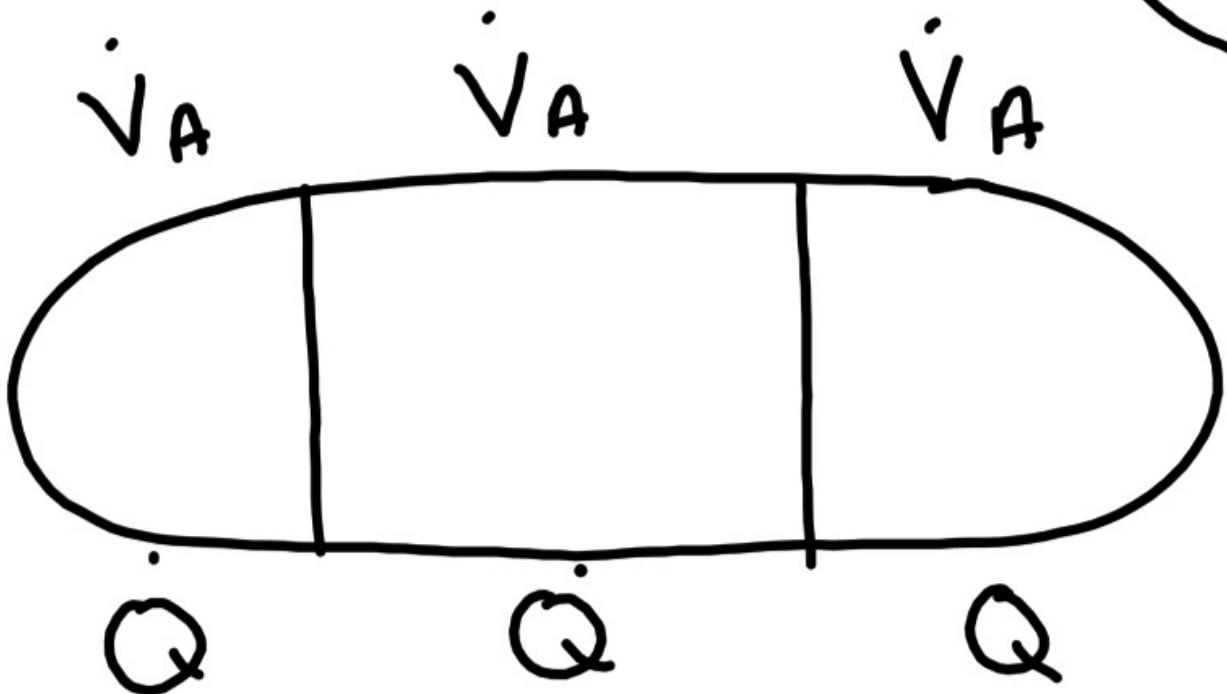


$P_{A\bar{O}_2$  has the  
biggest effect  
on  $\dot{Q}$



Rotates Prone Beds

Horizontal Lung  
Supine or Prone



residual  
differences  
disappear

Prone position  
has SaO<sub>2</sub> exchange  
value especially  
(in patients  
w. ARDS)

# Ventilation ( $\dot{V}_A$ ) / Perfusion ( $\dot{Q}$ ) Relationship

- Level of oxygen in alveoli ( ie ,  $PA_{O_2}$  ) has the greatest effect on perfusion
  - As  $PA_{O_2}$  decreases ... pulmonary arterioles vasoconstrict , which decreases perfusion
  - As  $PA_{O_2}$  increases ... pulmonary arterioles vasodilate , which increases perfusion

# Pulmonary Disease

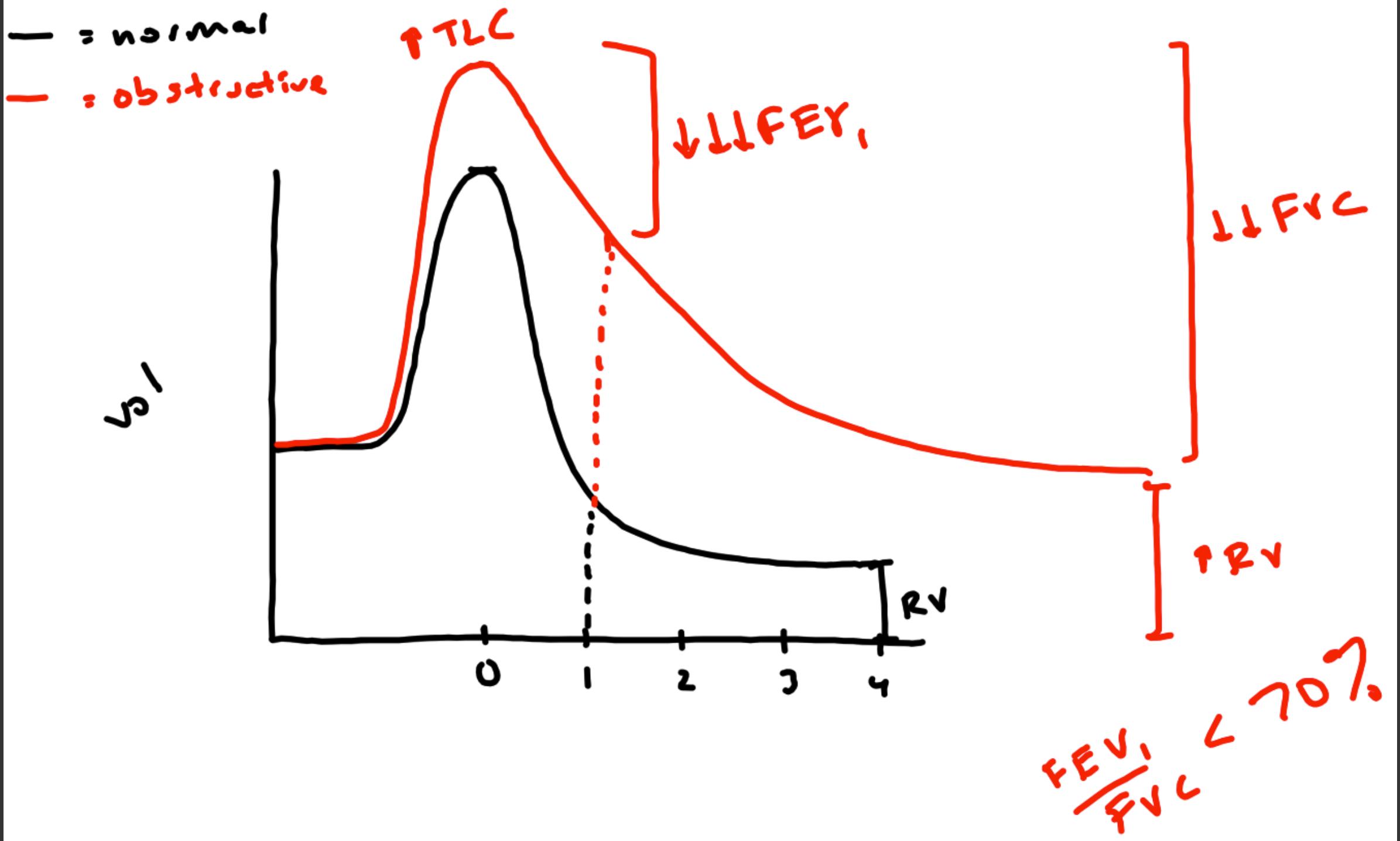
- Obstructive Pulmonary Disease
- Restrictive Pulmonary Disease

# Pulmonary Disease – Obstructive

- Increase in airway resistance ( airway obstruction )
- Air gets trapped in the lungs
  - Causes an increase in RV and thus an increase in FRC and TLC
- Changes in air flow
  - $FEV_1$  and FVC are reduced (  $FEV_1$  is reduced more )
  - $\therefore FEV_1 / FVC$  is greatly reduced
- Ventilation is decreased ( ie , hypoventilation )
  - Causes hypoxemia
  - Causes hypercapnia

# Pulmonary Disease – Obstructive

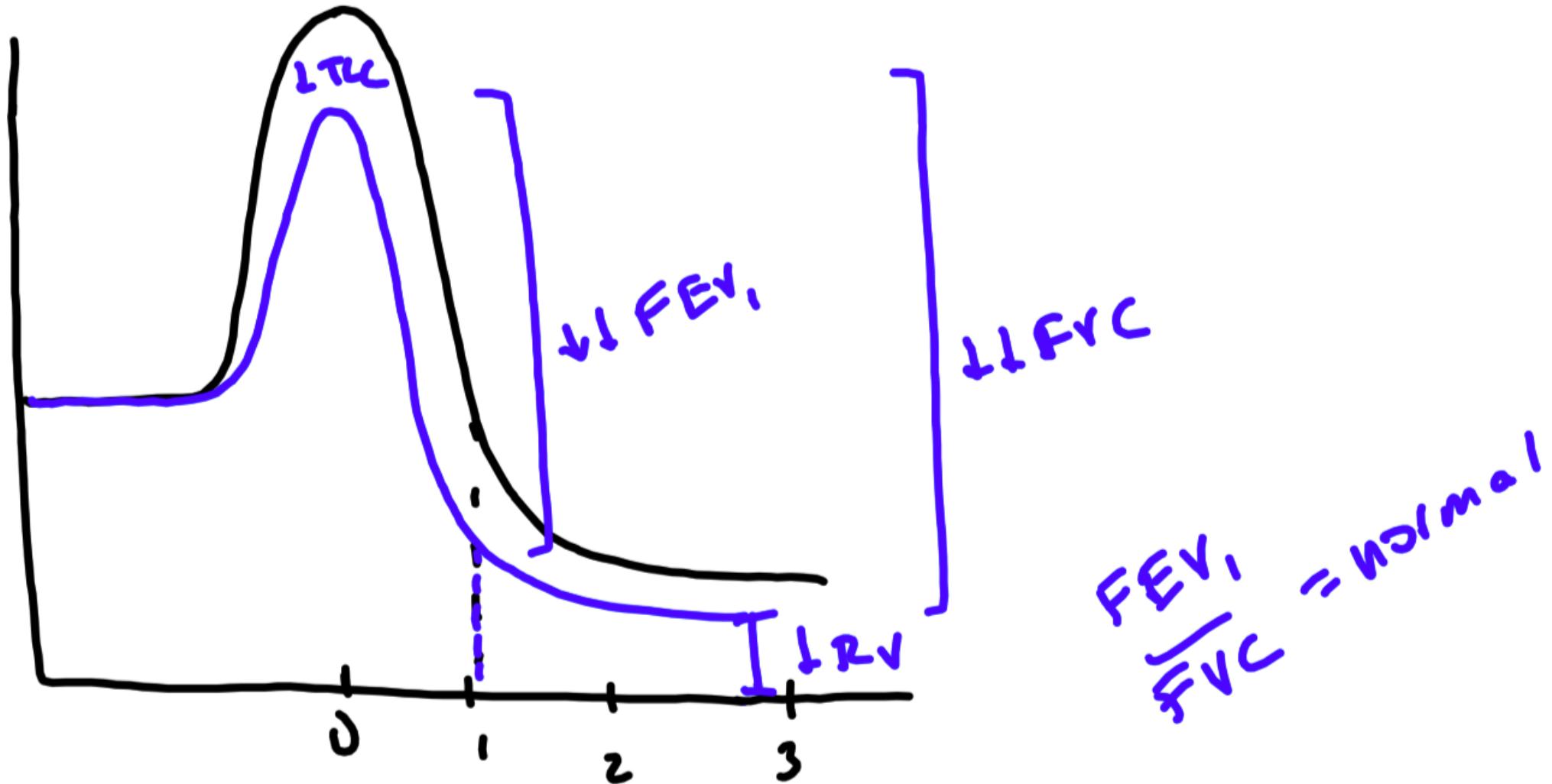
- Chronic Obstructive Pulmonary Disease ( COPD )
  - Emphysema
    - Loss of elastic fibers in walls of bronchioles and alveoli
      - Increase in compliance
      - Loss of elastic recoil causes air to be trapped
        - Causes obstruction to airflow
  - Chronic Bronchitis
    - Increased daily mucus production and airway inflammation for at least 3 months in 2 or more consecutive years
      - Causes airway obstruction
- Asthma
  - Not considered COPD but is caused by obstruction
  - Bronchoconstriction and inflammation cause airway obstruction



# Pulmonary Disease – Restrictive

- Great difficulty getting air into the lungs , even though there is no obstruction
  - All volumes and capacities are reduced
- Changes in air flow
  - Both  $FEV_1$  and FVC are reduced ... but reduced to the same degree
  - Therefore ,  $FEV_1 / FVC$  is normal
    - Can move air very well ( no obstruction ) but not very much air
- Ventilation is decreased ( ie , hypoventilation )
  - Causes hypoxemia
  - Causes hypercapnia

— = normal  
— = restrictive



	Obstructive	Restrictive
volumes and capacities	<p>↑ RV</p> <p>↳ ↑ FRC</p> <p>↳ ↑ TLC</p> <p>All other volumes and capacities decrease</p>	All volumes and capacities decrease
FEV <sub>1</sub> / FVC	<p>↓ ↓ ↓ ↓ FEV<sub>1</sub></p> <p>↓ ↓ FVC</p> <p>↓ ↓ <math>\frac{FEV_1}{FVC} &lt; 70\%</math></p>	<p>↓ ↓ ↓ ↓ FEV<sub>1</sub></p> <p>↓ ↓ ↓ ↓ FVC</p> <p><math>\frac{FEV_1}{FVC}</math> = normal</p>
V <sub>A</sub> PaO <sub>2</sub> PaCO <sub>2</sub>	<p>↓ V<sub>A</sub> → ↓ PaO<sub>2</sub></p> <p>→ ↑ PaCO<sub>2</sub></p> <p>↓ ↓ ↓ ↓ PaO<sub>2</sub> ↑ PaCO<sub>2</sub></p>	<p>↓ V<sub>A</sub> → ↓ PaO<sub>2</sub></p> <p>↓ ↓ ↓ ↓ PaO<sub>2</sub> ↑ PaCO<sub>2</sub></p>

\* Normal :  $\frac{FEV_1}{FVC} \rightarrow \frac{4,000}{5,000} = 80\%$

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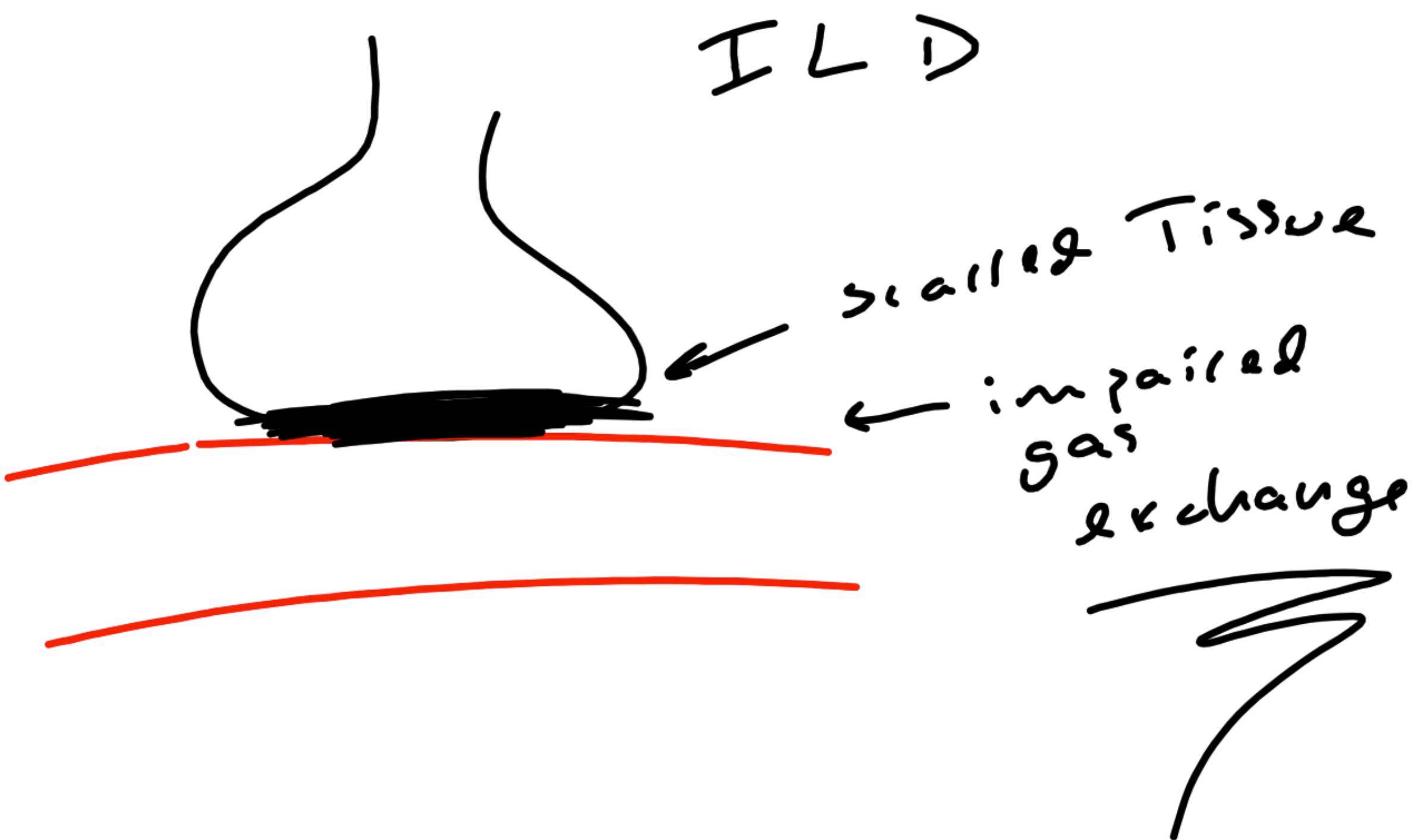
\* Obstructive :  $\frac{LLFEV_1}{LLFVC} \rightarrow \frac{1,000}{2,500} = 40\%$

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\* Restrictive :  $\frac{LLFEV_1}{LLFVC} \rightarrow \frac{2,000'}{2,500} = 80\%$

# Pulmonary Disease – Restrictive

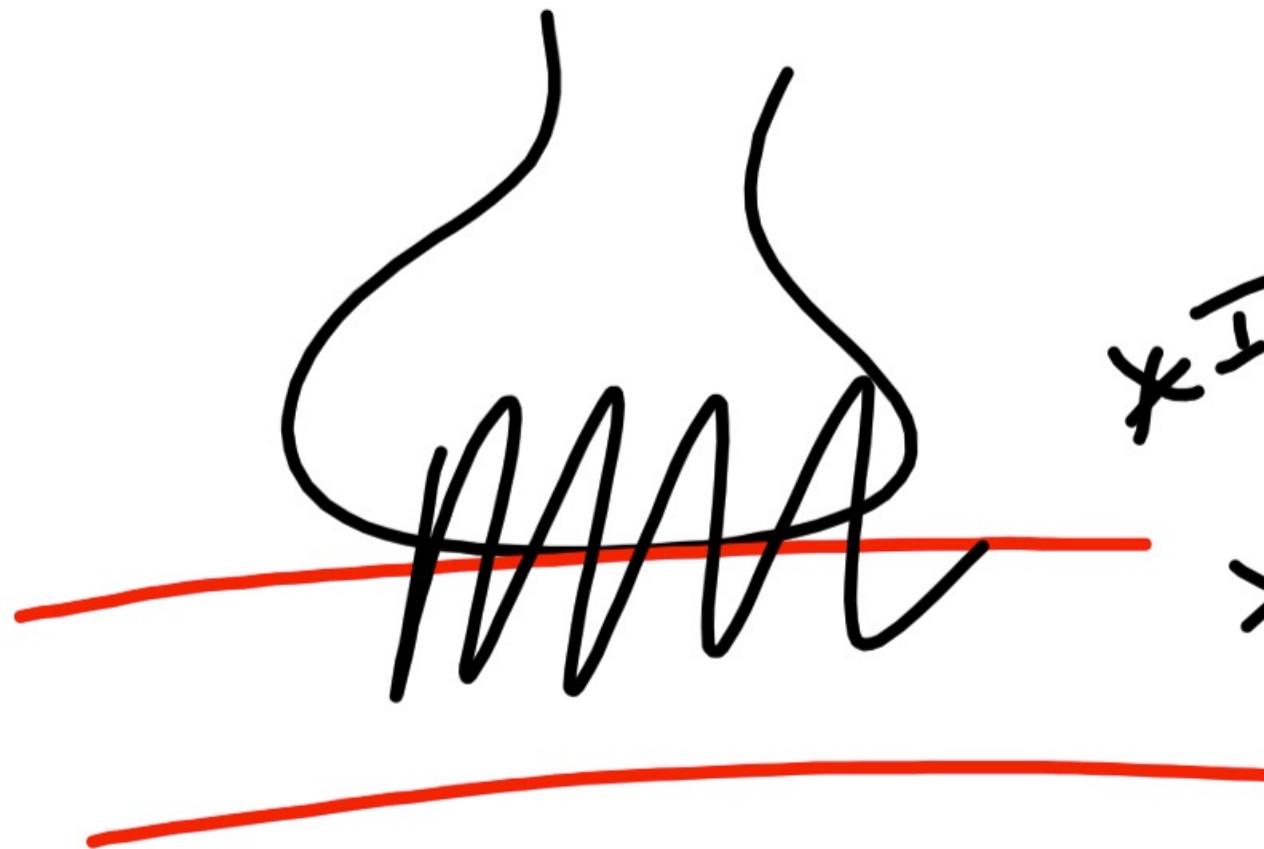
- Fibrotic Lung Disease / Interstitial Lung Disease
  - Lungs become fibrotic
    - Decrease in compliance
    - Failure of lungs to expand properly
      - Lowers ventilation
  - Fibrosis impairs gas exchange
    - Causes greater hypoxemia and hypercapnia
- Diseases that affect Respiratory Muscles
  - eg , amyotrophic lateral sclerosis , Guillain Barré , muscular dystrophy
  - Respiratory muscles unable to contract normally
    - Cannot produce normal changes in volume
      - Therefore , cannot cause appropriate changes in pressure
        - Lowers ventilation



# Pulmonary Disease – Restrictive

- Surfactant Deficiency Disorder
  - Most often seen in infants ( called infant respiratory distress syndrome )
  - Also called hyaline membrane disease
  - Lack of surfactant production
    - Decrease in compliance
    - Alveoli collapse
      - Lack of ventilation
- Acute Respiratory Distress Syndrome ( ARDS )
  - Diffuse alveolar and pulmonary capillary damage
    - Leads to fluid build up in alveoli
    - Decrease in compliance
    - Impairs gas exchange
      - Hypoxemia and hypercapnia

# ARDS



\* Impaired gas exchange  
\* Shift lung curv  
of excess fluid  
in lungs

# Sleep Apnea

- Sleep disorder characterized by apneic episodes
    - At least 5 per hour but can be greater than 100 per hour
    - Causes oxygen desaturation of approximately 3 to 4 %
  - Those afflicted are chronically tired
    - Do not get a restful night of sleep
  - Over 50% of those afflicted have hypertension
    - Most likely due to stimulation of sympathetics
      - Auto resuscitation reflex to breathe
        - Constant "startling"
      - Chemoreceptor reflex with increased level of  $CO_2$
      - Causes blood pressure to elevate
- Type Types :
    - Central Sleep Apnea
      - Loss in the drive to breathe
      - Respiratory network malfunctions
      - Central chemoreceptors malfunctions
    - Obstructive Sleep Apnea
      - Most prevalent type of sleep apnea (~ 90% of cases )
      - Physical obstruction of airways / collapse of airways
        - However , drive to breathe is present
        - Tend to snore
      - More prevalent in heavier individuals
        - Particularly heaviness at the face and neck

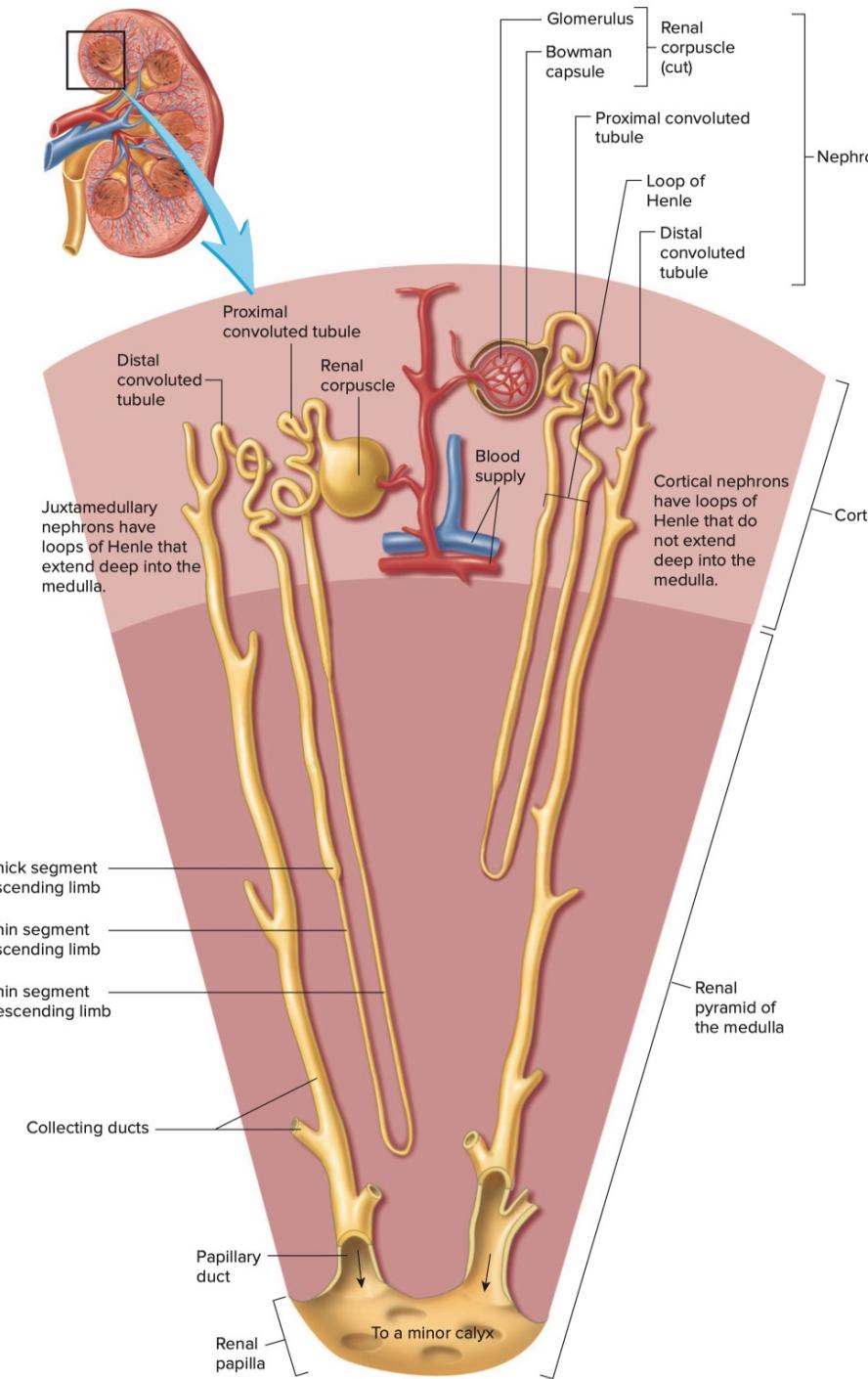
# Regulatory Functions of the Urinary System

- Regulates contents of blood
  - Maintains water and electrolyte balance
  - Maintains osmolarity of blood
  - Excretes wastes
- Regulates blood pressure
  - Via fluid volume and renin
- Regulates production of red blood cells
  - Erythropoietin
- Converts calcidiol into calcitriol ( most biologically active form of vitamin D<sub>3</sub> )

# Nephron

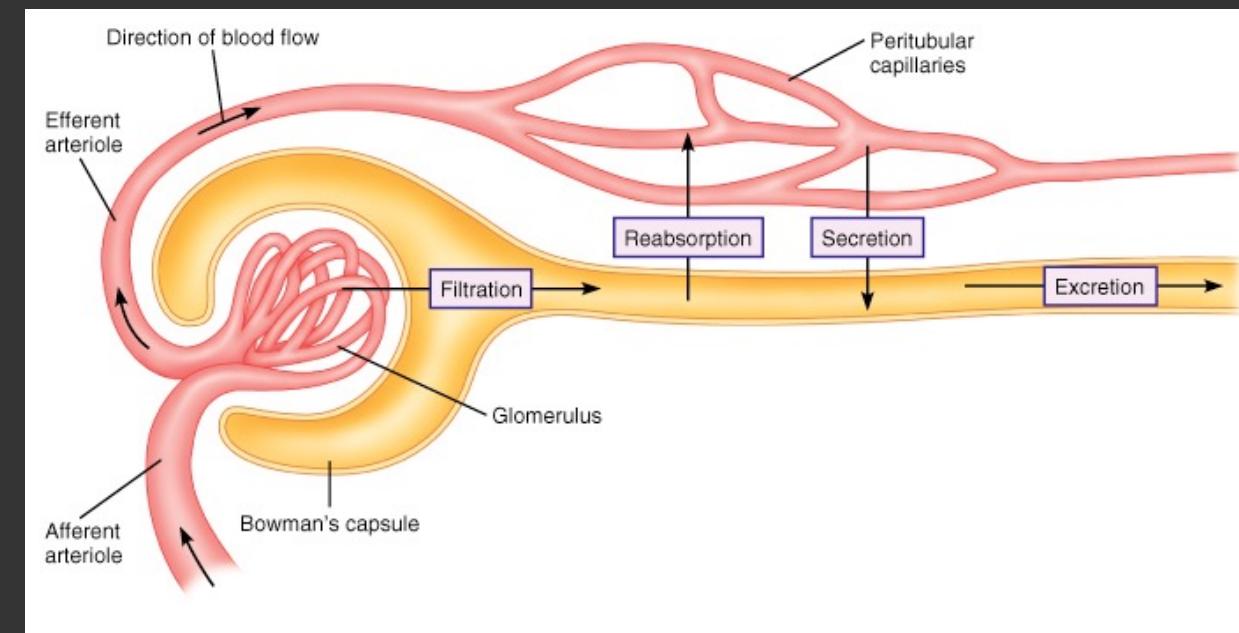
- Functional unit of the kidney
- Approximately one million per kidney
- Cortical Nephrons ( 80 % )
  - Bulk of nephron resides in cortex ( small portion descends into medulla )
  - Responsible for most regulatory functions
    - Accomplished via the functional relationship between the renal tubule and peritubular capillary
- Juxtamedullary Nephrons ( 20 % )
  - Descend deep within the medulla
  - Responsible for regulating osmolarity of the blood
    - Accomplished via the countercurrent exchanger
    - Structure made up of the loop of Henle and vasa recta

# Nephron

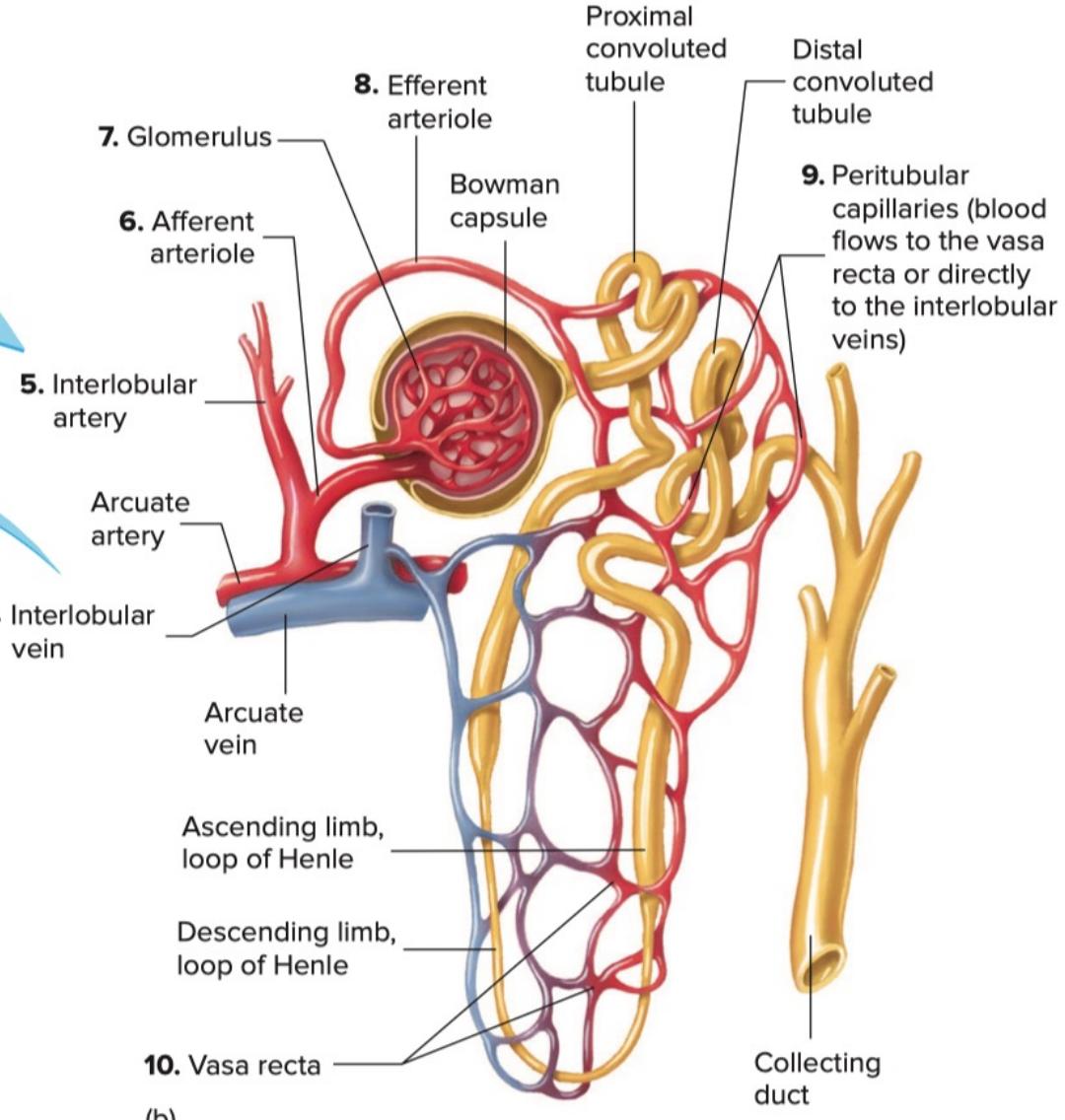
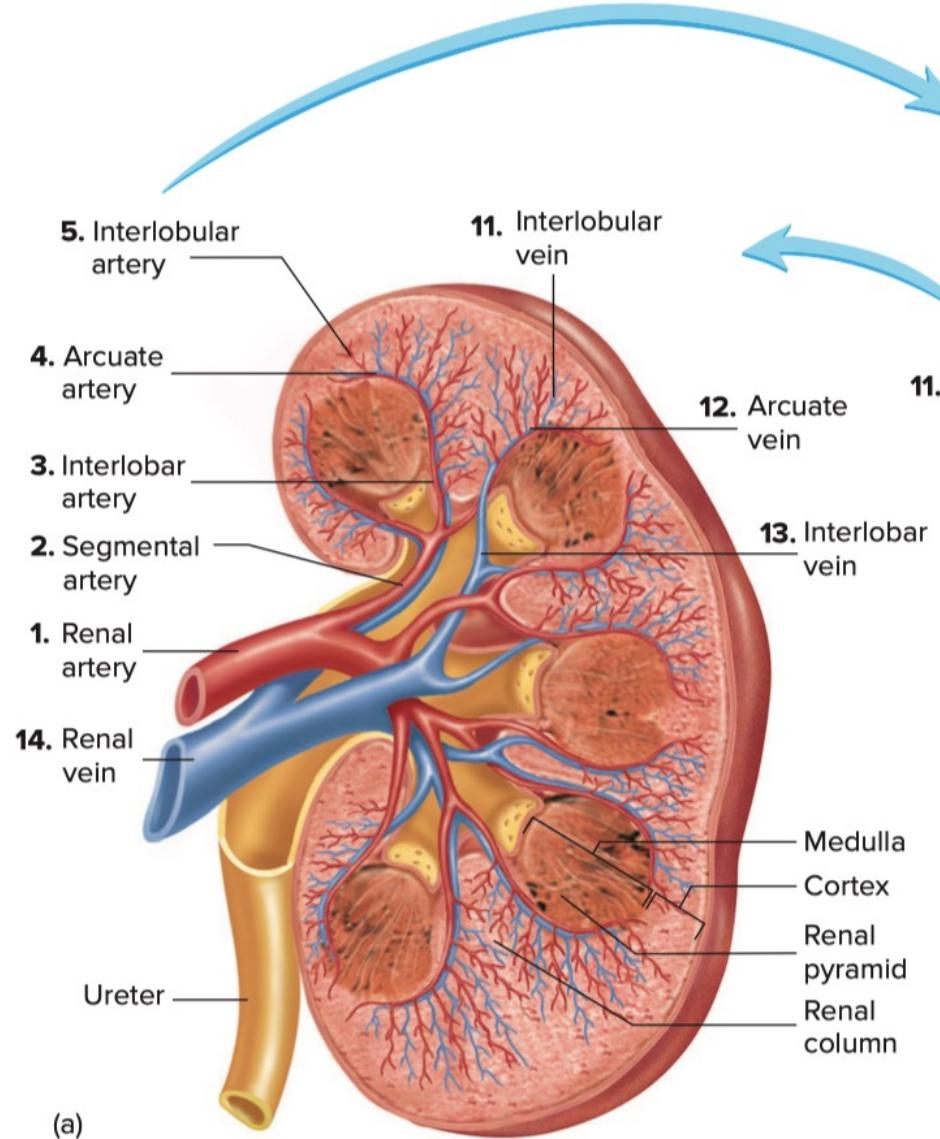


# Filtering of Blood

- Glomerular Filtration
  - Filtration of plasma
    - Glomerulus → Bowman's Capsule
- Tubular Reabsorption
  - Selective movement of filtrate
    - Keeps ion levels in blood normal
  - renal tubule → interstitial fluid → blood
- Tubular Secretion
  - Selective movement of substances
    - blood to interstitial fluid → renal tubule
  - Movement aided by active and passive processes
  - 20% of the plasma gets filtered per 1 run through the glomerulus

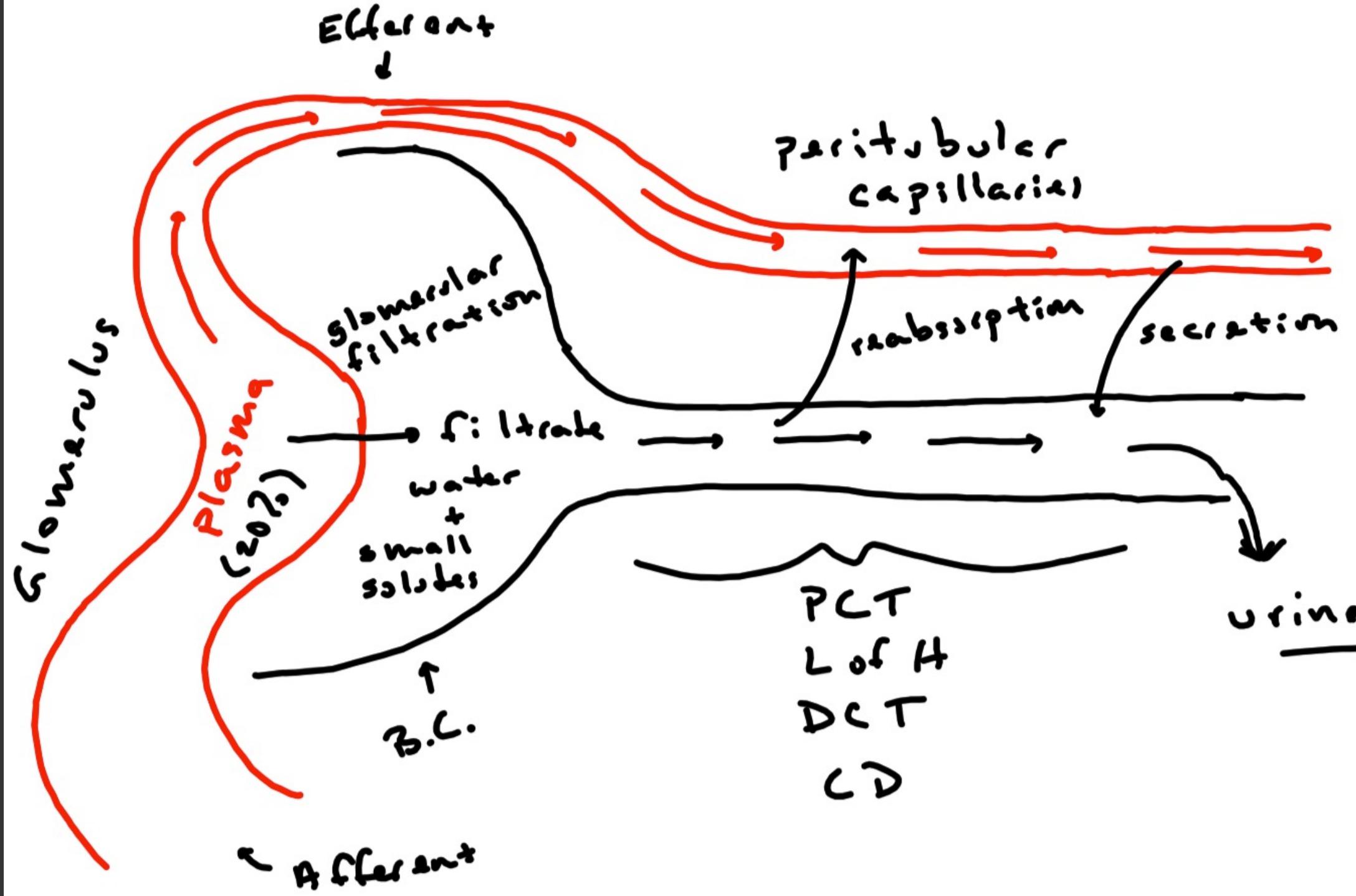


# Nephron



**FIGURE 26.7 Blood Flow Through the Kidney**

Numbers 1–14 show the sequence of blood flow through the kidney.  
(a) Blood flow through the larger arteries and veins of the kidney.  
(b) Blood flow through the arteries, capillaries, and veins that provide circulation to the nephrons.

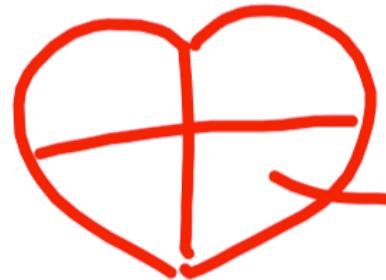


# Glomerular Filtration

- Filtration of plasma from glomerulus to Bowman's capsule
  - Fluid produced is known as the filtrate
    - Filtrate is devoid of large substances :
      - eg , RBCs , WBCs , platelets , protein , lipids
  - Glomerulonephritis = damage to the glomerulus
    - Large , otherwise restricted molecules are now filtered
    - eg , blood cells and / or proteins in urine ( hematuria and / or proteinuria )

# Glomerular Filtration Rate ( GFR )

- Renal Blood Flow Rate
  - Volume of blood that flows through the kidneys per minute
  - Product of the renal fraction ( ~ 20% ) and cardiac output
    - Renal fraction : percent of cardiac output that flows to kidneys , 20%
  - Renal blood flow rate = ( ~ 5,000 mL / min ) \* 20 %  $\approx$  1,000 mL / minute
- Renal Plasma Flow Rate
  - Volume of plasma that flows through the kidney per minute
  - Product of renal blood flow rate and plasma concentration
    - Plasma concentration is approximately 55 %
      - Can be calculated by : 100 % minus hematocrit
  - Renal Plasma Flow = ( 1,000 mL / minute ) \* 55 %  $\approx$  550 mL / minute
- Glomerular Filtration Rate ( GFR )
  - Volume of plasma that is filtered by the glomeruli per minute
    - Fluid known as filtrate
  - Product of renal plasma flow and filtration fraction ( ~ 20 % )
    - Filtration Fraction = percent of plasma that is filtered
  - $GFR = ( 550 \text{ mL / min} ) * 20 \% \approx 110 \text{ mL / minute}$
  - Therefore , ~ 110 mL of filtrate is produced per minute
    - This translates into ~ 160 liters / day , but 99% gets reabsorbed back into blood stream



C.O.  $\rightarrow$  5,000 ml blood/min

) 20% to the kidneys,  
(renal fraction)

RBF = 1,000 ml blood/min to the kidneys,  
55% of blood is plasma

Kidneys  
RPFR = 550 ml plasma/min

| 20% gets filtered  
(filtration fraction)

GFR = 110 ml filtrate/min

\* CHF  $\rightarrow$   $\downarrow CO \rightarrow \downarrow GFR$

\* Exercise  $\rightarrow$   $\uparrow CO$

$\hookrightarrow$  most will go to muscles

$\hookrightarrow$  less to kidneys

$\hookrightarrow$   $\downarrow GFR$

# How to Interpret GFR

- Normal GFR :

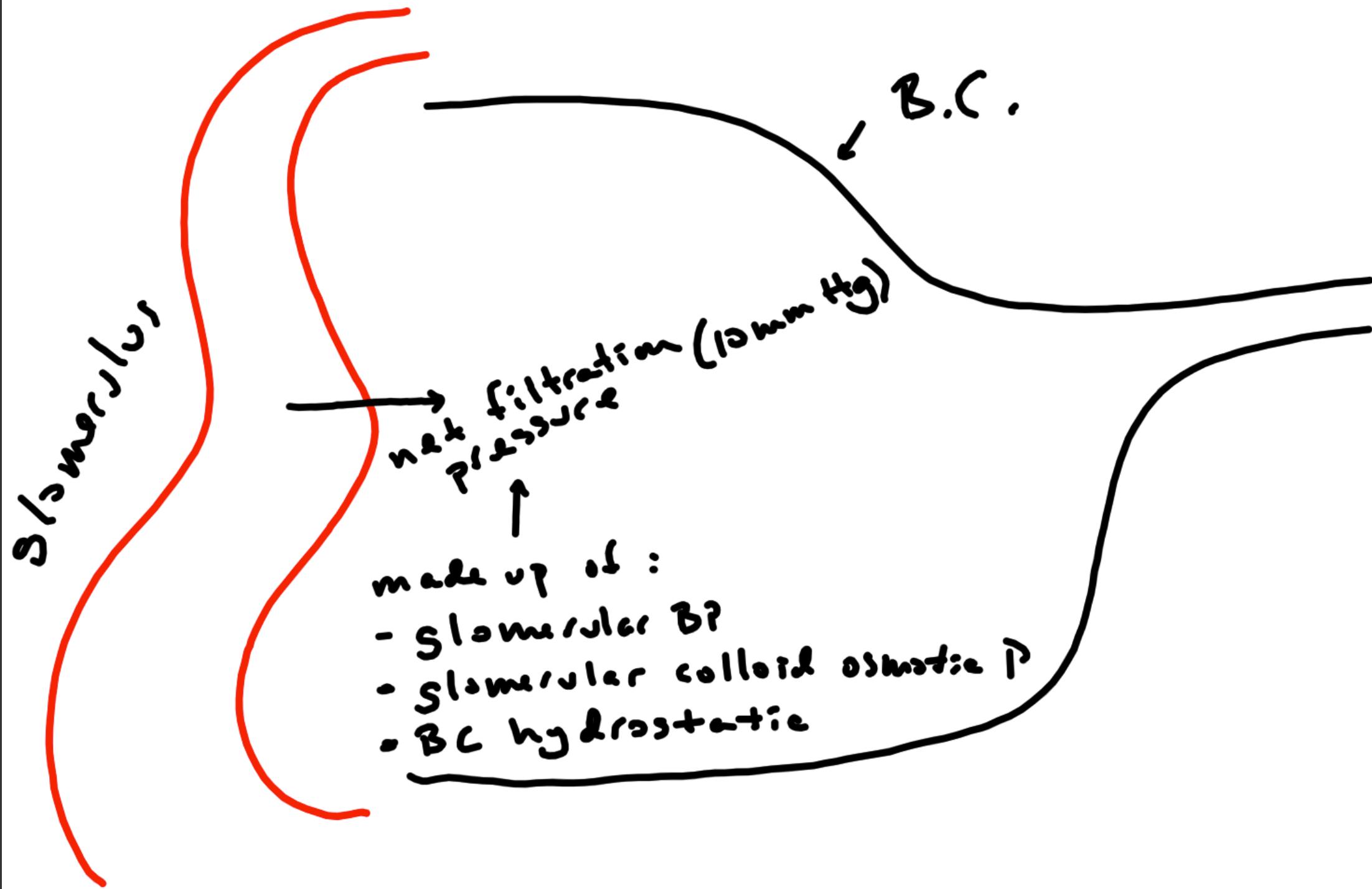
- Above 90 mL / min for most
- As low as 60 mL / min is still normal if there is no sign of kidney issues

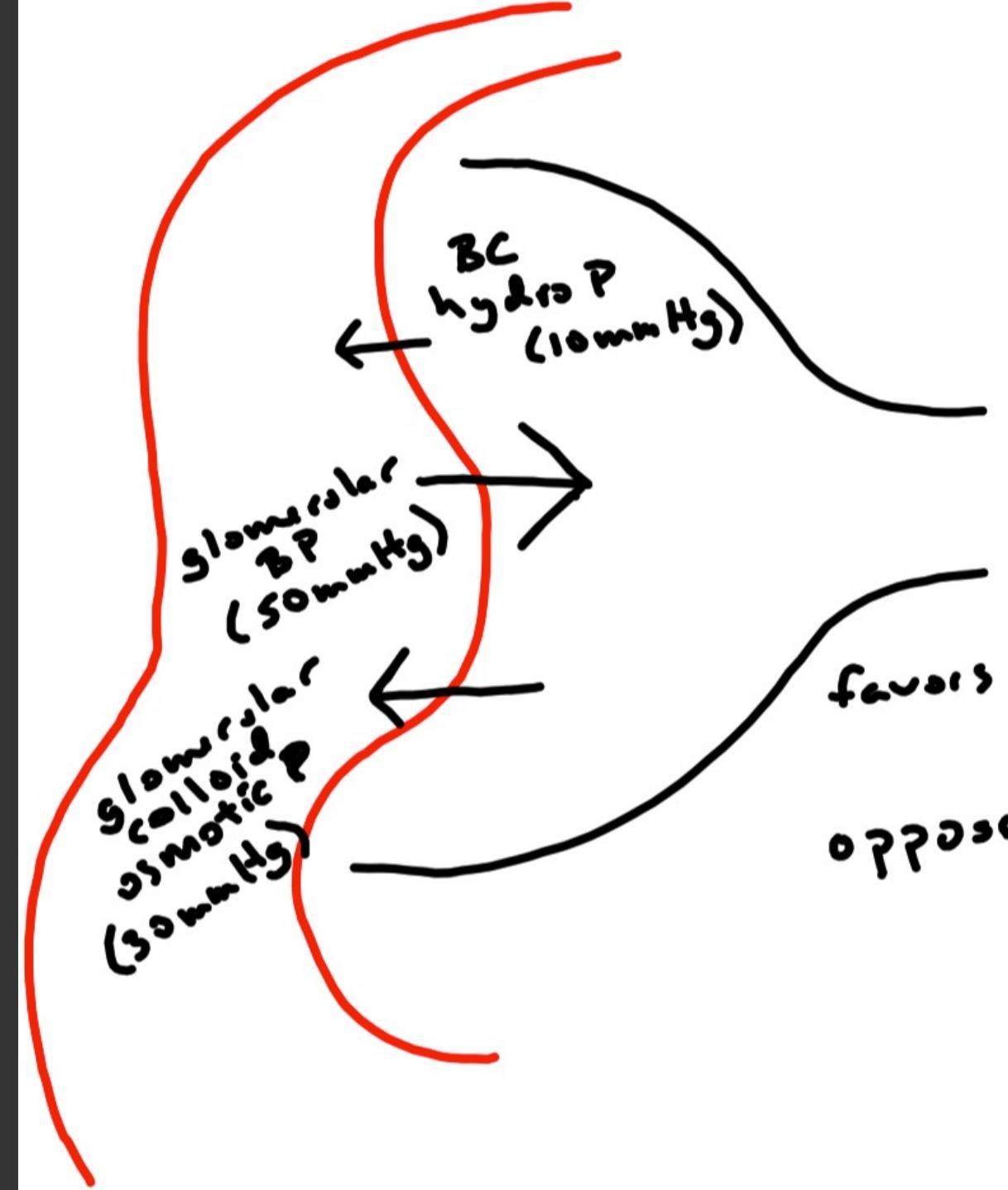
- Abnormal GFR :

- Below 60 mL / min = kidney damage
- Below 15 mL / min = end stage kidney disease

# Efficiency of Glomerular Filtration Rate

- Glomerulus is under high hydrostatic pressure
  - Efferent arteriole is smaller than afferent arteriole
    - Allows for positive net filtration pressure
- Glomerulus is highly coiled
  - Increases surface area
- Glomerulus is highly permeable
- Net Filtration Pressure :
  - Force favoring filtration versus force opposing filtration
    - Glomerular blood pressure ( favors ) ~ 50 mm Hg
    - Plasma colloid osmotic pressure ( opposes ) ~ 30 mm Hg
    - Bowman's capsule hydrostatic pressure ( opposes ) ~ 10 mm Hg
  - $\therefore \text{net filtration pressure} = 50 \text{ mm Hg} - ( 30 \text{ mm Hg} + 10 \text{ mm Hg} ) = 10 \text{ mm Hg}$ 
    - $\therefore 10 \text{ mm Hg}$  force that favors filtration
  - Filtration occurs if positive , net pressure



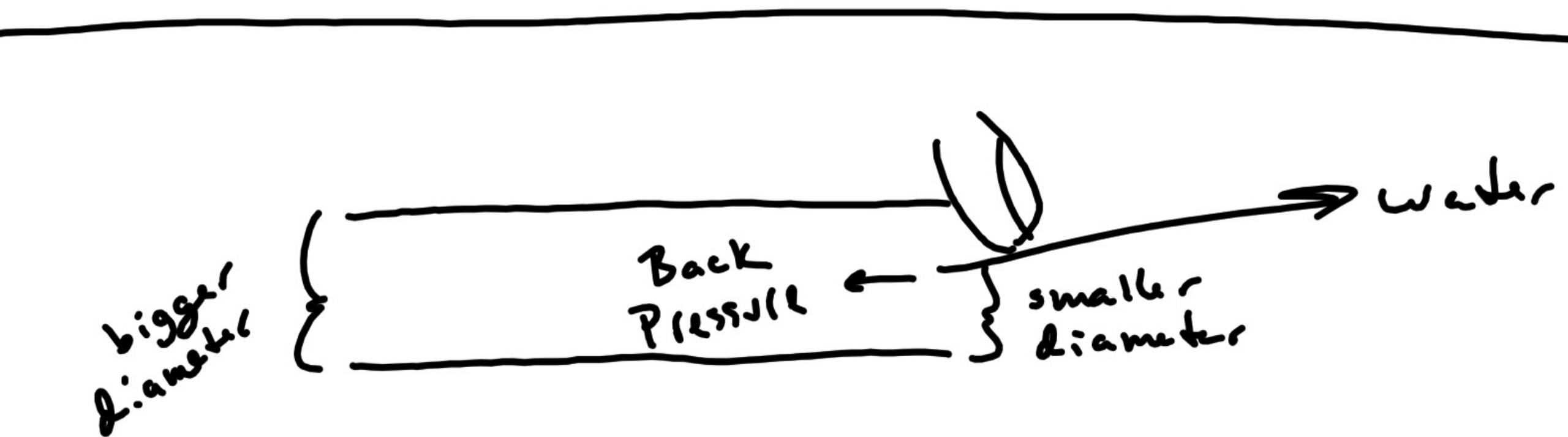
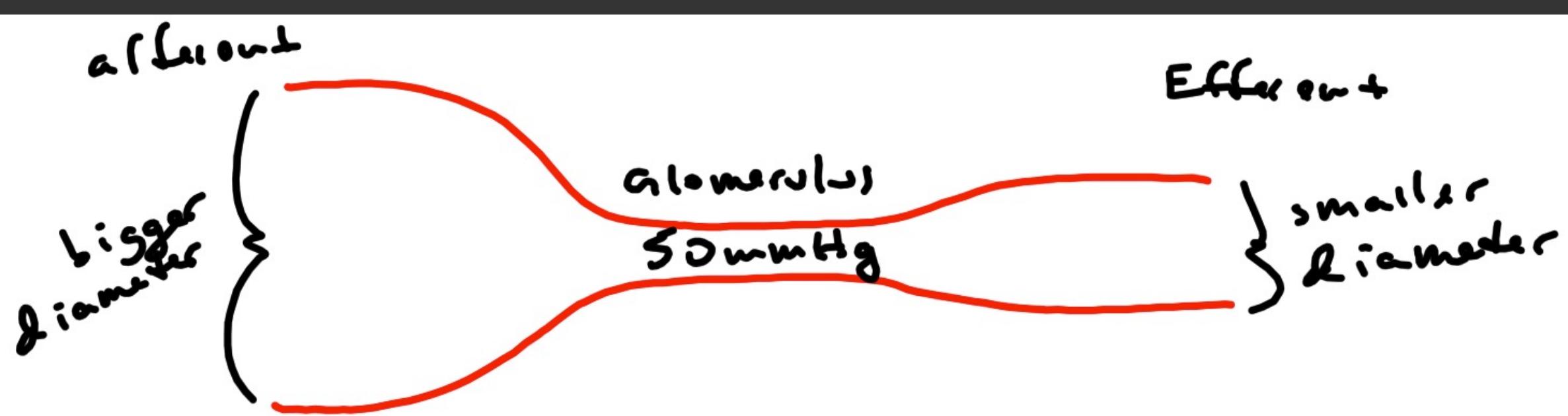


Net Filtration Pressure

favors → - glomerular BP : + 50 mm Hg  
- glomerular OP : - 30 mm Hg  
- BC hydro P : - 10 mm Hg

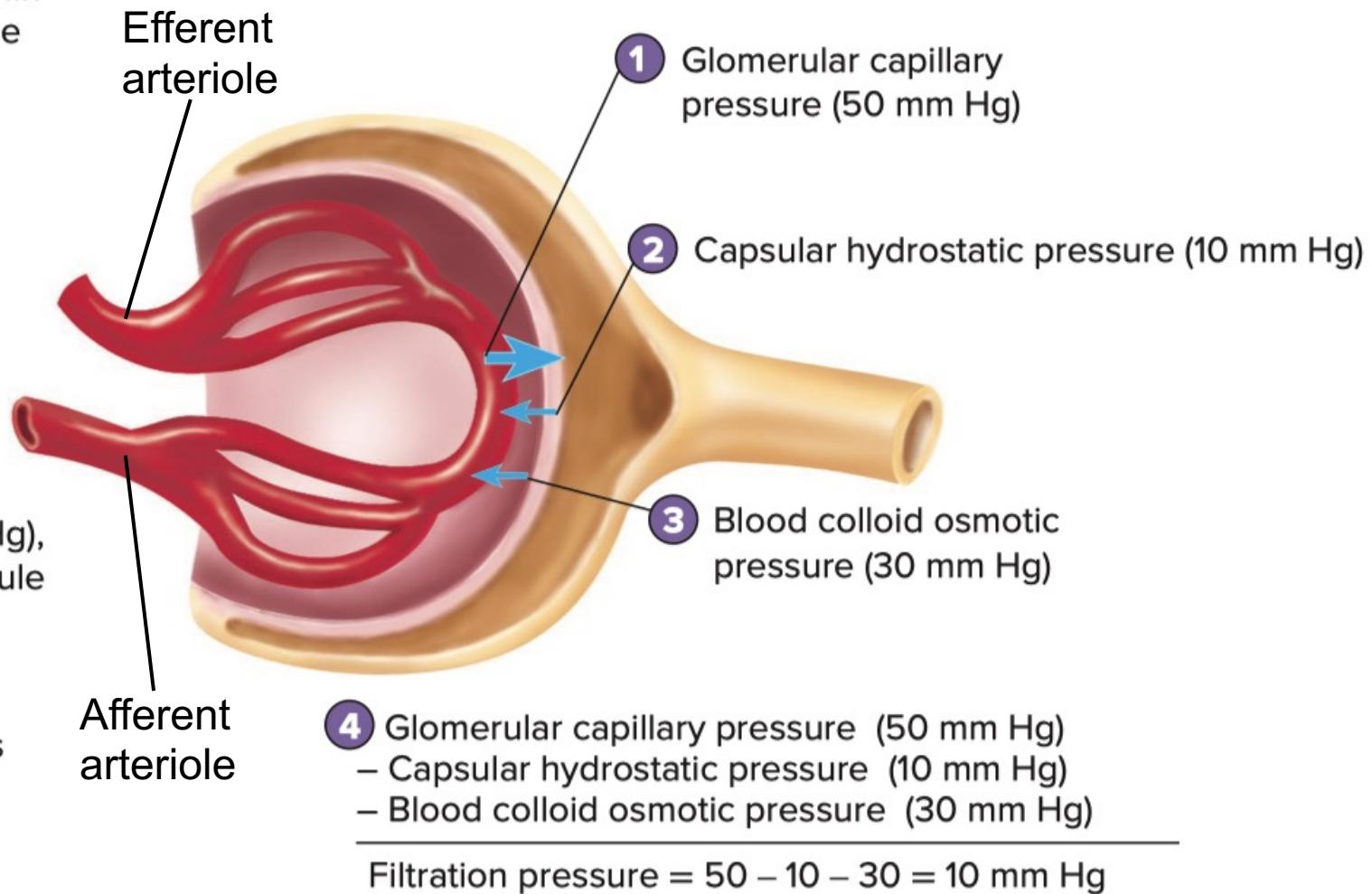
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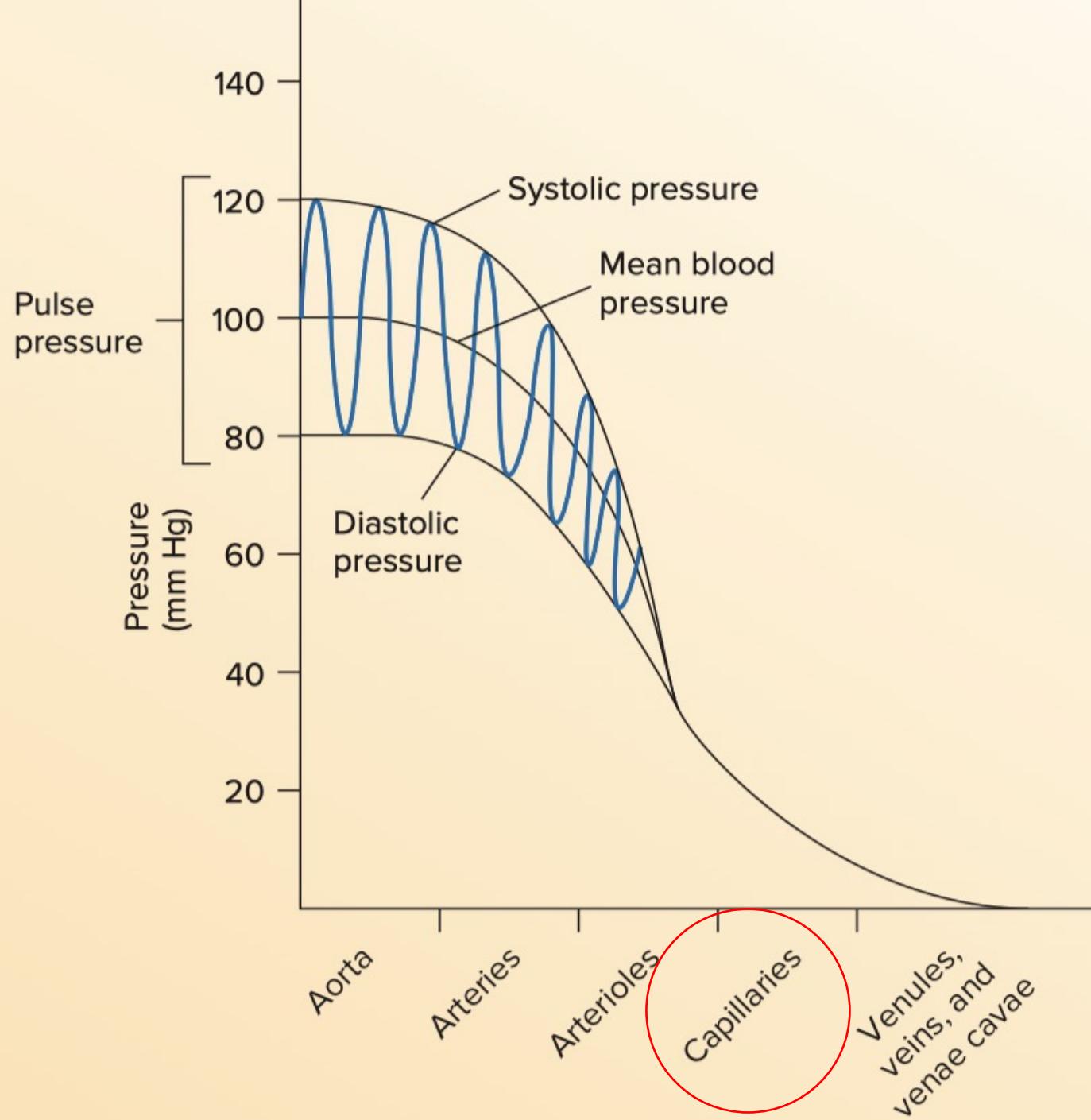
Oppose { + 10 mm Hg



# Net Filtration Pressure

- 1 Glomerular capillary pressure (GCP), the blood pressure (50 mm Hg) within the glomerulus, moves fluid from the blood into the Bowman capsule.
- 2 Capsular hydrostatic pressure (CHP), the fluid pressure inside the Bowman capsule (10 mm Hg), moves fluid from the Bowman capsule into the blood.
- 3 Blood colloid osmotic pressure (BCOP), produced by the concentration of blood proteins in the glomerular capillaries (30 mm Hg), moves fluid from the Bowman capsule into the blood by osmosis.
- 4 Filtration pressure is equal to the glomerular capillary pressure minus the capsular hydrostatic and blood colloid osmotic pressures.



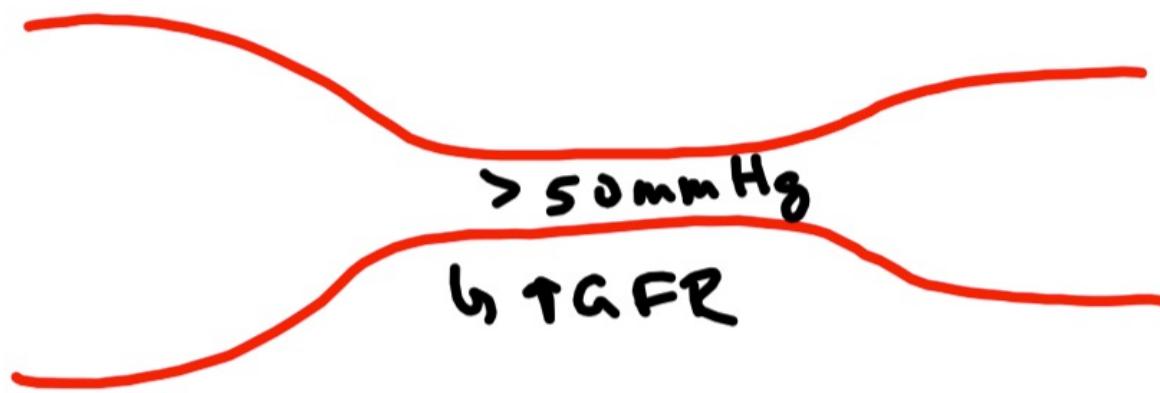


# Autoregulation of Glomerular Filtration

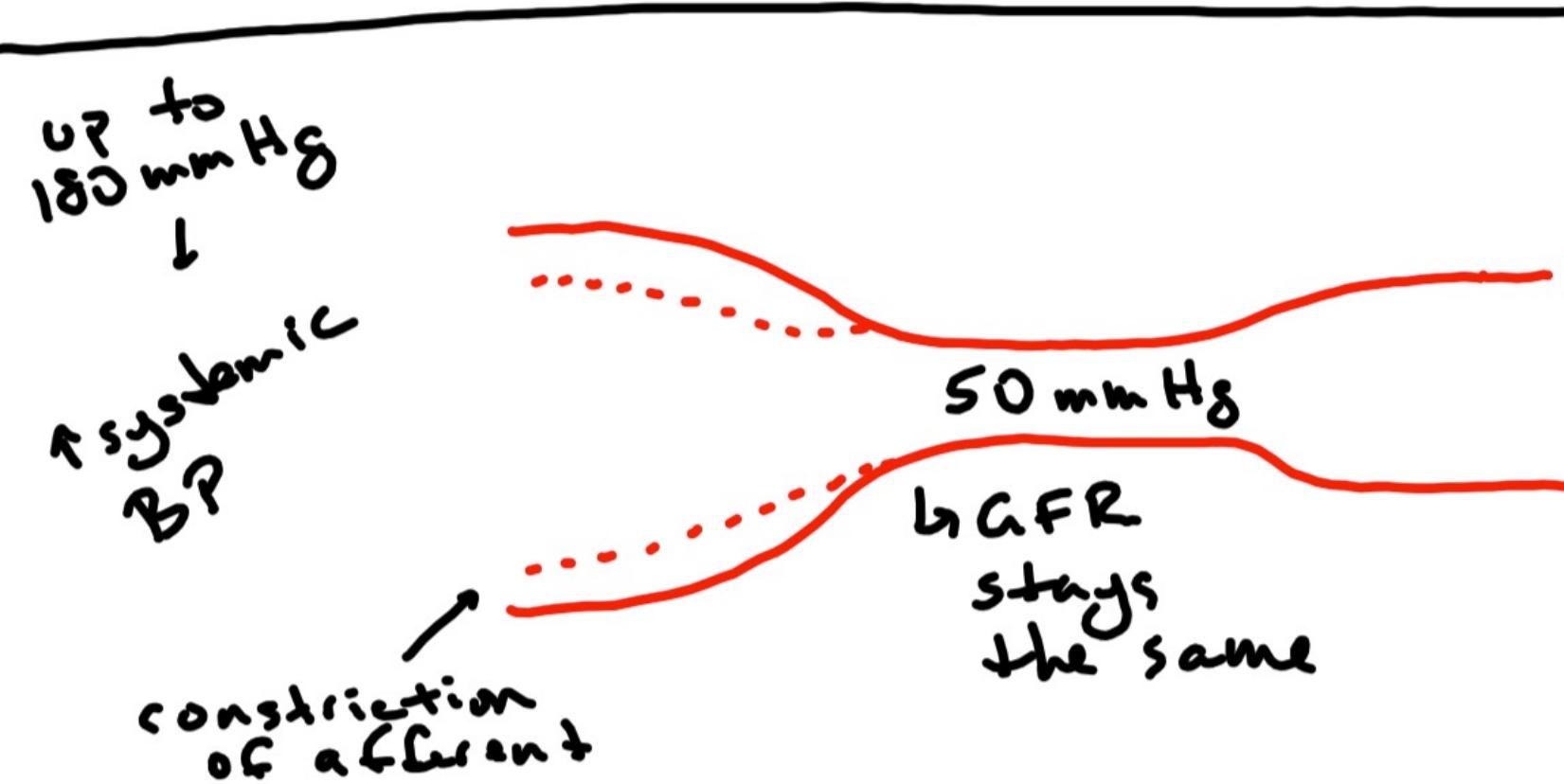
- Attempts to maintain a constant GFR
  - If GFR is too high , the kidneys are working too hard
  - If GFR is too low , the kidneys are not filtering plasma properly
- Involves changes in the degree of constriction of the afferent arteriole
  - In response to changes in blood pressure and filtrate flow
- Constant GFR is maintained with blood pressure of 90 to 180 mm Hg

# Autoregulation of Glomerular Filtration

- With an increase in systemic blood pressure :
  - This should cause an increase in GFR , but it does not ... Why?
  - Causes constriction of afferent arteriole to keep GFR constant
    - Maintains a normal glomerular blood pressure
      - Helps maintain a constant GFR
    - Maintains a normal renal plasma flow
      - Helps maintain a constant GFR
- With a decrease in systemic blood pressure :
  - This should cause a decrease in GFR , but it does not ... Why?
  - Causes dilation of afferent arteriole to keep GFR constant
    - Maintains a normal glomerular blood pressure
      - Helps maintain a constant GFR
    - Maintains a normal renal plasma flow
      - Helps maintain a constant GFR

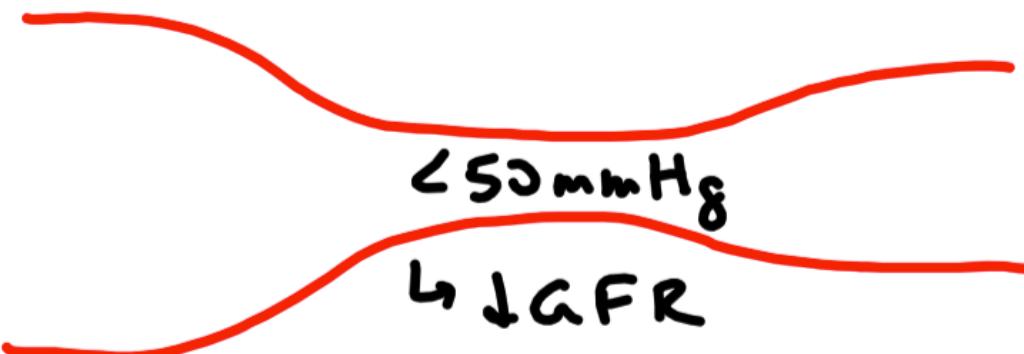


w/o autoregulation



w. autoregulation

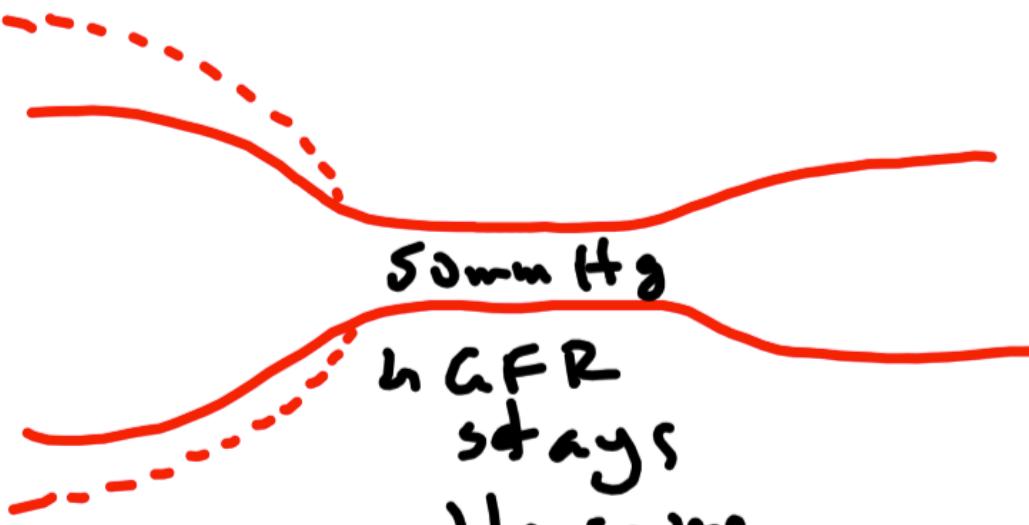
$\downarrow$  systemic  
BP



w/o  
auto regulation

down to  
90 mmHg  
 $\downarrow$   
systemic  
BP

dilation of afferent  $\rightarrow$



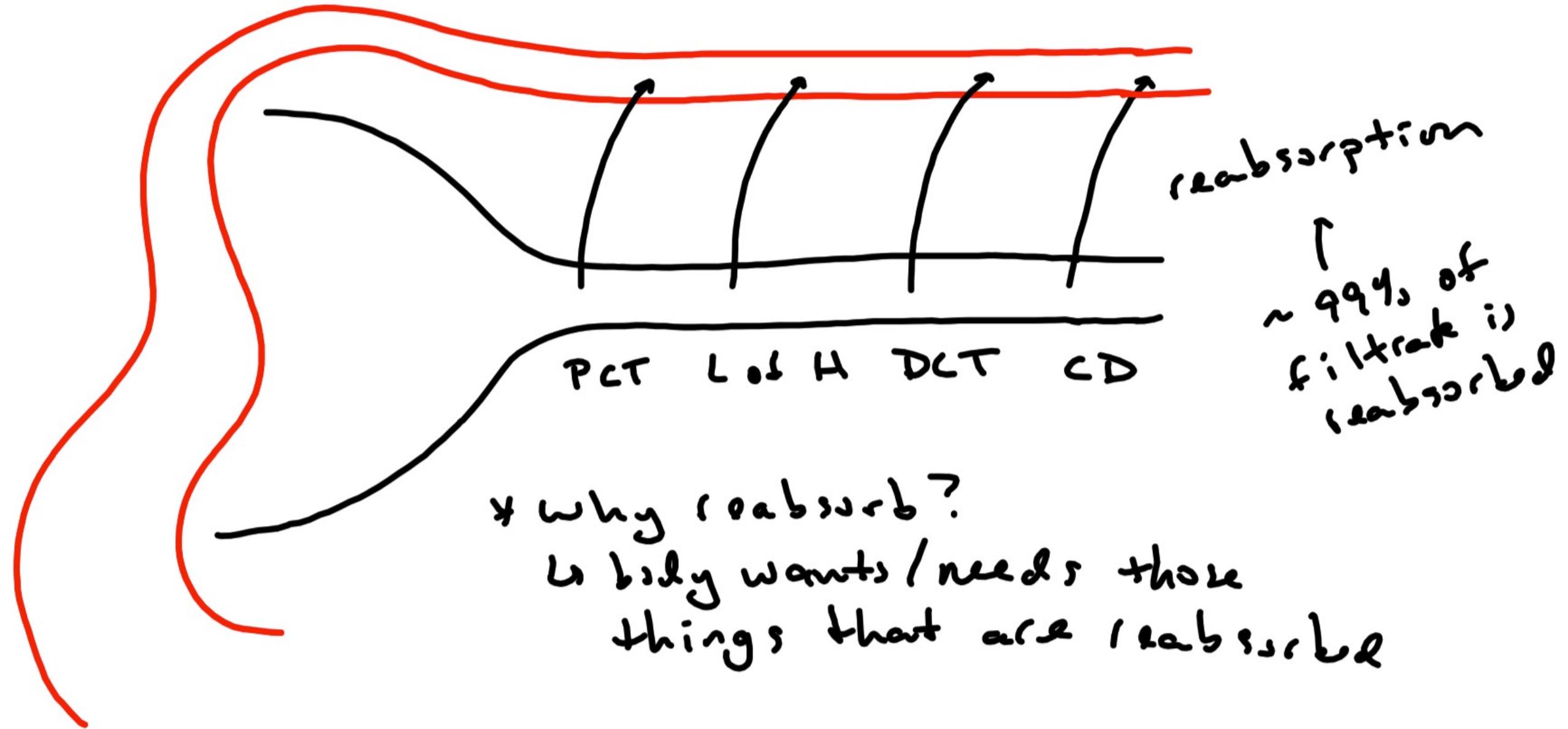
w.  
auto regulation

# Tubular Reabsorption

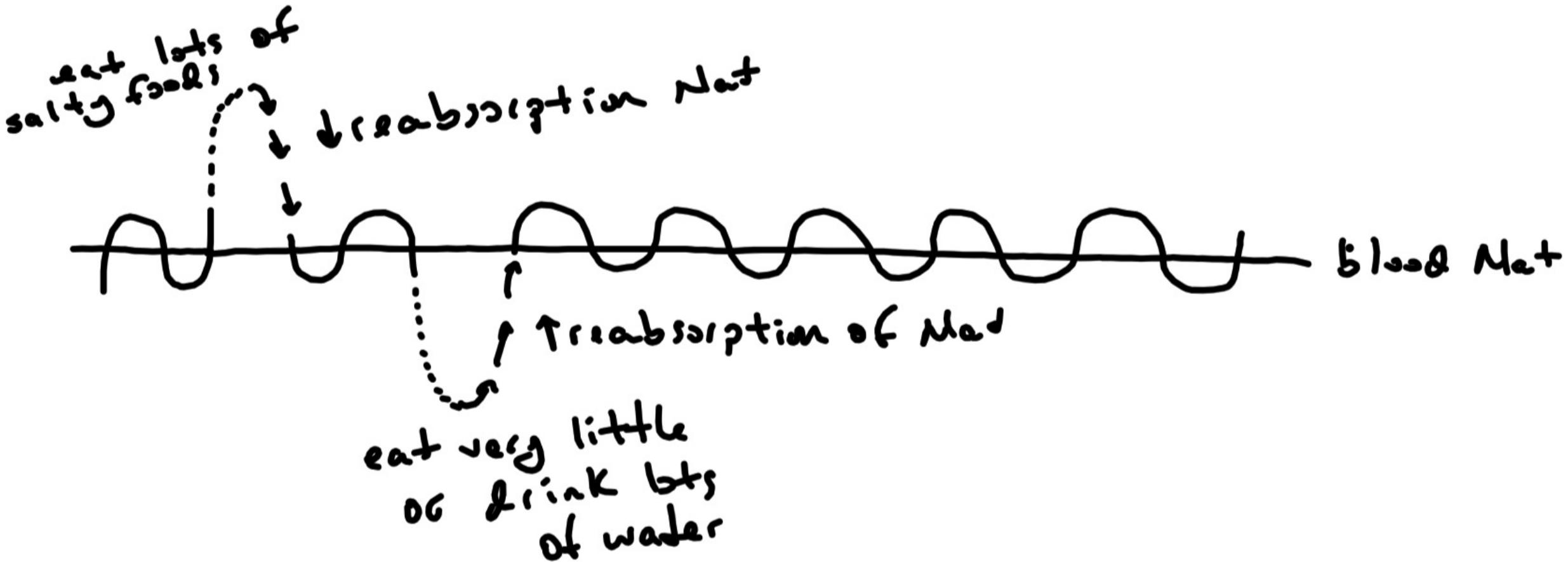
- 99 % of filtrate is reabsorbed
- Movement of water and solutes from renal tubule into peritubular capillaries
  - Reabsorption is enhanced in the peritubular capillaries
    - Peritubular capillaries are very permeable
- Highly selective
- Increased reabsorption of molecule “X” causes an increase in blood [ X ]
- Decreased reabsorption of molecule “X” causes a decrease in blood [ X ]

# Tubular Reabsorption

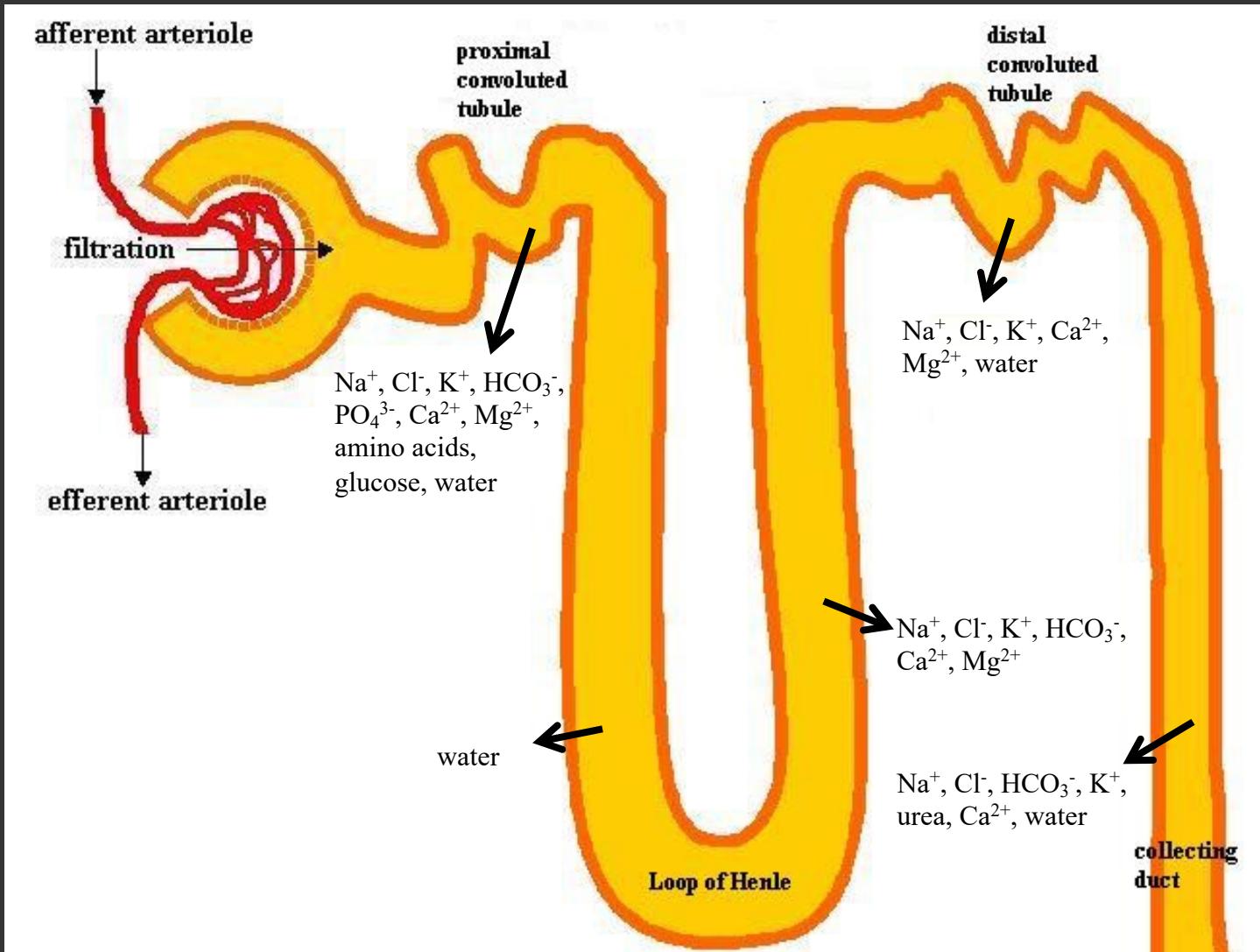
- Proximal convoluted tubule
  - $\text{Na}^+$ ,  $\text{Cl}^-$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ ,  $\text{Mg}^{2+}$ ,  $\text{HCO}_3^-$ ,  $\text{PO}_4^{3-}$ , amino acids, glucose, water
    - Water follows solutes osmotically
- Loop of Henle
  - Thin Segments
    - Descending Limb
      - Highly permeable to water
    - Ascending Limb
      - Impermeable to water
  - Thick Ascending Limb
    - $\text{Na}^+$ ,  $\text{Cl}^-$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ ,  $\text{Mg}^{2+}$ ,  $\text{HCO}_3^-$
    - Impermeable to water
- Distal convoluted tubule
  - $\text{Na}^+$ ,  $\text{Cl}^-$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ ,  $\text{Mg}^{2+}$ , water ( follows solutes osmotically )
- Collecting duct
  - $\text{Na}^+$ ,  $\text{Cl}^-$ ,  $\text{HCO}_3^-$ ,  $\text{K}^+$ , urea,  $\text{Ca}^{2+}$ , water ( follows solutes osmotically )



- \* ↑ reabsorption of  $X \rightarrow$  ↑ level of  $X$  in blood
- \* ↓ reabsorption of  $X \rightarrow$  ↓ level of  $X$  in blood



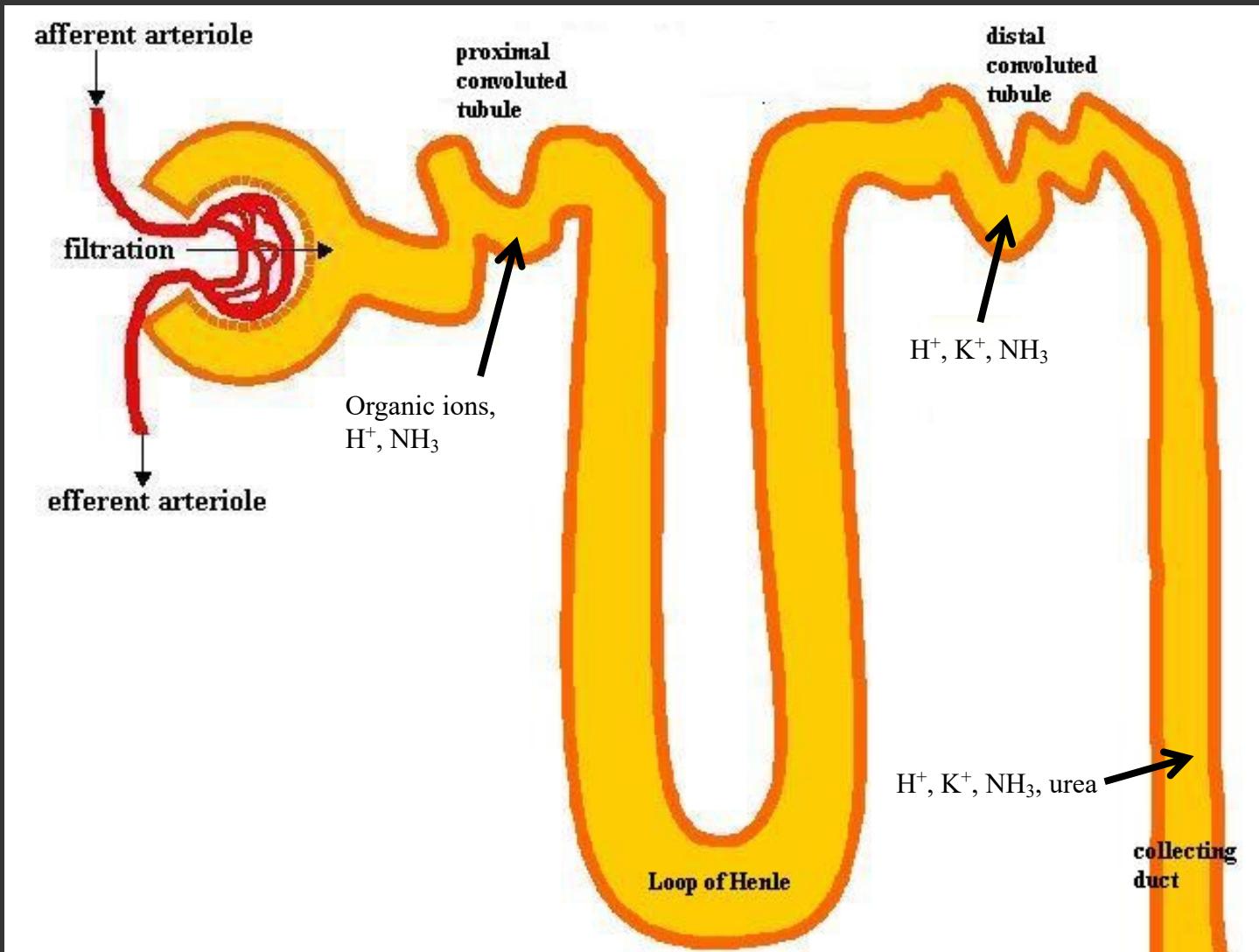
# Reabsorption

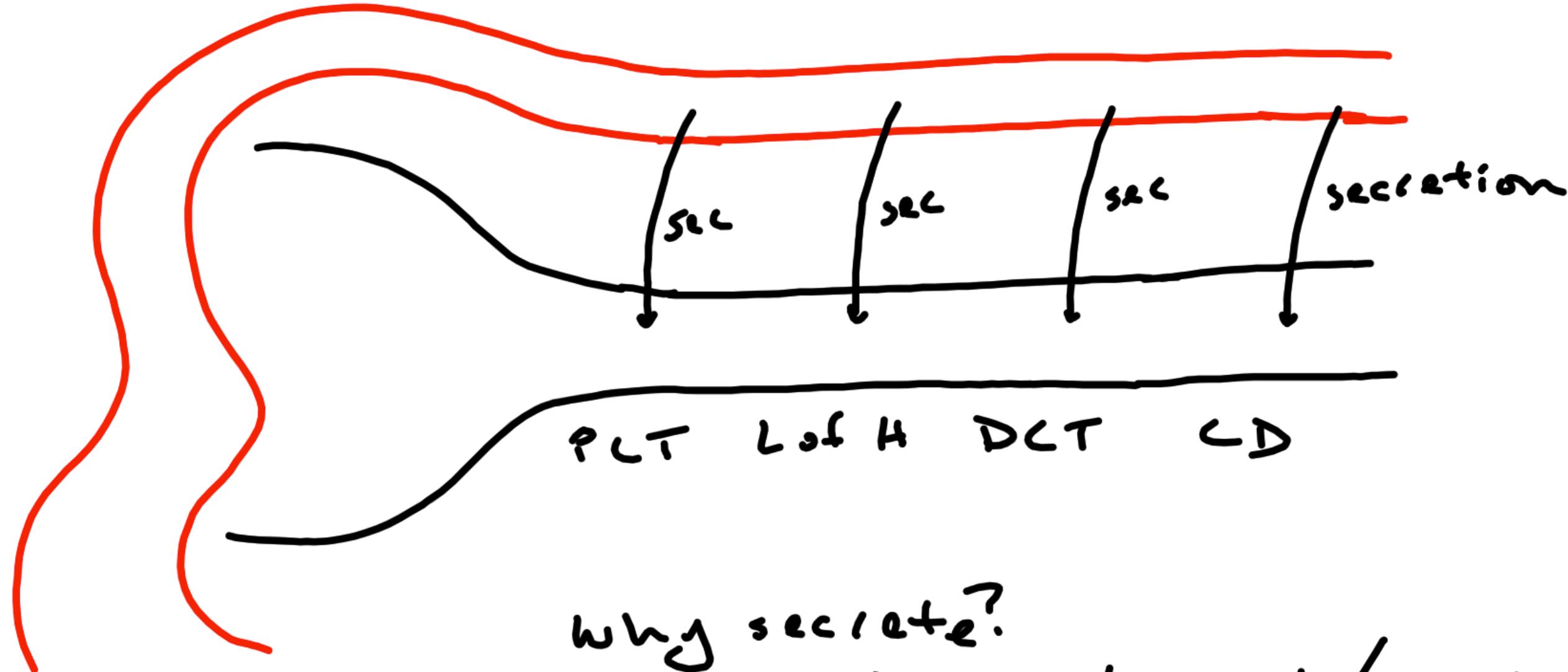


# Tubular Secretion

- Substances secreted into renal tubule from peritubular capillaries
- Mechanisms same as tubular reabsorption but in reverse direction
- Increased secretion of molecule “X” causes a decrease in blood [ X ]
- Decreased secretion of molecule “X” causes an increase in blood [ X ]
  
- Proximal Convoluted Tubule :
  - Organic ion transport
    - Cotransports organic acids with  $\text{Na}^+$ 
      - eg , uric acid , bile acids , antibiotics , creatinine , “drugs”
    - $\text{H}^+$  ,  $\text{NH}_3$  ( ammonia )
- Distal Convoluted Tubule :
  - $\text{H}^+$  ,  $\text{K}^+$  ,  $\text{NH}_3$  ( majority of  $\text{NH}_3$  secretion )
- Collecting Duct :
  - $\text{H}^+$  ,  $\text{K}^+$  ,  $\text{NH}_3$  , urea

# Secretion





why secrete?

body does not want/need  
what it is secreting

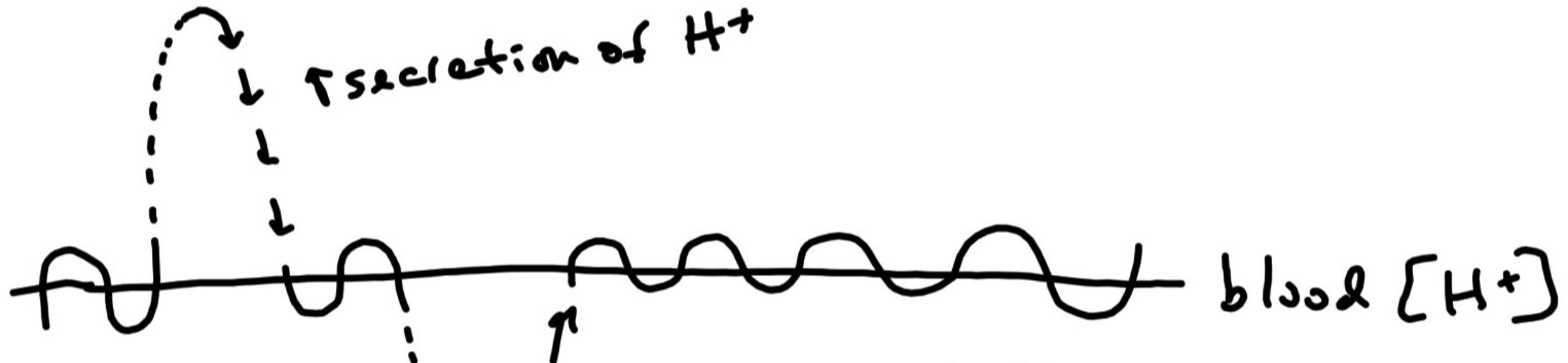
If ↑ secretion of X

↳ ↓ level of X in the blood

If ↓ secretion of X

↳ ↑ level of X in the blood

Ketoacidosis  $\leftarrow \uparrow [H^+]: \downarrow pH$



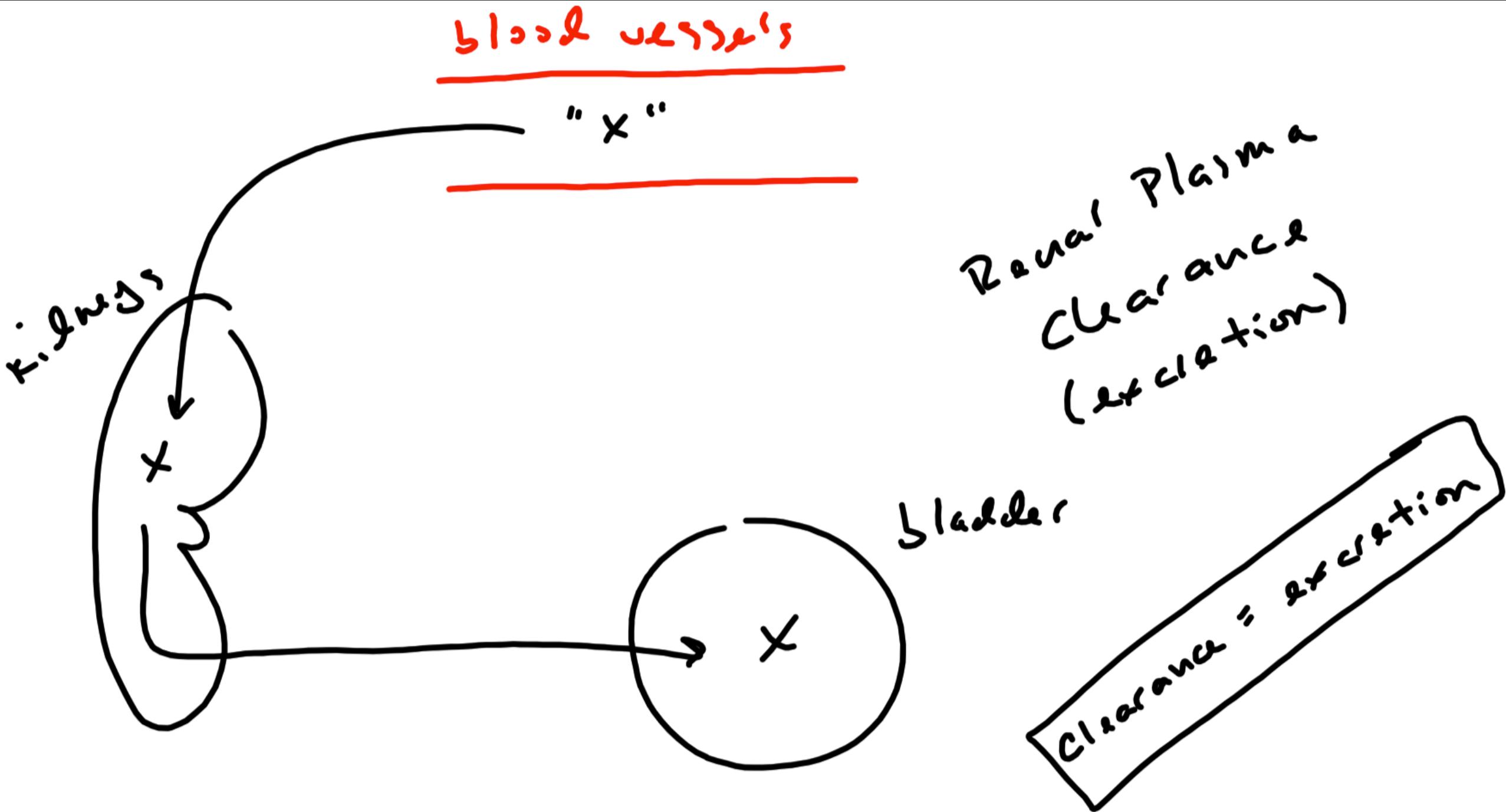
↓ secretion of H<sup>+</sup>

↑ secretion of H<sup>+</sup>

gastric vomiting  $\leftarrow \downarrow [H^+]: \uparrow pH$

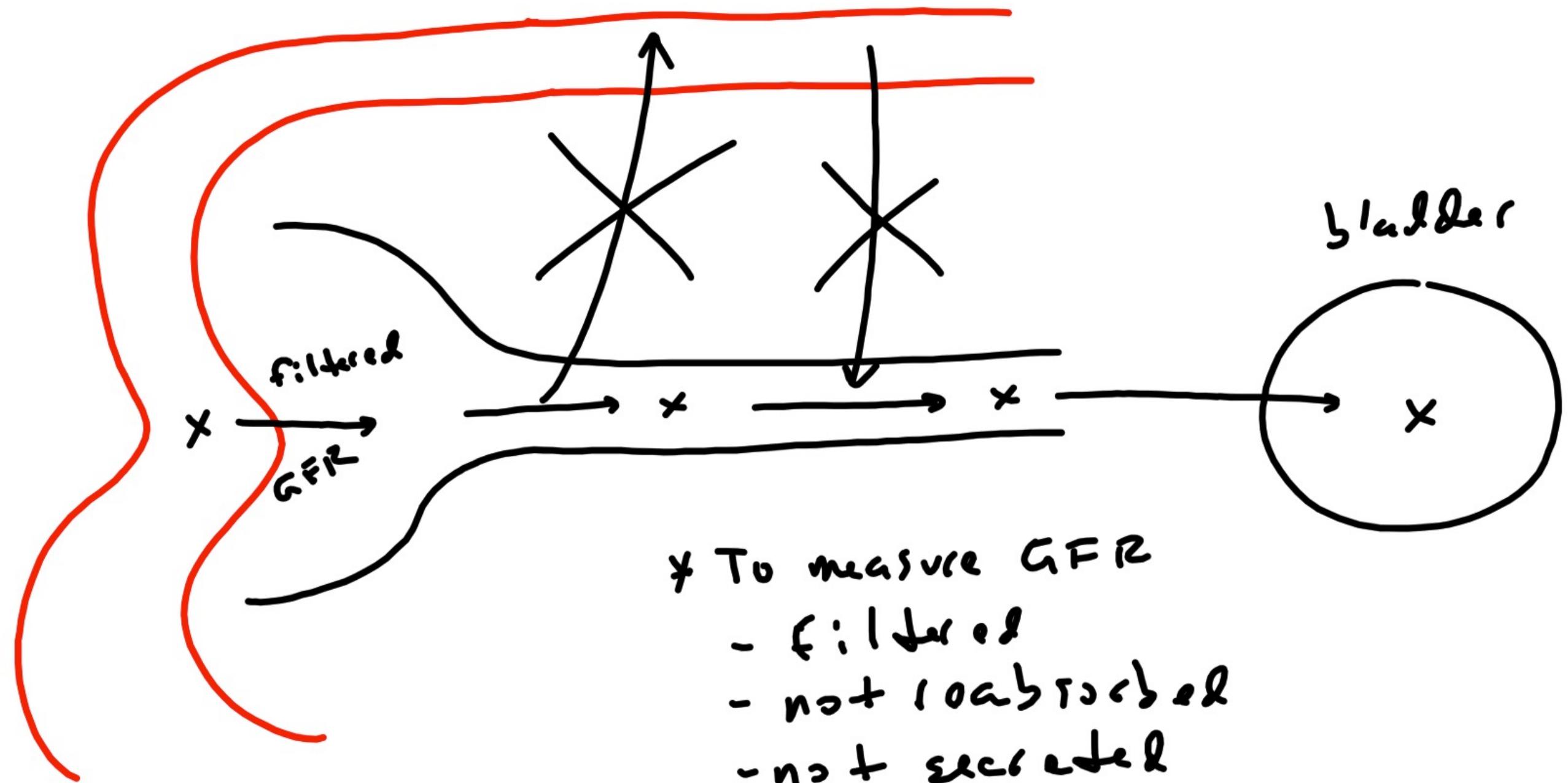
# Clearance to Estimate GFR

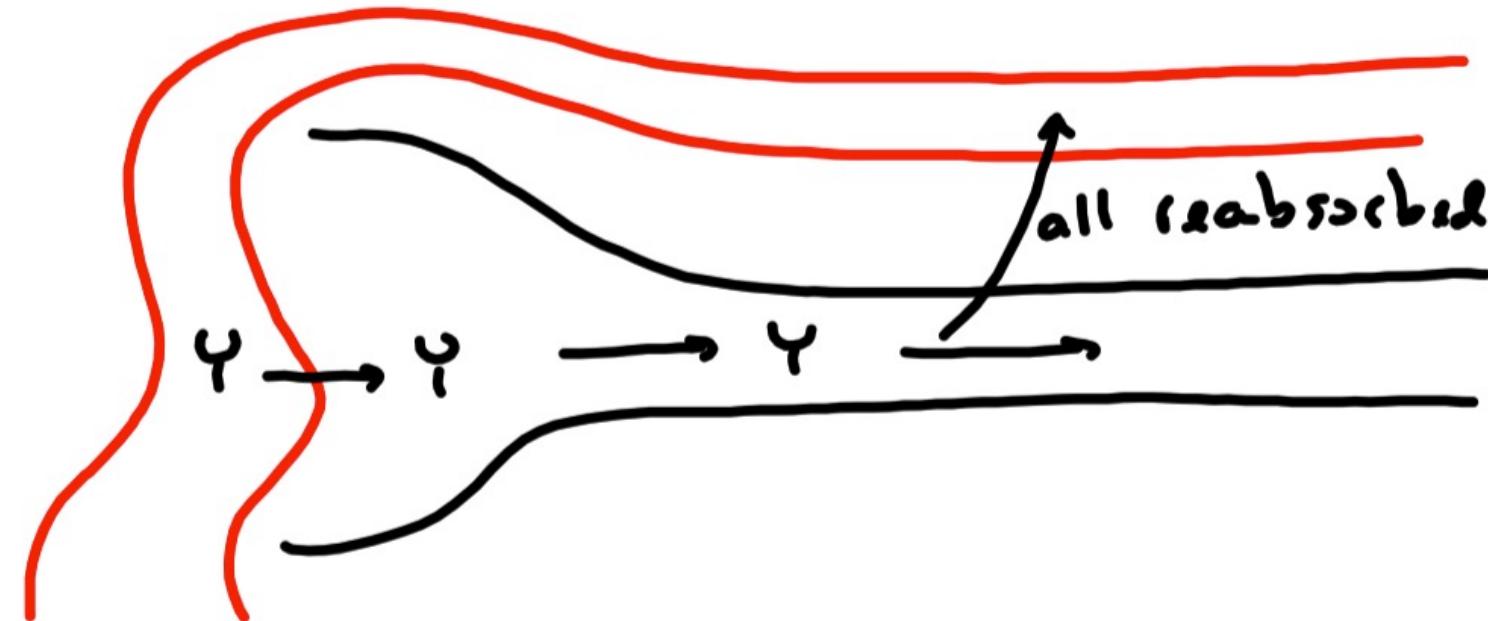
- Need a substance that is :
  - Freely filtered
  - Not reabsorbed
  - Not secreted
- Creatinine closely meets the above criteria
  - Produced naturally in the body as a waste product of the phosphagen system
  - Used routinely to calculate GFR



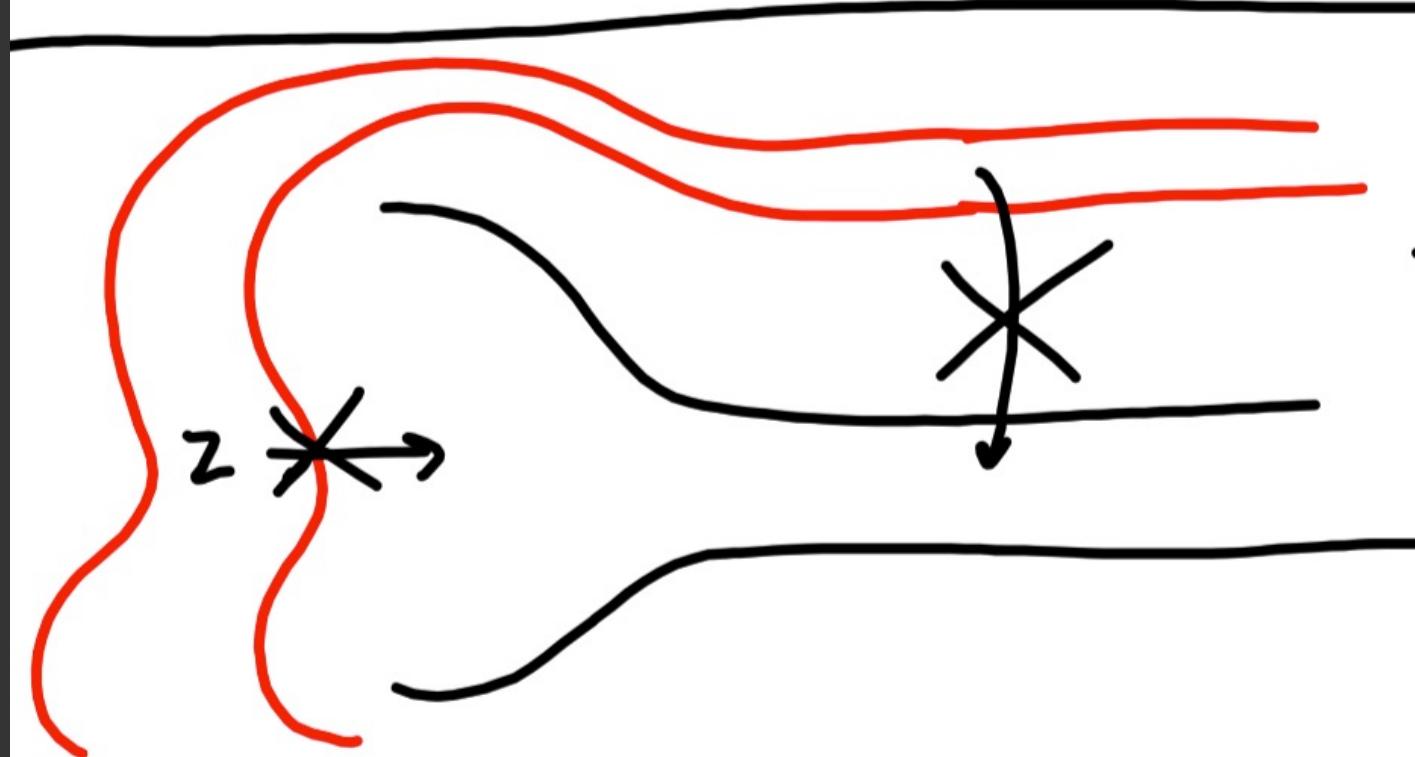
# Clearance to Estimate Renal Plasma Flow

- Need a substance that is :
  - Freely filtered
  - Not reabsorbed
  - Completely secreted
- Para-aminohippurate ( PAH ) comes close to meeting the above criteria





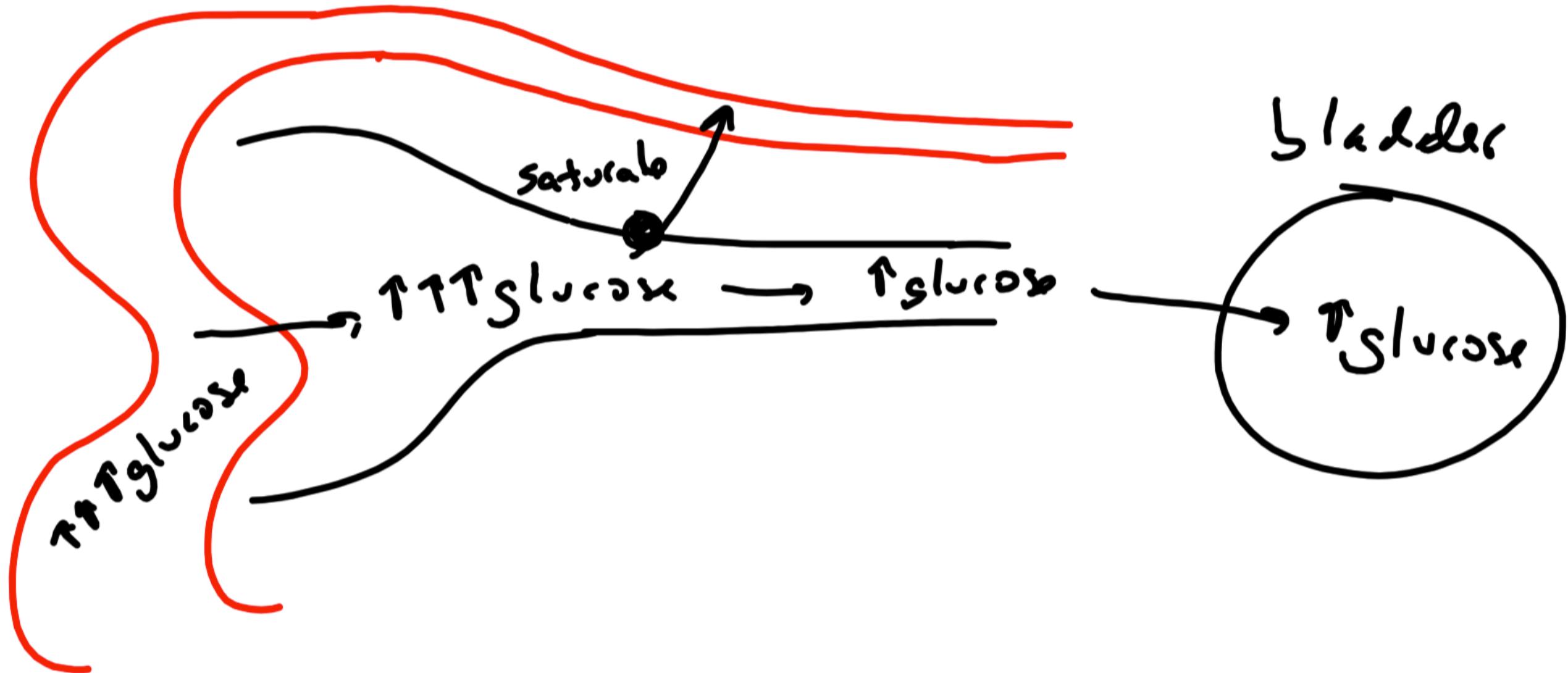
e.g. glucose  
bladder

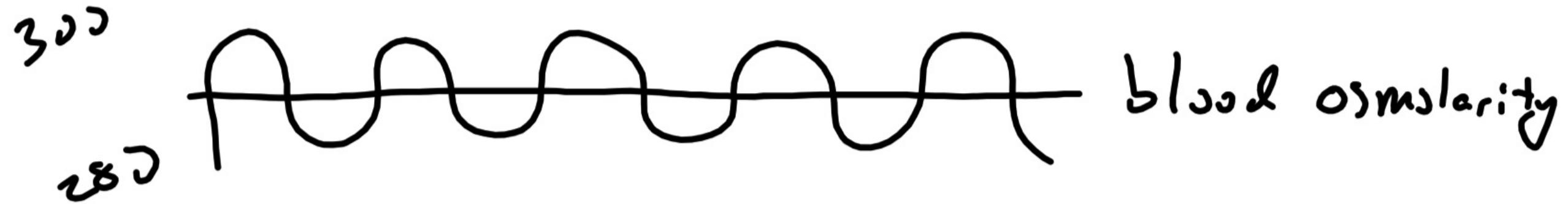


e.g. protein  
bladder



# Unterschied Diabetes Mellitus





# Summary of Clearance

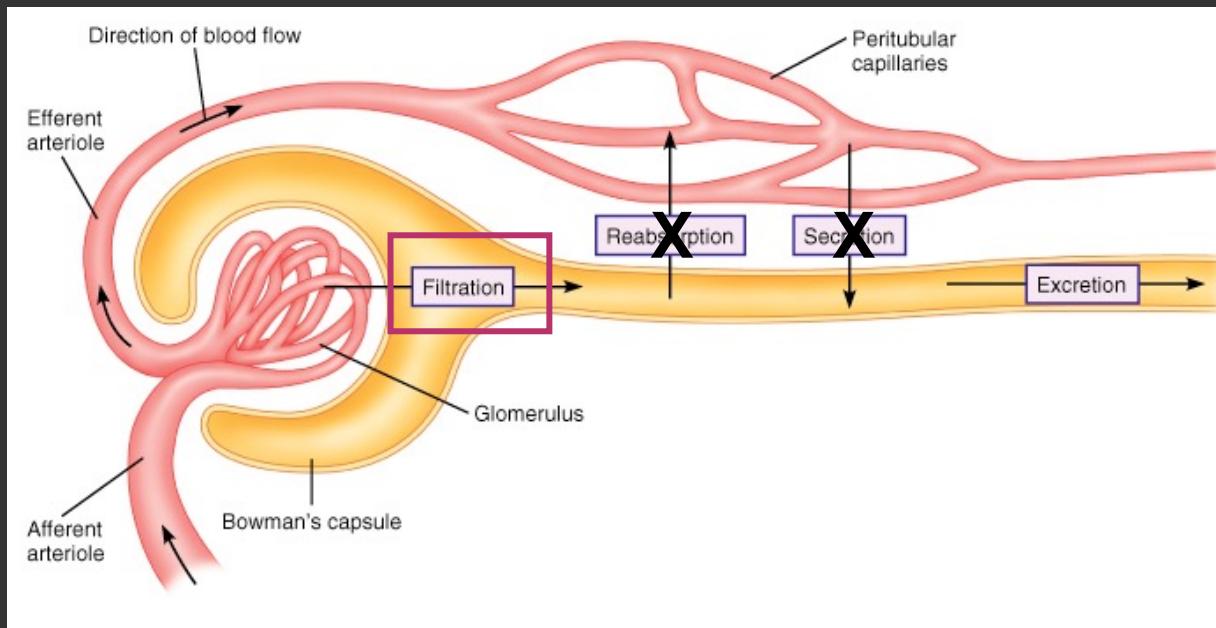
- If clearance equals GFR :
  - Substance is completely filtered and not reabsorbed and not secreted
- If clearance is zero :
  - Substance has been fully reabsorbed and not secreted
    - OR
  - not filtered and not secreted and not reabsorbed

# If Clearance Equals GFR

- Substance is completely filtered and not reabsorbed and not secreted
- Clearance of inulin ( clinically , clearance of creatine used to estimate GFR )

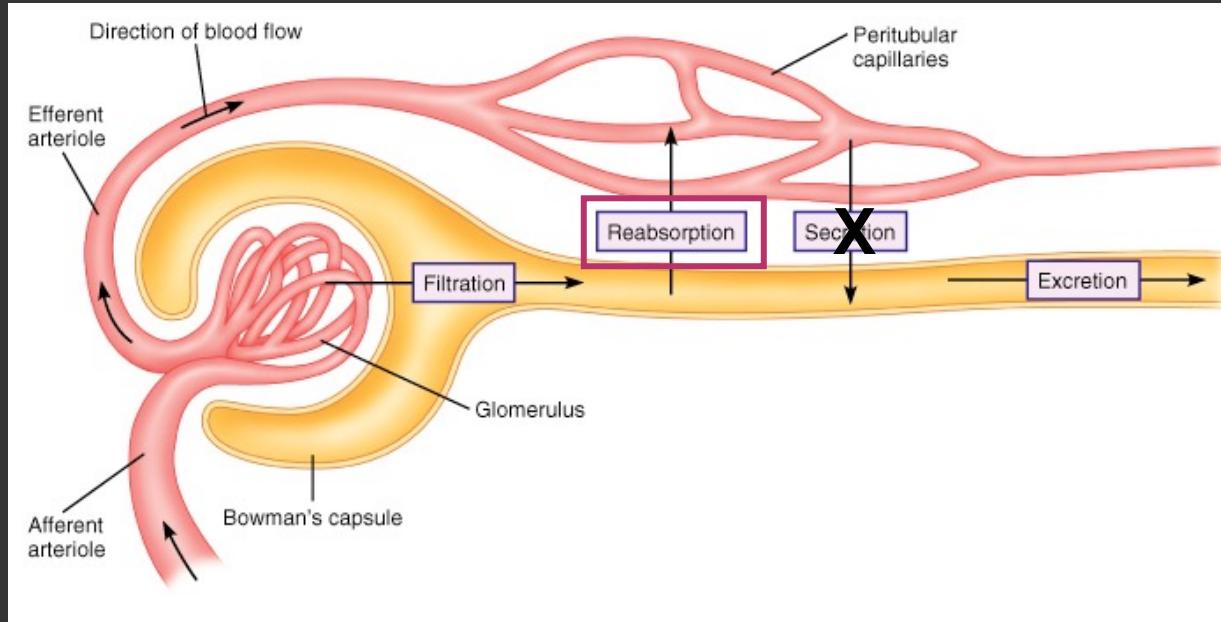


however, creatinine is secreted

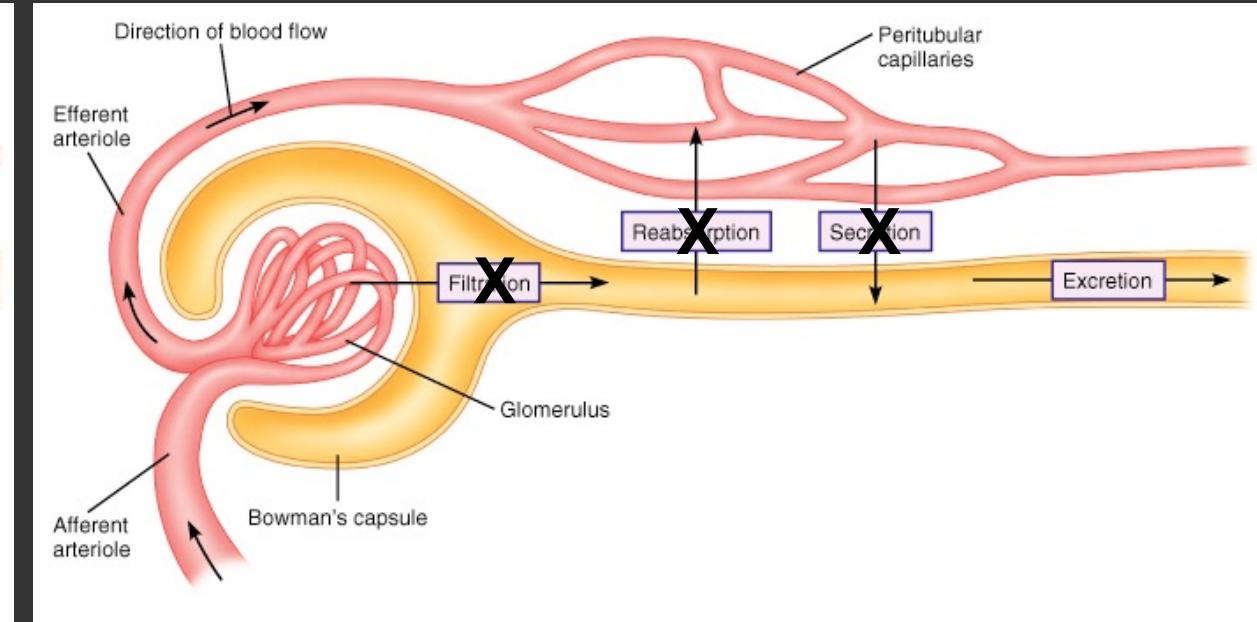


# If Clearance is Zero

- Substance has been fully reabsorbed and NOT secreted
  - or
- Substance has been not filtered and not secreted and not reabsorbed



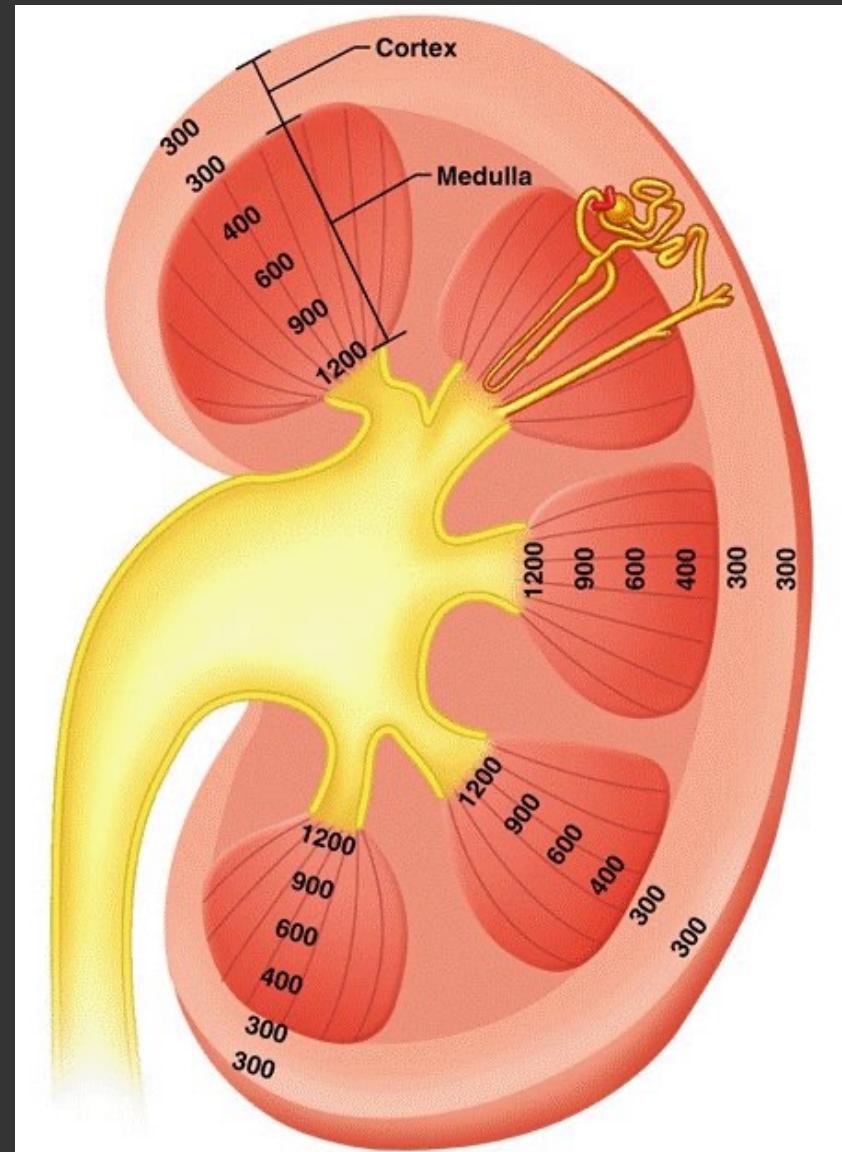
eg , glucose



eg , protein

# Countercurrent Exchanger

- Anatomic relationship between juxtamedullary nephron loop of Henle and the vasa recta
- Creates a very large osmotic gradient within the medulla
  - Osmolarity at the cortex-medulla junction is  $\sim 300$  mOsM
  - Osmolarity progressively increases to  $\sim 1,200$  mOsM deep within the medulla
  - Large osmotic gradient is used to regulate blood osmolarity



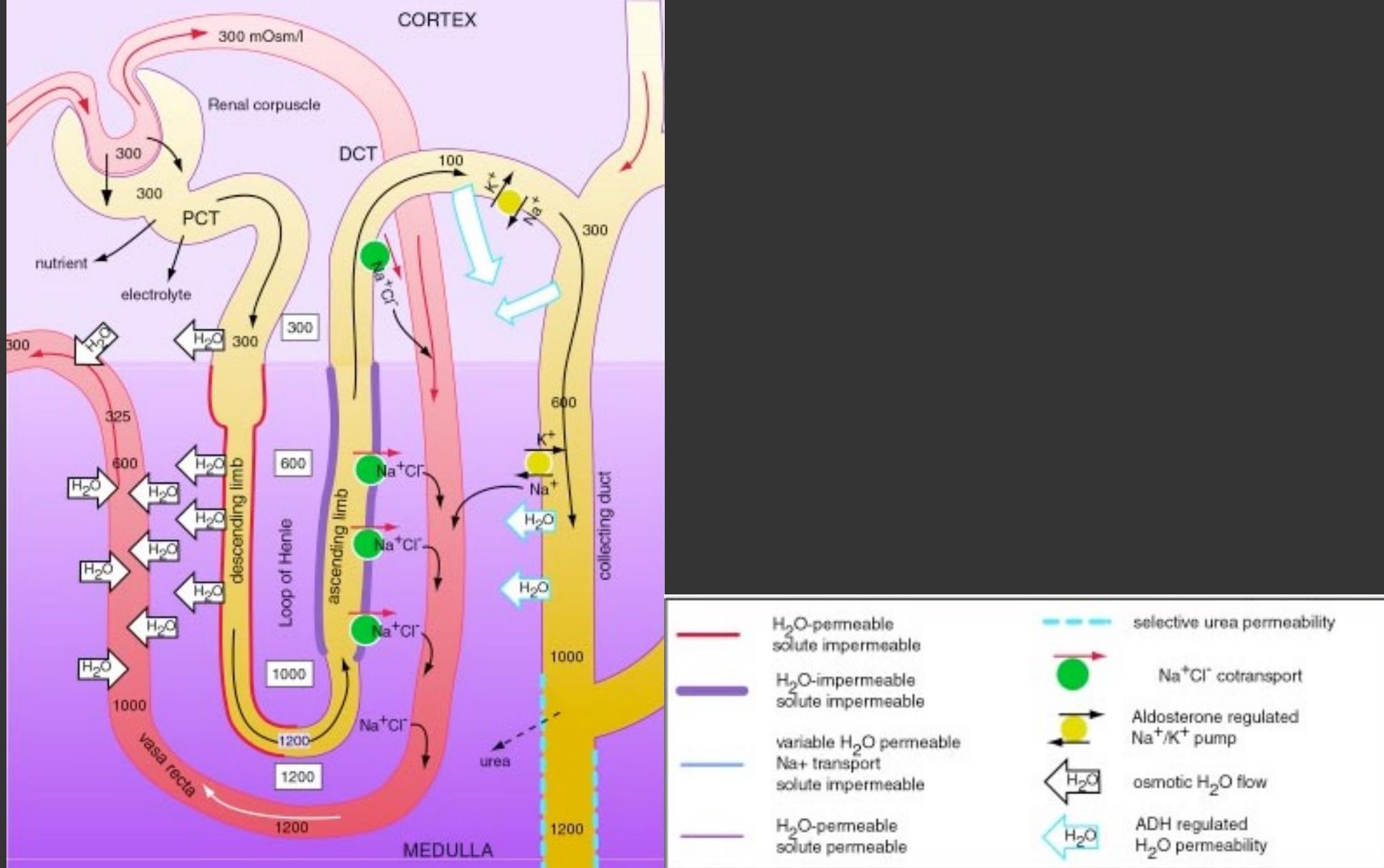
# Factors Involved in Countercurrent Exchange

- Thin descending limb of the loop of Henle
  - Permeable to water
  - Transport of water ( ie , osmosis ) out of limb
    - Progressively concentrates filtrate from 300 mOsM to 1,200 mOsM as it descends into the medulla
    - Some of the water is reabsorbed by the vasa recta
      - Progressively dilutes blood from 1,200 mOsM to 300 mOsM as it ascends towards the cortex
      - Helps maintain osmotic gradient of medullary interstitial fluid
- Thin and thick ascending limbs of the loop of Henle
  - Impermeable to water
  - Permeable to  $\text{Na}^+$  ,  $\text{Cl}^-$  ( transport of  $\text{Na}^+$  and  $\text{Cl}^-$  out of limbs )
    - Progressively concentrates medulla to 1,200 mOsM
    - Progressively dilutes the filtrate back towards 300 mOsM as it ascends towards the cortex
    - $\text{Na}^+$  and  $\text{Cl}^-$  reabsorbed by the vasa recta
      - Progressively concentrates the blood towards 1,200 mOsM as it descends into the medulla
      - Helps maintain osmotic gradient within the medulla

# Factors Involved in Countercurrent Exchange

- Distal convolute tubule dilutes filtrate to 100 mOsM
  - Transport of  $\text{Na}^+$  and  $\text{Cl}^-$  out of tubule
    - ∵ filtrate entering collecting duct has osmolarity of 100 mOsM

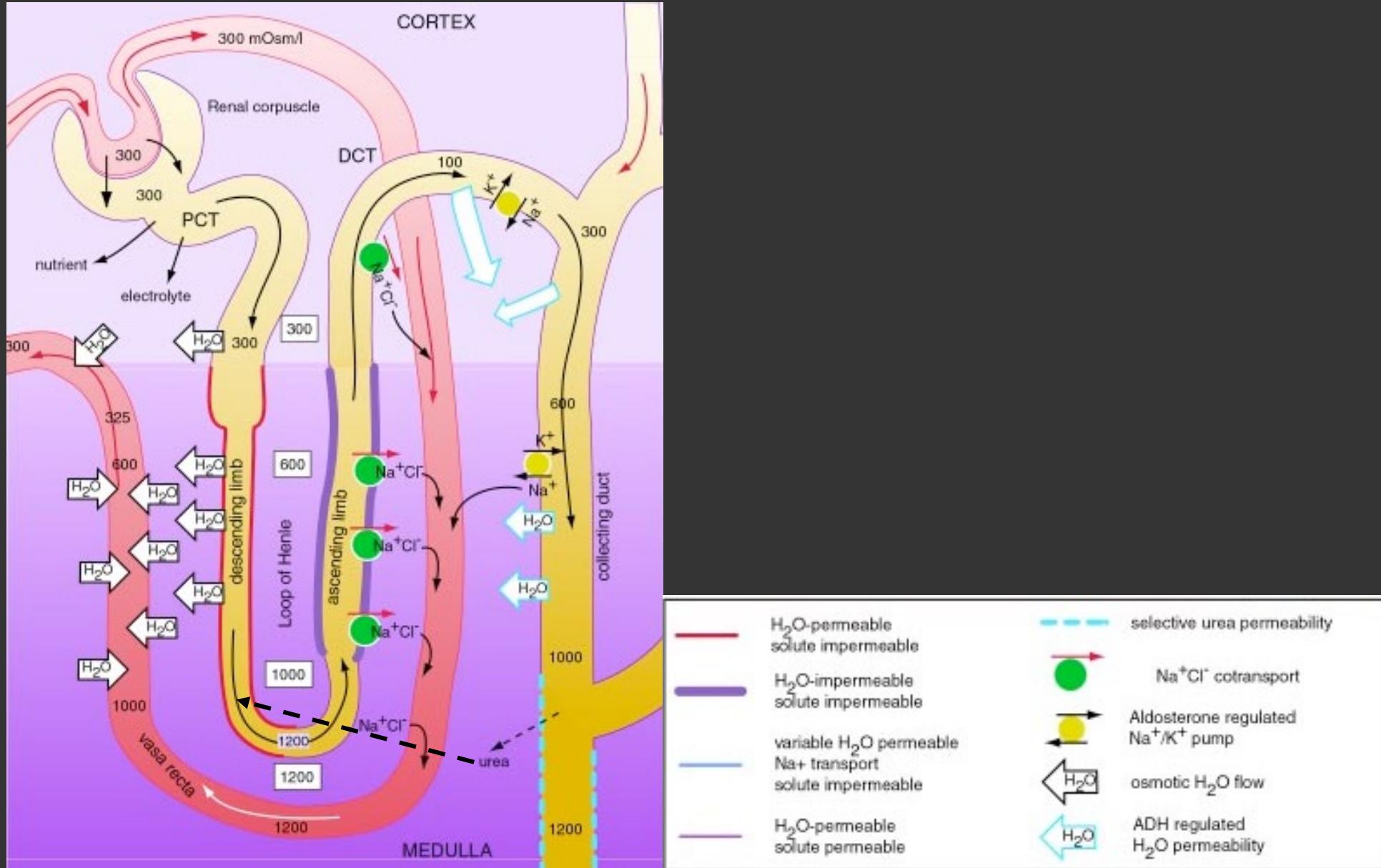
# Factors Involved in Countercurrent Exchange



# Factors Involved in Countercurrent Exchange

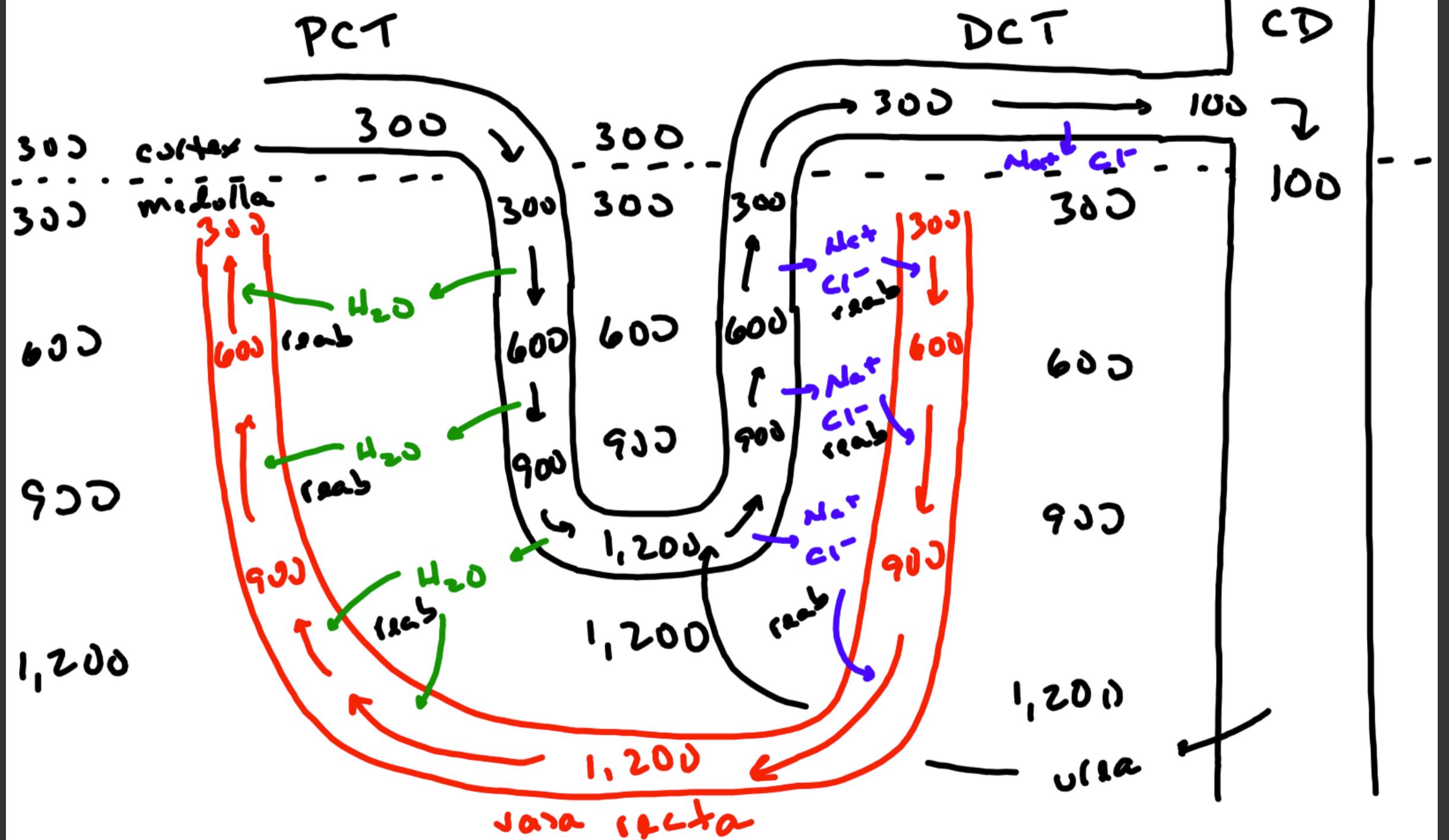
- Contribution of urea to the osmotic gradient within the medulla
  - Transport of urea out of the collecting duct to the medullary interstitial fluid
    - Aids in concentrating the medullary fluid
  - Urea is then secreted by the descending limb of the loop of Henle
    - Aids in concentrating the filtrate
    - Re-circulates to the collecting duct

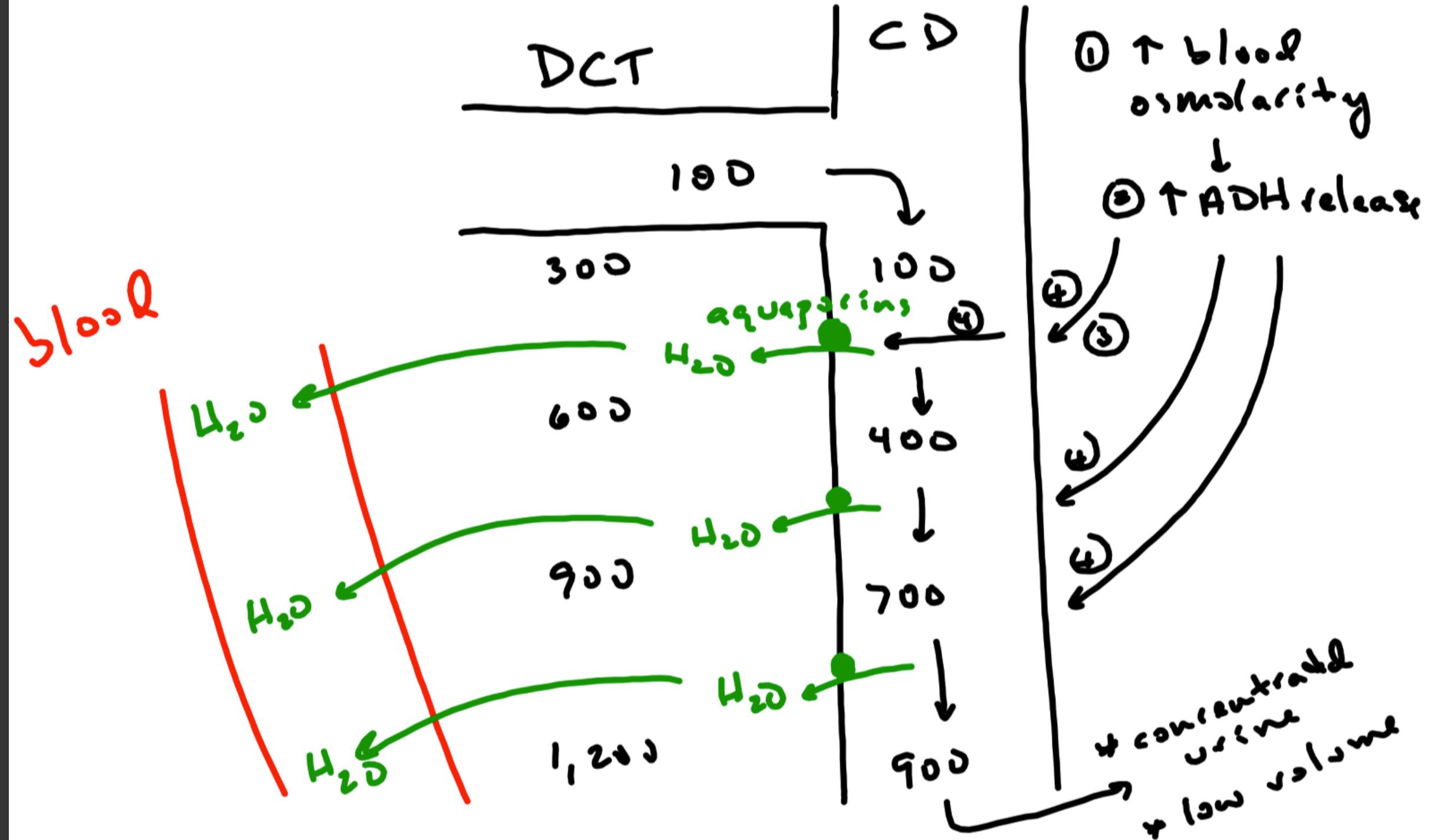
# Factors Involved in Countercurrent Exchange



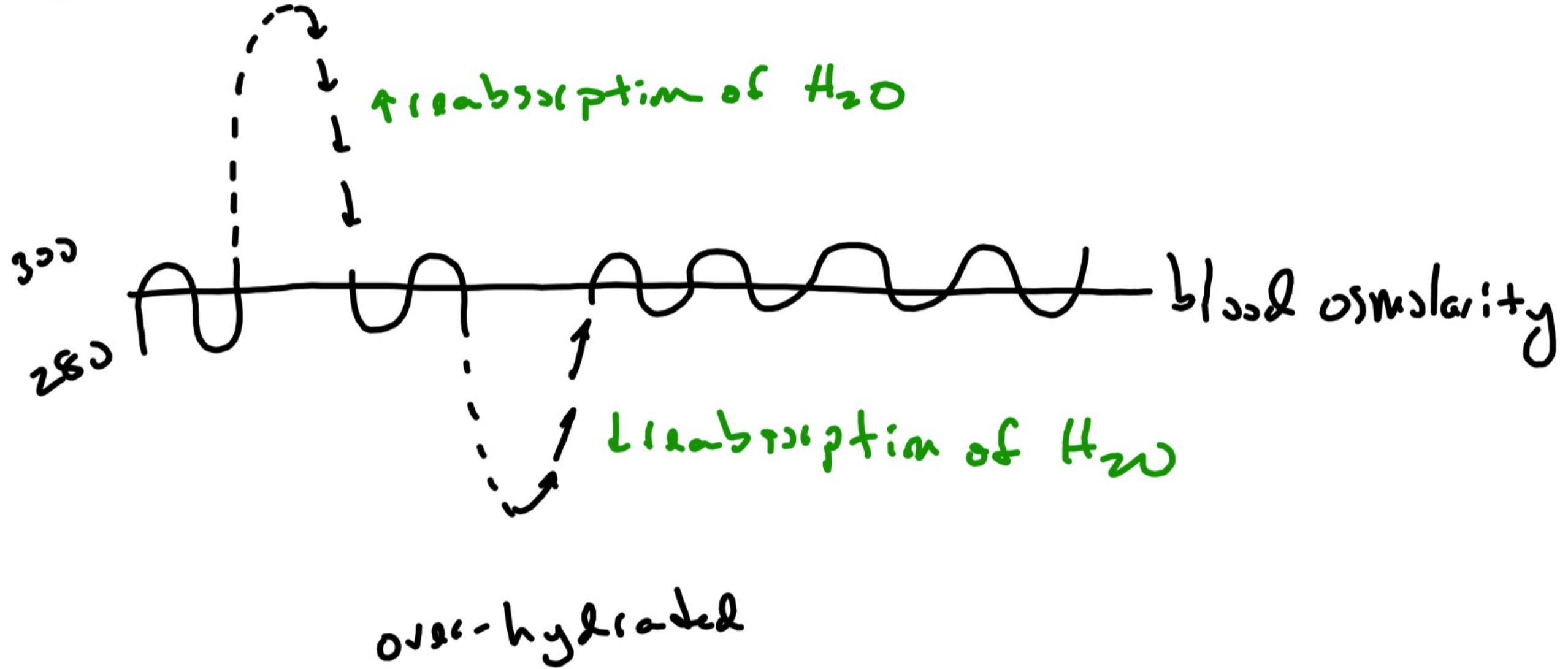
# Regulation of Blood Osmolarity via ADH

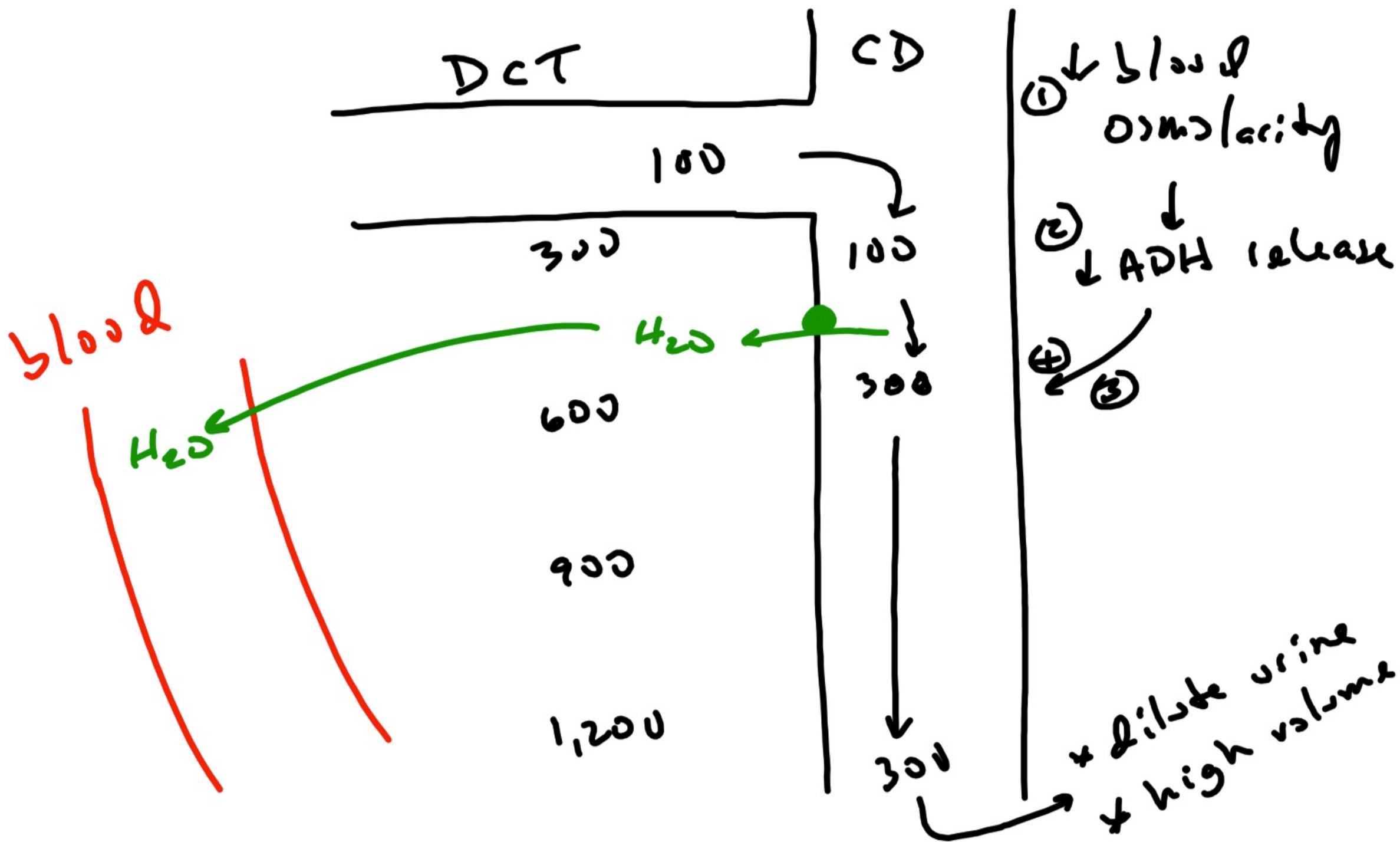
- ADH increases permeability of water at distal convoluted tubule and collecting duct.
  - Stimulates the incorporation of aquaporins ( ie , water channels )
  - Increases water reabsorption at distal convoluted tubule and collecting duct
    - Osmosis driven by the osmotic gradient within the medulla
  - Increased level of ADH released when blood osmolarity is high
    - Causes more water to be reabsorbed
      - Thus decreases blood osmolarity towards normal
      - Urine consequently has a higher osmolarity
  - Decreased level of ADH released when blood osmolarity is low
    - Causes less water to be reabsorbed
      - Thus increases blood osmolarity toward normal
      - Urine consequently has a lower osmolarity





dehydration





~~✓~~ ADH (diabetes insipidus)

↳ no aquaporins

↳ CD is impermeable to  $H_2O$

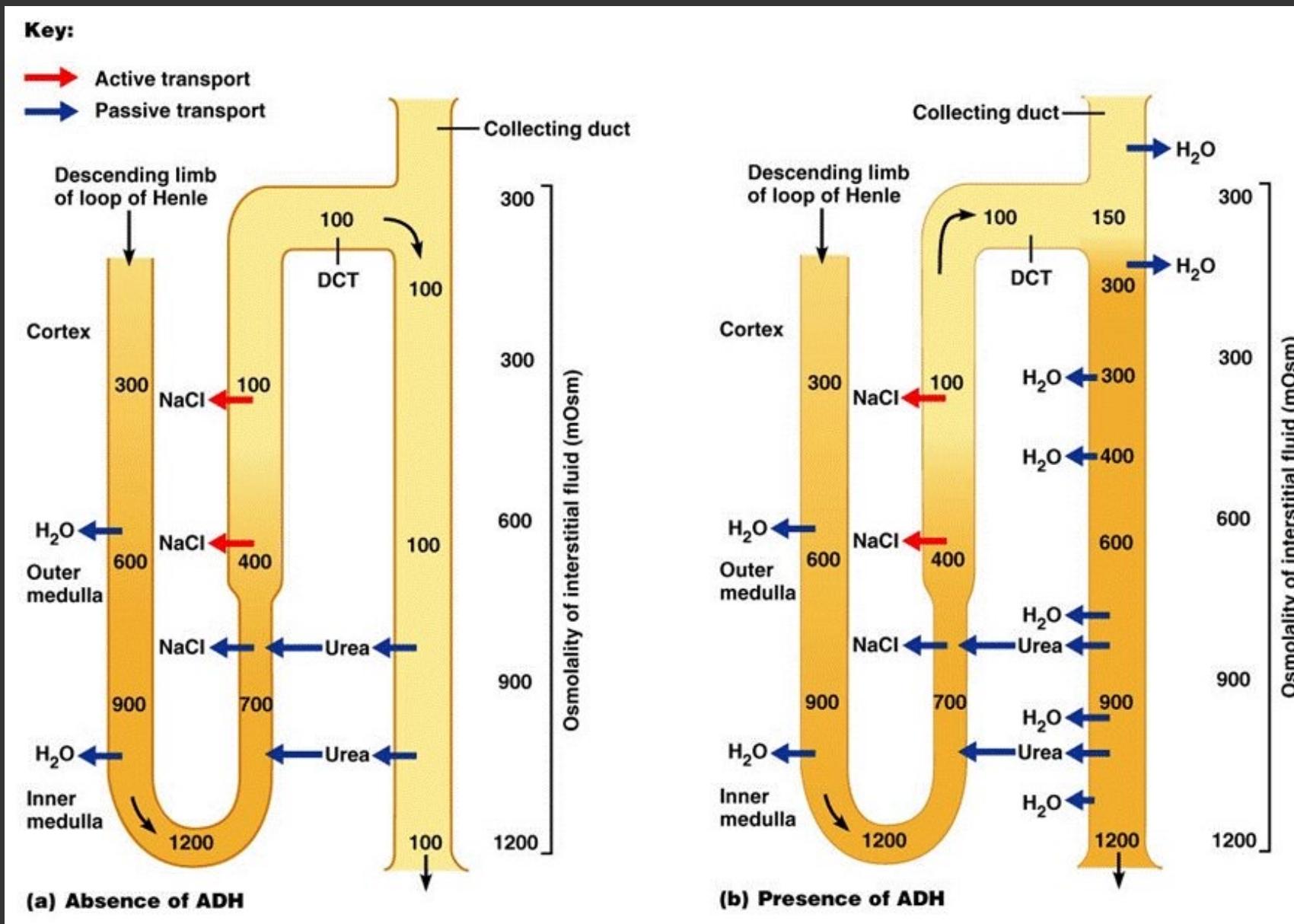
↳ lots of dilute urine

(osmolarity = 100)



high  
blood  
osmolarity

# Regulation of Blood Osmolarity



# Diuretics

- Drugs that cause excretion of water
- Used to treat , for example , edema and hypertension
- Loop Diuretics ( eg , Lasix )
  - Most powerful of the diuretics
  - Work in ascending limbs of the loop of Henle
  - Decrease blood K<sup>+</sup>
- Thiazides ( eg , Metolazone )
  - Work mainly in distal convoluted tubule
  - Decrease blood K<sup>+</sup>
- Aldosterone Antagonists ( eg , Inspra )
  - Work mainly in distal convoluted tubule
  - Does NOT decrease blood K<sup>+</sup>
    - ∴ potassium sparing

\* Pathophysiological changes in reabsorption and secretion lead to changes in [blood] of "things."  
↳ How?

- kidney disease
- medications

# Urine

- Approximately 1.5 to 2 liters per day
- 96 % water
- 2.5 % nitrogenous wastes ( eg , ammonia , urea , uric acid , creatinine )
- 1.5 % salts and traces of other substances
- pH : 4.6 to 8.0
- Osmolarity of between 300 and 900 mOsM
  - Can be as low as 100 and as high as 1,200 mOsM
- Specific Gravity = a weight of a solution compared to that of an equal volume of distilled water
  - Determined by two things :
    1. osmolarity of urine
    2. Size of particles in urine
  - Normally between 1.010 and 1.030
    - Higher value indicates more and / or larger particles in urine
    - Lower value indicates less and / or smaller particles in urine
- Healthy urine is sterile

## \* Specific Gravity (SG)

- $\uparrow$  SG w. ↑ osmolarity and/or bigger solutes
- $\downarrow$  SG w. ↓ osmolarity and/or smaller solutes

# Micturition / Urination

- Anuria = no urine output
  - Urinary Retention = urine is produced but is not voided
    - Due to severe obstruction that completely prevents flow of urine ( eg , tumor )
  - Urinary Suppression = urine is not produced by the kidneys
    - Renal disease
- Oliguria = decreased urine output
  - eg , dehydration
  - eg , obstruction ( eg , kidney stone , small tumor )
  - eg , renal disease
- Polyuria = excess urine output
  - eg , over-hydration
  - eg , diabetes insipidus ( low ADH ) = dilute urine due to excess water secretion
  - eg , diabetes mellitus = concentrated urine due to excess glucose in urine
    - Patients drink lots of water because they feel thirsty
      - Thirst due to increased blood osmolarity
- Dysuria = urine expelled painfully
  - eg , obstruction ( eg , kidney stone , small tumor )
  - eg , urinary tract or bladder infection
  - eg , venereal disease

# Patient A

Urine Vol = 600ml  
(oliguria)

Osmolarity = 870

SG = 1.025

↑  
dehydrated

# Patient B

Urine Vol = 600ml  
(oliguria)

Osmolarity = 800

SG = 1.040

↑  
dehydrated +  
glomerulonephritis