Definitions

- Eupnea = normal quite 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

Nares

Nasal Cavity

Pharynx

Larynx

Trachea

Bronchi

Bronchioles

Terminal Bronchioles

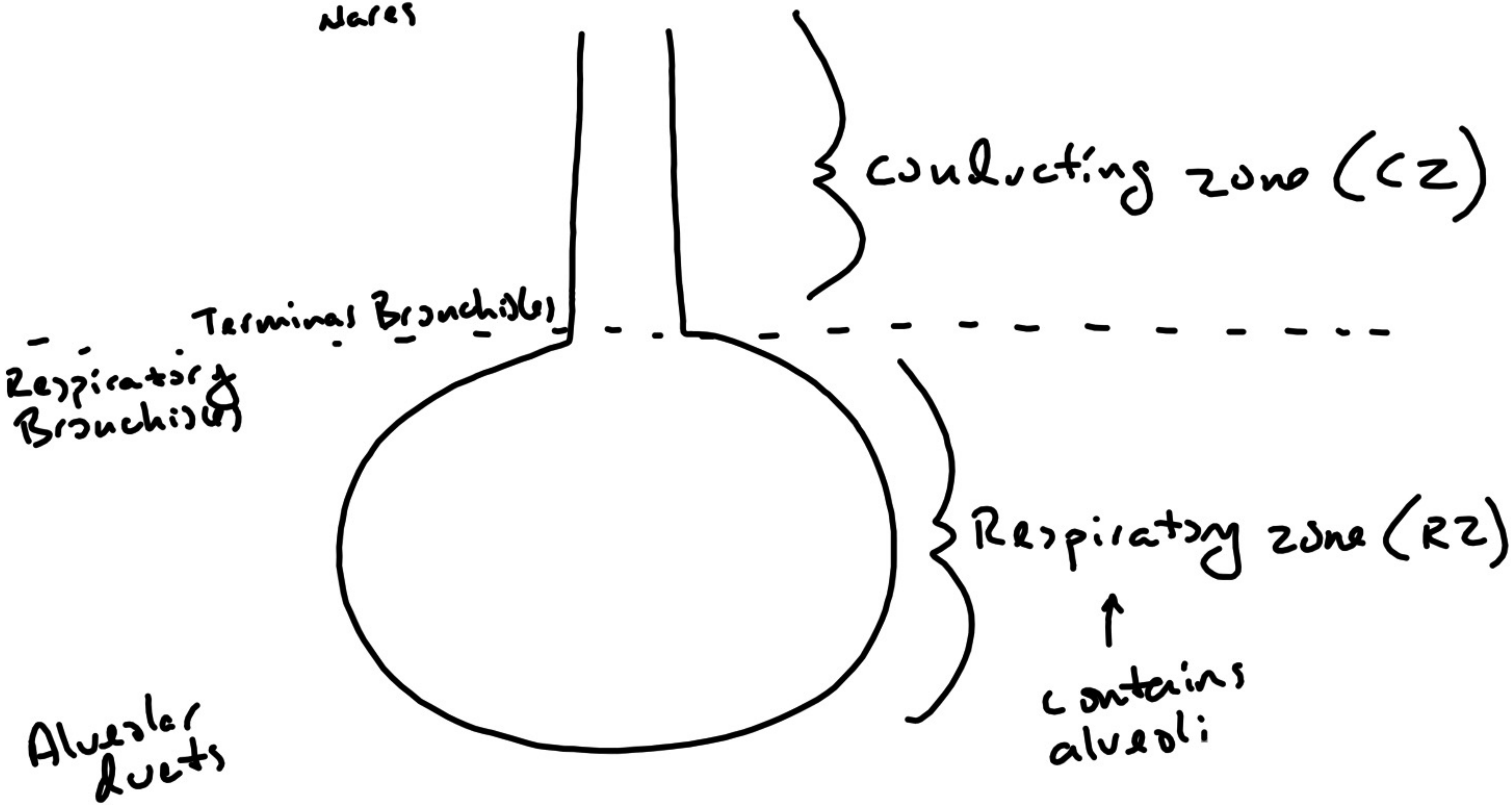
Conducting Zone

Respiratory Bronchioles

Alveolar Ducts

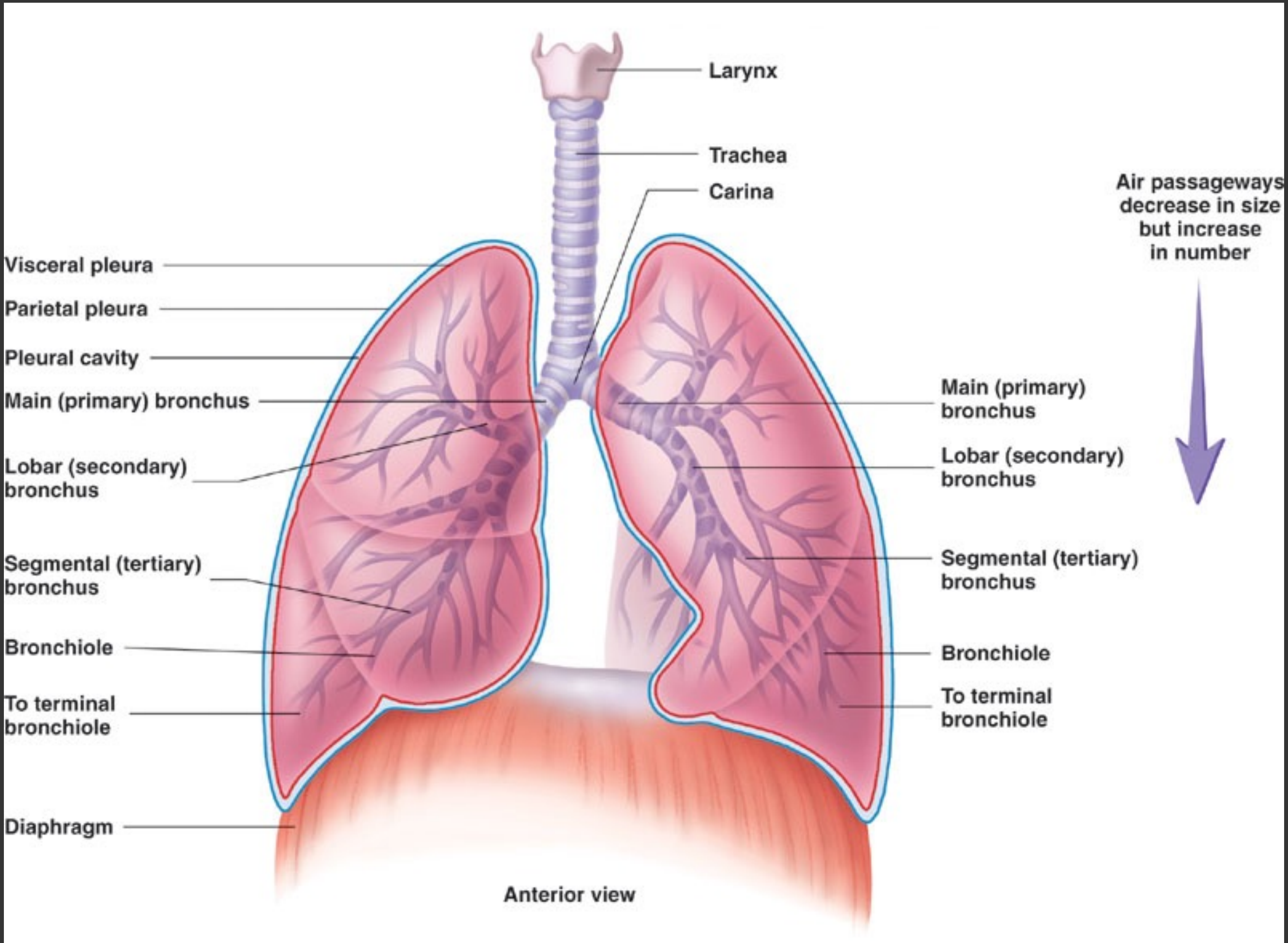
Alveoli

Respiratory Zone



Nares
conducting zone (CZ)
Terminal Bronchiole(s)
Respiratory Bronchiole(s)
Respiratory zone (RZ)
contains alveoli
Alveolar ducts

Respiratory System – Airways – Conducting Zone



Respiratory System – Airways – Conducting Zone

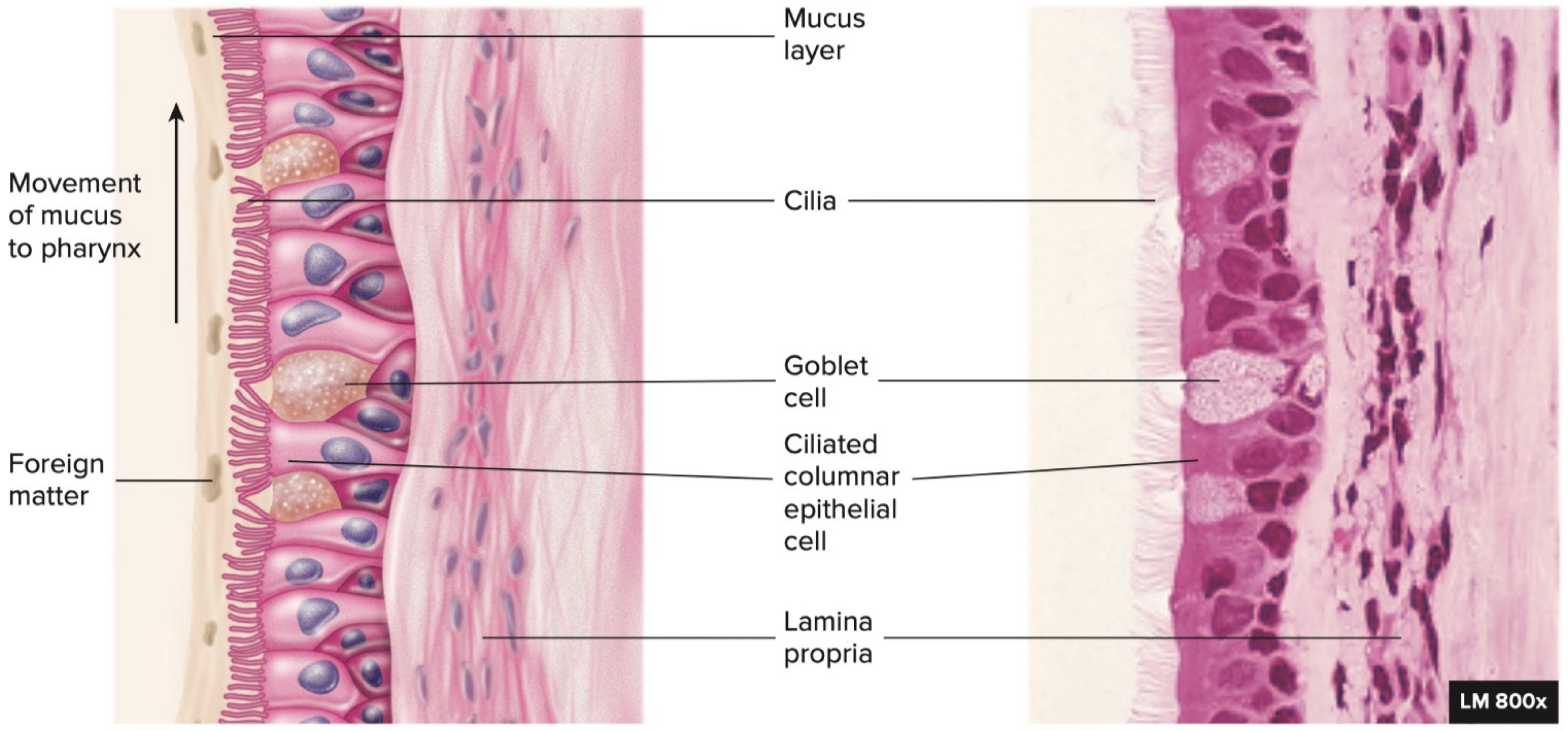
- Functions :

1. Controls the volume of air into and out of the respiratory tract
    - Controlled by airway smooth muscle tone
        - eg , β-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

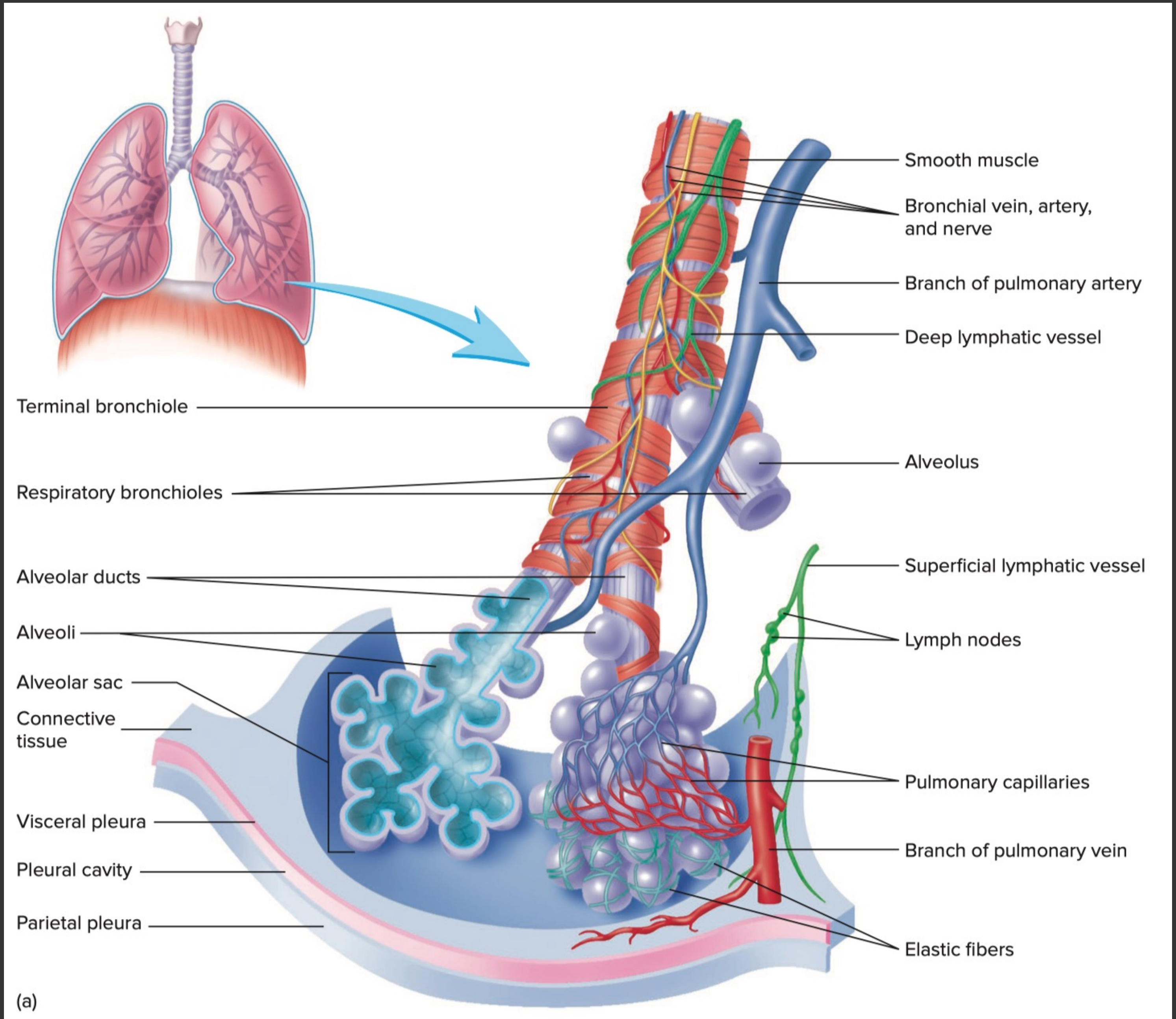


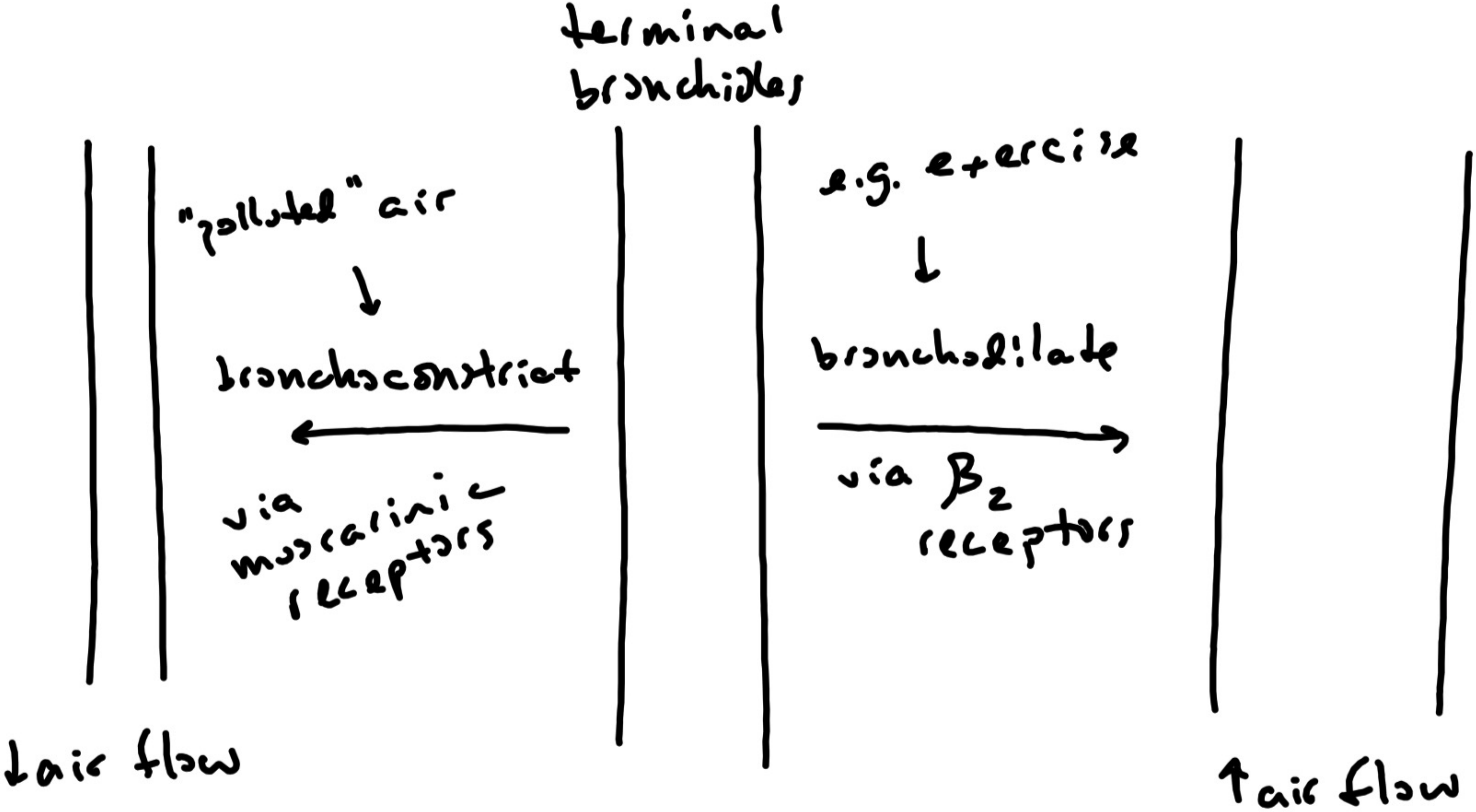
Respiratory System – Airways – Respiratory Zone

- 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



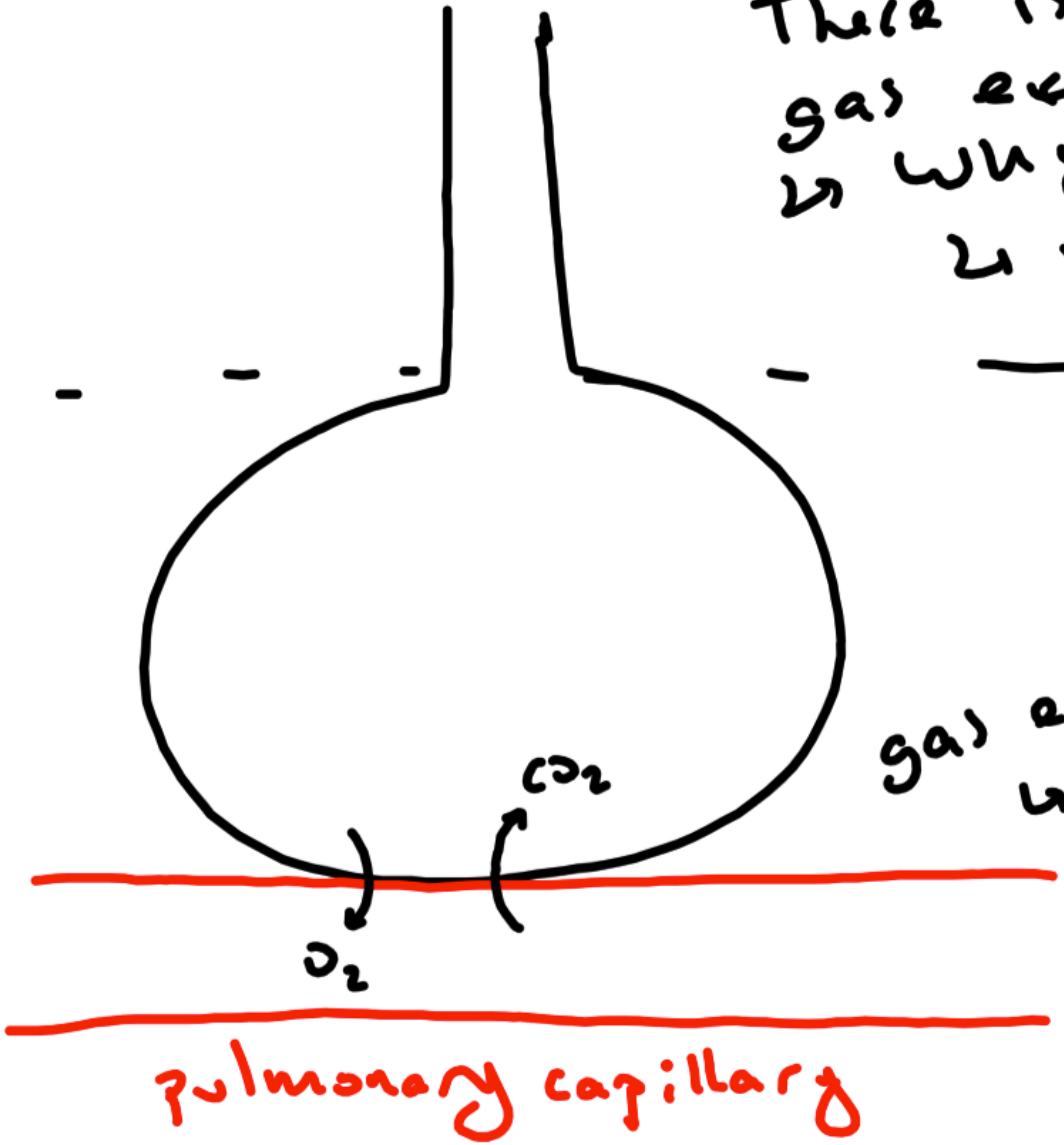


terminal bronchioles
"polluted" air
bronchoconstrict
via muscarinic receptors
↓ air flow
e.g. exercise
bronchodilate
via β_2 receptors
↑ air flow

CZ

There is no gas exchange
↳ why?
↳ no alveoli

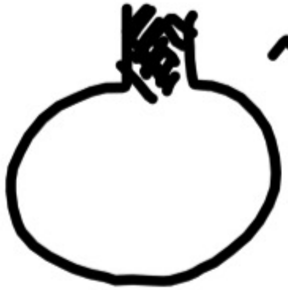
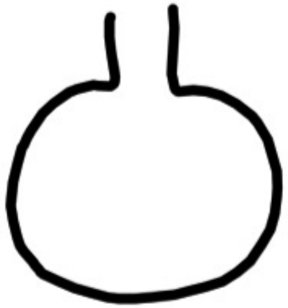
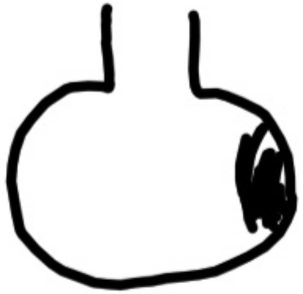
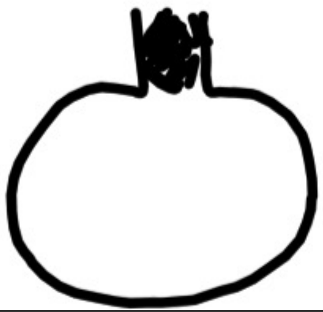
RZ



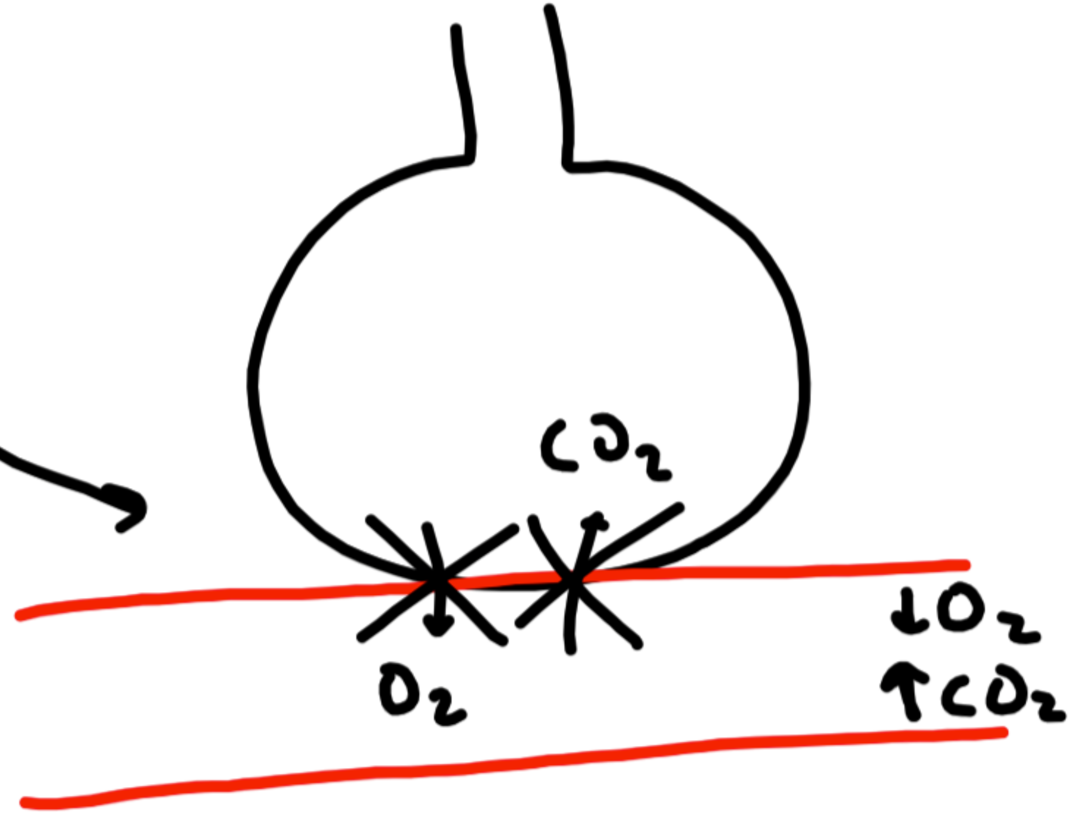
contains alveoli
↓
gas exchange
↳ to oxygenate the blood and to get rid of excess CO_2

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
- Physiological Dead Space
  - Combination of anatomic and alveolar dead spaces

	Normal (healthy)	Abnormal
Anatomic	 ~150ml	 ~150ml
Alveolar	 ∅	 ~110ml
Physiologic	 ~150ml	 ~260ml

Alveolar Dead Space



$$\uparrow \text{Physiologic D.S.} \longrightarrow \left.\begin{array}{l}\downarrow \text{blood } O_2\\ \uparrow \text{blood } CO_2\end{array}\right\}\text{BAD}$$

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

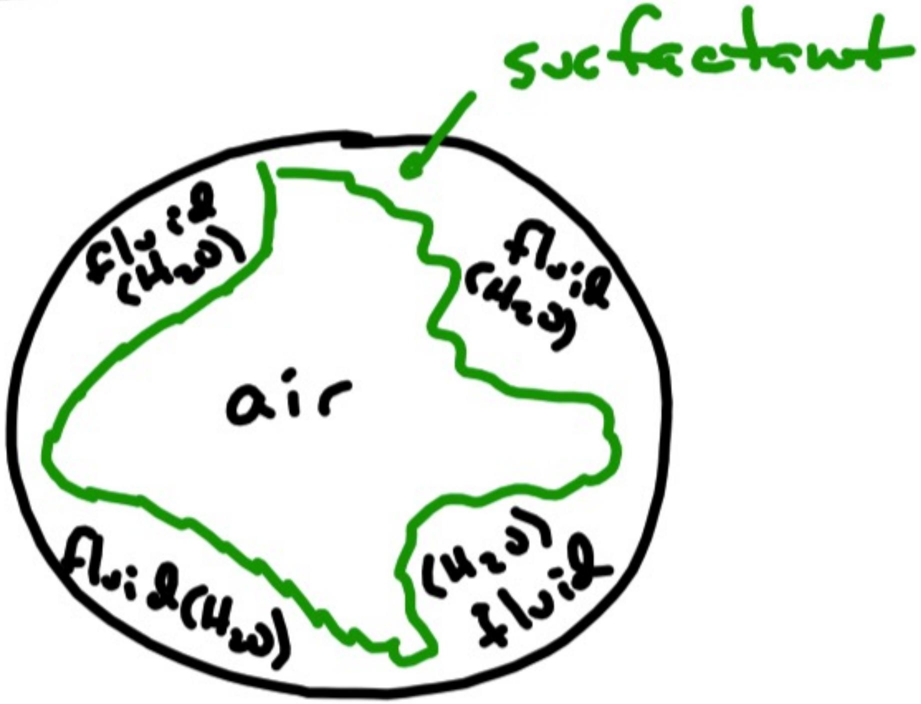
$$P = \frac{2 \ * T}{r}$$

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

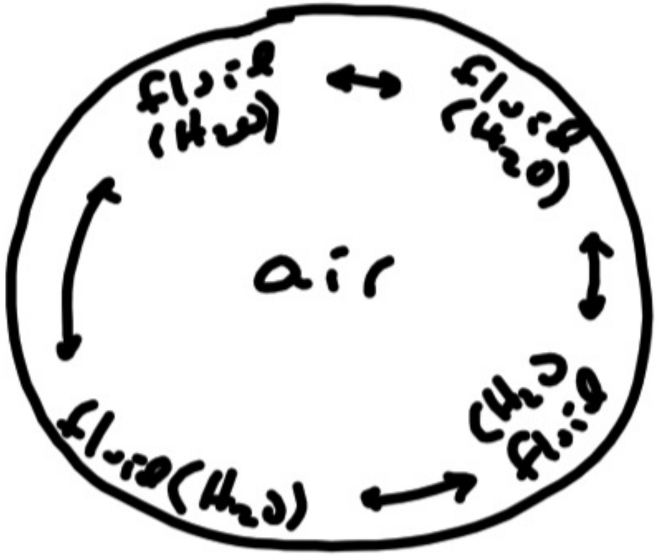
with surfactant	w/o surfactant

with surfactant



H_2O molecules "hidden" from each other
↳ low surface tension
↳ low collapsing pressure
↳ alveoli remain inflated

w/o surfactant



H_2O molecules "mingle"
↳ ↑↑↑ surface tension
↳ ↑↑↑ collapsing pressure
↳ alveoli collapse
↳ stiff lung

Respiratory System – Lungs

- An increase in compliance indicates the lung is too "stretch"
  - 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

e.g. emphysema

* ↑ compliance
  - ↳ loss/destruction of elastin fibers

thin rubber band

thick rubber band

---

e.g. interstitial lung disease

* ↓ compliance
  - ↳ damage and scarring of elastin fibers
  - ↳ loss of surfactant
    - ↳ alveoli will collapse (atelectasis) ← surfactant 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

Right Ventricle

↓

Pulmonary Arteries

↓

Pulmonary Capillaries ⟶ perfusion of alveoli

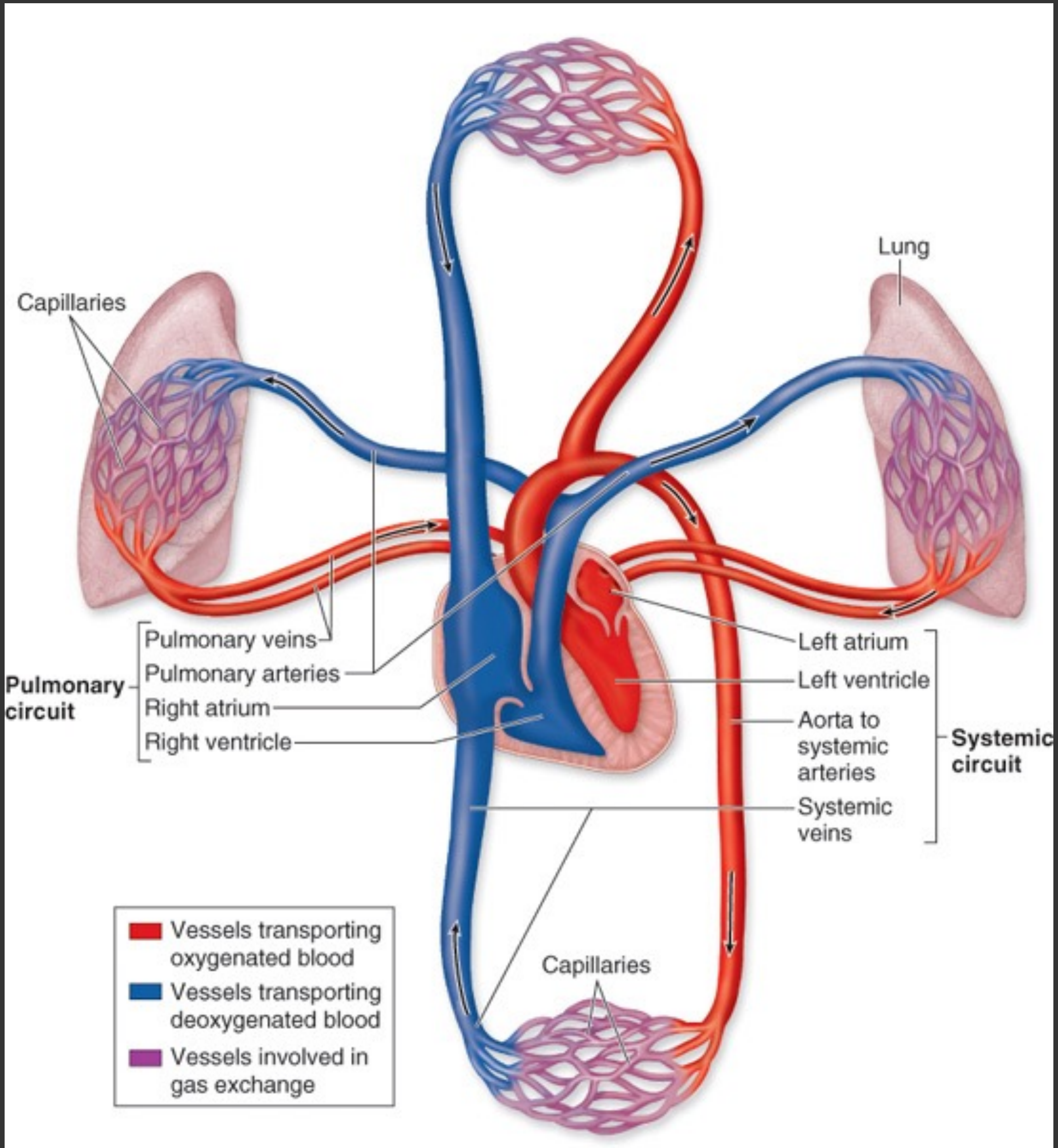
↓

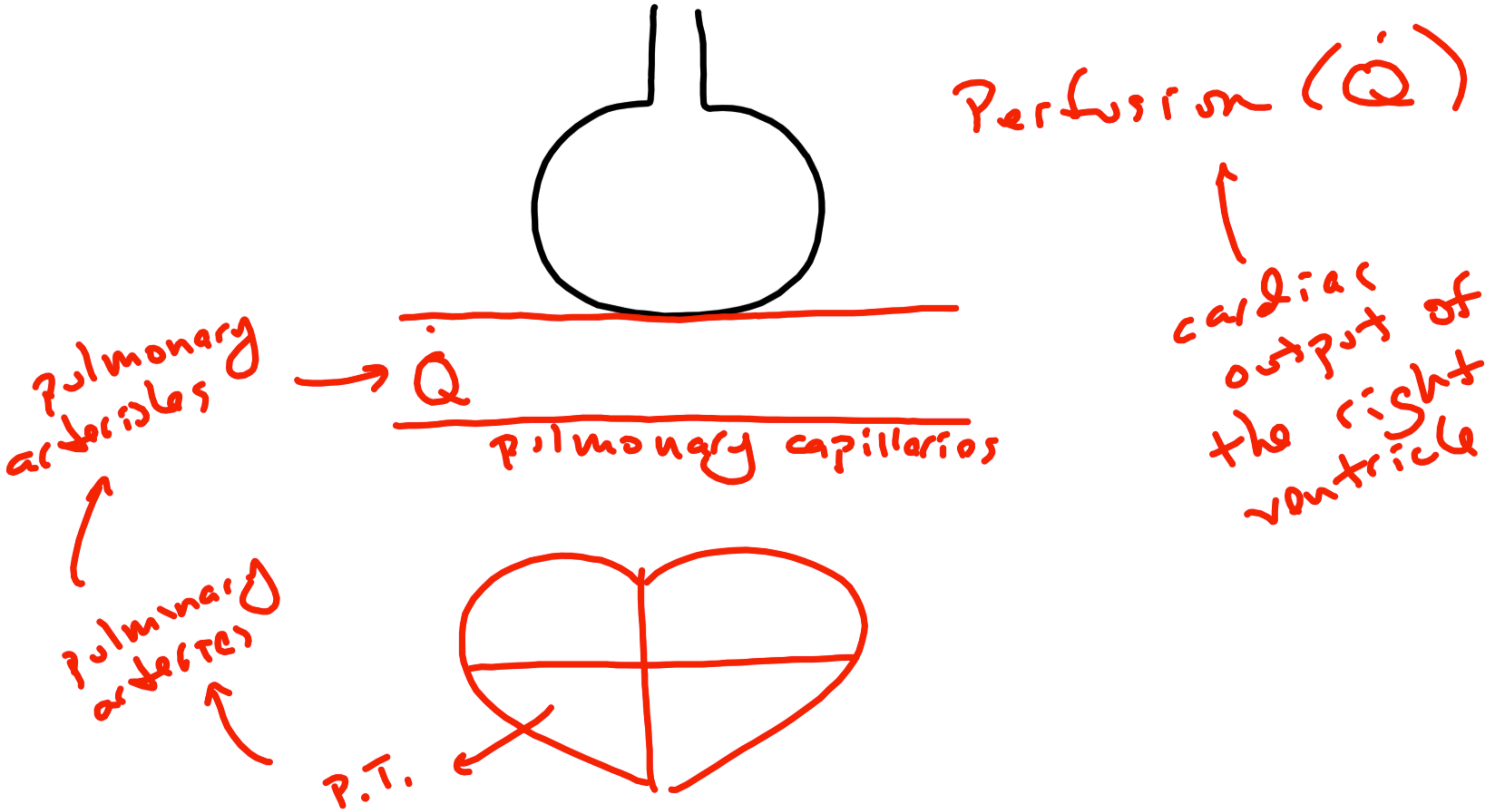
Pulmonary Veins

↓

Left Atrium

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




Perfusion ($\dot{Q}$)
cardiac output of the right ventricle
pulmonary arterioles
$\dot{Q}$
pulmonary capillaries
pulmonary arteries
P.T.

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

Left Atrium

↓

Left Ventricle

↓

Aorta

↓

Bronchial Arteries

↓

Systemic Capillaries → lung tissue

↓

Bronchial Veins

↓

Right Atrium

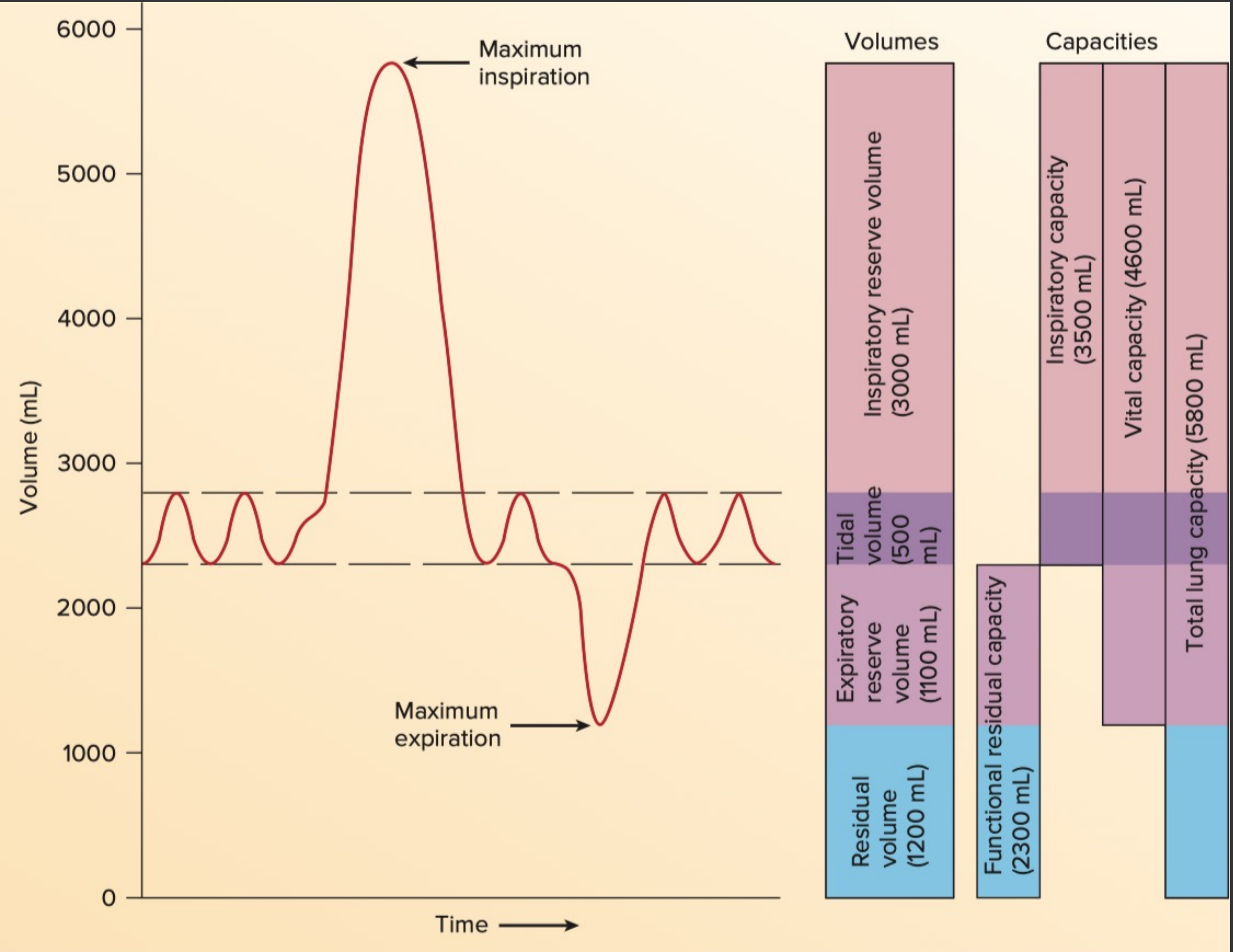
Spirometry

- Measurement of Lung Volumes and Lung Capacities

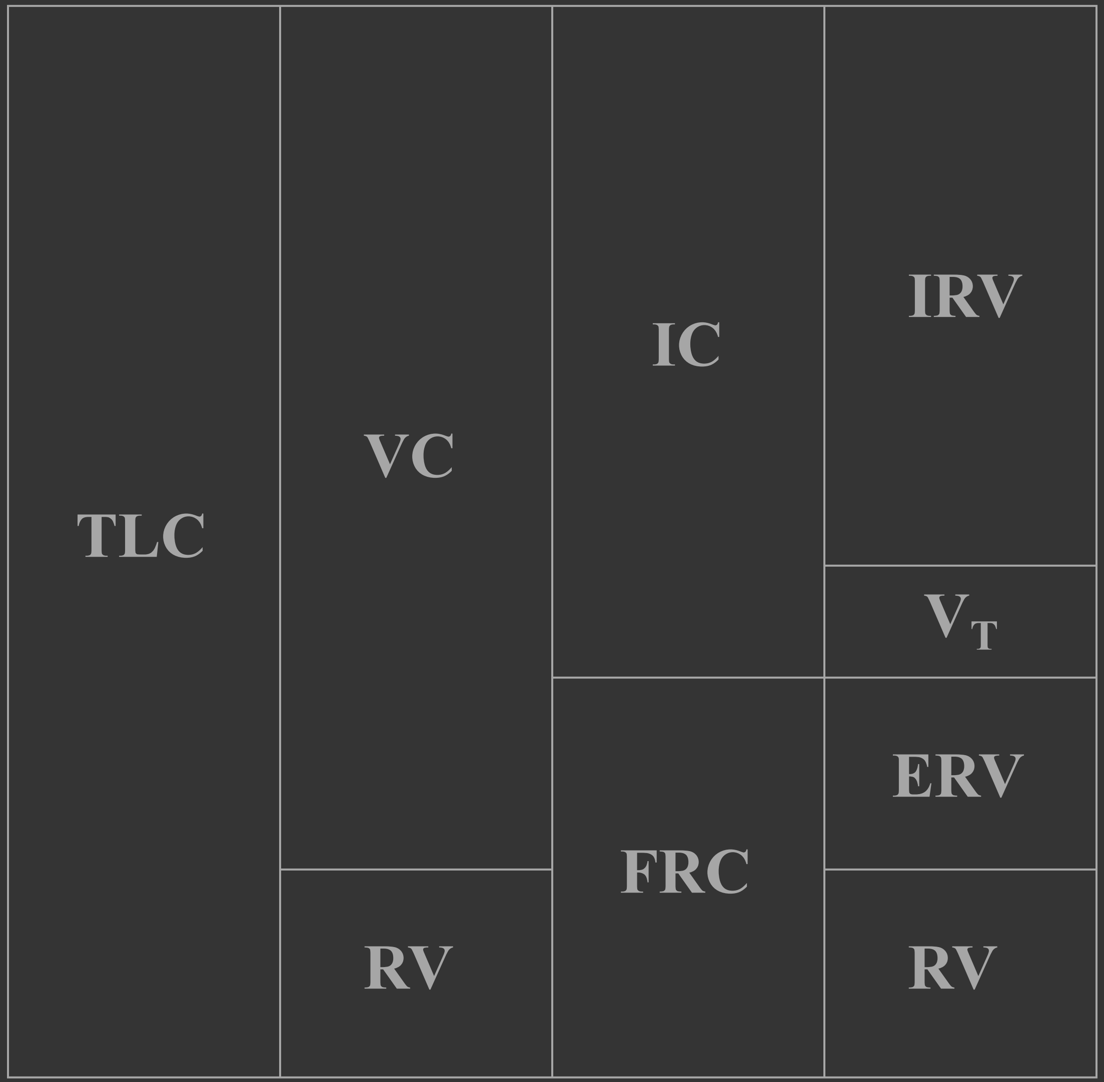
Spirometry

- 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 + ERF
  - 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

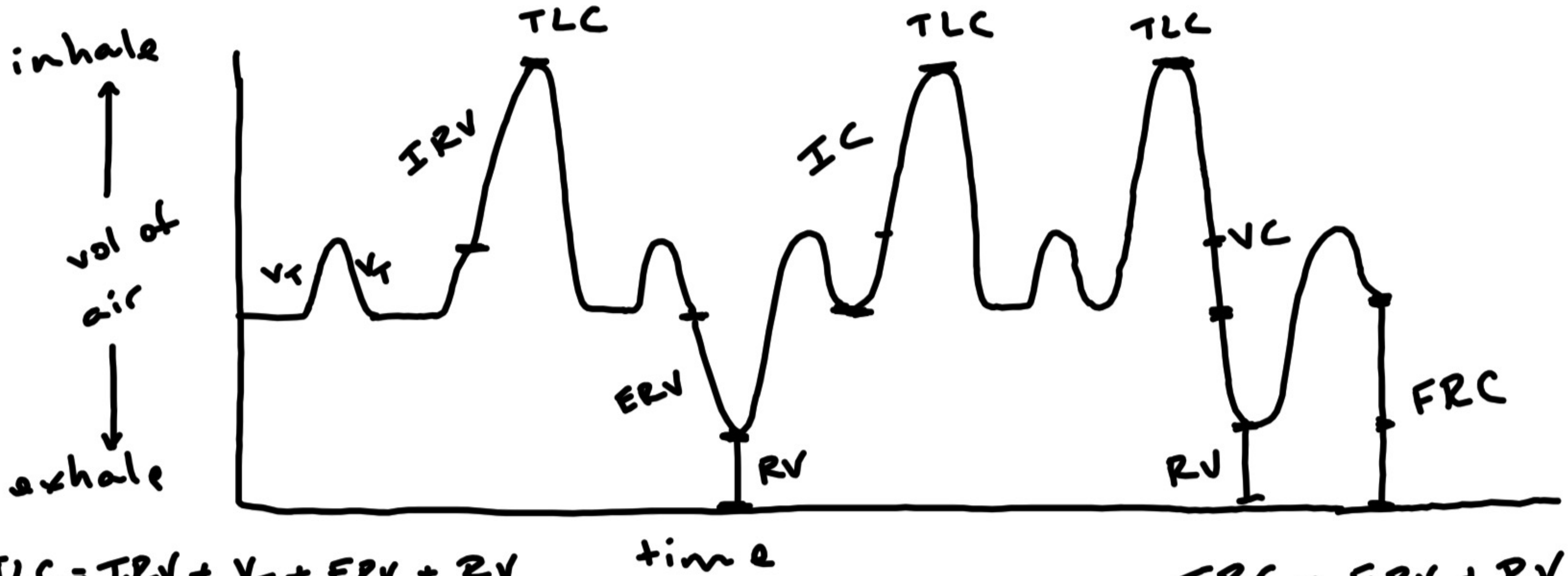


Lung Volumes and Capacities



$$IC = V_T + IRV$$

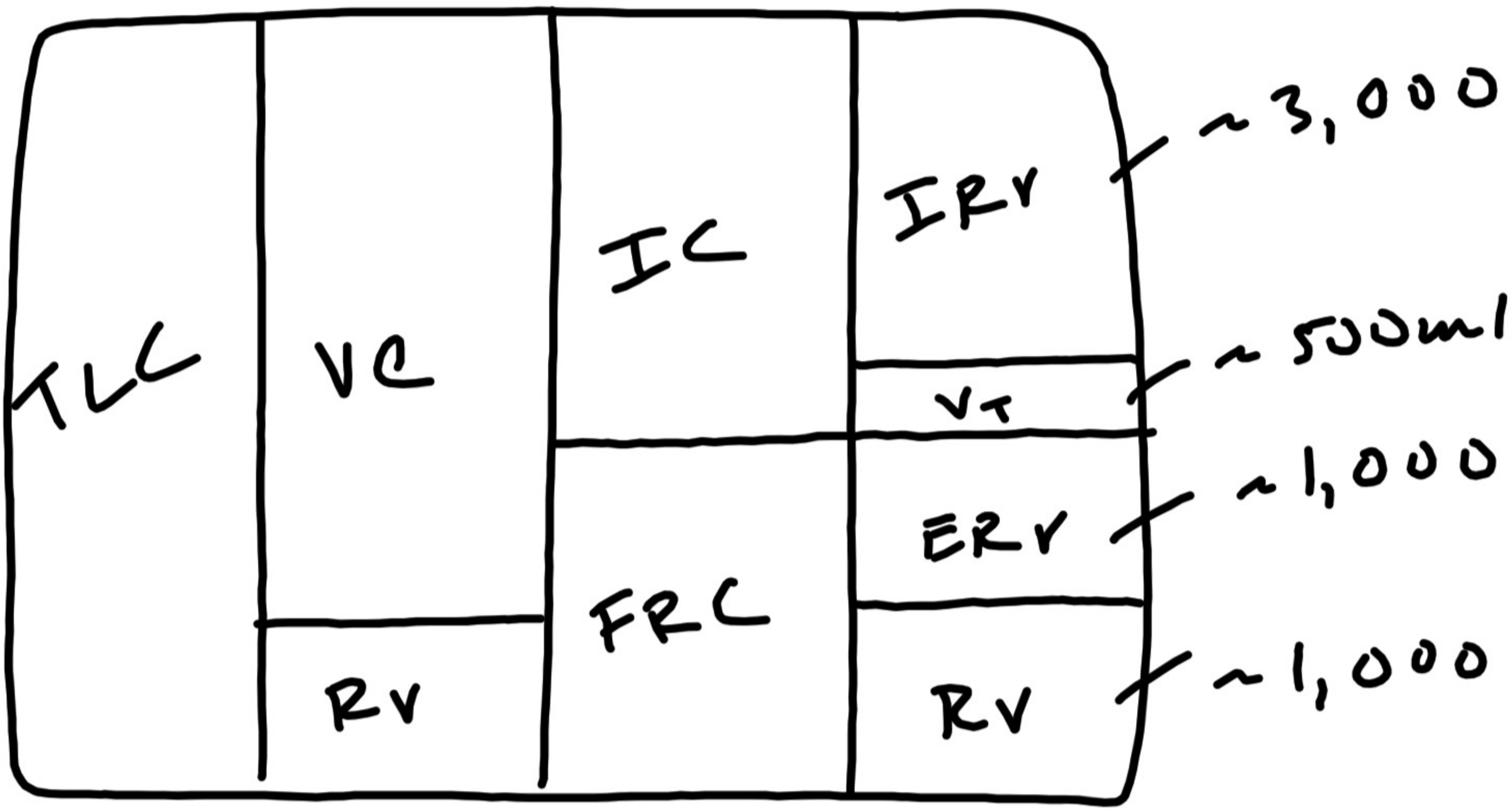
$$\begin{aligned} VC &= IRV + V_T + ERV \\ &= IC + ERV \end{aligned}$$



$$\begin{aligned} TLC &= IRV + V_T + ERV + RV \\ &= VC + RV \\ &= IC + FRC \end{aligned}$$

$$FRC = ERV + RV$$

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


TLC
VC
RV
IC
FRC
IRV
V_T
ERV
RV
~3,000
~500ml
~1,000
~1,000

$$VC = 6{,}200$$

$$\left.\begin{aligned} FRC &= 2{,}500 \\ IC &= 3{,}200 \end{aligned}\right\} 5{,}700$$

$$RY? = 500$$

Forced Vital Capacity (FVC)

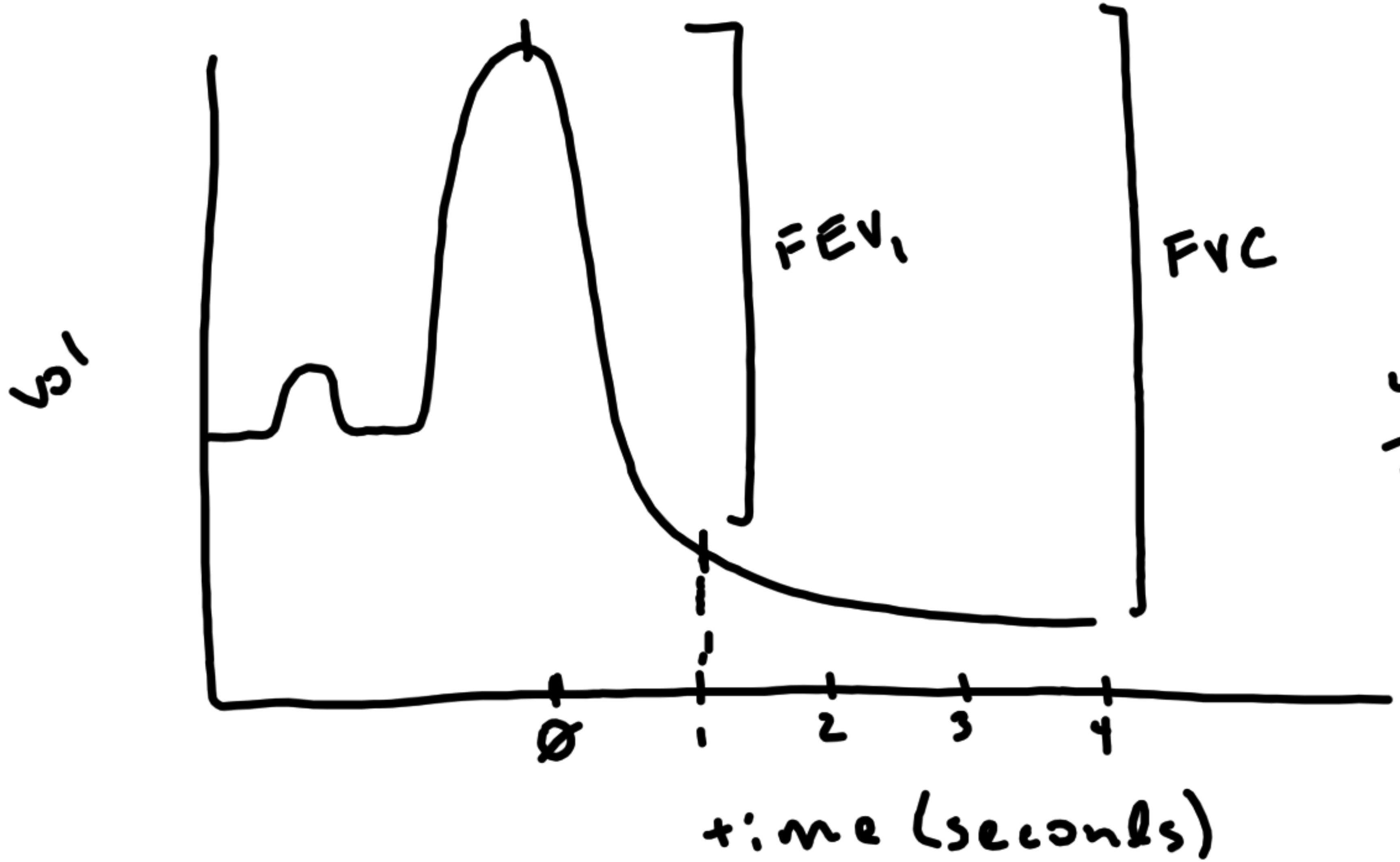
- FVC :
  - Volume of air forcefully expired after a maximal inspiration
  - Normal FVC ≈ 5,00 mL

- FEV_1
  - Volume of air forcefully expired during the first second
  - Normal FEV_1 ≈ 3,500 to 4,000 mL

$$\frac{FEV_1}{FVC} * 100\ \%$$

- Normal FEV_1 / 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

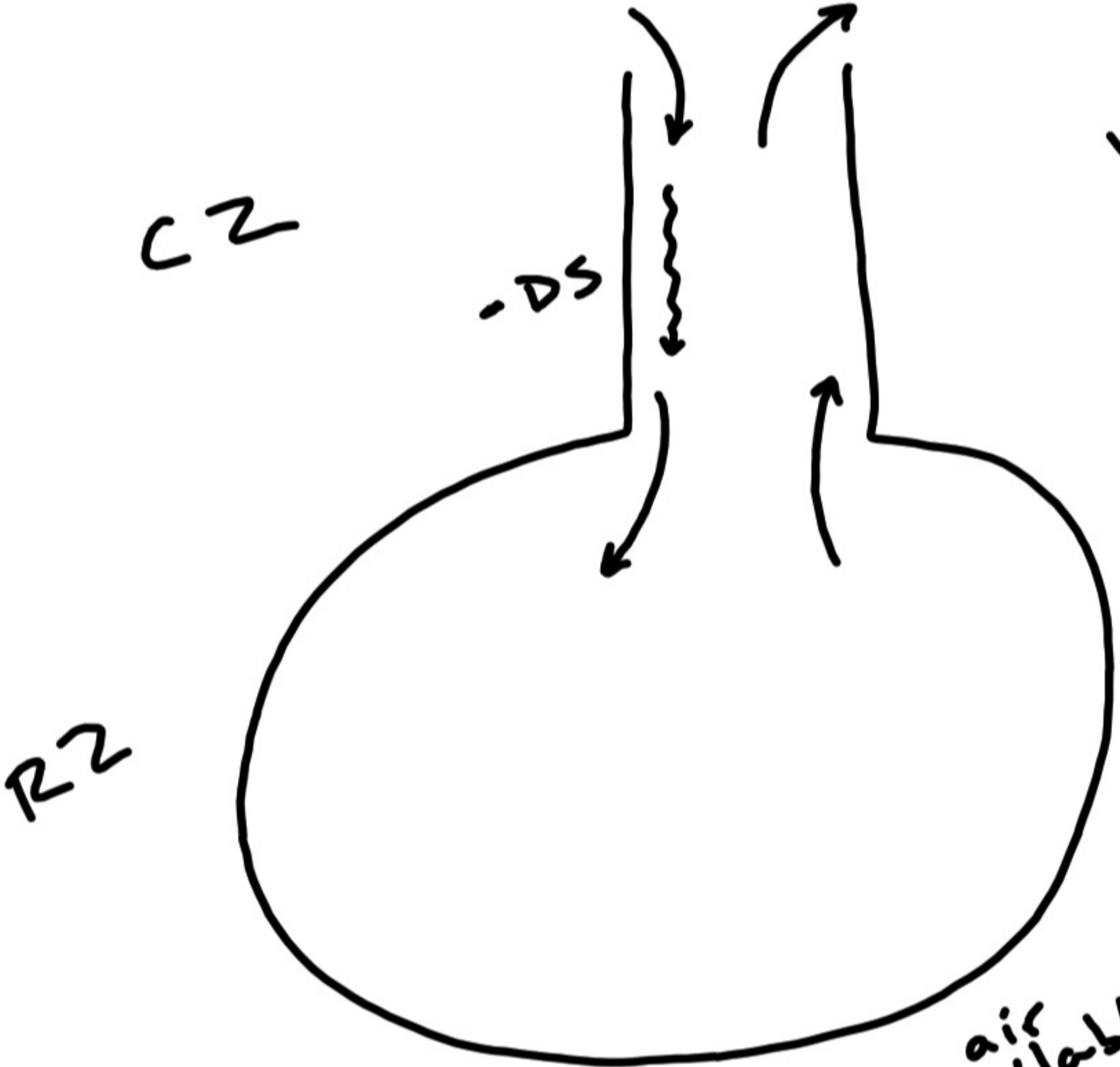


$$\frac{FEV_1}{FVC} \cdot 100 = 70 \text{ to } 80\%$$

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

Pulmonary Ventilation

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



$\dot{V}_E$: volume of air in or out of CZ per minute

$\dot{V}_E = (V_T) \times (RR)$

$\dot{V}_A$: volume of air in or out of RZ per minute

$\dot{V}_A = (V_T - DS) \times (RR)$

air available for gas exchange

Breathing

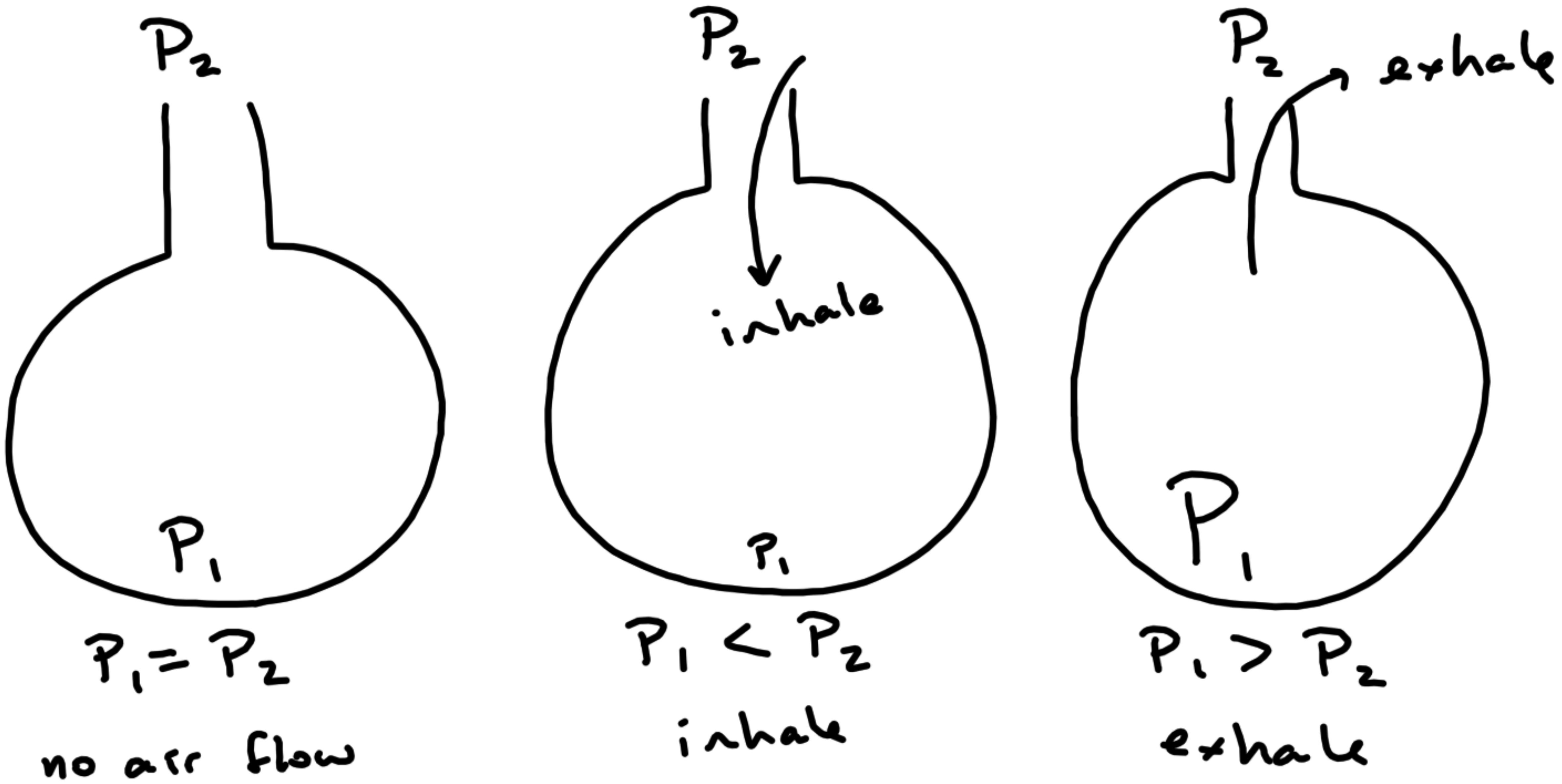
- Movement of air into and out of the lung (requires pressure gradients)
- Air Flow (Poiseuille's Law)

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

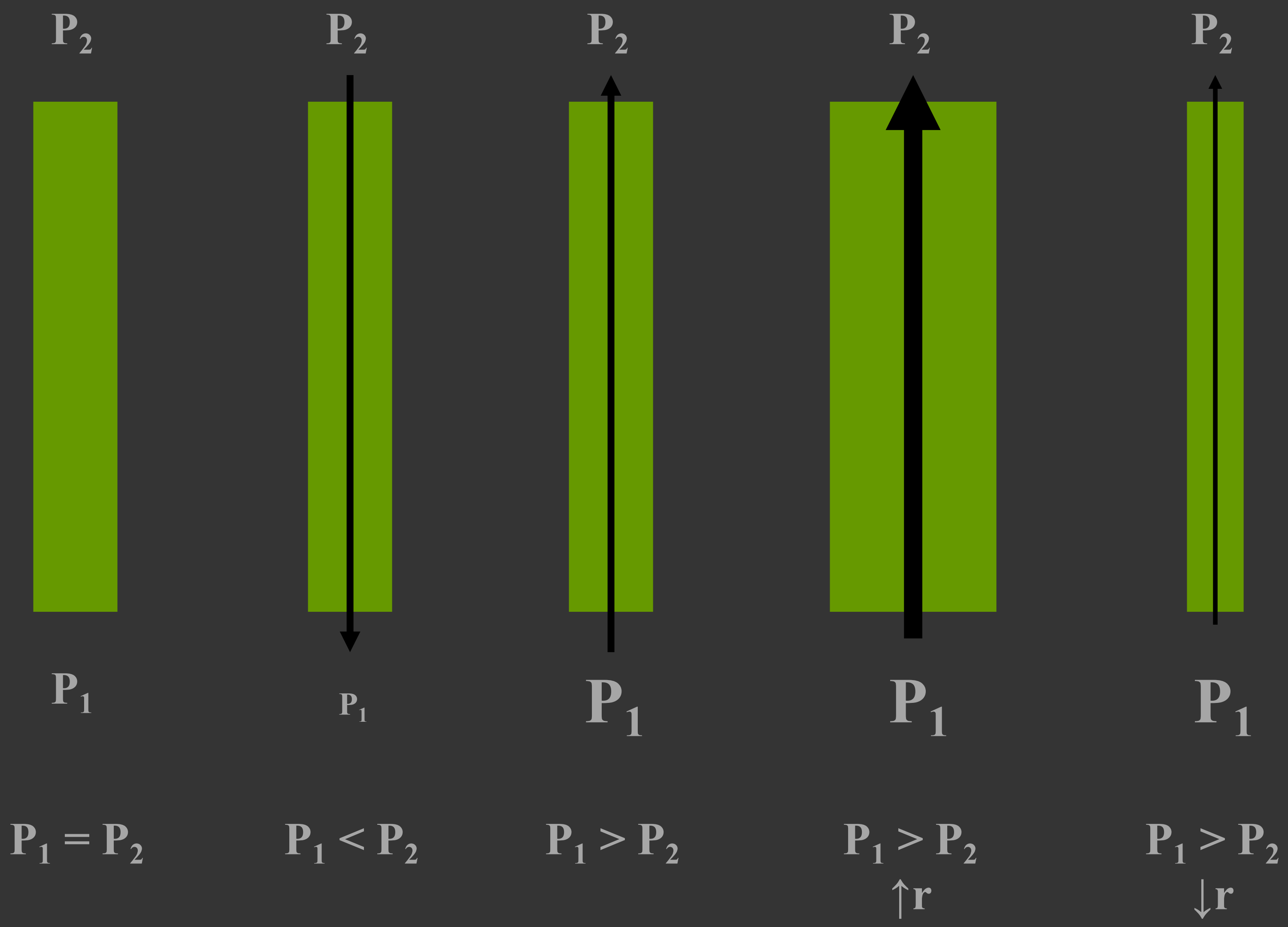
  P_1 = pressure at point 1 (inside the lung)
  P_2 = pressure at point 2 (outside the lung)
  r = radius of airway

- $(P_1 - P_2)$ is equal to pressure gradient
- If $P_1 = P_2$, there is no pressure gradient for air to flow
- If $P_1 \neq P_2$, 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

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



Air Flow , Pressure , and Resistance



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

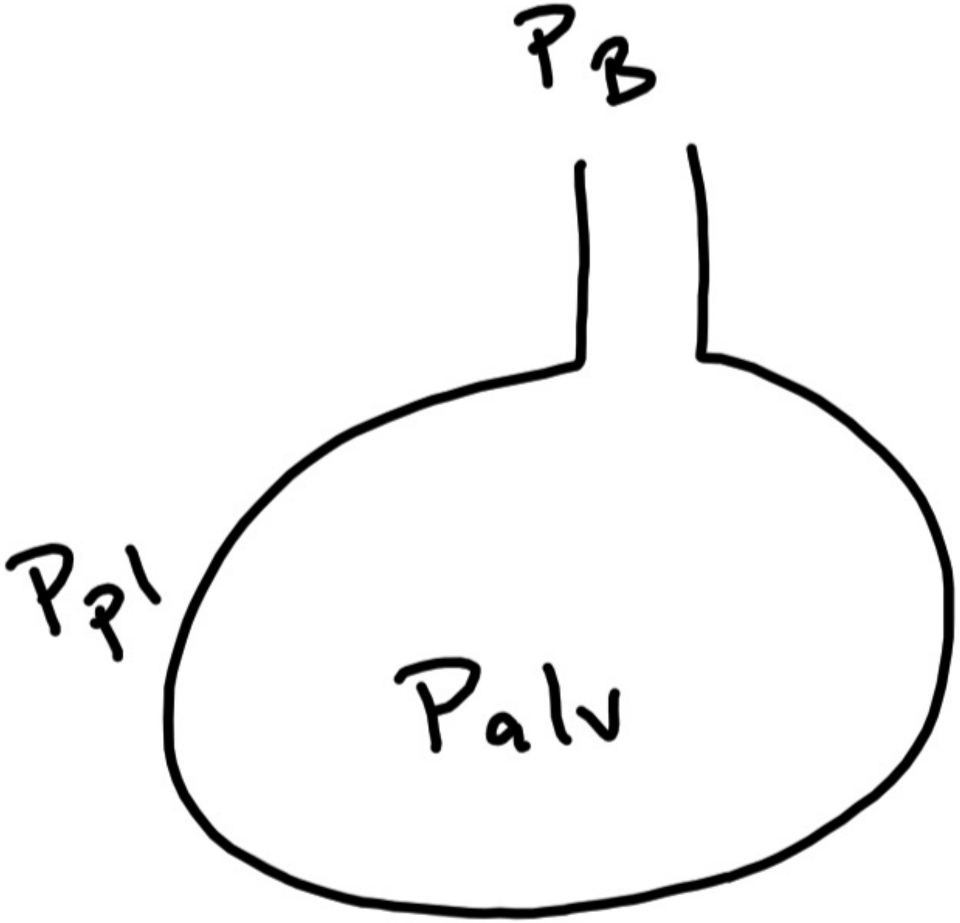
$$P = \frac{nRT}{V}$$

$\uparrow V \rightarrow \downarrow P$

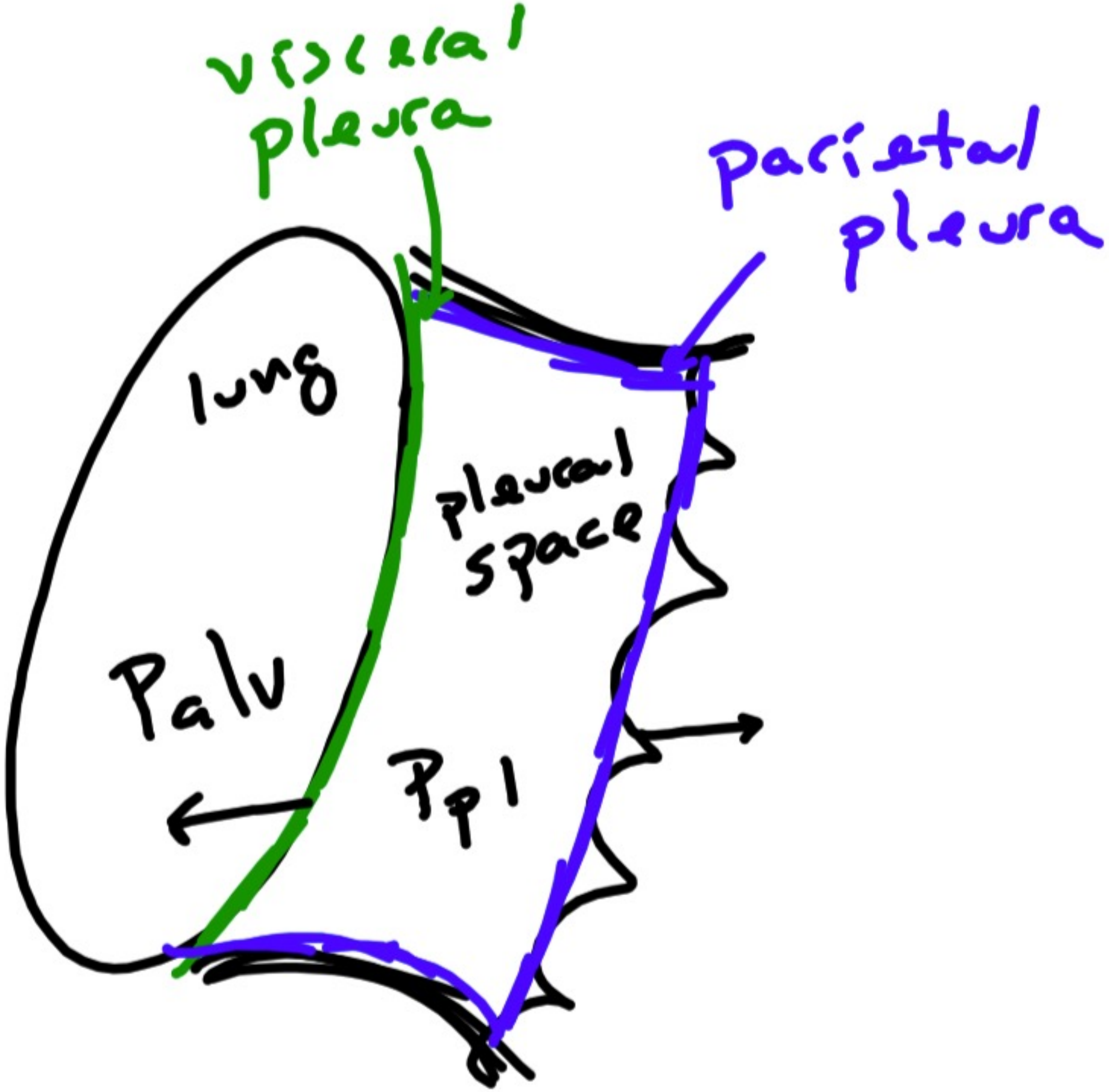
$\downarrow V \rightarrow \uparrow P$

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



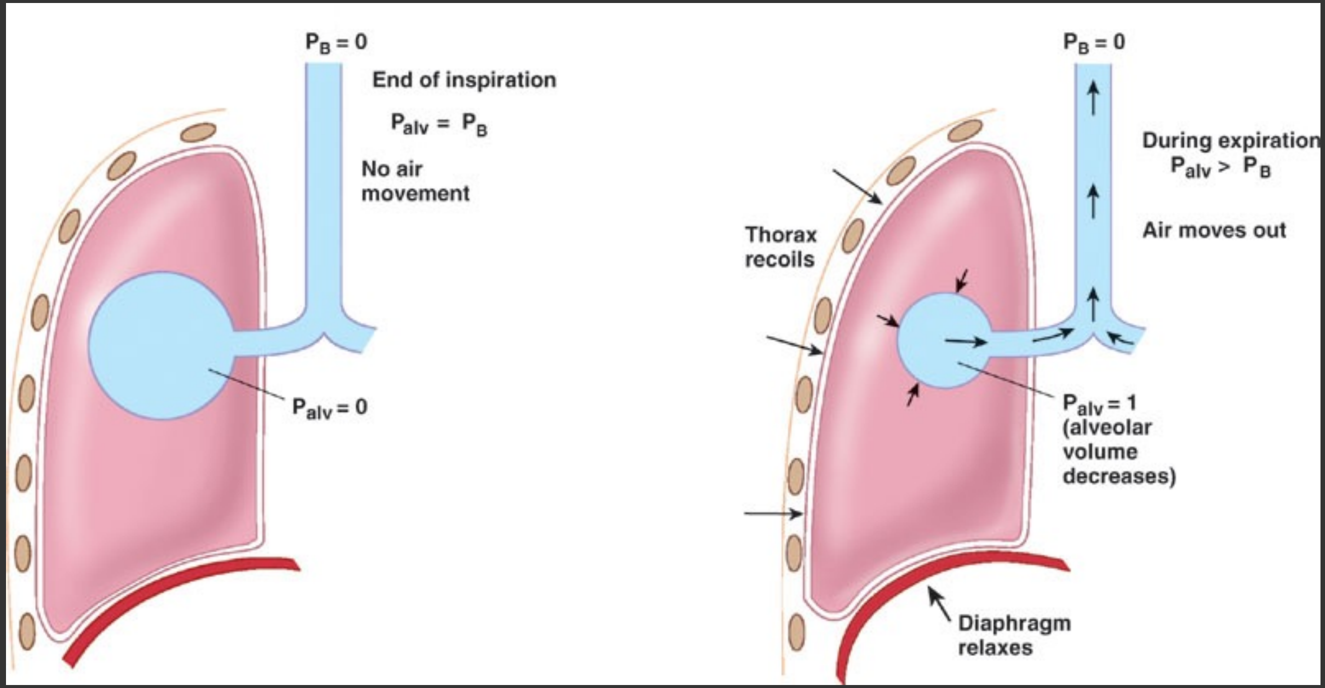
PB
Ppl
Palv

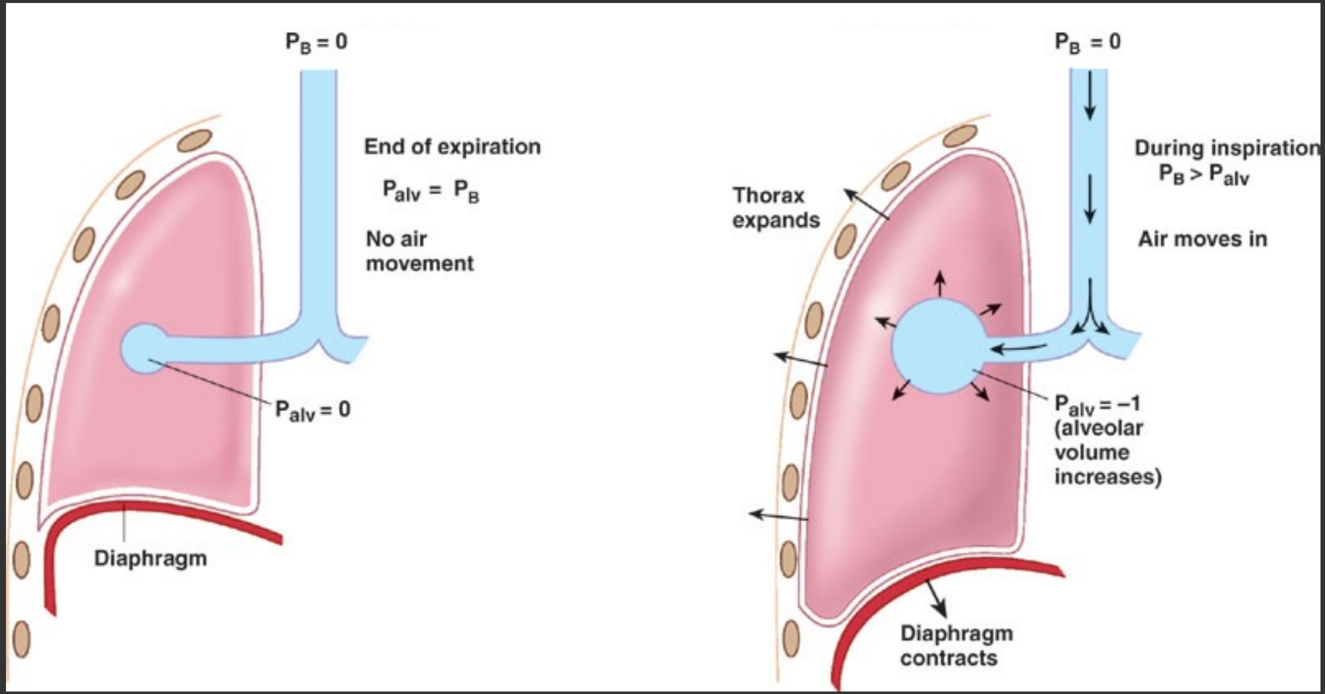


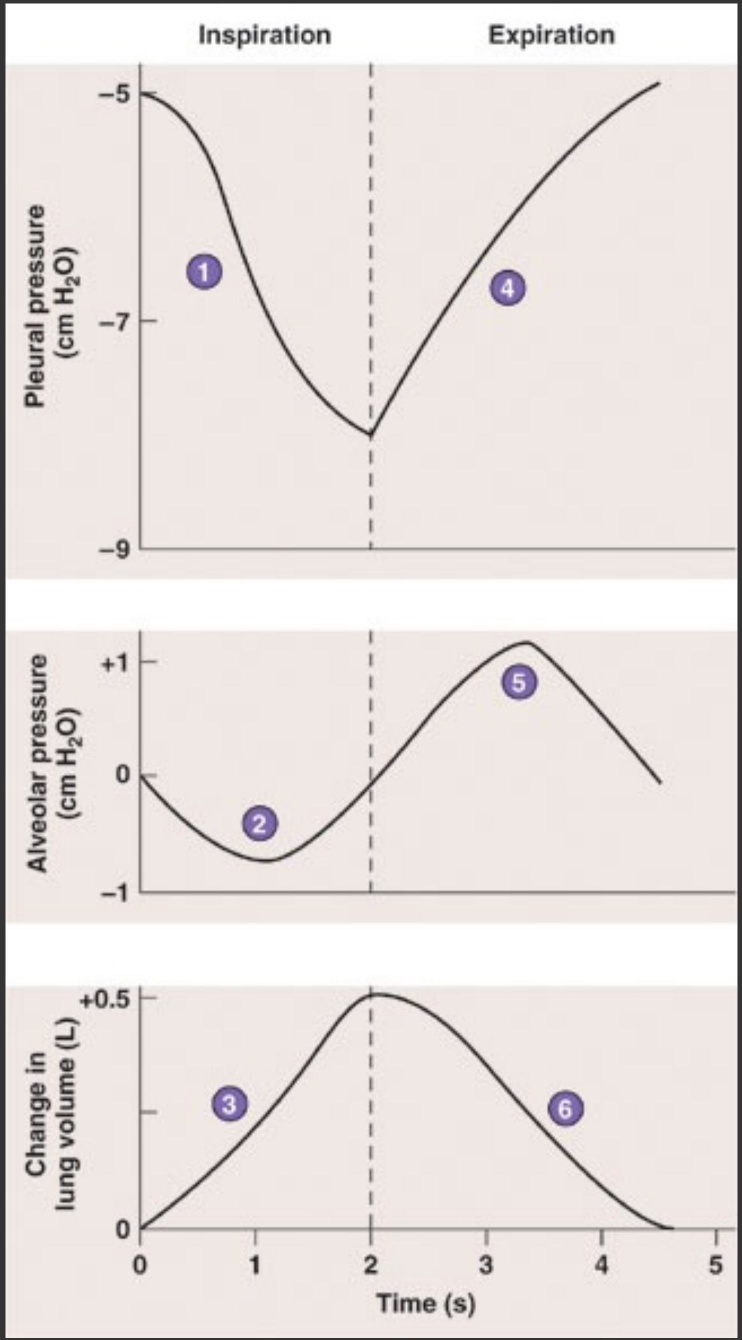
visceral pleura
parietal pleura
lung
pleural space
Palv
Ppl

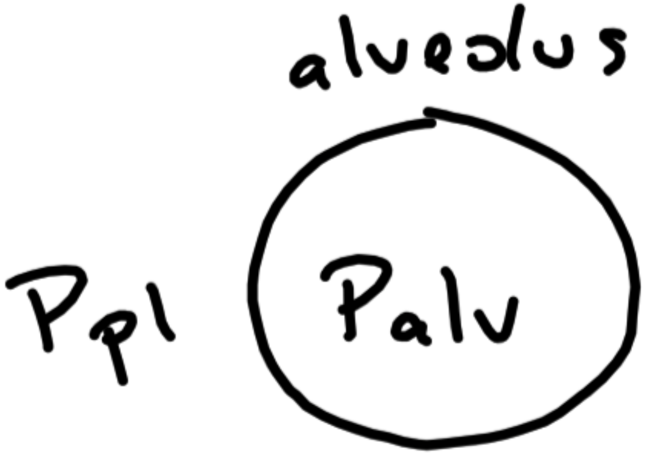
Breathing Cycle

- End of Expiration
  - P_B and P_{alv} are both equal
    - (ie , ~ 1,000 cm H_2O)
    - No pressure gradient
      - No air flow
  - P_{pl} is less than P_{alv}
    - P_{pl} is 5 cm H_2O less than P_{alv} (ie , 995 cm H_2O)
- During Inspiration
  1. Contraction of respiratory muscles
  2. Increases thoracic cavity volume , which then increases pleural space volume
  3. P_{pl} decreases towards 992 cm H_2O causing alveoli to inflate
  4. Increases alveolar volume
  5. P_{alv} decreases towards 999 cm H_2O
  6. P_{alv} is less than PB now
  7. Air into lung down pressure gradient
  8. Air filling the alveoli causes P_{alv} to increase back towards 1,000 cm H_2O
- End of Inspiration
  1. Thoracic cavity has stopped expanding (thoracic cavity at its greatest volume)
  2. P_{pl} is 992 cm H_2O (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 cm H_2O
  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 cm H_2O
  4. Decreases alveolar volume toward resting levels
  5. P_{alv} increases above P_B towards 1,001 cm H_2O
  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 to 1,000 cm H_2O


$P_B = 0$
End of inspiration
$P_{alv} = P_B$
No air movement
$P_{alv} = 0$
$P_B = 0$
During expiration
$P_{alv} > P_B$
Air moves out
Thorax recoils
$P_{alv} = 1$ (alveolar volume decreases)
Diaphragm relaxes


$P_B = 0$
End of expiration
$P_{alv} = P_B$
No air movement
$P_{alv} = 0$
Diaphragm
$P_B = 0$
During inspiration
$P_B > P_{alv}$
Air moves in
Thorax expands
$P_{alv} = -1$ (alveolar volume increases)
Diaphragm contracts

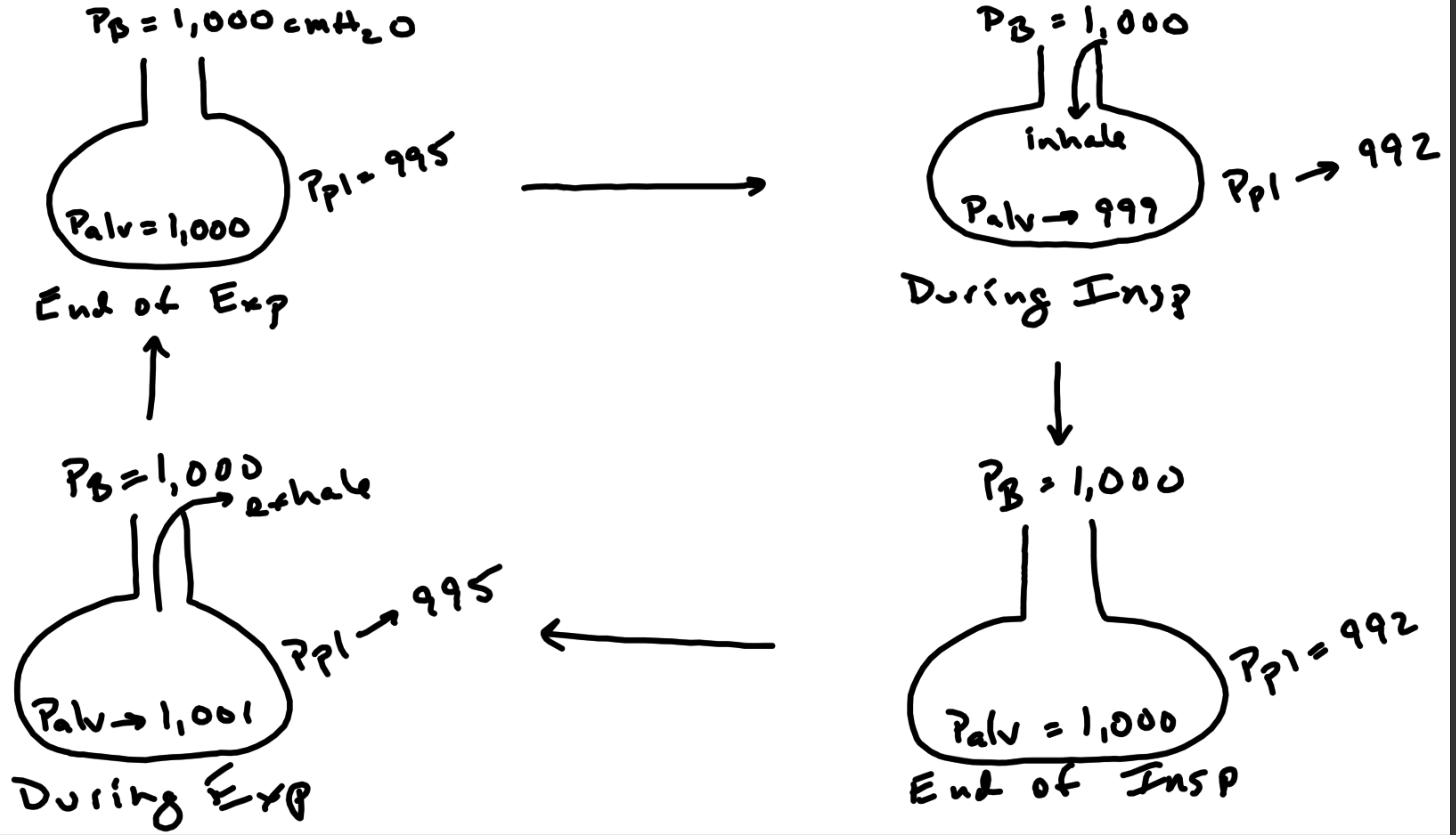

Inspiration
Expiration
Pleural pressure ($cm\ H_2O$)
−5
−7
−9
1
4
Alveolar pressure ($cm\ H_2O$)
+1
0
−1
2
5
Change in lung volume (L)
+0.5
0
3
6
0
1
2
3
4
5
Time (s)



$P_{pl} < P_{alv}$

← help keep the alveoli inflated

$\uparrow P_{pl}$	$\downarrow P_{pl}$
$\downarrow$	$\downarrow$
$\downarrow$ alveolar volume	$\uparrow$ alveolar volume
$\downarrow$	$\downarrow$
$\uparrow P_{alv}$	$\downarrow P_{alv}$



PB = 1,000 cmH2O
Ppl = 995
Palv = 1,000
End of Exp
PB = 1,000
inhale
Ppl → 992
Palv → 999
During Insp
PB = 1,000
Ppl = 992
Palv = 1,000
End of Insp
PB = 1,000
exhale
Ppl → 995
Palv → 1,001
During Exp

During Insp

Respiratory muscles contract

↓

↑ Thoracic Cavity Volume

↓

↑ Pleural Space Volume

↓

↓ Ppl

↓

↑ alveolar volume

↓

↓ Palv

↓

inhale

During Exp

Respiratory muscles relax

↓

↓ Thoracic Cavity Volume

↓

↓ Pleural Space Volume

↓

↑ Ppl

↓

↓ alveolar volume

↓

↑ Palv

↓

exhale

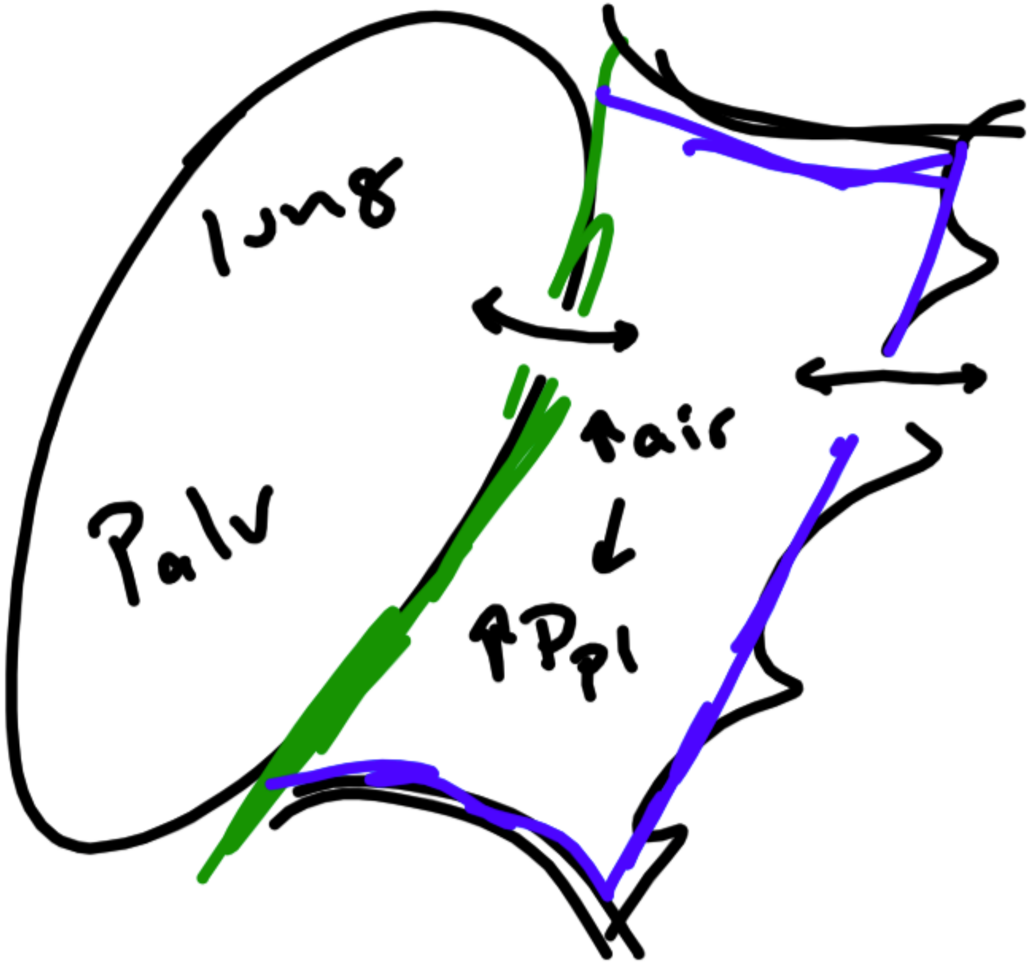
Pneumothorax

- 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

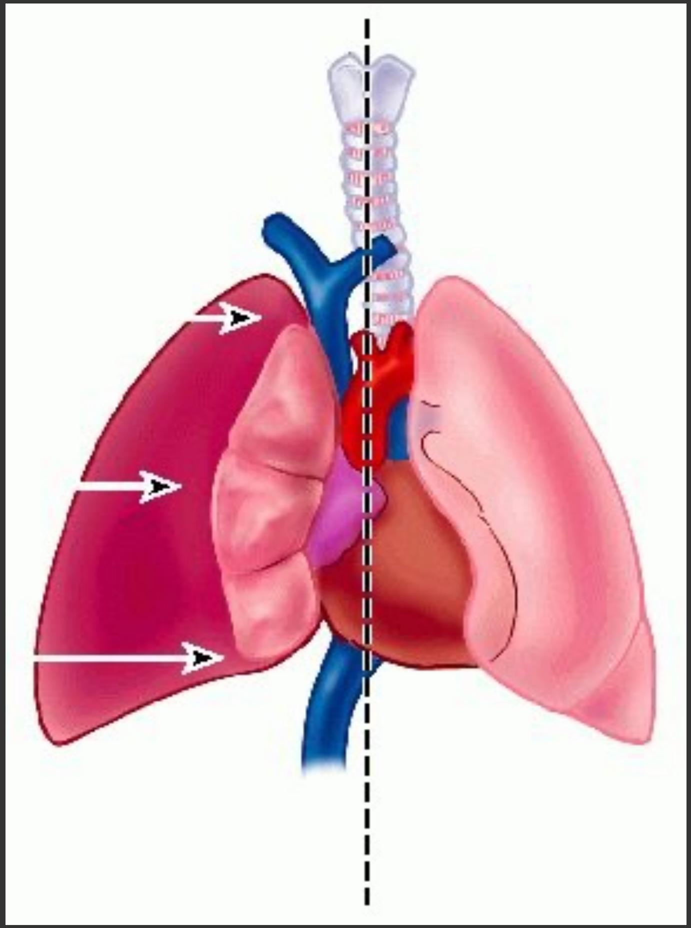
- Tension pneumothorax
  - P_{pl} is more positive than P_{alv}
    - Pushes structures on opposite side of thoracic cavity (ie , the heart)
      - Can lead to dangerous decrease in cardiac output and blood pressure

Simple Pneumo



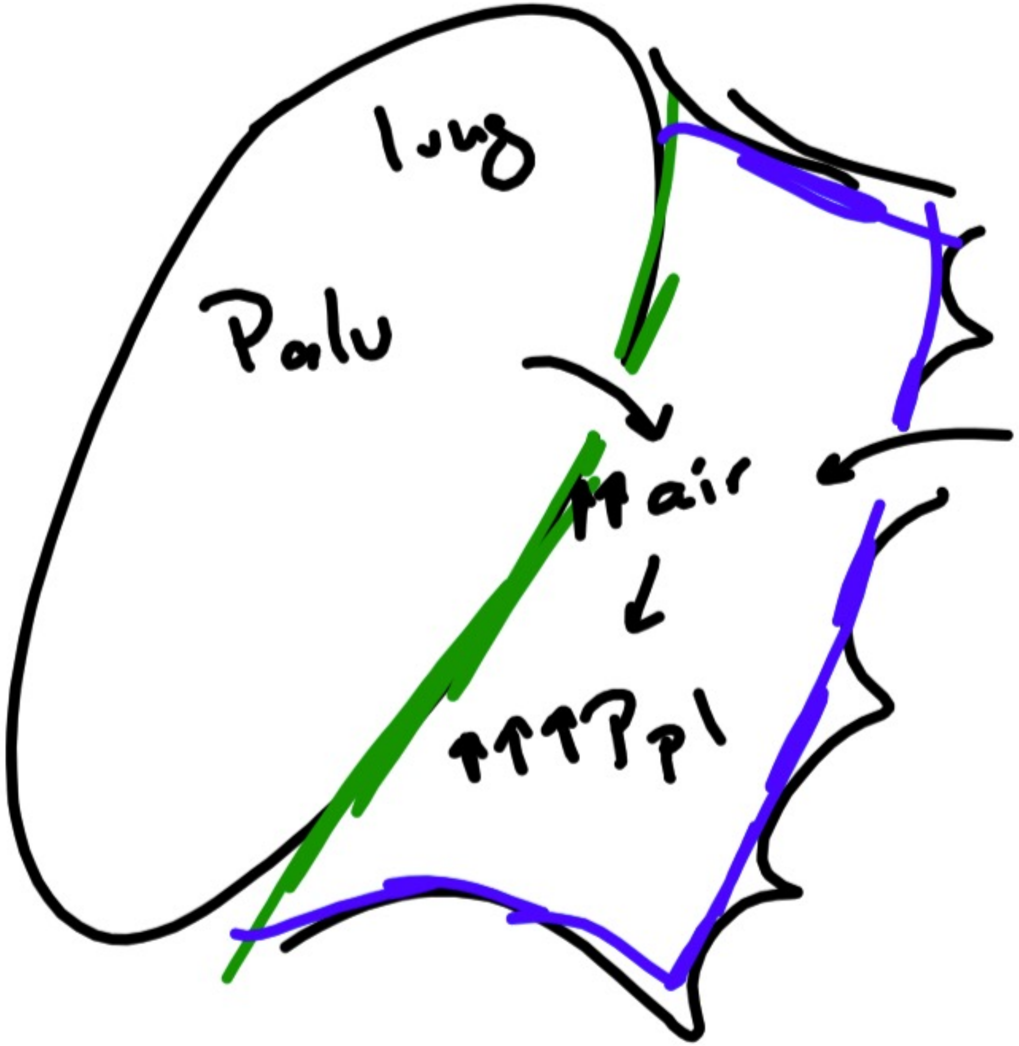
$P_{pl} = P_{alv}$

Tension Pneumothorax



Right-sided tension pneumothorax

Tension Pneumo



$P_{pl} > P_{alv}$

Severe Tension Pneumo

↓

"Squeeze Heart"

↓

↓↓↓↓ heart contractility

↓

↓↓↓↓ SV

↓ ← ↑↑ HR

↓↓ CO

↓

↓↓ BP

↓

↓↓ blood flow

↓

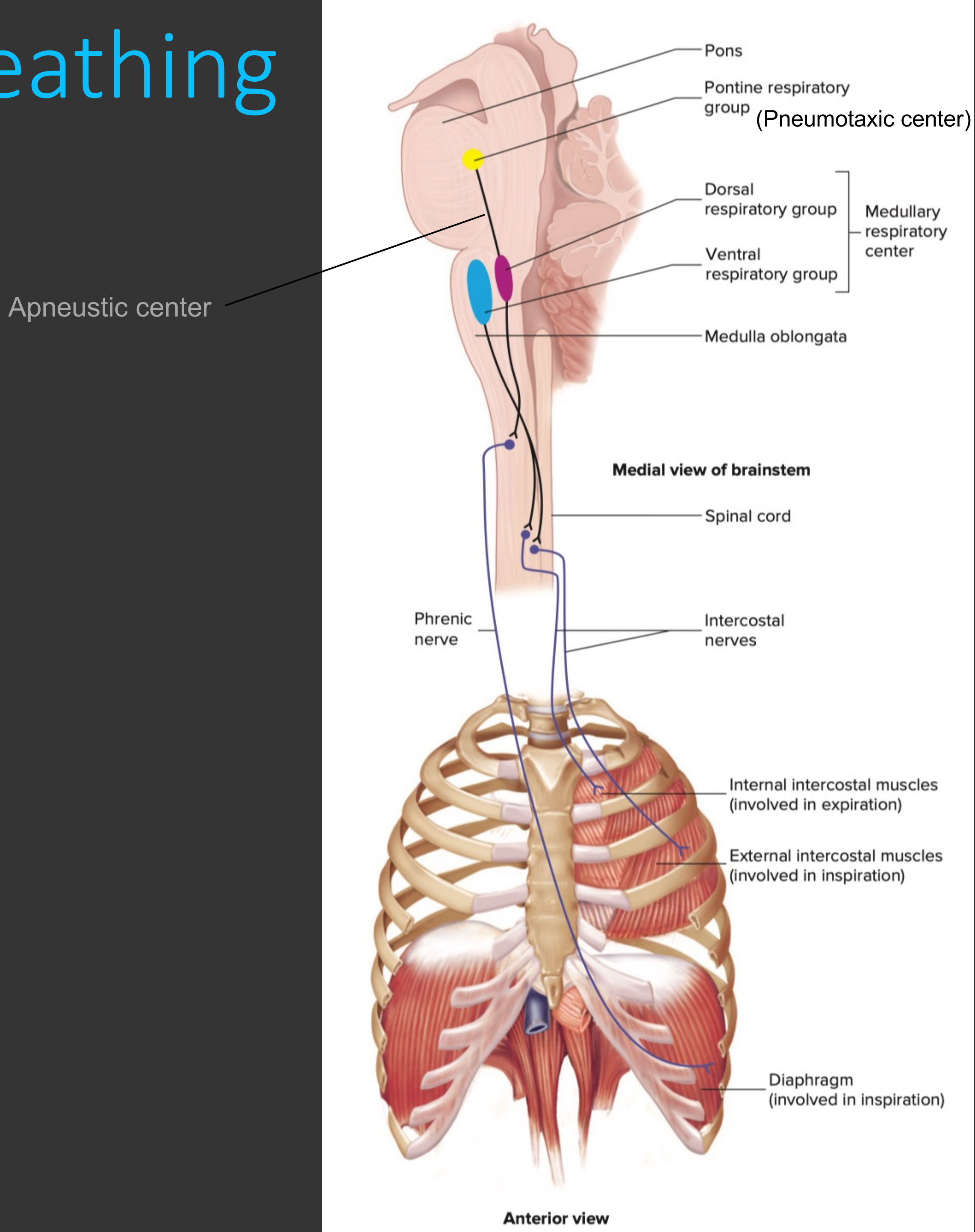
organ failure → death

$MAP = (CO) \times (TPR)$

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 exteroreceptors

Regulation of Breathing



Inputs to Respiratory Centers

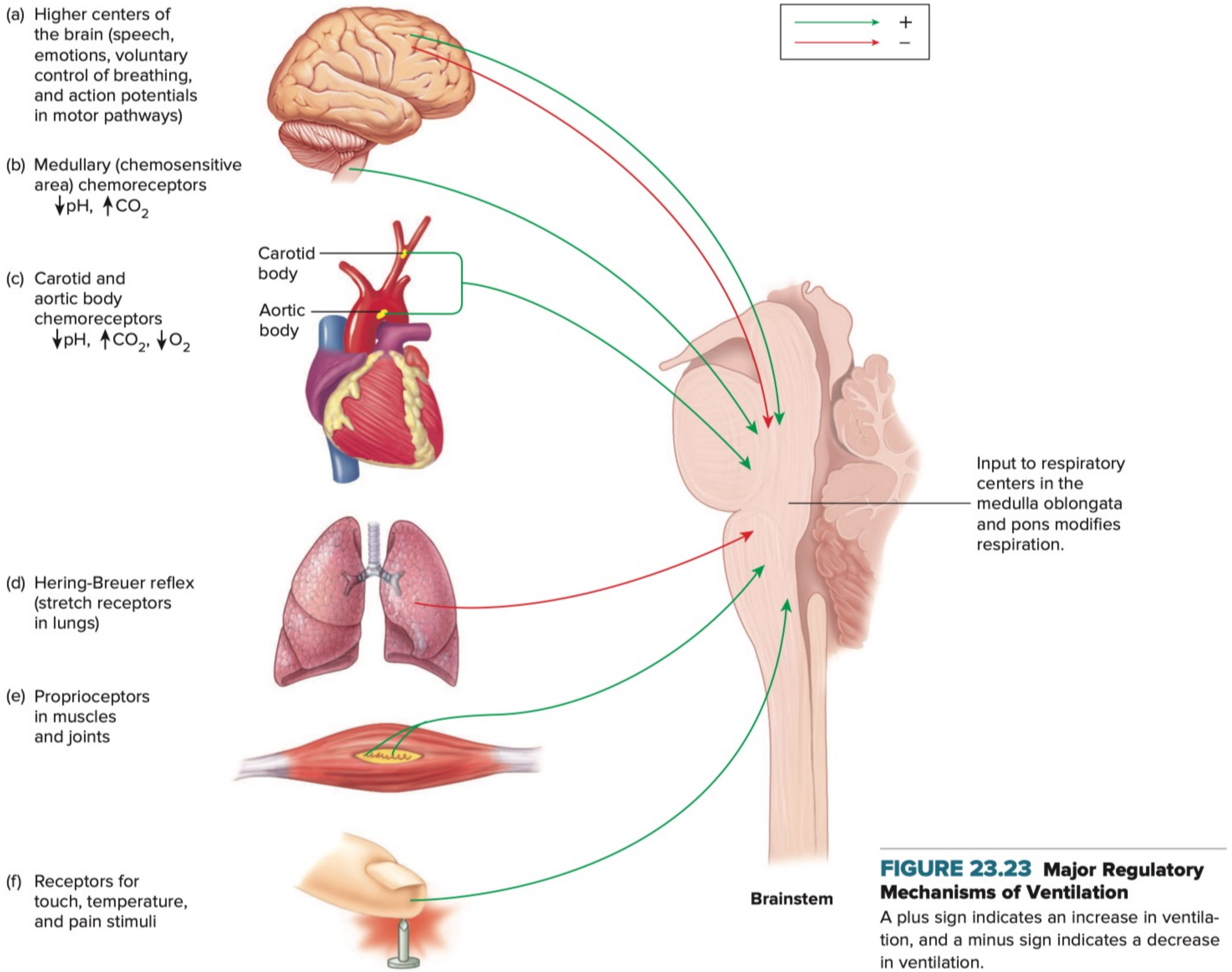


FIGURE 23.23 Major Regulatory Mechanisms of Ventilation

A plus sign indicates an increase in ventilation, and a minus sign indicates a decrease in ventilation.

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_2 levels (mainly central chemoreceptors)
  - CO_2 is the main stimulus to breathing
- Monitor arterial O_2 levels (mainly peripheral chemoreceptors)
  - O_2 stimulates breathing only in extreme instances ($PO_2 < 60$ mm Hg)

Cerebrum
(thoughts)

Hypothalamus
(emotion)

+ −

+ −

Respiratory Center

VRG	DRG
↓ pre-Böt	

+ −

Respiratory center

+ irritant receptors → cough

Chemoreceptors (central & peripheral)

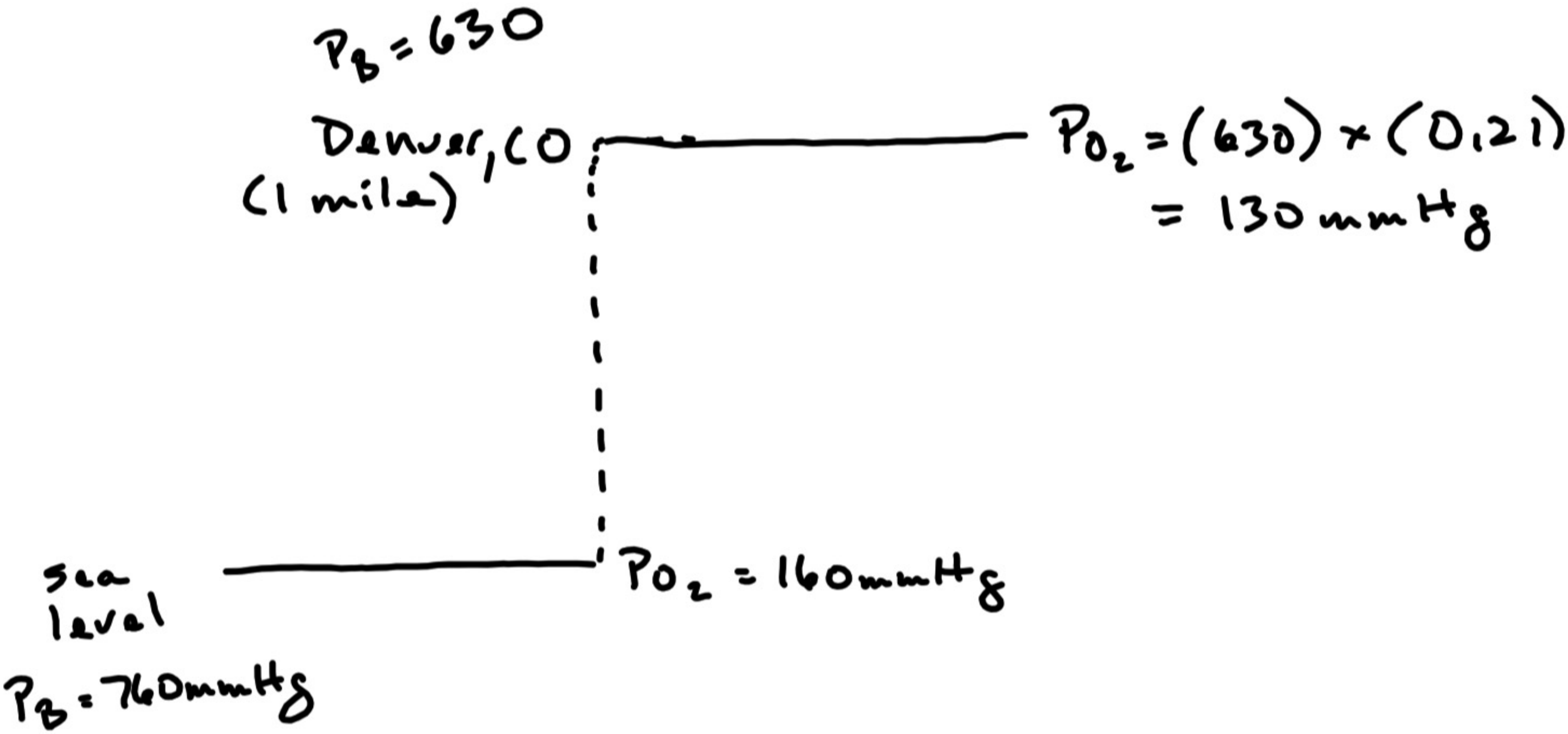
└ detect level of CO_2 and O_2 in the blood

← main drive to breathe is the level of CO_2

$\uparrow CO_2 \rightarrow$ stim $\downarrow CO_2 \rightarrow$ 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
  - $\therefore$ partial of pressure of oxygen (P_{O_2}) = (760 mm Hg) * (0.21) ≈ 160 mm Hg
  - $\therefore$ 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)
$P_{O_2} = (630) \times (0.21)$
$= 130\ mmHg$
sea
level
$P_{O_2} = 160\ mmHg$
$P_B = 760\ mmHg$

Partial Pressures

- Partial pressures in dry air at sea level
  - $P_{O_2} = (760\ mm\ Hg) * 0.21 = 160\ mm\ Hg$
  - P_{CO_2} = negligible
- Partial pressures in conducting zone
  - $P_{O_2} = (760\ mm\ Hg - 47\ mm\ Hg) * 0.21 = 150\ mm\ Hg$
  - 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
  - $\therefore$ 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
  - $\therefore$ 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 O2 during aerobic cellular respiration
  - $\therefore$ gradient for O_2 to diffuse from interstitial space into cells

* Room Air : 21% O_2
* Supplemental Oxygen

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

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

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

$100\%: P_{O_2} = (760) \times (1) = 760\ mmHg$

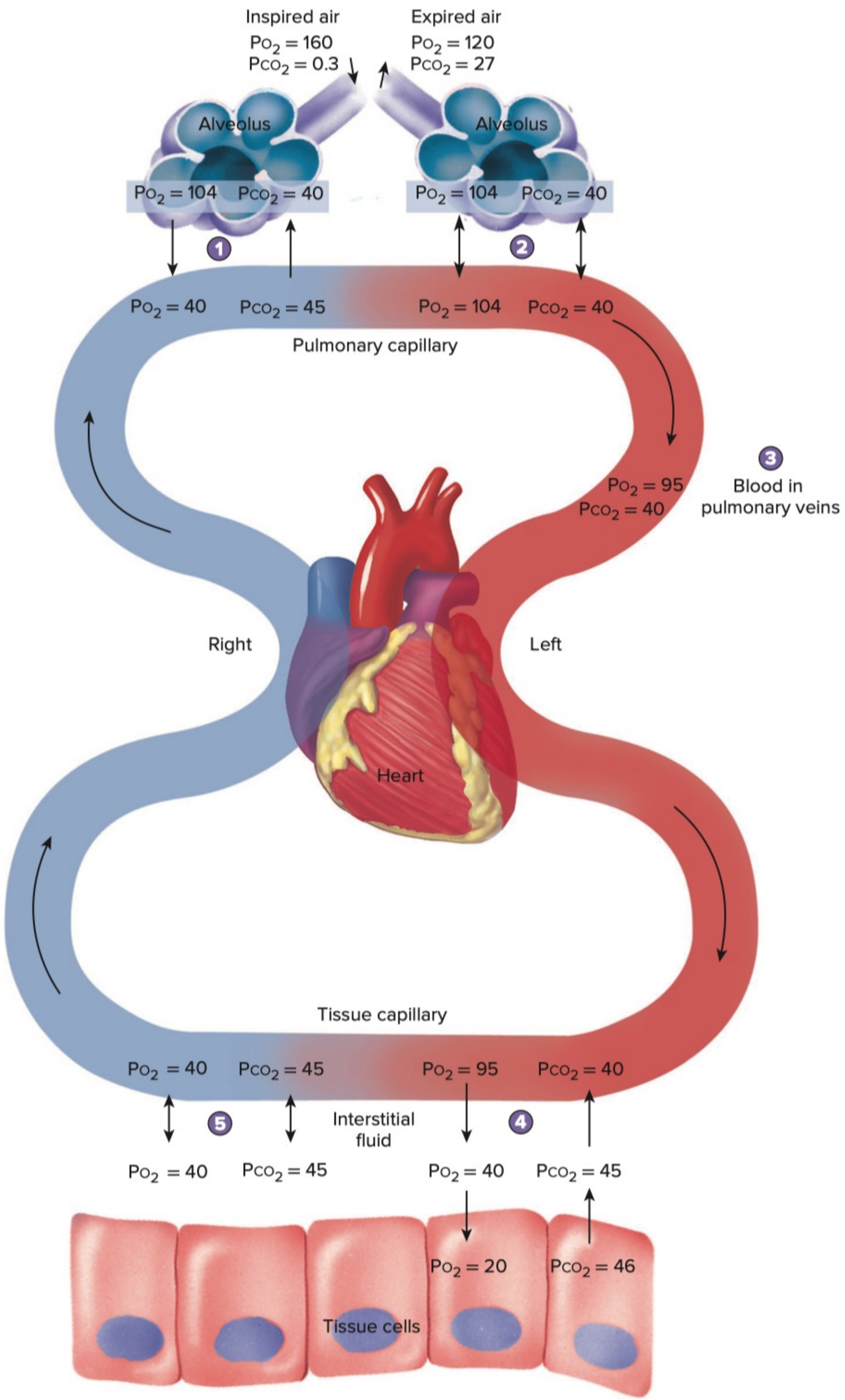
1 Oxygen diffuses into the arterial ends of pulmonary capillaries, and CO_2 diffuses into the alveoli because of differences in partial pressures.

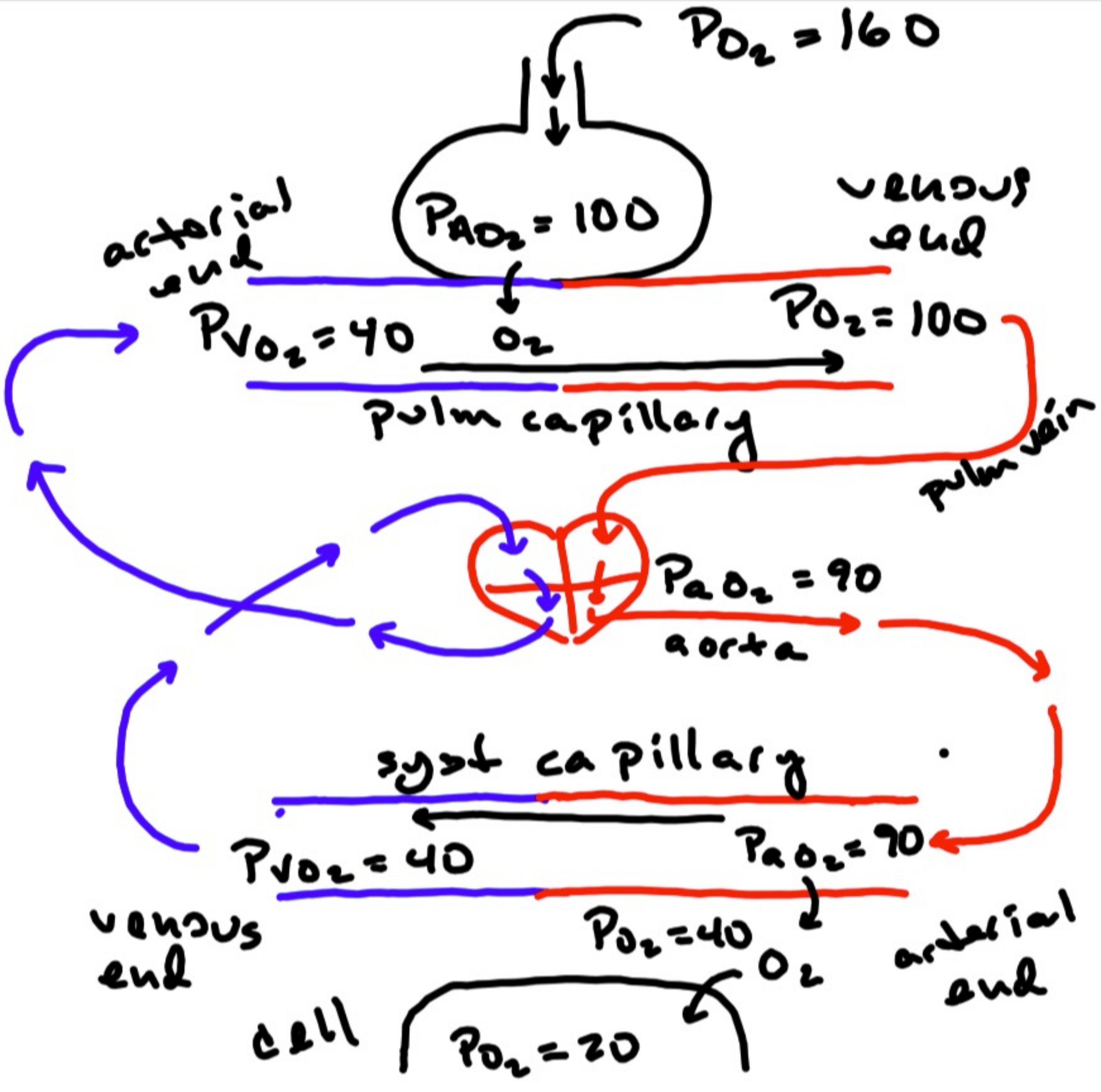
2 As a result of diffusion at the venous ends of pulmonary capillaries, the P_{O_2} in the blood is equal to the P_{O_2} in the alveoli, and the P_{CO_2} in the blood is equal to the P_{CO_2} in the alveoli.

3 The P_{O_2} 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.

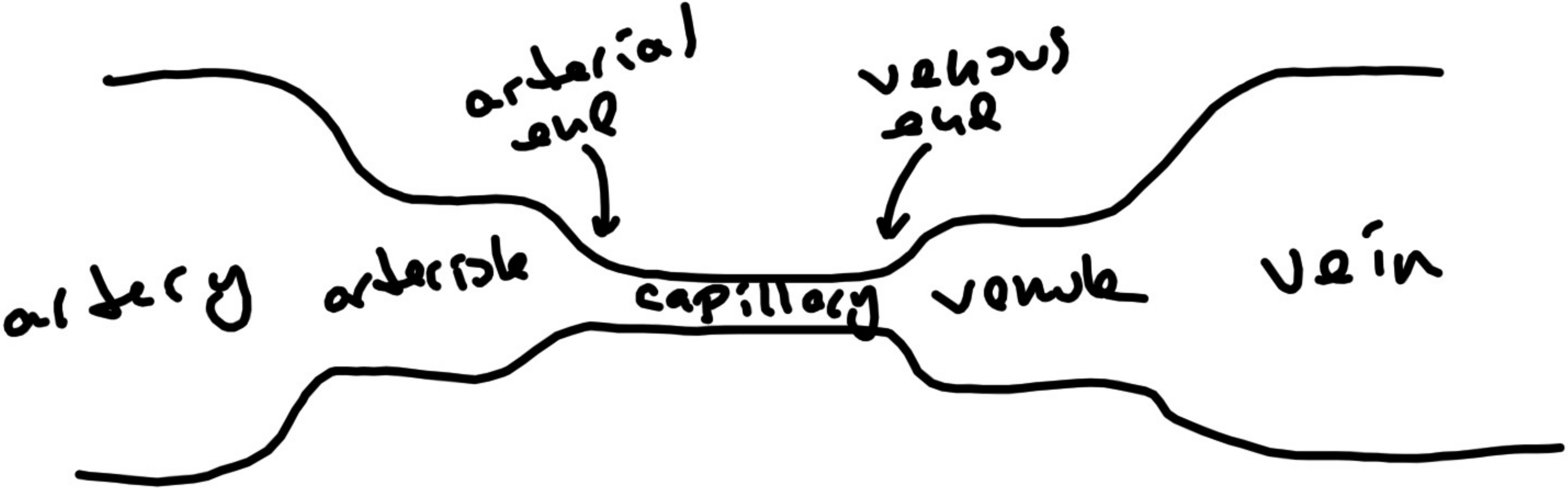
4 Oxygen diffuses out of the arterial ends of tissue capillaries, and CO_2 diffuses out of the tissue because of differences in partial pressures.

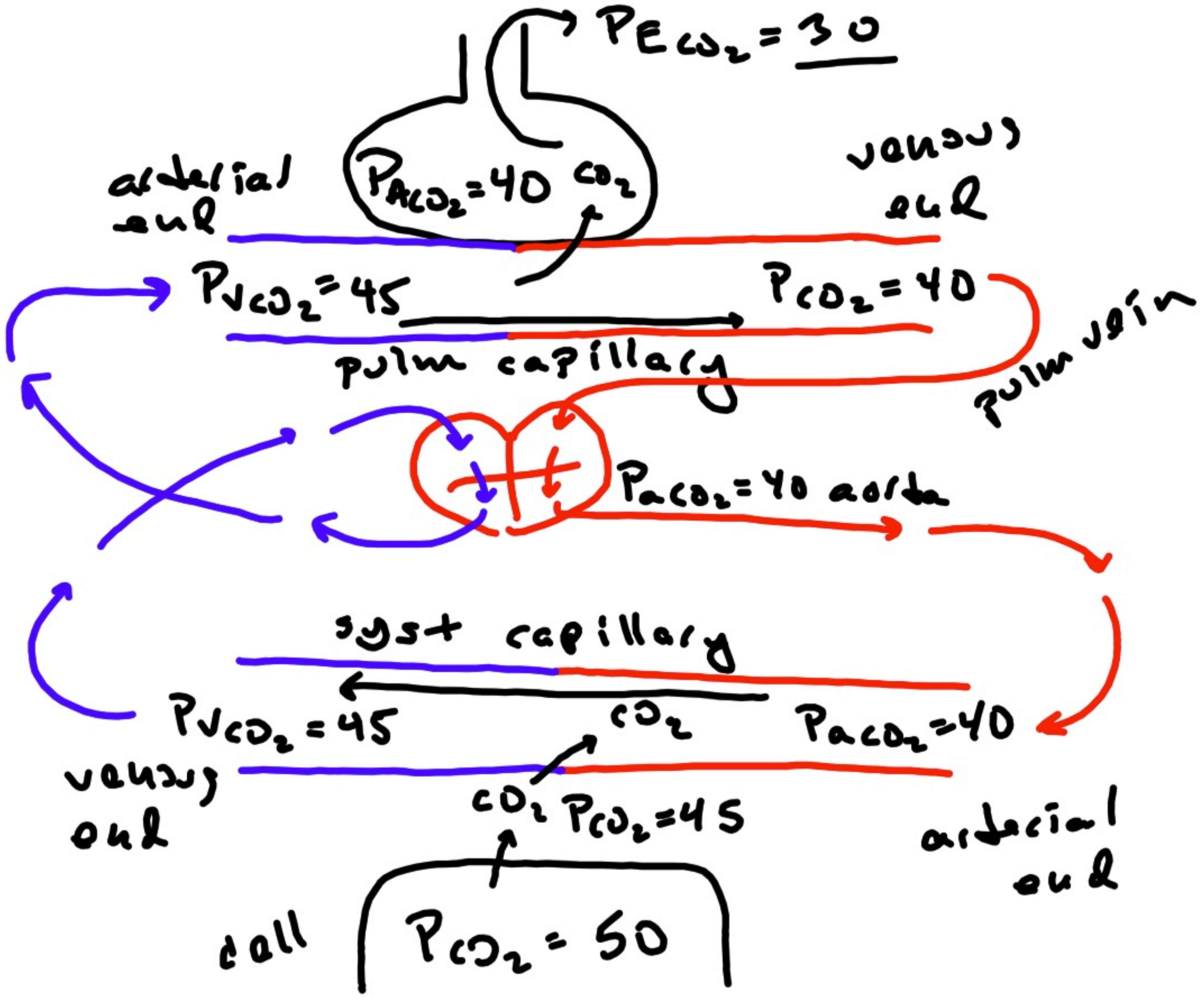
5 As a result of diffusion at the venous ends of tissue capillaries, the P_{O_2} in the blood is equal to the P_{O_2} in the tissue, and the P_{CO_2} in the blood is equal to the P_{CO_2} in the tissue. Go back to *step 1*.





$P_{O_2} = 160$
$P_{AO_2} = 100$
arterial end
venous end
$P_{VO_2} = 40$
O_2
$P_{O_2} = 100$
pulm capillary
pulm vein
$P_{aO_2} = 90$
aorta
syst capillary
$P_{VO_2} = 40$
$P_{aO_2} = 90$
venous end
$P_{O_2} = 40$
O_2
arterial end
cell
$P_{O_2} = 20$


arterial
end
venous
end
artery
arteriole
capillary
venule
vein



$P_{ECO_2} = 30$
$P_{ACO_2} = 40$
CO_2
arterial end
venous end
$P_{\bar{v}CO_2} = 45$
$P_{CO_2} = 40$
pulm capillary
pulm vein
$P_{aCO_2} = 40$ aorta
syst capillary
$P_{\bar{v}CO_2} = 45$
CO_2
$P_{aCO_2} = 40$
venous end
CO_2 $P_{CO_2} = 45$
arterial end
cell
$P_{CO_2} = 50$

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
  - $\therefore$ 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
  - $\therefore$ 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
  - $\therefore$ 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

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

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

Gas Transport

- Oxygen is transported in two different ways :
  - Dissolved (~ 1.5 %)
  - Hemoglobin (~ 98.5 %)

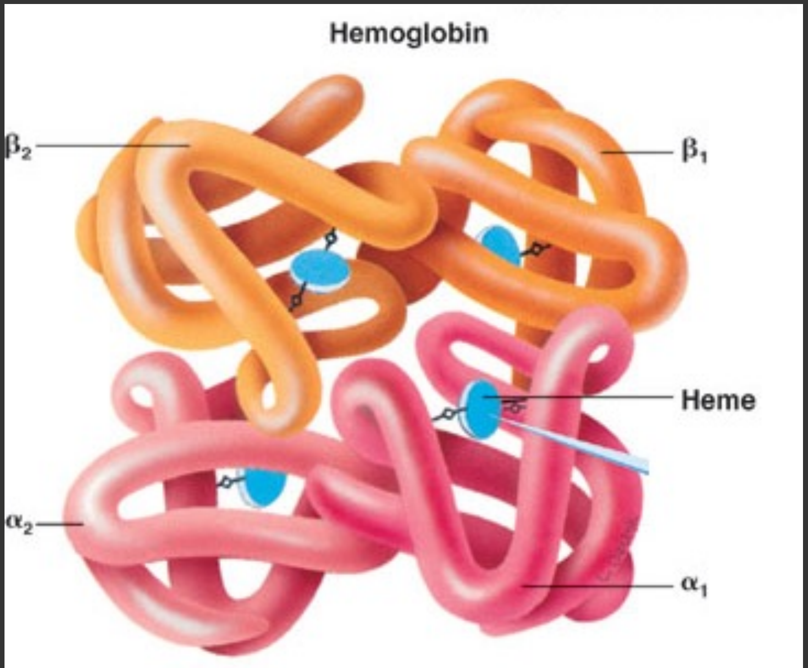
- Carbon dioxide is transported in three different ways
  - Dissolved (~ 5 to 30 %)
  - Hemoglobin (~ 5 to 10 %)
  - Bicarbonate (~ 60 to 90 %)

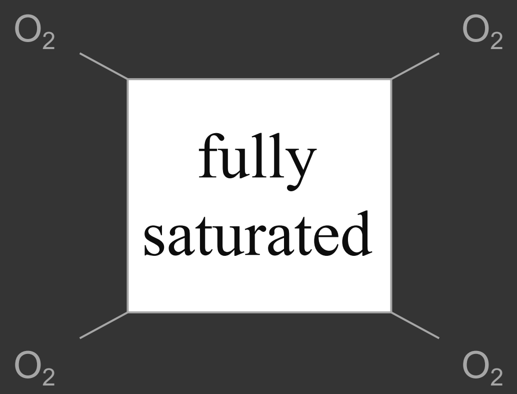
Gas Transport

- 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

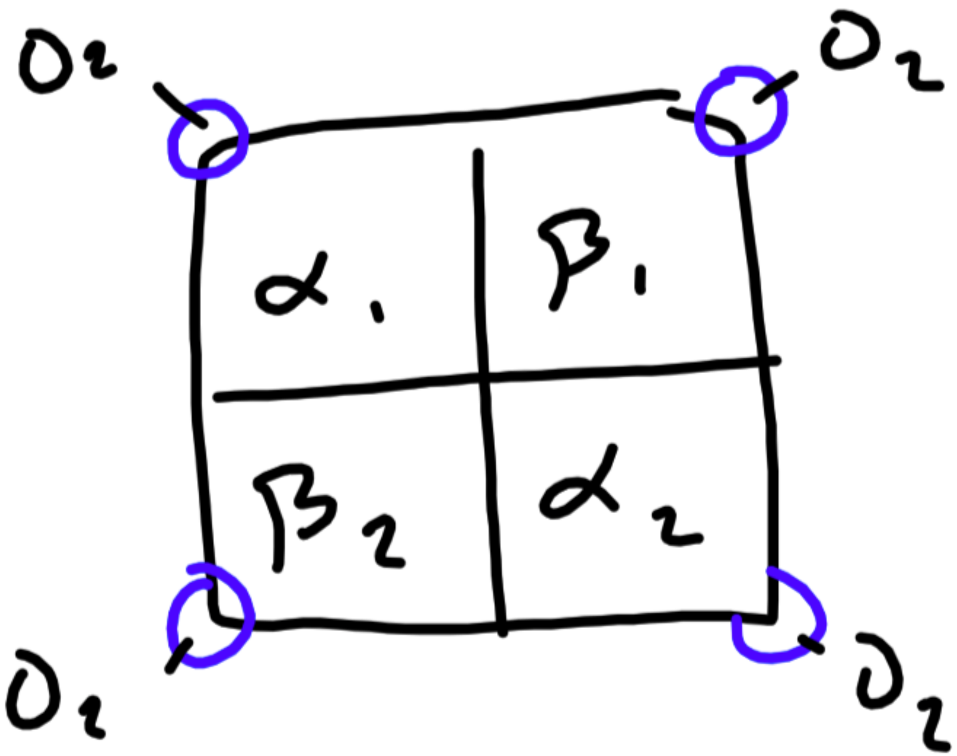
Gas Transport

- 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





Hb



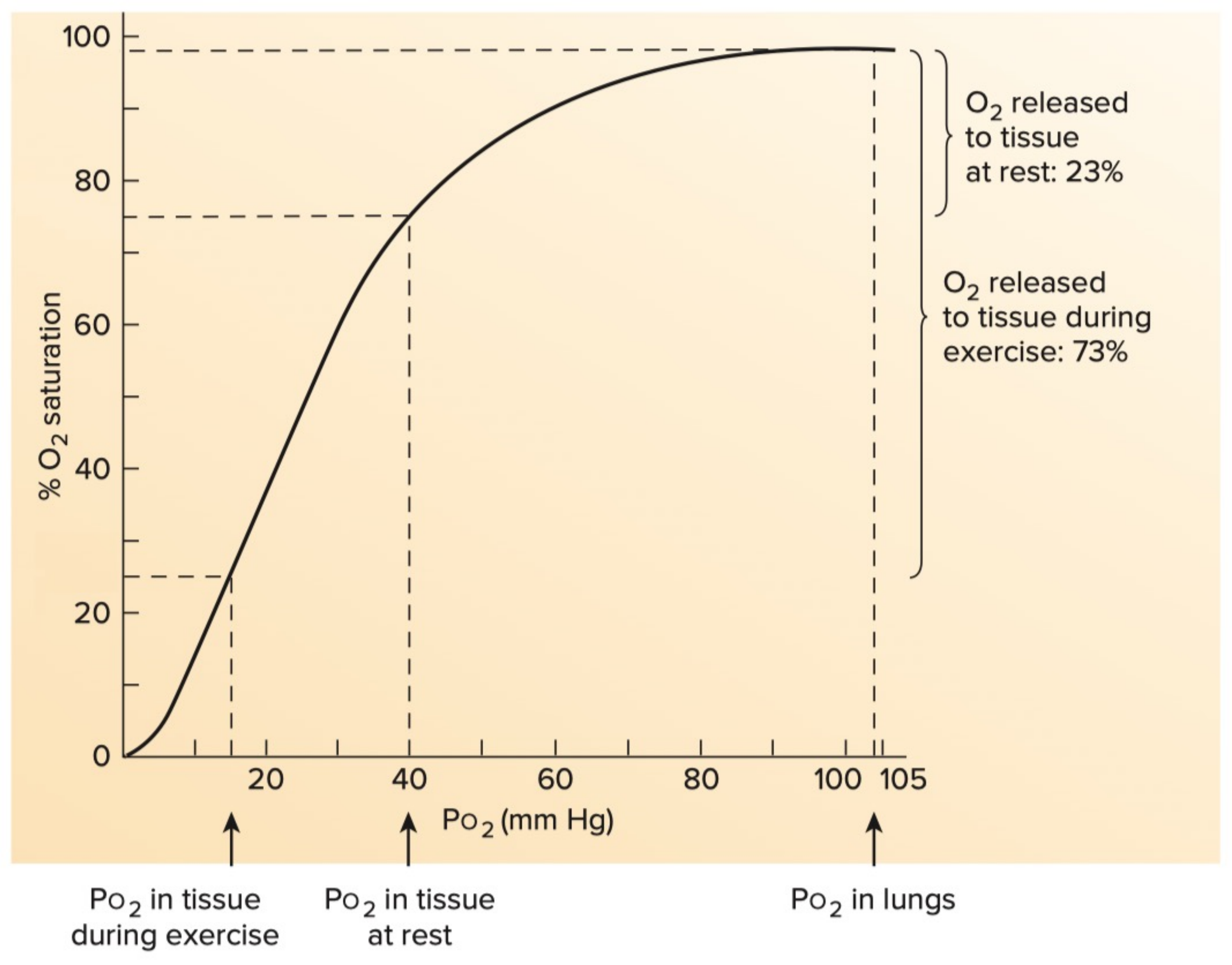
fully saturated

* 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
  - At a P_{O_2} of 90 mm Hg :
    - SaO_2 is approximately 100 %
  - At a P_{O_2} of 40 mm Hg :
    - SaO_2 is approximately 75 %



Oxygen–Hemoglobin Binding

- Affected By :
  - CO_2 / pH
  - Temperature
  - 2,3-biphosphoglycerate
  - Carbon monoxide

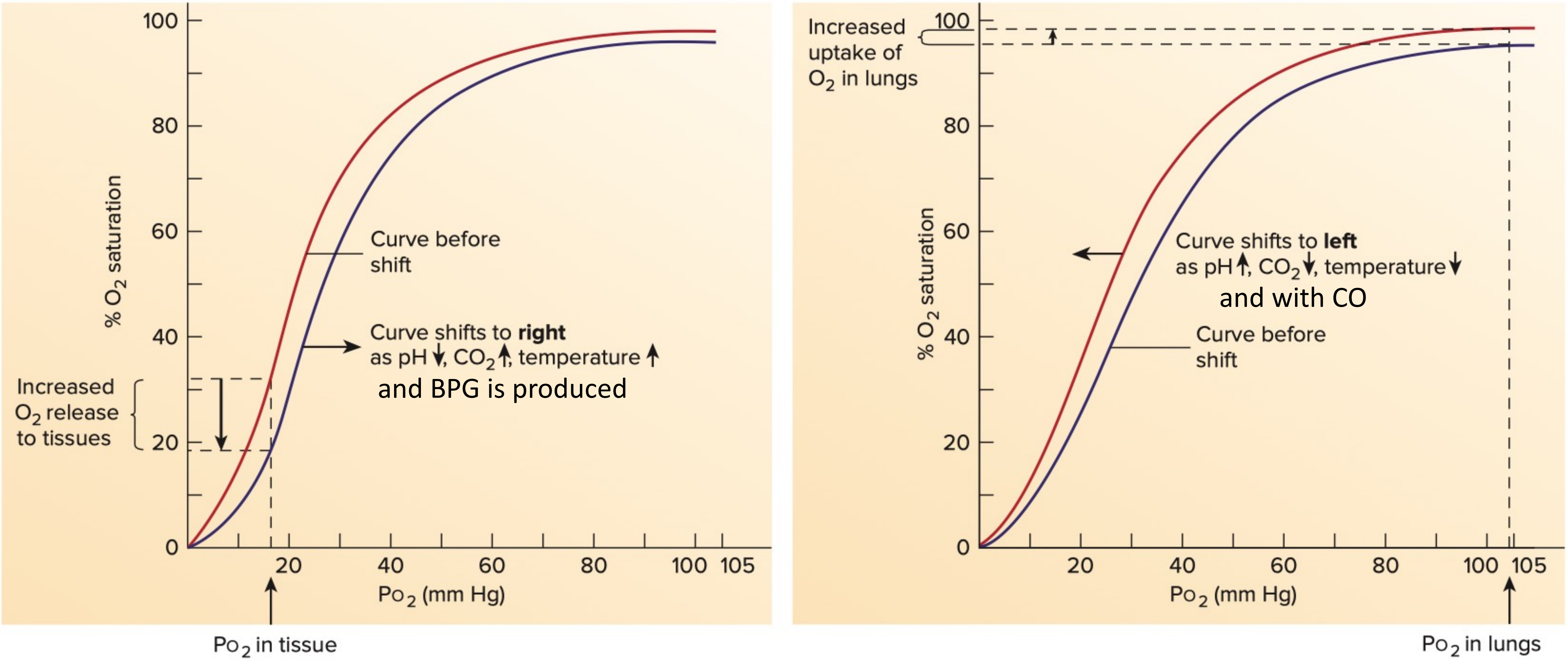
Altering Oxygen–Hemoglobin Binding

- 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

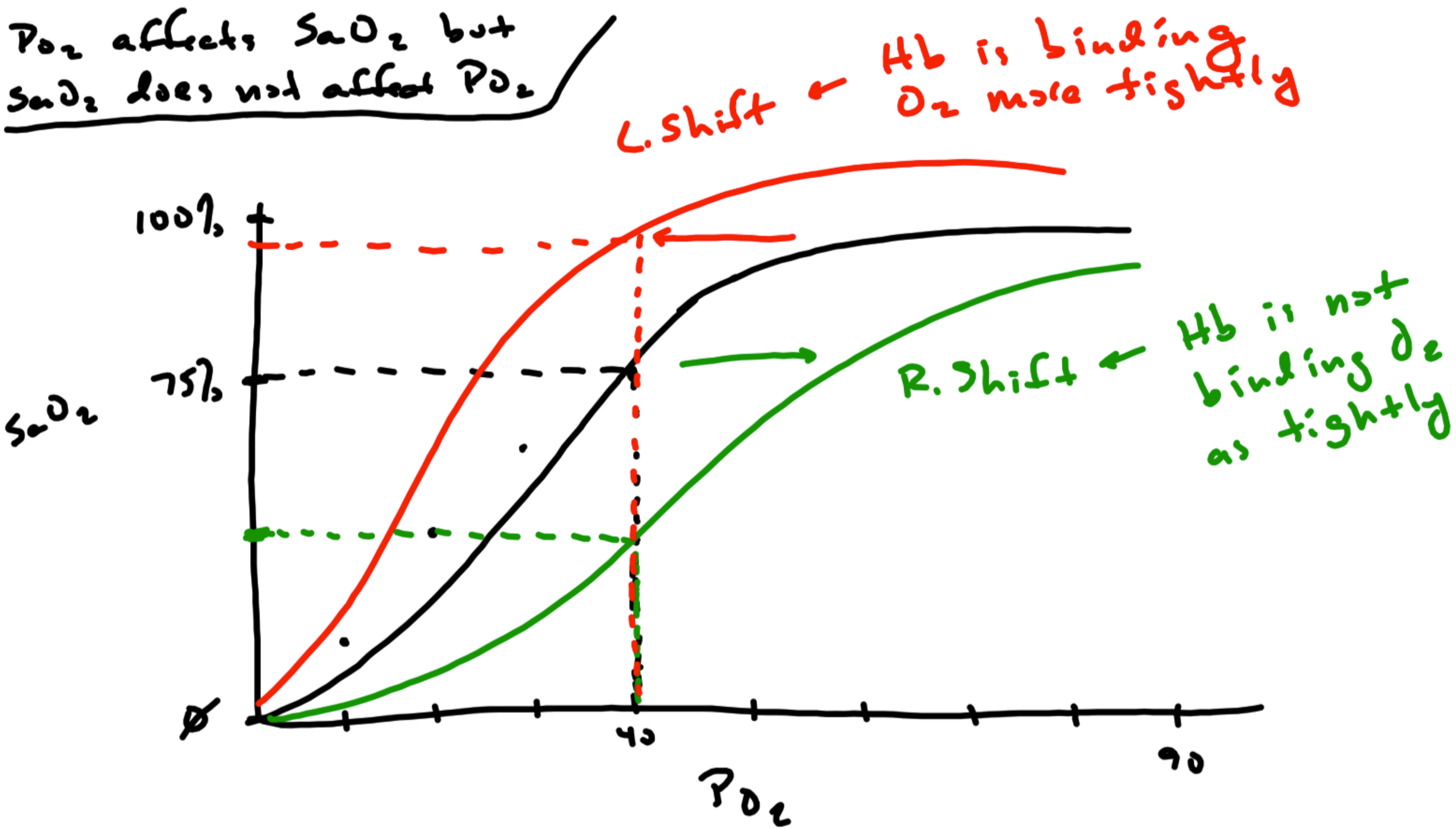
Altering Oxygen–Hemoglobin Binding

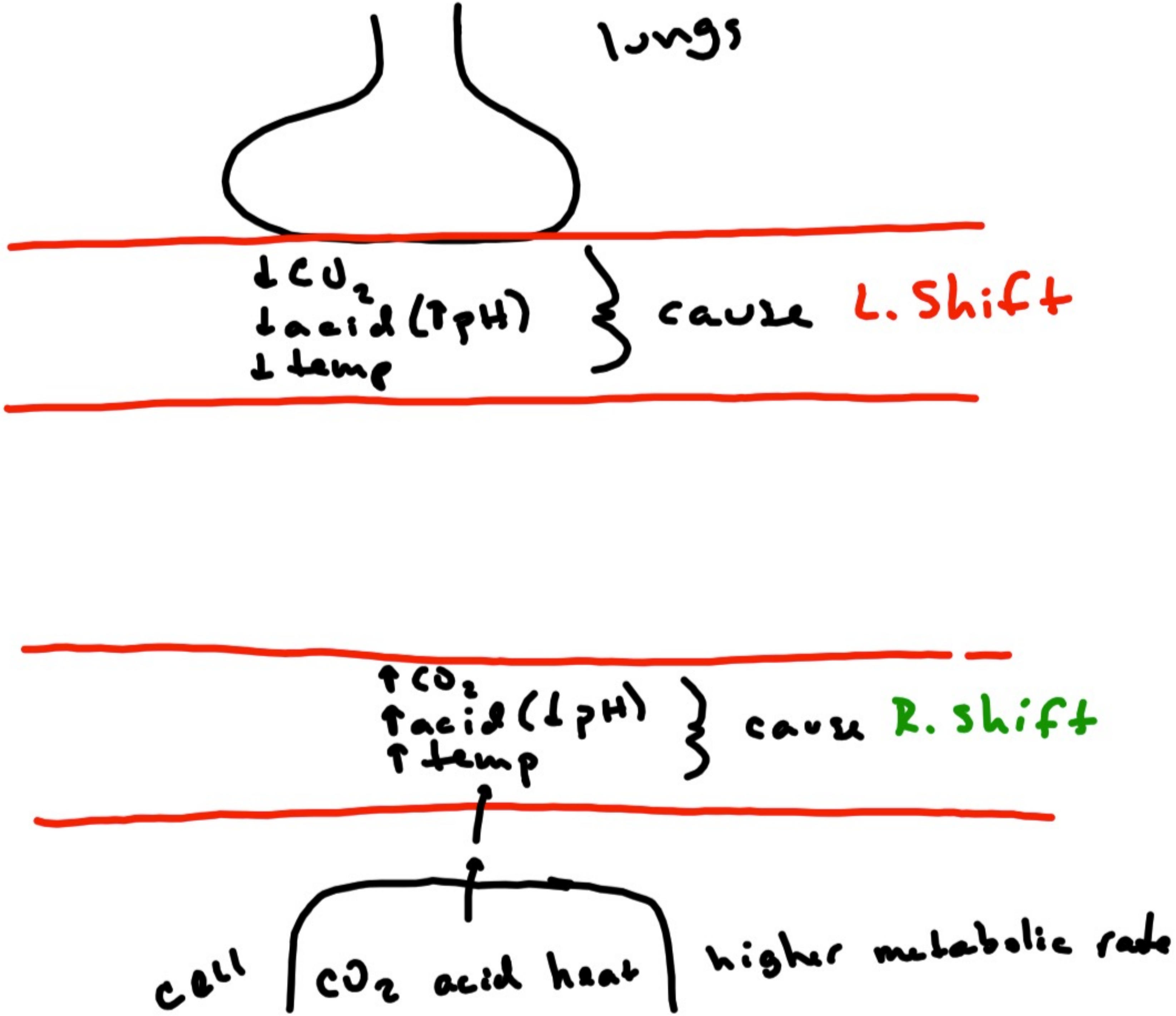


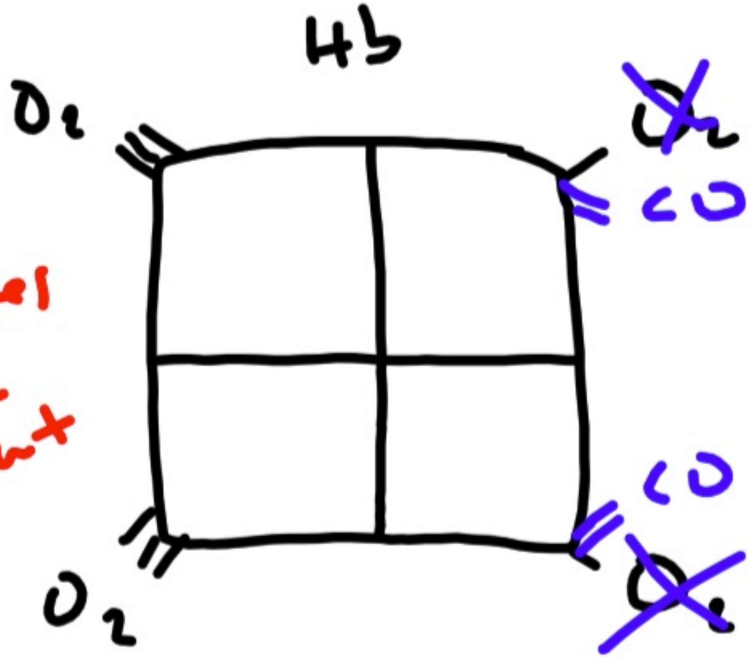
(a) **In the tissues, the oxygen-hemoglobin dissociation curve shifts to the right.** As pH decreases, Pco_2 increases, or temperature increases, the curve (*red*) shifts to the right (*blue*), resulting in an increased release of O_2.

(b) **In the lungs, the oxygen-hemoglobin dissociation curve shifts to the left.** As pH increases, Pco_2 decreases, or temperature decreases, the curve (*blue*) shifts to the left (*red*), resulting in an increased ability of hemoglobin to pick up O_2.

PO_2 affects SaO_2 but SaO_2 does not affect PO_2




lungs
↓ CO_2
↓ acid (↑ pH)
↓ temp
cause L. Shift
↑ CO_2
↑ acid (↓ pH)
↑ temp
cause R. Shift
cell
CO_2 acid heat
higher metabolic rate



L. shift at the sides where O_2 is present

* 2 - big problems

① ↓ SaO_2

② Hb does not "let go" of O_2

↓↓↓ 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_2 (i.e. cause a right shift in the O_2 – Hb binding curve)	**Increase the Affinity of Hb for O_2** (i.e. cause a left shift in the O_2 – Hb binding curve)
↓ pH	↑ pH
↑ CO_2	↓ CO_2
↑ temperature	↓ 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

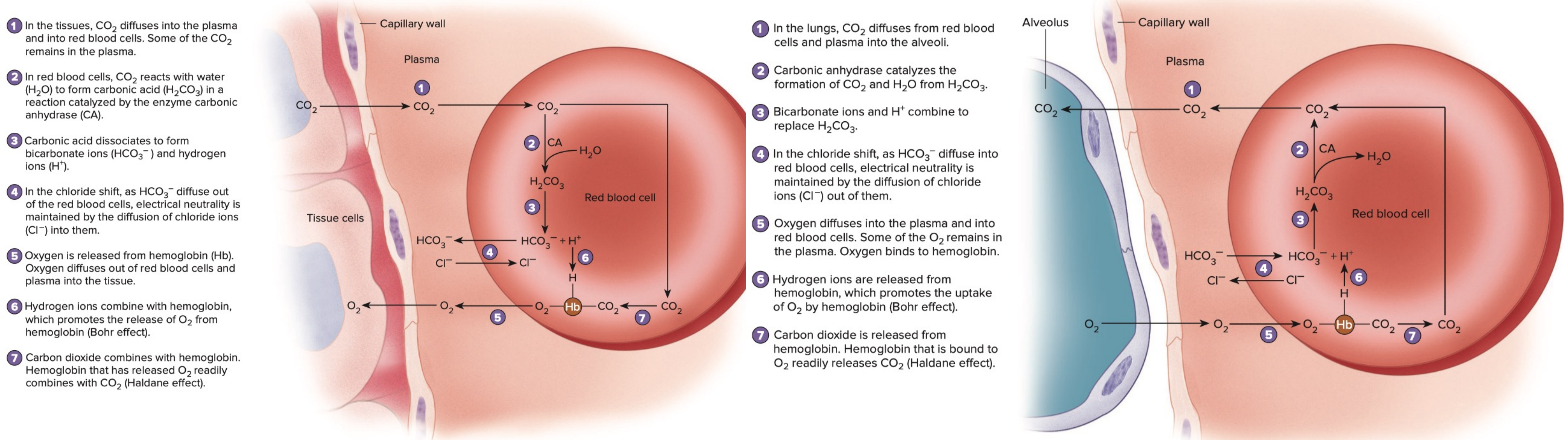
	O_2 Capacity	O_2 content
arterial	20	20
venous	20	15

less because 25% of O_2 was given to cells by Hb (at rest)

Carbon Dioxide Transport

- Transported by hemoglobin : ~ 5% in arterial blood … ~ 10% in venous blood
- Carbaminohemoglobin
- Transported as HCO_3^- : ~ 90% in arterial blood … ~ 60% in venous blood

CO_2 Carried as HCO_3^-



(a) **Gas exchange in the tissues**

(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 ($\dot{V}_A$)

* $\uparrow \dot{V}_A \longrightarrow \uparrow P_{A_{O_2}}$ and $\downarrow P_{A_{CO_2}}$

$$\downarrow \qquad\qquad \downarrow$$

$\uparrow P_{a_{O_2}}$ and $\downarrow P_{a_{CO_2}}$

---

* $\downarrow \dot{V}_A \longrightarrow \downarrow P_{A_{O_2}}$ and $\uparrow P_{A_{CO_2}}$

$$\downarrow$$

$\downarrow P_{a_{O_2}}$ and $\uparrow P_{a_{CO_2}}$

Pulmonary Ventilation

- Minute Ventilation ($\dot{V}_E$) = volume of air moved into the lungs per minute
  - $\dot{V}_E = \text{Tidal Volume} * \text{Respiratory Rate}$
  - $\frac{500\ \text{mL}}{1\ \text{breath}} * \frac{12\ breaths}{1\ minute} = \frac{6{,}000\ \text{mL}}{1\ \text{minute}}$

- Alveolar Ventilation ($\dot{V}_A$) = amount of air available for gas exchange per minute
  - $\dot{V}_A = (\text{Tidal Volume} - \text{Dead Space}) * \text{Respiratory Rate}$
  - $\frac{500\ \text{mL} - 150\ \text{mL}}{1\ \text{breath}} * \frac{12\ breaths}{1\ minute} = \frac{4{,}200\ \text{mL}}{1\ \text{minute}}$
  - 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)

Right Ventricle

↓

Pulmonary Arteries

↓

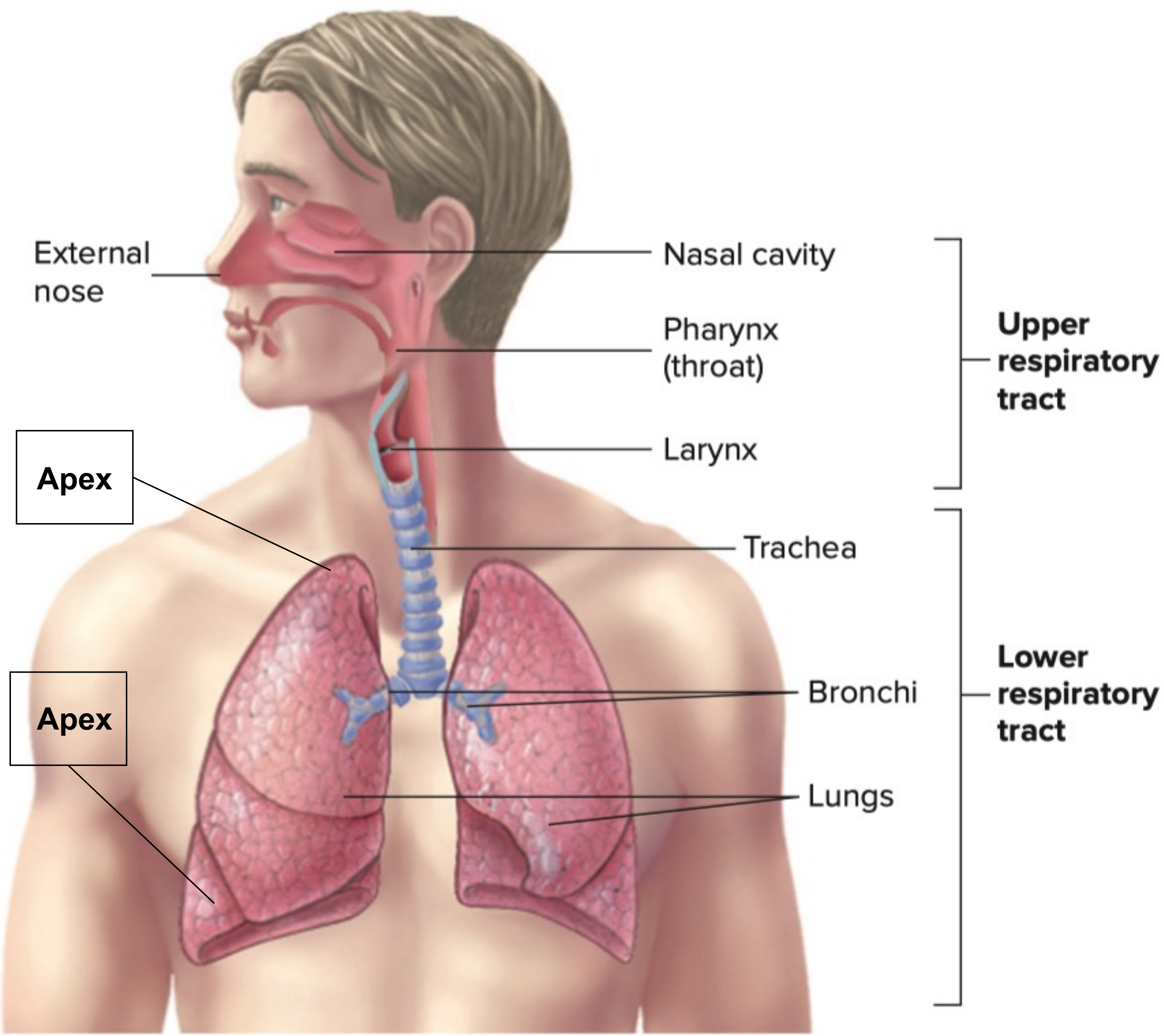
Pulmonary Capillaries ⟶ perfusion of alveoli

↓

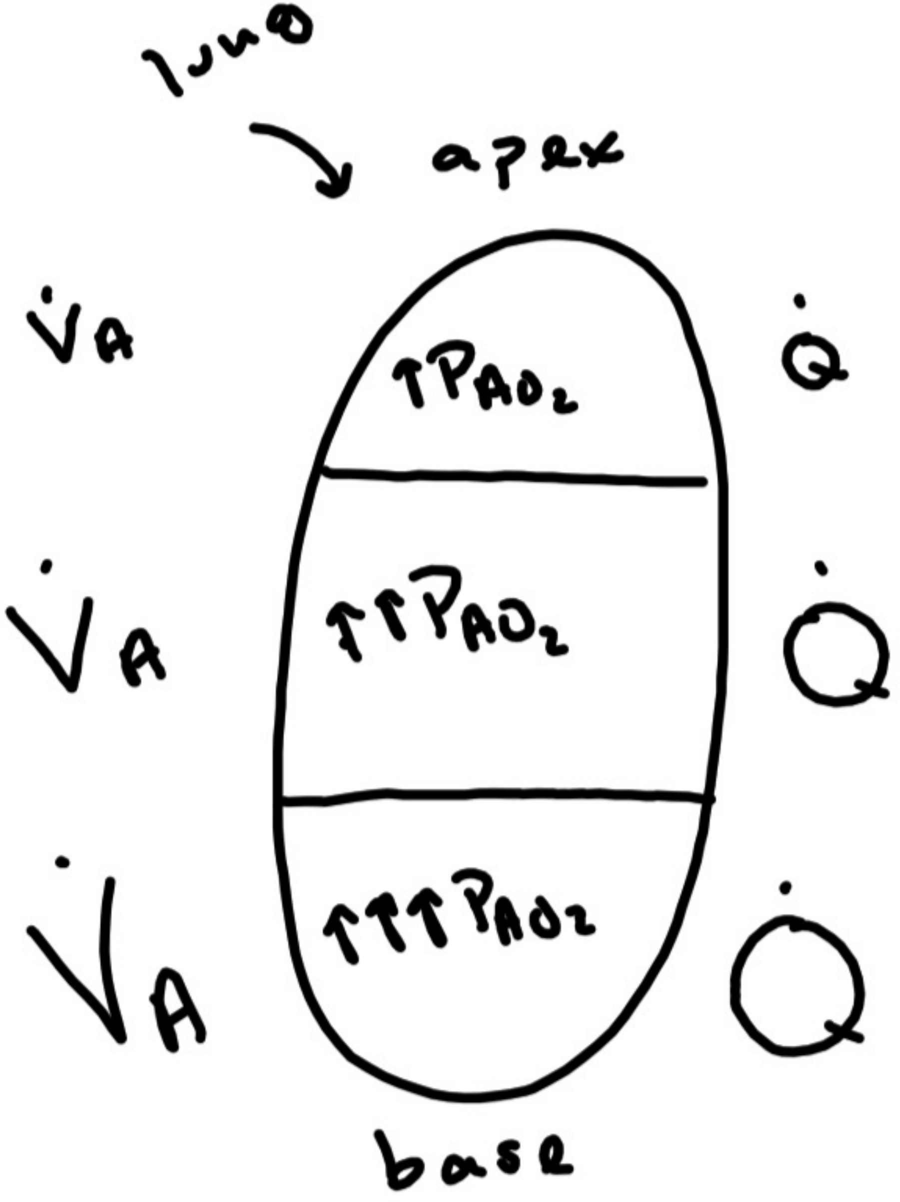
Pulmonary Veins

↓

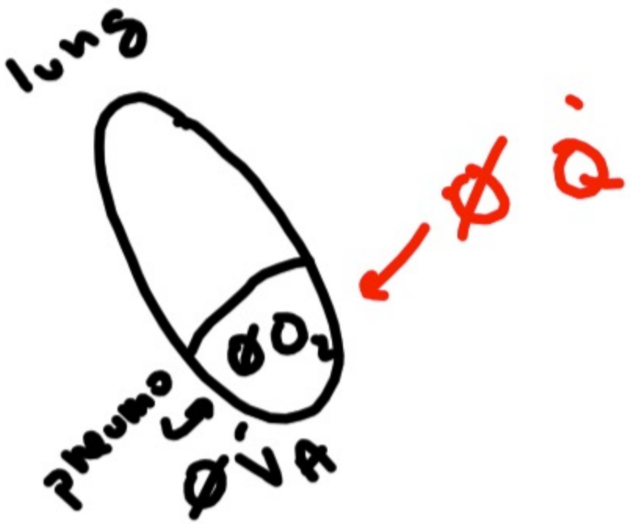
Left Atrium


External nose
Nasal cavity
Pharynx (throat)
Larynx
Upper respiratory tract
Apex
Trachea
Bronchi
Lungs
Apex
Lower respiratory tract

Upright Lung



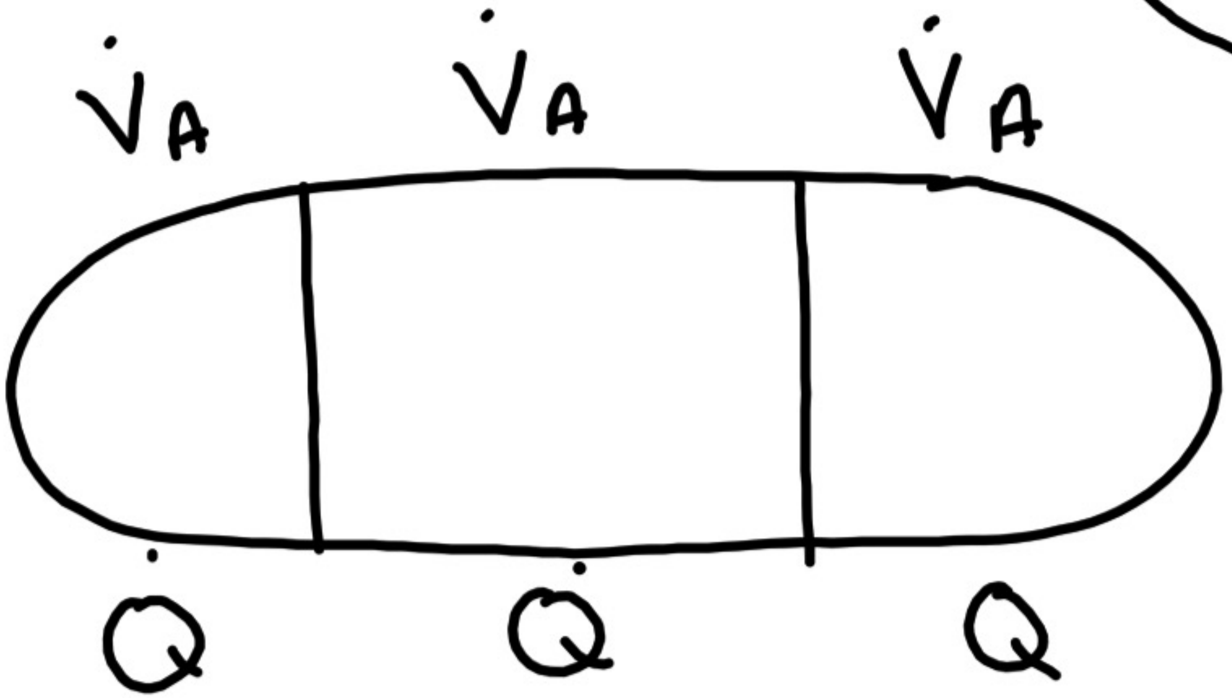
P_{AO_2} has the biggest effect on $\dot{Q}$



Roto Prone Beds

Horizontal Lung

supine or prone



regional differences disappear

Prone position has gas 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

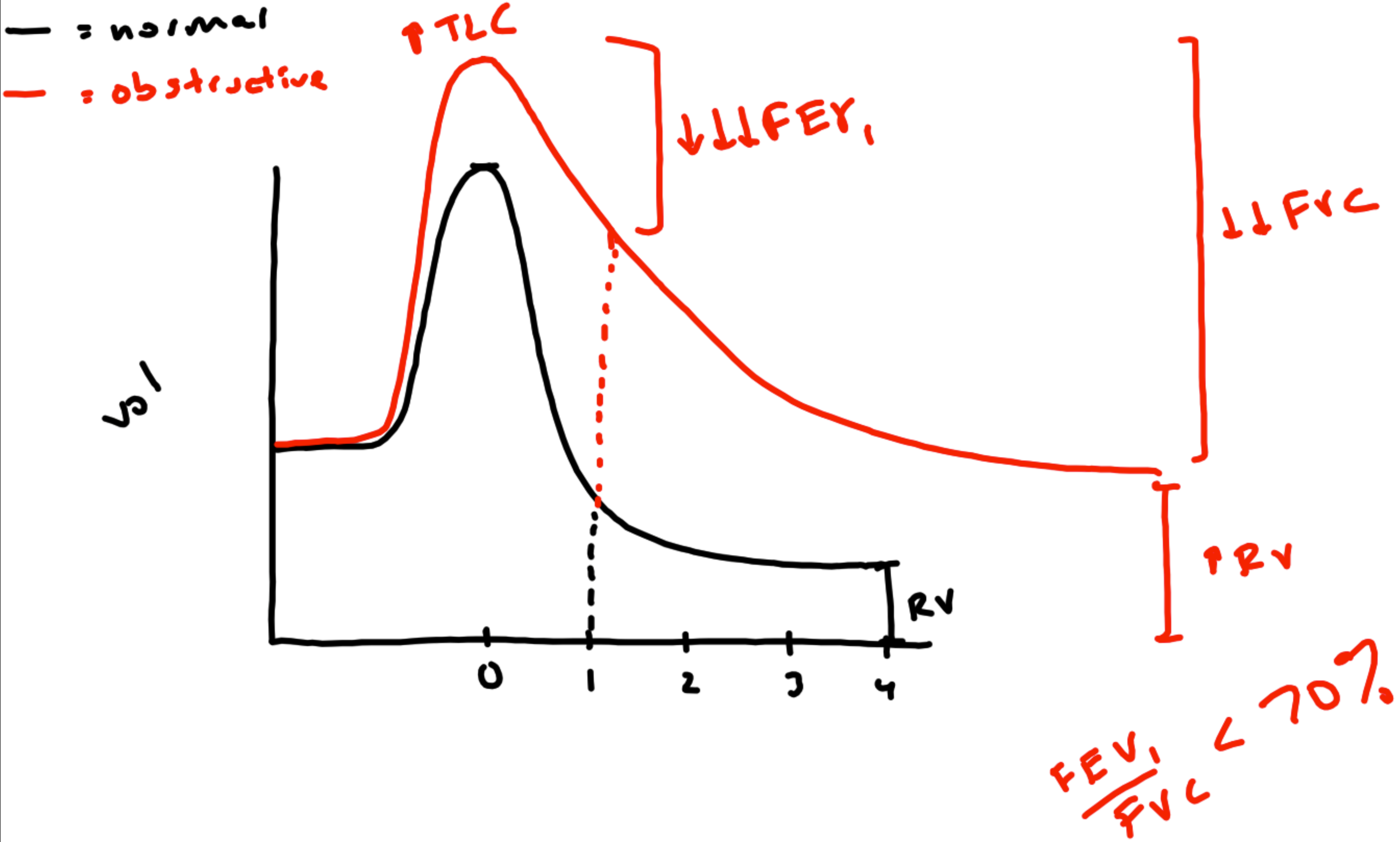
- Obstructive Pulmonary Disease
- Restrictive Pulmonary Disease

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

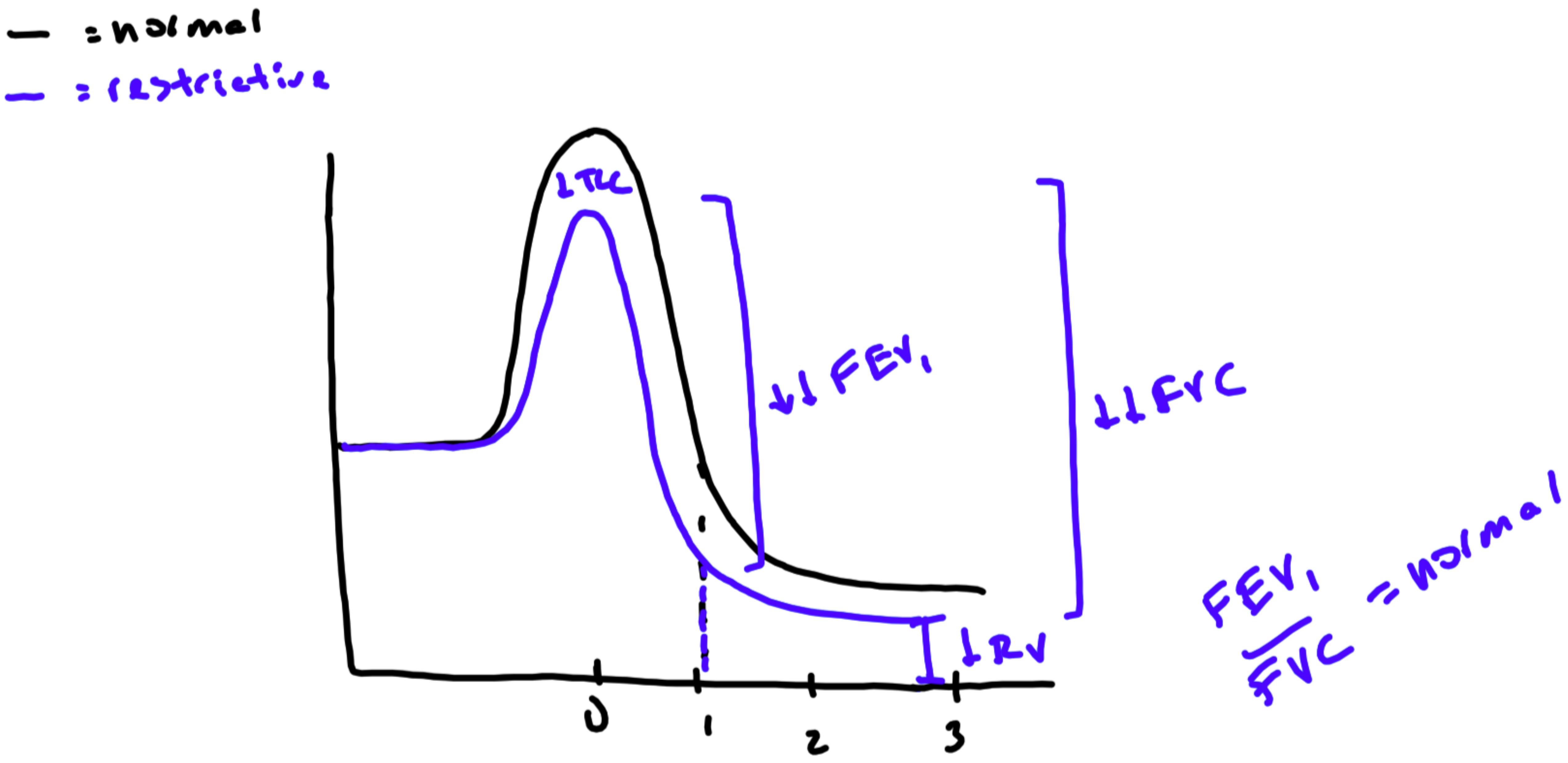
Pulmonary Disease – Obstructive

- 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


— = normal
— = obstructive
↑TLC
↓↓FEV1
↓↓FVC
↑RV
RV
vol
0
1
2
3
4
FEV1/FVC < 70%

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
↓TLC
↓↓ FEV1
↓↓ FVC
↓RV
0
1
2
3
FEV1 / FVC = normal

	Obstructive	Restrictive
volumes and capacities	$\uparrow RV$ ↳ $\uparrow FRC$ ↳ $\uparrow TLC$ All other volumes and capacities decreases	All volumes and capacities decrease
FEV_1/FVC	$\downarrow\downarrow\downarrow\downarrow FEV_1$ $\downarrow\downarrow FVC$ $\downarrow\downarrow \frac{FEV_1}{FVC} \leftarrow <70\%$	$\downarrow\downarrow\downarrow\downarrow FEV_1$ $\downarrow\downarrow\downarrow\downarrow FVC$ $\frac{FEV_1}{FVC}$ = normal
$\dot{V}_A$ PaO_2 $PaCO_2$	$\downarrow \dot{V}_A \rightarrow \downarrow P_AO_2$ $\rightarrow \uparrow P_ACO_2$ $\downarrow PaO_2$ $\uparrow PaCO_2$	$\downarrow \dot{V}_A \rightarrow \downarrow P_AO_2$ $\rightarrow \uparrow P_ACO_2$ $\downarrow PaO_2$ $\uparrow PaCO_2$

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

---

* Obstructive : $\frac{\downarrow\downarrow\downarrow FEV_1}{\downarrow\downarrow FVC} \rightarrow \frac{1,000}{2,500} = 40\%$

---

* Restrictive : $\frac{\downarrow\downarrow FEV_1}{\downarrow\downarrow FVC} \rightarrow \frac{2,000}{2,500} = 80\%$

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

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

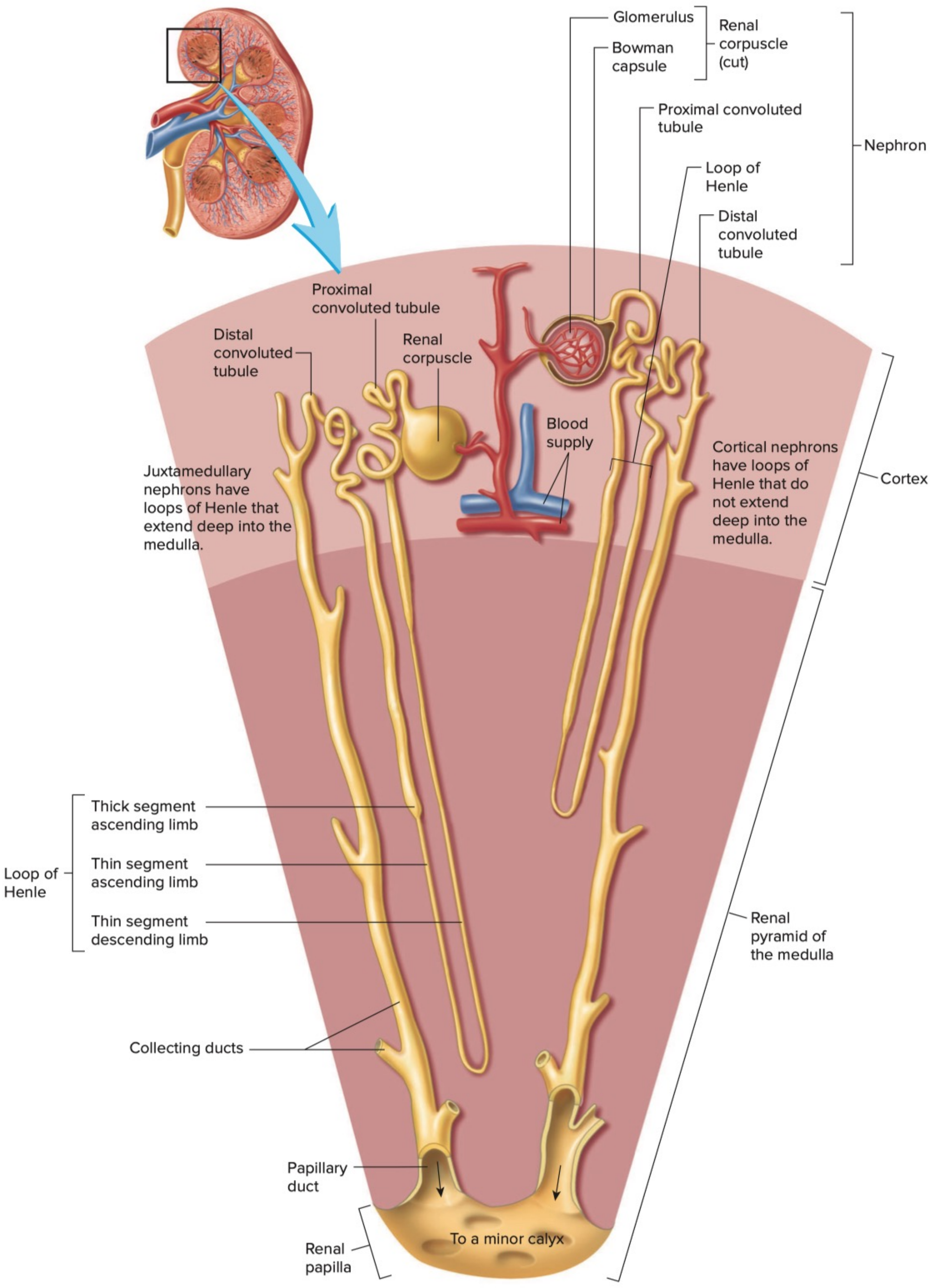
Regulatory Functions of the Urinary System

- 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_3)

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

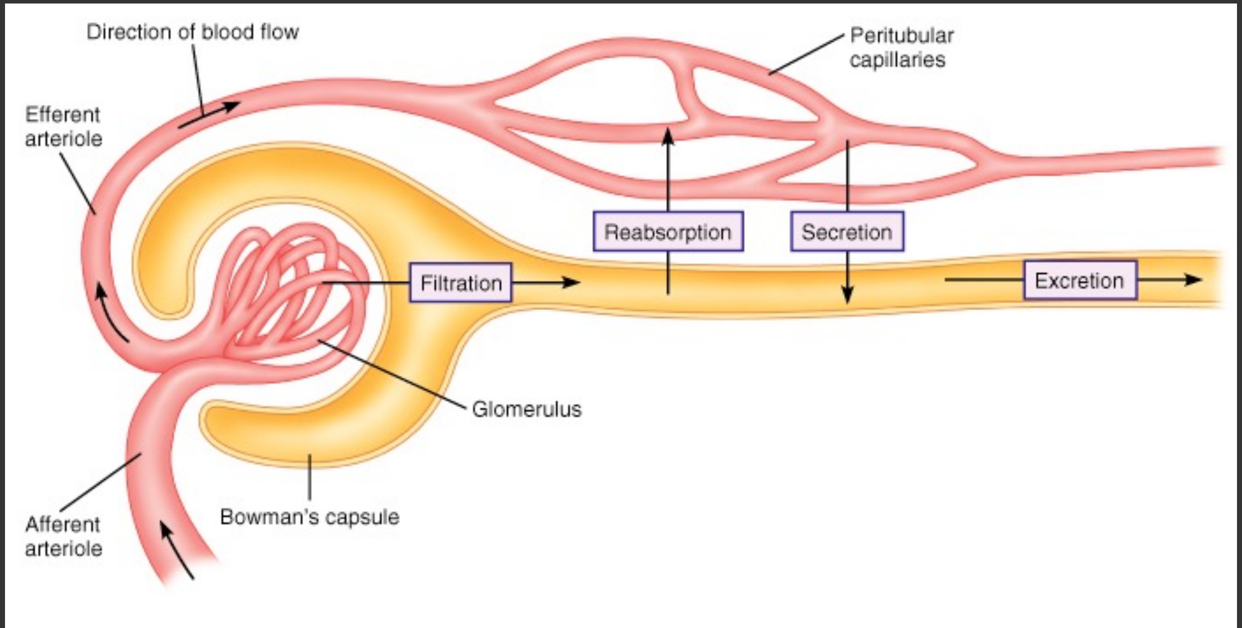
Nephron



Glomerulus
Bowman capsule
Renal corpuscle (cut)
Proximal convoluted tubule
Loop of Henle
Distal convoluted tubule
Nephron
Proximal convoluted tubule
Distal convoluted tubule
Renal corpuscle
Blood supply
Juxtamedullary nephrons have loops of Henle that extend deep into the medulla.
Cortical nephrons have loops of Henle that do not extend deep into the medulla.
Cortex
Loop of Henle
Thick segment ascending limb
Thin segment ascending limb
Thin segment descending limb
Renal pyramid of the medulla
Collecting ducts
Papillary duct
Renal papilla
To a minor calyx

Filtering of Blood

- Glomerular Filtration
  - Filtration of plasma
    - Glomerulus ➡️ Bowman's Capsule
- Tubular Reabsorption
  - Selective movement of filtrate
    - renal tubule ➡️ interstitial fluid ➡️ blood
- Tubular Secretion
  - Selective movement of substances
    - blood to interstitial fluid ➡️ renal tubule
  - Movement aided by active and passive processes



Nephron

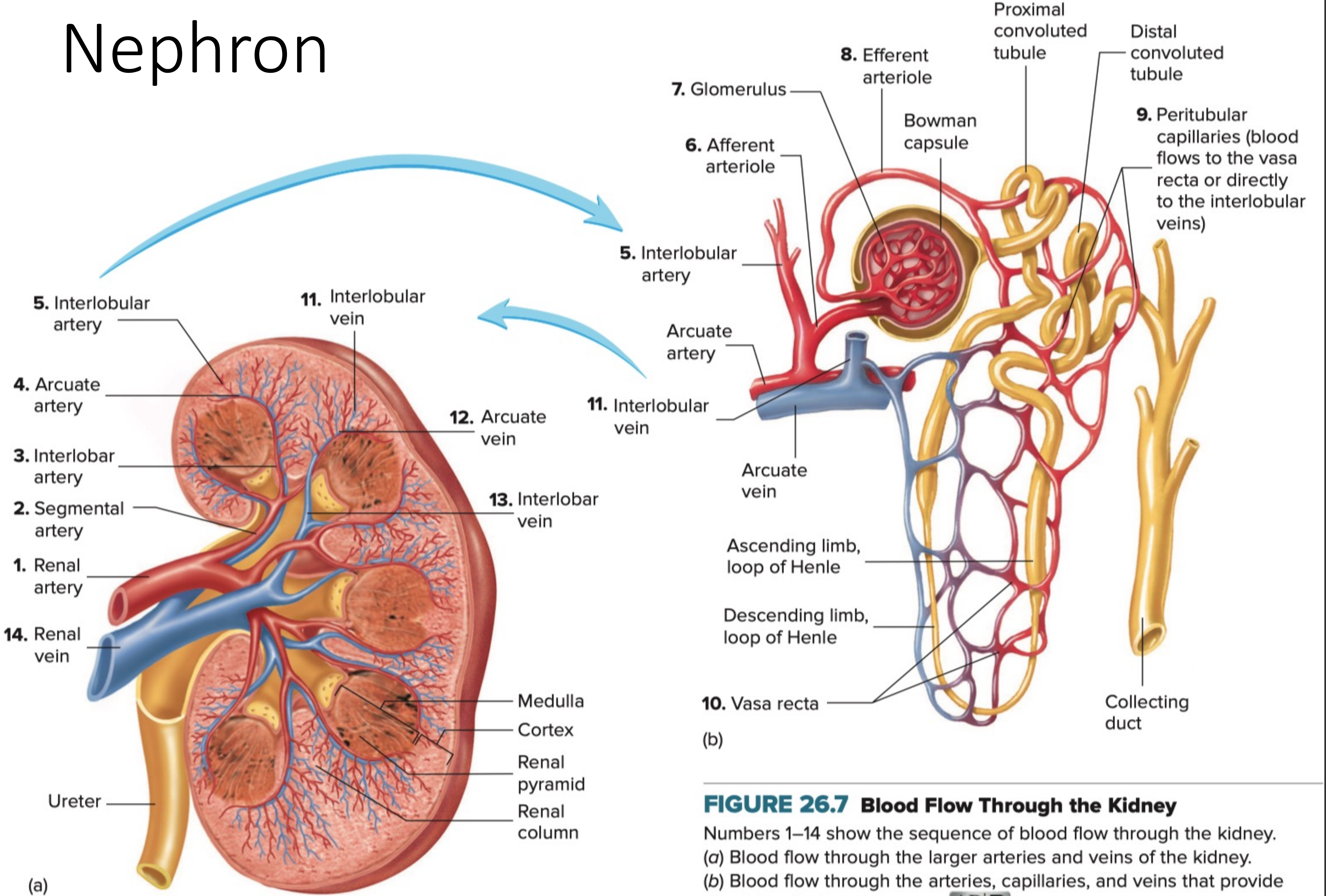


FIGURE 26.7 Blood Flow Through the Kidney

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. AP|R

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
  - Renal blood flow rate = (~ 5,000 mL / min) * 20 % ≈ 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 % ≈ 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 mL / min) * 20 % ≈ 110 mL / minute
  - Therefore , ~ 110 mL of filtrate is produced per minute
    - This translates into ~ 160 liters / day

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
  - ∴ net filtration pressure = $50\ mm\ Hg - (\ 30\ mm\ Hg + 10\ mm\ Hg\ ) = 10\ mm\ Hg$
    - ∴ 10 mm Hg force that favors filtration

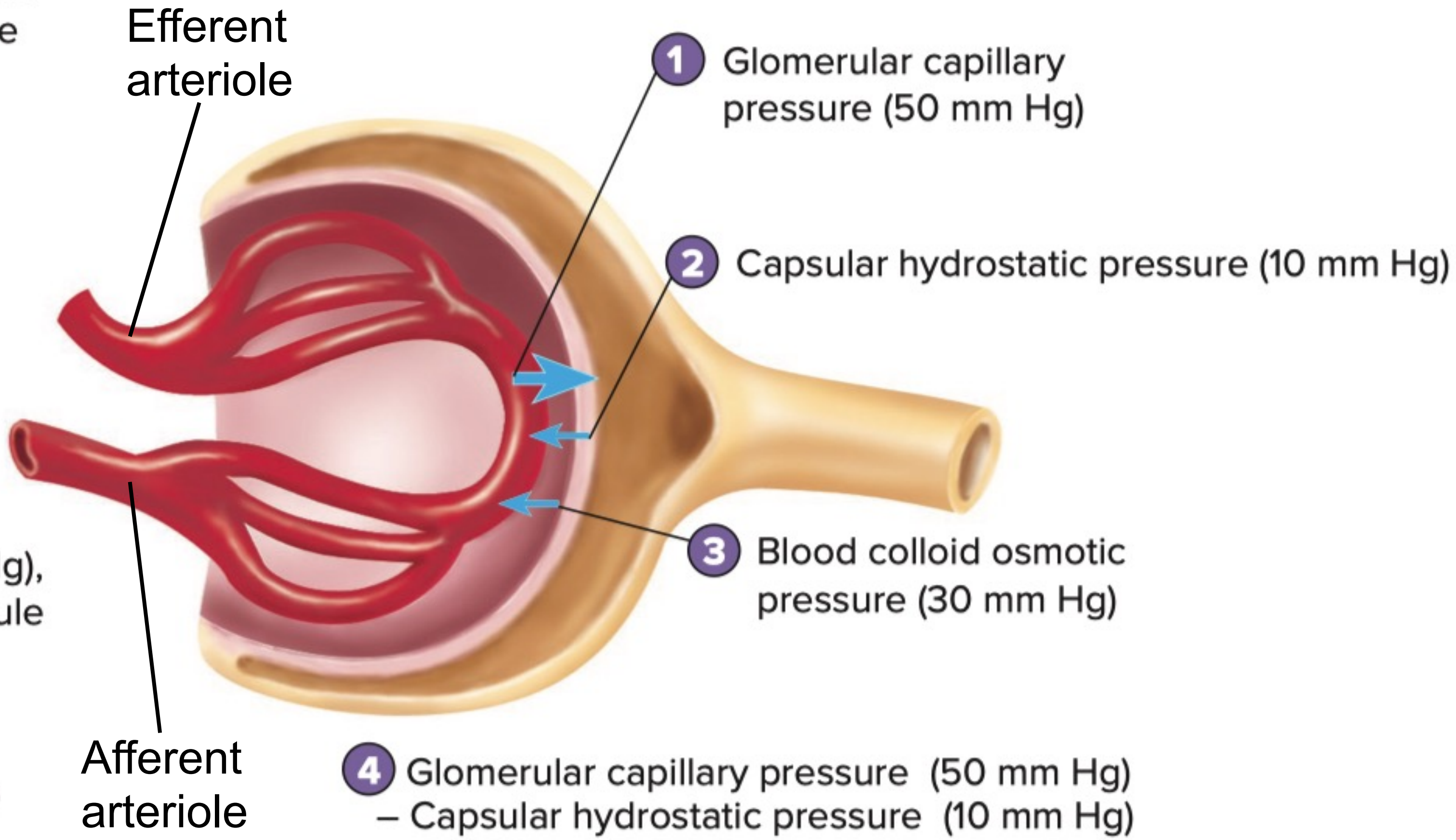
Net Filtration Pressure

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.

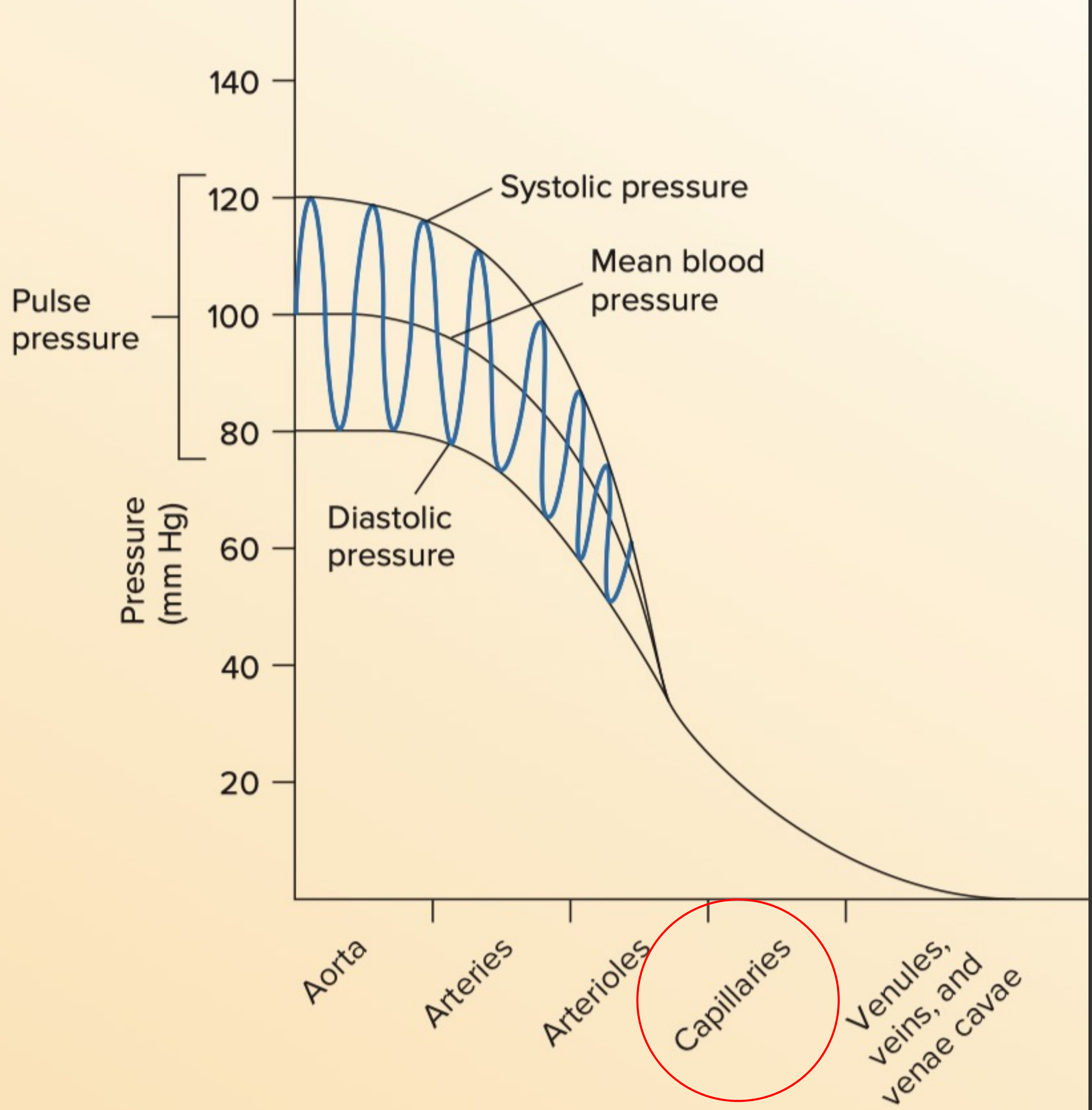
3. Blood colloid osmotic pressure (BCOP), produced by the concentration of blood proteins in the glomerular capillaries (30 mm Hg), moves fluid from the Bowman capsule into the blood by osmosis.

4. Filtration pressure is equal to the glomerular capillary pressure minus the capsular hydrostatic and blood colloid osmotic pressures.



4 Glomerular capillary pressure (50 mm Hg)
– Capsular hydrostatic pressure (10 mm Hg)
– Blood colloid osmotic pressure (30 mm Hg)

Filtration pressure = 50 – 10 – 30 = 10 mm Hg


140
120
100
80
60
40
20
Pulse
pressure
Pressure
(mm Hg)
Systolic pressure
Mean blood
pressure
Diastolic
pressure
Aorta
Arteries
Arterioles
Capillaries
Venules,
veins, and
venae cavae

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

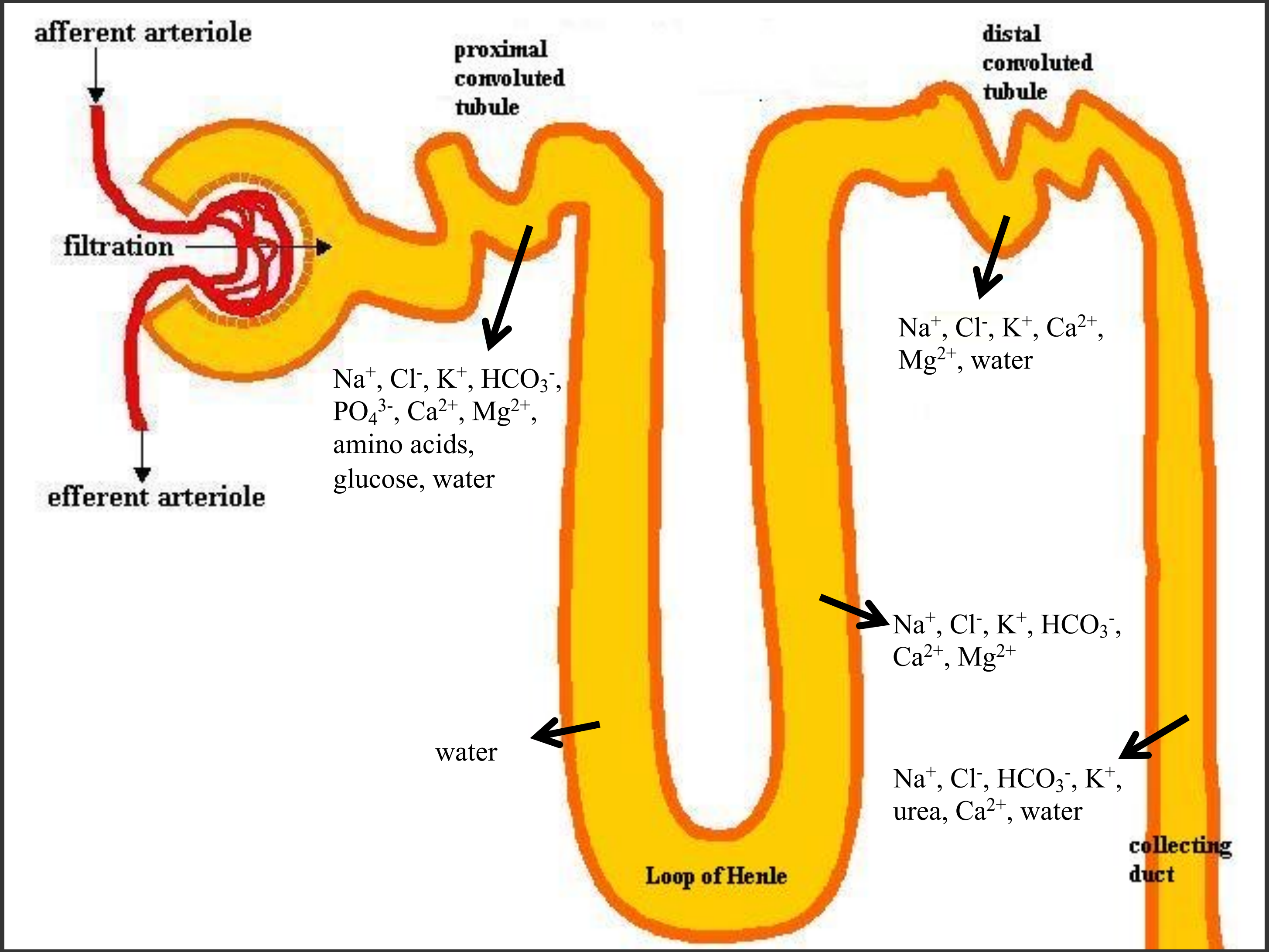
Tubular Reabsorption

- 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
  - Na^+, Cl^-, K^+, Ca^{2+}, Mg^{2+}, HCO_3^-, 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
    - Na^+, Cl^-, K^+, Ca^{2+}, Mg^{2+}, HCO_3^-
    - Impermeable to water
- Distal convoluted tubule
  - Na^+, Cl^-, K^+, Ca^{2+}, Mg^{2+}, water (follows solutes osmotically)
- Collecting duct
  - Na^+, Cl^-, HCO_3^-, K^+, urea, Ca^{2+}, water (follows solutes osmotically)

Reabsorption

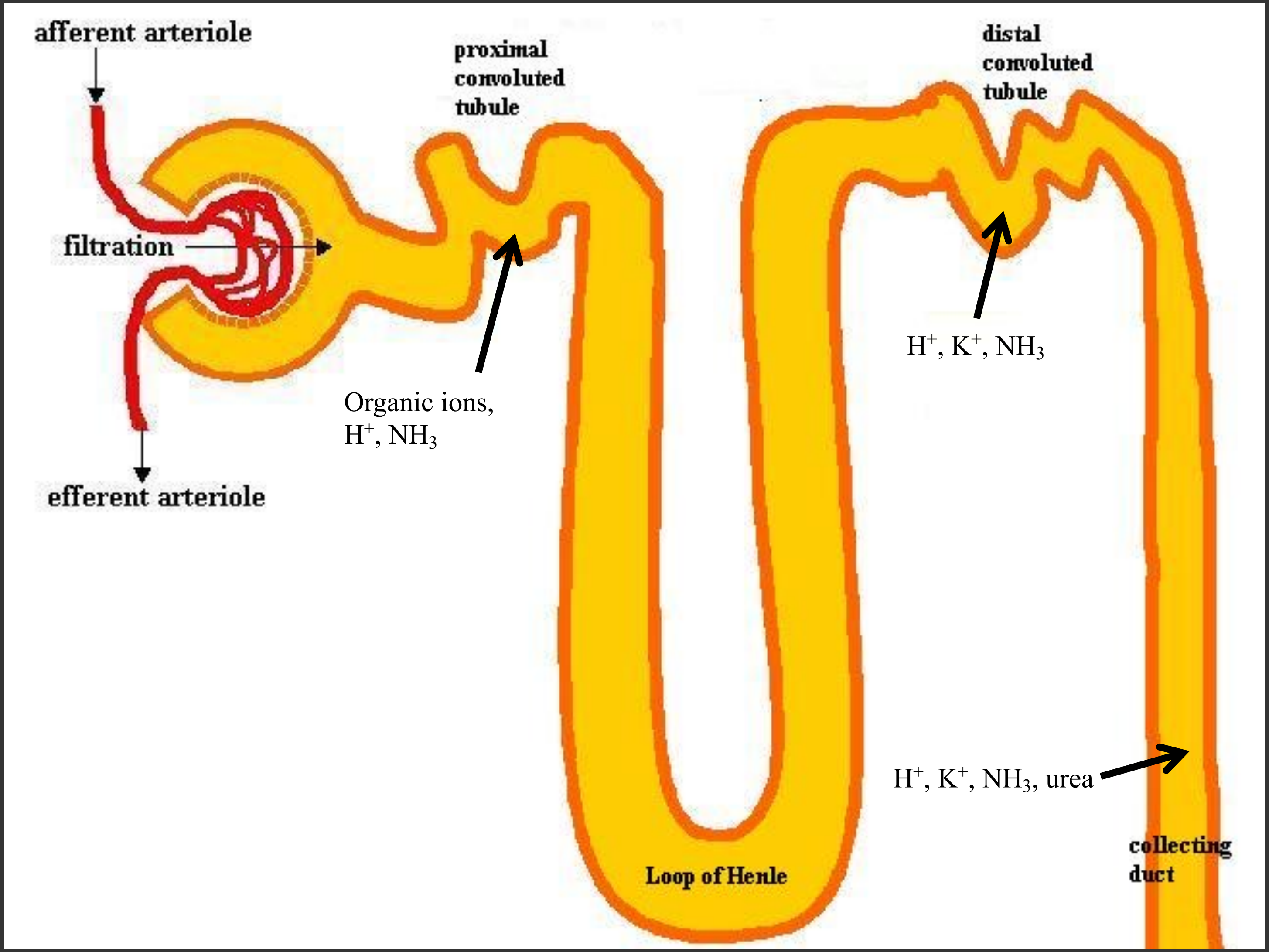


Tubular Secretion

- 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 Na^+
      - eg , uric acid , bile acids , antibiotics , creatinine , "drugs"
  - H^+ , NH_3 (ammonia)
- Distal Convoluted Tubule :
  - H^+ , K^+ , NH_3 (majority of NH_3 secretion)
- Collecting Duct :
  - H^+ , K^+ , NH_3 , urea

Secretion



afferent arteriole
proximal convoluted tubule
distal convoluted tubule
filtration
H^+, K^+, NH_3
Organic ions, H^+, NH_3
efferent arteriole
H^+, K^+, NH_3, urea
collecting duct
Loop of Henle

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

Summary of Clearance

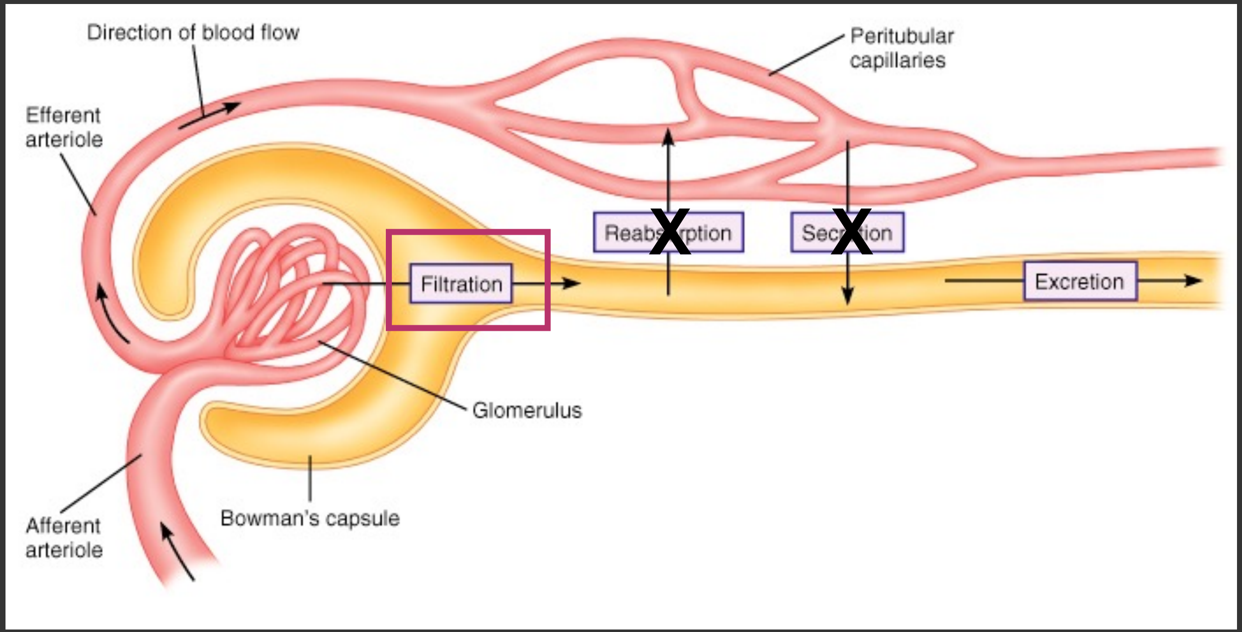
- If clearance equals GFR :
  - Substance is completely filtered and not reabsorbed and not secreted

- 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

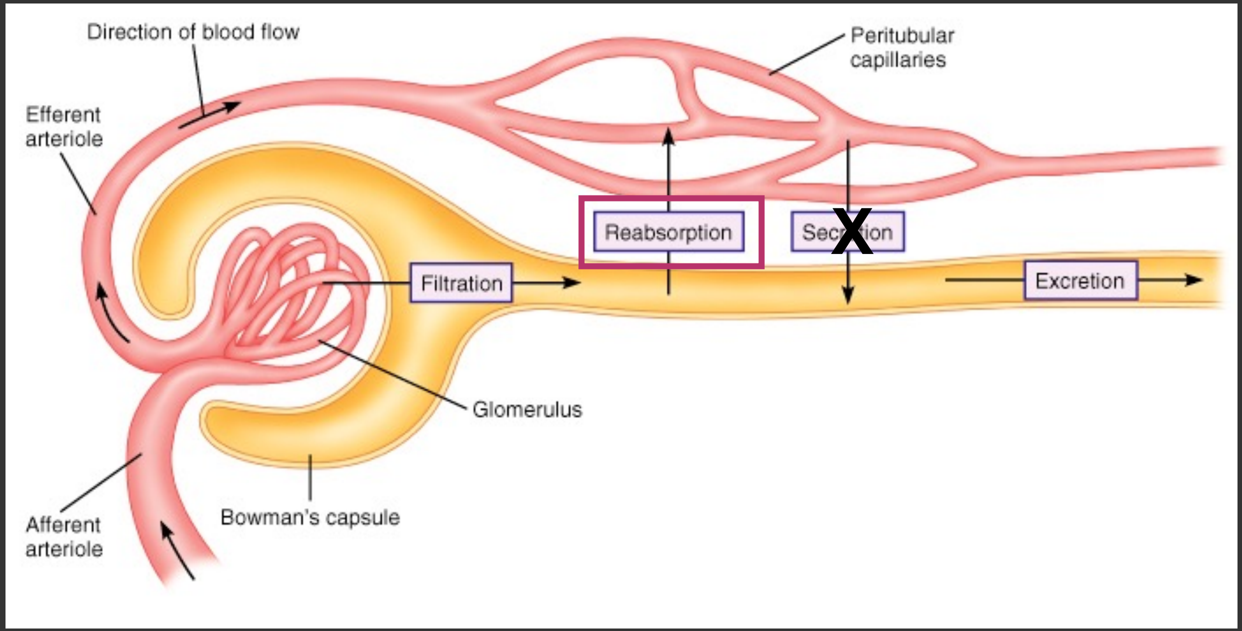
- Substance is completely filtered and not reabsorbed and not secreted
- Clearance of inulin (clinically , clearance of creatine used to estimate GFR)

however, creatinine is secreted

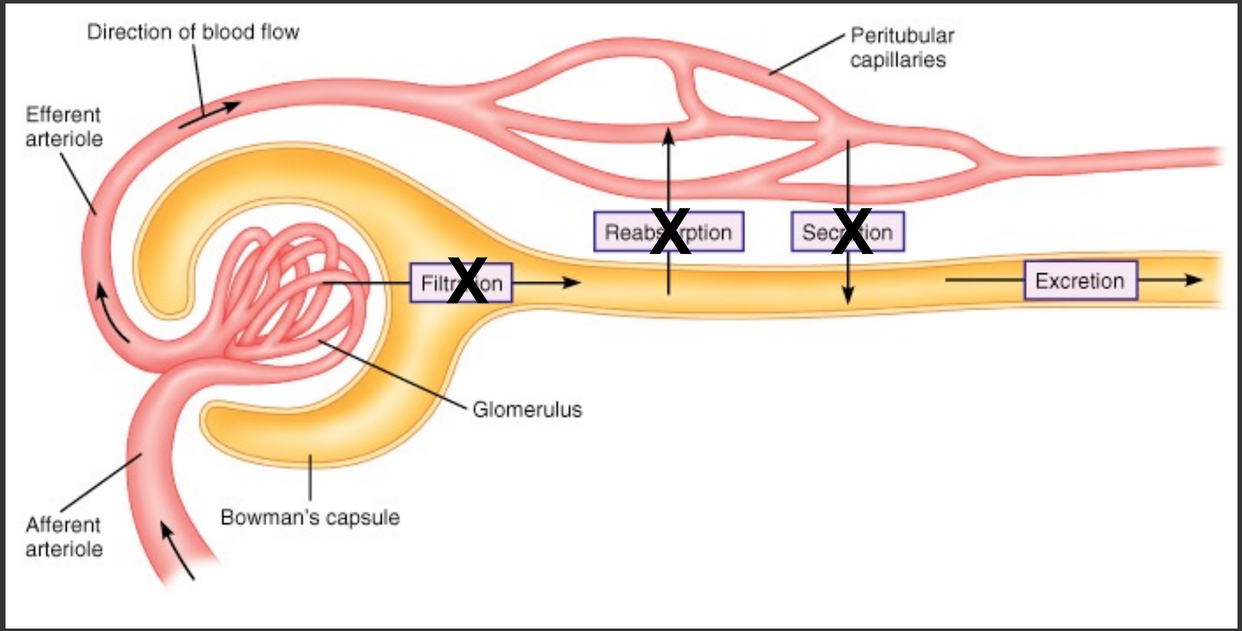


If Clearance is Zero

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



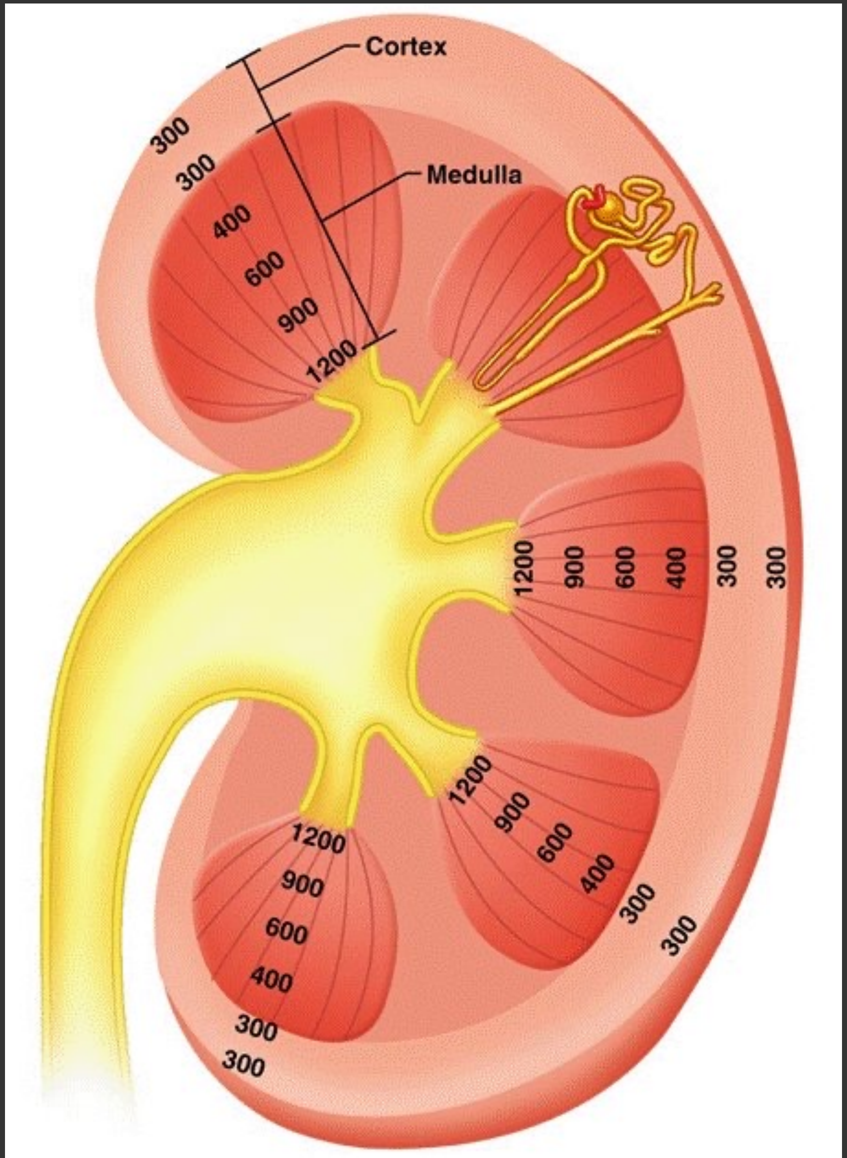
eg , glucose



eg , protein

Countercurrent Exchanger

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



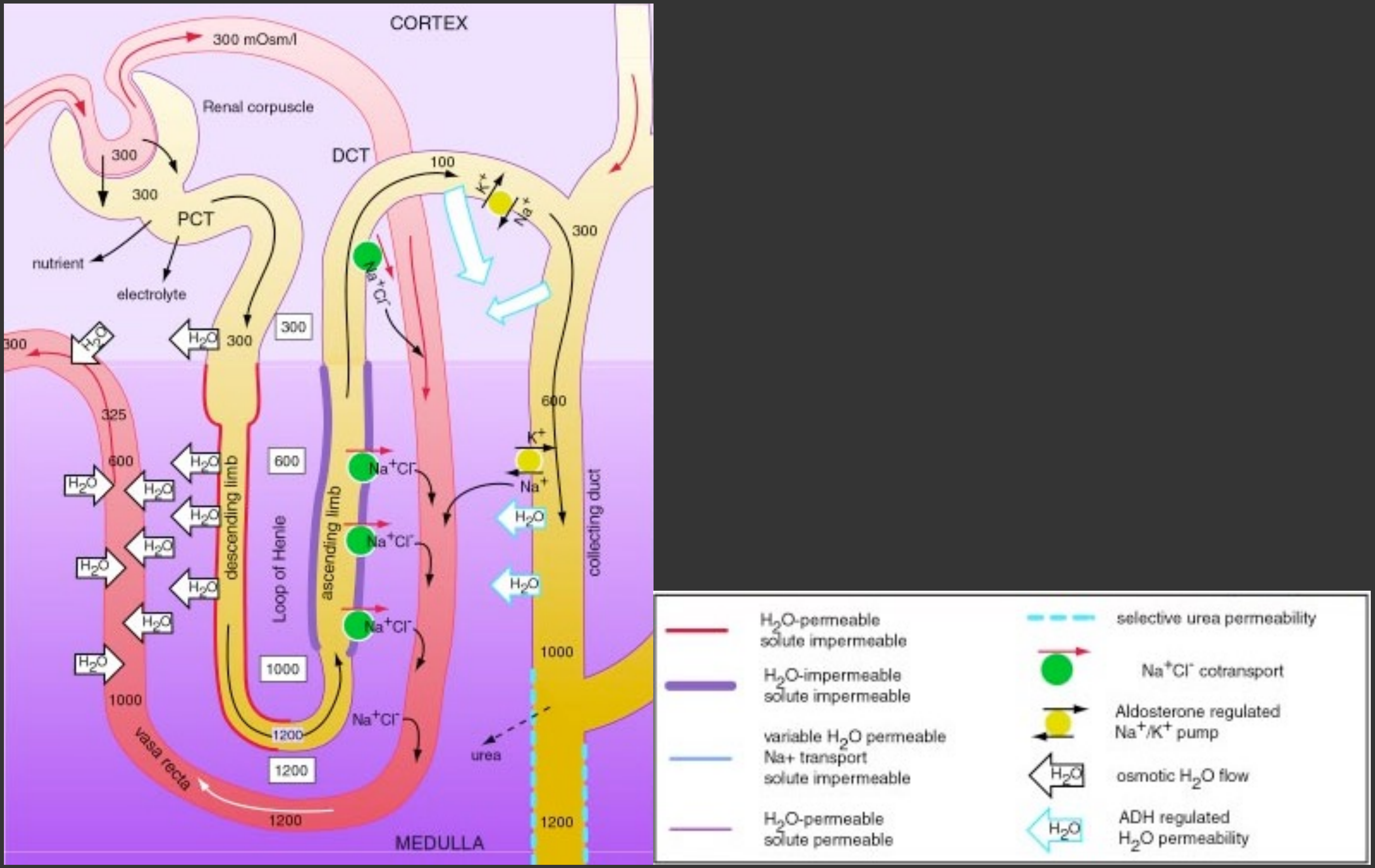
Factors Involved in Countercurrent Exchange

- 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 Na^+ , Cl^- (transport of Na^+ and 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
    - Na^+ and 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 Na^+ and Cl^- out of tubule
    - ∴ filtrate entering collecting duct has osmolarity of 100 mOsM

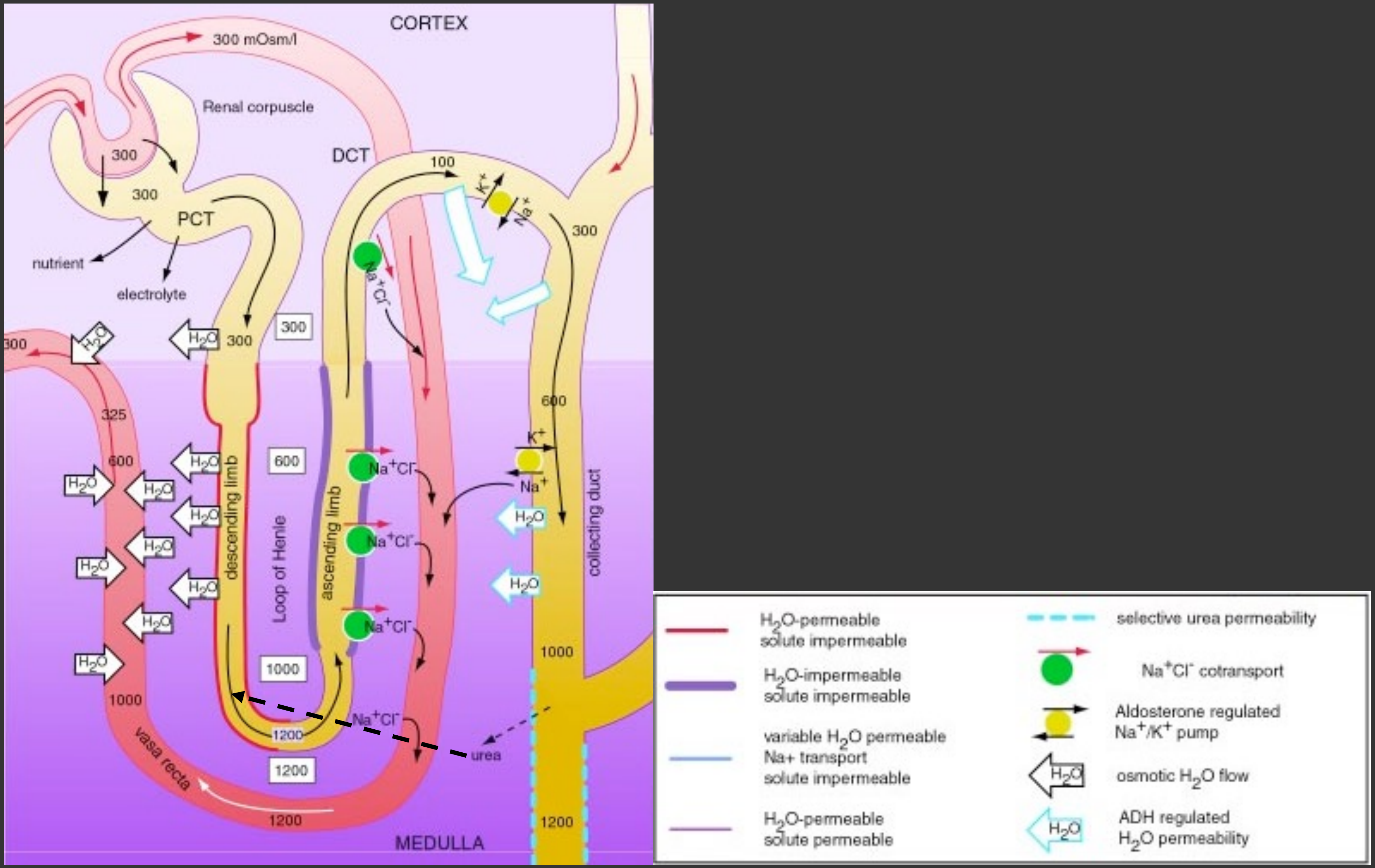
Factors Involved in Countercurrent Exchange



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

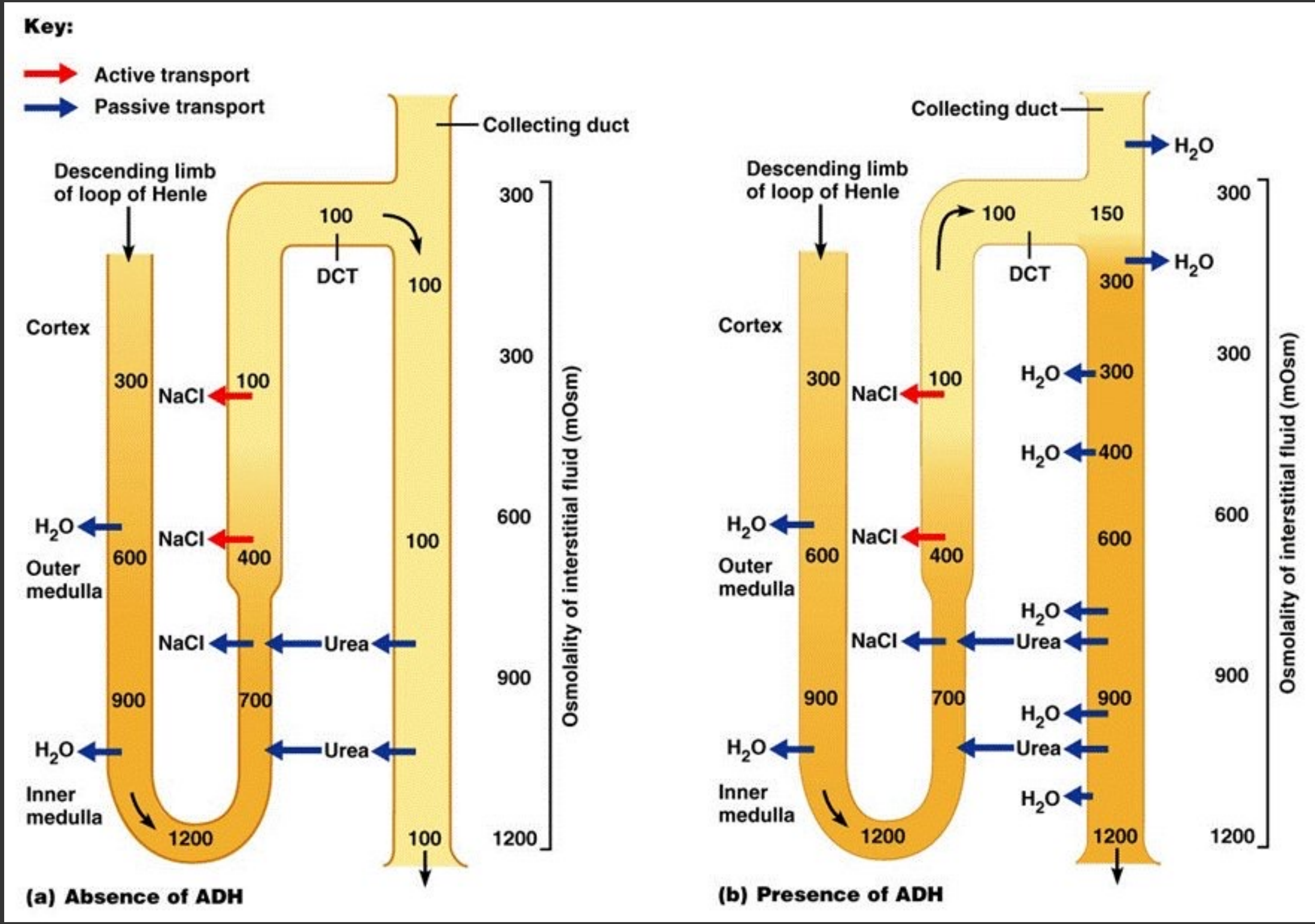
Factors Involved in Countercurrent Exchange



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

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^+
- Thiazides (eg , Metolazone)
  - Work mainly in distal convoluted tubule
  - Decrease blood K^+
- Aldosterone Antagonists (eg , Inspra)
  - Work mainly in distal convoluted tubule
  - Does NOT decrease blood K^+
    - ∴ potassium sparing

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

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