Respiratory Physiology

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Textbook of medical physiology, by A.C. Guyton and John E, Hall

First Jordan Edition

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- In general the **10** lectures will cover the following Respiratory Physiology Topics:
- 1. Overview: causes of hypoxia…One lecture
- 2. Mechanics of Breathing (Lung Ventilation)…one lecture.
- 3. Airway Resistance…COPD…2 lectures.
- 4. Lung Compliance…1 lectures…Lung fibrosis, IRDS and ARDS
- 5. Pulmonary circulation ….Ventilation-Perfusion Ratio…1 lecture.
- 6. Gas Exchange and Transport…2 lectures
- 7. Regulation of Lung Ventilation, high altitude, exercise
- etc…2 lectures.
- 8. Pulmonary Function Test and Pathophysiology (lung Diseases) and Clinical Applications…one lecture.

The non-respiratory functions of the respiratory system

- **The non-respiratory functions of the respiratory system (Note: *Most of these non-respiratory functions of the lungs will not be covered in this course*):**
- - Helps blood and lymph flow (venous return)
- - Acid base balance. Regulation of pH which dependents on rate of CO2 release
- - Pulmonary capillary remove any air bubble which might otherwise
- reach systemic circulation
- - Airways remove airborne particles
- - Ventilation contribute to heat loss and water loss. Regulation of body temperature by evaporation of water from the respiratory passages to help heat loss from the body
- - Important reservoir of blood
- - Phonation
- BP regulation by converting AI to AII
- - Metabolic functions such as:
- - Conversion of angiotensin I to AII
- - Synthesis and removal of bradykinin and PGs
- - Storage and release of serotonin and histamine
- - inactivation of noradrenaline and adrenaline
- - synthesis of peptides like substance P and opiates
- - secretion of heparin by mast cells
- - secretion of immunoglobulins in the bronchial mucus

Introduction

- RS and CVS systems are highly interconnected: fact: lung disease probably will develop heart failure and vice versa; for example: left heart failure will result in pulmonary edema and decreased O2 supplied by the lung due to lung disease will result in right heart failure (corpulmonale)

- Hypoxia is decreased O_2 utilization by the cells
- What are the Potential Causes of Hypoxia
- **Causes**
  - inadequate oxygenation of lungs
    - Atmosphere…high altitude
    - decrease muscle activity ..paralysis
  - pulmonary disease
  - inadequate transport.. anemia and heart failure
  - inadequate usage as septicemia and CN poisoning

Introduction

- Respiration is the process by which the body takes in and utilizes oxygen and gets rid of CO_2.
- Exchange of gases
- Directionality depends on gradients “Pressure difference “!
  - From atmosphere to blood -And from blood to tissues
- *Three determinants of respiration*
- Respiration depends on three things: the lungs, the blood, and the tissues.

Basics of the Respiratory System

Respiration

- What is respiration?
  - **Respiration** = the series of exchanges that leads to the uptake of oxygen by the cells, and the release of carbon dioxide to the lungs
    - Step 1 = ventilation
      - Which includes: Inspiration & expiration
    - Step 2 = exchange between alveoli (lungs) and pulmonary capillaries (blood)
      - Referred to as *External Respiration*
    - Step 3 = transport of gases in blood
    - Step 4 = exchange between blood and cells
      - Referred to as *Internal Respiration*
  - **Cellular respiration** = use of oxygen and ATP synthesis

- ***The lungs:*** The lungs must be adequately ventilated and be capable of adequate gas exchange.
- **Ventilation**: is determined by the activity of the control system (respiratory center), the adequacy of the feedback control systems (neural and hormonal), and the efficiency of the effector system (muscles of respiration).
- **Gas exchange**: depends on the patency of the airways, the pressure gradient across the alveolar-capillary membrane, the diffusability of individual gases and the area and thickness of the exchange membrane.

- ***The Blood:***
- The blood must pick up, carry and deliver O_2 and CO_2 in amounts that are appropriate to the body's need. It depends in the presence of adequate amount of the correct type of Hb, the cardiac output, and local perfusion.
-

- ***The Tissues:***
- Individual cells must be capable of taking up and utilizing O_2 properly.
- **Hypoxia can therefore result from a fault at any point along this lungs-blood-tissue chain.**

Functions of the respiratory system

- The primary function of the respiratory system is to deliver sufficient amount of O_2 from the external environment to the tissues and to remove CO_2 that is produced by cellular metabolism to the surrounding atmosphere….Therefore, it is homeostasis of O_2, CO_2, H^+

One more time: To achieve these goals:

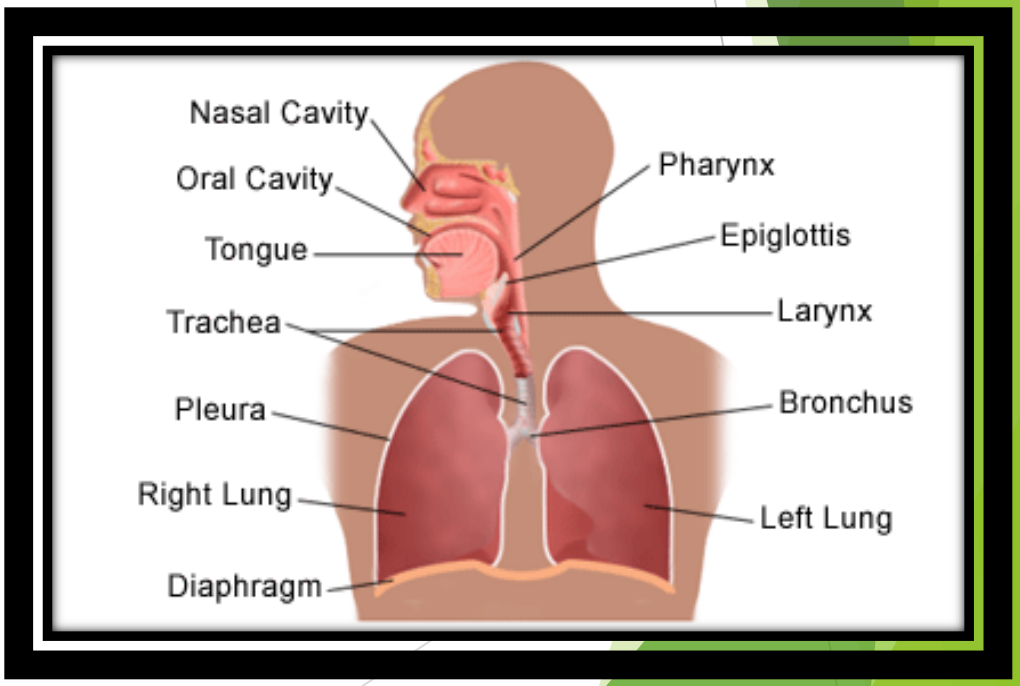
respiration can be divided into four major functions:

(1) *Pulmonary ventilation*

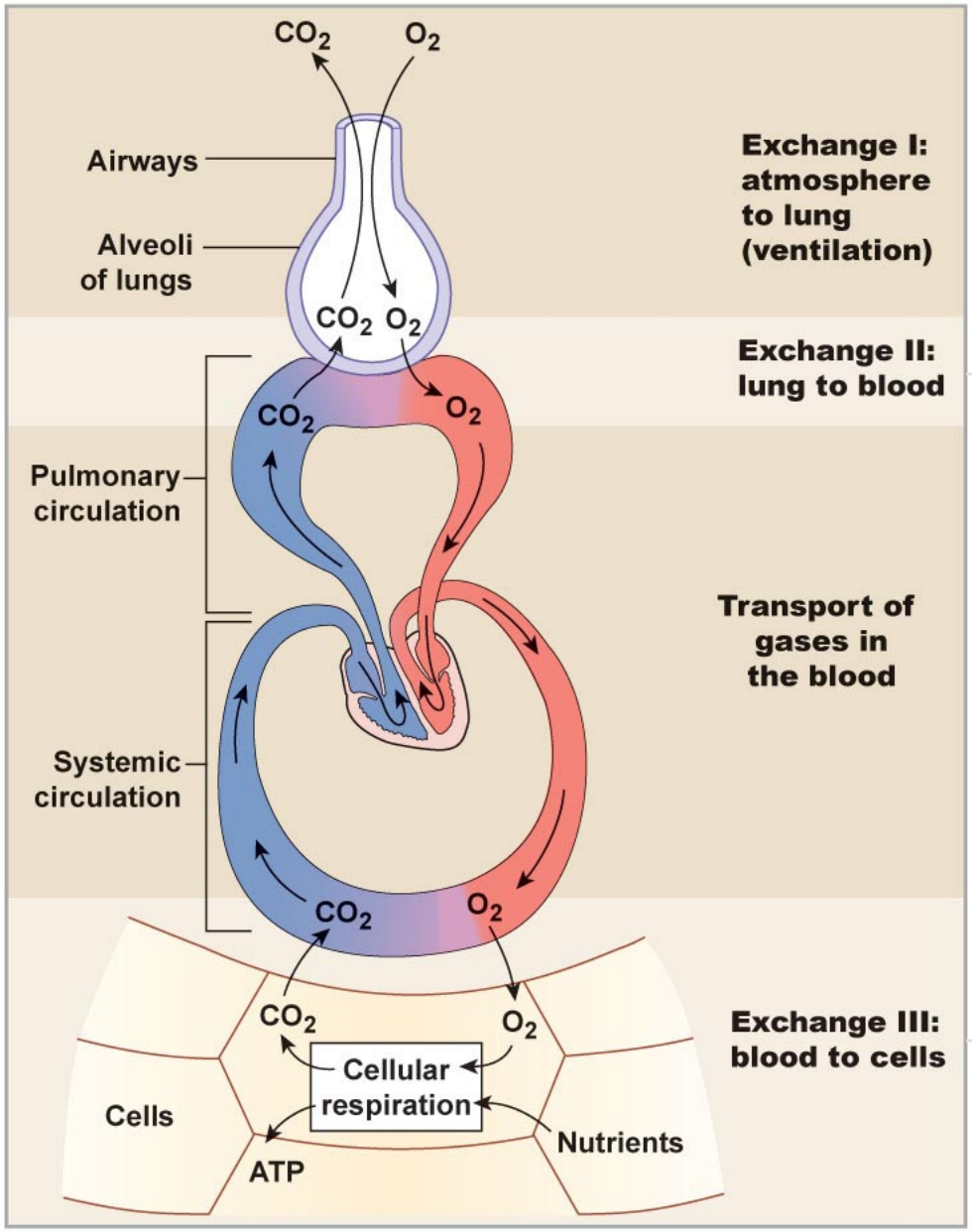
(2) *Diffusion*

(3) *Transport of* O_2 *&* CO_2*. (perfusion)*

(4) *Regulation of ventilation*.



Schematic View of Respiration



External Respiration

Internal Respiration

Partial Pressures of Gases in Inspired Air and Alveolar Air

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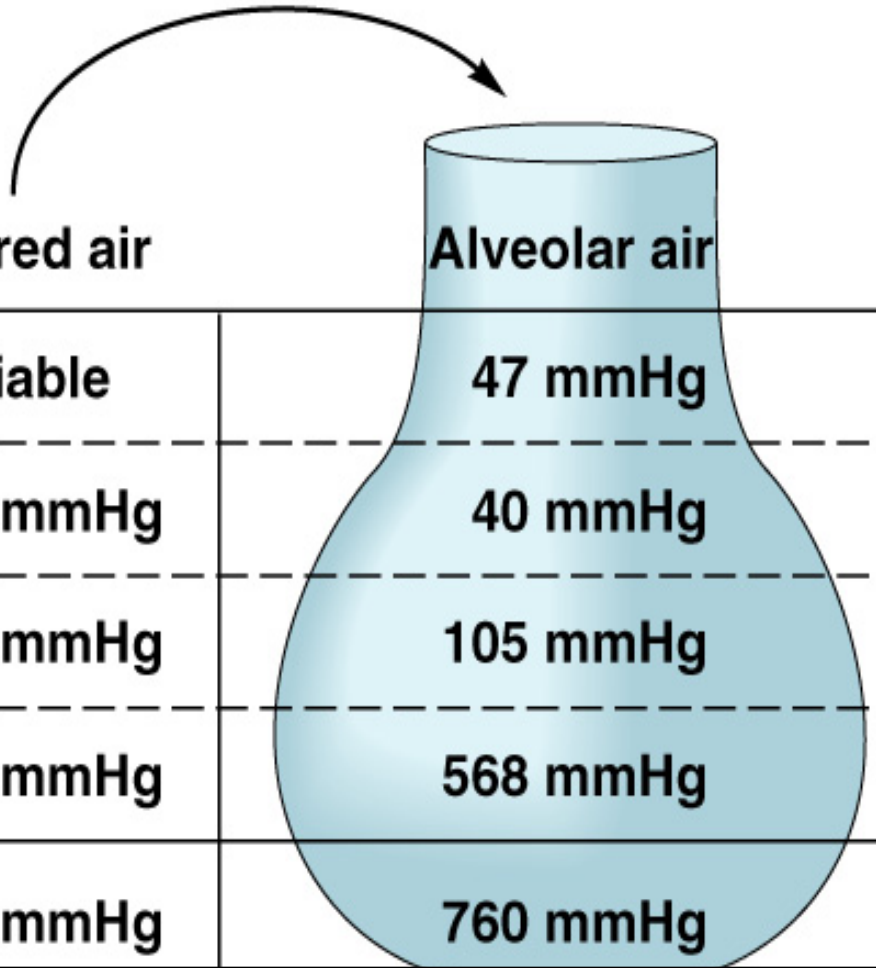
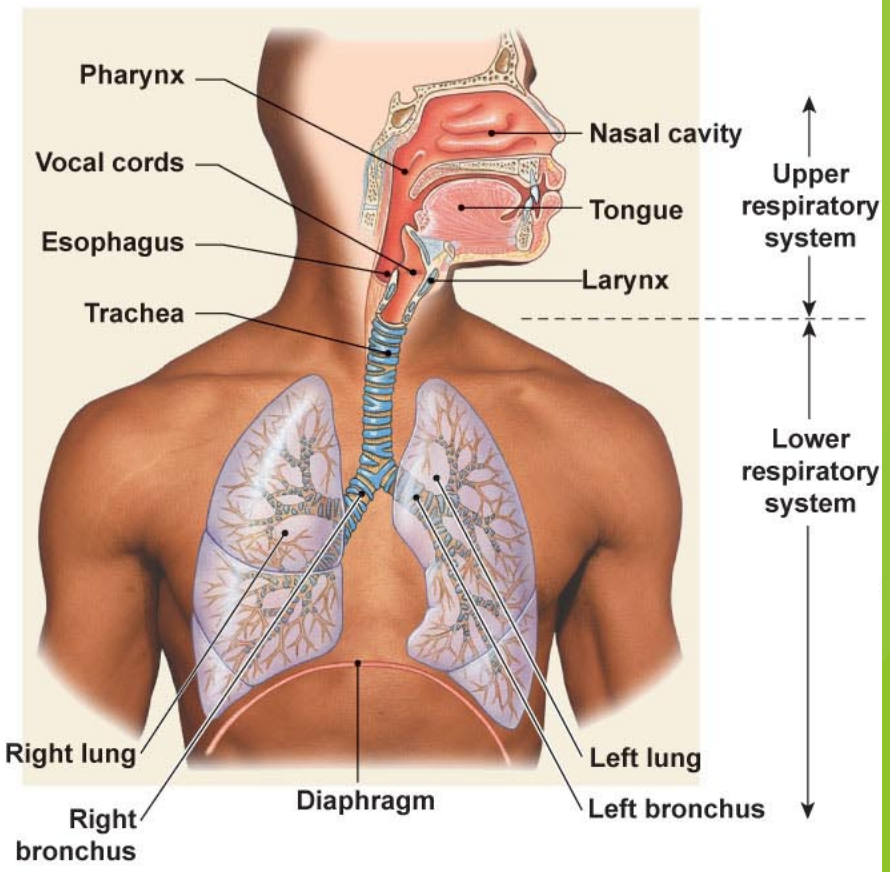


	Inspired air	Alveolar air
H_2O	Variable	47 mmHg
CO_2	000.3 mmHg	40 mmHg
O_2	159 mmHg	105 mmHg
N_2	601 mmHg	568 mmHg
Total pressure	760 mmHg	760 mmHg

Basics of the Respiratory System

Functional Anatomy

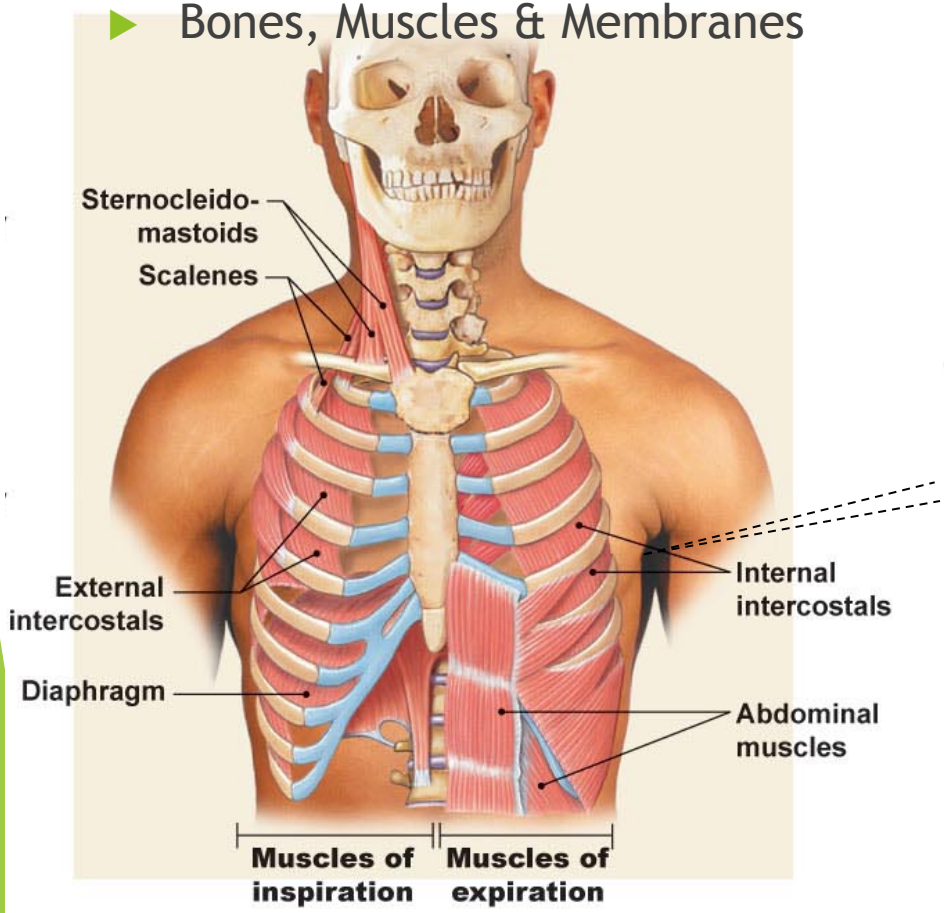
- What structural aspects must be process of respiration?
  - The conducting zone
  - The respiratory zone
  - The structures involved with ventilation
    - Skeletal & musculature
    - Pleural membranes
    - Neural pathways
- All divided into
  - Upper respiratory tract
    - Entrance to larynx
  - Lower respiratory tract
    - Larynx to alveoli (trachea to lungs)

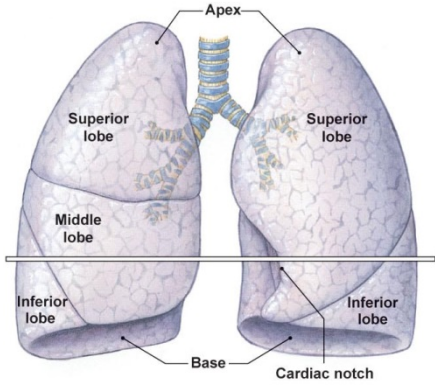


Basics of the Respiratory System

Functional Anatomy

- Bones, Muscles & Membranes

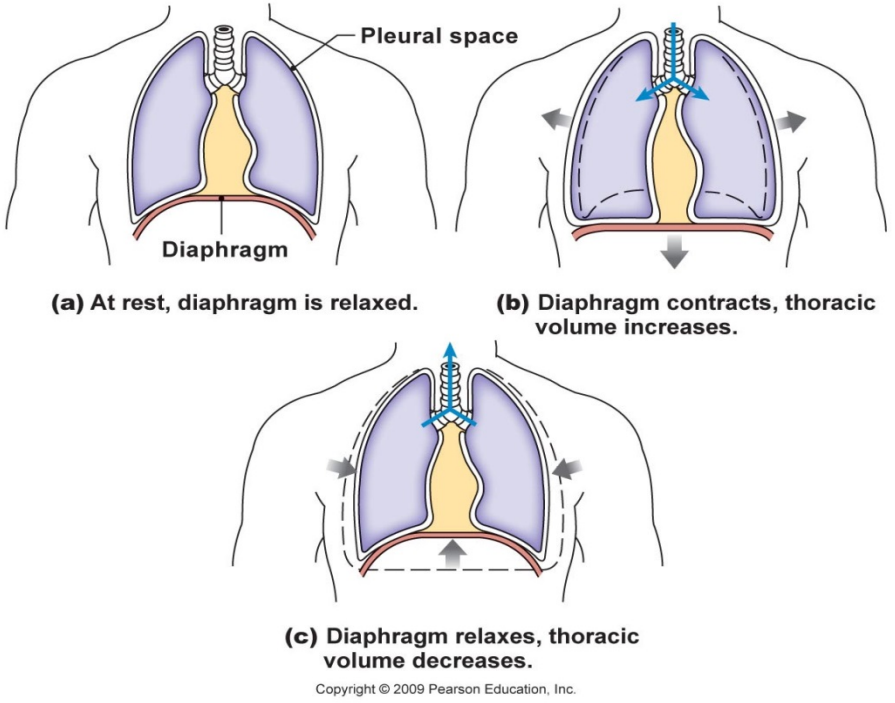




Basics of the Respiratory System

Functional Anatomy

- Function of these Bones, Muscles & Membranes
  - Create and transmit a pressure gradient
    - Relying on
      - the attachments of the muscles to the ribs (and overlying tissues)
      - The attachment of the diaphragm to the base of the lungs and associated pleural membranes
      - The cohesion of the parietal pleural membrane to the visceral pleural membrane
      - Expansion & recoil of the lung and therefore alveoli with the movement of the overlying structures



Basics of the Respiratory System
Functional Anatomy

- Pleural Membrane Detail
  - Cohesion between parietal and visceral layers is due to serous fluid in the pleural cavity
    - Fluid (30 ml of fluid) creates an attraction between the two sheets of membrane
    - As the parietal membrane expands due to expansion of the thoracic cavity it "pulls" the visceral membrane with it
      - And then pulls the underlying structures which expand as well
    - Disruption of the integrity of the pleural membrane will result in a rapid equalization of pressure and loss of ventilation function= pneumothorax and collapsed lung

Basics of the Respiratory System: Functional Anatomy

- The Respiratory Tree
  - connecting the external environment to the exchange portion of the lungs…Trachea being generation zero (we may also call it “branch” or “division”)…we have 23 generations/branches/divisions
  - similar to the vascular component
  - larger airway = high velocity
    - small cross-sectional area
  - smaller airway = low velocity
    - large cross-sectional area

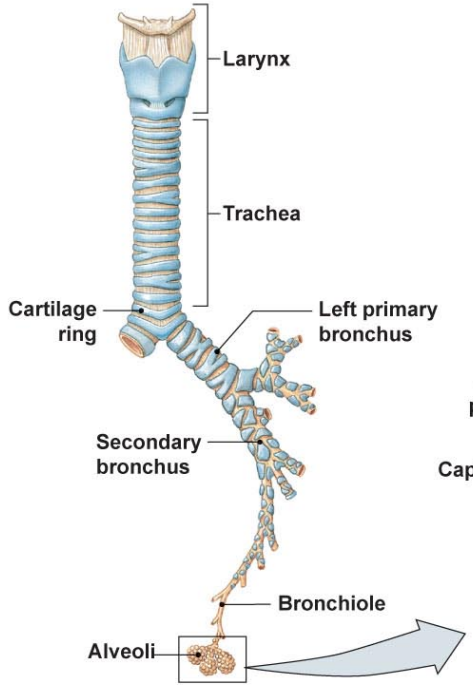
Basics of the Respiratory System

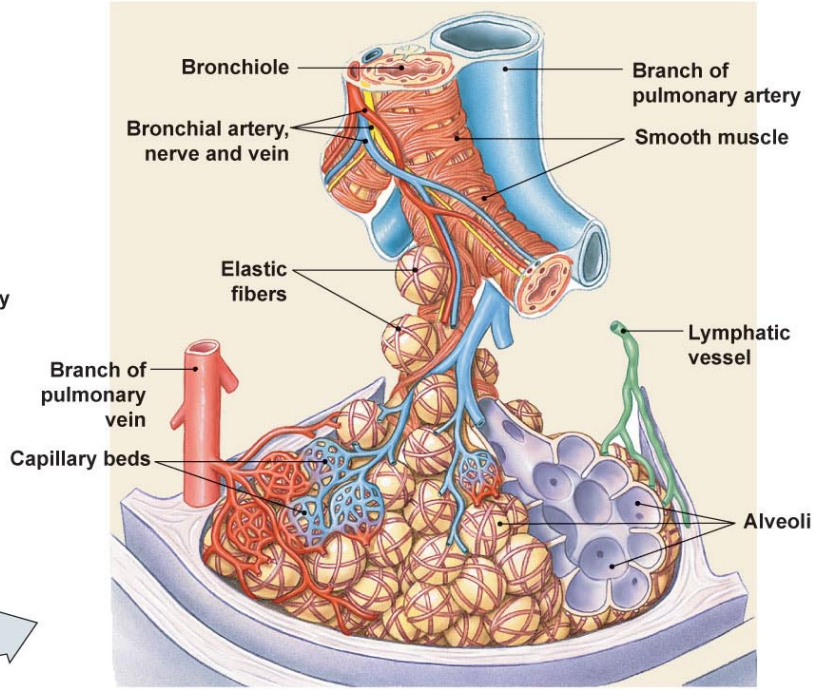
Functional Anatomy

- The Respiratory Tree
  - Upper respiratory tract is for all intensive purposes a single large conductive tube
  - The lower respiratory tract starts after the larynx and divides again and again…and again to eventually get to the smallest regions which form the exchange membranes
    - Trachea
    - Primary bronchi
    - Secondary bronchi
    - Tertiary bronchi
    - Bronchioles
    - Terminal bronchioles
    - Respiratory bronchioles with start of alveoli outpouches
    - Alveolar ducts with outpouchings of alveoli

conductive portion…first 16 branches

exchange portion…last 7

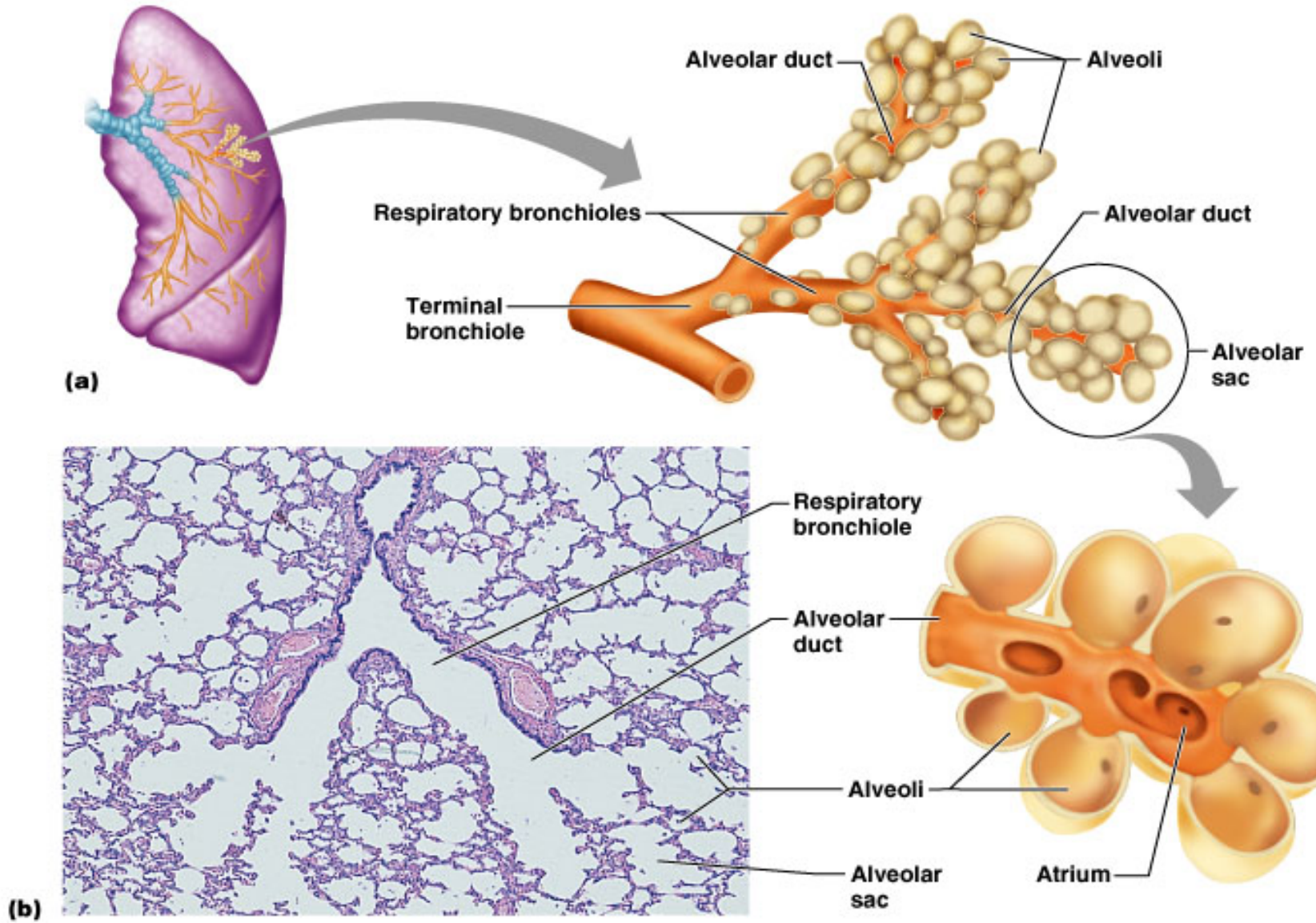




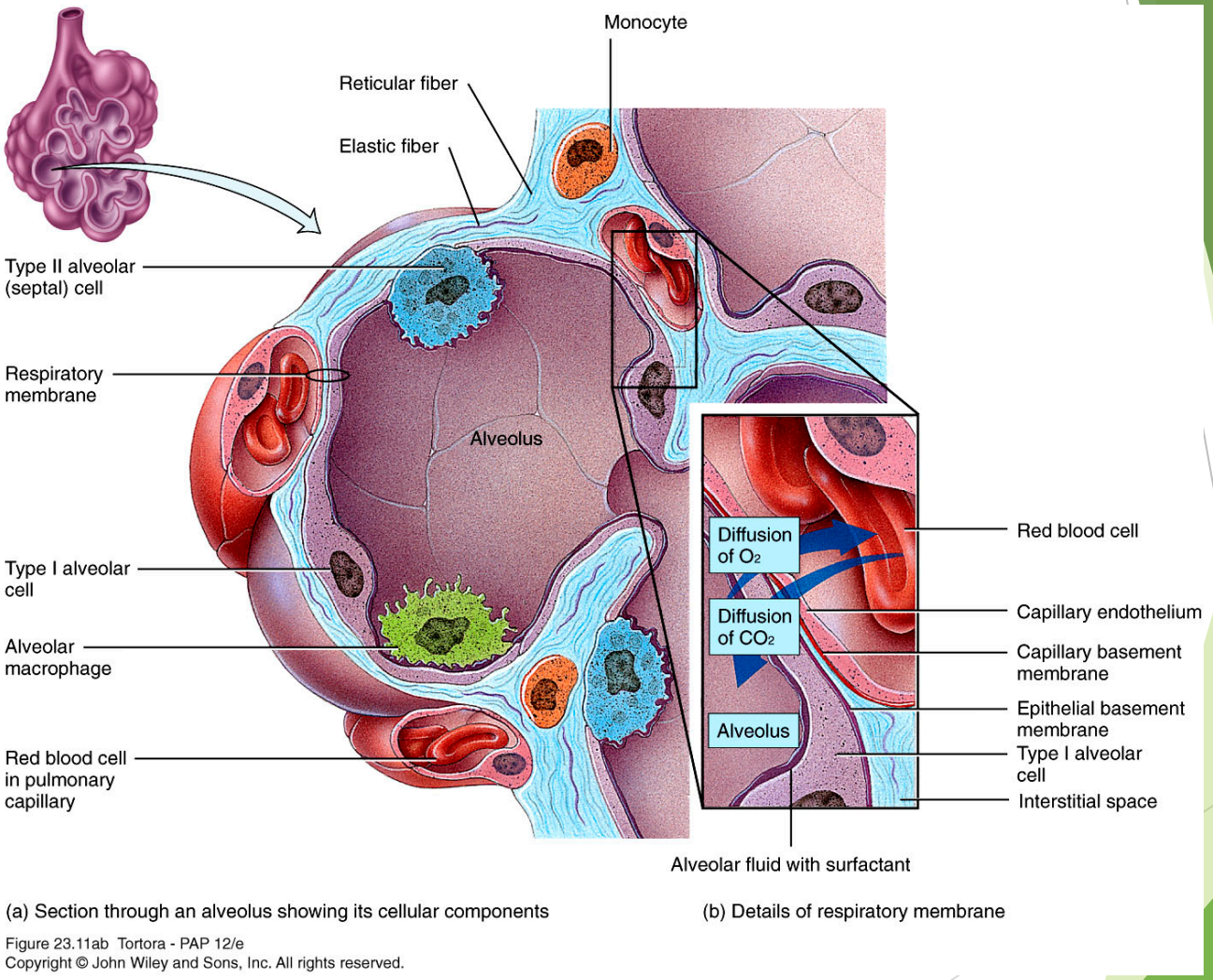
	Name	Division	Diameter (mm)	How many?	Cross-sectional area (cm^2)
Conducting system	Trachea	0	15-22	1	2.5
	Primary bronchi	1	10-15	2	↓
	Smaller bronchi ↓	2	↓	4 ↓	↓
		3			
		4	1-10		
		5			
		6-11		1×10^4	
Exchange surface	Bronchioles	12-23	0.5-1	2×10^4 ↓ 8×10^7	100 ↓ 5×10^3
	Alveoli	24	0.3	$3\text{-}6 \times 10^8$	$>1 \times 10^6$

Cartilage and its protection

- The first 10 generations have cartilage and thus have support and therefore are somehow not collapsible structures
- 12^{th} to 16^{th} are called bronchioles (diameter < 1 mm) lack cartilage….and thus are collapsible
- From 0-16 is the conductive zone…ADS (2 ml/kg BW)
- From 17-23 is the respiratory zone…
- Some times 17^{th} -19^{th} are called Transitional zone
- 20^{th} to 22^{nd} are called alveolar ducts (0.5 mm in diameter) and are completely lined with alveoli
- Alveoli can intercommunicate through the pores of Kohn


Alveolar duct
Alveoli
Respiratory bronchioles
Alveolar duct
Terminal bronchiole
Alveolar sac
(a)
Respiratory bronchiole
Alveolar duct
Alveoli
Alveolar sac
Atrium
(b)

Components of Alveolus



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Basics of the Respiratory System

Functional Anatomy

- Anatomic Dead space : Definition…Function

Raises incoming air to 37 Celsius

- Warm
- Humidify
- Filter
- Vocalize

Raises incoming air to 100% humidity …PH_2O=47 mmHg

Forms mucociliary escalator

Basics of the Respiratory System Functional Anatomy

- **What is the function of the respiratory zone?**
  - Exchange of gases …. Due to
  - Alveoli have a volume of 5-6 liters. A sphere of this volume has a surface area of 0.16 m^2. However the alveolar surface area is 50-100 m^2. (150-times more)
    - Type I alveolar cells (simple squamous Epithelium…flat cells).
    - The surface area of the alveoli available for diffusion is about the size of a tennis court
    - Associated huge network of pulmonary capillaries
      - 80-90% of the space between alveoli is filled with blood in pulmonary capillary networks
    - Exchange distance is less than 1 μm from alveoli to blood!
  - Protection
    - Free alveolar macrophages (dust cells) **Alveolar macrophage** is the **garbage man** of the alveoli and thus clean the alveoli.
    - Surfactant produced by type II alveolar cells (septal cells)

Respiratory Physiology
Gas Laws

- Basic Atmospheric conditions
  - Pressure is typically measured in mm Hg
  - At sea level, atmospheric pressure is 760 mm Hg
  - Atmospheric components
    - Nitrogen = 78% of our atmosphere $PN_2 \approx$ 600 mmHg
    - Oxygen = 21% of our atmosphere $PO_2 \approx$ 160 mmHg
    - Carbon Dioxide = .033% of our atmosphere, and for practical purposes we will consider $PCO_2 \approx$ zero mmHg…we ignore it.
    - Water vapor, krypton, argon, …. Make up the rest...but bcs we consider dry atmospheric air we are going to ignore them too.

- **Consider PO_2 and PCO_2 in different compartments.**

	Atmospheric	ADS	A	a	v	E
PO_2	160	150	102	102	40	120
PCO_2	0	---	40	40	45	28
PH_2O	Dry	47	47	47	47	47
PN_2	600	563→	571	571	571	566
Total P	**760**	**760**	**760**	**760**	**704**	**760**

How to calculate alveolar P_AO_2 A=stands for alveolar

$$P_AO_2 = P_IO_2 - (PCO_2/R)$$ I=stands for inspired

$$PO_2 = 150 - (40/0.8) = 100$$

R is respiratory exchange ratio ~0.8 we will come back to this concept…don't worry

In a normal person alveolar $P_AO_2 \approx$ a P_aO_2 …the difference is less than 5 mmHg for reasons to be discussed later (V/Q ratio)

The same concept: $P_ACO_2 = P_aCO_2$.

A few laws to remember

Dalton's law…the partial pressure law
Fick's Laws of Diffusion…
Ohm's law which is the most important law in physiology (not only respiratory!)
Boyle's Law: volume versus pressure
Ideal Gas Law…conversion between units PV=nRT

Respiratory Physiology

Gas Laws

- **Dalton's Law**
  - Law of Partial Pressures
    - "In a mixture of gases, each gas will exert a pressure independent of other gases present"
    - In a mixture of gases each gas behaves as if it is the only gas available in that mixture

      Or
    - The total pressure of a mixture of gases is equal to the sum of the individual gas pressures.
  - What does this mean in practical application?
    - If we know the total atmospheric pressure (760 mm Hg) and the relative abundances of gases (% of gases)
      - We can calculate individual gas effects!
      - P_{atm} x % of gas in atmosphere = Partial pressure of any atmospheric gas
        - PO_2 = 760mmHg x 21% (.21) = **160 mm Hg**
    - Now that we know the partial pressures we know the gradients that will drive diffusion!

Again: Dalton's Law

In a gas mixture the pressure exerted by each individual gas in a space is independent of the pressure exerted by other gases.

$$P_{atm} = PH_2O + PO_2 + PN_2$$

$$P_{gas} = \%\ \text{total gases} * P_{total}$$

Respiratory Physiology

Gas Laws

- Fick's Laws of Diffusion
  - Things that affect rates of diffusion of gases
    - Distance to diffuse…thickness of the respiratory membrane
    - ΔP for that gas
    - Diffusing molecule sizes …least important
    - Temperature…usually it is stable 37C
  - In healthy individuals, most of the above variables are constant with the exception ΔP
    - So it all comes down to partial pressure gradients of gases… determined by Dalton's Law!

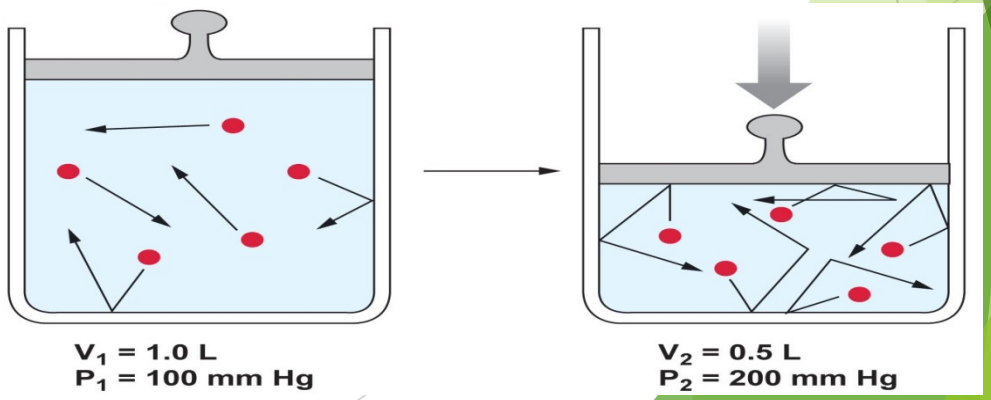
Fick's Law

- **Fick's Law defines diffusion of gas**
- **GAS Diffusion=Area*ΔPressure *Diffusion Coefficient /Distance**
- **Diffusion Coefficient = Solubility/(Molecular weight)^{½}**
- MW has small effect bcs it is the square root of MW

Respiratory Physiology

Gas Laws

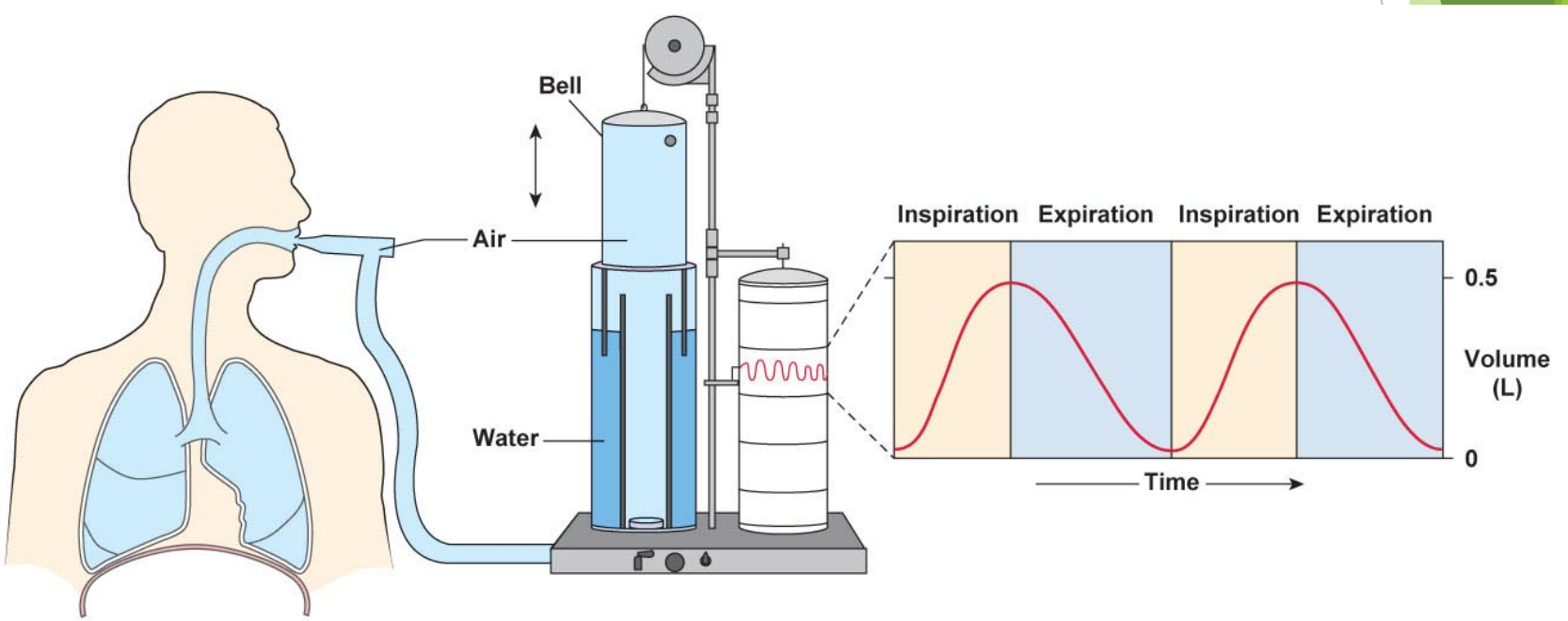
- Boyle's Law
  - Describes the relationship between pressure and volume…this law helps you to understand how we breath in and out.
    - "the pressure and volume of a gas in a system are inversely related if the temperature is kept constant
    - $P_1V_1 = P_2V_2$



Respiratory Physiology

Gas Laws

- How does Boyle's Law work in us?
  - As the thoracic cavity (container) expands the volume increases and pressure goes down
    - If it goes below 760 mm Hg what happens?
  - As the thoracic cavity shrinks the volume must go down and pressure goes up
    - If it goes above 760 mm Hg what happens



Respiratory Physiology

Gas Laws

- Ideal Gas law
  - The pressure and volume of a container of gas is directly related to the temperature of the gas and the number of molecules in the container
  - PV = nRT
    - n = moles of gas
    - T = absolute temp
    - R = universal gas constant @ 8.3145 J/K·mol
- Why Do we care? It helps you to convert PCO_2 (mmHg) to $[CO_2]$ in mmol/l later when you consider acid-base disturbance in renal physiology

Respiratory Physiology

Gas Laws

- Henry and his law

At a constant temperature, the amount of a given gas dissolved in a given type and volume of liquid is directly proportional to the partial pressure of that gas multiplied by the solubility of a gas in a

** Solubility has a constant which is different for each gas*

Using this law you can predict how much O_2 and CO_2 are available in dissolved form.

Solubility hardly change, but PO2 and PCO2 can both change

Partial Pressures of Gases in Blood

- When a liquid or gas (blood and alveolar air) are at equilibrium:
  - The amount of gas dissolved in fluid reaches a maximum value (Henry's Law).
- Depends upon:
  - Solubility of gas in the fluid.
  - Temperature of the fluid.
  - Partial pressure of the gas.
- .

Ventilation

- To makes Inspiration possible? (Mechanics)
  - Biological answer
    - Contraction of the inspiratory muscles causes an increase in the thoracic cavity size, thus allowing air to enter the respiratory tract
  - Physics answer
    - As the volume in the thoracic cavity increases (due to inspiratory muscle action) the pressure within the respiratory tract drops below atmospheric pressure, creating a pressure gradient which causes molecular movement to favor moving into the respiratory tract
  - Cause of Expiration? What you think? How this process is reversed?

Mechanics of Breathing

Airflow is governed by the basic flow equation, which relates flow to driving force (pressure) & airways resistance.

Always remember Ohm's law: Flow is directly proportional to the driving force and inversely proportional to the resistance

Flow = pressure difference (driving force) / resistance = ΔP/R

- 1. By positive Pressure Breathing: **resuscitator**: P at the nose or mouth is made higher than the alveolar pressure (P_{alv}). This is artificial type of breathing…not normal physiological breathing
- 2. By negative Pressure Breathing: P_{alv} is made less than P_{atm}**. This is normal pattern of breathing**
- It is the pressure difference between the two opposite ends of the airways: ($P_{alv} - P_{atm}$)
- **If R is large then ΔP must be large too to keep flow constant, we recognize the magnitude of airway resistance from the ΔP needed…indirectly**.
- .

Inhalation or inspiration

- Inhalation is active bcs it involves contraction of:
  - Diaphragm – most important muscle of inhalation
    - Flattens, lowering dome when contracted
    - Responsible for 75% of air entering lungs during normal quiet breathing
  - External intercostal muscles (not internal intercostal muscles!)
    - Contraction elevates ribs
    - Responsible 25% of air entering lungs during normal quiet breathing
  - Accessory muscles for dee and forceful inhalation
- When thorax expands…lungs expand too and intra-pulmonic (intra-alveolar) pressure drops… which create a driving force for air flow. Parietal and visceral pleurae adhere tightly

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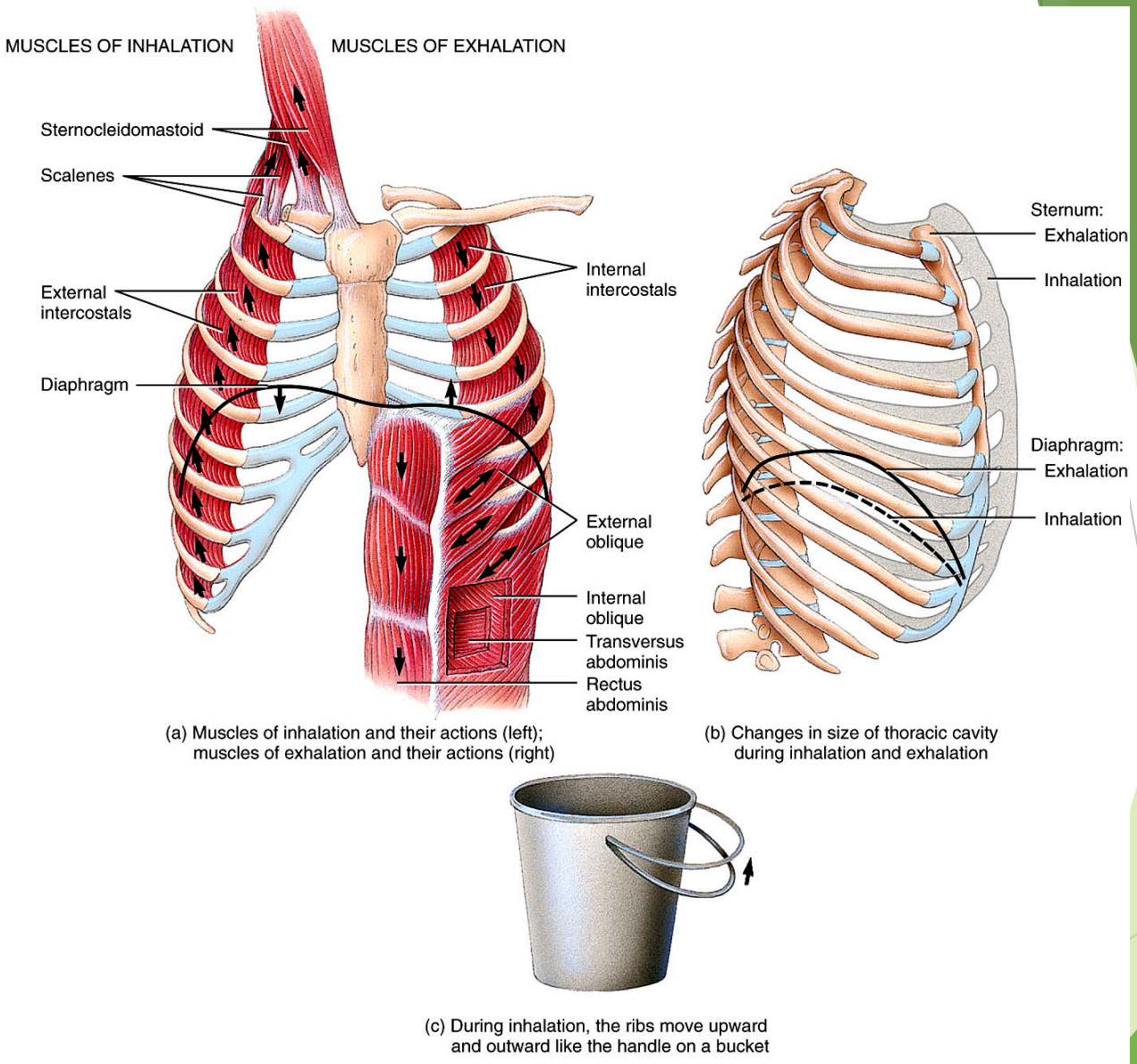

(a) Muscles of inhalation and their actions (left); muscles of exhalation and their actions (right)

(b) Changes in size of thoracic cavity during inhalation and exhalation

(c) During inhalation, the ribs move upward and outward like the handle on a bucket

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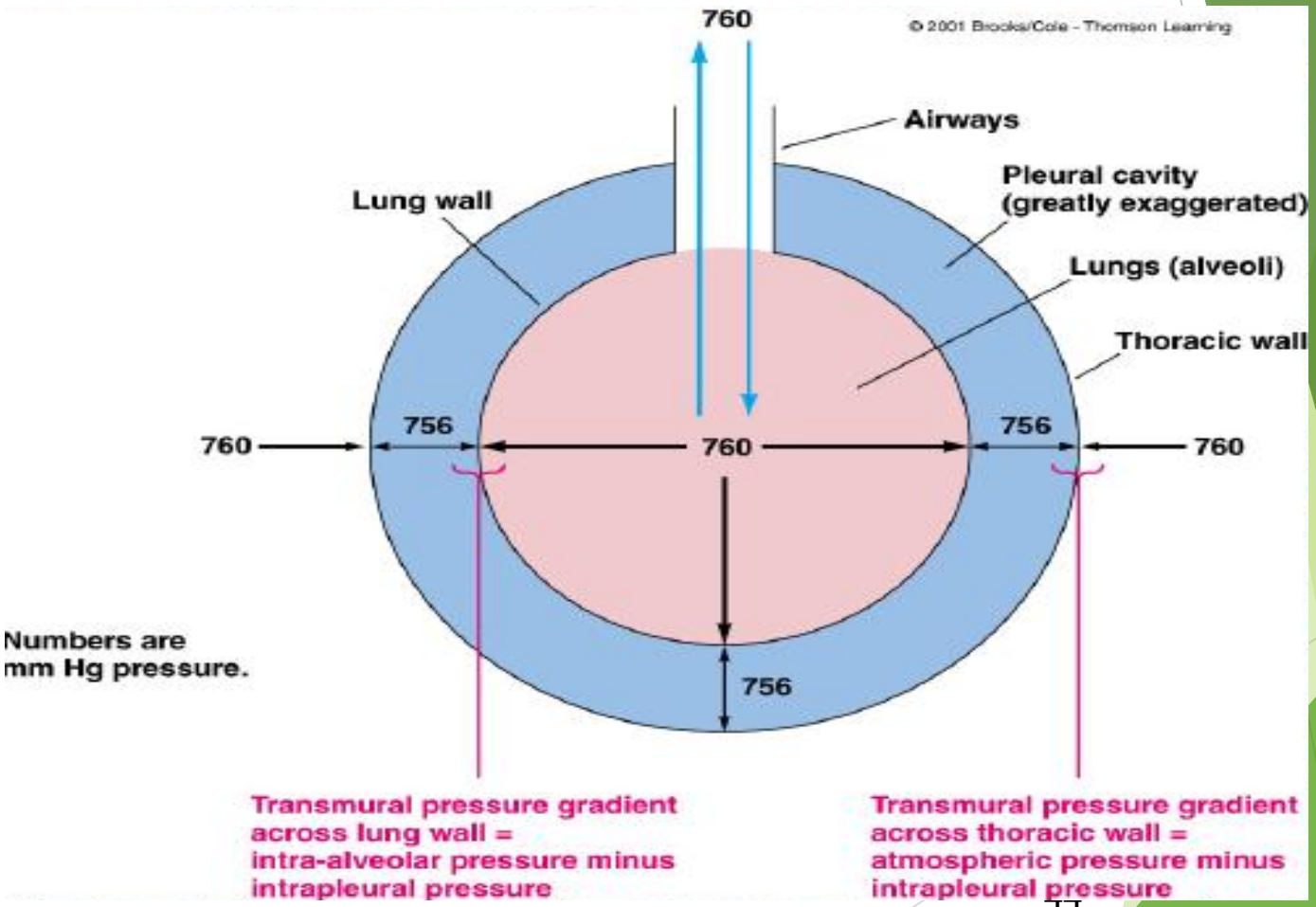
Ventilation

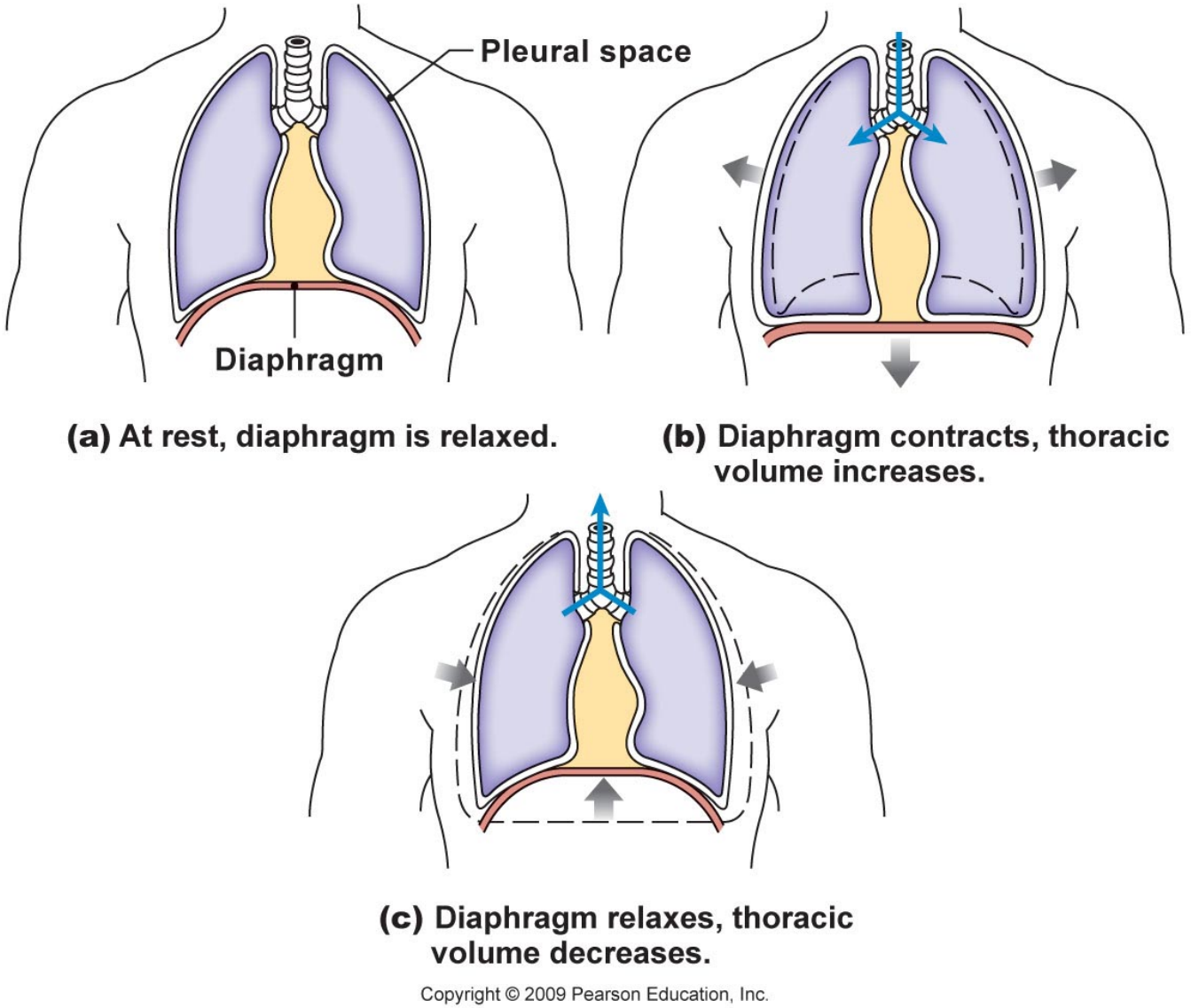
- Inspiration
  - Occurs as alveolar pressure drops below atmospheric pressure… becomes less than atmospheric and thus we call this pattern as: **negative pressure breathing**
    - For convenience atmospheric pressure = 0 mm Hg
      - A negative value (-) indicates pressure below atmospheric P
      - A positive (+) value indicates pressure above atmospheric P
    - At the start of inspiration (time = 0),
      - atmospheric pressure = alveolar pressure=zero mmH
      - No driving force (Ohm's)…No net movement of gases!
      - At time 0 to 2 seconds
      - Expansion of thoracic cage and corresponding pleural membranes and lung tissue causes alveolar pressure to drop to -1 mm Hg (negative)
      - Now…air enters the lungs down the partial pressure gradient

Respiratory pressures



Ventilation

Besides the diaphragm (only creates about 60-75% of the volume change) what are the muscles of inspiration & expiration?



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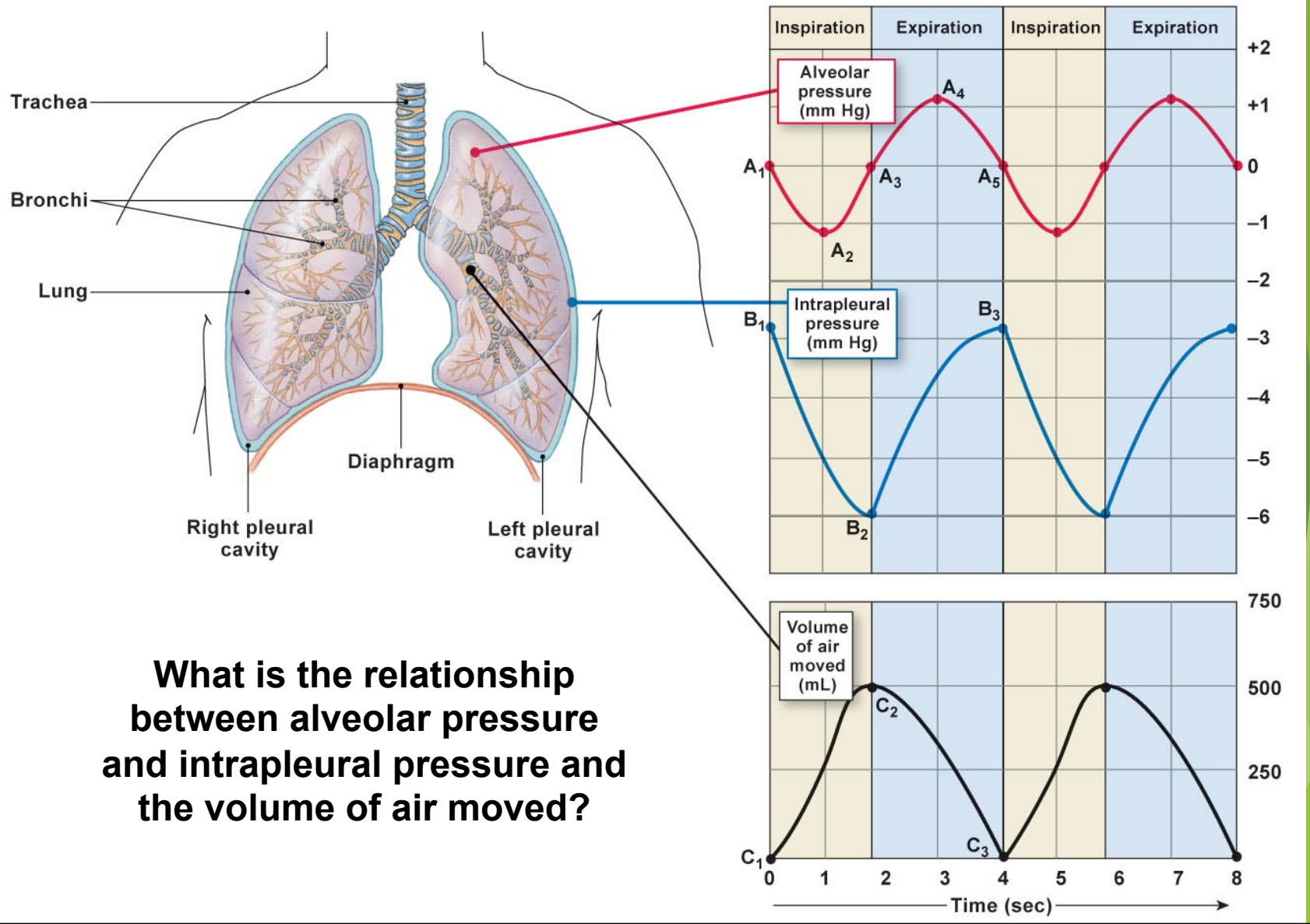
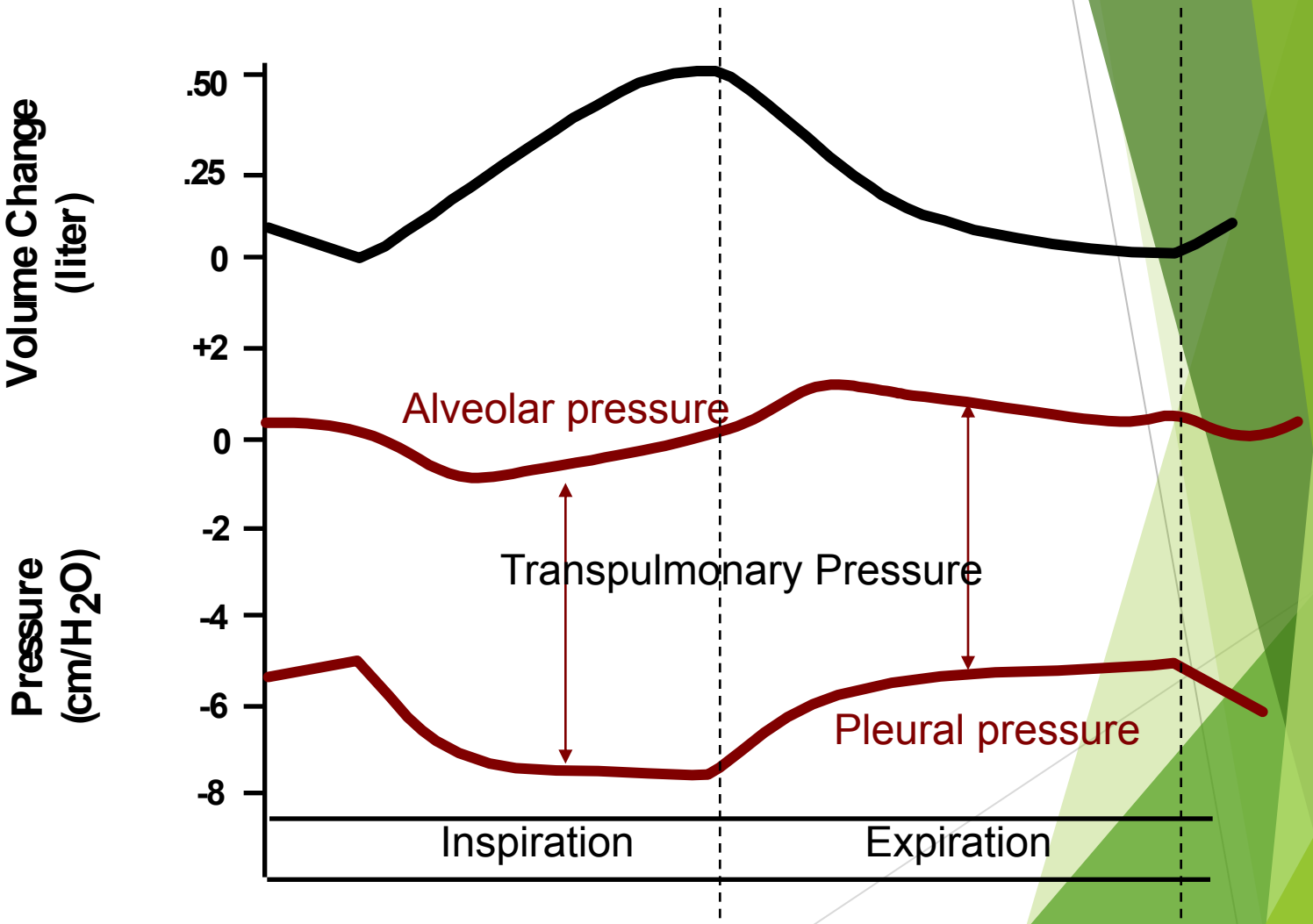
Ventilation



What is the relationship between alveolar pressure and intrapleural pressure and the volume of air moved?

Ventilation

- Expiration
  - Occurs as alveolar pressure elevates above atmospheric pressure due to a shrinking thoracic cage
    - At time 2-5 seconds
      - Inspiratory muscles relax, elastic tissue of corresponding structures initiates a recoil back to resting state
      - This decreases volume and correspondingly increases alveolar pressure to 1 mm Hg
        - This is above atmospheric pressure, causing…?
    - At time 5 seconds
      - Atmospheric pressure once again equals alveolar pressure and there is no net movement

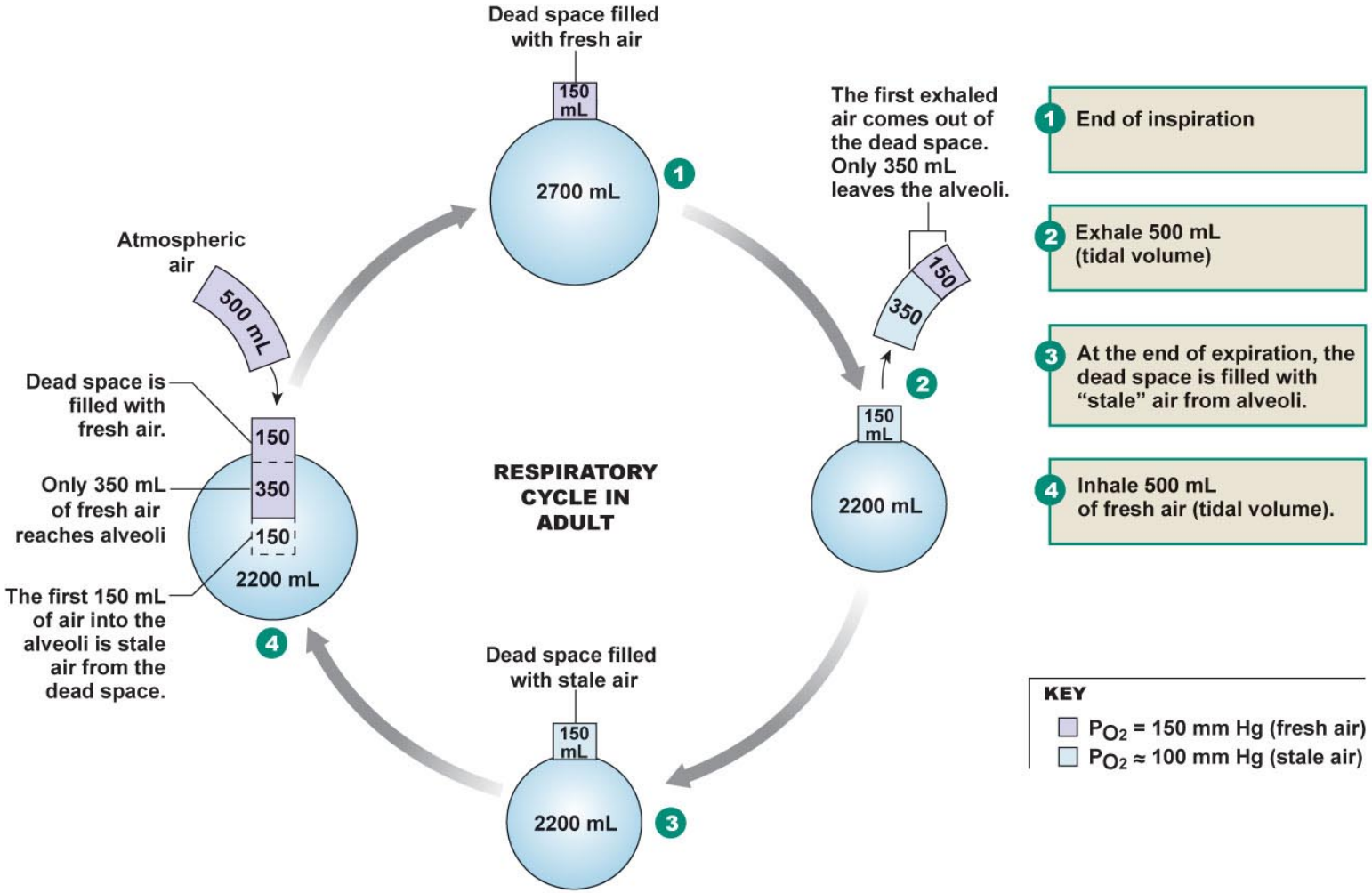

Volume Change (liter)
.50
.25
0
+2
0
-2
-4
-6
-8
Pressure (cm/H2O)
Alveolar pressure
Transpulmonary Pressure
Pleural pressure
Inspiration
Expiration

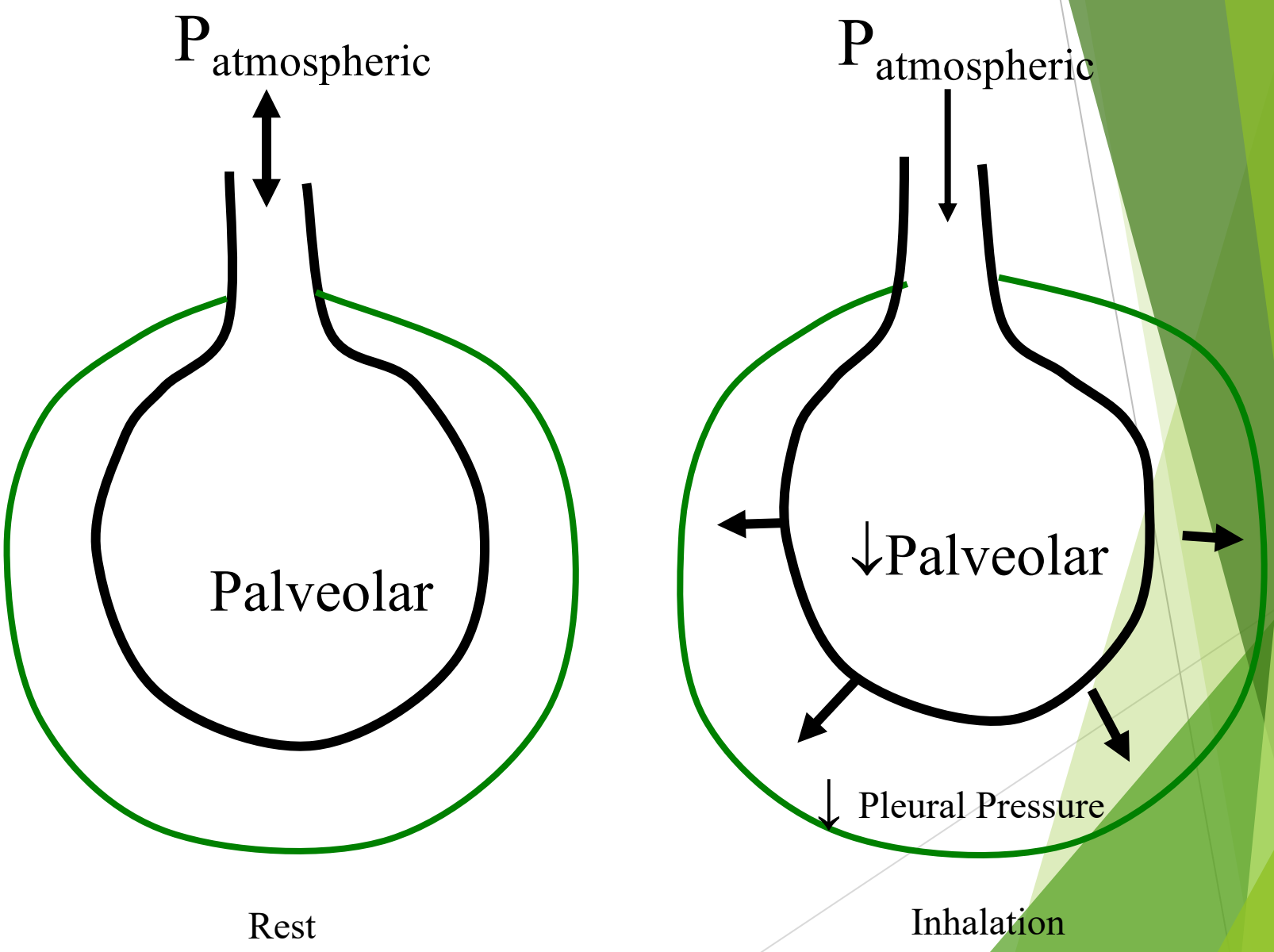
Ventilation

- What are the different respiratory patterns?
  - Quiet breathing (resting)
  - Forced inspirations & expirations (exercise)
- Respiratory volumes follow these respiratory patterns…
- Definition of HYPERVENTILATION is when alveolar ventilation is more than CO_2 production $\rightarrow$ decrease $PaCO_2$
- HYPOVENTILATION is when alveolar ventilation is LESS than CO2 production $\rightarrow$ increase PaCO2

Ventilation

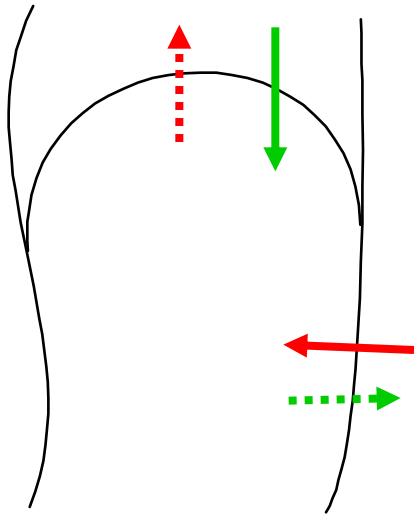
The relationship between minute volume (total pulmonary ventilation) and alveolar ventilation & the subsequent “mixing” of air




P atmospheric
Palveolar
Rest
P atmospheric
↓Palveolar
↓ Pleural Pressure
Inhalation

Mechanics Of Respiration

- Expiration
  - Active
    - Abdominals
    - decrease chest volumes



Active exhalation abdominal compression

Active inspiration abdominal relaxation

Exhalation/ expiration

- Pressure in lungs greater than atmospheric pressure
- Normally passive – muscle relax instead of contract
  - Based on elastic recoil of chest wall and lungs from elastic fibers and surface tension of alveolar fluid
  - Diaphragm relaxes and become dome shaped
  - External intercostals relax and ribs drop down
- Exhalation only active during forceful breathing

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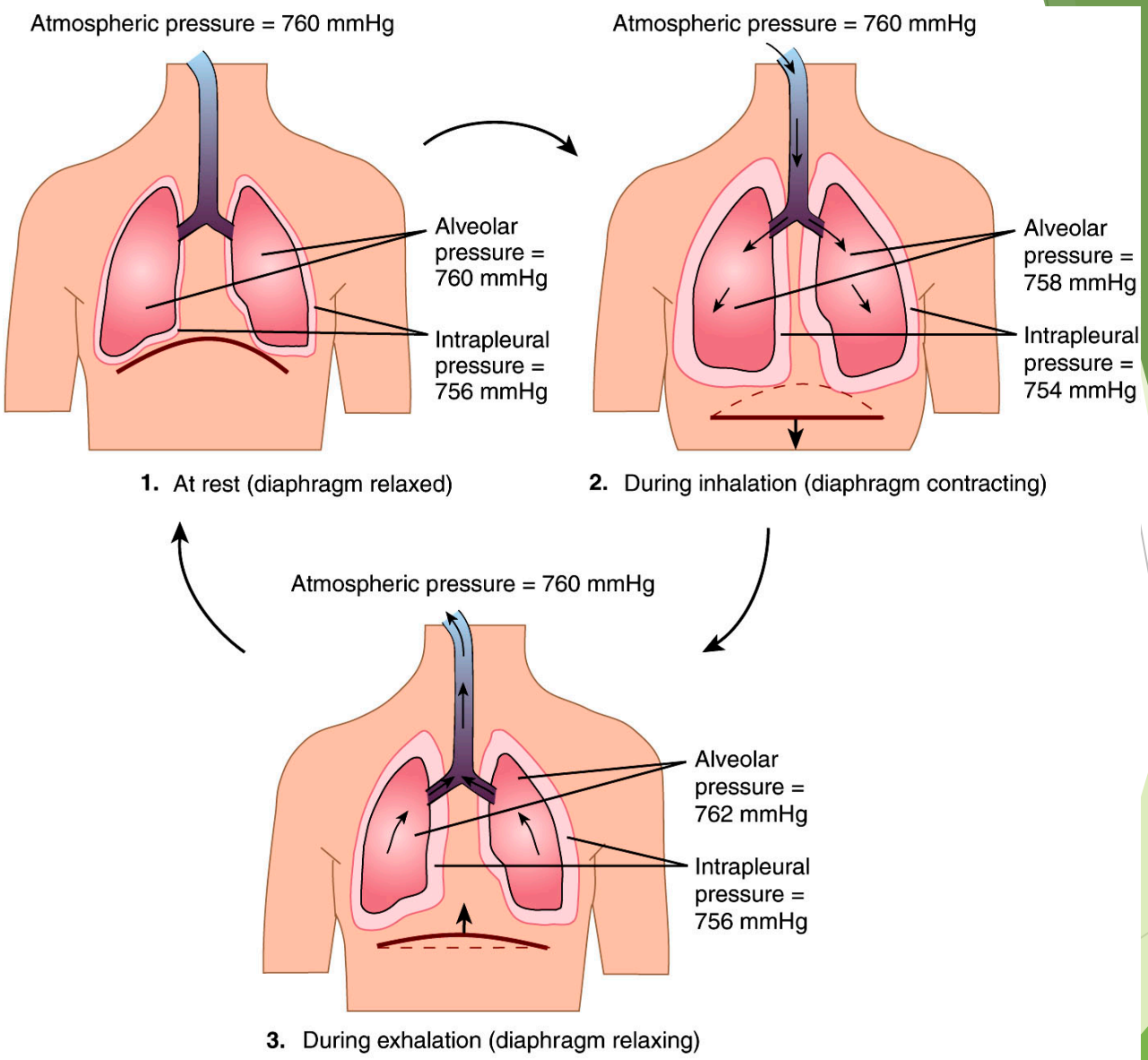

Figure 23.14 Tortora - PAP 12/e

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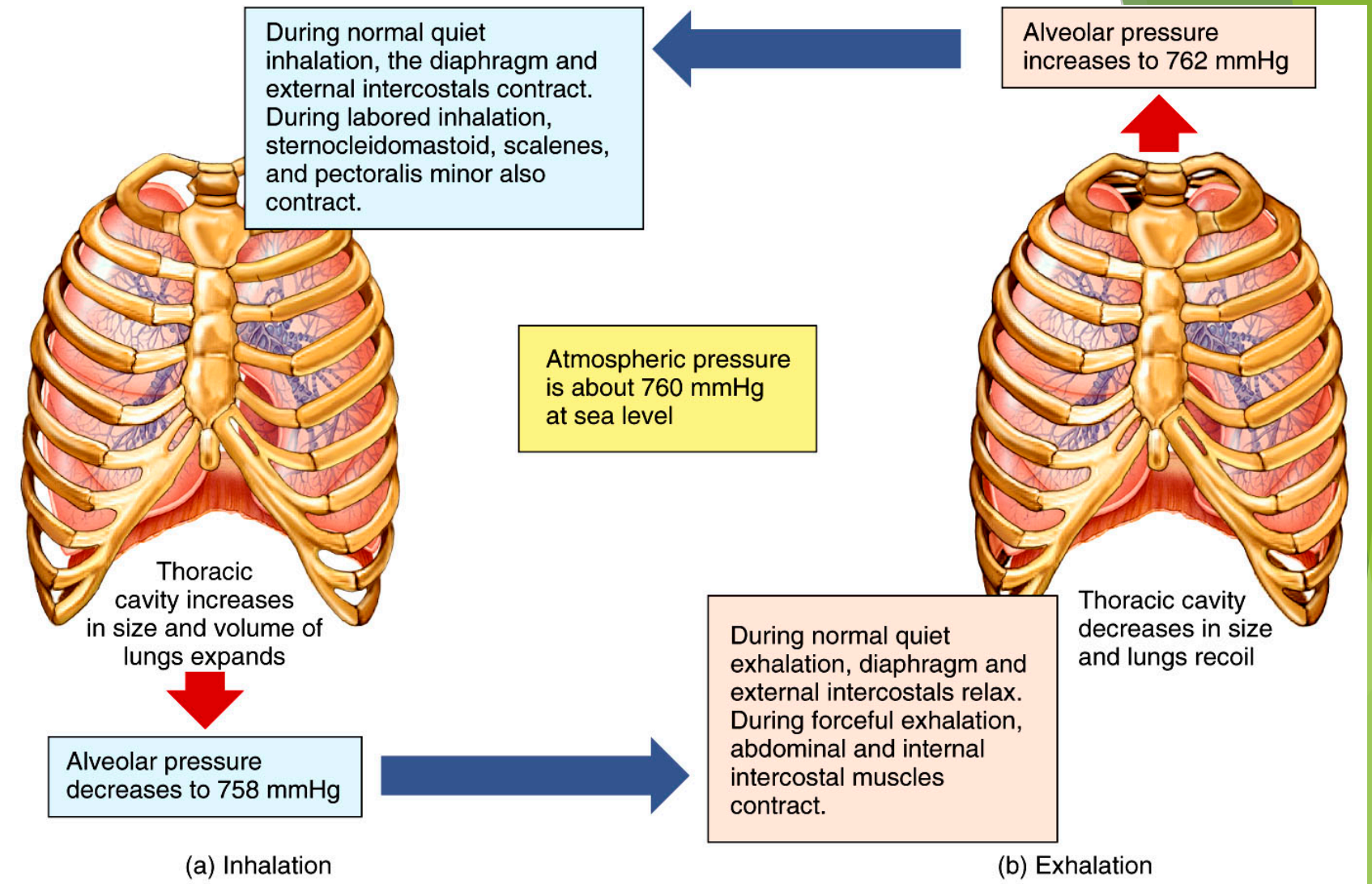

Figure 23.15 Tortora - PAP 12/e

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Respiratory Minute ventilation

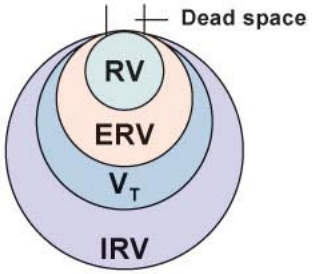
- Respiratory Minute ventilation RMV (respiratory rate times tidal volume 0.5 L * 12=6L/min). if you remember how the cardiac output is calculated then it is easy for you to understand
- RMV: Q=HR * SV… it is the same principle
- RMV=RR * V_T
- Anatomical dead space ventilation and alveolar ventilation
- RMV= ADS ventilation + alveolar ventilation

PFT Pulmonary Function Tests

- **Lung Volumes and Capacities**
- **Other tests will be discussed too. Diffusing Capacity of the Lung for Carbon Monoxide will be also discussed, but with Gas Exchange lecture**

Ventilation e-learning

The four lung volumes



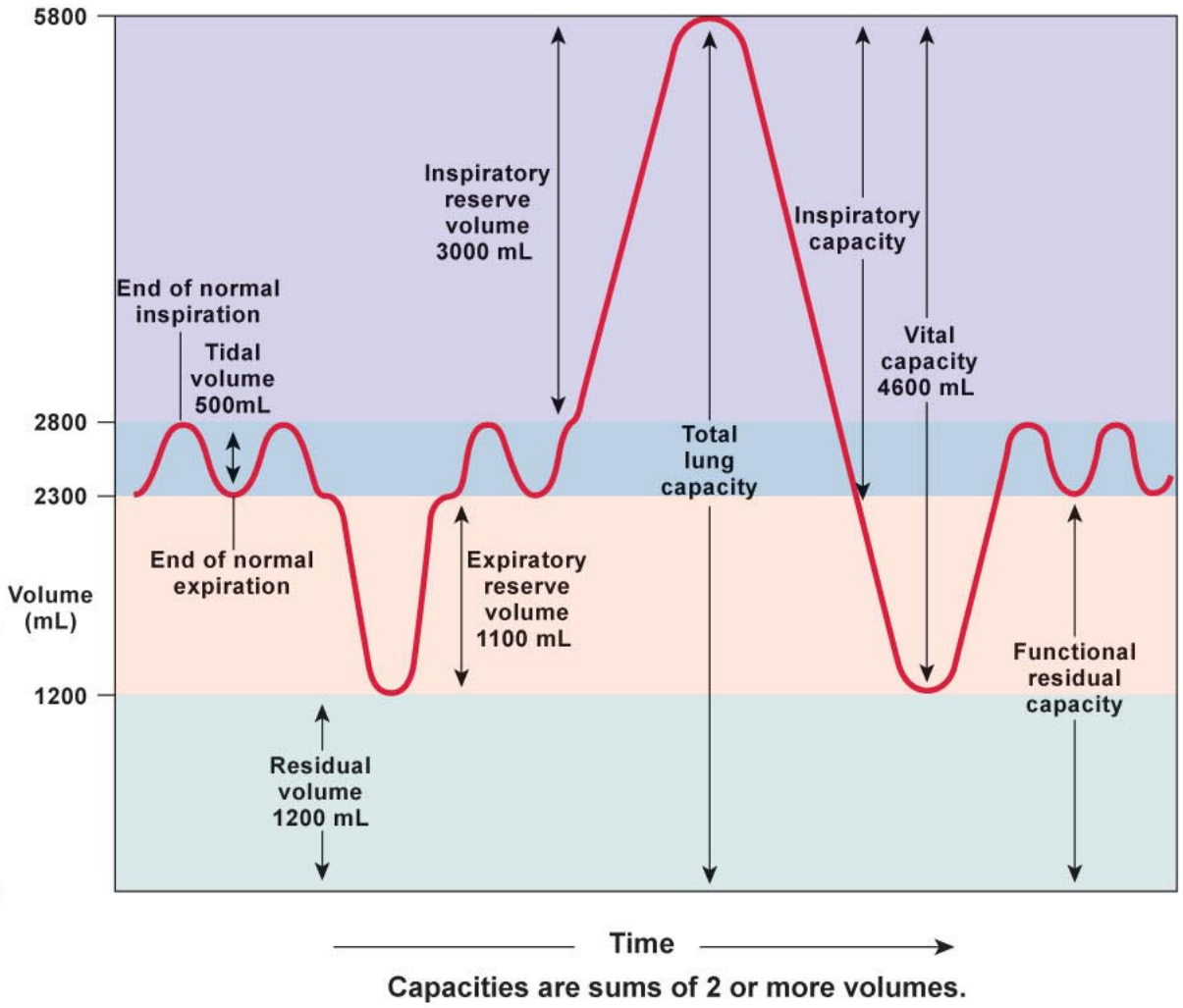
KEY

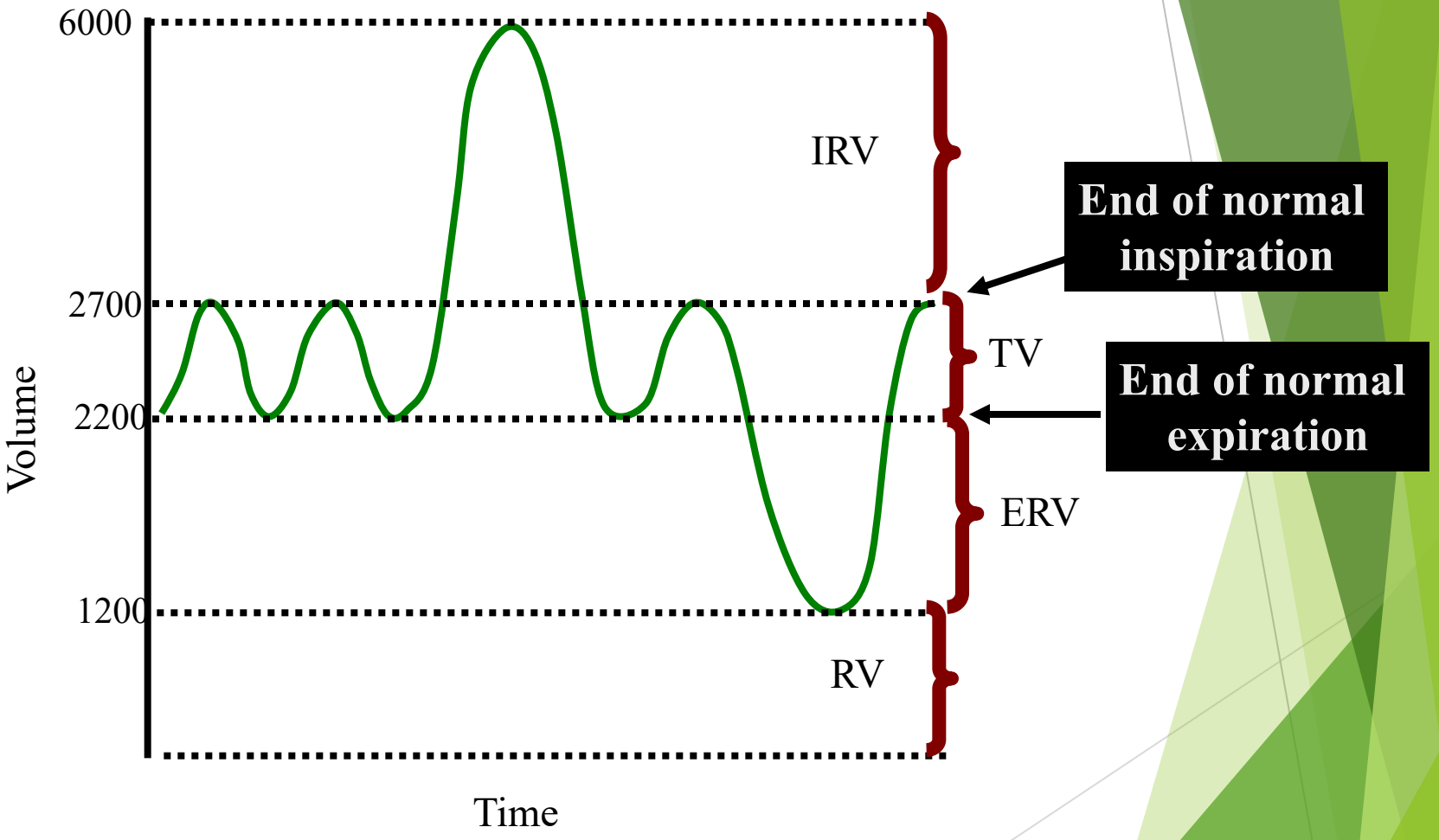
RV = Residual volume
ERV = Expiratory reserve volume
V_T = Tidal volume
IRV = Inspiratory reserve volume

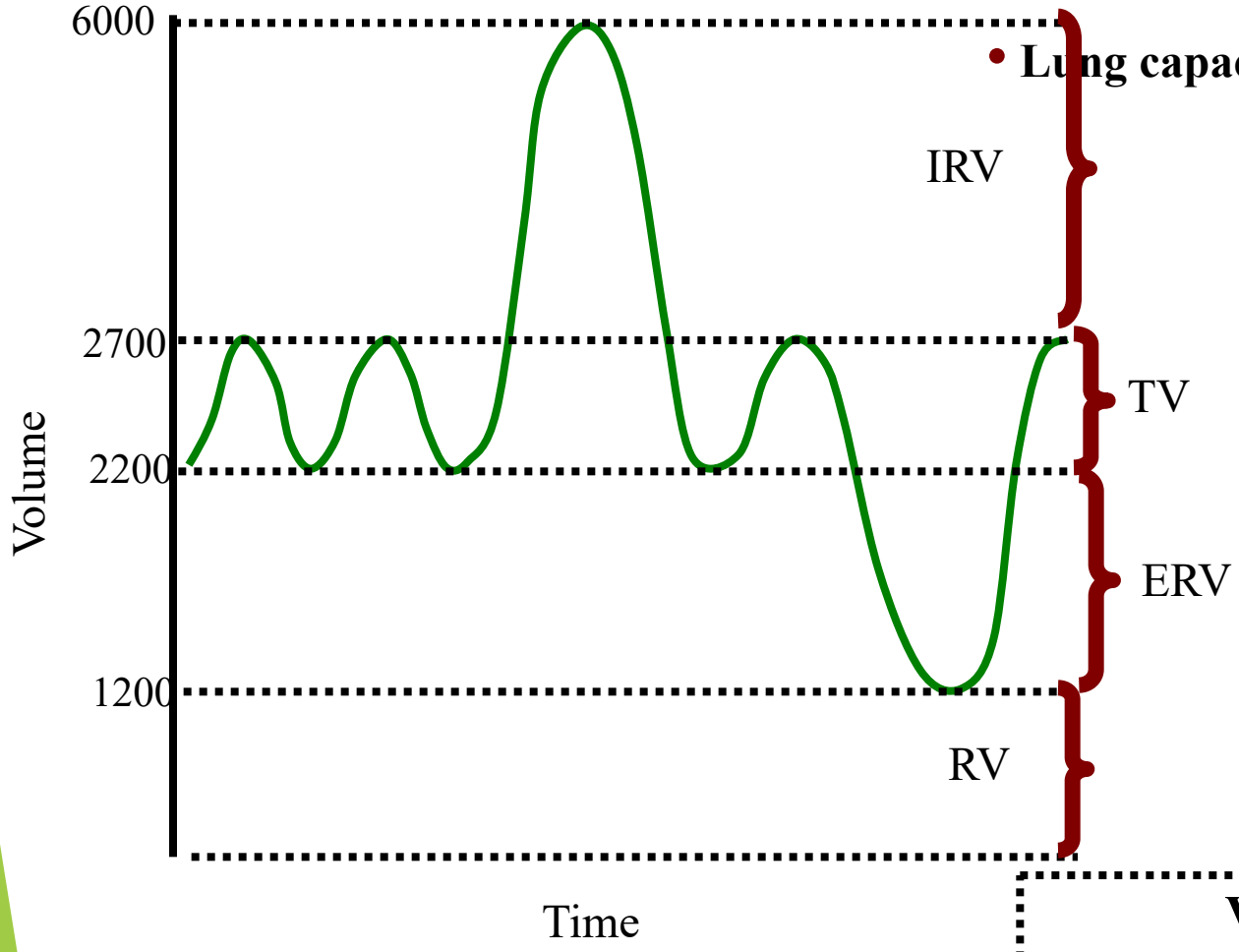
Pulmonary volumes

		Males	Females	
Vital capacity	IRV	3000	1900	Inspiratory capacity
	V_T	500	500	
	ERV	1100	700	Functional residual capacity
Residual volume		1200	1100	
		5800 mL	4200 mL	

A spirometer tracing showing lung volumes and capacities.



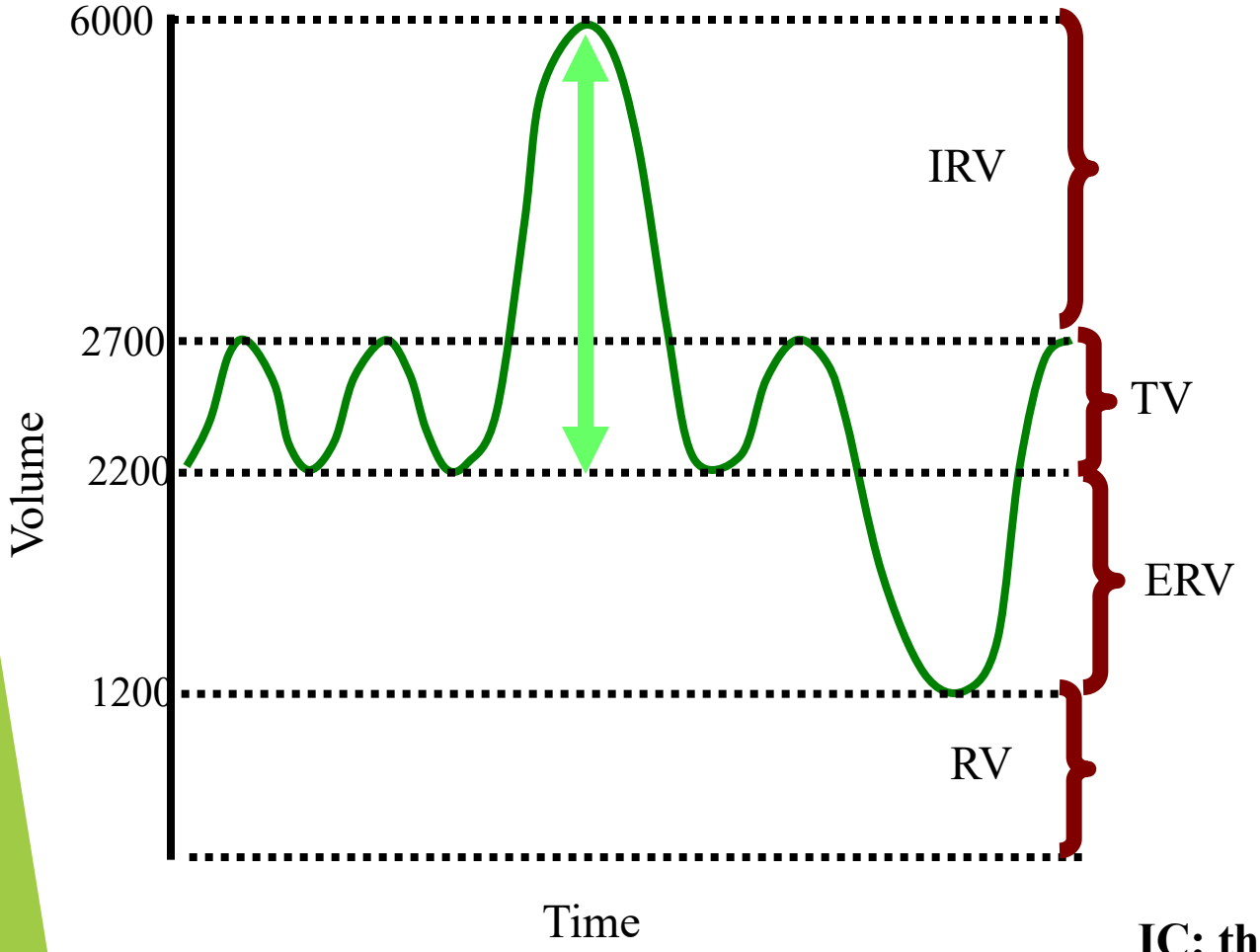

6000
2700
2200
1200
Volume
Time
IRV
TV
ERV
RV
End of normal inspiration
End of normal expiration



- **Lung capacity is the sum of two or more lung volumes**

V_T: Tidal Volume
IRV: Inspiratory Reserve Volume
ERV: Expiratory Reserve Volume
RV: Residual Volume

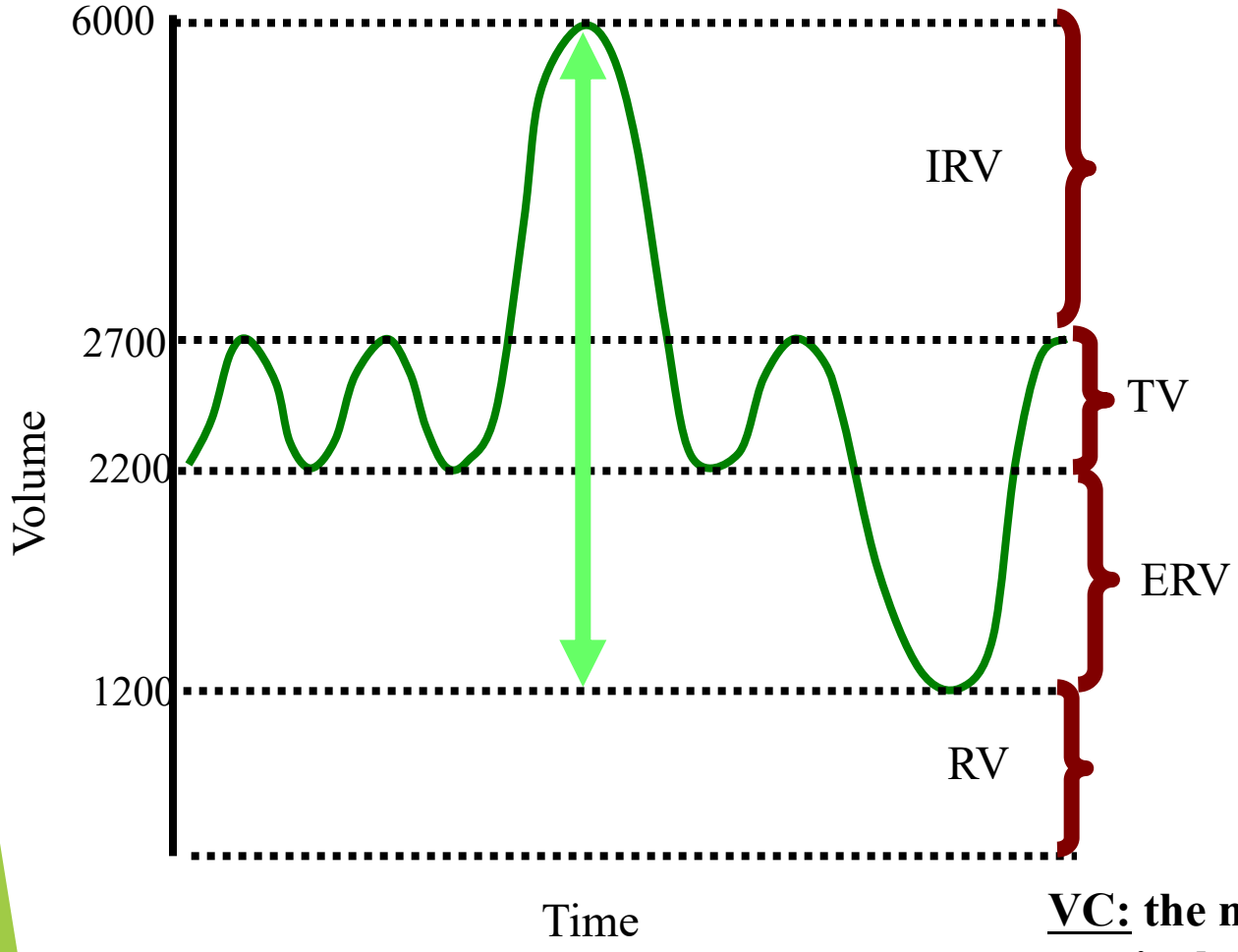
apacity (IC)



$$IC = V_T + IRV$$

IC: the maximum amount of air that can be inspired following a normal expiration

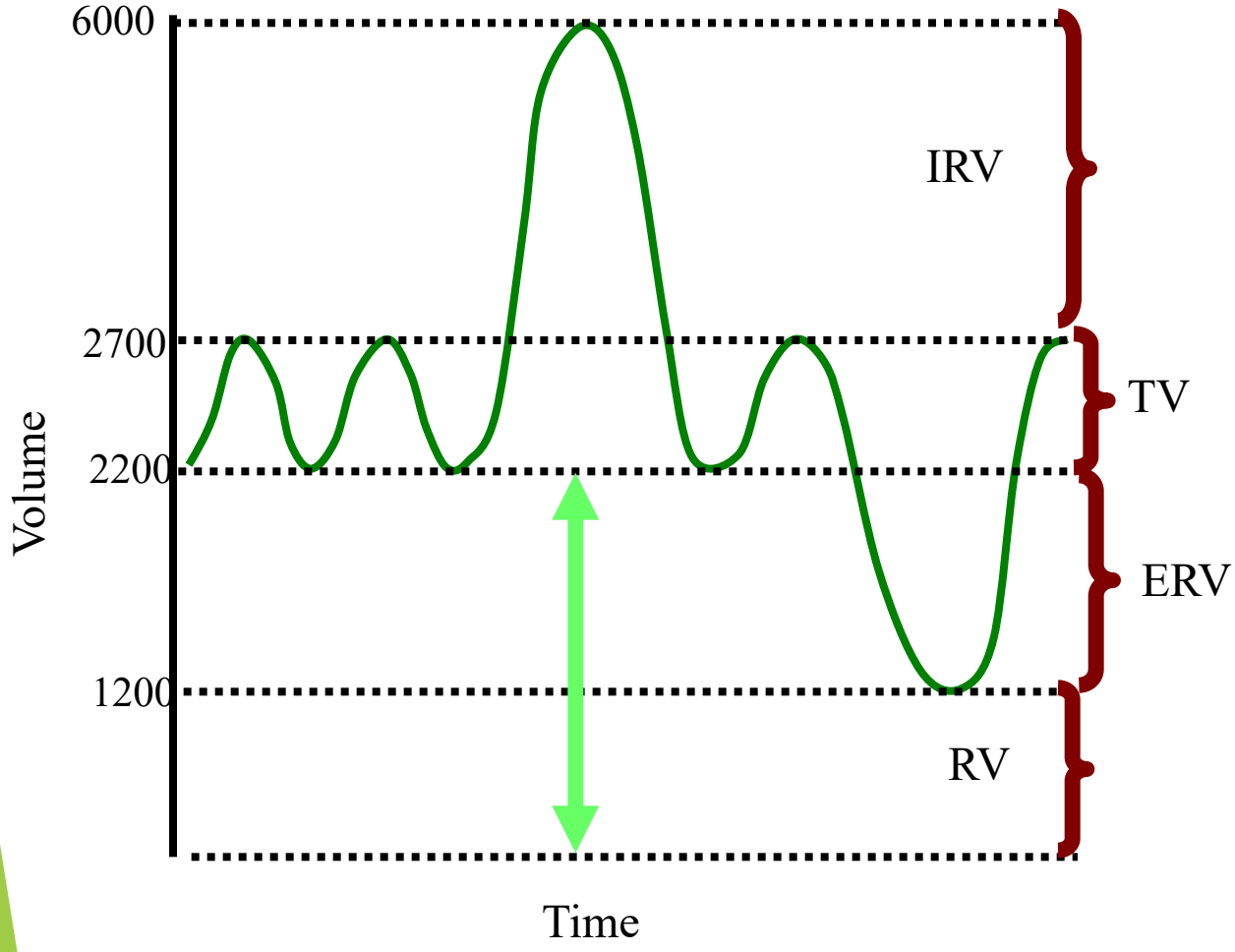
(VC)



VC = IRV + V_T + ERV

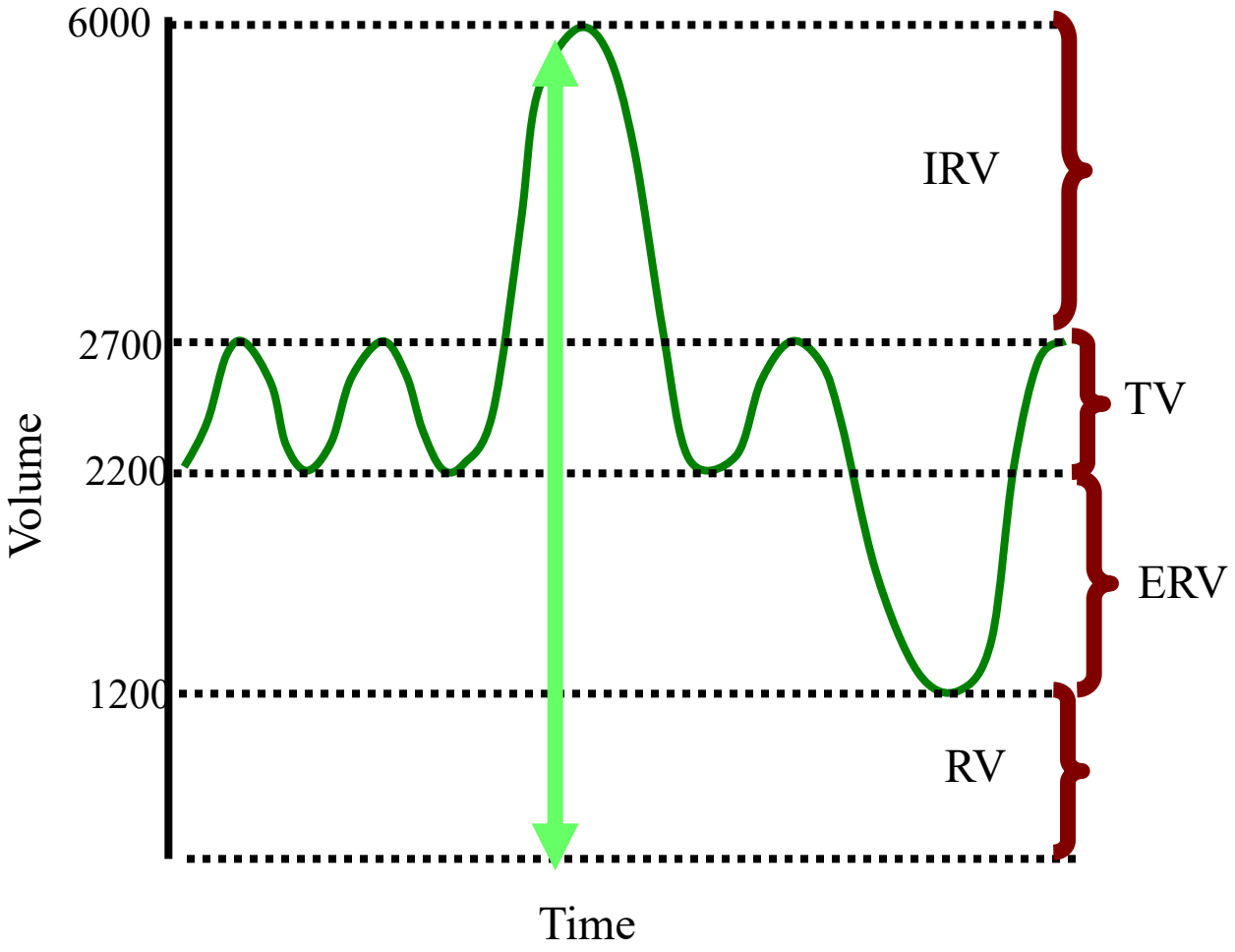
<u>VC:</u> the maximum amount of air that can be expired following a maximal inspiration

al



FRC = ERV + RV

FRC: the amount of air remaining in the lungs following a normal expiration.



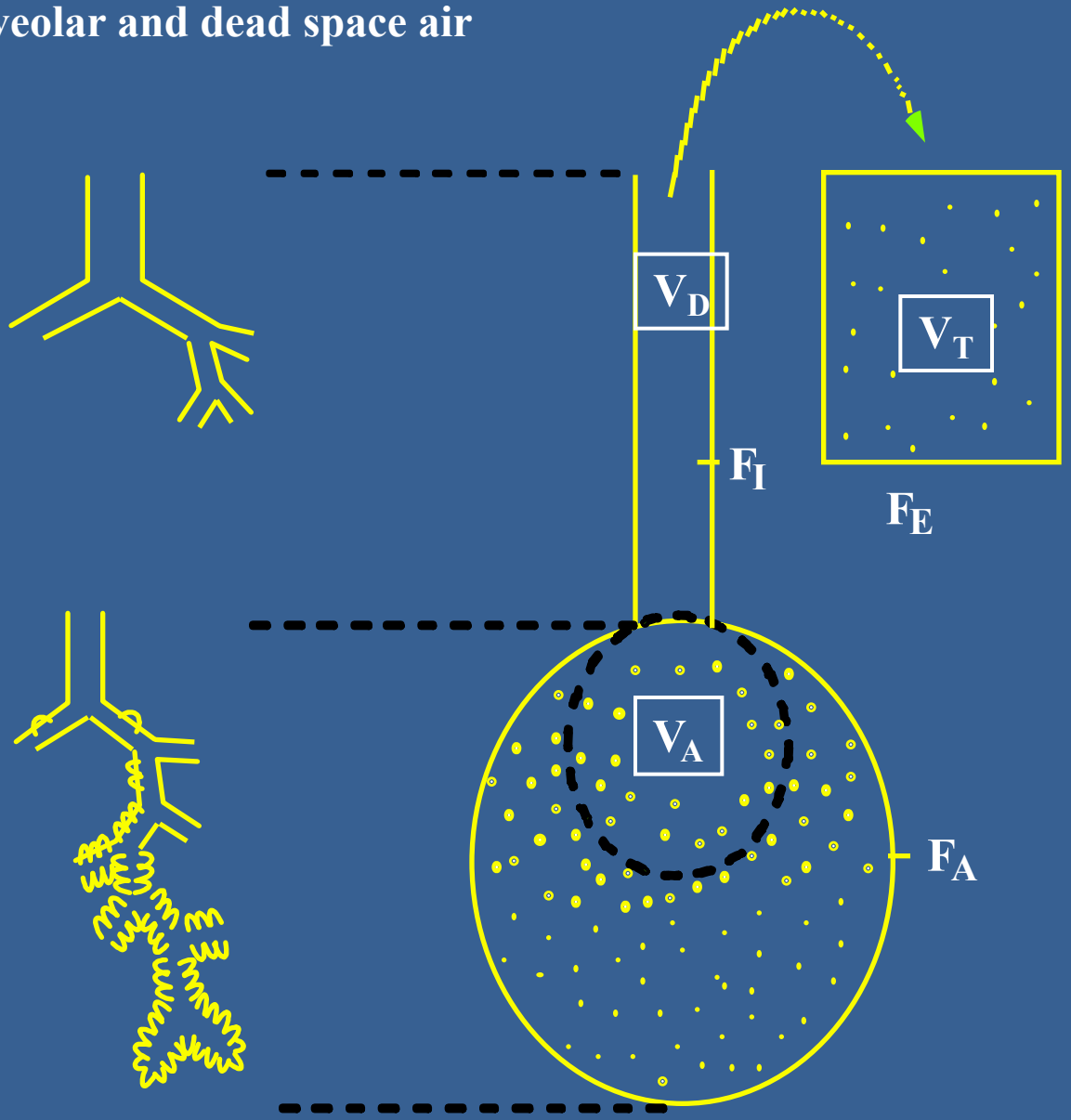
TLC = IRV + V_T + ERV + RV

TLC: the amount of air in the lungs at the end of a maximal inspiration.

ation

- Minute ventilation or RMV: Total amount of air moved into and out of respiratory system per minute
- Respiratory rate or frequency RR: Number of breaths taken per minute
- Anatomic dead space: Part of respiratory system where gas exchange does not take place ≈ 150 ml in an adult (2 ml/kg)
  - Physiological dead space=ADS + alveolar wasted volume
- Alveolar ventilation: How much air per minute enters the parts of the respiratory system in which gas exchange takes place

Expired air has alveolar and dead space air



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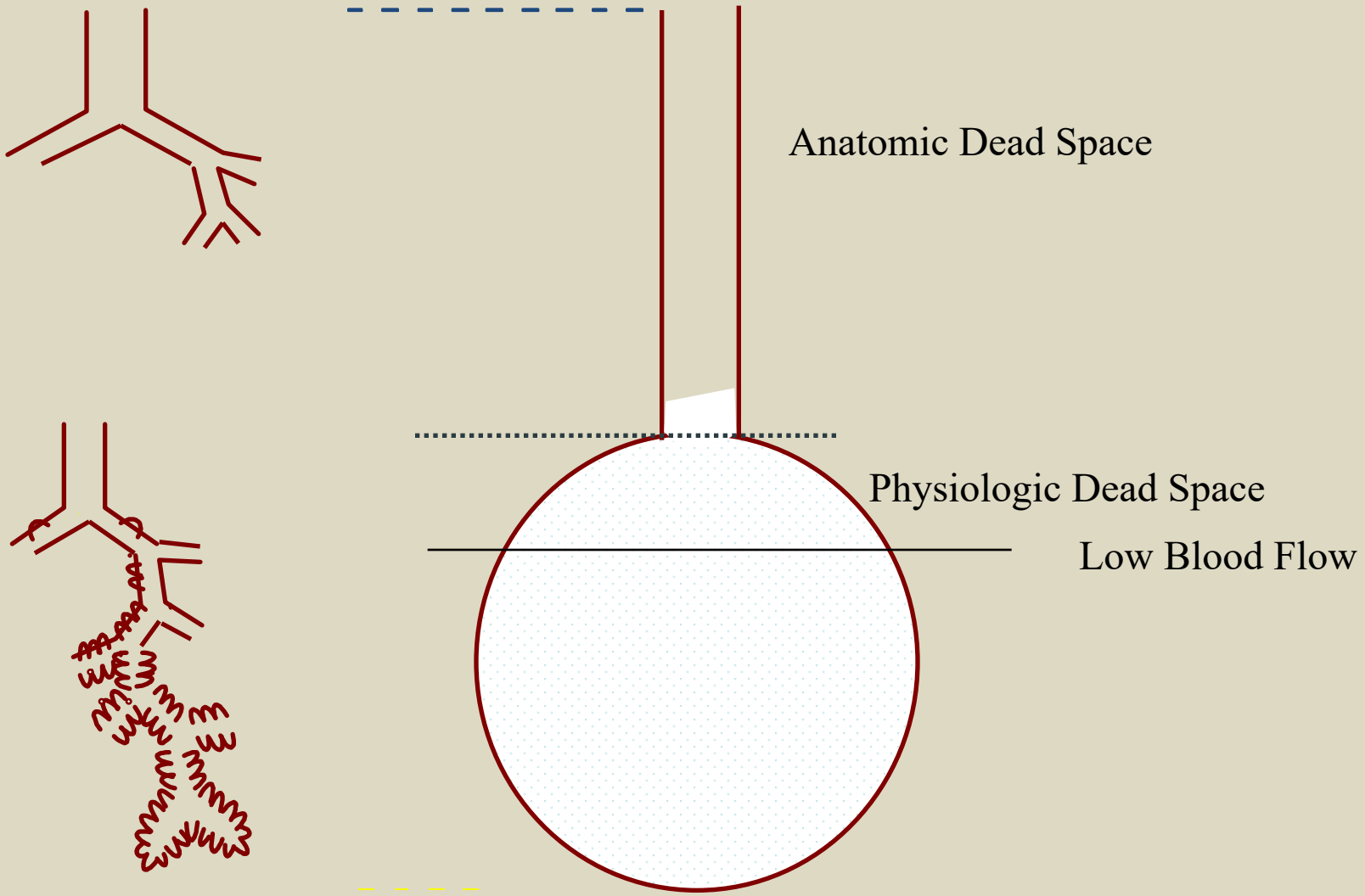
- ANATOMICAL: *Anatomical dead space is the volume of air that does not participate in gas exchange*
  - 150 ml (or 2 ml/Kg body weight)
- PHYSIOLOGICAL
  - Depends on ventilation-perfusion ratio (V/Q)
  - **Physiologic Dead Space = Anatomic Dead Space + alveolar dead space**

$$V_D \quad VT \; \frac{PaCO_2 \quad PECO_2}{PaCO_2}$$



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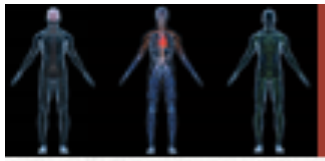
V/Q ratio and the generation of ADS and PDS in the apex and base



Lung Ventilation/Perfusion Ratios

- Functionally:
  - Alveoli at apex are underperfused (overventilated).
  - Alveoli at the base are underventilated (overperfused).

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	Ventilation (L/min)	Blood flow (L/min)	Ratio
Apex	0.24	0.07	3.40
Base	0.82	1.29	0.63

Next Time…

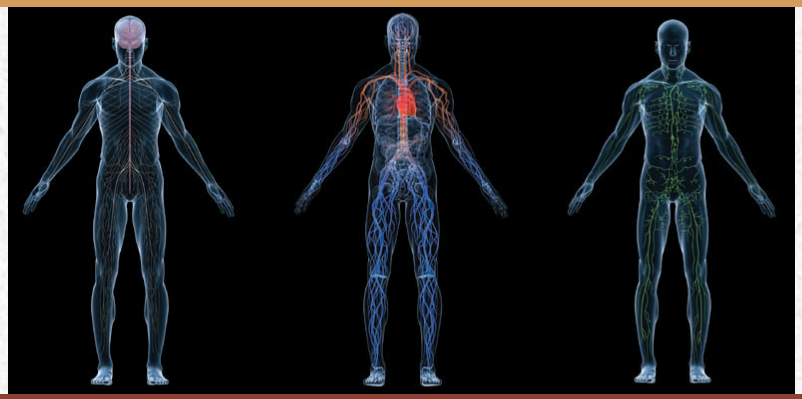
- Airway Resistance Lecture 3-4
-

UNIT VII

GUYTON AND HALL *Textbook of*

Medical Physiology

TWELFTH EDITION



Chapter 41:

Regulation of Respiration

Slides by Robert L. Hester, PhD

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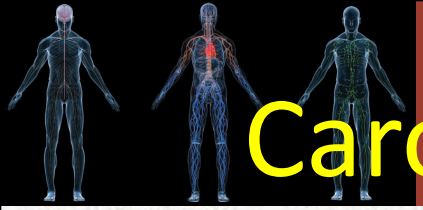

Carotid blood flow (ml/g/min)

Tissue	Blood flow (ml/g/min)	A-V difference (Vol %)	Flow ml/min	O_2 consumption ml/min
Heart	0.8	11	250	27
Brain	0.5	6.2 (25-30% Extraction)	750-900	
Skeletal Muscle	0.03	6	1200	70
Liver	0.6	3.4 Reconditioner organ		
SKIN	0.1			
Kidney	4.2	1.4	1250	18
Carotid bodies	20	0.5	0.6	

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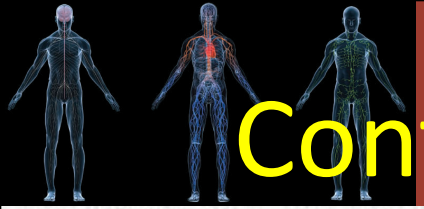

Control of Breathing....Introduction

- Q: What the controller system is going to do?
- A: Homeostasis of O_2, CO_2, H^+…Normal ABGs
- Q: How? What are the tools?
- A: by: ↑ventilation or ↓ventilation
- Q: What is the feedback system…nature of the receptor?
- A: ↓ $PaCO_2$, ↑$PaCO_2$, ↓ PaO_2 (below 60 mmHg), ↓ H+, and finally ↑H+
- **Note: ↑PaO_2 has almost no effect on the controller system**

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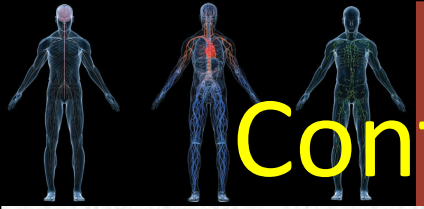

Control Of Breathing ….Introduction

- Again: The main goal of the respiratory system is to maintain normal ABGs: O_2, CO_2, and pH
- The controller center receives feedback response from O_2, CO_2, and pH
- What are the tools: Manipulating ventilation
- Sensor and response: Peripheral and central nervous system

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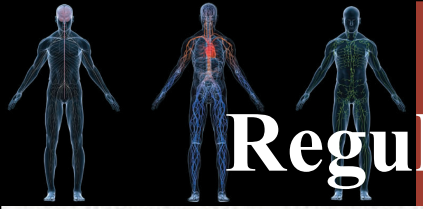

Regulation of Respiration ….Introduction

- Sensors…receptor… afferent pathway
  - gather information regarding CO2, O2, and pH
- Central controller
  - integrate signals…translation…output orders…the efferent pathway.
- Effectors
  - Respiratory muscles…receive the output from the respiratory center and produce a response that change the controlled condition.

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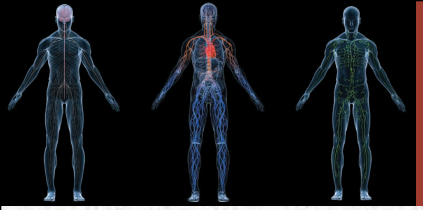

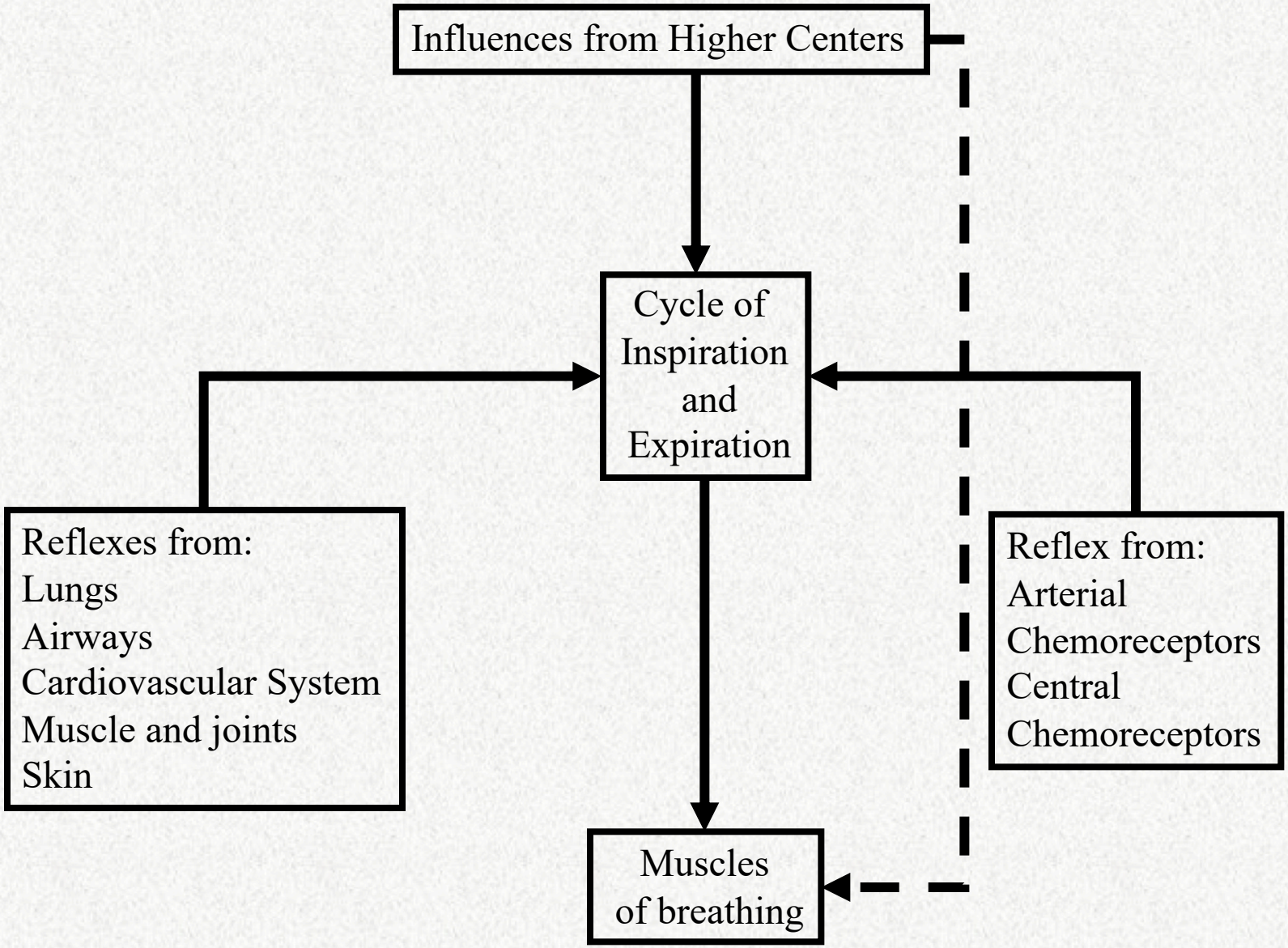

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How alveolar ventilation V_A affects P_ACO_2 and P_ACO_2

P_AO_2 depends on :

1. O_2 delivery to alveoli (Alveolar Ventilation V_A).
2. Rate of O_2 absorption to blood (O_2 Consumption VO_2)

$$P_AO_2 \propto (V_A/VO_2)$$

HYPERVENTILATION is when alveolar ventilation is more than CO_2 production → decrease P_aCO_2

HYPOVENTILATION is when alveolar ventilation is LESS than CO_2 production → increase P_aCO_2

$$P_ACO_2 = (VCO_2/V_A)* K$$

K"= constant (= 0.863 mmHg. lit/ml).

If ventilation is doubled then P_ACO_2 decreases to ½

If ventilation is halved then PCO_2 is doubled…keeping CO_2 production constant.....*See the two graphs in the next two slide.*

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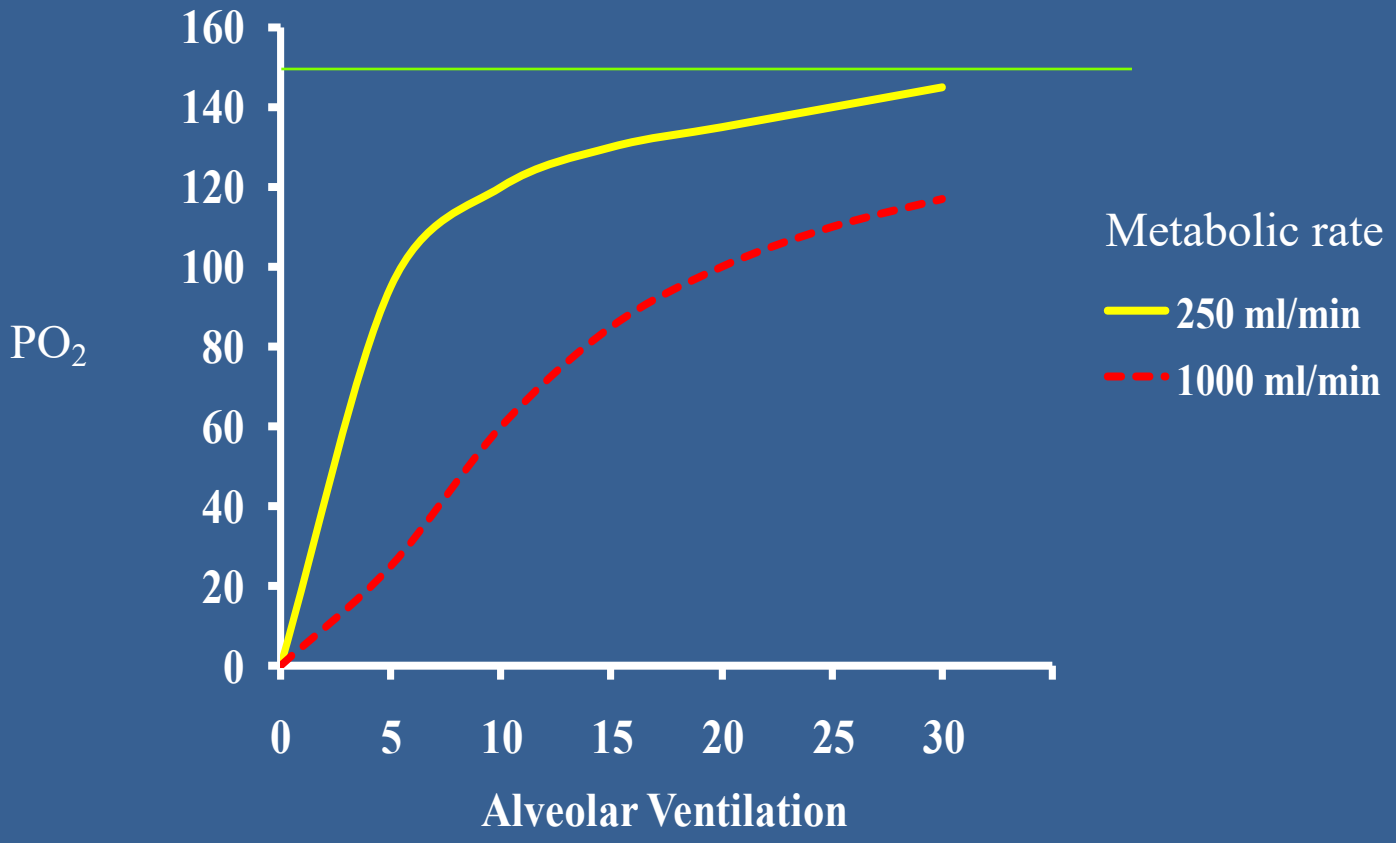
Partial pressure of oxygen in alveoli



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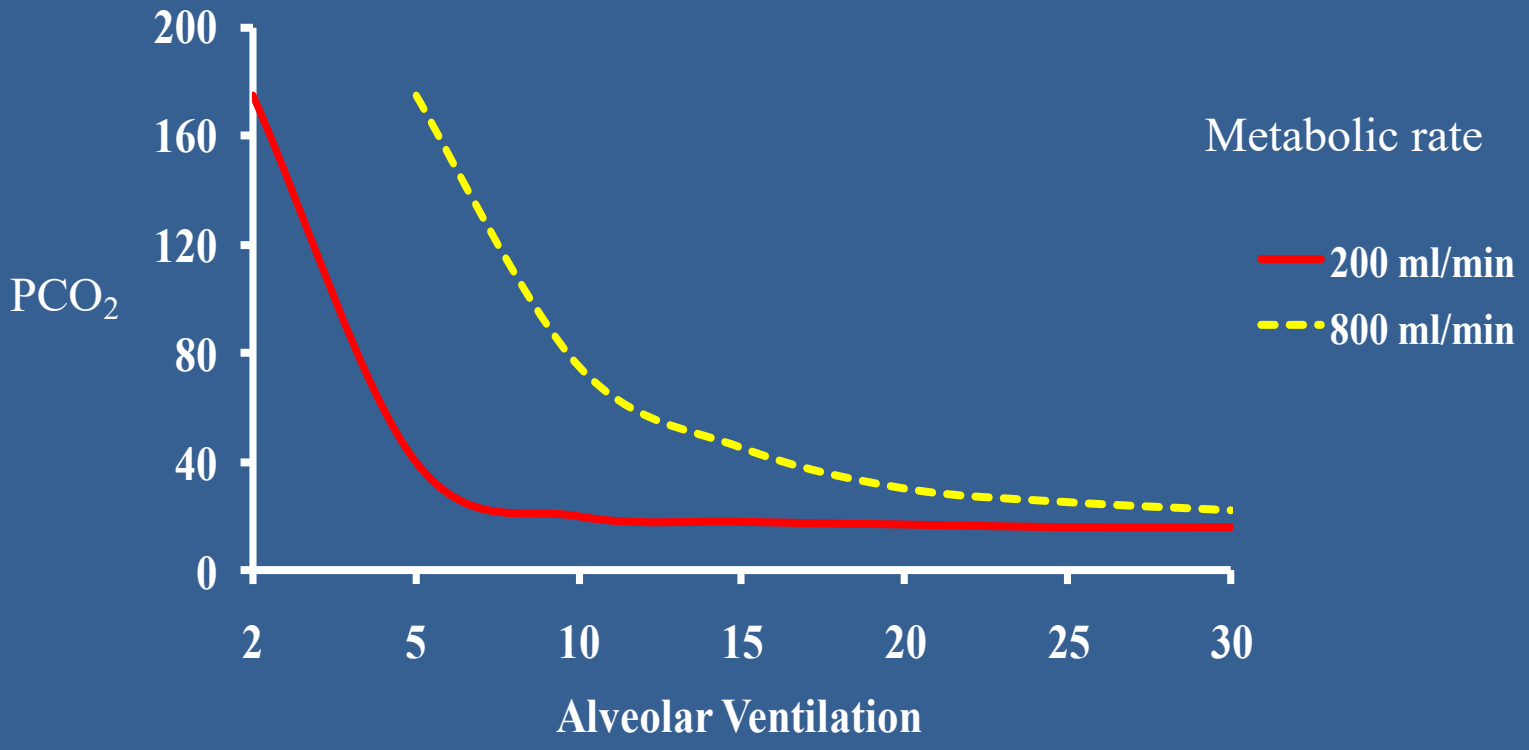
Partial pressure of CO_2 in alveoli



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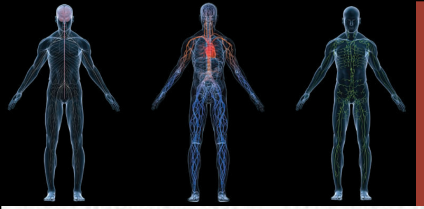

Question

Metabolic rate is doubled but alveolar ventilation is not changed. What happens to systemic arterial PCO_2?

A. Increases

B. Decreases

C. no change

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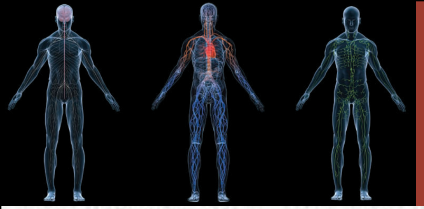

Question

In which of the following conditions is alveolar PO_2 increased and alveolar PCO_2 decreased

A. Breathing air with 19% PO_2

B. Increased alveolar ventilation and unchanged metabolism

C. Decreased alveolar ventilation and unchanged metabolism

D .Increased metabolism and unchanged alveolar ventilation

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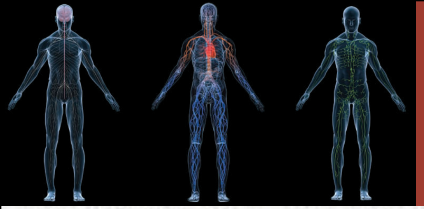

Question

What is the effect of anemia on ventilation?

A. decrease ventilation

B. increase ventilation

C. no change in ventilation.

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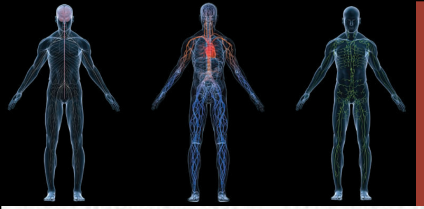

Question

Breathing CO acutely will __?__ respiration?

A. increase

B. decrease

C. not change

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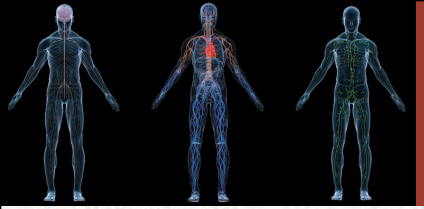

Answer

Breathing CO will not change respiration?

Arterial PO_2 does not change, PCO_2 does not change

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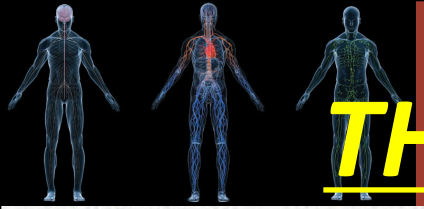

THE RESPIRATORY CENTER

- It is a loose collection of inspiratory and expiratory neurons situated in the medulla oblongata of the brain stem. Is not a discrete identifiable center in the strict anatomical sense. When inspiratory neurons are active, expiratory neurons are inhibited and vise versa.

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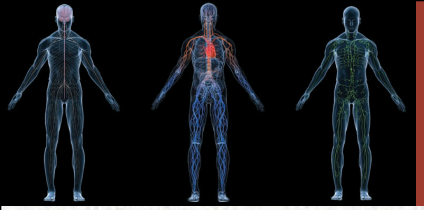
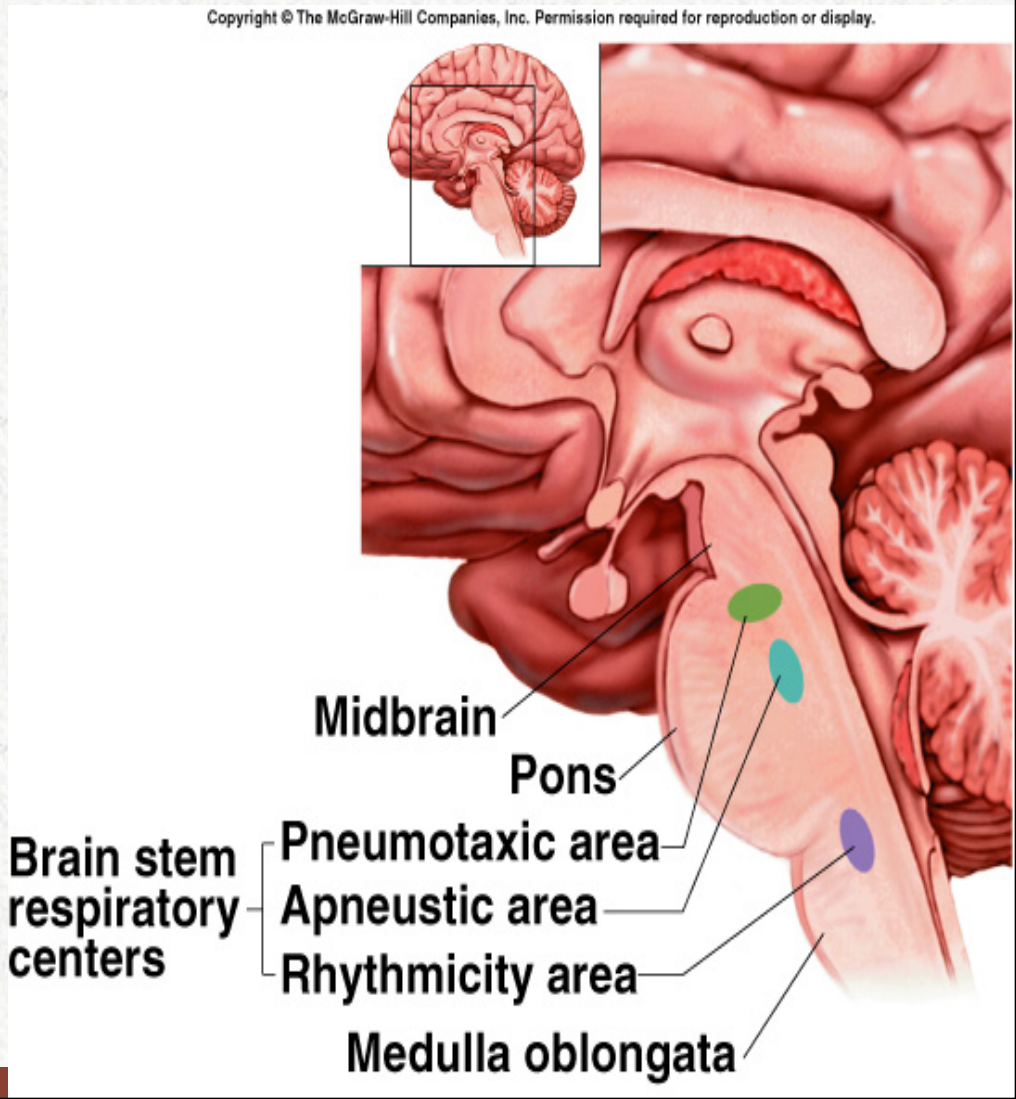


Brain Stem Respiratory Centers

- Neurons in the reticular formation of the medulla oblongata form the rhythmicity center:
  - Controls automatic breathing.
  - Consists of interacting neurons that fire either during inspiration (I neurons) or expiration (E neurons).



Respiratory Center

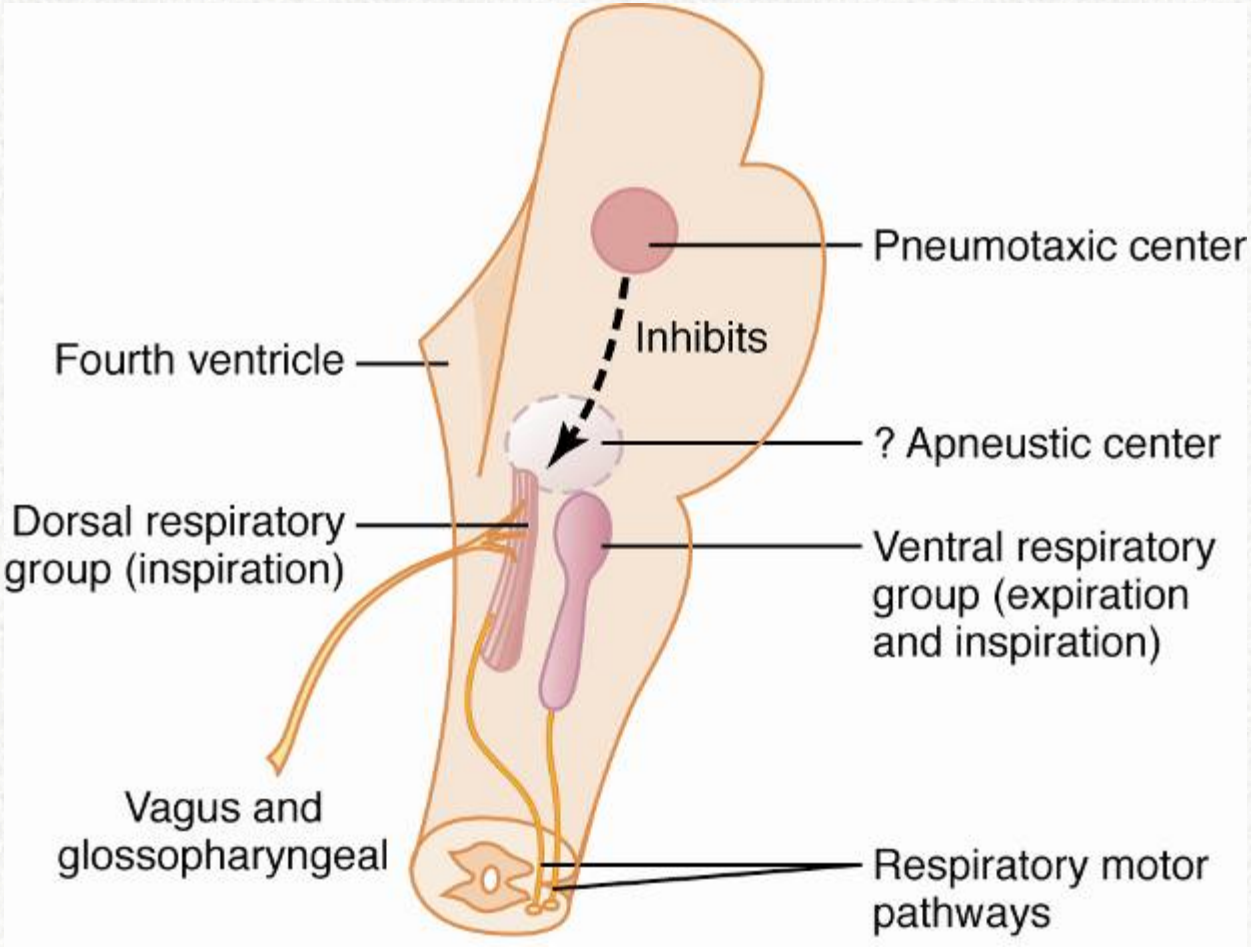


Figure 41-1

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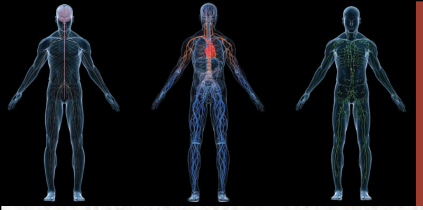
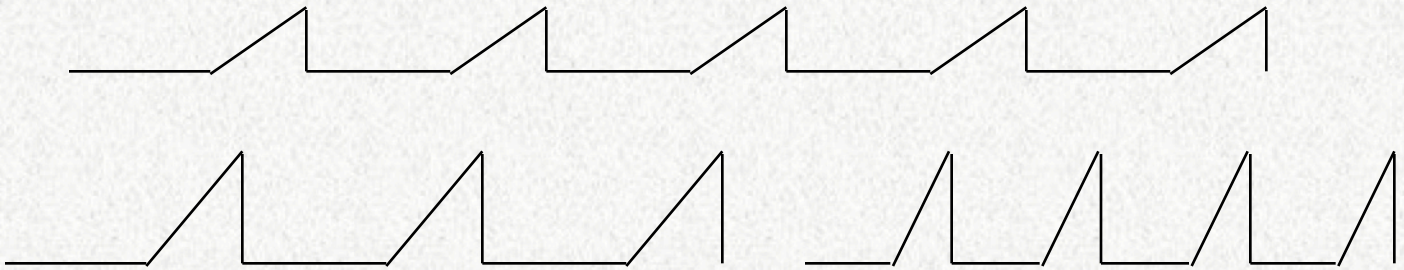


Medullary Respiratory Center

Dorsal respiratory group

- inspiration, intrinsic nerve activity



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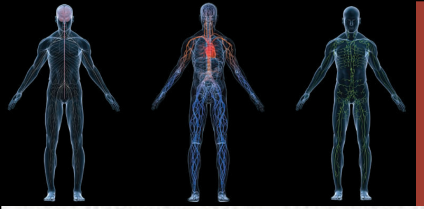

Respiratory Center

- Ventral Respiratory Group
  - Inactive during quiet respiration
  - Active respiration
  - Projections from the Dorsal Respiratory Group

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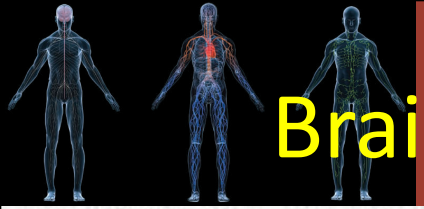

Brain Stem Respiratory Centers (continued)

- "I" neurons project to, and stimulate spinal motor neurons that innervate respiratory muscles.
- Expiration is a passive process that occurs when the I neurons are inhibited.
- Activity varies in a reciprocal way.

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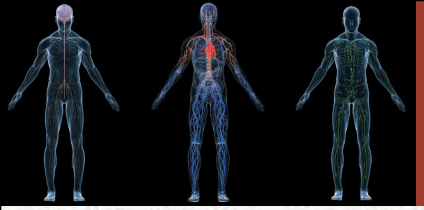

Rhythmicity Center

- "I" neurons located primarily in dorsal respiratory group (DRG):
  - Regulate activity of phrenic nerve.
    - Project to and stimulate spinal interneurons that innervate respiratory muscles.
- "E" neurons located in ventral respiratory group (VRG):
  - Passive process.
    - Controls motor neurons to the internal intercostal muscles.
- Activity of E neurons inhibit I neurons.
  - Rhythmicity of I and E neurons may be due to pacemaker neurons located in the upper part of the VRG.

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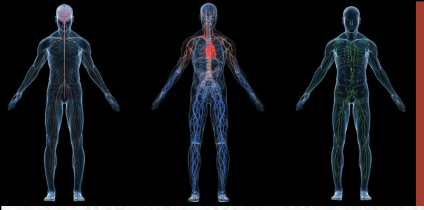

Pons Respiratory Centers

- Activities of medullary rhythmicity center is influenced by pons.
- Apneustic center:
  - Promotes inspiration by stimulating the I neurons in the medulla.
- Pneumotaxic center:
  - Antagonizes the apneustic center.
  - Inhibits inspiration and thus increase RR.
- **It is the Switch of** inspiration and modulate respiratory system

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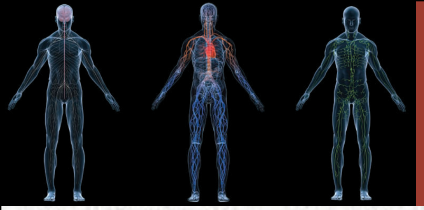
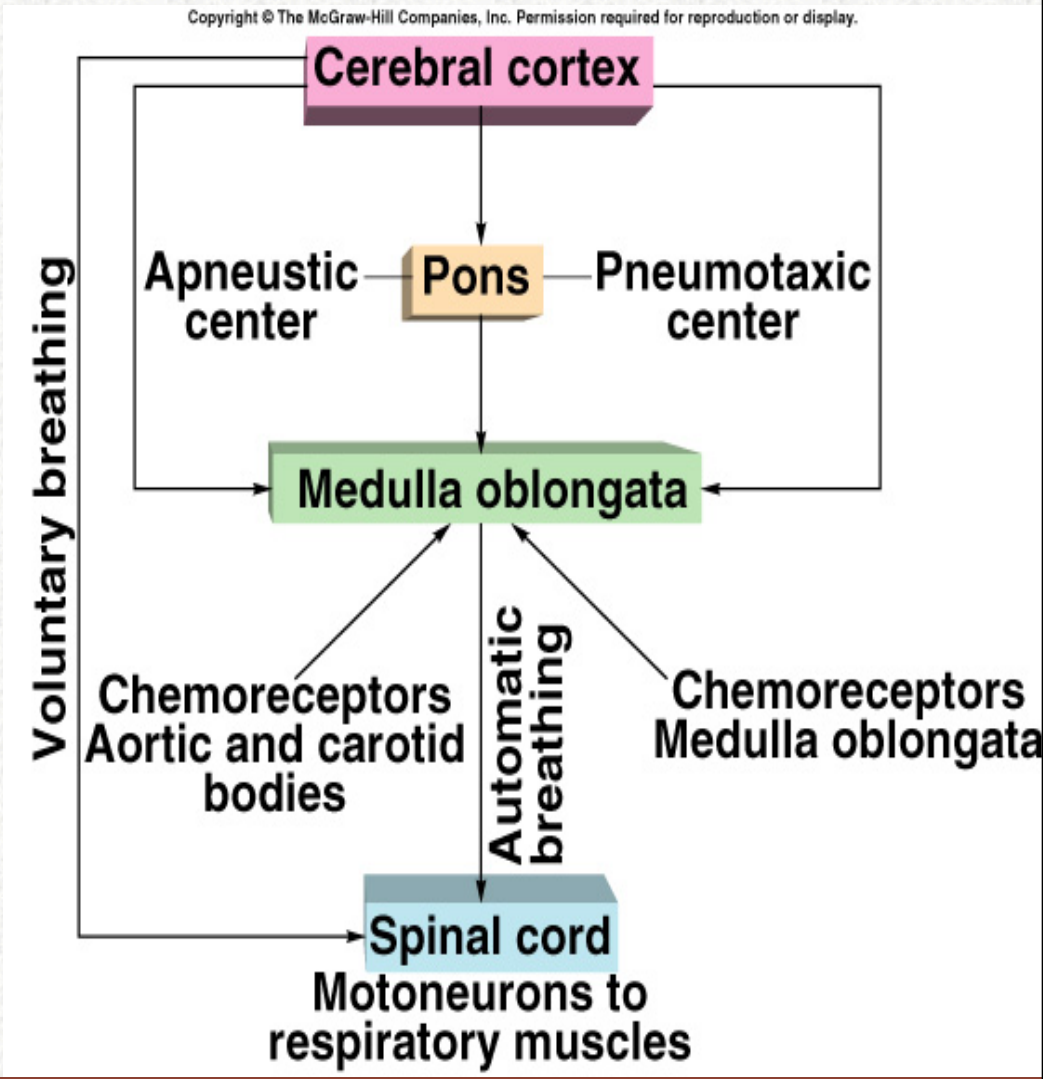


Chemoreceptors

- 2 groups of chemo-receptors that monitor changes in blood PCO_2, PO_2, and pH.
- Central:
  - Medulla…chemosensitive area…sensitive to H+
- Peripheral:
  - Carotid and aortic bodies.
    - Control breathing indirectly via sensory nerve fibers to the medulla (X, IX). Sensitive to O2



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Effects of Blood P_{CO_2} and pH on Ventilation

- Chemoreceptor input modifies the rate and depth of breathing.
  - Oxygen content of blood decreases more slowly because of the large "reservoir" of oxygen attached to hemoglobin. HbO_2 dissociation curve is sigmoidal
  - Central Chemoreceptors are more sensitive to changes in PCO_2 through the H+

- $H_20 + C0_2 \longleftrightarrow H_2C0_3 \longleftrightarrow H^+ + HC0_3^-$

- Rate and depth of ventilation adjusted to maintain arterial PCO_2 equals to 40 mm Hg.

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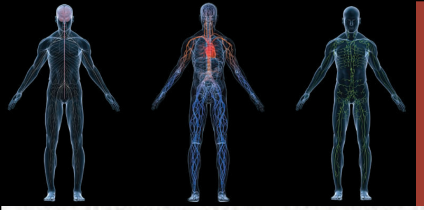

Chemoreceptor Control

- Central chemoreceptors:

  More sensitive to changes in arterial $PC0_2$ through H+

- **$H_20 + CO_2 \longrightarrow H_2C0_3 \longrightarrow H^+$**
- H^+ cannot cross the blood brain barrier.
- CO_2 can cross the blood brain barrier and will form H_2CO_3.
  - H^+ lowers pH of CSF fasters than it lowers blood pH…no enough buffers in CSF
    - Directly stimulates central chemoreceptors.

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Chemoreceptor Control of Breathing

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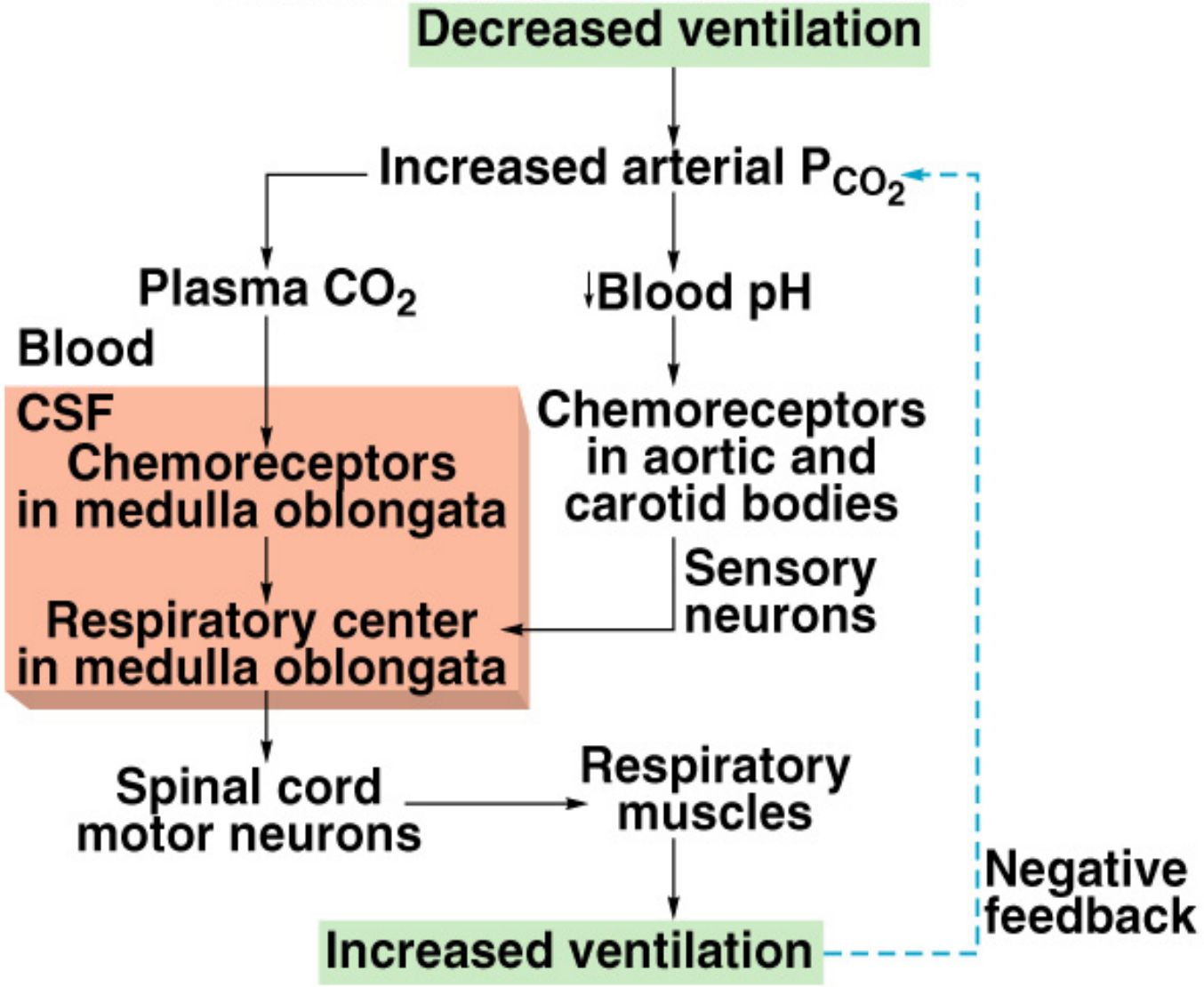

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Effects of Blood PO_2 and PCO2 on Ventilation

- **O_2 and CO_2 potentiation effect**
  - Low PO_2 Influences chemoreceptor sensitivity to changes in POC_2….potentiation
  - High PCO_2 enhances sensitivity of carotid bodies to fall in PO_2…..potentiation
- Hypoxic drive:
  - Emphysema blunts the chemoreceptor response to PCO_2…because kidneys correct pH in chronic situation. By making more $HC0_3^-$ which buffers the fall in CSF pH. Therefore, giving the COPD patient pure O_2 to breath will suppress ventilation…since the low PO_2 is the one which drives ventilation in this patient…don't remove the drive!

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Effects of Pulmonary Receptors on Ventilation

- Lungs contain receptors that influence the brain stem respiratory control centers via sensory fibers in vagus.
  - Unmyelinated C fibers can be stimulated by:
    - Histamine and bradykinin:
      - Released in response to noxious agents.
  - Irritant receptors are rapidly adaptive receptors.

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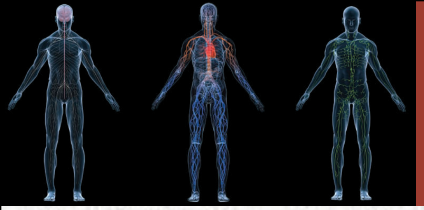

Lung receptors

- **Pulmonary Stretch Receptors**

- Located in smooth muscle of large and small airway and minimize work of breathing by inhibiting large tidal volumes

- **Hering-Breuer reflex**" are Pulmonary stretch receptors activated during inspiration.
- Inhibits respiratory centers to prevent undue tension on lungs.
- Hering Breuer inflation reflex can be easily manifested in dogs & cats but not in man (unless $V_T \geq 1.5$ liters). So its function in man is uncertain. However, in newborn where V_T is small, it may be important.

- Irritant receptors
  - Nasal mucosa, upper airways, possibly alveoli
  - Bronchoconstriction which lead to cough and sneeze
- J receptors
  - Located in the capillary wall, interstitium
  - Lung disease and edema (pulmonary congestion)
  - Rapid shallow breathing (tachypnea)

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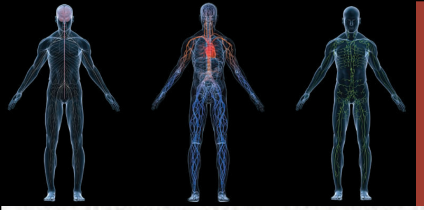

Other Reflexes

- Arterial Baroreceptors
  - Stimulation by elevated blood pressure results in brief apnea and bronchodilation
- Muscles and Tendons
  - Muscles of respiration as well as skeletal muscles, joints and tendons
  - Adjust ventilation to elevated workloads

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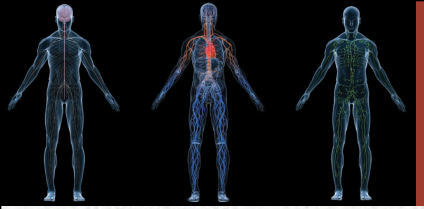

Chemical Control of Respiration

- Carbon Dioxide works centrally through H^+
- Oxygen works peripherally at the carotid and aortic bodies.

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Chemosensitive Area of Respiratory Center

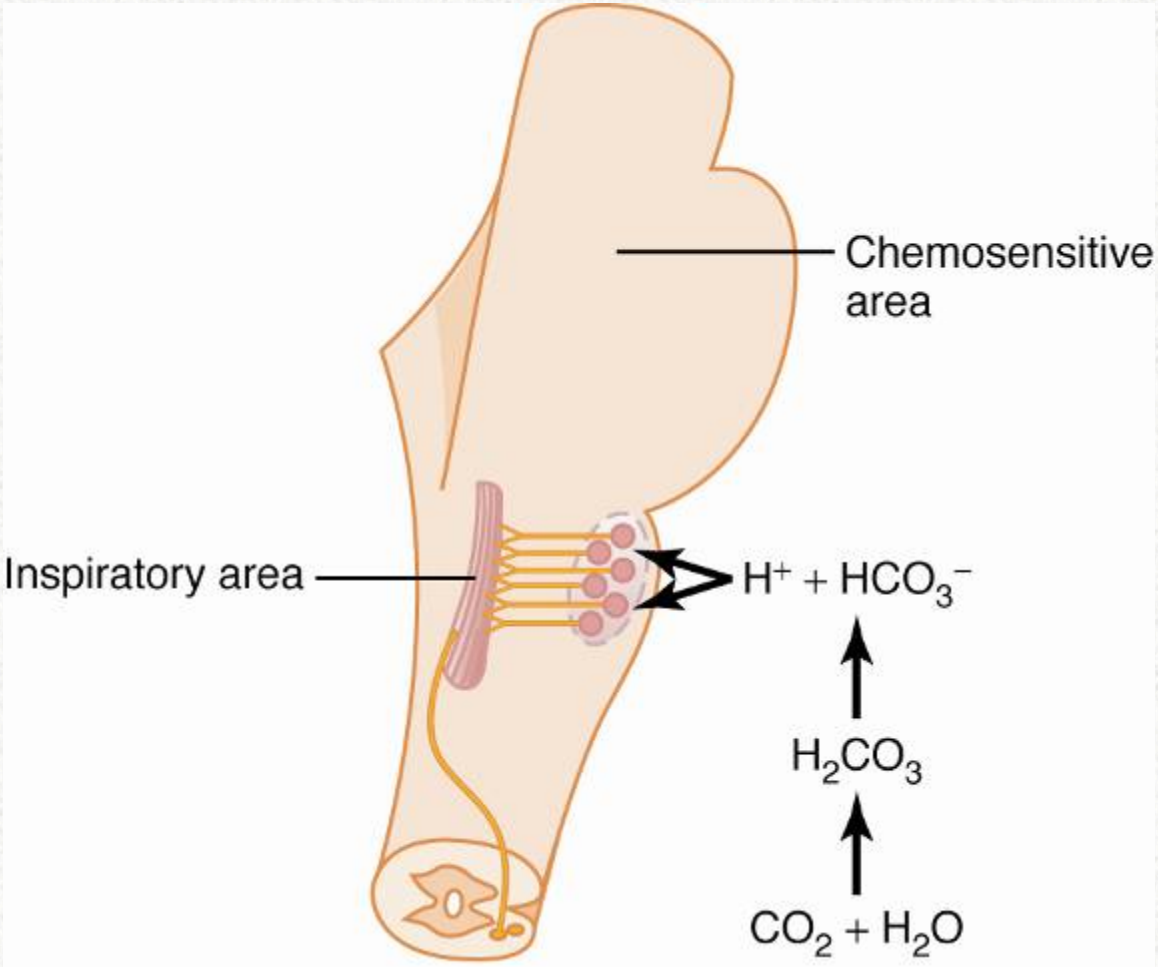

Figure 41-2

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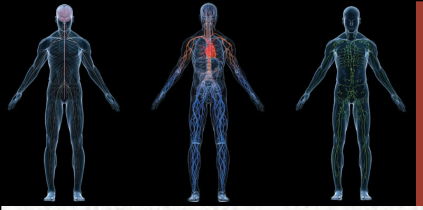
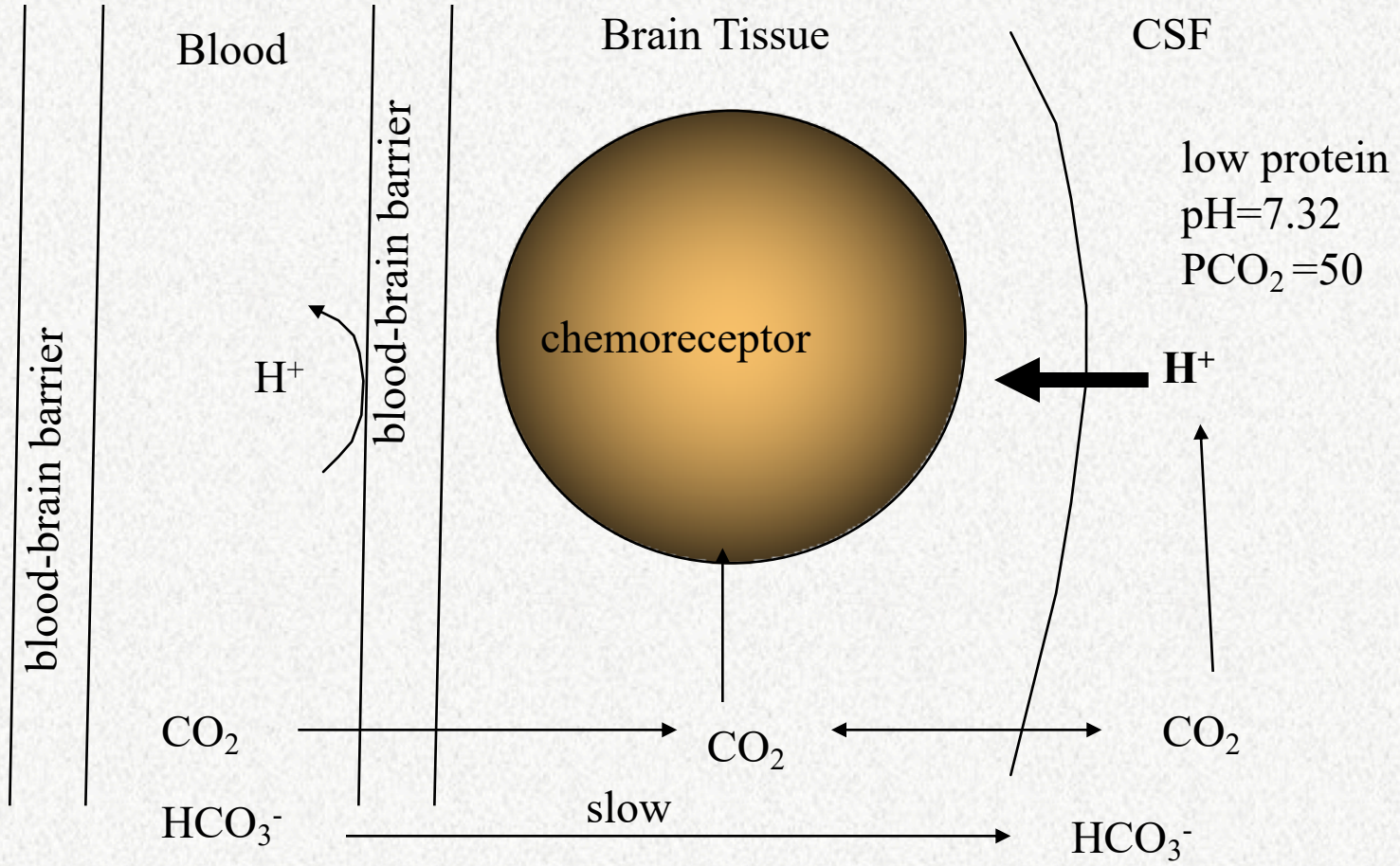


Chemosensitive Area of Respiratory Center



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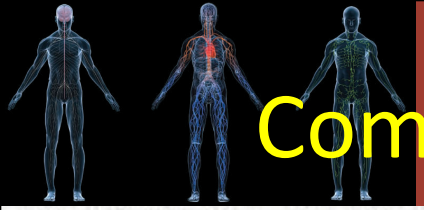

Comparison between Blood and CSF

	CSF	***BLOOD***
HCO_3^-	24	28
protein	<45 mg%	6-8 g%
pH	7.32	7.4

CSF have less buffering capacity…and thus pH is shifted faster

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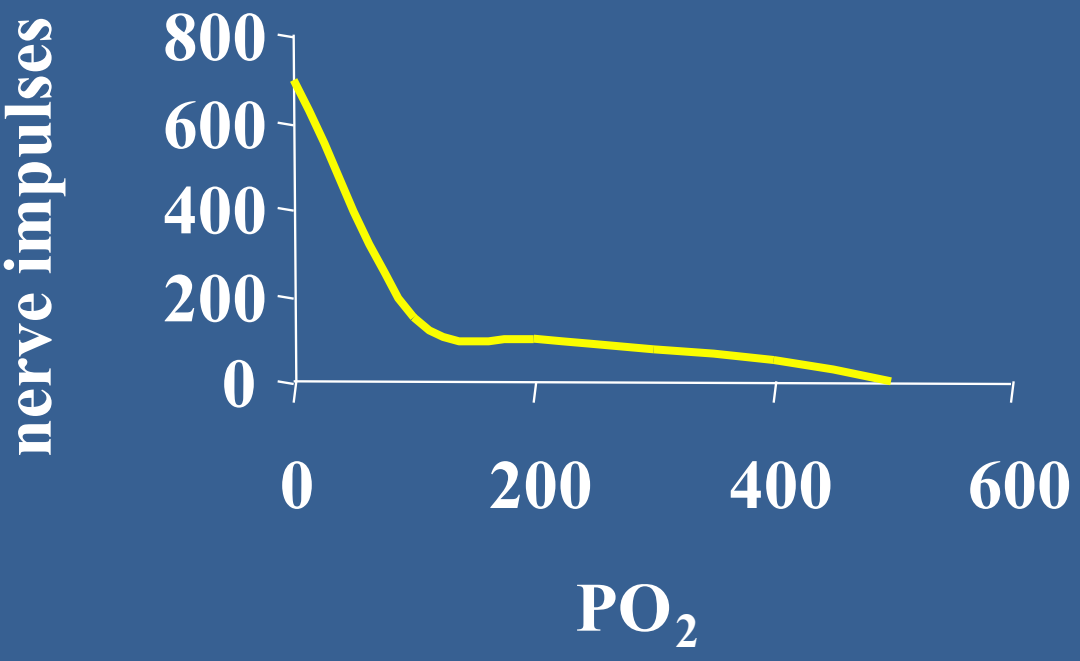
Peripheral Chemoreceptors

- Carotid bodies at the bifurcation of the common carotid artery.
  - –responds mainly (not only) to oxygen (PO_2<60 mmHg)
  - –-responds to carbon dioxide and hydrogen ion…one seventh of the central response but 5 times faster



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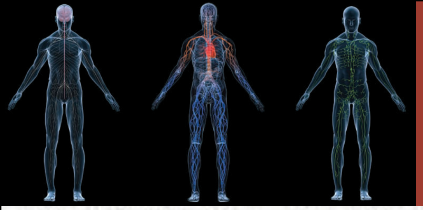
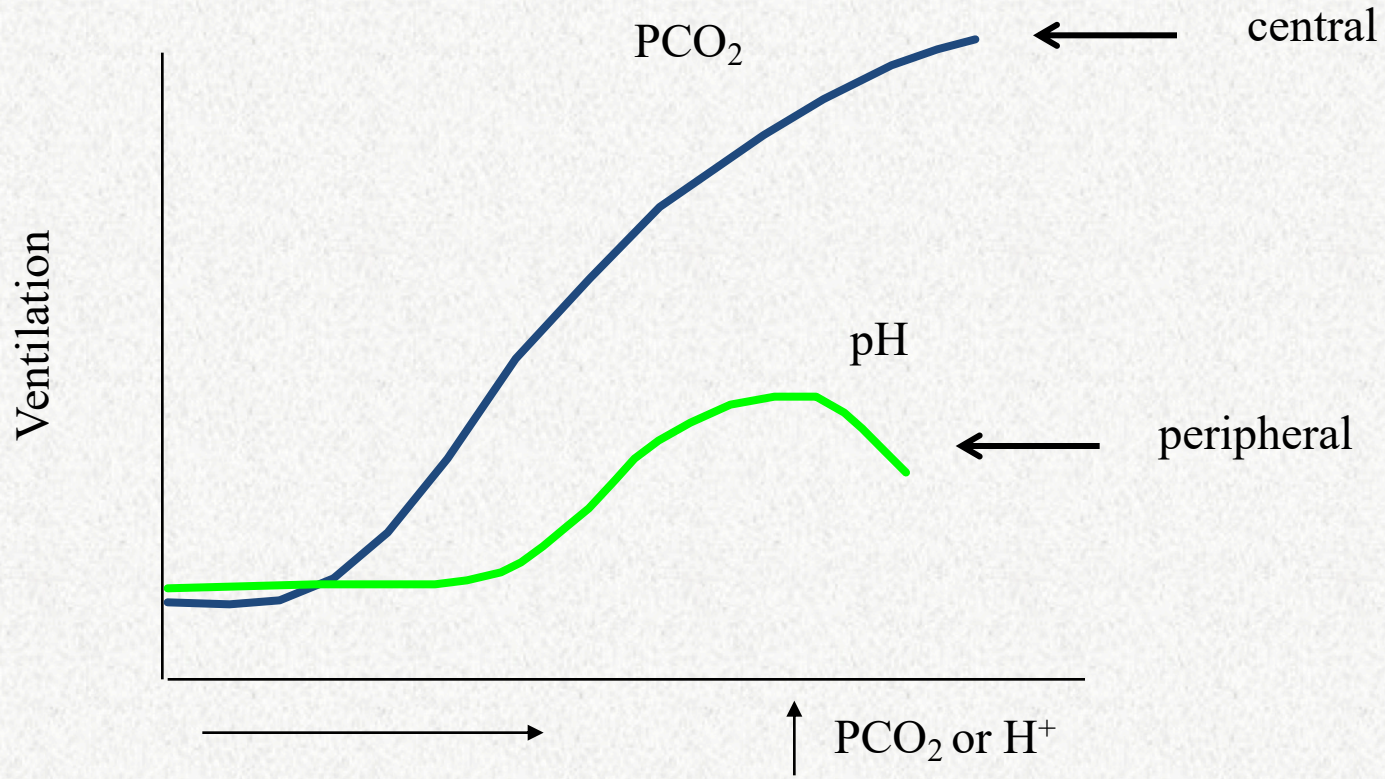


Control of Respiration



Changes in arterial PCO_2 have greater effect than changes in arterial pH

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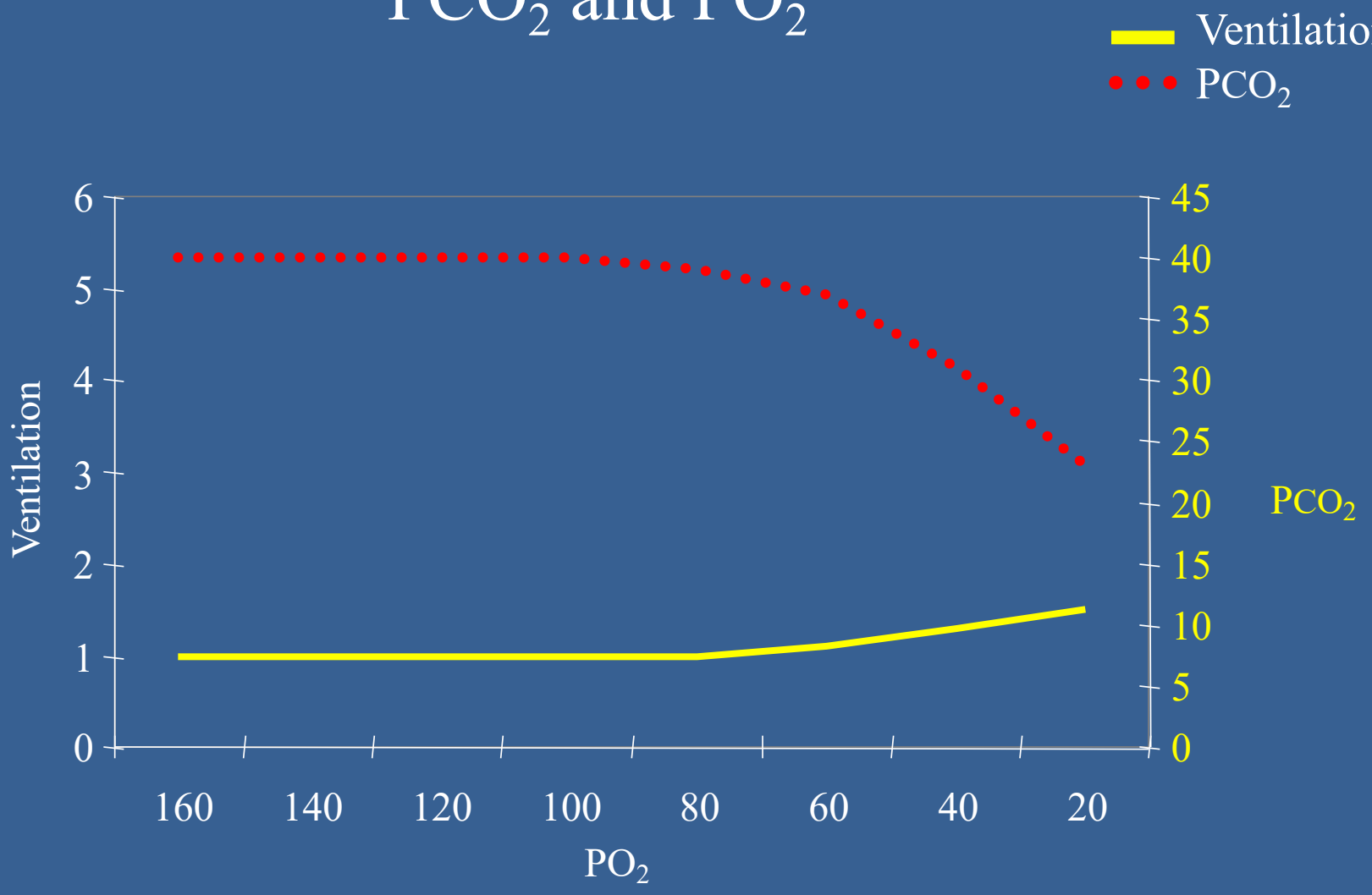
PCO_2 and PO_2



Hypoxic increase in ventilation inhibited by fall in PCO_2

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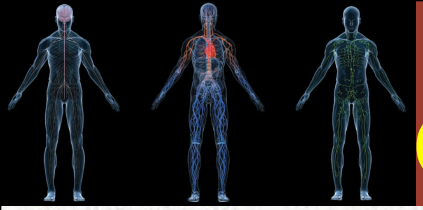

Chemoreceptor Control (continued)

- Peripheral chemoreceptors mainly stimulated by $\downarrow PO_2$
- $H_2O + CO_2 \longrightarrow H_2CO_3 \longrightarrow H^+$
- Stimulated by rise in $[H^+]$ of arterial blood.
  - Increased $[H^+]$ stimulates peripheral chemoreceptors.

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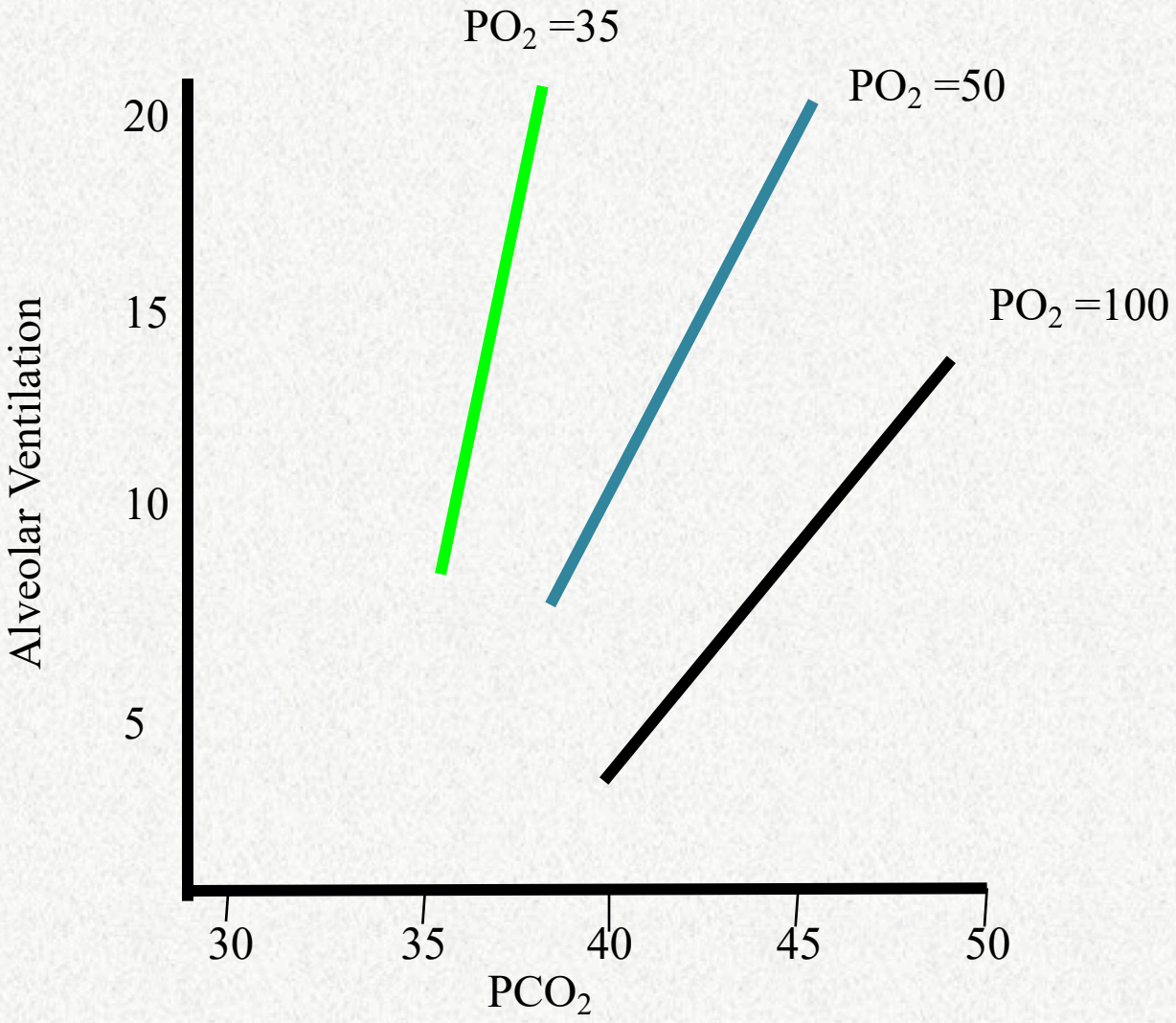
Carbon dioxide response curve at different O2 levels



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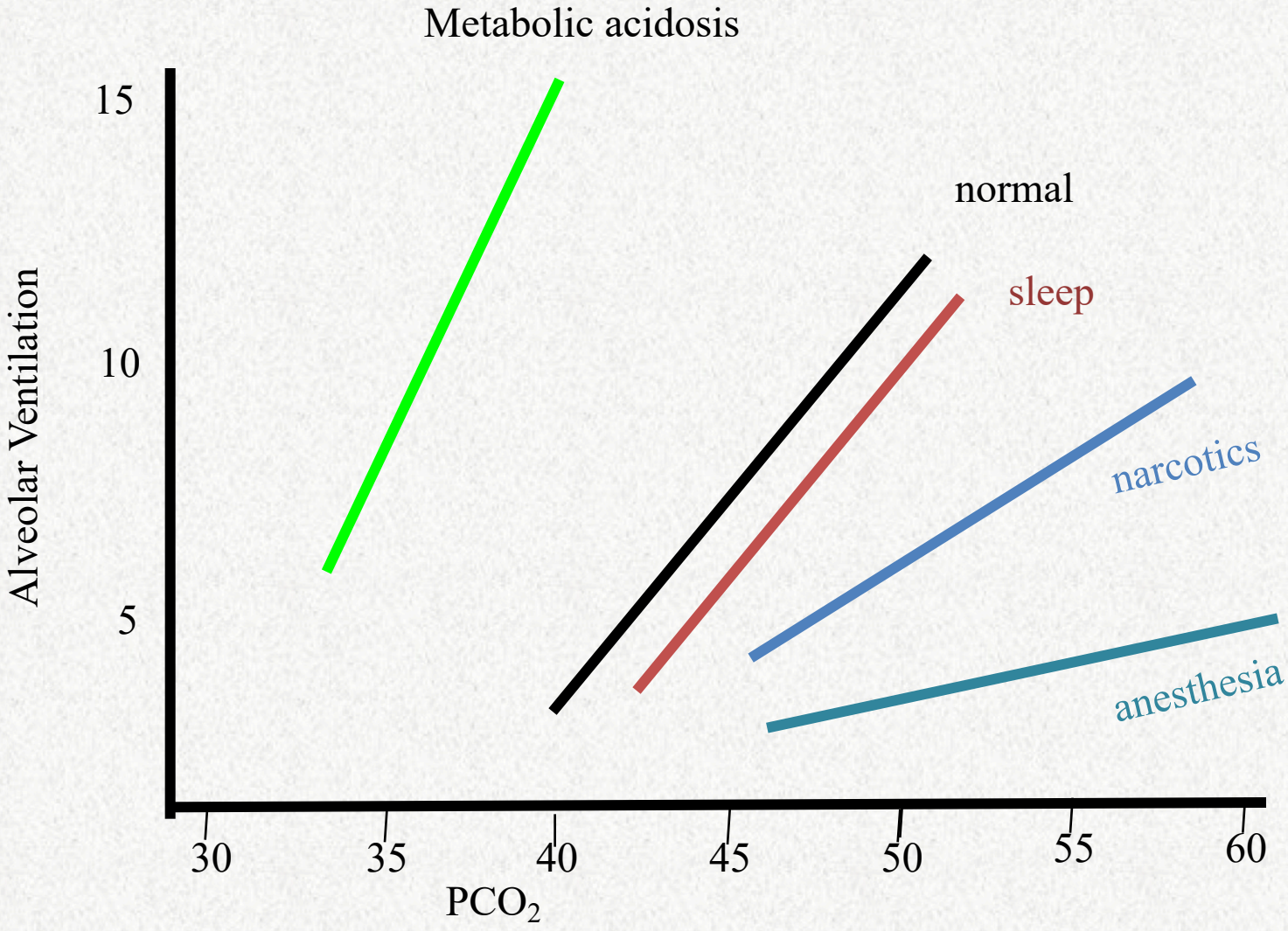
Carbon dioxide response curve under different conditions



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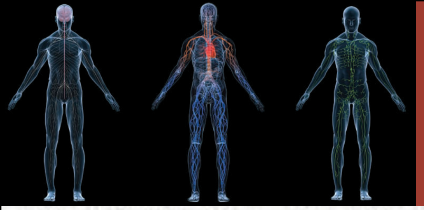

Summary

- Carbon dioxide is major stimulus for increased respiration
- Acts on chemosensitive area through H^+
- Peripheral chemoreceptors are mainly affected by low PO2
- If P_{CO_2} is constant low oxygen can be important
- Questions?
  - Why is oxygen's effect on respiration blunted?
  - Explain ventilatory drive during severe lung disease…see next slide for answer.

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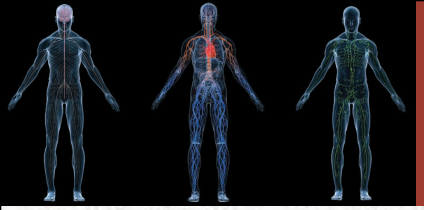

CO_2 Retention

- Severe lung disease, COPD
- Develop hypoxemia and hypercapnia
- Respiratory drive is due to low PO2
- Renal control of acid-base balance
- Treat with hight % oxygen inhibits respiratory drive
- High levels of PCO_2
- Minimal levels of oxygen, monitor blood gases

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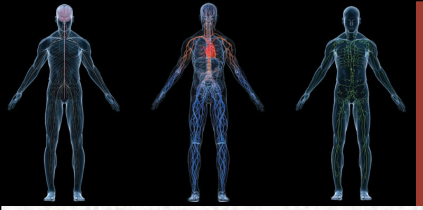
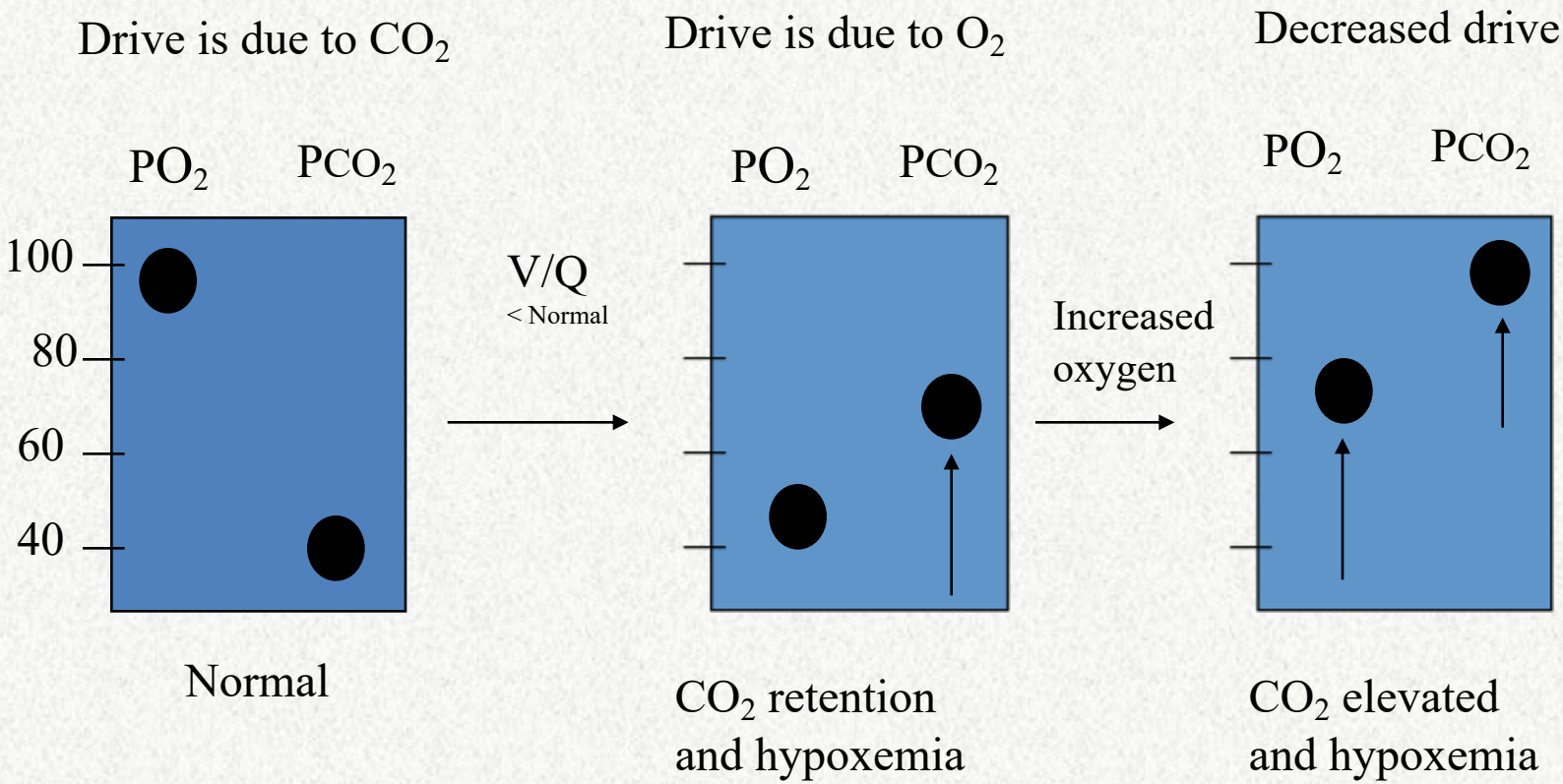


CO_2 Retention



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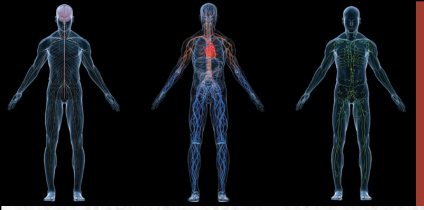

Respiration During Exercise

- Linear increase in ventilation with increasing oxygen consumption. Ventilation increase linearly until it reaches VO_{2max}.
- O_2 consumption at rest is 250 ml/min. In exercise it increases 20 folds (5,000 ml/min).
- arterial P_{O_2}, P_{CO_2} and pH **do not change** during exercise
- In the contrary, P_aCO_2 may decrease slightly…
- Q: What drives ventilation during Exercise?

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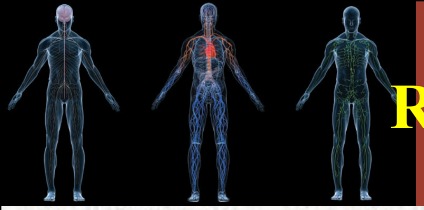

Respiration During Exercise…..Time wise

- Ventilation ↑ immediately (instantaneously) with the onset of exercise, then it gradually ↑ to final value which is determined by the severity of the exercise. The more strenuous the exercise the greater the initial rise at the onset & the higher the final level of ventilation. Following exercise there is an immediate decrease in ventilation followed by a more gradual return to the resting level.
- Because of the initial ↑ in ventilation (before muscle movement) the P_aCO_2 would decrease slightly. And then exercising muscles would produce CO_2 which then returns to normal level which stays at that level until the end of exercise. When muscles stop exercising (end of exercise) ventilation decrease instantly which cause ↑ P_aCO_2, again stimulates the respiratory center which ↑ ventilation slightly and then again decreasing slightly but remains high because of the oxygen debt.

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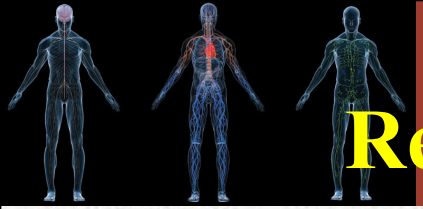

Respiration During Exercise…Drive

- Overflow of signals from cortex
- Body movements
- Increased body temperature
- Designed to control P_{CO_2}
- Learned response
- Conclusion: we are not sure regarding the exact mechanism responsible for increased ventilation during exercise.

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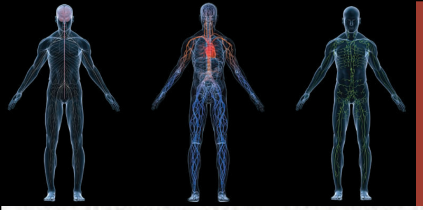

Other Factors to Influence Respiration

- Voluntary control
- Activity from vasomotor center
- Body temperature
  - increased production of carbon dioxide
  - direct effect on respiratory center
- Irritants
- Anesthesia

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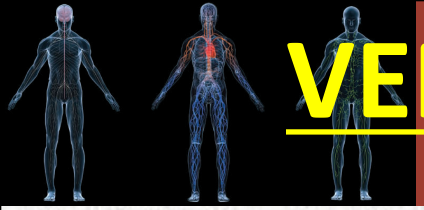

VENTILATION AT HIGH ALTITUDE

		Breathing Air			Breathing Pure O_2	
Height (feet)	Air	Inspired PO_2	P_AO_2	P_ACO_2	P_AO_2	P_ACO_2
0	760	160	100	40		
10,000	523	110	67(77)	36(23)		
20,000	350	73	40(53)	24(10)	262	40
29,029 (8848 m) Mount Everest	226	47	18(30)	24(7)	139	40

**In parenthesis are acclimatized values

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PO_2 Responses to High Altitude

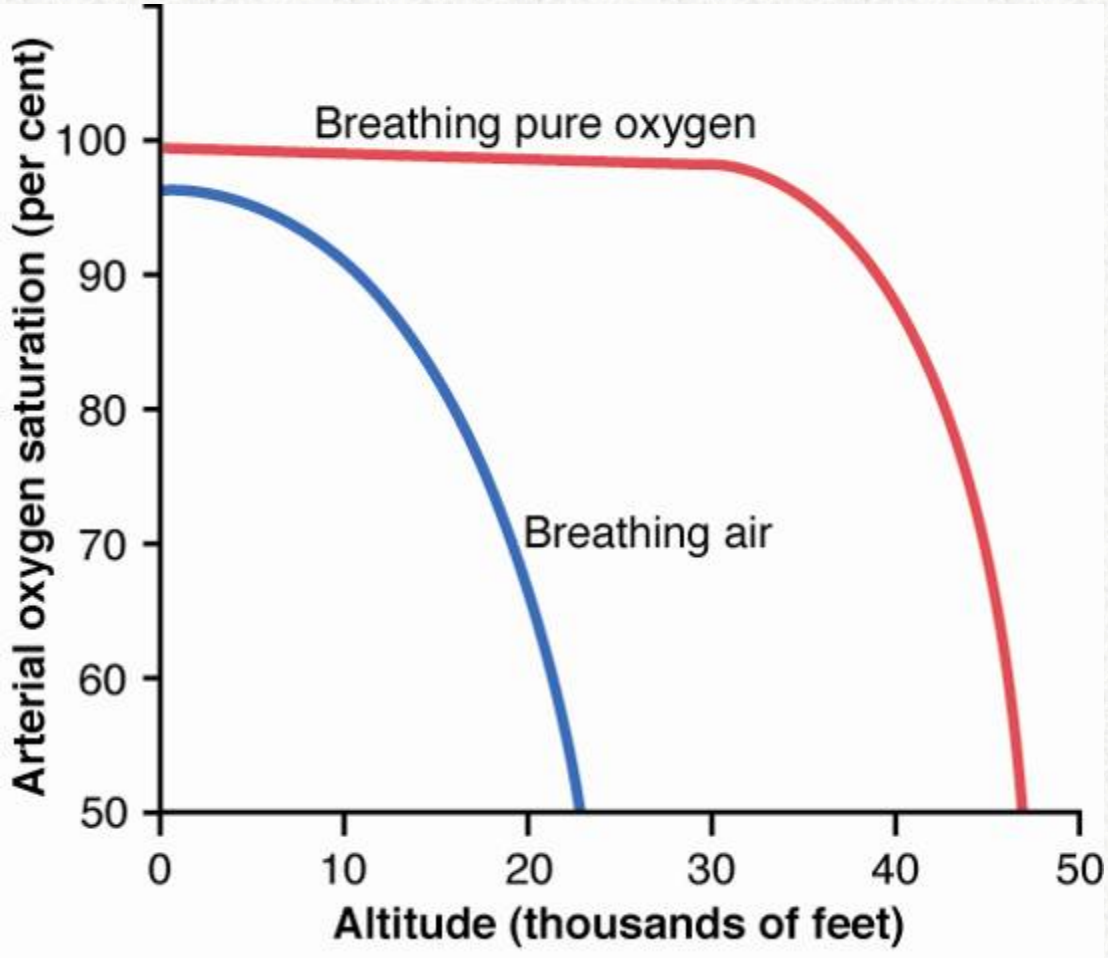

Figure 43-1

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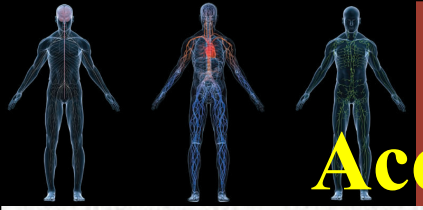

Acclimatization….continue

- Increased ventilation
  - due to decreased P_{O_2}
  - increase slowed by decreased P_{CO_2}
  - It increases 70% in the first day and 400-500% in the coming few days.
- Increased hematocrit (content)
- Increased diffusing capacity
- Increased capillarity

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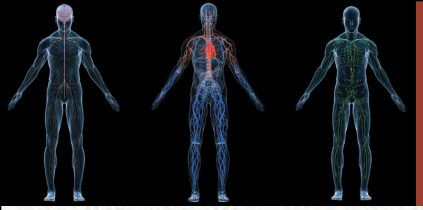

Hematocrit Responses during Acclimatization

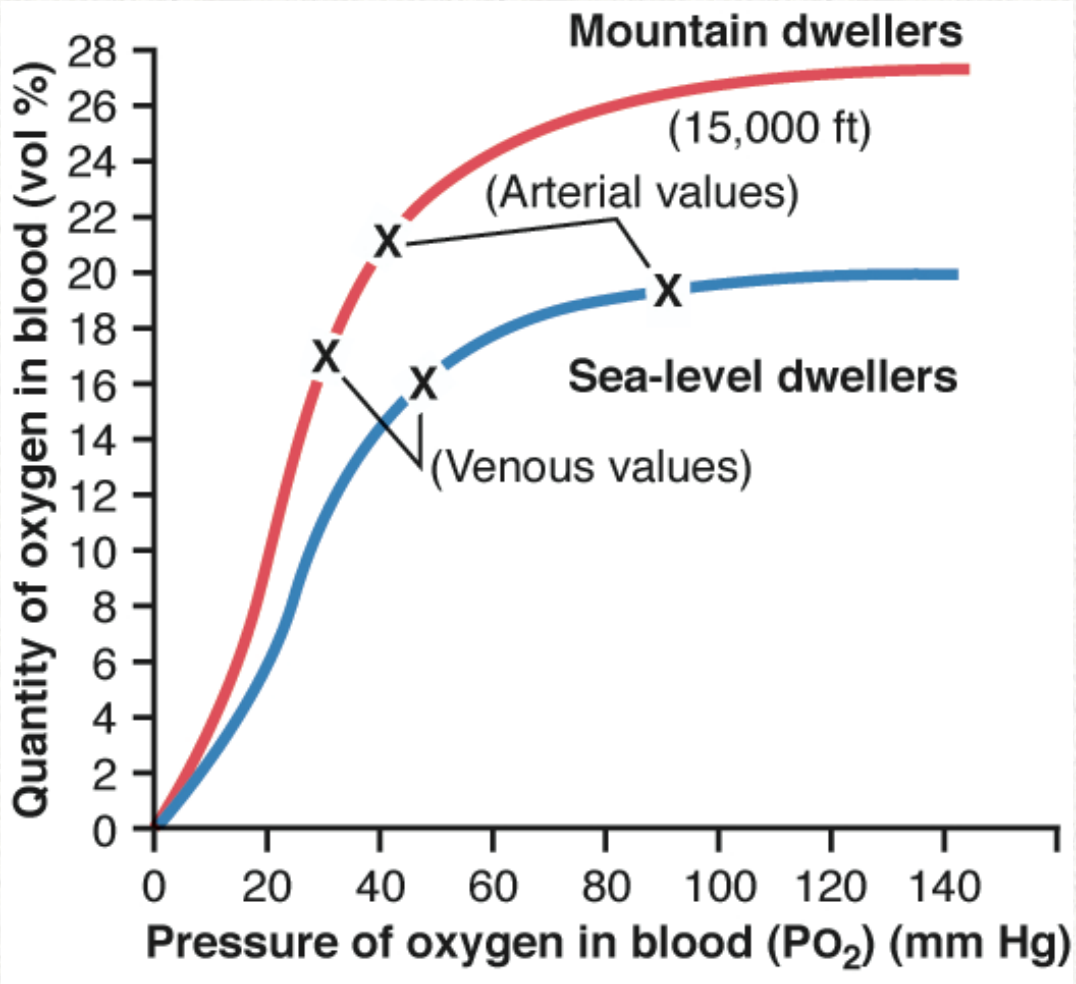

Figure 43-2

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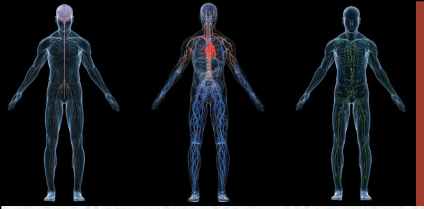

Mountain Sickness

- Chronic mountain sickness
  - increase in red cell mass
  - increase in pulmonary arterial pressure
  - enlargement of right heart
- Acute mountain sickness
  - acute cerebral edema
  - acute pulmonary edema

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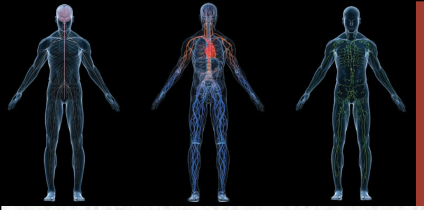

Question

What is atmospheric PO_2 at 10,000 ft (barometric pressure = 508 mmHg)?

Person has normal alveolar ventilation

A. 95 mmHg

B. 106

C. 149

D. 159

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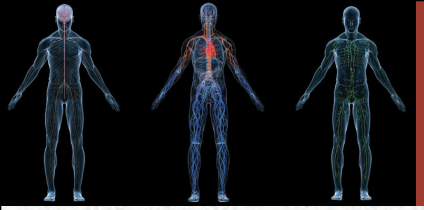

Answer

508*0.21=106

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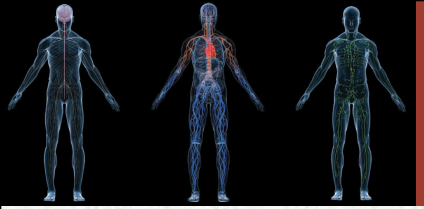

- See you again next semester in renal Physiology…
  - GOOD LUCK

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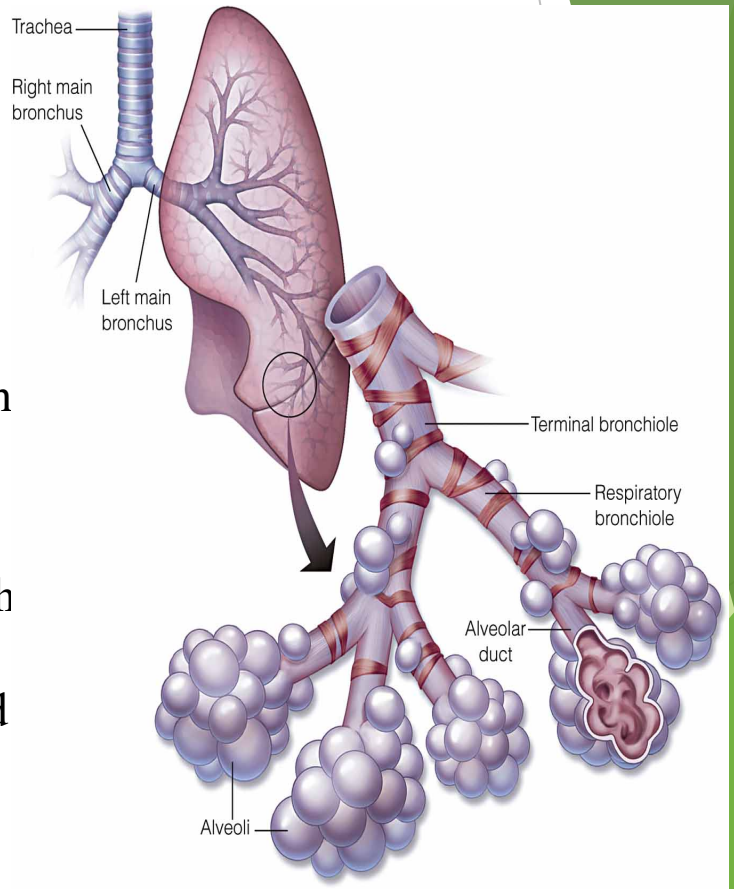
Lung Diseases...three families

- **Prevalence of lung disease depends on the population, but in general we have three families:**
- **1. obstructive is 70%,**
- **2. restrictive is 20-25% and**
- **3. vascular the rest 5-10%**
- Obstructive Diseases: Increased resistance to flow
- Restrictive Diseases: Decreased expansion of the lungs

Introduction

- Bronchial asthma and COPD (chronic obstructive pulmonary disease) are obstructive pulmonary diseases that affected millions of people all over the world
- Asthma is a serious global health problem with an estimated 300 million affected individuals
- COPD is the fourth leading cause of death in the world and further increases in its prevalence and mortality can be predicted



COPD

1. Emphysema 2. Chronic bronchitis ±3. Bronchial asthma…only when it becomes chronic

1. ↑ Compliance: mainly in emphysema, due to destruction of the elastic fibers,
2. ↑ FRC:
3. . ↑ Airway R. more fluctuation during dynamic phases mainly in asthma.

Smoking inhibits cilia → accumulation of mucus → bacterial growth → chronic bronchitis.

Smoking induces hyperplasia of Goblet cells → excessive mucus secretion → bacterial growth → chronic bronchitis

Chronic bronchitis….excessive mucous production

Asthma….constriction of bronchioles

Chronic Obstructive Pulmonary Disease

- **Chronic pulmonary emphysema**
  - infection (secretions)
  - Obstruction→ turbulence → wheezes
  - loss of parenchyma…loss of surface area available for diffusion …hypoxemia…hypoxia
  - **Consequences**

    - high airway resistance

    - decreased diffusing capacity

    - pulmonary hypertension…increase pulmonary vascular resistance

logy

Resistance to airflow

- Lumen
- excessive secretions
- obstruction due to aspiration

– Airway

- contraction of smooth muscle
- hypertrophy of bronchial wall

– outside of airway

- destruction of the elastin fibersparenchyma

The work of Breathing:

$W = \Delta P \times \Delta V$

Normally 0.5 L X 5 cm H_2O = 0.25 J……*One Joule is equal to = 10 L X cm H_2O = J*

50% of the work of breathing is used to expand the lungs and 50% to expand the chest wall.

The work of breathing is used to overcome:

1) Elastic forces (70%) (Contribution to the total work of breathing): They are under static (no-flow conditions). Two types:

A) Elastic fibers (one third)

B) Surface tension (two thirds).

2) Non elastic forces (30%) (Only present during the dynamic phase of breathing). Again two types:

A) 20% is the tissue viscous resistance, it occurs only during tissue movement. It is frictional R which resists a change in shape. It always opposes motion (during inspiration and during expiration)

B) 80% is due to air way resistance:

$T_{Total} = P_{Elastic} + P_{Nonelastic}$

$P_{Elastic}$: elastic recoil P

$P_{Nonelastic}$: Is the pressure to overcome resistance to airflow.

When no air movement takes place $T_{Total} = E_{Elastic}$

Always remember Ohm's law: Flow is directly proportional to the driving force and inversely proportional to the resistance
Flow = pressure difference / resistance = ΔP/R….
What is the ΔP? It is the pressure difference between the two opposite ends of the airways: ($P_{alv} - P_{atm}$)
If R is large then ΔP must be large too in order to keep air flow constant.
Boyle's law: The pressure and the volume of a gas are inversely related if the temperature is constant.
$R_{airways}$ resides mainly in large airways. In contrast, the small airways have small tiny diameter, but large cross sectional area, thus they offer little resistance to airflow.

The French physician Jean Leonard Marie **Poiseuille's**

$$V = (\Delta P)/ \pi r^4/8\eta l$$

***The most important point to remember is R is inversly proportional to $1/ r^4$

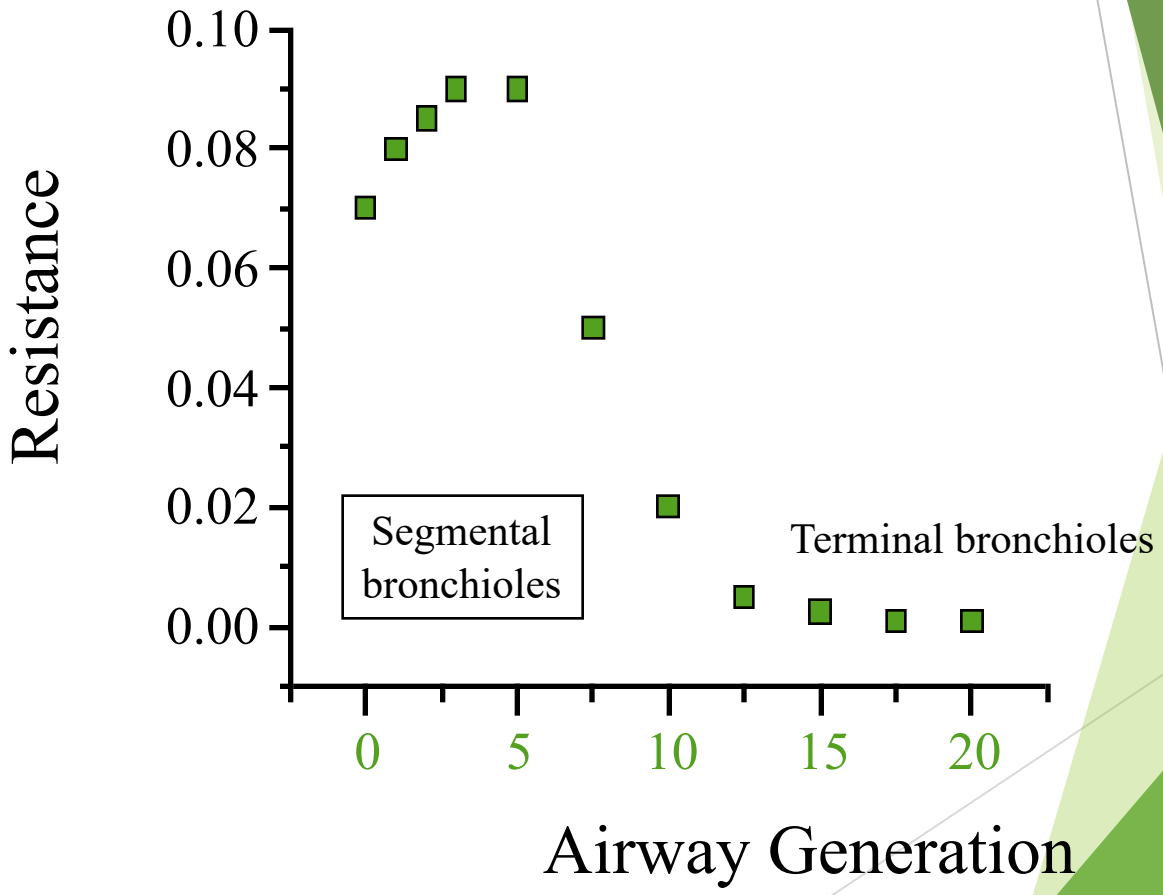
Small change in "r" results in huge change in R.

Air flow = $(P_{atm} - P_{alv})/R$

Remember the four Take home messages: Discussed In the lecture

1. Normally: R is small and negligible
2. Normally: R resides in large airways not in the small ones
3. Small airways participate in the increase in R disease condition.
4. R, when increased is Manifested mainly during expiration rather than during inspiration.

Airway Resistance



Ventilation

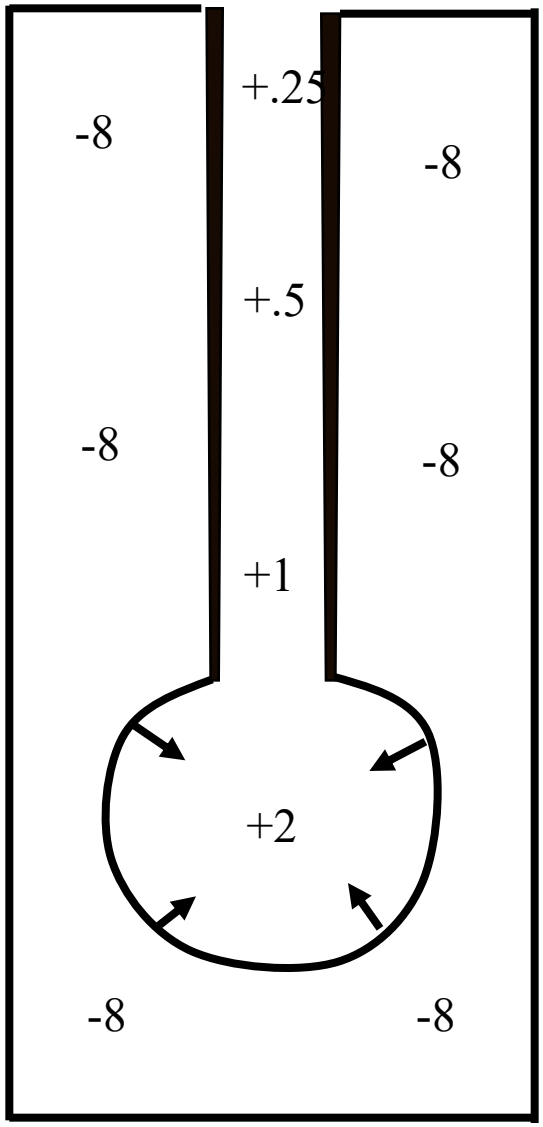
Airway diameter & other factors that affect airway resistance?

FACTOR	AFFECTED BY	MEDIATED BY
Length of the system	Constant; not a factor	
Viscosity of air	Usually constant; humidity and altitude may alter slightly	
Diameter of airways		
Upper airways	Physical obstruction	Mucus and other factors
Bronchioles	Bronchoconstriction	Parasympathetic neurons (muscarinic receptors), histamine, leukotrienes
	Bronchodilation	Carbon dioxide, epinephrine (β_2-receptors)

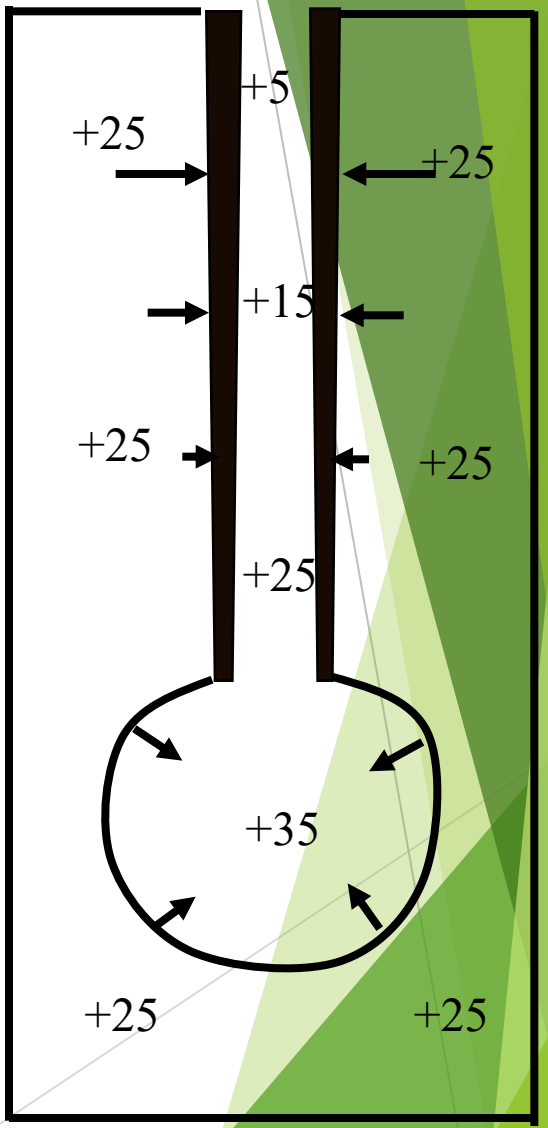
Pulmonary Disorders (continued)

- **Emphysema:**
  - **Is Chronic progressive condition**
    - **Alveolar tissue is destroyed leading to decrease surface area available for diffusion**
    - **Decreases ability of bronchioles to remain open during expiration…bcz of destruction of elastic fibers which keep small airways open,,,obstruction comes from ouside**
    - **Cigarette smoking stimulates macrophages and leukocytes to secrete protein digesting enzymes that destroy tissue.**

ed Exhalation



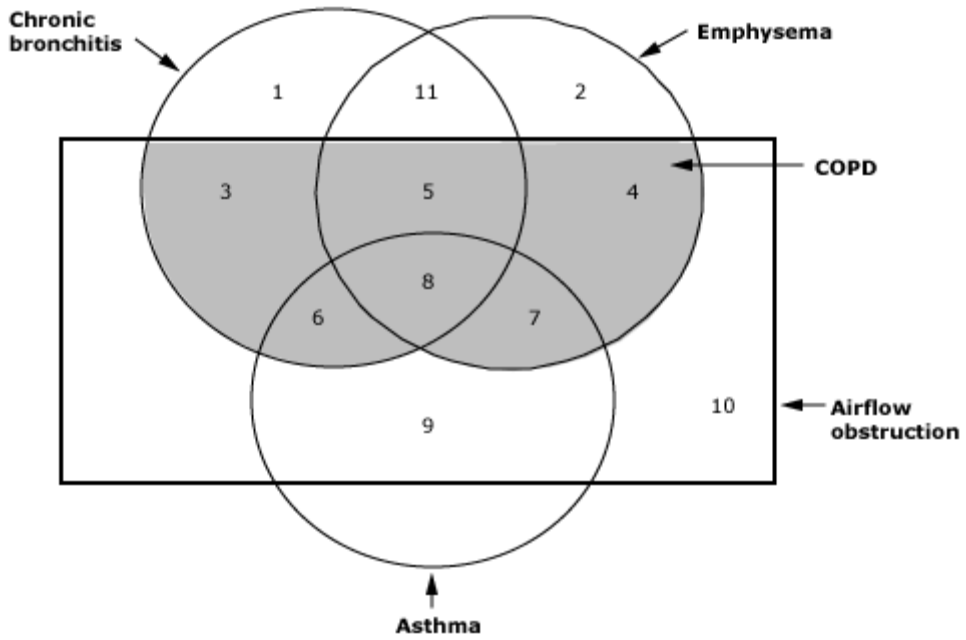
Passive Expiration



Forced Expiration

Control of Bronchiolar Diameter

- Nervous
  - Sympathetics
    - β_2 receptors dilate (salbutamol, dobutamine, albuterol, fenoterol, terbutaline).
  - Parasympathetics
    - Acetylcholine constrict bronchioles
- Humoral
  - Histamine, acetylcholine >> Constrict
  - Adrenergic (β agonists) >> Relax


Chronic bronchitis
Emphysema
1
11
2
COPD
3
5
4
8
6
7
10
Airflow obstruction
9
Asthma

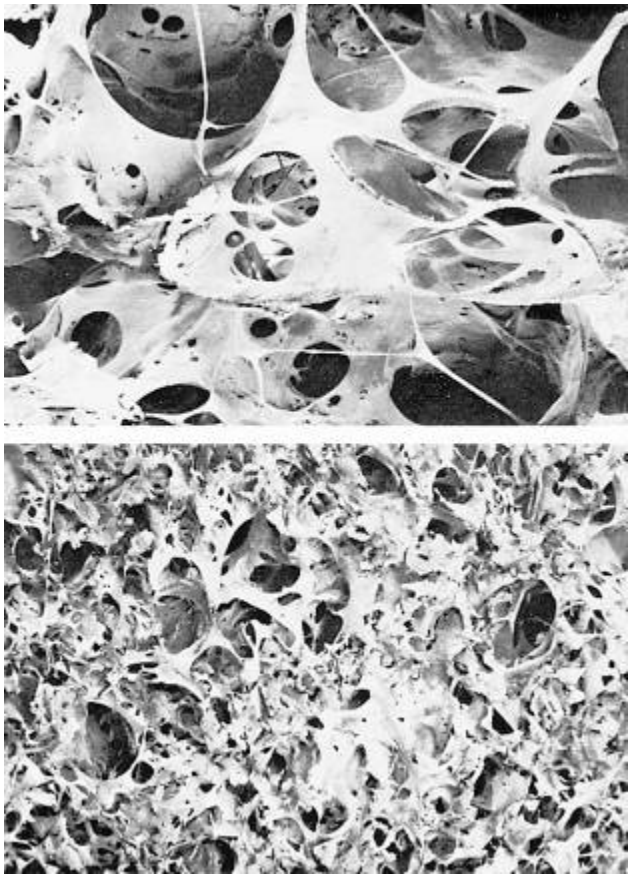
Pursed Lip Breathing in COPD patients

Collapse of your airways on expiration, as your lungs are getting smaller as you breathe out. This is a particularly serious problem in people with Emphysema, as the elastic supporting lung structure helping to keep the airways open is deficient.

Pursed Lip Breathing simply imposes a slight obstruction to expiration air flow at the mouth, which generates a back pressure throughout the airways, and therefore a stenting effect to help prop open the airways and assist expiration and lung emptying. It must be emphasized, the amount of pressure supplied by you by pursing your lips together must, as usually described, be "minimal," or "gentle."

Restrictive Diseases

- Decreased expansion of the lungs
- Lung volumes
  - reduced VC, FRC, RV and normal airway resistance
- Diffuse Interstitial Pulmonary Fibrosis
  - thick collagen deposits
- Pneumothorax



Emphysematous Lung

Normal Lung

Figure 42-4

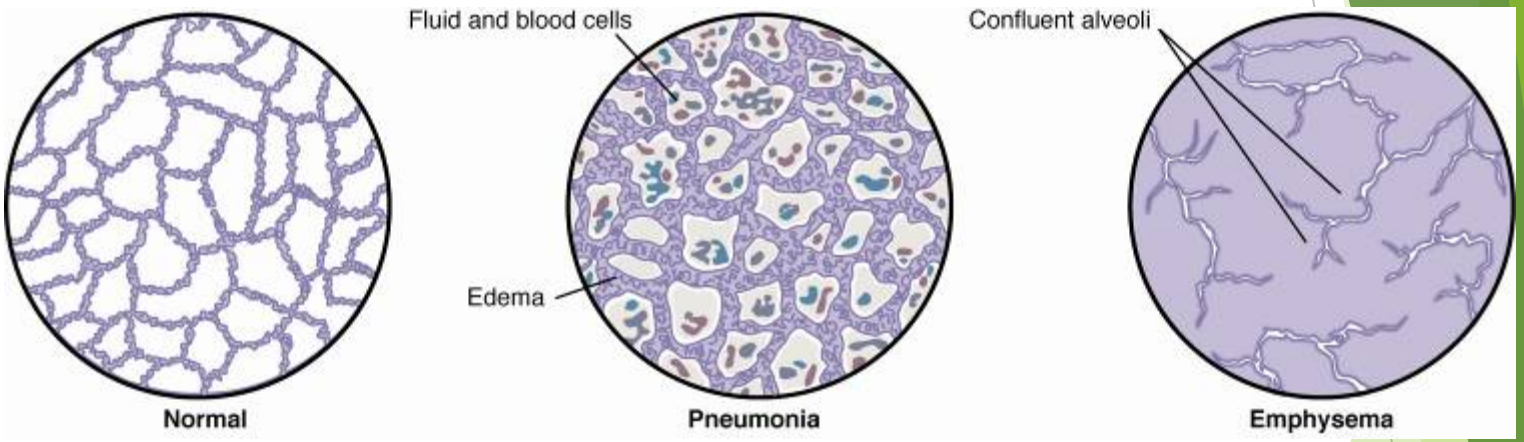

Fluid and blood cells
Edema
Confluent alveoli
Normal
Pneumonia
Emphysema

Figure 42-5

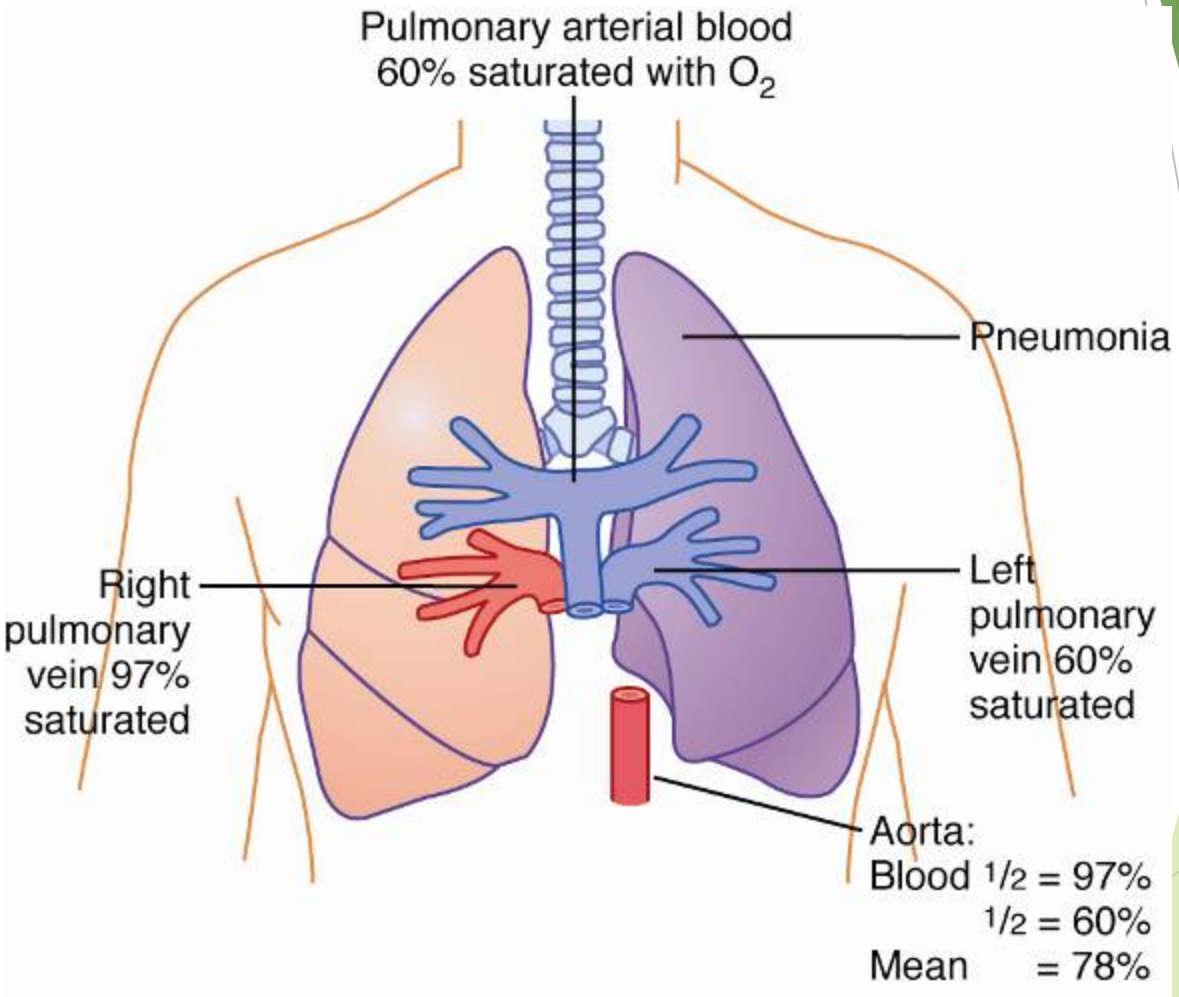

Pulmonary arterial blood
60% saturated with O_2
Pneumonia
Right
pulmonary
vein 97%
saturated
Left
pulmonary
vein 60%
saturated
Aorta:
Blood 1/2 = 97%
1/2 = 60%
Mean = 78%

Figure 42-6

ology

- Atelectasis
  - collapse of alveoli
    - airway obstruction
    - lack of surfactant

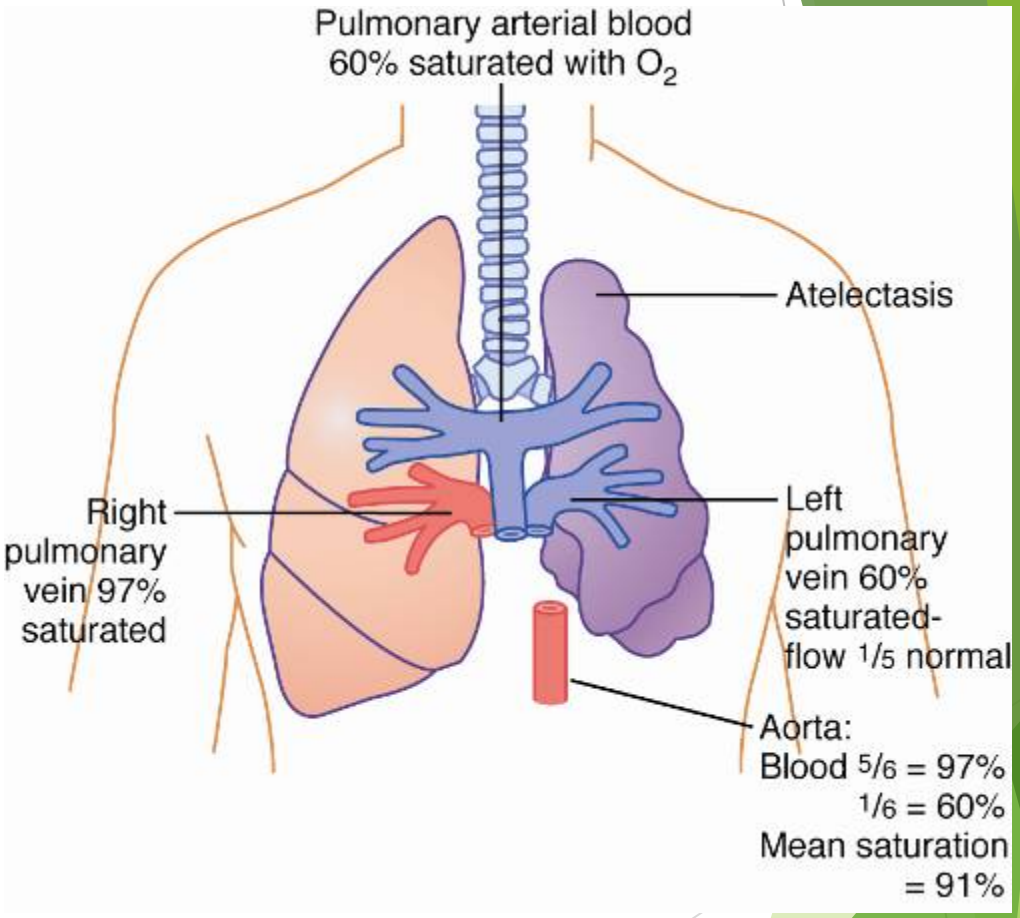


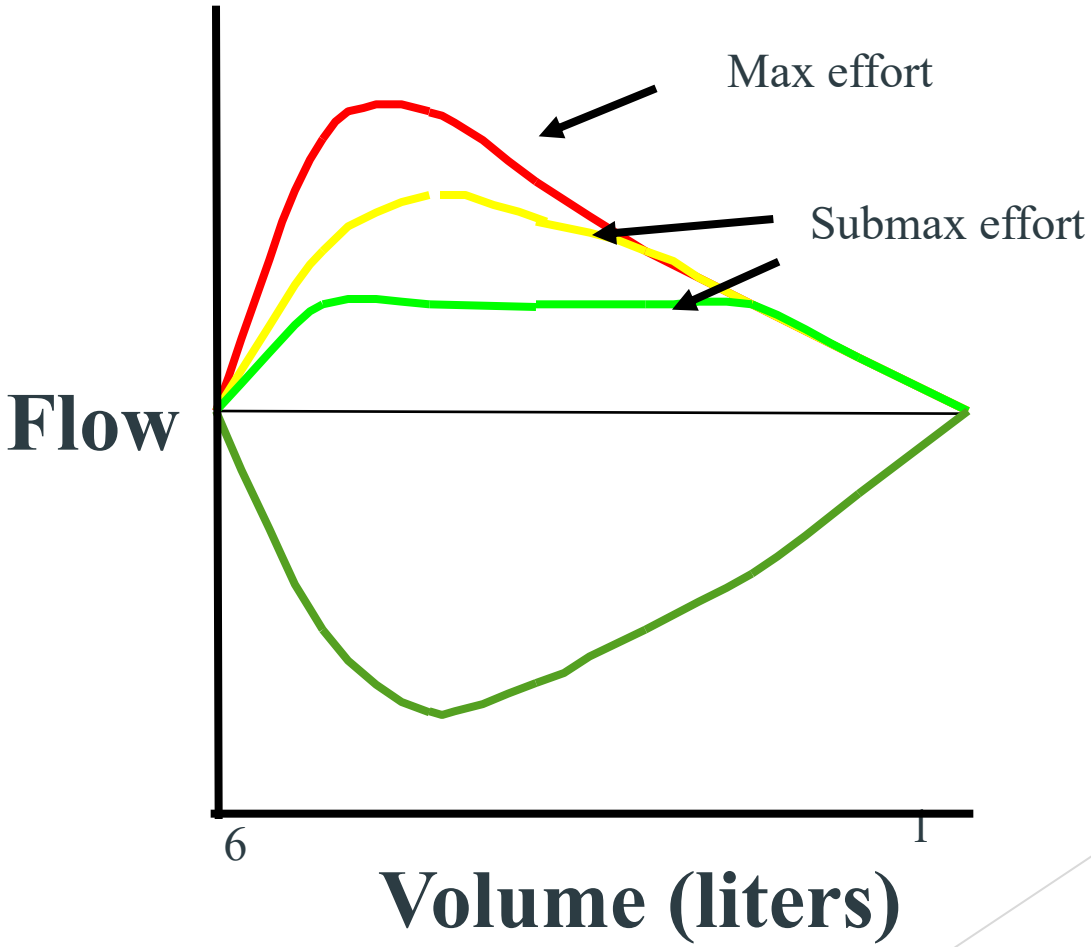
Figure 42-7

y Function Tests in Obstruction: Go to the e-learning videos

des an objective assessment of airflow obstruction and is important in staging asthm
l diagnosis of asthma, after treatment is started and symptoms have stabilized, and
netry is used to measure the rate of airflow during maximal expiratory effort after m
n differentiating between obstructive and restrictive lung disorders. In asthma (an ob
ced expiratory volume in 1 second (FEV1) is usually decreased, **the forced vital capa**
atio FEV1/FVC is decreased. In restrictive disorders the FEV1 and FVC are both decre
.
urements are usually done before and after administration of a β_2 agonists (salbutam
rol, terbutaline).. Reversibility with the use of a bronchodilator is defined as an incr
ts with severe asthma may need a short course of oral steroid therapy before the

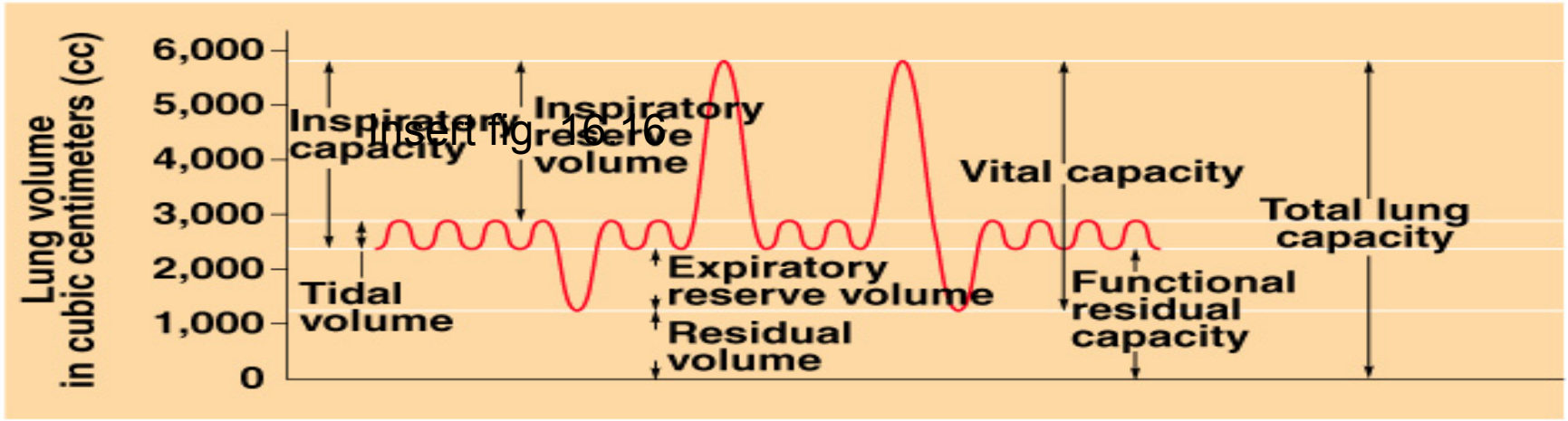
n Spirometry

is an example of a volume-time curve. It shows the amount of air expired from the l


Max effort
Submax effort
Flow
6
1
Volume (liters)

Pulmonary Function Tests

- Assessed by spirometry.
- Subject breathes into a closed system in which air is trapped within a bell floating in H_20.
- The bell moves up when the subject exhales and down when the subject inhales.



Insert fig 16.16

Terms Used to Describe Lung Volumes and Capacities

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Table 16.3 Terms Used to Describe Lung Volumes and Capacities

Term	Definition
Lung Volumes	The four nonoverlapping components of the total lung capacity
Tidal volume	The volume of gas inspired or expired in an unforced respiratory cycle
Inspiratory reserve volume	The maximum volume of gas that can be inspired during forced breathing in addition to tidal volume
Expiratory reserve volume	The maximum volume of gas that can be expired during forced breathing in addition to tidal volume
Residual volume	The volume of gas remaining in the lungs after a maximum expiration
Lung Capacities	Measurements that are the sum of two or more lung volumes
Total lung capacity	The total amount of gas in the lungs after a maximum inspiration
Vital capacity	The maximum amount of gas that can be expired after a maximum inspiration
Inspiratory capacity	The maximum amount of gas that can be inspired after a normal tidal expiration
Functional residual capacity	The amount of gas remaining in the lungs after a normal tidal expiration

nses

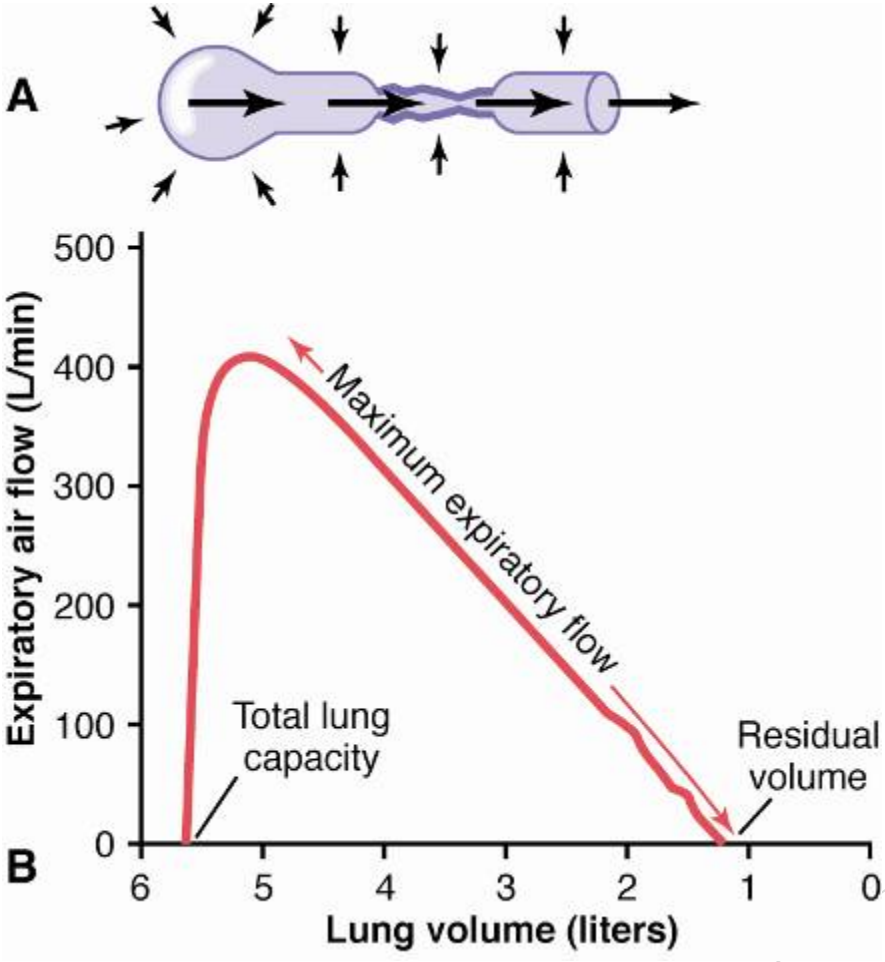


Figure 42-1

Dynamic Flow - Volume Loops

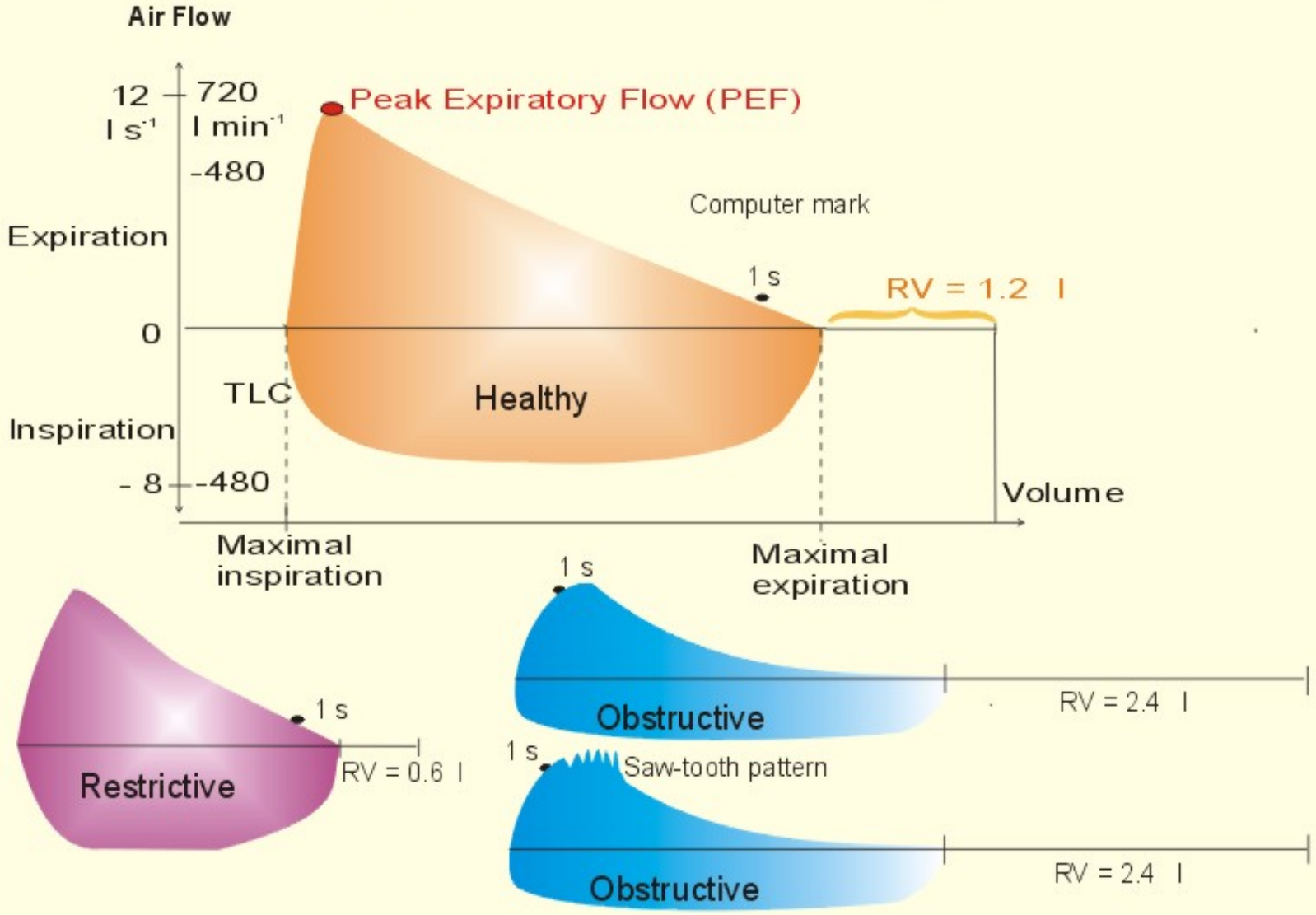


Fig. 13-6

KMc

onses

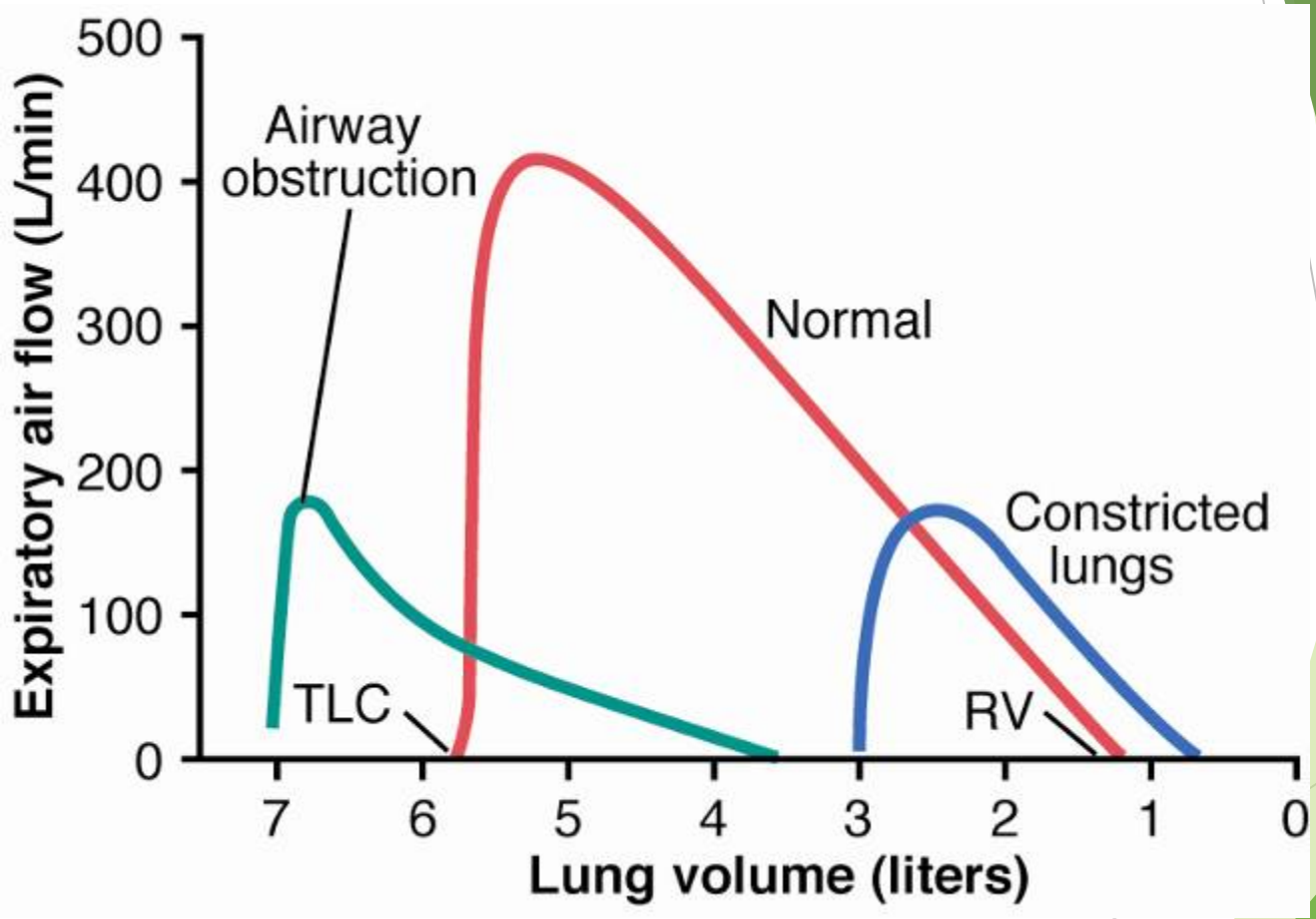


Figure 42-2

city

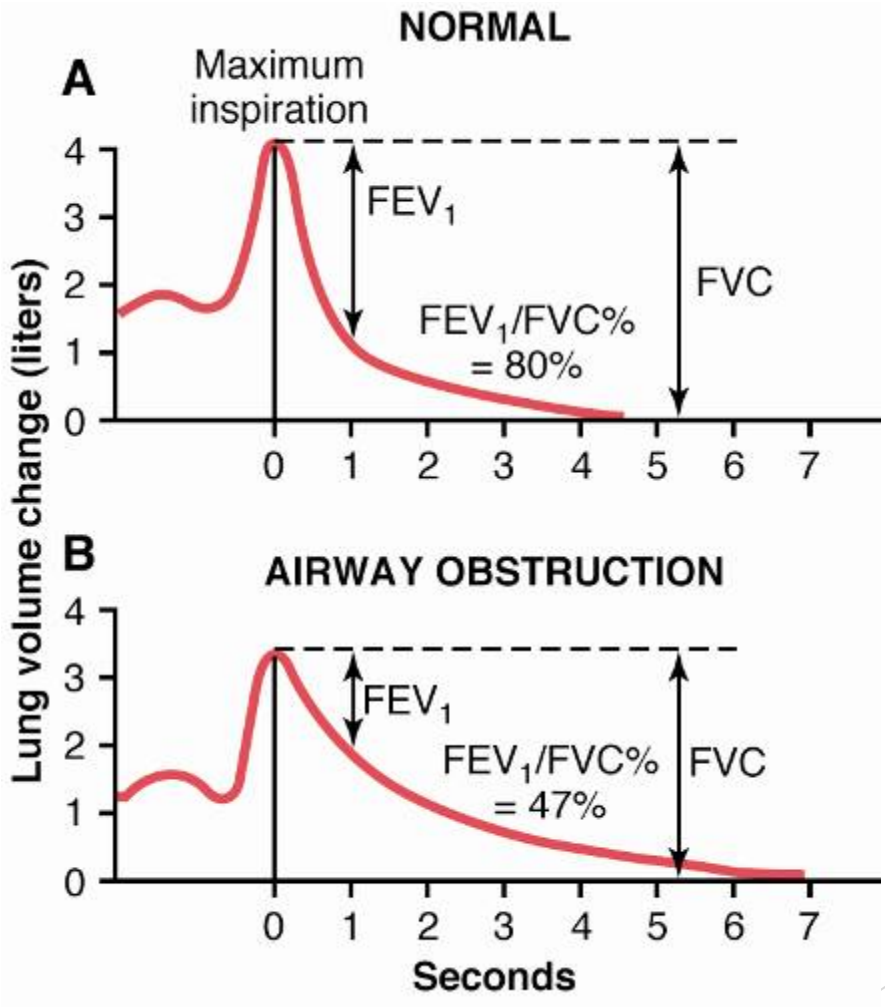


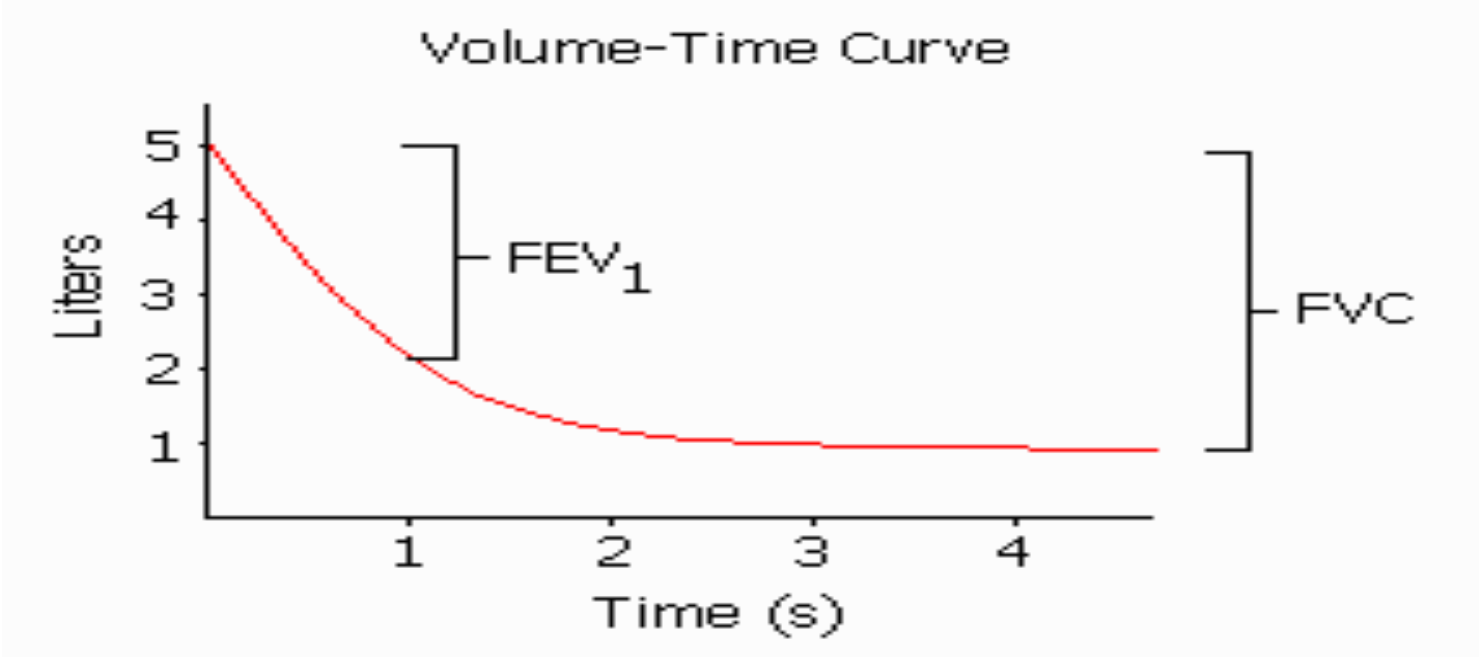
Figure 42-3

Staging of COPD based on FEV_1

GOLD: **G**lobal **I**nitiative of chronic obstructive **L**ung **D**isease

FEV_1 values (expressed as a percentage of **predicted**) may classify the severity of the COPD

	FEV_1 compared to predicted for age/ gender/ height
GOLD Stage I	$FEV_1 \geq 80\%$
GOLD Stage II	$50\% \leq FEV_1 < 80\%$
GOLD Stage III	$30\% \leq FEV_1 < 50\%$
GOLD Stage IV	$FEV_1 < 30\%$



Restrictive and Obstructive Disorders

- Restrictive disorder:
  - Vital capacity is reduced.
  - FVC is normal.
- Obstructive disorder:
  - Diagnosed by tests that measure the rate of expiration.
    - VC is normal.
    - FEV_1 is < 80%.

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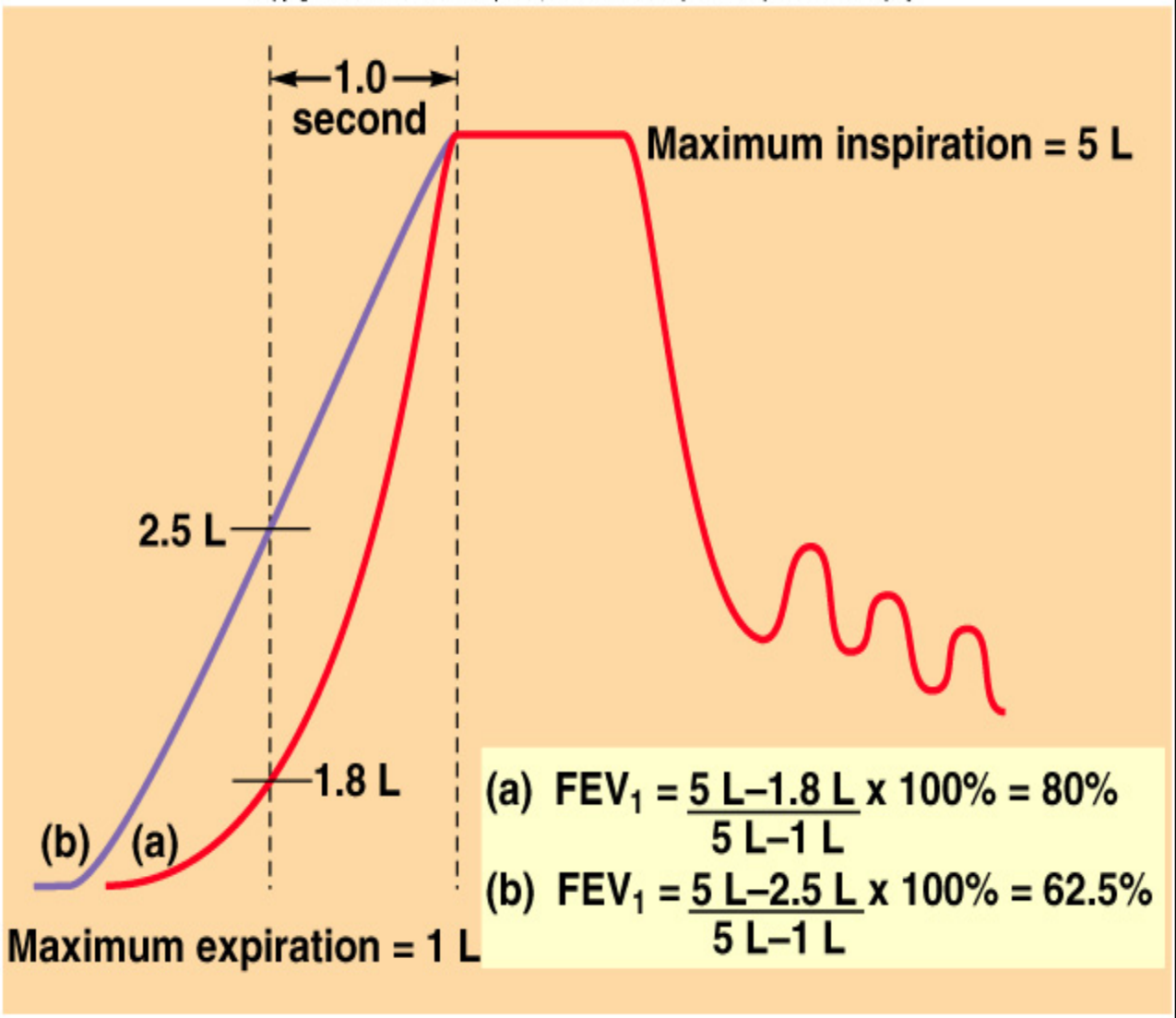

Closing volume (CV) *is the volume of air that can be exhaled after the gravitationally dependent airways have closed down. The point at which the closure begins during expiration is called the closing point which is normally reached near to residual volume. If its reached before the end of normal* V_T*, then the V/Q ratio falls sharply. By the mid-forties, CV equals FRC in the lying position and by the mid-sixties it equals FRC in the erect position. It increases in smokers, pulmonary congestion, pulmonary edema, chronic bronchitis, and excessive bronchial secretions. Any condition which interfere with diaphragmatic movement such as, tight clothing, obesity, pregnancy, ascites, phrenic paralysis, obesity, pneumothorax*

ABG

- An **arterial blood gas** (**ABG**) is a blood test that is primarily performed using blood from an artery. It involves puncturing an artery with a thin needle and syringe and drawing a small volume of blood. The most common puncture site is the radial artery at the wrist, but sometimes the femoral artery or other sites are used. The blood can also be drawn from an arterial catheter.

- The test is used to determine the pH of the blood, the partial pressure of carbon dioxide and oxygen, and the bicarbonate level. Many blood gas analyzers will also report concentrations of lactate, hemoglobin, several electrolytes, oxyhemoglobin, carboxyhemoglobin .

Components of the Arterial Blood Gas

The arterial blood gas provides the following values:

pH

Measurement of acidity or alkalinity, based on the hydrogen (H+) ions present.

The normal range is 7.35 to 7.45

PaO_2

The partial pressure of oxygen that is dissolved in arterial blood.

The normal range is 80 to 100 mm Hg.

SaO_2

The arterial oxygen saturation.

The normal range is 95% to 100%.

$PaCO_2$

The amount of carbon dioxide dissolved in arterial blood.

The normal range is 35 to 45 mm Hg.

HCO_3^-

The calculated value of the amount of bicarbonate in the bloodstream.

The normal range is 22 to 26 mEq/liter

B.E.

The base excess indicates the amount of excess or insufficient level of bicarbonate in the system.

The normal range is –2 to +2 mEq/liter.

(A negative base excess indicates a base deficit in the blood.)

Oxygen Therapy

- Atmospheric
- Hypoventilation
- impaired alveolar membrane
- anemia, abnormal hemoglobin
- inadequate tissue use

erapy

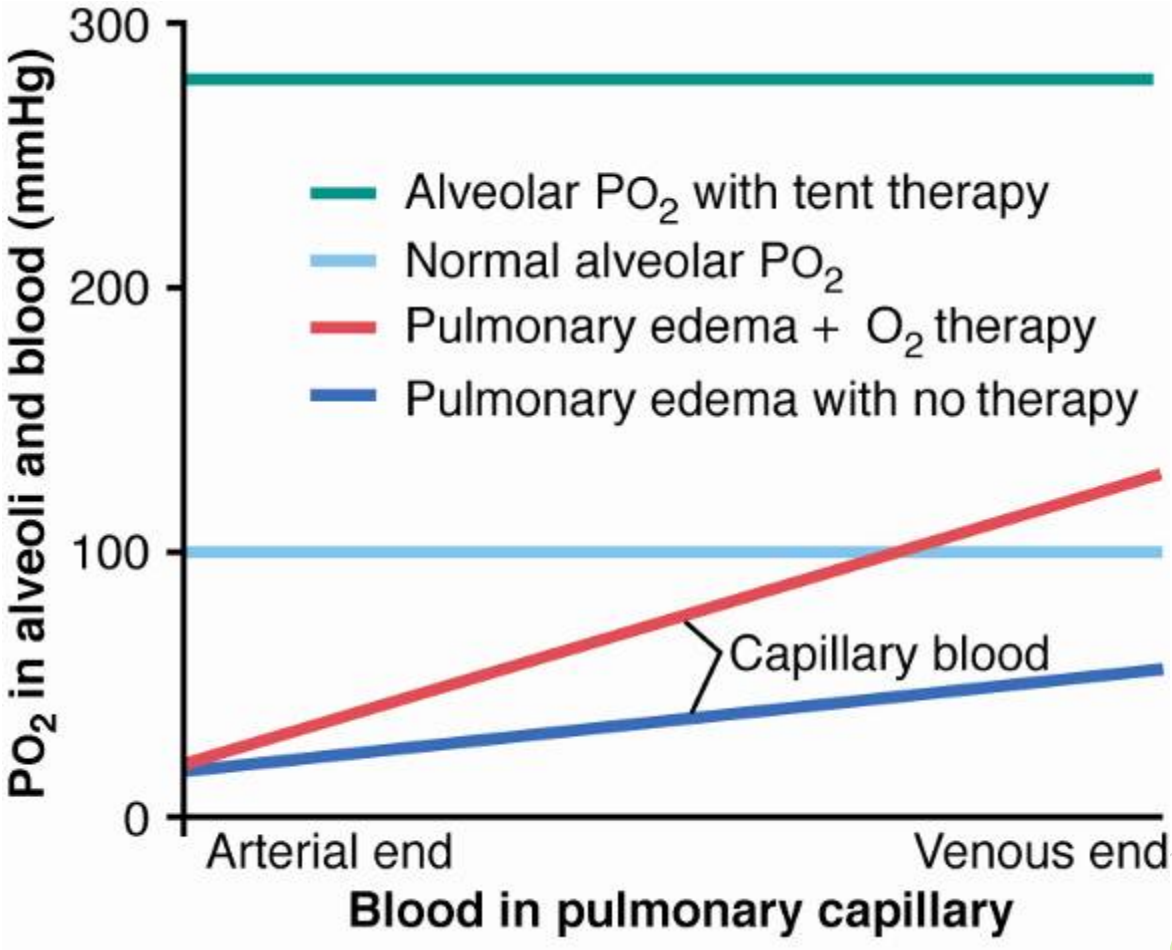

Figure 42-8

THANK YOU

Next Time…

- Compliance

UNIT VII

GUYTON AND HALL *Textbook of*
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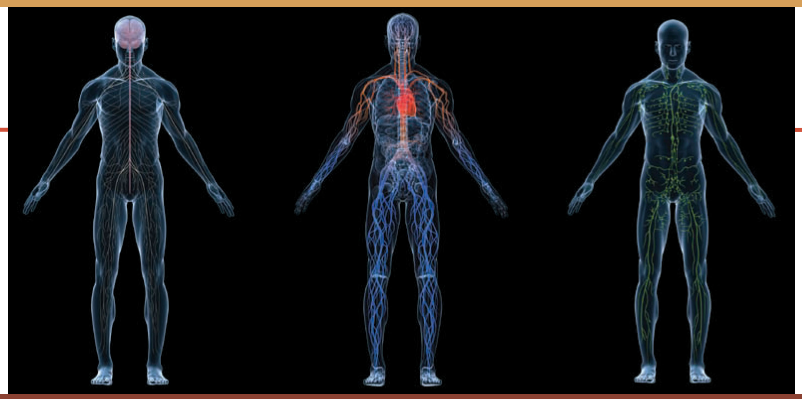

CHAPTER 37:

Lung Compliance

Slides by Robert L. Hester, PhD

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Work of breathing

Work in the respiratory system is of 2 major types (discussed in the previous lecture):

1. *Work to overcome elastic forces (70%):* that required to expand the lungs against the lung and chest elastic forces. Two third is duo to surface tension and one third is duo to elastic fibers.
2. *Work to overcome non-elastic forces (30%):* that required to overcome:
    1. The viscosity of the lung and chest wall structures (20%).
    2. *Airway resistance work (80%):* that required to overcome airway resistance to movement of air into the lungs.

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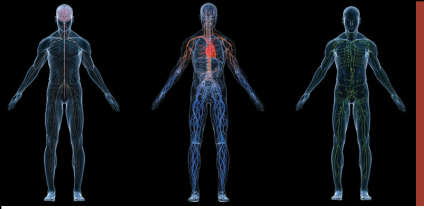

Minimal Volume

- The lungs, if alone, (outside the body) or during open-chest surgery, will collapse up to 150 ml air **= minimal volume MV (this is not anatomic dead space volume even though it is 150 ml)**. MV is used for medico legal purposes (WHY?). MV is also known as unstressed volume or resting volume of the lung.

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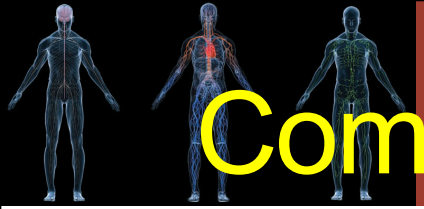

Compliance

- Distensibility (stretchability):
  - How easy the lungs can expand. How much force we need to expand the lung? If the force is small, then the lung is stretchable.
- It is the change in lung volume per unit change in transpulmonary pressure.

  $\Delta V/\Delta P$
- Lung is 100 times more distensible than a child balloon. **This means, 100 times more distending pressure is required to inflate a child toy balloon than to inflate the lung.**
  - Compliance is reduced when distension is difficult.

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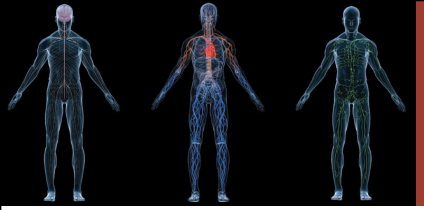

Compliance…cont.

COMPLIANCE is the ability of the lung to stretch

Specific compliance = C/FRC to correct for differences in lung volume between a child and an adult.

C_L = 200ml/cm H_2O. For the lung alone

C_W = 200ml/cm H_2O. For the thoracic wall alone

C_S = 100ml/cm H_2O. S stands for lung-thorax system (For both)

Inflating one balloon is easier than inflating two balloons, one inside the other. The two balloons are the lung and the thorax.

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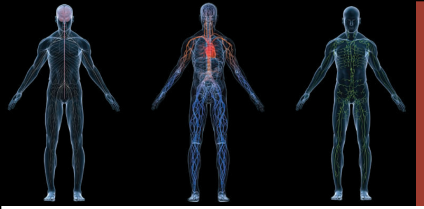

Elasticity

- Tendency to return to initial size after distension.
- High content of elastin proteins.
  - If the lung is very elastic and resist distension…this means high recoil tendency or high collapsing forces Too much recoil tendency is bad (high collapsing forces) and too little recoil tendency is also bad (high compliance).
- Elastic tension increases during inspiration.

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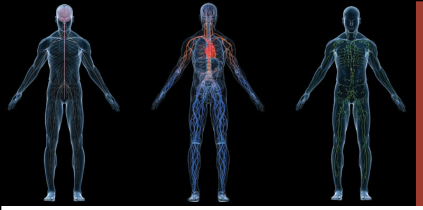
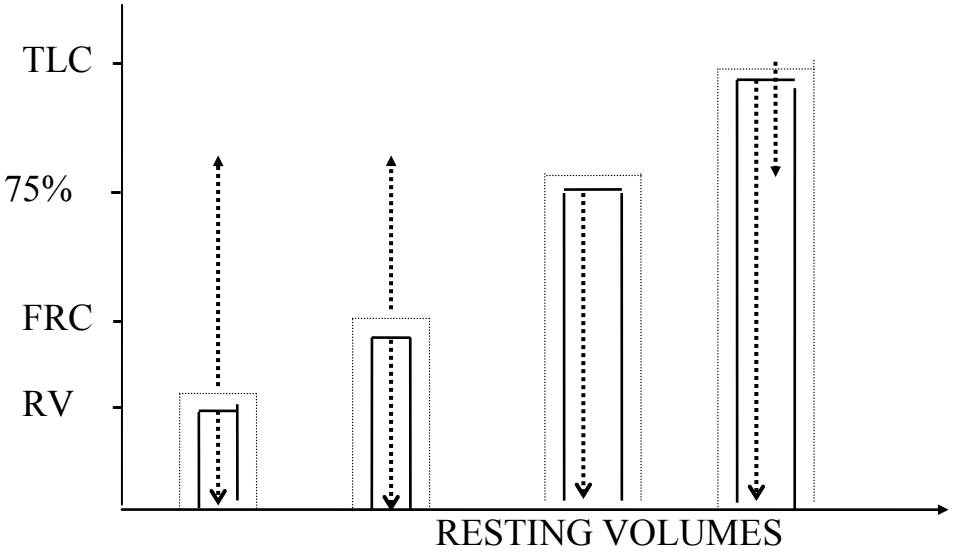


RESTING VOLUMES



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BINDING BETWEEN LUNGS & THORAX.

- Lungs are covered by a visceral pleura & the mediastinum & chest wall are lined by parietal pleura. Both pleural surfaces are covered with a thin film of fluid & the intermolecular forces of this film between the two surfaces holds the lungs against the thorax. It is like two glasses slide over each others but not easily separated.

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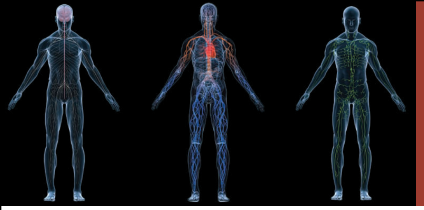

Intrapleural Pressure

- The magnitude of the intrapleural pressure equals the separate elastic forces of the lungs or chest wall rather than the sum of their combined forces. It reflects either the strength of the collapsing elastic lung tissue or the strength of the expanding chest wall force
- Since chest wall elasticity usually remains unchanged in respiratory pathology, "P_{pl}" reflects the elastic strength of the lungs. At all volume P_{pl} reflects how strongly the lungs are tending to collapse. P_{pl} can be measured using a tube inside the esophagus.

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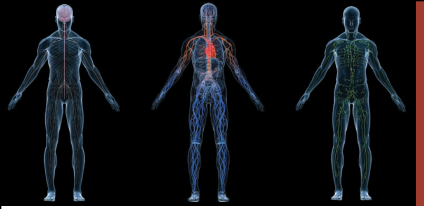

Relaxation Curve

- When generating the **Relaxation Curve**, all respiratory muscles (inspiratory & expiratory) are relaxed and we plot volume versus intra-alveolar pressure.
- At each lung volume we can study whether the lung-chest wall system is tending to expand or to relax.
- Relaxation curve is generated under static conditions when no air flow occurs.
- Under these conditions, Ppl reflects the strength of the elastic forces of the chest wall

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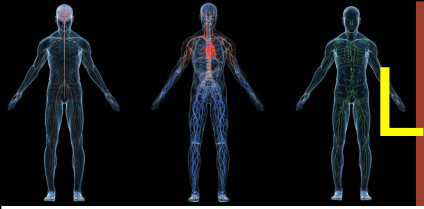

Lung-Thorax Resting Volume

- In vivo, we can't measure P_{alv} below residual volume.
- To move the system from FRC you need to apply force such as muscle contraction…but to bring it back to its resting volume (FRC) is passive. This is another way to look at inspiration is active and expiration being passive process.

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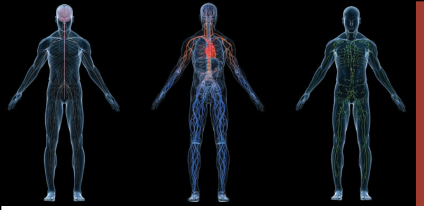

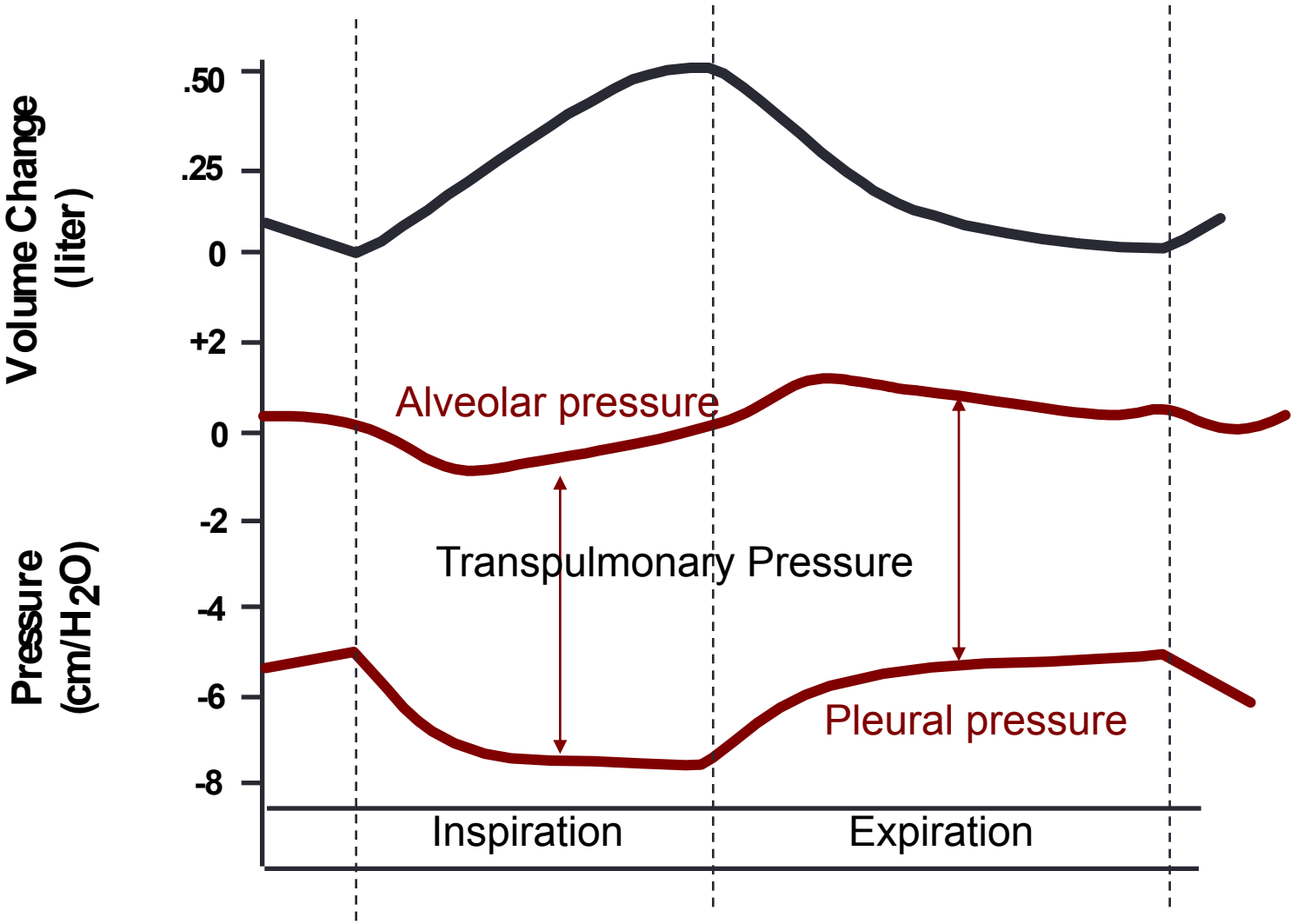

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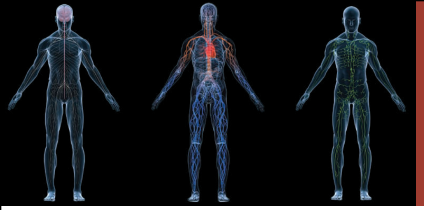
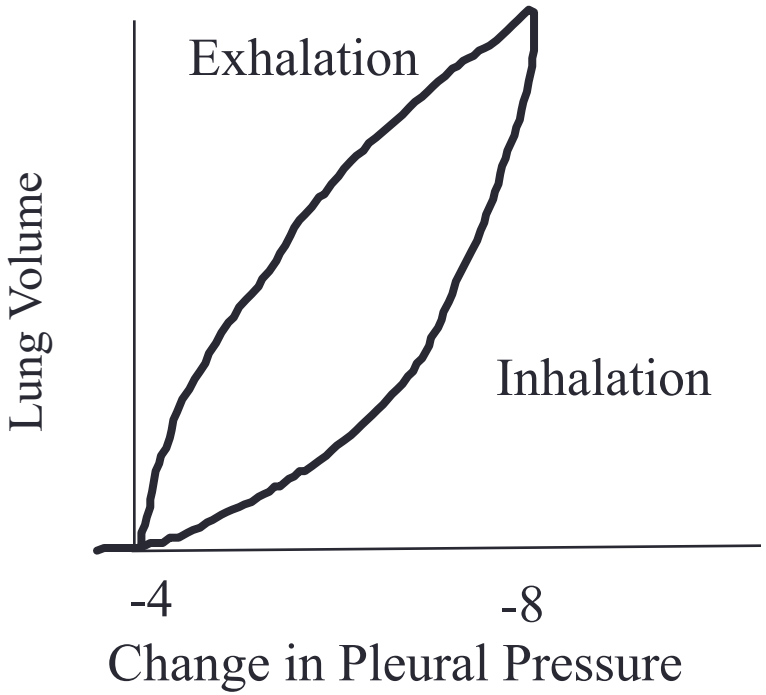


COMPLIANCE OF LUNGS

- Determined by elastic forces
- Elastic forces
  - lung tissue… one third
  - surface tension…two thirds



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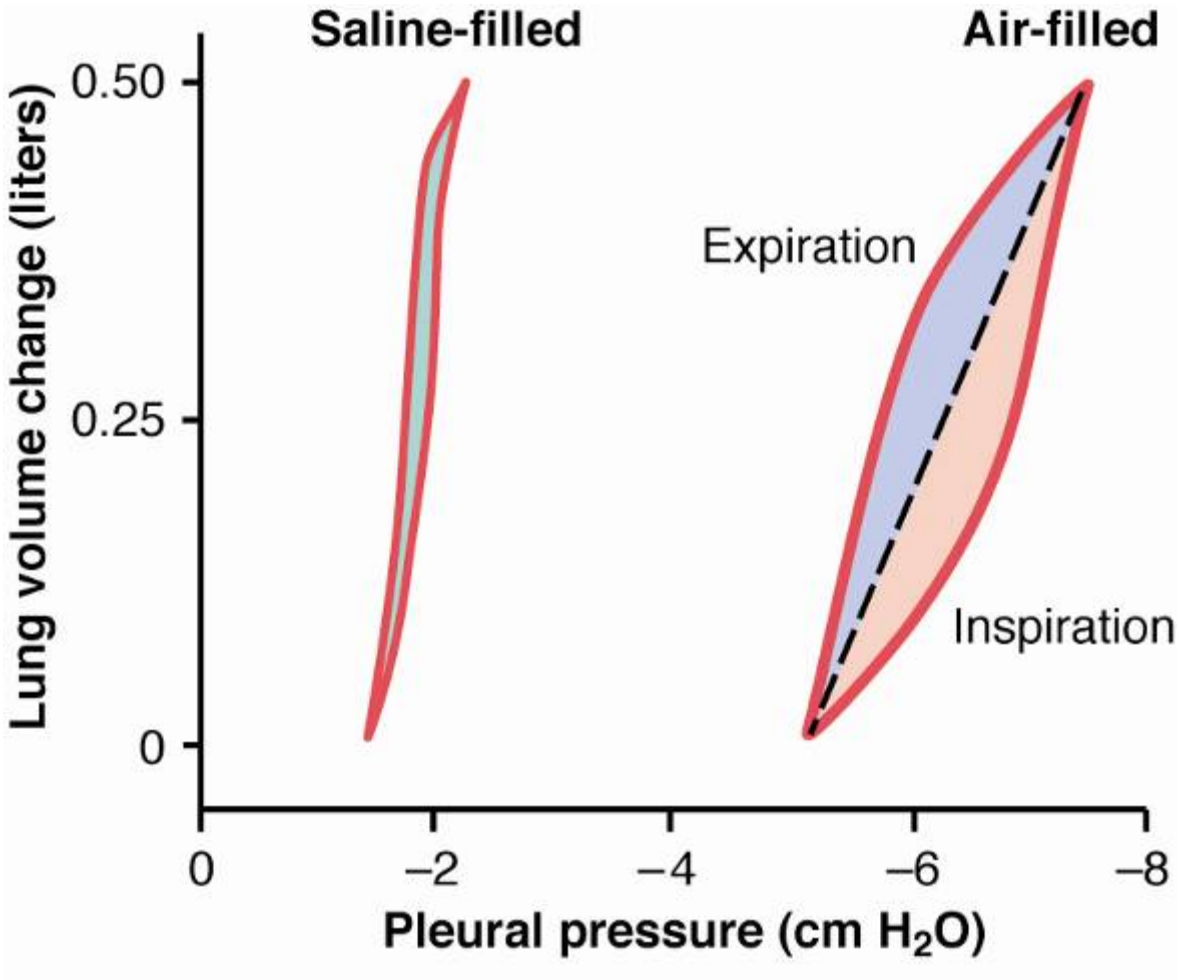
Compliance of Lungs



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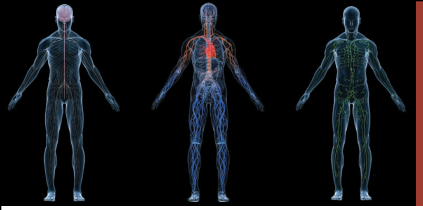

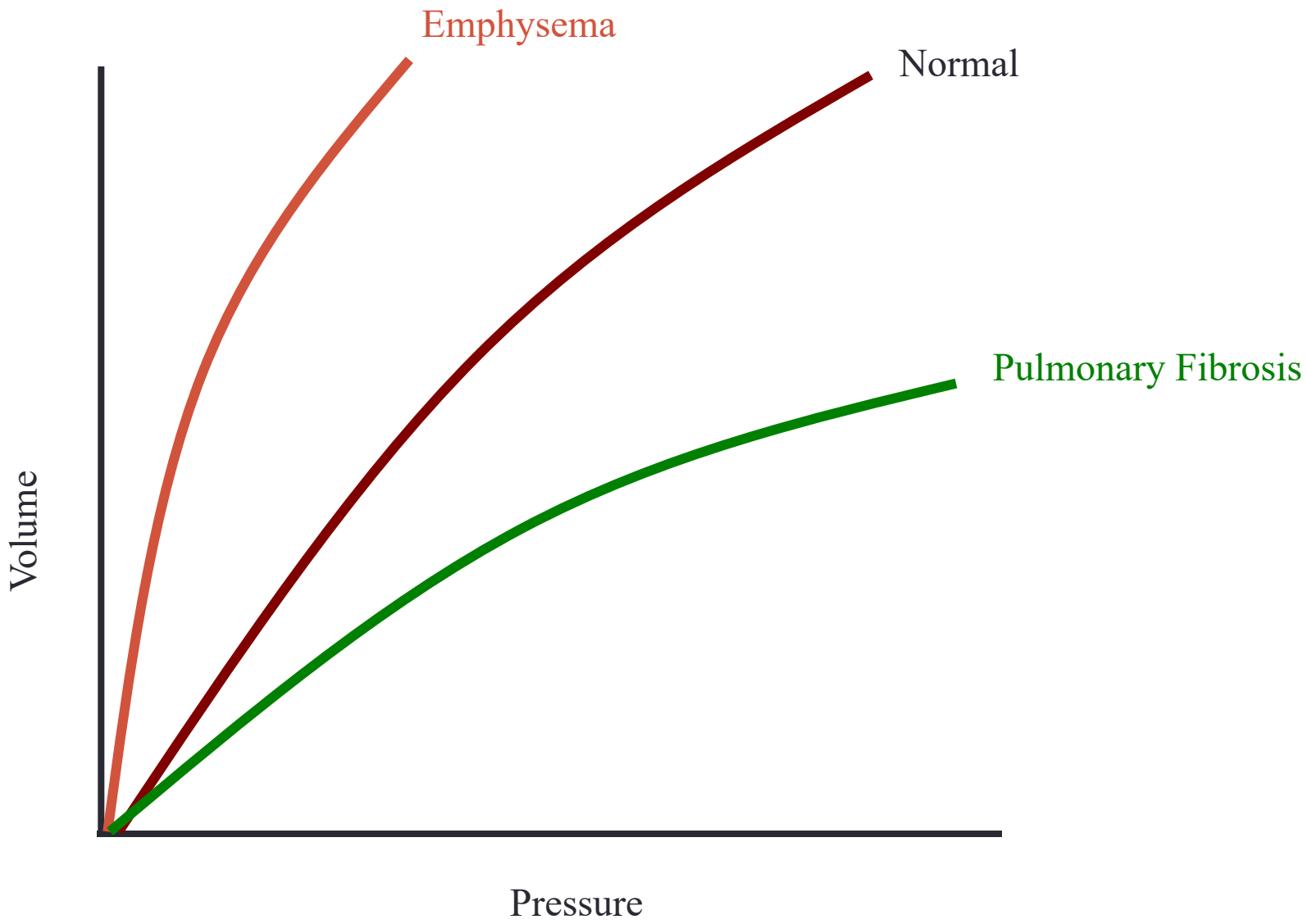

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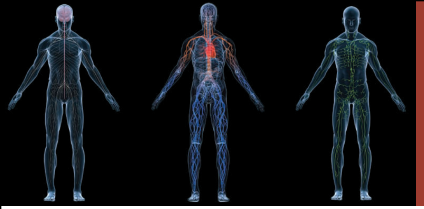

Compliance of Lungs

Surface tension T can be looked as a collapsing force which is going to collapse the alveoli…

- T is duo to attraction of water molecules at air-water interface
- T is reduced by the presence of surfactant

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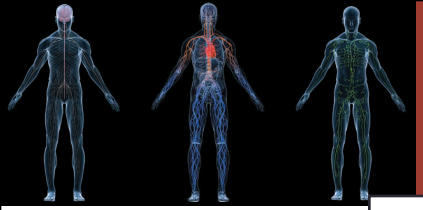
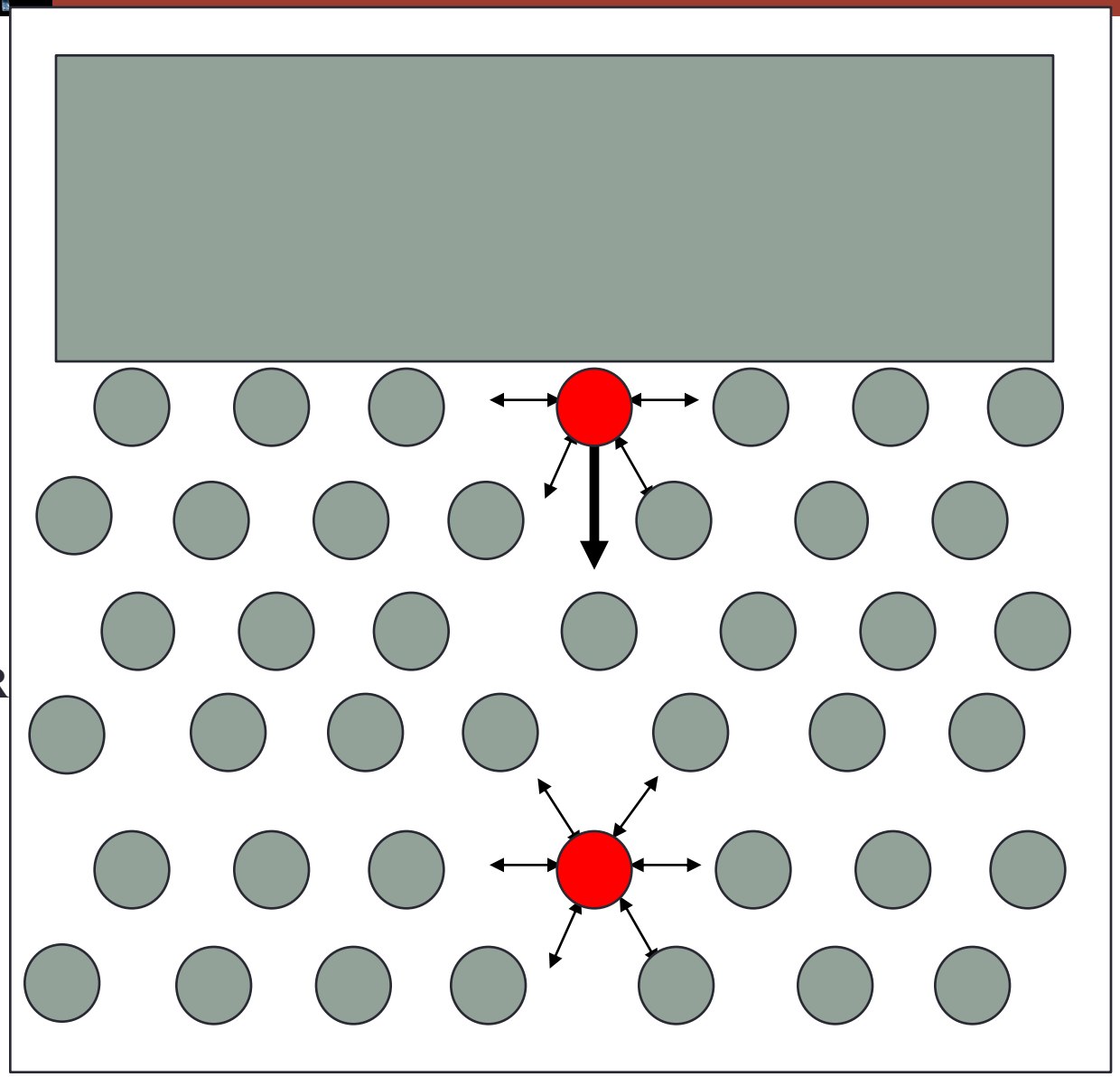


SURFACE TENSION- asymetrical forces acting at an air/water interface produce a net force acting to decrease surface area



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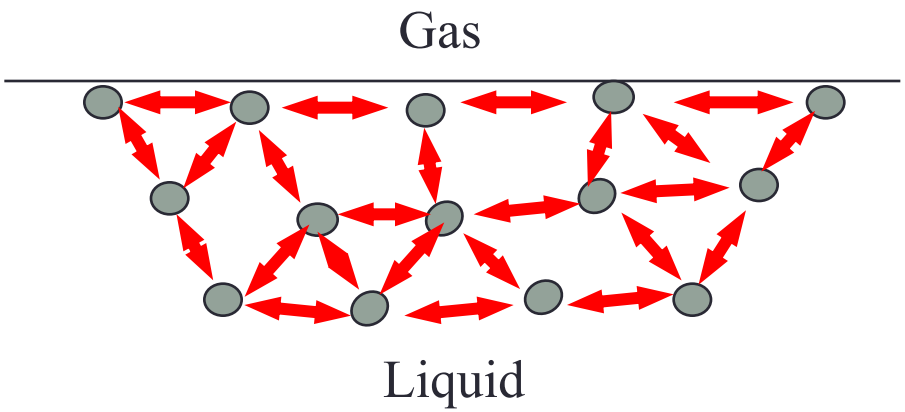
Surface Tension and recoil of the lung

Molecular interactions resulting from hydrogen bonds between water molecules in liquid but not between water and air.



When water forms a surface with air, the water molecules on the surface of the water have an especially strong attraction for one another. Therefore, the water surface is always attempting to contract.

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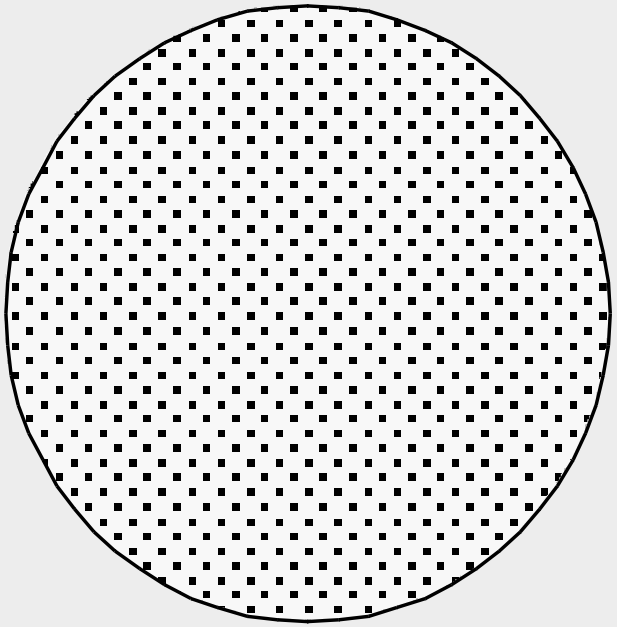
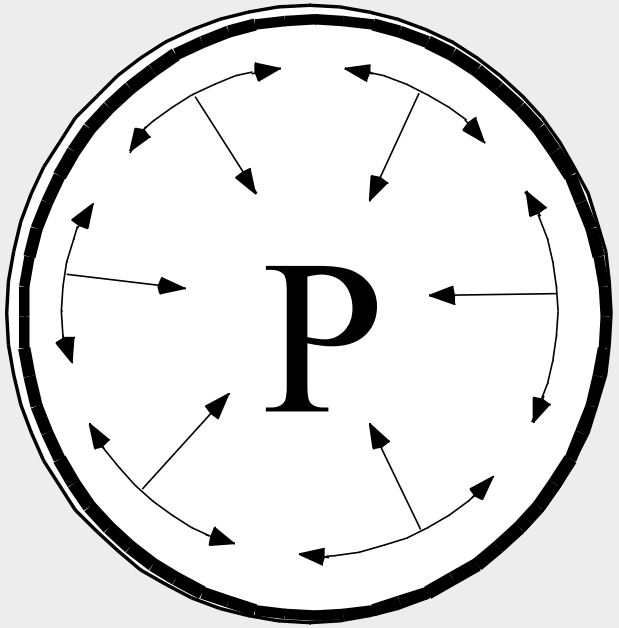
Liquid filled alveolus



No Surface Tension

Because there is no air/water interface

Gas filled alveolus with thin liquid layer



+ Surface Tension

Recoil Pressure

Compliance

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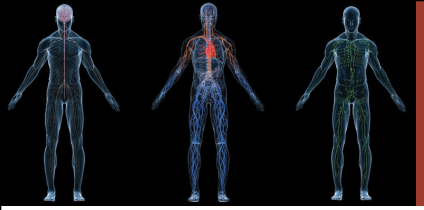


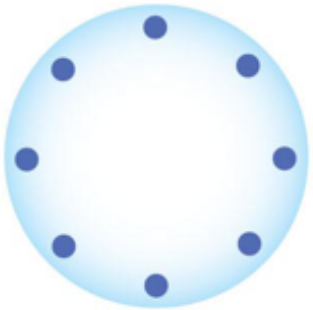
Surfactant

- ***Surfactant***: Means surface-active agent
- Surfactant is produced by Alveolar type II cells
  - It is Glyco(2%)-lipo(90%)-protein(8%) plus calcium ions.
  - Disrupts the surface tension & cohesion of water molecules
  - Maturation of surfactant needs T_4, prolactin, estrogen, and other steroids
    - prevents alveoli from sticking together during expiration

Law of LaPlace: P = 2T/r

P = pressure
T = surface tension
r = radius

According to the law of LaPlace, if two bubbles have the same surface tension, the small bubble will have higher pressure.



r = 2
T = 2
P = (2 × 2)/2

r = 1
T = 1
P = (2 × 1)/1

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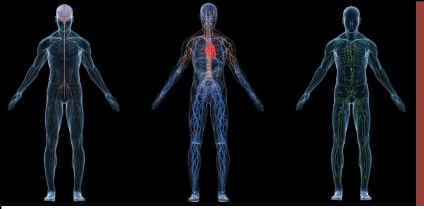

Laplace's Law

$$T = P \times r / 2 \text{ or } P = 2T/r$$

P = pressure required to prevent alveolar collapse <u>at rest</u>
T = surface tension
r = radius…

- The smaller the radius , the larger the pressure required to prevent collapse…this point is important in IRDS where alveolar diameter is extremely small.

  - If T = 2; r = 2; P = 2
  - If T = 2; r = 4; P = 1

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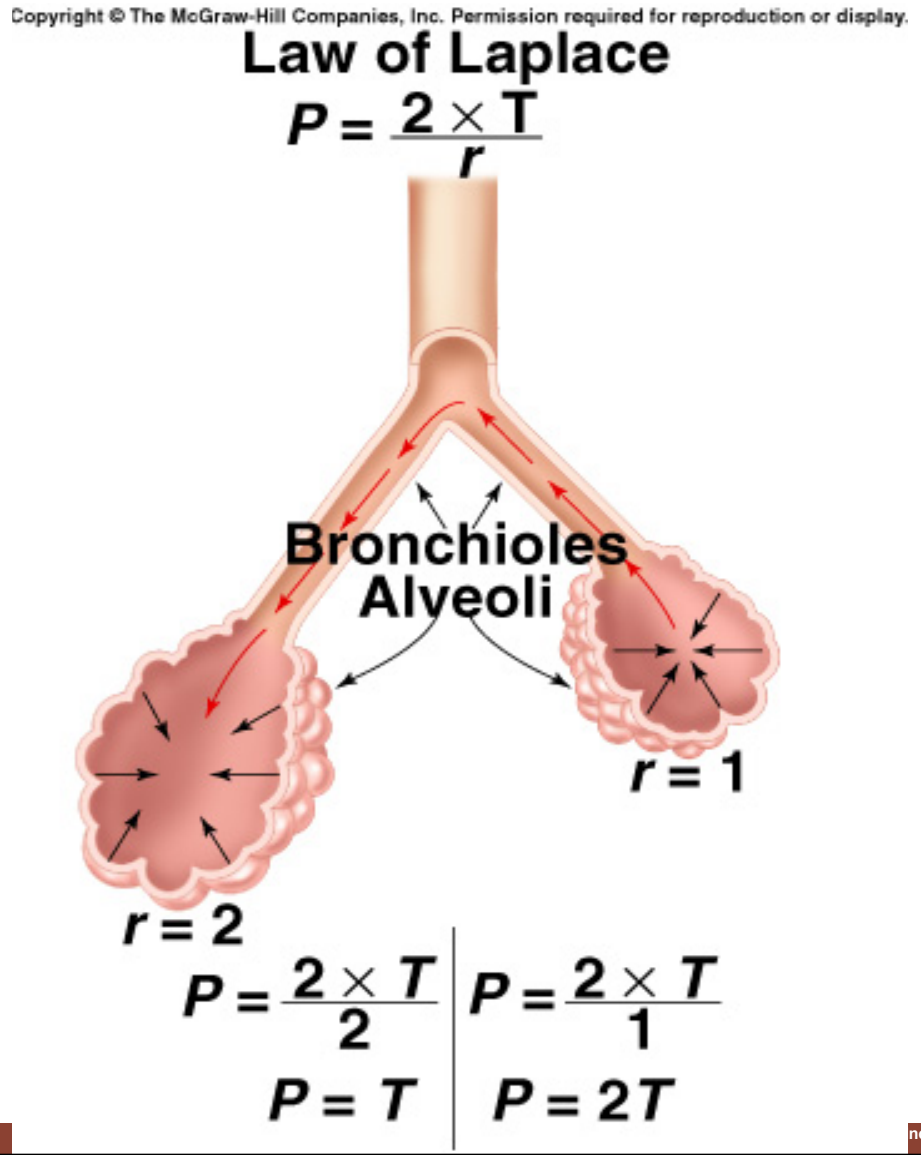
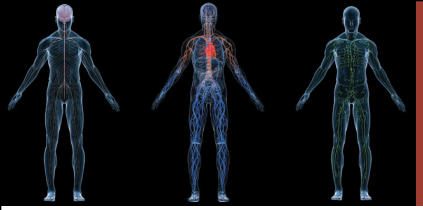
Surface Tension… Law of Laplace (continued)

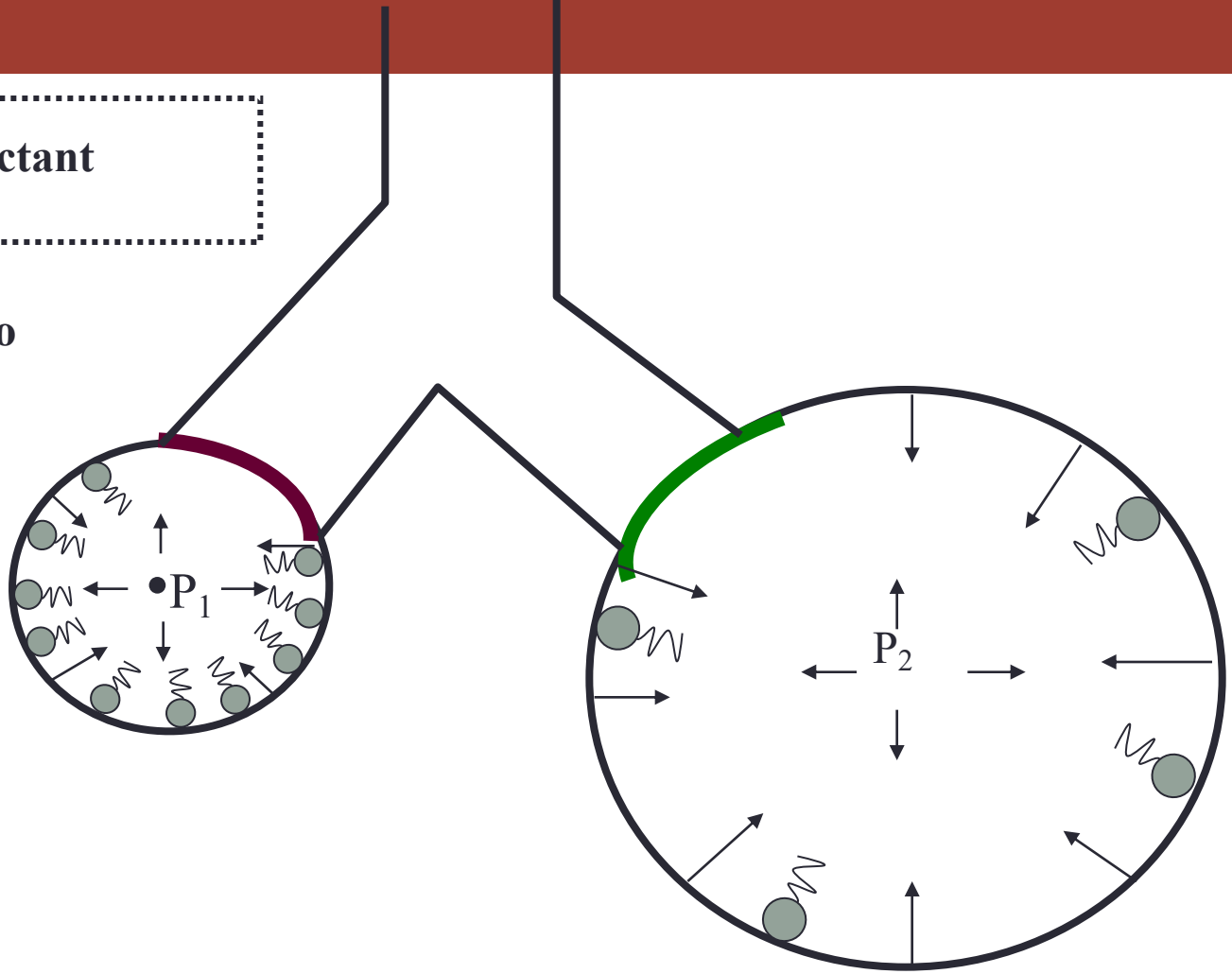
- Law of Laplace:
  - Pressure in pleural cavity is directly proportional to surface tension; and inversely proportional to radius of alveoli.
  - Pressure in smaller alveolus would be greater than in larger alveolus, if surface tension were the same in both.





Pulmonary surfactant

P_1 = Pressure required to prevent alveoli #1 from collapsing.



P_2 = Pressure required to prevent alveoli #2 from collapsing.

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Deficiency of Surfactant causes collapse of the lungs

- IRDS: Respiratory distress syndrome (in premature babies)
- ARDS: Acute Respiratory distress syndrome in adults and children
- Since lung inflation requires large pleural pressure drops, deep breaths are difficult for patients with Restrictive Ventilatory Defects RVD; These patients exhibit shallow and rapid breathing patterns.

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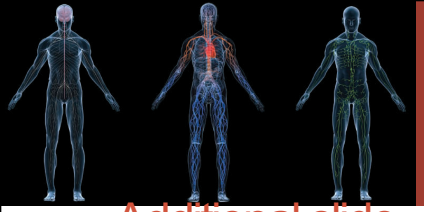

Additional slide…just take a look…you don't have to memorize any of the following numbers

Berlin criteria for ARDS severity

PaO_2/FiO_2 ratio	Inference
200 - 300 mm Hg	Mild ARDS
100 - 200 mm Hg	Moderate ARDS
< 100 mm Hg	Severe ARDS

ARDS is characterized by an acute onset within 1 week, bilateral radiographic pulmonary infiltrates, respiratory failure not fully explained by heart failure or volume overload, and a PaO_2/FiO_2 ratio < 300 mm Hg

ARDS

	Mild	Moderate	Severe
Timing	Acute onset within 1 week of a known clinical insult or new/worsening respiratory symptoms		
Hypoxemia	PaO_2/FiO_2 201–300 with PEEP/CPAP ≥ 5	PaO_2/FiO_2 ≤ 200 with PEEP ≥ 5	PaO_2/FiO_2 ≤ 100 with PEEP ≥ 10
Origin of Edema	Respiratory failure associated to known risk factors and not fully explained by cardiac failure or fluid overload. Need objective assessment of cardiac failure or fluid overload if no risk factor are present		
Radiological Abnormalities	Bilateral opacities*	Bilateral opacities*	Opacities involving at least 3 quadrants*
Additional Physiological Derangement	N/A	N/A	$V_{E\,Corr}$ > 10 L/min or C_{RS}<40 ml/cmH_2O

*Not fully explained by effusions, nodules, masses, or lobar/lung collapse; use training set of CXRs; $V_{E\,Corr} = V_E \times PaCO_2/40$ (corrected for Body Surface Area)

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UNIT VII

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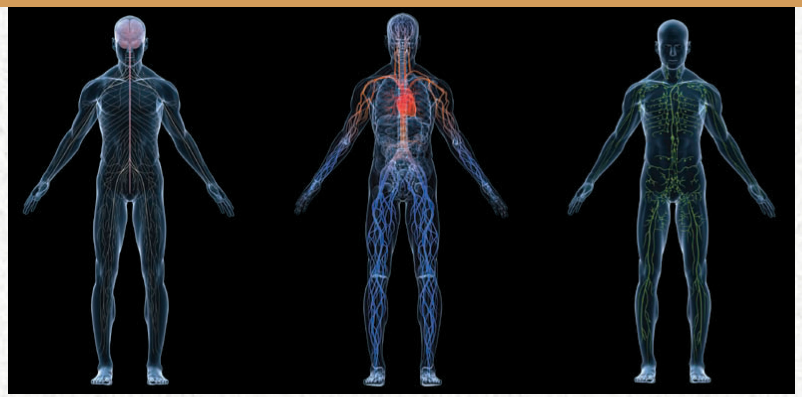

Chapter 38:

Pulmonary Circulation, Pulmonary Edema, Pleural Fluid

Slides by Robert L. Hester, PhD

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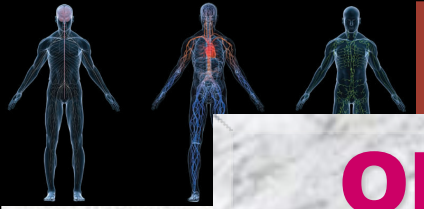

Objectives

- Describe the pulmonary circulation
- Describe the pulmonary blood pressures
- List the factors that affect diffusion
- Explain the factors that affect O_2 and CO_2 diffusion
- Composition of air in the respiratory pathway
- Describe the lung zones of perfusion
- Explain how the lungs accommodate extra flow
- Describe the Ventilation/Perfusion ratio

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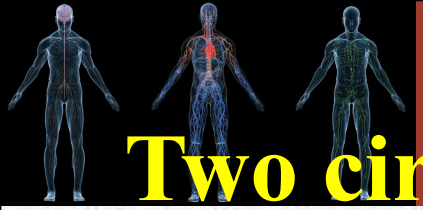

Two circulations in the respiratory system

- **Bronchial Circulation**
  - Arises from the aorta.
  - Part of systemic circulation (oxygenated).
  - Receives about 1-2% of left ventricular output.
  - Supplies the supporting tissues of the lungs, including the connective tissue, septa, and bronchi.
  - It empties into the pulmonary veins and eventually into left atrium
  - The blood flow into left side is greater by 2%...do you think left ventricular output is equal to right ventricular output?

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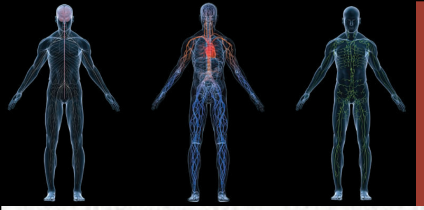

PULMONARY BLOOD FLOW

- Pulmonary Pressures
  - Pulmonary artery pressure
    - systolic 25 mmHg
    - diastolic 8 mmHg
    - mean 15 mmHg
    - capillary 10 mmHg
- Left Atrial and Pulmonary Venous Pressures = 2 (1-5) mm Hg (estimated)
- *Pulmonary wedge pressure* = 5 mm Hg (usually its 2 to 3 mm Hg greater than the left atrial pressure)

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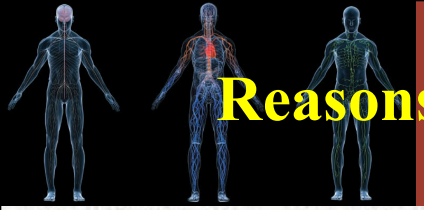

Reasons Why Pressures Are Different in Pulmonary and Systemic Circulations

- Gravity and Distance:
  - Distance above or below the heart adds to, or subtracts from, **both** arterial and venous pressure
  - Distance between Apex and Base affected by gravity

Systemic	
Aorta	100 mmHg
Head	50 mmHg
Feet	180 mmHg

Pulmonary	
Mean PA	**15 mmHg**
Apex	**2 mmHg**
Base	**25 mmHg**

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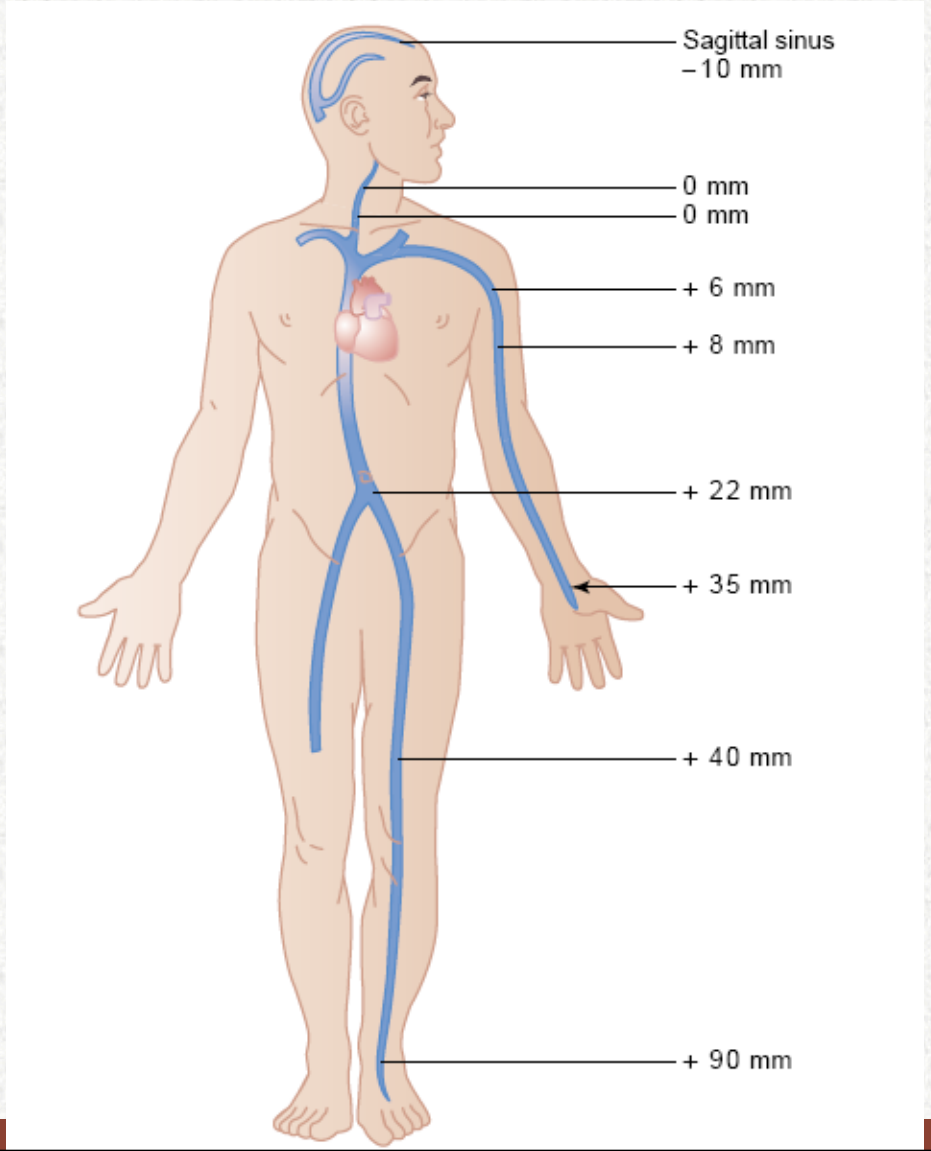
Effect of hydrostatic pressure on venous pressure in the standing position



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Difference between pulmonary capillary & that of systemic

	Pulmonary capillary	Systemic capillary
Pc	10 mm Hg	17 mm Hg
Πc	28 mmHg	28 mmHg
Pi	- 5 mmHg	Zero
Πi	14 mmHg*	7 mmHg

:
*

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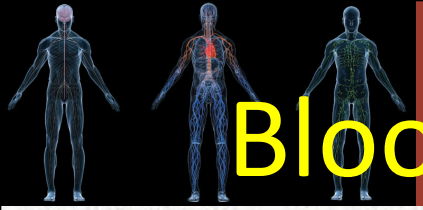

Blood Flow to Different Organs

Tissue	Blood flow (ml/g/min)	A-V O_2] difference (Vol %)	Flow ml/min	O_2 consumption ml/min
Heart	0.8	11	250	27
Brain	0.5	6.2 (25-30% Extraction)	750-900	
Skeletal Muscle	0.03	6	1200	70
Liver	0.6	3.4 Reconditioner organ		
SKIN	0.1			
Kidney	4.2	1.4 Reconditioner organ	1250	18
Carotid bodies	20	0.5 Reconditioner organ	0.6	

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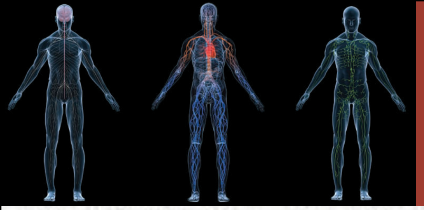

The composition of alveolar air reflects the harmony by which respiratory & cardiovascular systems are working: Ventilation: Perfusion Ratio (V/Q).

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Pressure in the different areas of the lungs

- At the top, 15 mm Hg less than the pulmonary arterial pressure at the level of the heart
- At the bottom, 8 mm Hg greater than the pulmonary arterial pressure at the level of the heart.
- 23 mm Hg pressure difference between the top and the bottom of the lung
- These differences have effects on blood flow through the different areas of the lungs.

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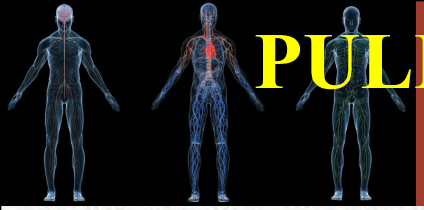

PULMONARY RESISTANCE TO FLOW

- Pressure drop of 12 mmHg (P_m-P_{RA})
- Flow of 5 l/min
- Resistance 1/7 systemic circulation

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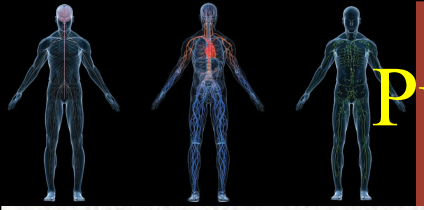

Pulmonary Capillary Dynamics

- **Outward Forces**
  - Pulmonary capillary pressure 10 mmHg
  - Interstitial colloid osmotic pressure 14 mmHg
  - Negative interstitial pressure 5 mmHg
  - **Total 29 mmHg**
- **Inward Forces**
  - Plasma osmotic pressure 28 mmHg
- **Net filtration pressure 1 mmHg**
- **Lymphatic vessels take care of this extra filtrate**
- There is plenty lymphatics which empty in the right lymphatic duct to prevent the occurrence of pulmonary edema. The left apex empties in the thoracic duct.

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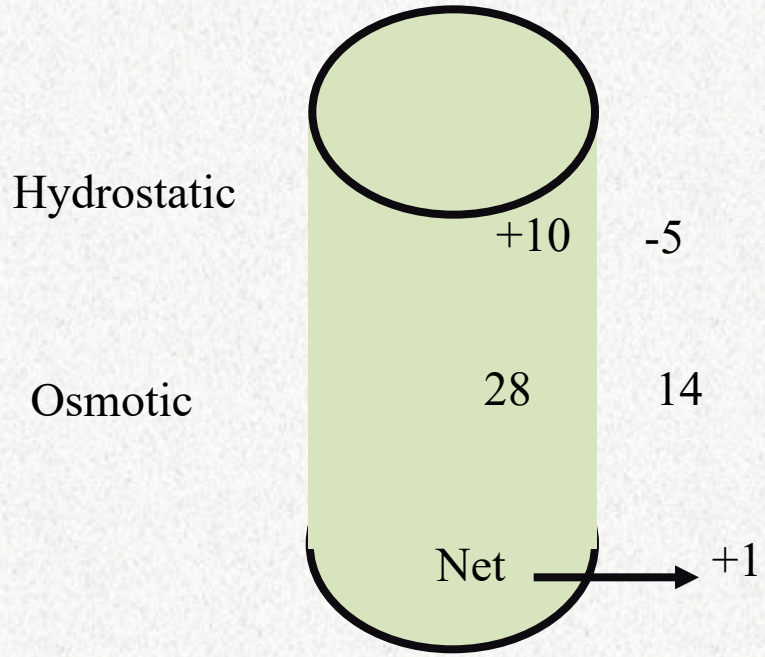
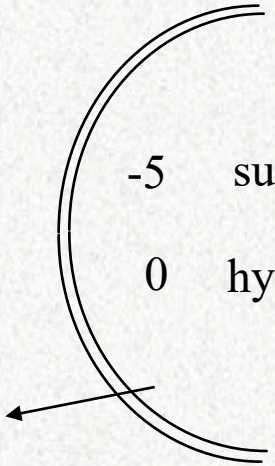
Pulmonary Capillary Dynamics





Lymphatic pump…mainly Rt lyn

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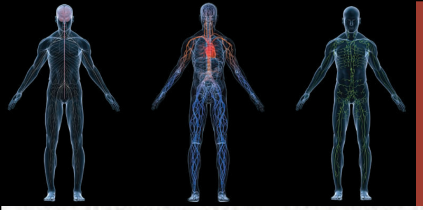
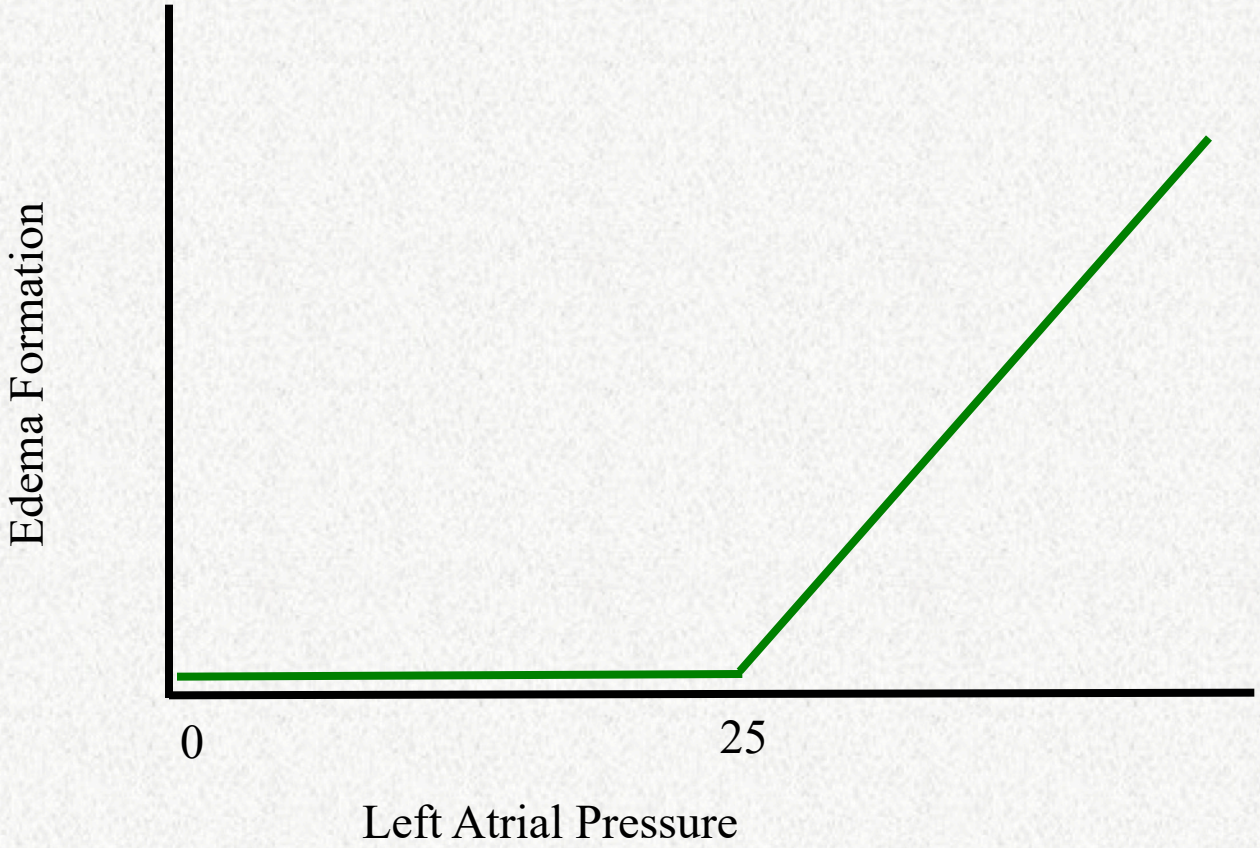


Heart Failure and Pulmonary Edema



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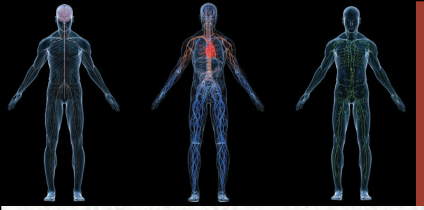

Pulmonary Edema

- Causes of pulmonary edema
  - left heart failure
  - damage to pulmonary membrane: infection or noxious gas such as , chlorine, sulfur dioxide
- Safety factor
  - negative interstitial pressure
  - lymphatic pumping

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Three Zones of Pulmonary Blood Flow

- The alveolar capillaries are distended by the blood pressure inside them and compressed by the alveolar air pressure on their outsides.
- If the alveolar air pressure (Palv) becomes greater than the pulmonary capillary blood pressure (Ppc), the capillaries will close and there is no blood flow.
- There are three possible *patterns* of blood flow (zones of pulmonary blood flow) under different normal and pathological lung conditions.

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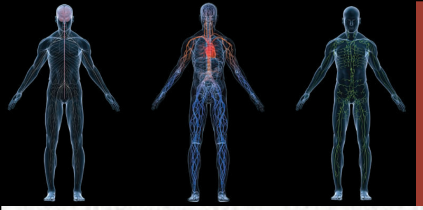
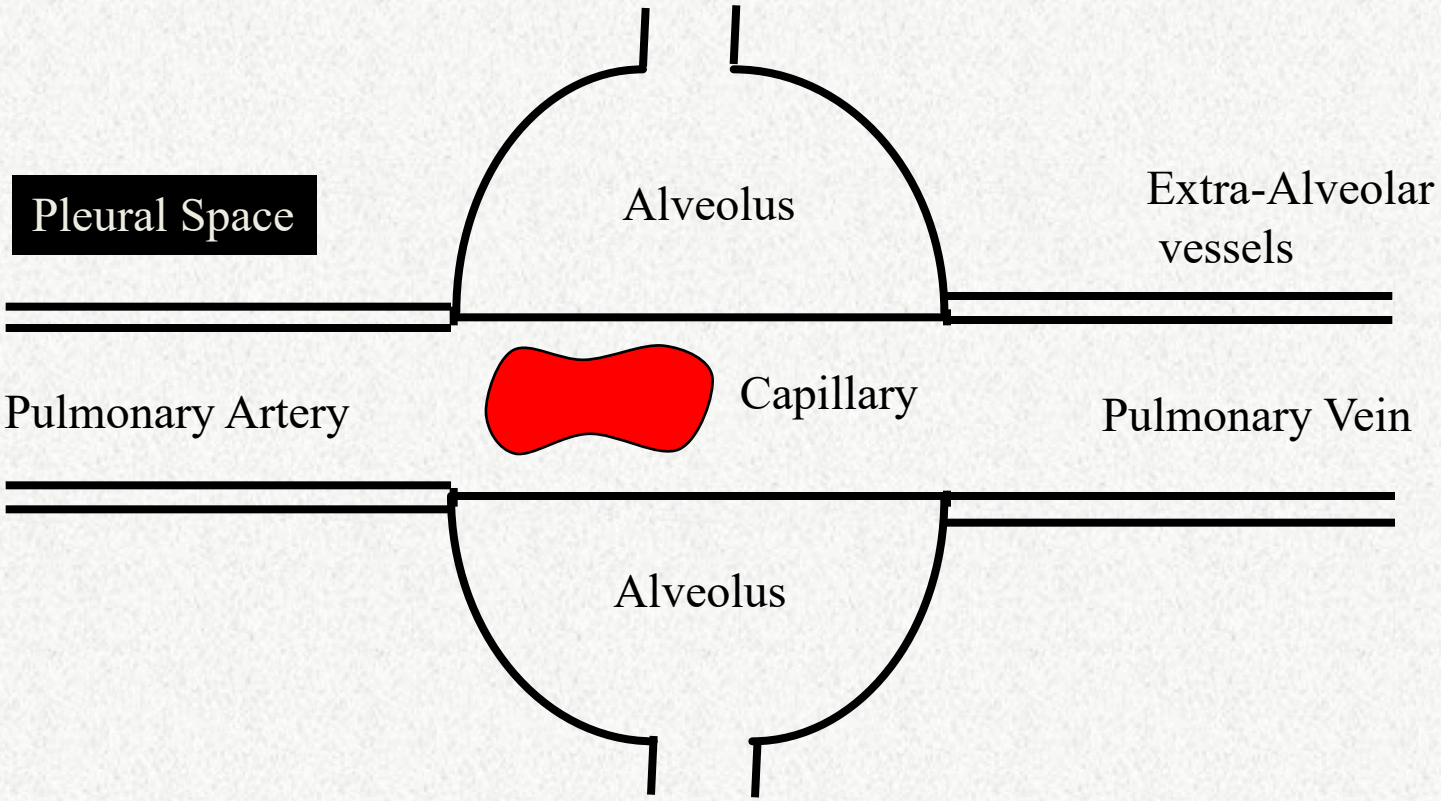


ALVEOLAR and "EXTRA-ALVEOLAR" VESSELS



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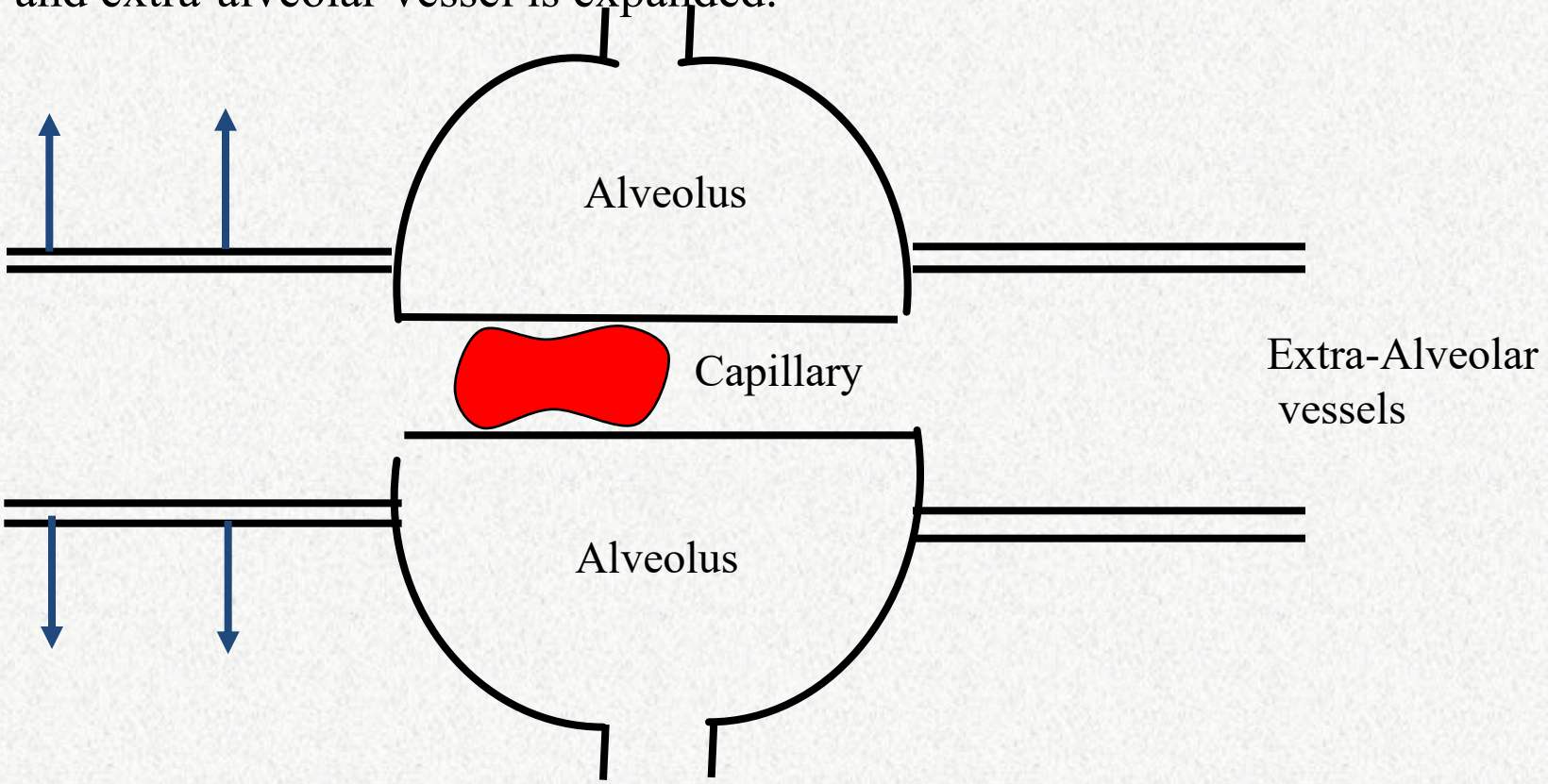
ALVEOLAR and "EXTRA-ALVEOLAR" VESSELS

Pleural Pressure (-)….during inflation…alveolar capillary is compressed and extra-alveolar vessel is expanded.



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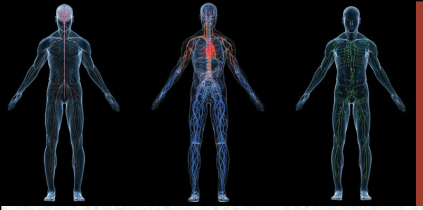

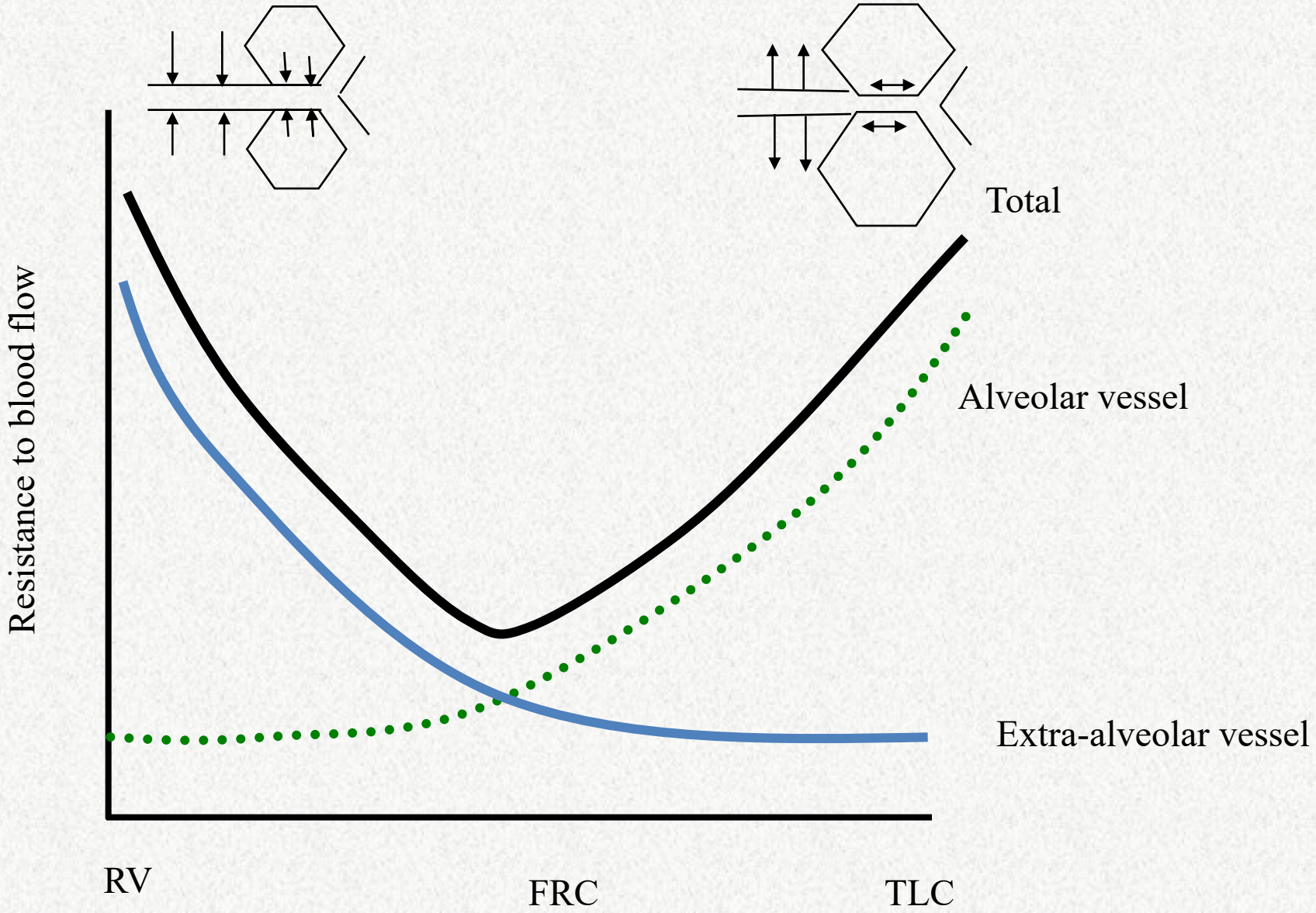

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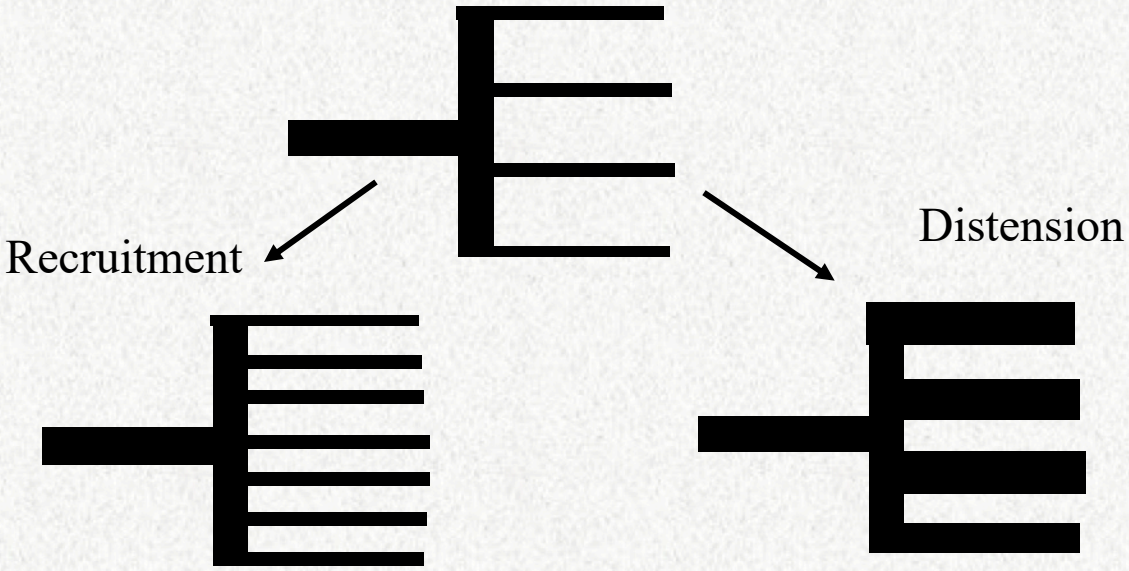
Recruitment and Distension increases Pulmonary blood flow

Pulmonary blood vessels are much more compliant than systemic blood vessels. Also the system has a remarkable ability to promote a decrease in resistance as the blood pressure rises.

***This achieved by two mechanisms*:**

Recruitment: by increasing the number of open capillaries

Distension: by distending all the capillaries and increasing the rate of flow



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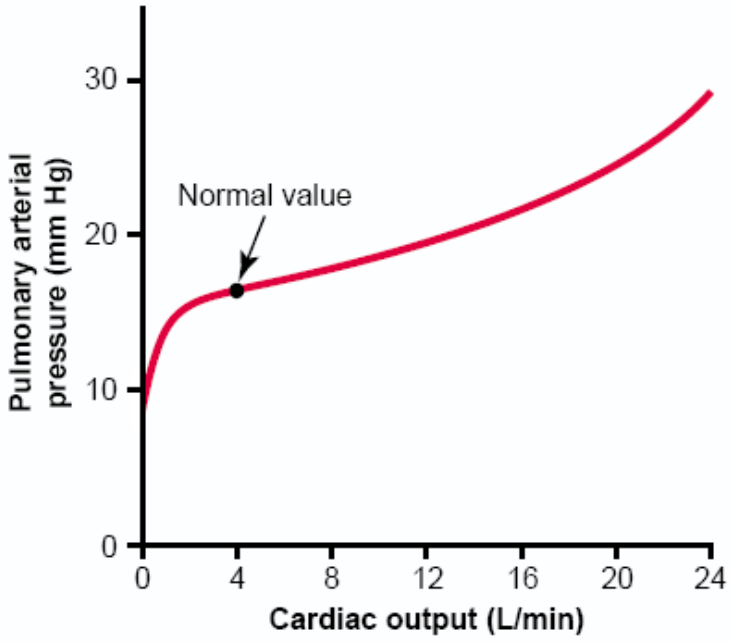
Effect of Increased Cardiac Output on Pulmonary Blood Flow and Pulmonary Arterial Pressure During Heavy Exercise

Recruitment and Distension decrease pulmonary vascular resistance, so that the pulmonary arterial pressure rises very little even during maximum exercise. During Exercise, Q might increase 5 times but still Pm increase slightly because of the decrease in pulmonary vascular resistance.



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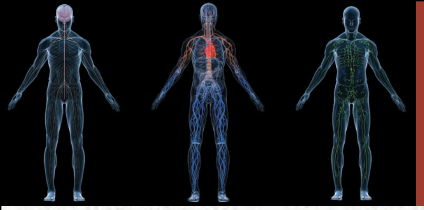

PULMONARY BLOOD FLOW

- Blood Volume…the numbers were given to you in the first lecture Wednesday…do you remember?
  - Approximately 450 ml
  - 190 ml in the arterial part
  - 190 ml in the venous part
  - 70 ml inside the capillaries
  - Some of this blood Can shift to systemic circulation

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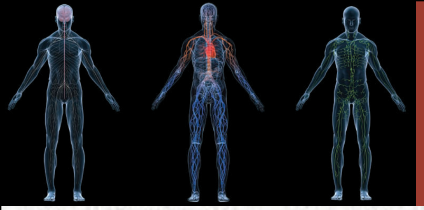

MEASUREMENT OF PULMONARY BLOOD FLOW

Fick Principle for cardiac output estimation…this slide and the next slide was discussed in the cardiovascular system module…"**cardiac output estimation**"… we don't need to discuss this slide and the next one in the respiratory module

$$V_{O_2} = Q(Ca_{O_2} - Cv_{O_2})$$

V_{O_2} = Oxygen Consumption

Ca_{O_2} = Arterial Content

Q = Blood flow

Cv_{O_2} = Venous Content

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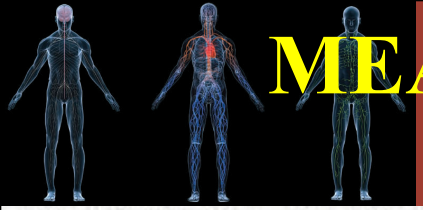

MEASUREMENT OF PULMONARY BLOOD FLOW

$$V_{O_2} = Q(Ca_{O_2} - Cv_{O_2})$$

Ca_{O_2} = 20 ml O_2/100 ml blood

V_{O_2} = 250 ml/min

Cv_{O_2} = 15 ml O_2/100 ml blood

$$Q = \frac{250 \text{ ml } O_2/\text{min}}{(20\text{-}15) \text{ ml } O_2/100 \text{ ml blood}} = \frac{250 \text{ ml } O_2}{\text{min}} * \frac{100 \text{ ml blood}}{5 \text{ ml } O_2}$$

$$Q = 5000 \text{ ml blood /min}$$

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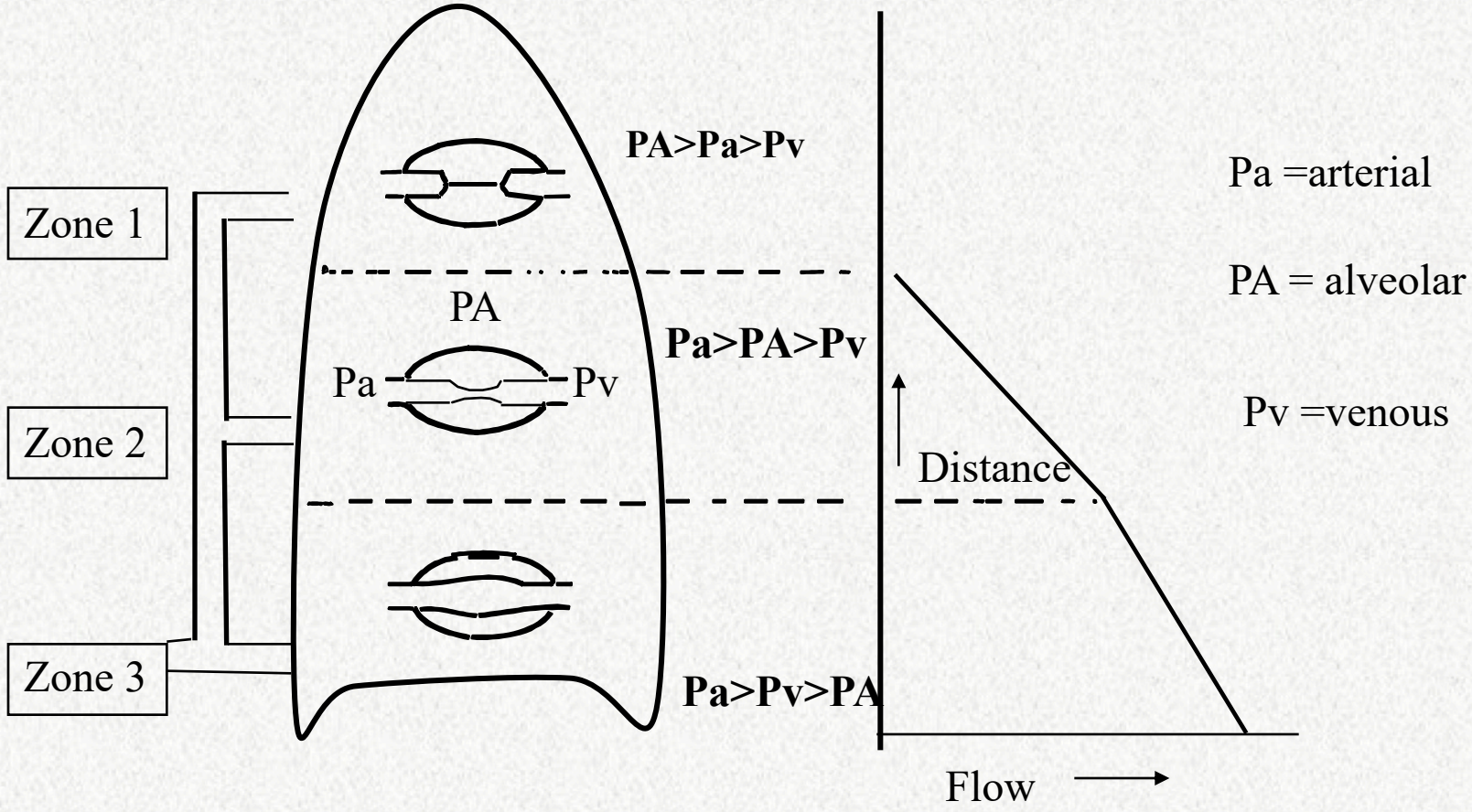
Hydrostatic Effects on Blood Flow



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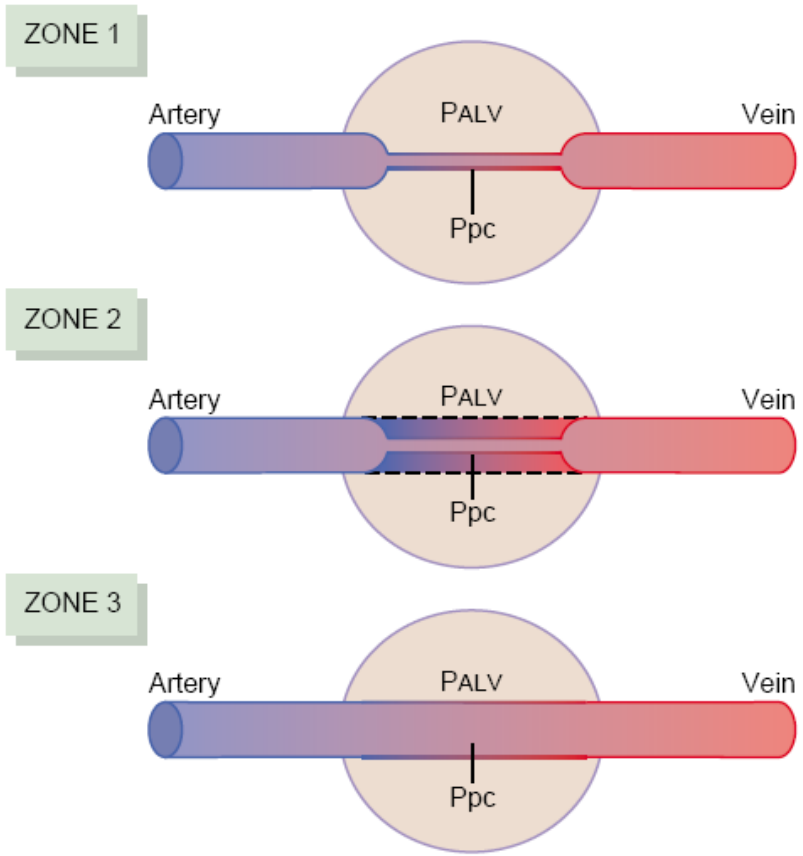
Zones of Pulmonary Blood Flow



- *Zone 1:*
  - ✓ ***no flow***
  - ✓ alveolar air pressure (Palv) is higher than pulmonary arterial pressure (Ppc) during any part of cardiac cycle…This zone does not exist in human lung.
- *Zone 2:*
  - ✓ ***intermittent flow***
  - ✓ systolic arterial pressure higher than alveolar air pressure, but diastolic arterial pressure below alveolar air pressure.
- *Zone 3:*
  - ✓ ***continuous flow***
  - ✓ pulmonary arterial pressure (Ppc) remain higher than alveolar air pressure at all times.

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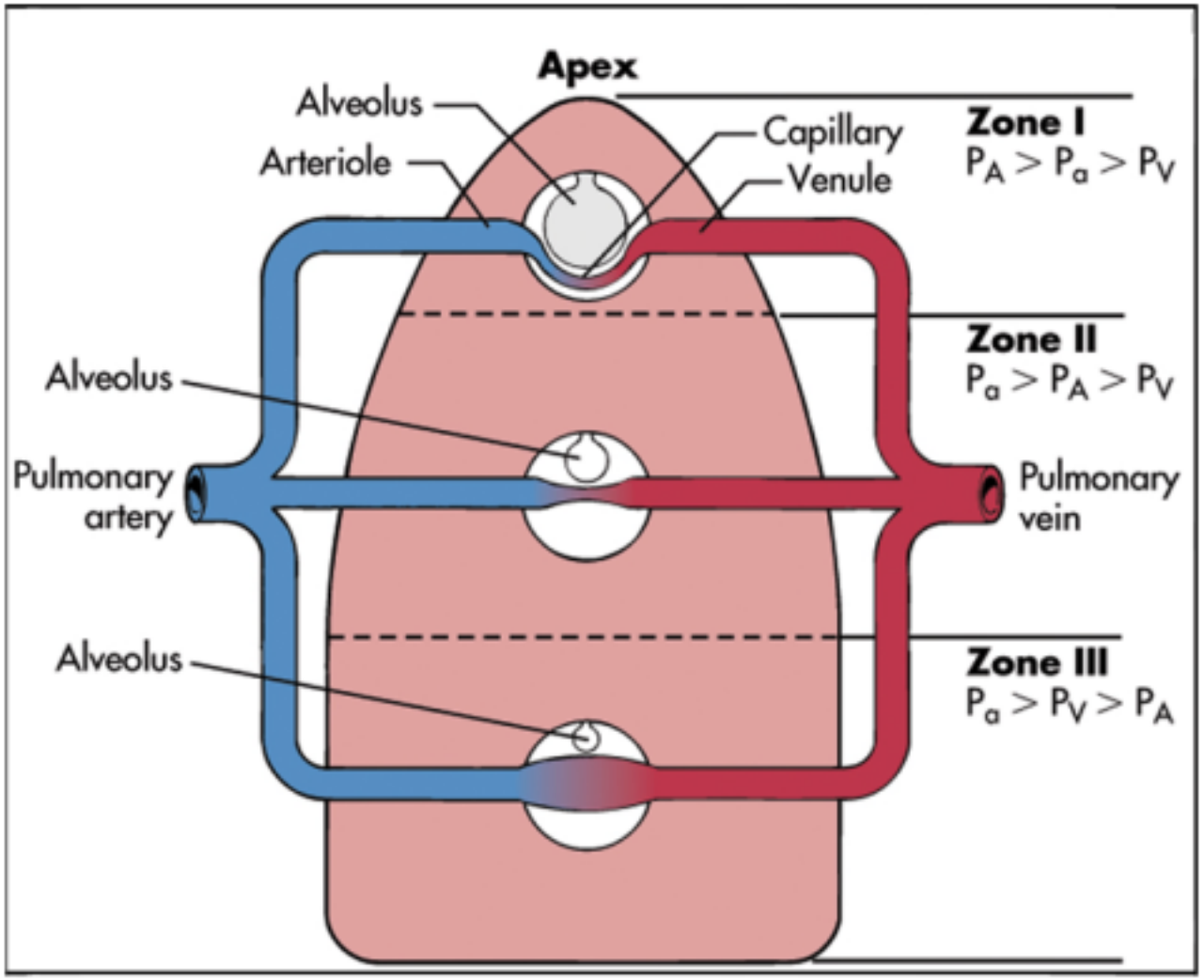
Zones of Pulmonary Blood Flow



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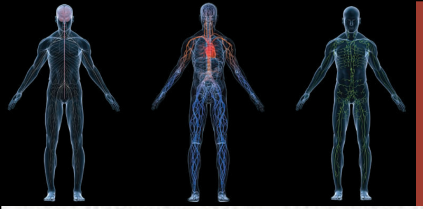

Zones of a normal lung

- Normally, the lungs have 2 zones for blood flow
  - zone 2 (intermittent flow) at the apices.
  - zone 3 (continuous flow) in all the lower areas.
- In normal lungs, Zone 2 begins 10 cm above the mid-level of the heart to the top of the lungs.

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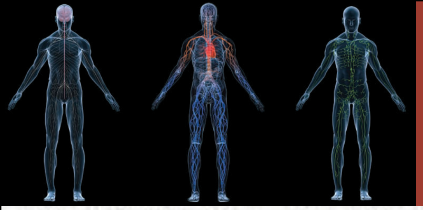
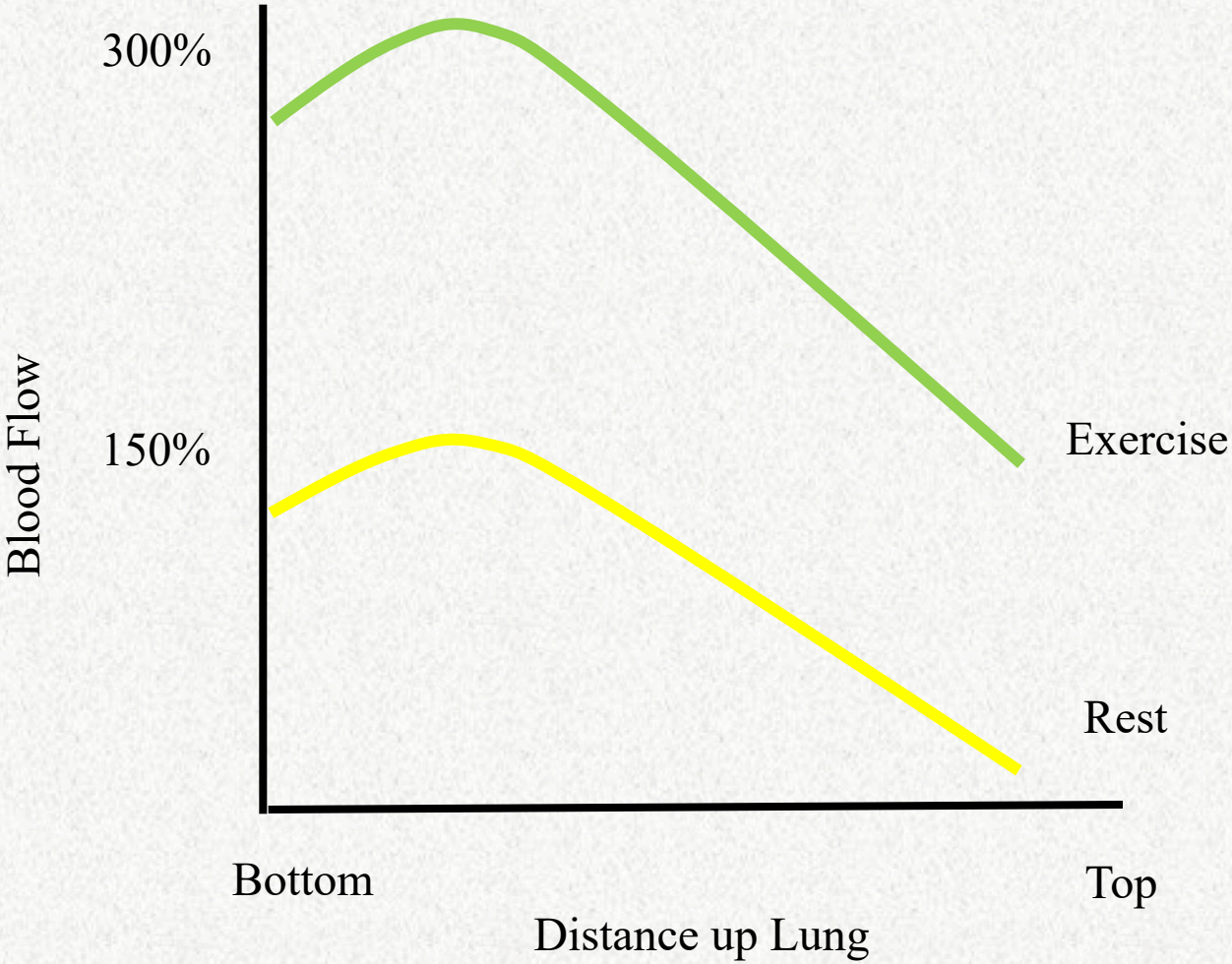


DISTRIBUTION OF BLOOD FLOW



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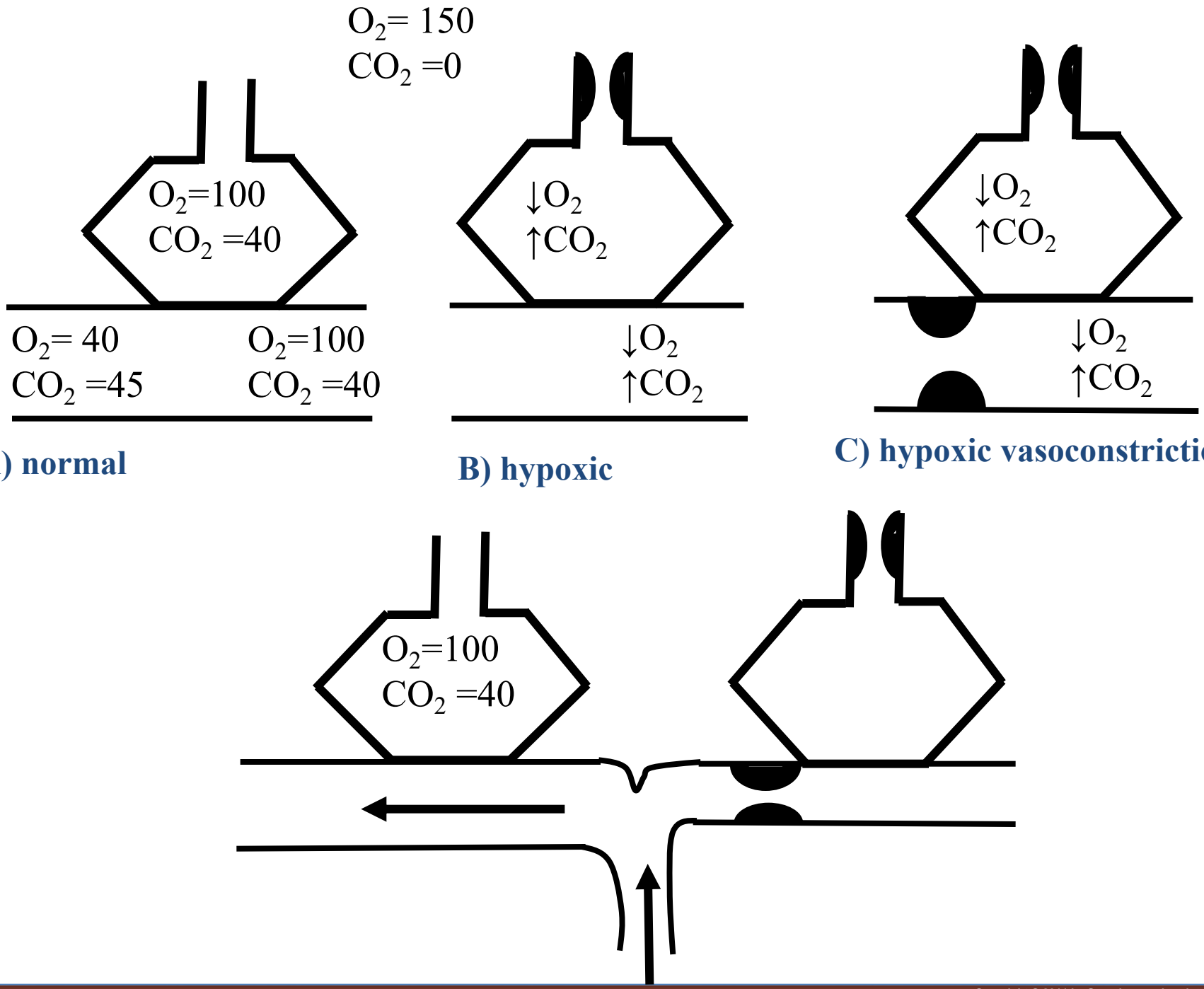

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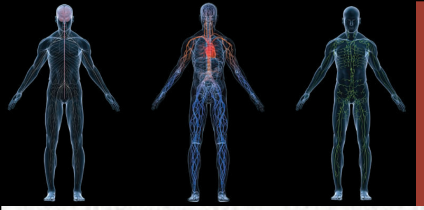

Pulmonary Circulation

- Rate of blood flow through the pulmonary circulation is = rate of flow through the systemic circulation.
  - Driving pressure in pulmonary circulation is only 10 mm Hg.
- Pulmonary vascular resistance is low.
  - Low pressure pathway produces less net filtration than produced in the systemic capillaries.
    - Avoids pulmonary edema.
- Autoregulation:
  - Pulmonary arterioles constrict when alveolar PO_2 decreases.
  - Matches ventilation/perfusion ratio.

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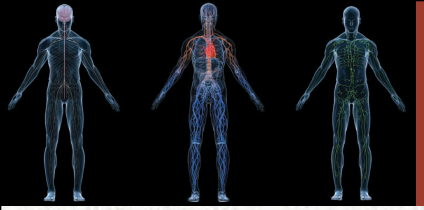

Lung Ventilation/Perfusion Ratios

- Functionally:
  - Alveoli at apex are underperfused (overventilated).
  - Alveoli at the base are underventilated (overperfused).

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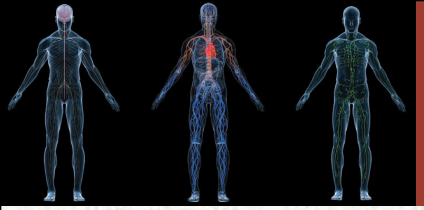
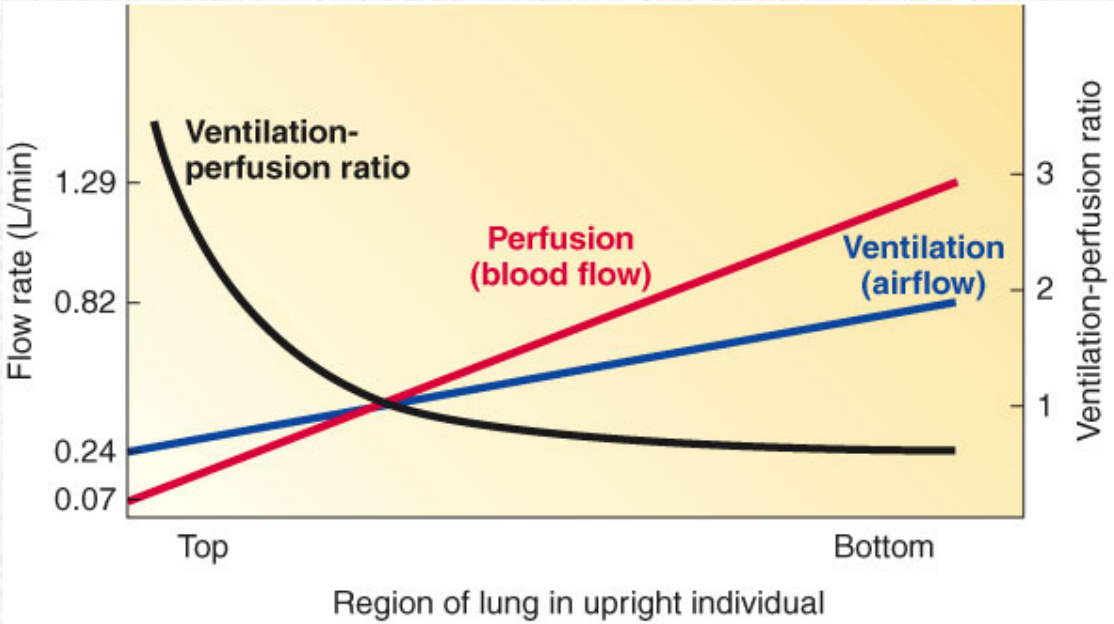
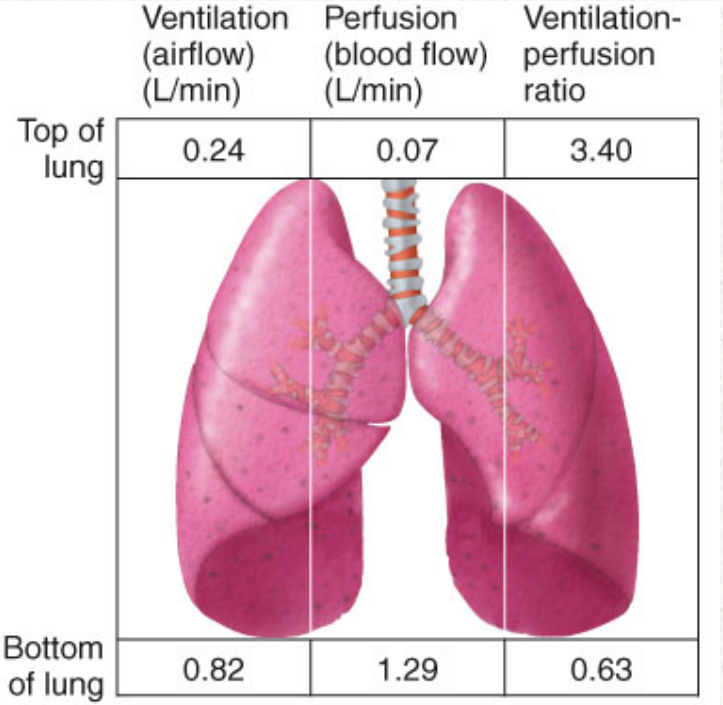
	Ventilation (L/min)	Blood flow (L/min)	Ratio
Apex	0.24	0.07	3.40
Base	0.82	1.29	0.63





(a) Regional ventilation and perfusion rates and ventilation-perfusion ratios in the lungs



(b) Ventilation and perfusion rates and ventilation-perfusion ratios at top and bottom of lungs

Fig. 13.24, p. 485

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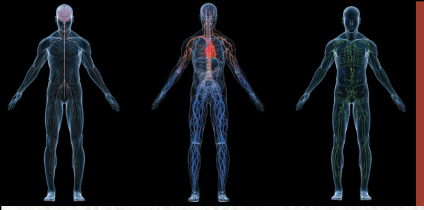
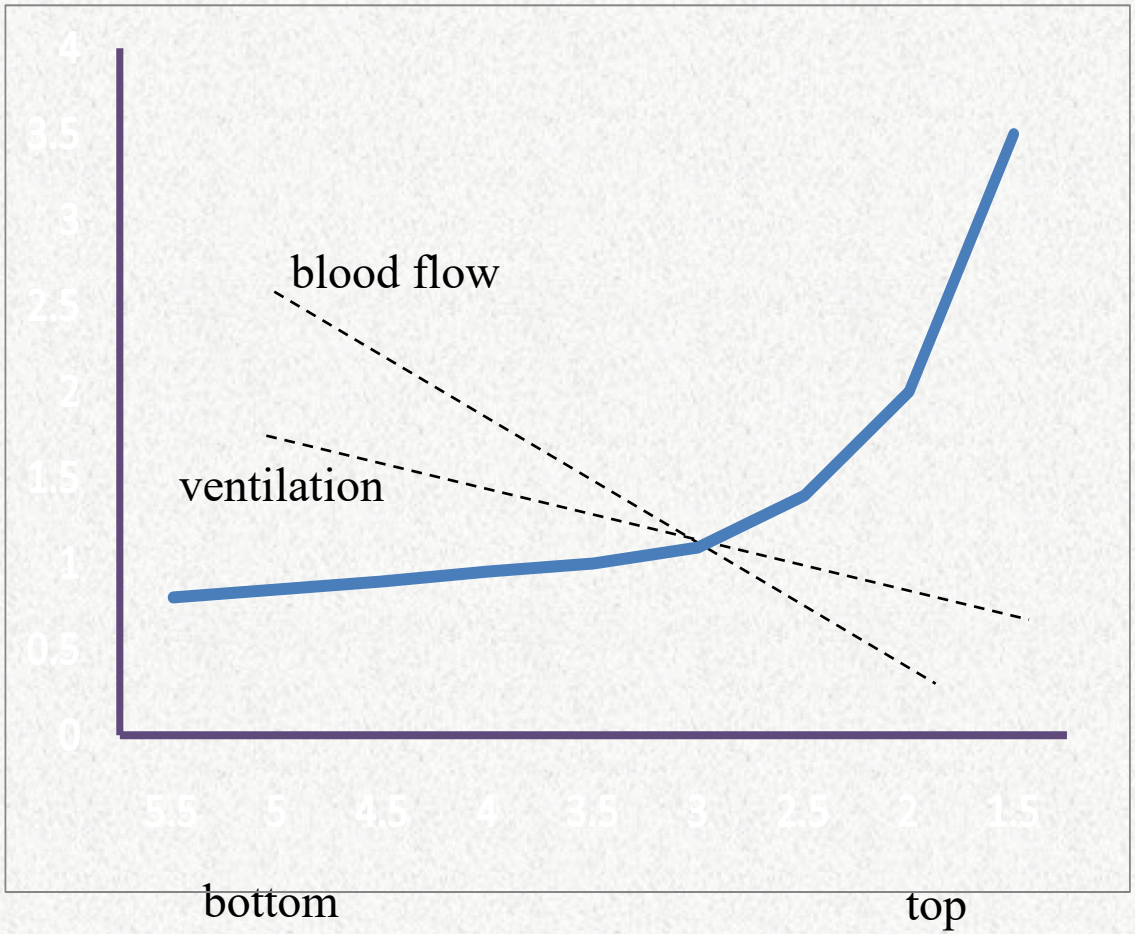


Regional V/Q Ratio



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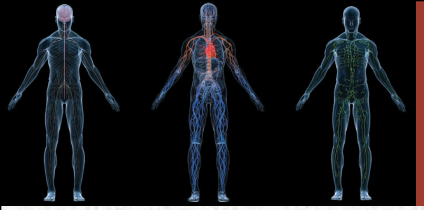

V/Q Ratio

- V/Q is ↑ in:
- 1. pulmonary embolism.
- 2. emphysema.
- 3. cigarette smokers.
- 4. pulmonary hyperventilation
- Whenever V/Q ↑
- 1. alveolar dead space ↑.
- 2. mixed expired P_ECO_2 ↓.
- 3. mixed expired P_EO_2 ↑.

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Question

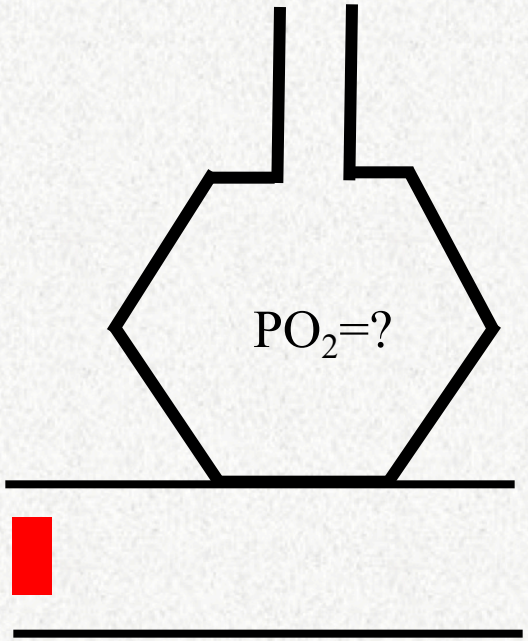
An alveoli that has normal ventilation and no blood flow (V/Q=0) has an alveolar PO_2 of

A. 40 mmHg

B. 100 mmHg

C. 149 mmHg

D. 159 mmHg



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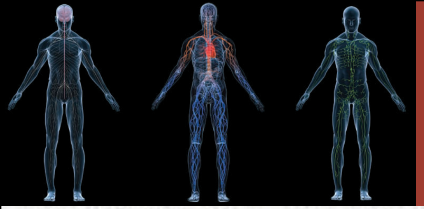

Ventilation/perfusion

- Relationship between adequate flow and adequate ventilation is the V/Q ratio
- V/Q = (4.2 l/min)/ (5 l/min) = 0.84
- If there is no diffusion impairment then the PO_2 and PCO_2 between an alveolus and end capillary blood are usually the same. P_AO_2-P_aO_2≈zero

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Ventilation/Perfusion Ratios

- The ratio of alveolar ventilation to pulmonary blood flow = **0.84** (4.2 L/min ÷ 5 L/min).

- When the ventilation (V) is zero, but there is adequate perfusion (Q) of the alveolus, the V/Q is **zero**.
- when there is adequate ventilation, but zero perfusion, the ratio V/Q is **infinity**.
- At a ratio of either zero or infinity, there is no exchange of gases through the respiratory membrane of the affected alveoli

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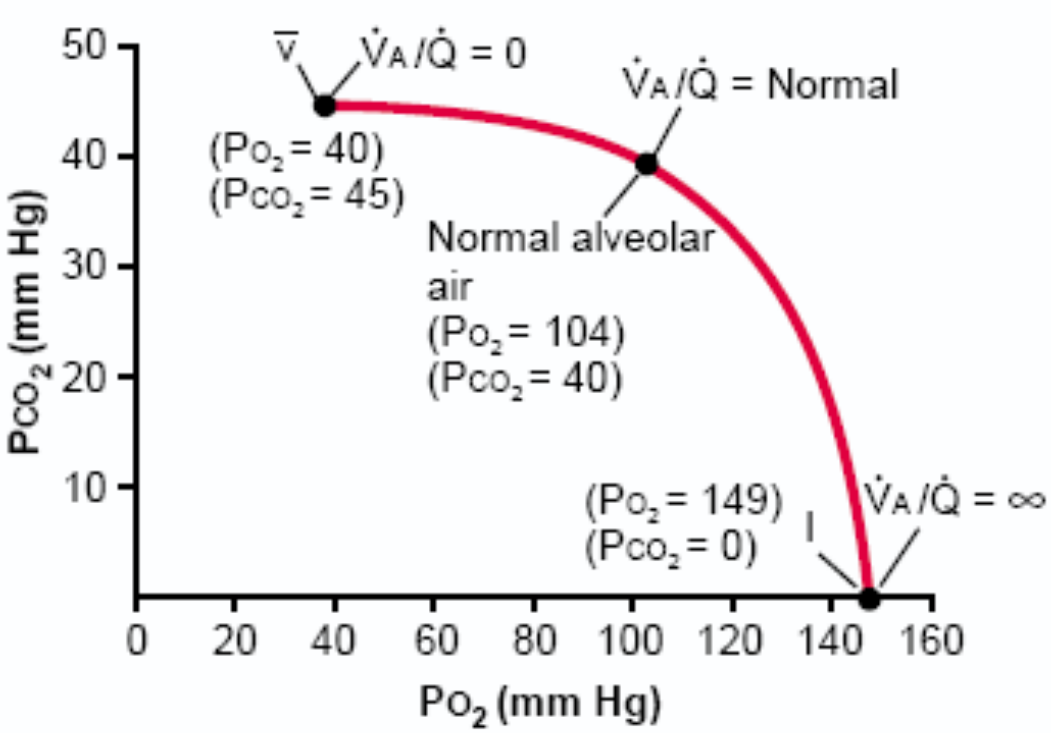
V/Q ratio



physiologic shunt:
The total amount of shunted blood per minute.

physiologic dead space:
Alveolar + anatomical dead spaces

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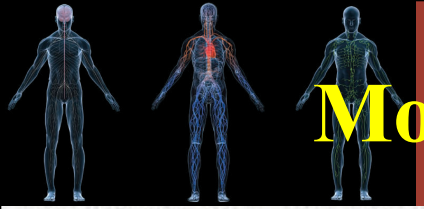

Movement of Air in and Out of Lungs

- Pleural Pressures
  - Resting -4 mmHg
  - Inspiration -6 mmHg
  - In the upright position at rest the basal intrapleural P is

–2 mm Hg, while apical intrapleural P equals –7 mm Hg.

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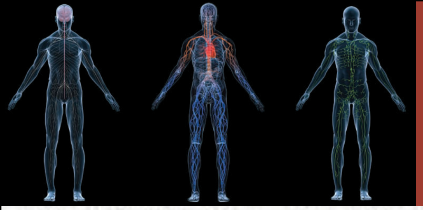

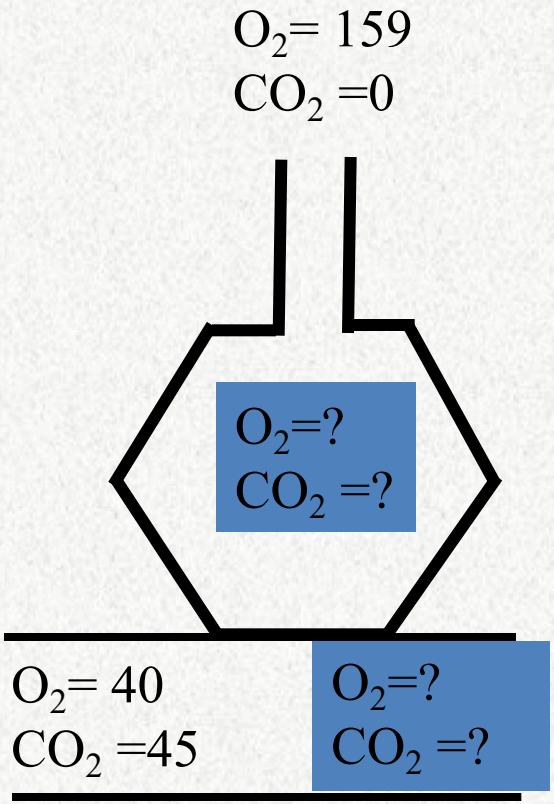

V/Q =0.8

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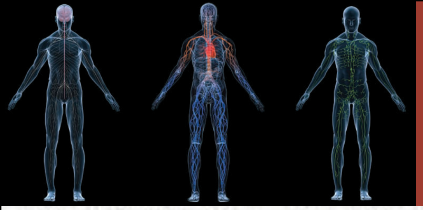

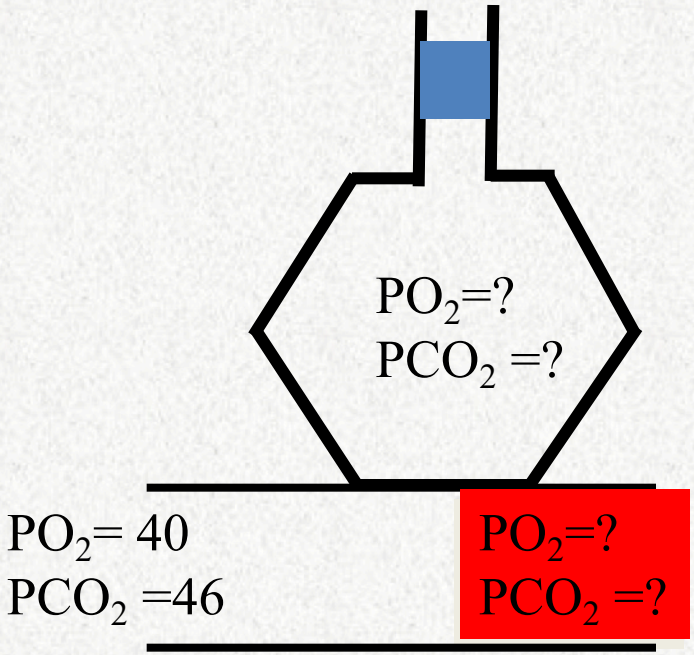

$$V/Q = 0$$

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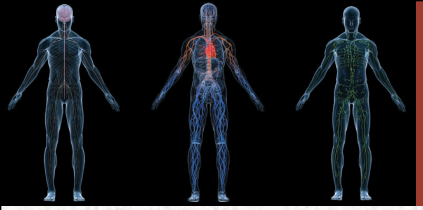

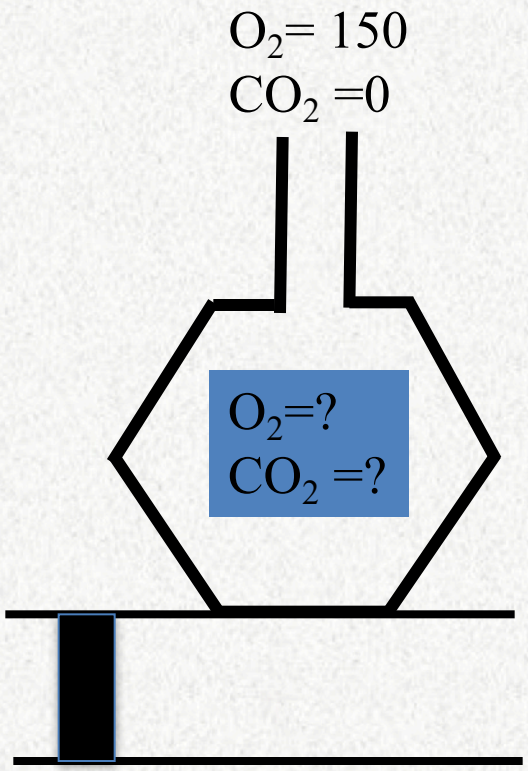

$$V/Q = \infty$$

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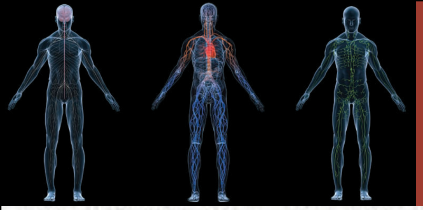

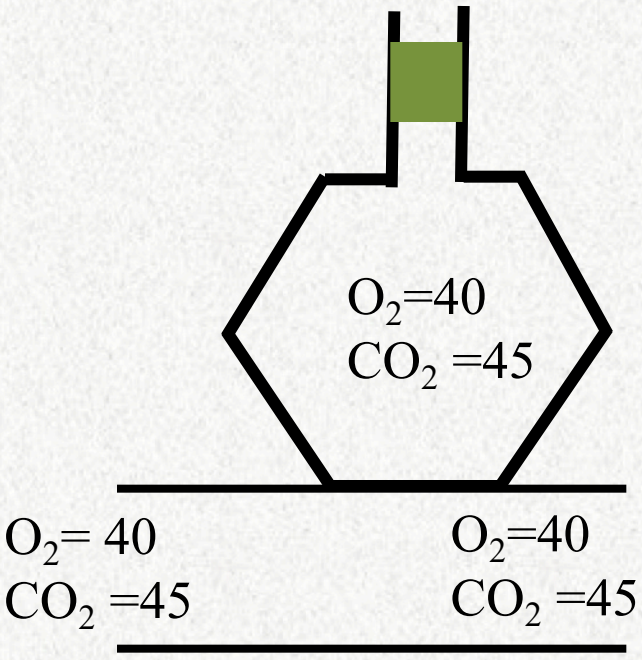

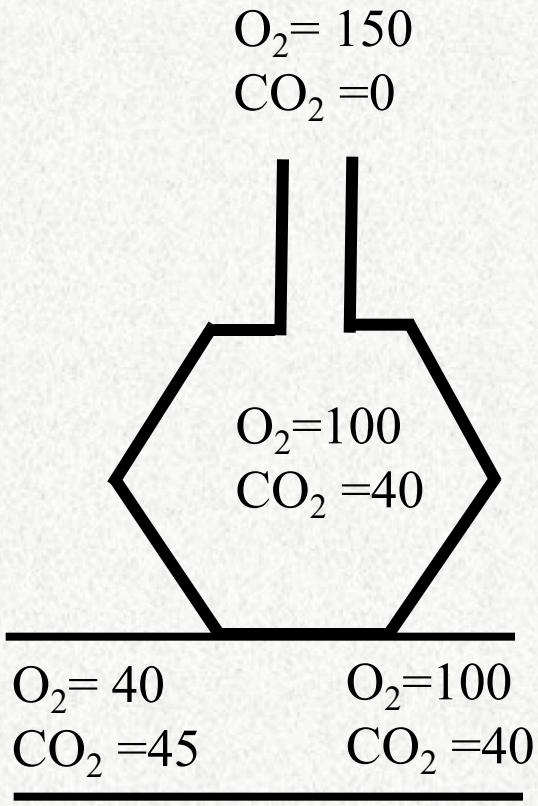

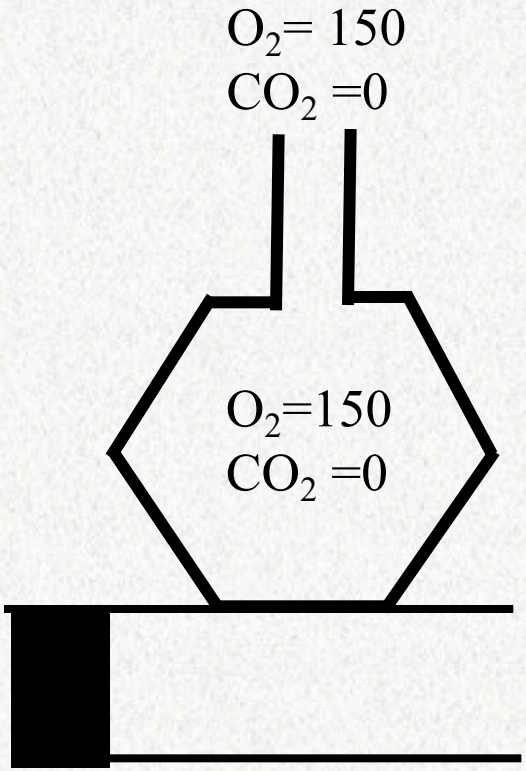

V/Q = 0

V/Q =normal

V/Q = ∞

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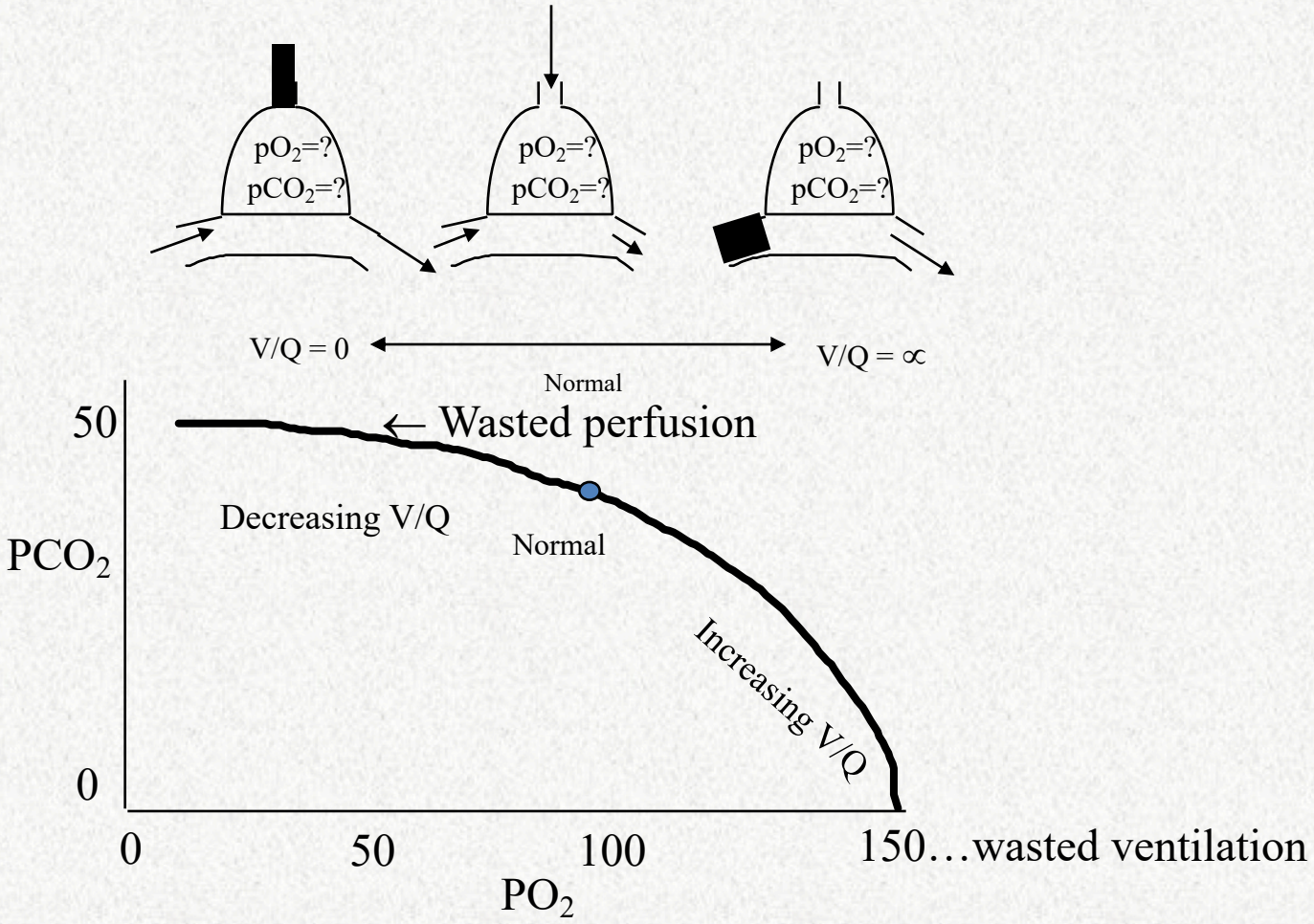
Ventilation/perfusion



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Abnormal VA/Q in the Upper and Lower Normal Lung.

- **Upper part of the lung**
  - Less blood flow and less ventilation; but blood flow is considerably less than ventilation.
  - Therefore, V/Q is 3.4 times higher than the normal value
  - This causes a moderate degree of *physiologic dead space*.
- **The bottom of the lung**
  - Slightly too little ventilation in relation to blood flow
  - Va/Q as low as 0.6 times the normal value.
  - A small fraction of the blood fails to become normally oxygenated, and this represents a *physiologic shunt*.
  - Assuming perfusion is adequate … hyperventilation makes alveolar air like atmospheric air …. Hypoventilation makes alveolar air like venous blood.

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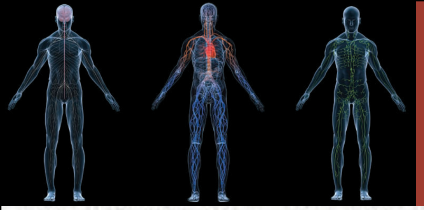

V/Q ratio

- Physiologic shunt
  - V/Q ration is less than normal bcs of low ventilation
- Physiologic dead space…alveolar wasted volume
  - V/Q > normal
- Abnormalities
  - Upper lung V/Q =3
  - Lower lung V/Q =0.5

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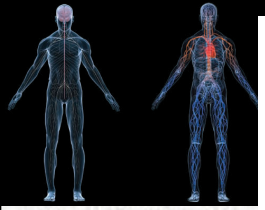
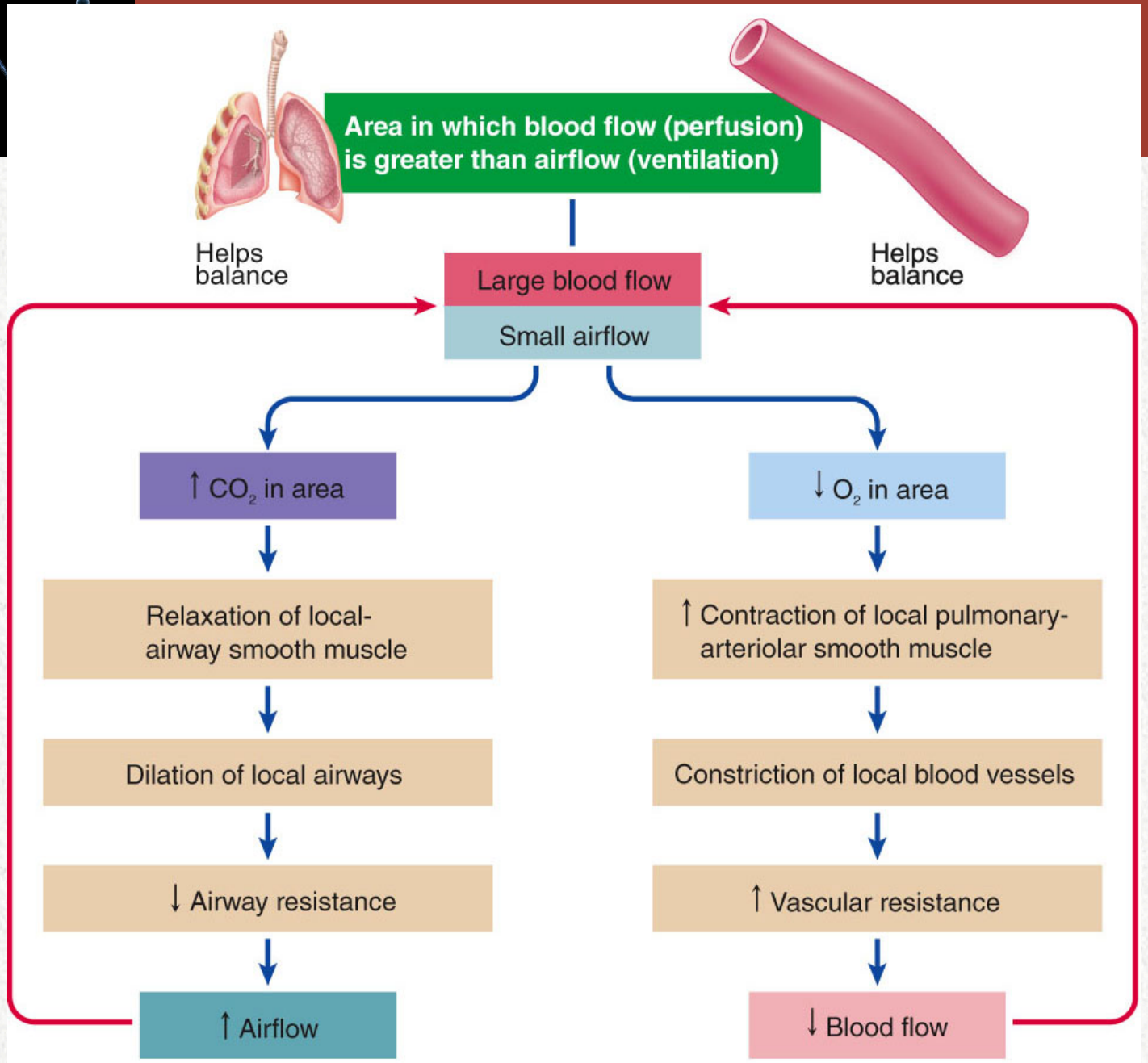
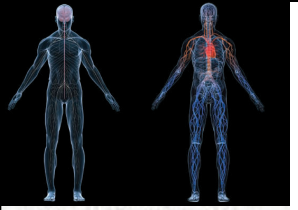
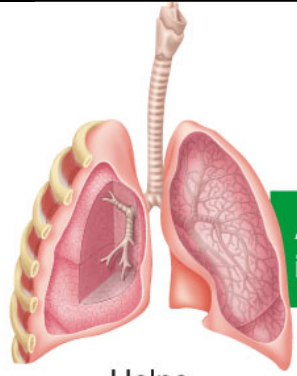




(a) Local controls to adjust ventilation and perfusion to lung area with large blood flow and small airflow

Fig. 13-23a, p. 484





(b) Local controls to adjust ventilation and perfusion to a lung area with large airflow and small blood flow

Fig. 13.23b, p. 484

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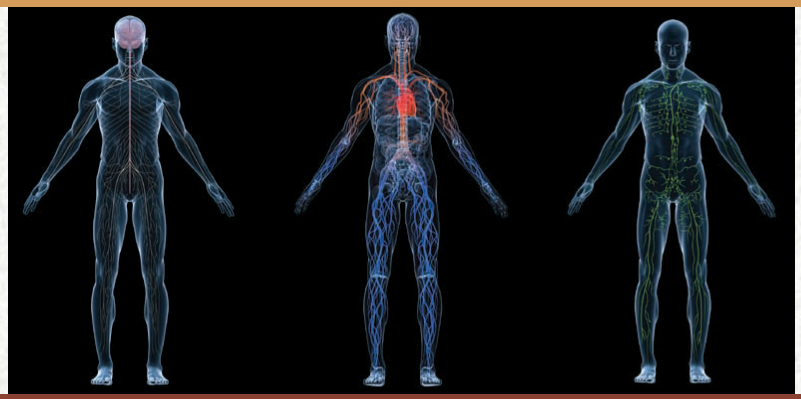
UNIT VII

GUYTON AND HALL *Textbook of*

Medical Physiology

TWELFTH EDITION



Chapter 40:

Transport of Oxygen and Carbon Dioxide in Blood and Tissue Fluids

Slides by Robert L. Hester, PhD

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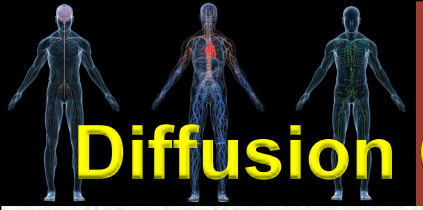

Diffusion Capacity of The Respiratory Membrane

It is the volume of gas that diffuses through the membrane each minute for pressure difference of one mm Hg.

- Normal value for O_2 is **21** ml/min/mm Hg
- Normal value for CO_2 is about 20 times greater than O_2.
- During muscular exercise, increase 2-3 times due to
  - recruitment and distension of capillaries.
  - Improvement in ventilation/ Perfusion ratio
- Lungs receive blood from
  - Pulmonary artery - deoxygenated blood
  - Bronchial arteries – oxygenated blood to perfuse muscular walls of bronchi and bronchioles

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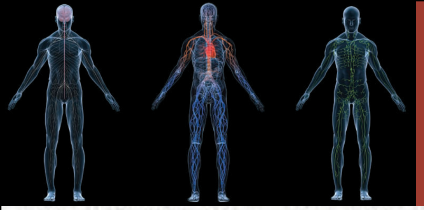

Respiratory Membrane

1. The gases of respiratory importance are highly soluble in lipids. Therefore they can easily diffuse through tissues, including the respiratory membrane….. The respiratory membrane is composed of 6 layers: Thickness is only 0.25 – 0.6 μ. to allow rapid diffusion of gases

- A layer of slight fluid lining the alveolus and containing surfactant
- Alveolar epithelium
- Epithelial basement membrane
- Interstitial space
- Capillary basement membrane
- Capillary endothelial membrane.

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Factors affecting the rate of gas diffusion through The respiratory membrane

- **The surface area of the membrane is 50-100 m^2..difficult to estimate**
- **The pressure difference across the respiratory membrane….this also is very difficult to estimate**
- **Diffusion coefficient:** depends on its **solubility** of the gas and square root of its **molecular weight** (makes MW least important factor)…easy to estimate

Diff.Coef= (Gas's solubility / √ MW)

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Basics of the Respiratory System

- Characteristics of exchange membrane
  - High volume of blood through huge capillary network results in
    - **Low vascular resistance through lungs**
      - **P**ulmonary circulation = 5L/min through lung
      - Systemic circulation = 5L/min through entire body
    - Pulm.Capillary hydrostatic blood pressure is low (7-10 mmHg)
    - This Means
      - » Filtration is not a main theme here, we do not want a net loss of fluid into the lungs as rapidly as the systemic tissues
      - » Any excess fluid is still returned via lymphatic system

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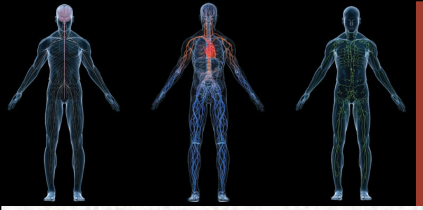

Determinants of Diffusion

Ficks Law

$$\text{Diffusion} = \frac{(P_1 - P_2) * \text{Area} * \text{Solubility}}{\text{Thickness} * \sqrt{\text{MW}}}$$

- Pressure Gradient
- Area
- Distance
- Solubility and MW are fixed
- Area and thickness are the characteristic of the membrane
- Solubility and MW are the characteristic of the gas

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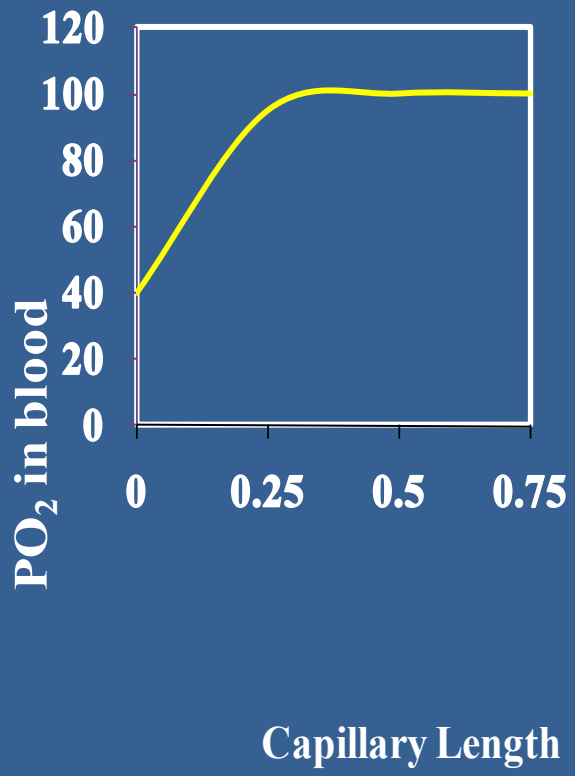
Diffusion Capacity

- Oxygen
  - Diff capacity 22 ml/min/mmHg * gradient of 11 mmHg
  - 250 ml/min diffusion of oxygen



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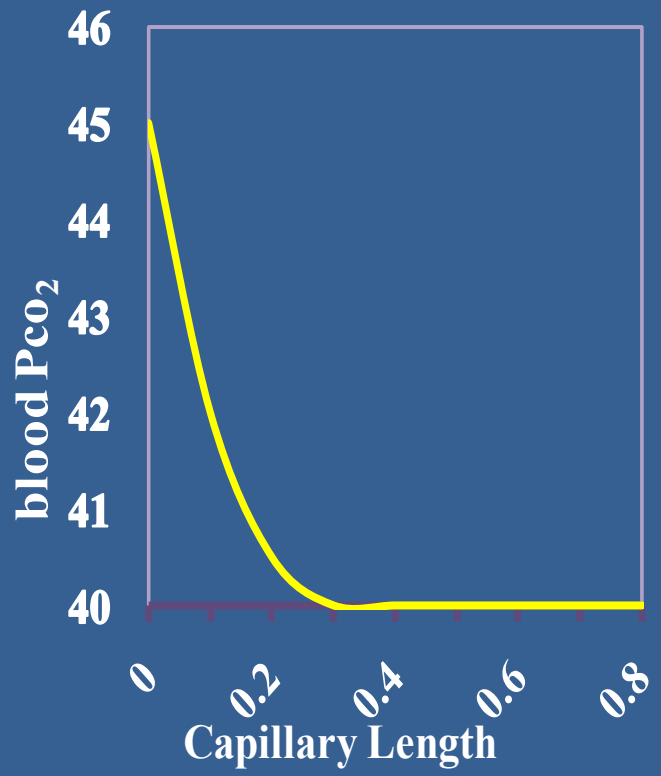
Diffusion Capacity

- Carbon Dioxide
  - Diff capacity 400 ml/min/mm Hg * gradient < 1 mmHg
  - 200 ml/min diffusion of carbon dioxide



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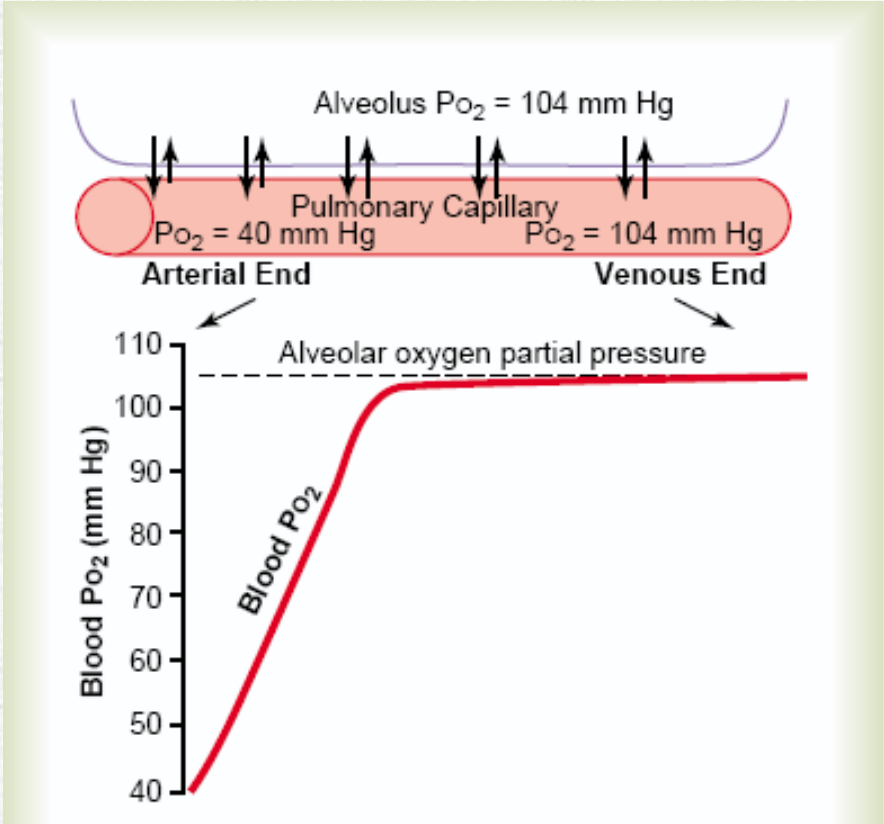
Oxygen Diffusion from the Alveoli to the Pulmonary circulation

- O_2 diffuses into the pulmonary capillaries because the PO_2 in the alveoli is high. Note: O_2 utilizes less than one third of the respiratory membrane…perfusion-limited
- PO_2 in the pulmonary capillaries increased very fast (1/3 distance) it takes 0.3 sec leaving the rest 0.5 sec with no more exchange. In pathophysiology look at the next slide



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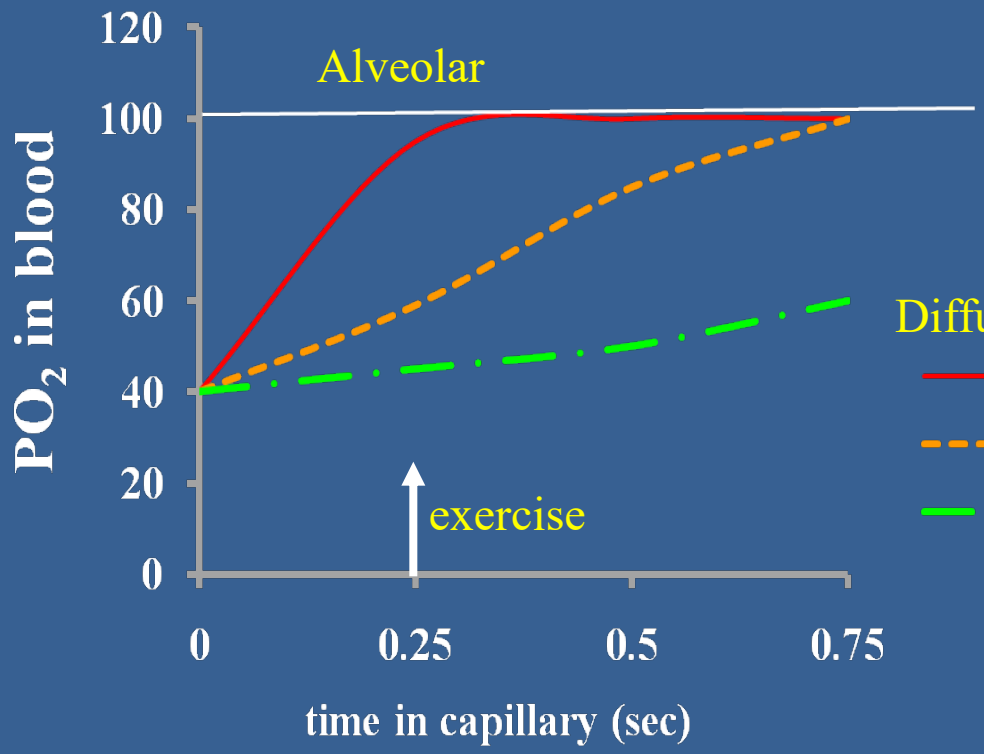
Uptake of Oxygen in Lungs



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Why PO_2 arterial <Alveolar PO_2?

- **P_AO_2 =100 while systemic P_aO_2 is only 95 mm Hg?**
- **1. Venous admixture (pollution)**
- **A. BRONCHIAL Circulation**: 50% goes back to right atrium, and 50% to left atrium.
- **B. Cardiac veins**
- **C. Pulmonary Circulation:** 2% of all venous blood doesn't pass through pulmonary capillaries (A-V anastomosis) "physiological shunted blood".
- **2. Low VA/Q in the base of the lung.**

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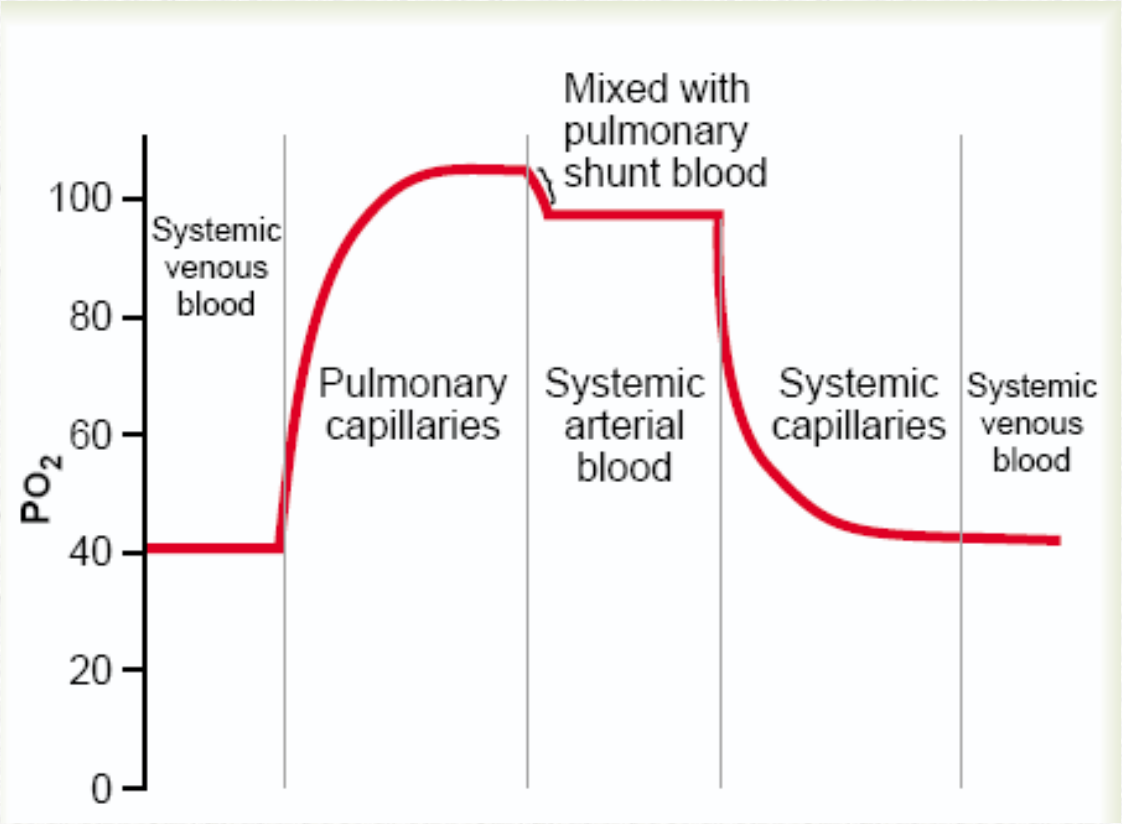
Transport in arterial blood & Pulmonary shunt flow

Due to the bronchial circulation the arterial PO_2 falls to 95 mm Hg



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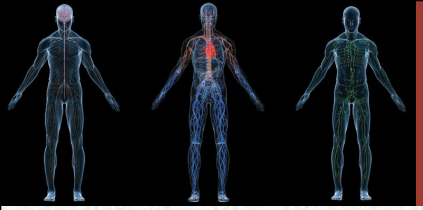
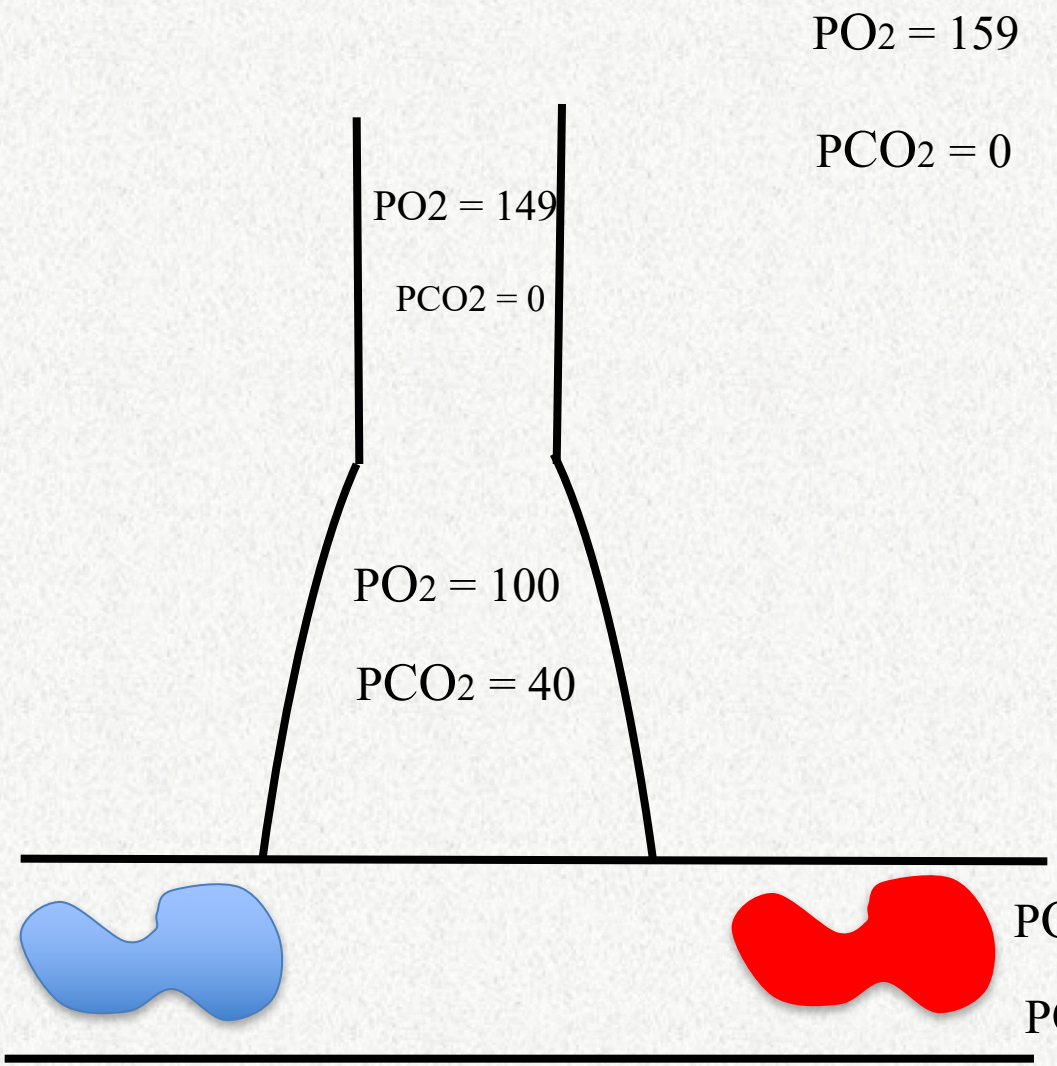


Alveolar and Blood Gases



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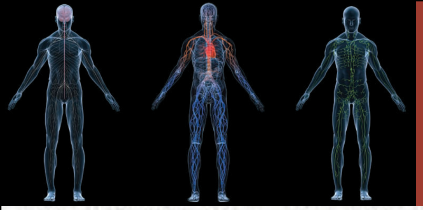
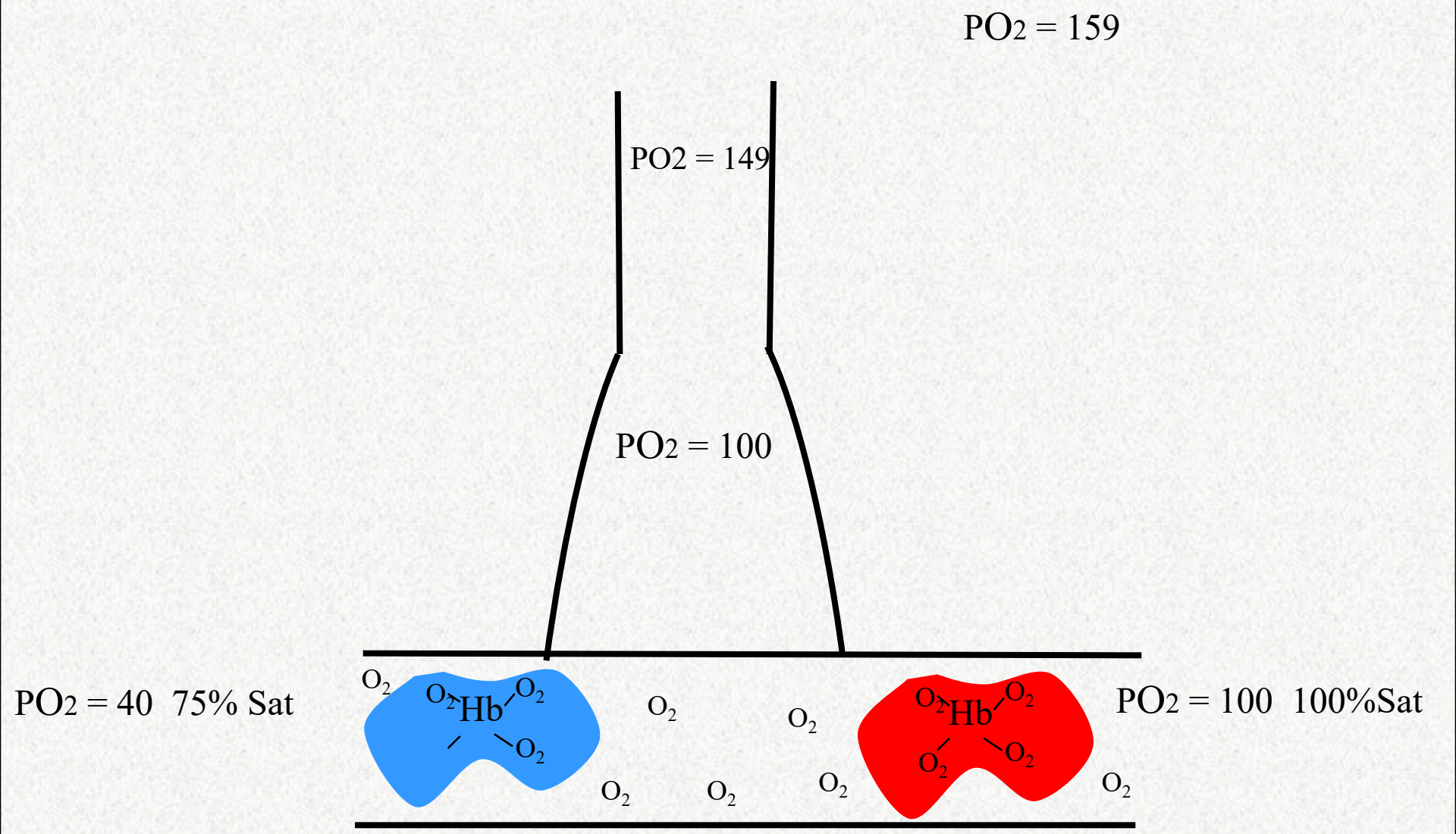


Alveolar and Blood PO_2



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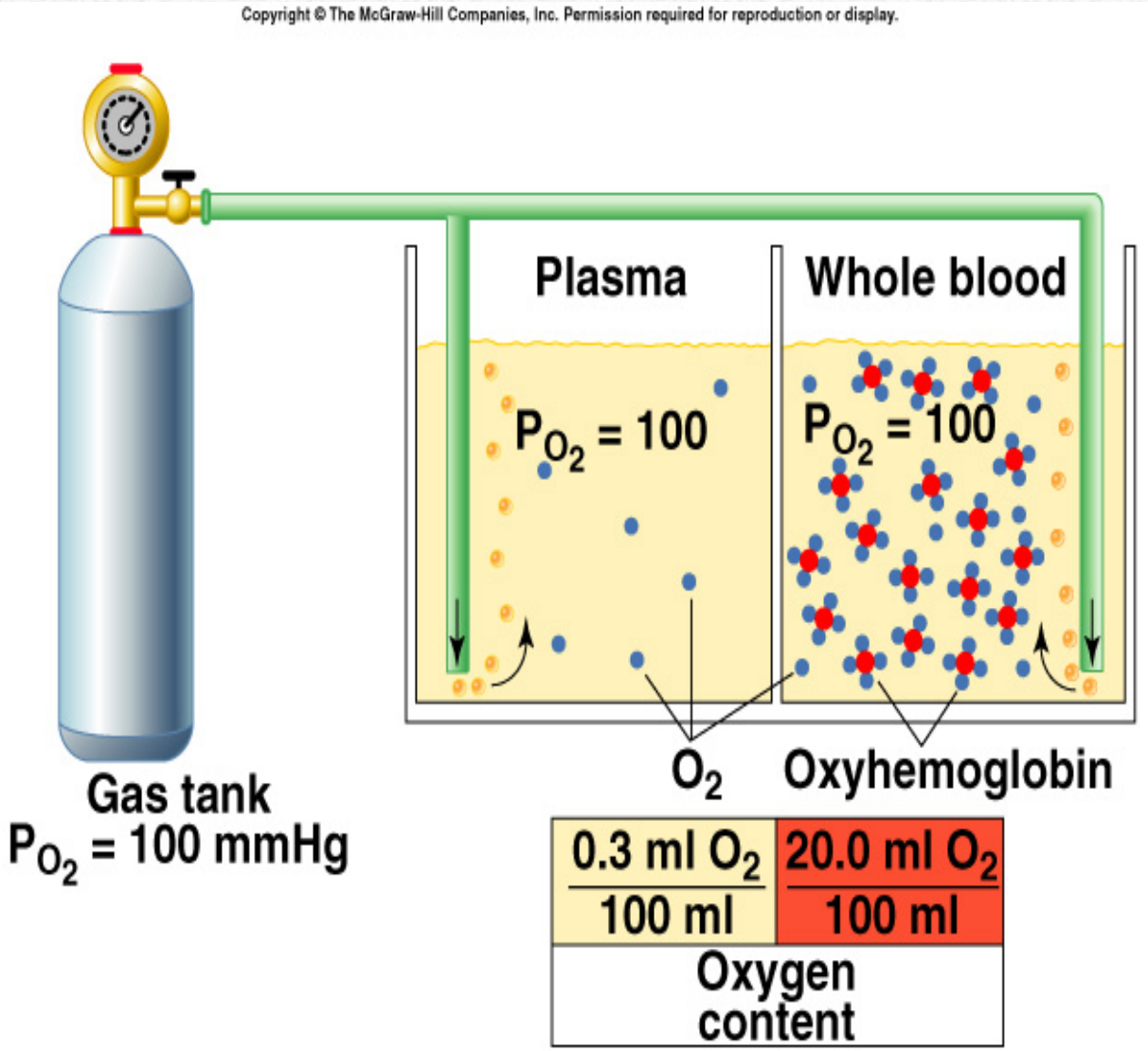
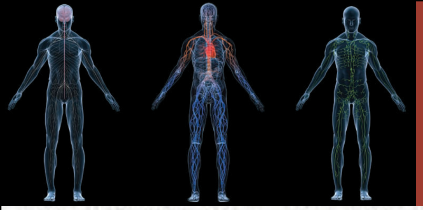
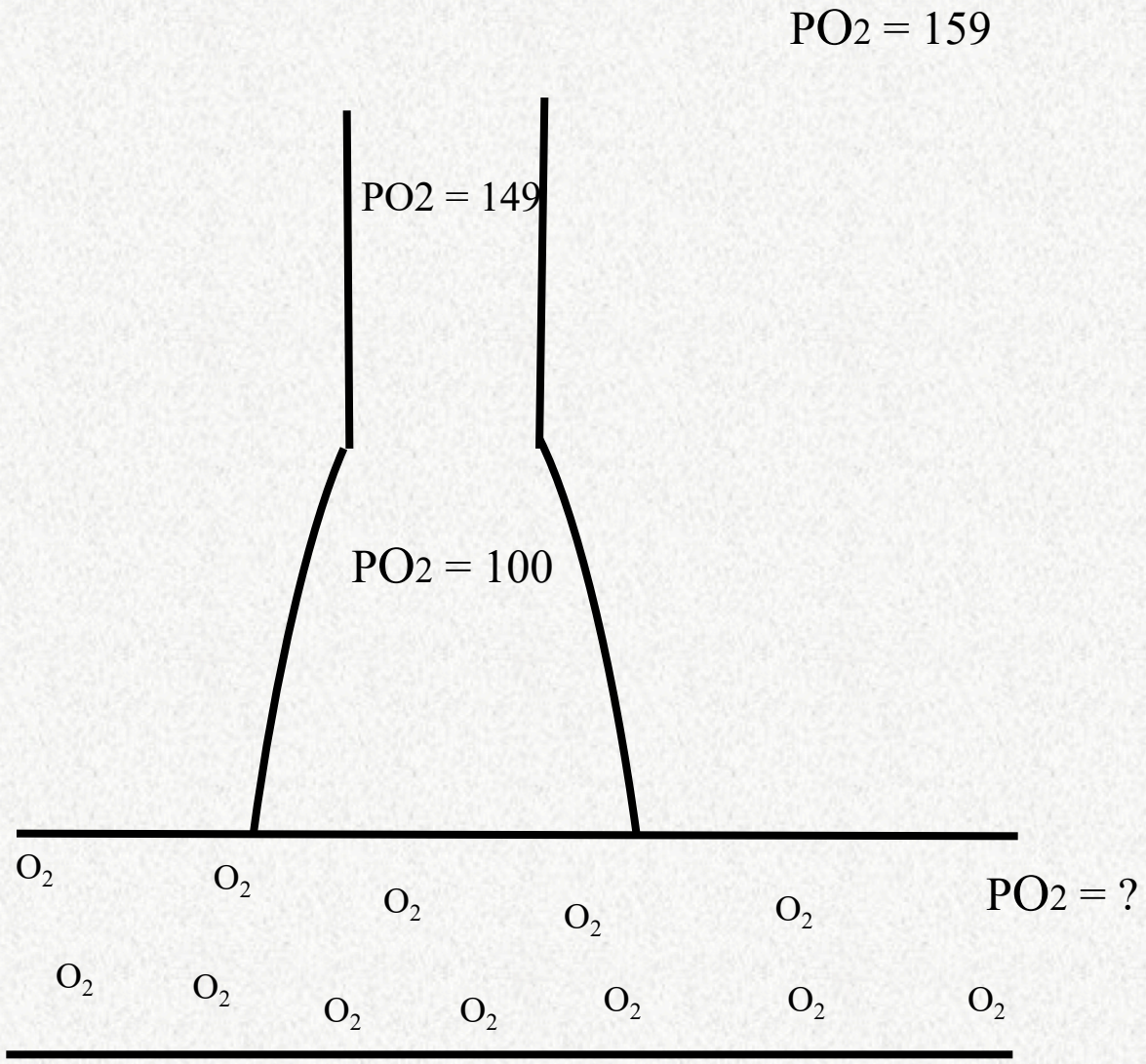
Hemoglobin and 0_2 Transport

C= 5 million per µl blood
million Hb/RBC.
h Hb has 4 polypeptide
ins and 4 hemes.
he center of each heme
up is 1 atom of iron
t can combine with 1
ecule 0_2.





Alveolar and Blood PO_2



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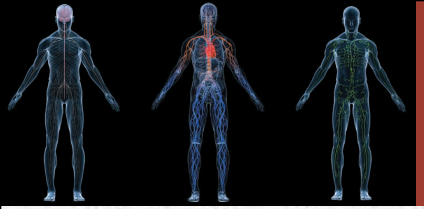

Question….

A vasodilator is infused into a paralyzed muscle. What happens to PO_2 within that muscle?

A. Increases

B. Decreases

C. No change

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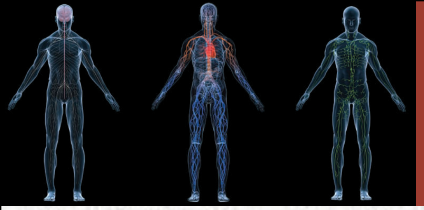

Question

Arterial PO_2 is 100 mmHg and content is 20 ml O_2/dl.
What is arterial PO_2 if ½ of all of the red cells are removed?

A. PO_2 = 0 mmHg
B. PO_2 =30 mmHg
C. PO_2 =50 mmHg
D. PO_2 =60 mmHg
E. PO_2 =100 mmHg

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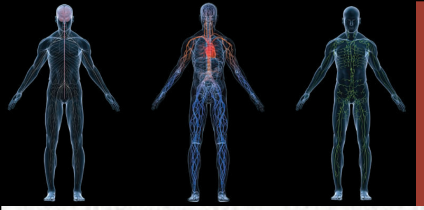

Question

Systemic arterial PO_2 is 100 mmHg and hematocrit is 40%. What is systemic arterial PO_2 if blood is added to increase hematocrit to 50?

A. PO_2 = 50 mmHg
B. PO_2 =70 mmHg
C. PO_2 =100 mmHg
D. PO_2 =120 mmHg
E. PO_2 =149 mmHg

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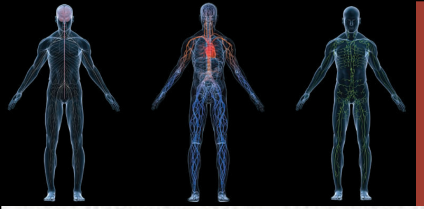

Hypothetical

- What happens to ***mixed venous*** PO_2 in an anemic person?
- Normal
- Lower
- Higher

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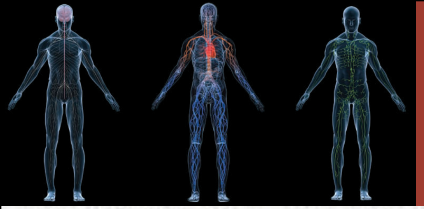

Question

A person is breathing from a gas tank containing 45% oxygen. What is the alveolar PO_2?

A. 149 mmHg

B. 250 mmHg

C. 270 mmHg

D. 320 mmHg

E. 340 mmHg

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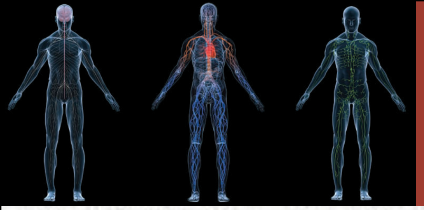

Answer

760-47=713

713*0.45 = 321 mmHg = inspired PO_2

Alveolar PO_2 = 321-(40/0.8)= 321-50 =

271 mmHg

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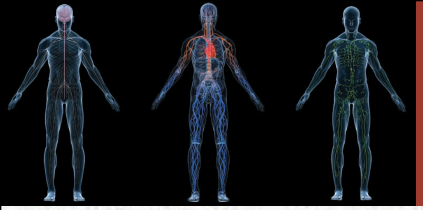
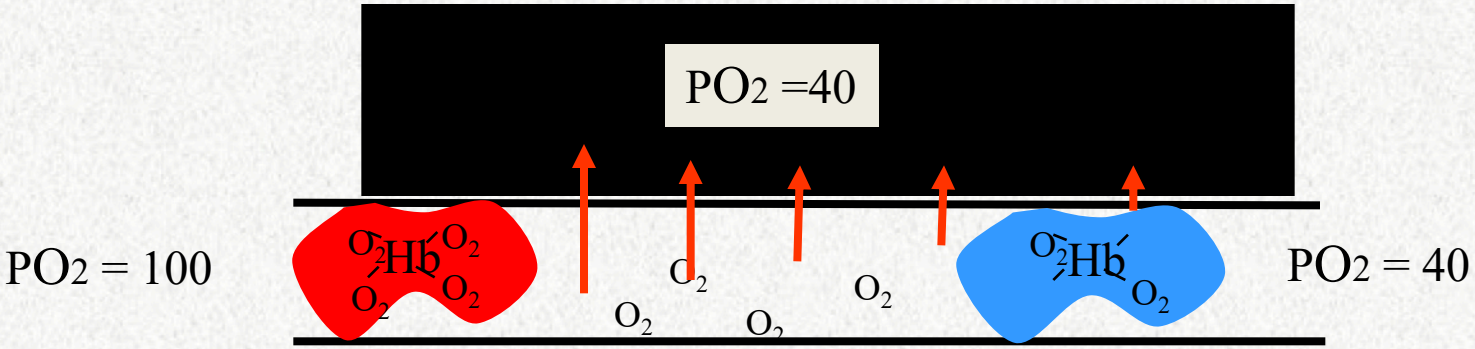
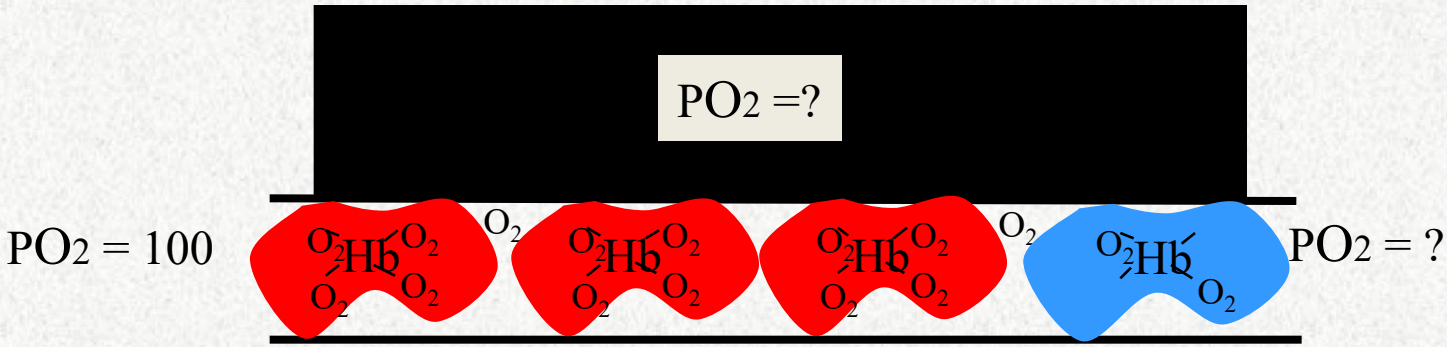


Blood and Muscle PO_2



Increased Flow and normal metabolism



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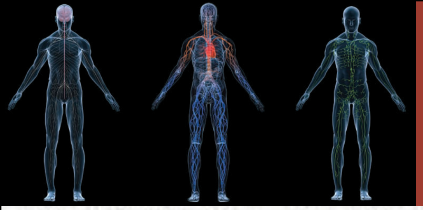
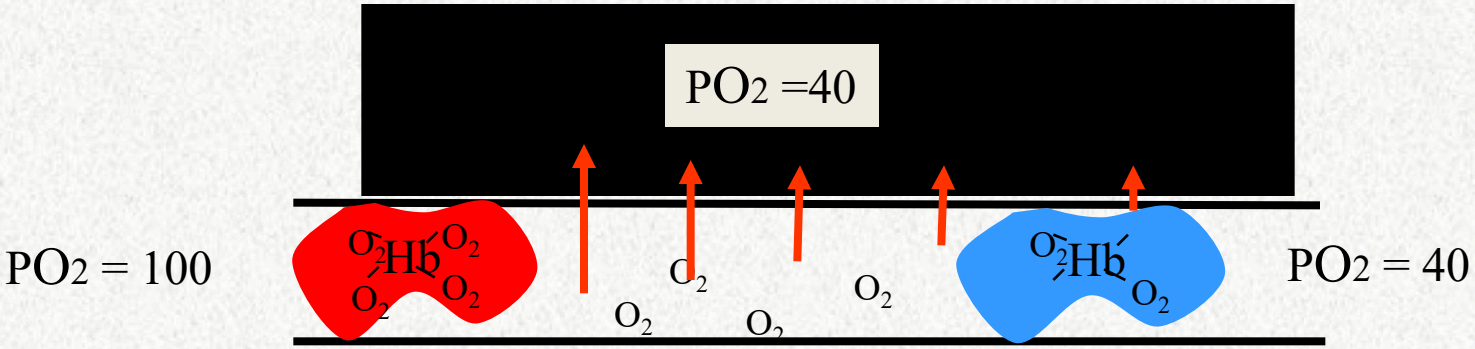


Blood and Muscle PO_2



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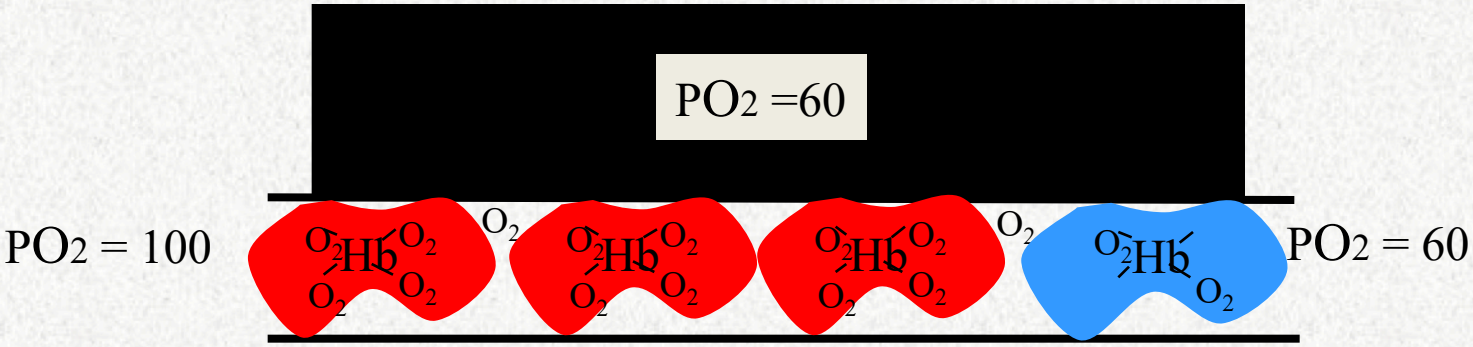

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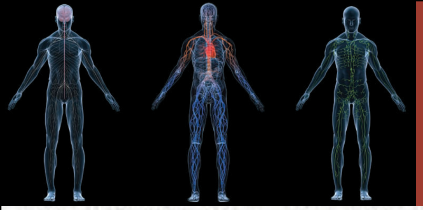
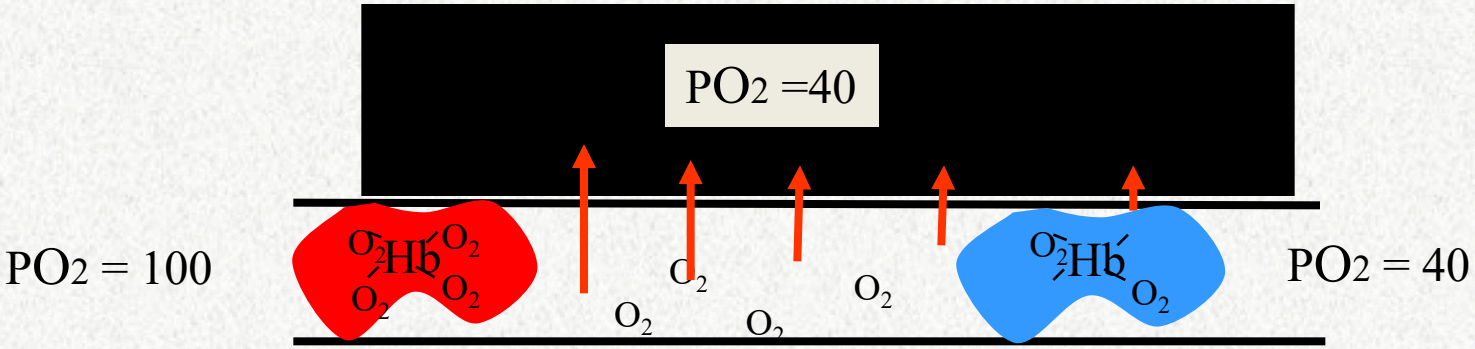
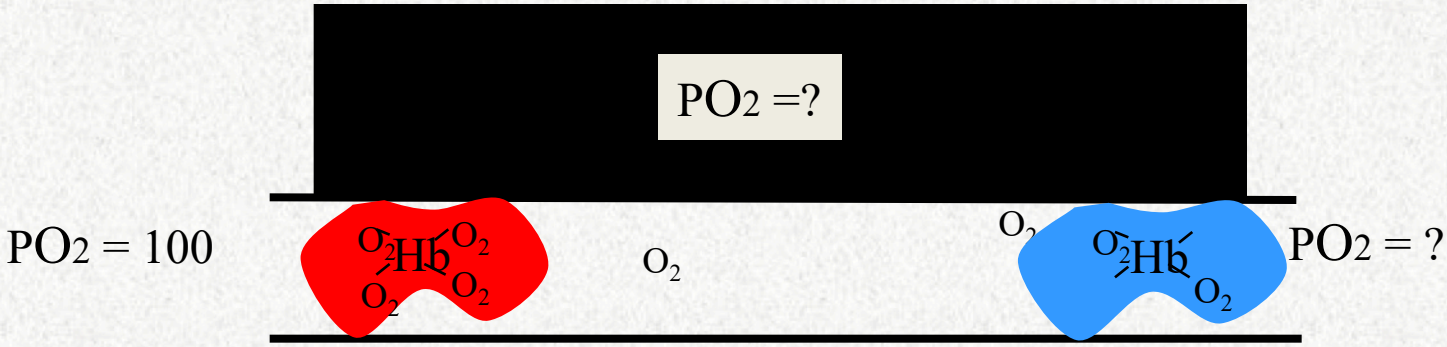


Blood and Muscle PO_2



Increased Metabolism and normal blood flow



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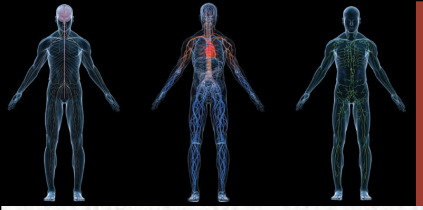

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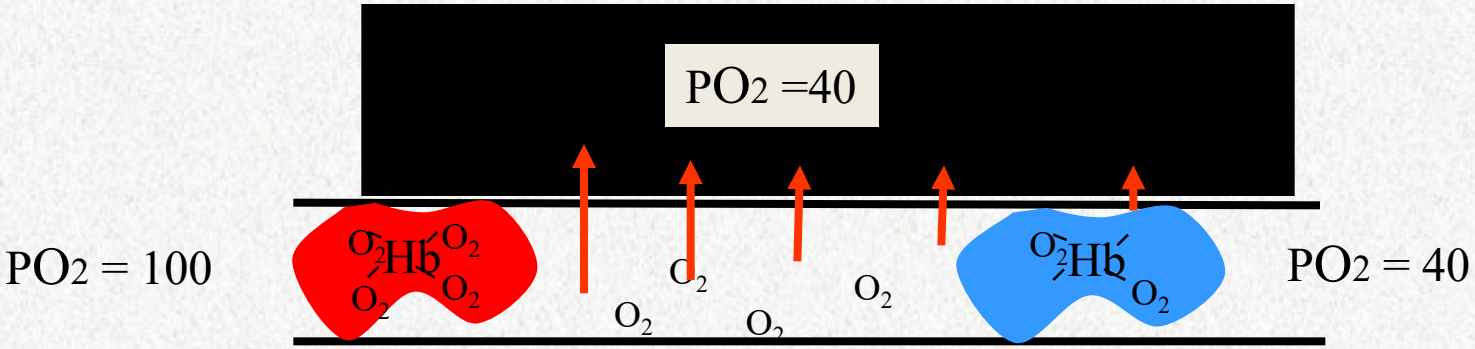

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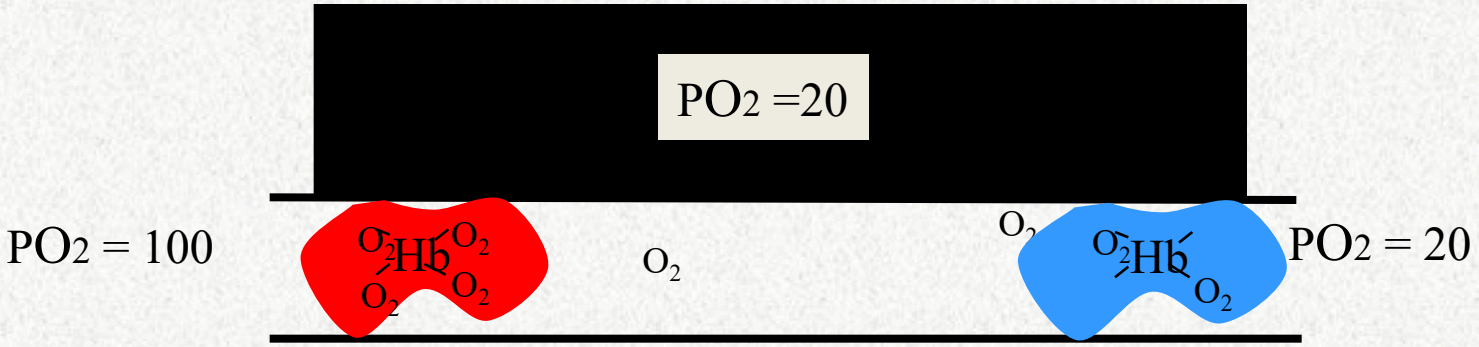

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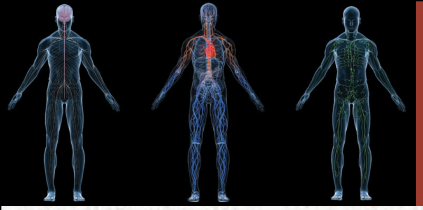
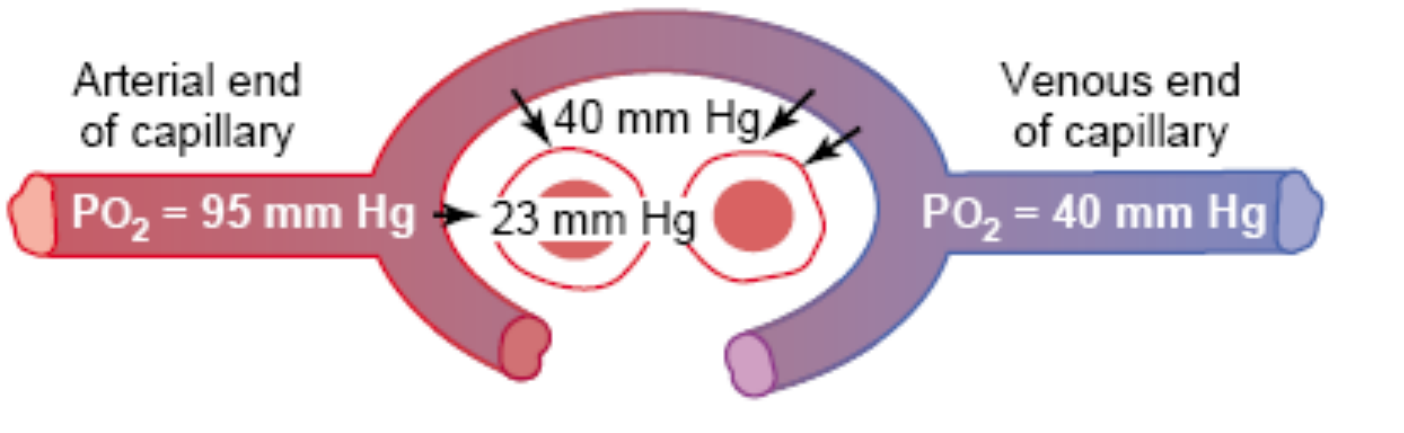


PO_2 in systemic circulation (Diffusion from peripheral capillaries)

- Oxygen is always being used by the cells. Therefore, the intracellular PO_2 in the peripheral tissue cells remains lower than the PO_2 in the peripheral capillaries.



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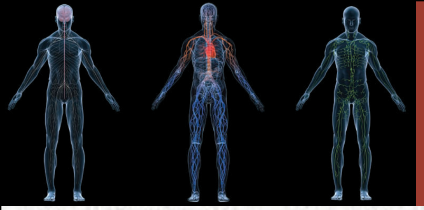

Increased Blood Flow to Tissue

- Normal blood flow
  - 200 ml O_2/lit of arterial blood * 5 lit blood/min= 1000 ml/min
  - VO_2/min…250 ml are consumed at rest (25%)
- **Utilization Coefficient or (Extraction ratio):**
- Is the % of blood that gives up its O_2 as it passes through tissue capillaries. Normally is 25%. In exercise 75% - 85%. In some local tissues with extremely high metabolic rate → 100%.

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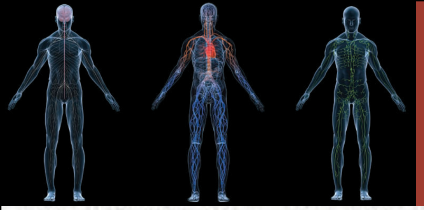

O_2 Uptake during Exercise

- VO_2 increases during exercise until it reaches VO_2max…what limits VO_2max…lung? CVS? number of mitochondria?
- Increased cardiac output and thus muscle blood flow and extraction ratio…all make more O_2 available to the exercising tissues
- Decreased transit time…Normal lung can still oxygenate blood beside this issue
- Increased diffusing capacity
  - Opening up of additional capillaries
  - Better ventilation/perfusion match
- Equilibration even with shorter time

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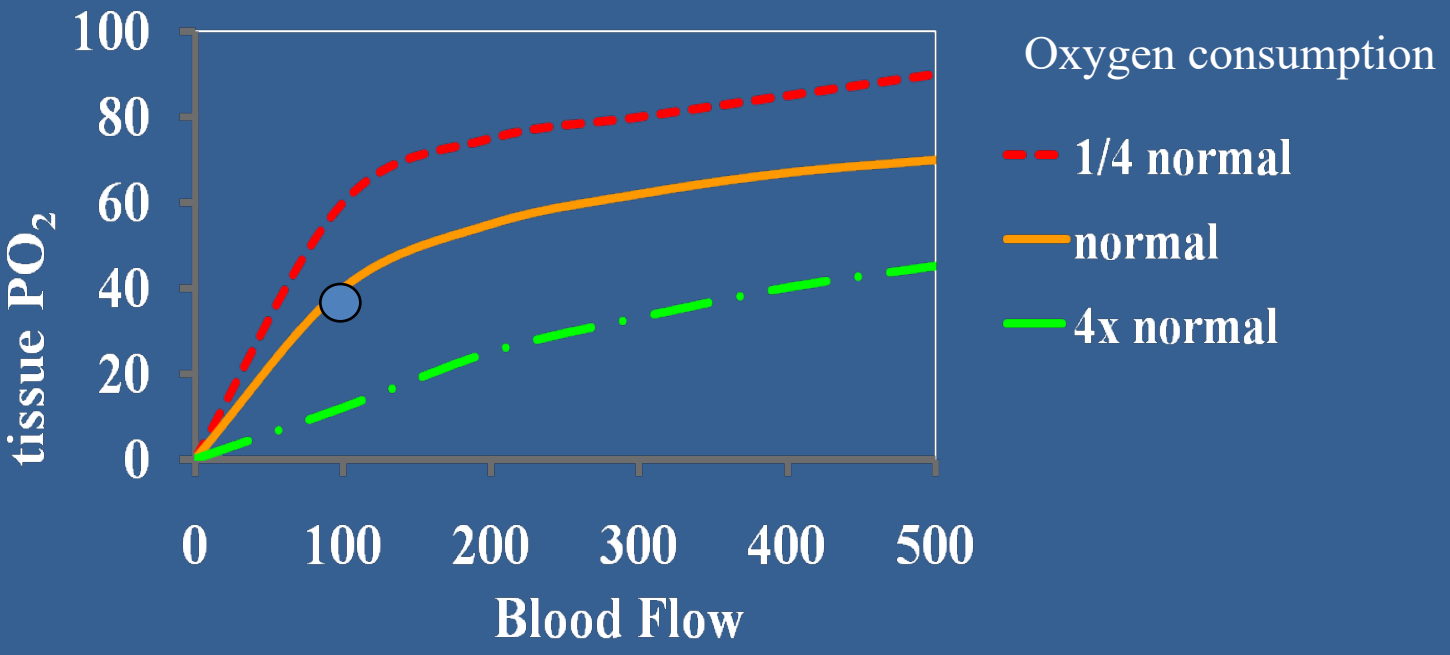
Diffusion of Oxygen at the Tissue



- Arterial blood has PO_2 of 95-100 mmHg
- Tissue has a PO_2 of 30-40 mmHg
- Tissue PO_2 is determined by balance of O2 delivery and O2 usage.

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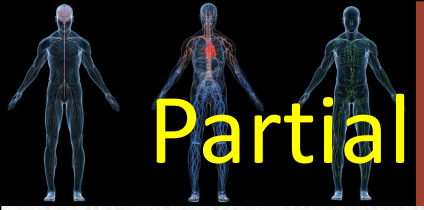

Partial Pressures of Gases in Inhaled Air

PN_2	=0.786	x 760mm Hg	= 597.4 mmHg
P_{O2}	=0.209	x 760mm Hg	= 158.8 mmHg
P_{H2O}	=0.004	x 760mm Hg	= 3.0 mmHg
P_{CO2}	=0.0004	x 760mm Hg	= 0.3 mmHg
$P_{other\ gases}$	=0.0006	x 760mm Hg	= 0.5 mmHg
		TOTAL	= 760.0 mmHg

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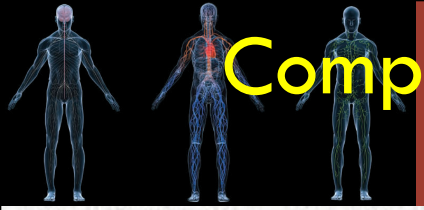

Composition of Alveolar Air—Its Relation to Atmospheric Air

	Inhaled Atmospheric Air		Humidified Air	Alveolar Air	Expired Air
	mm Hg	%	mm Hg	mm Hg	mm Hg
PN_2	597	78.6	563	569	566
PO_2	**159**	**20.8**	**149**	**104**	**120**
PCO_2	0.3	0.04	0.3	**40**	27
PH_2O	**3.7**	**0.5**	**47**	**47**	**47**
Total	760	100	760	760	760

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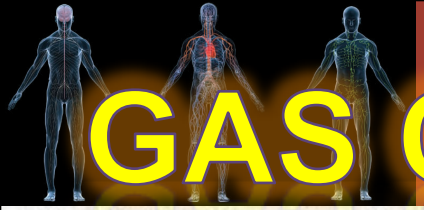

GAS CONTENT OF BLOOD.

- One DL of Blood Contains 15 g of Hemoglobin
- One DL of arterial Blood Contains 20 ml of O_2
- **Arterial Blood**
  (PO_2 95 mm Hg;
  PCO_2 40 mm Hg;
  Hb 97% Saturated)
- **Venous Blood**
  (PO_2 40 mm Hg;
  PCO_2 45 mm Hg;
  Hb 75% Saturated)

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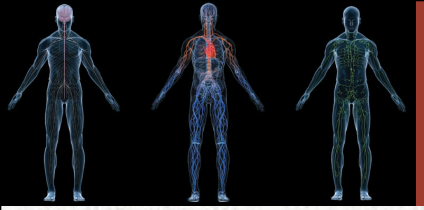

Oxygen Transport

- Partial Pressure (mm Hg)
  - driving force for diffusion
- Percent Saturation (no units)

  $\underline{HbO_2}$

  $(Hb+O_2)$ is called oxyHb
- Content (ml O_2/100 ml blood)
  - The absolute quantity of oxygen in the blood is the most important among others

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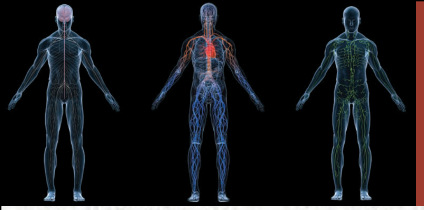

Transport of Oxygen in Blood

- Henry's law
- Dissolved oxygen=PaO_2 X Solubility of O_2 Solubility 0.003 ml O_2/100 ml blood
- - In normal blood; the [O_2] in its dissolved form is equal to= 0.3 ml O_2/100 ml blood
  - Normal oxygen consumption 250 ml O_2/min
  - Would require 83 l/min blood flow
- Hemoglobin
  - 97% of the transported O2 is in this form

$$O_2 + Hb \rightleftharpoons HbO_2$$

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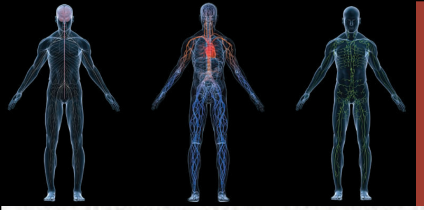

Law of dissolved gases

Oxygen	0.024
Carbon dioxide	0.57
Carbon monoxide	0.018
Nitrogen	0.012
Helium	0.008

- Much more CO_2 is dissolved in blood than O_2 because CO_2 is 20 times more soluble.
- The air we breathe is mostly N_2, very little dissolves in blood due to its low solubility.

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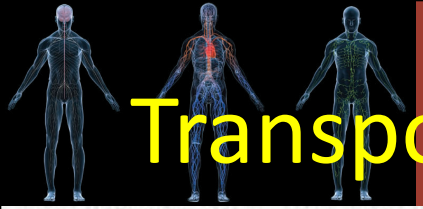

Transport of Oxygen and Carbon Dioxide

- Oxygen transport
  - Only about 1.5% is in the dissolved form (in plasma)
  - 98.5% bound to hemoglobin in red blood cells
    - Heme portion of hemoglobin contains 4 iron atoms – each can bind one O_2 molecule
    - Only dissolved portion can diffuse out of blood into cells
    - Oxygen must be able to love (bind, associate, load, increase affinity) and hate dissociate (hate, unload
    - decrease affinity).

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Why Hb is inside the RBCs and not circulating freely in the plasma

- 2,3 BPG is inside RBC. If no DPG the HbO_2 curve is no more sigmoidal, it becomes like that for myoglobin…a mutase in RBC convert 1,3 BPG to 2,3 BPG

- . NADH-met-Hb reductase inside RBC converts methHb (ferric) to reduced Hb (ferrous).

- Protection against degradation enzymes in plasma.

- Protection against filtration through the kidneys.

- Presence of C.A. which converts CO_2 to HCO3, otherwise by using Acetazolamide (CA inhibitor) PCO_2 reaches 80 mmHg

- Prevent ↑ in blood viscosity.

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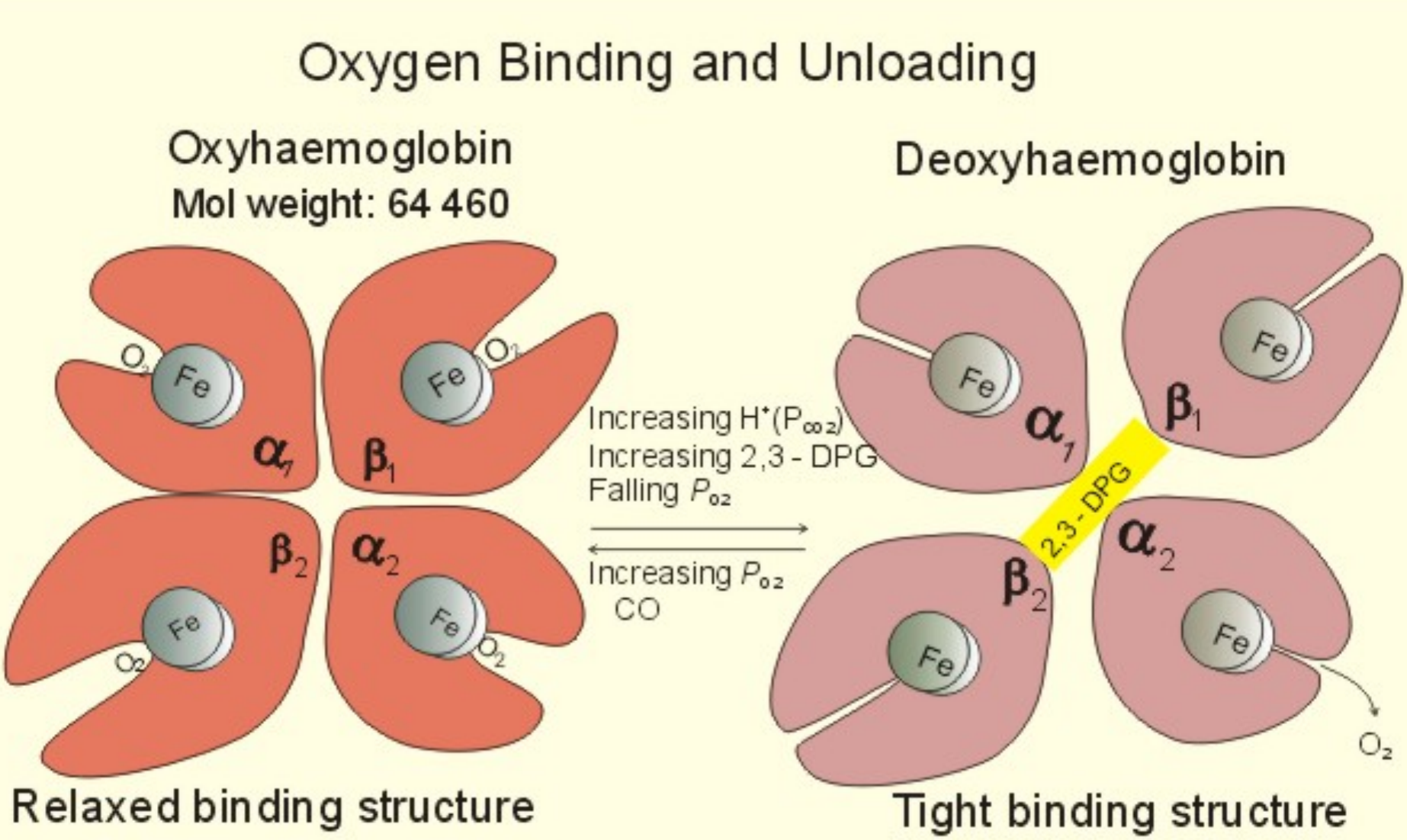

- **The total amount of Oxygen carried by Hb in blood depends upon:**
  - **The percentage saturation of Hb.**
  - **The amount of Hb in the blood.**

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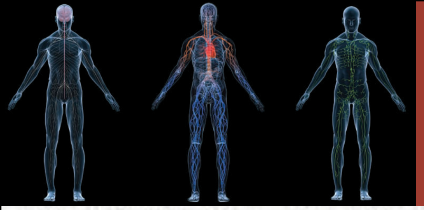

Hemoglobin

- Oxyhemoglobin:
  - Normal heme contains iron in the reduced form (Fe^{2+}).
  - Fe^{2+} shares electrons and bonds with oxygen.
- Deoxyhemoglobin:
  - When oxyhemoglobin dissociates to release oxygen, the heme iron is still in the reduced form.
  - Hemoglobin does not lose an electron when it combines with 0_2.

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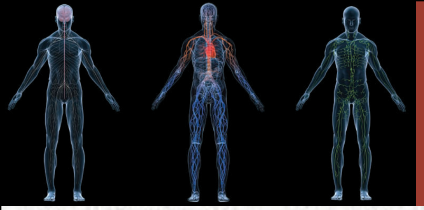

Hemoglobin (continued)

- Methemoglobin:
  - Has iron in the oxidized form (Fe^{+++}).
    - Blood normally contains a small amount. but ferric Fe^{+3} which is useless because it does not release O_2. NADH-meth-Hb reductase can convert ferric to ferrous form
- Carboxyhemoglobin:
  - The reduced heme is combined with carbon monoxide.
  - The bond with carbon monoxide is **250** times stronger than the bond with oxygen.
    - Therefore, transport of O_2 to tissues is impaired.

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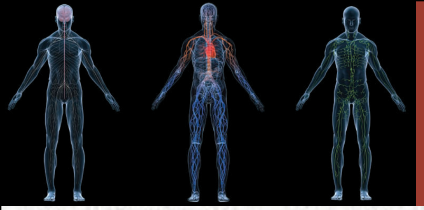

Hemoglobin (continued)

- Oxygen-carrying capacity of blood determined by its hemoglobin concentration.
  - Anemia:
    - [Hemoglobin] below normal.
  - Polycythemia:
    - [Hemoglobin] above normal.
  - Hemoglobin production controlled by erythropoietin.
    - Production is stimulated by the decrease in renal PO_2
- Loading/unloading depends:
  - PO_2 of environment.
  - Affinity between hemoglobin and O_2.

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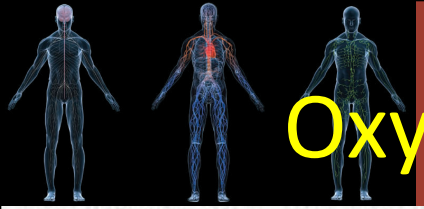

Oxyhemoglobin Dissociation Curve

- Graphic illustration of the % oxyhemoglobin saturation at different values of PO_2.
  - Loading and unloading of O_2.
    - Steep portion of the sigmoidal curve, small changes in PO_2 produce large differences in % saturation (unload more O_2).
- Decreased pH, increased temperature, increased 2,3 DPG, and increase PCO_2 all will decrease affinity of hemoglobin for O_2→ greater unloading of O_2 → Shift of the Hb-O_2 dissociation curve to the right. Hb hates O_2 or the so called decrease affinity.

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Oxyhemoglobin Dissociation Curve

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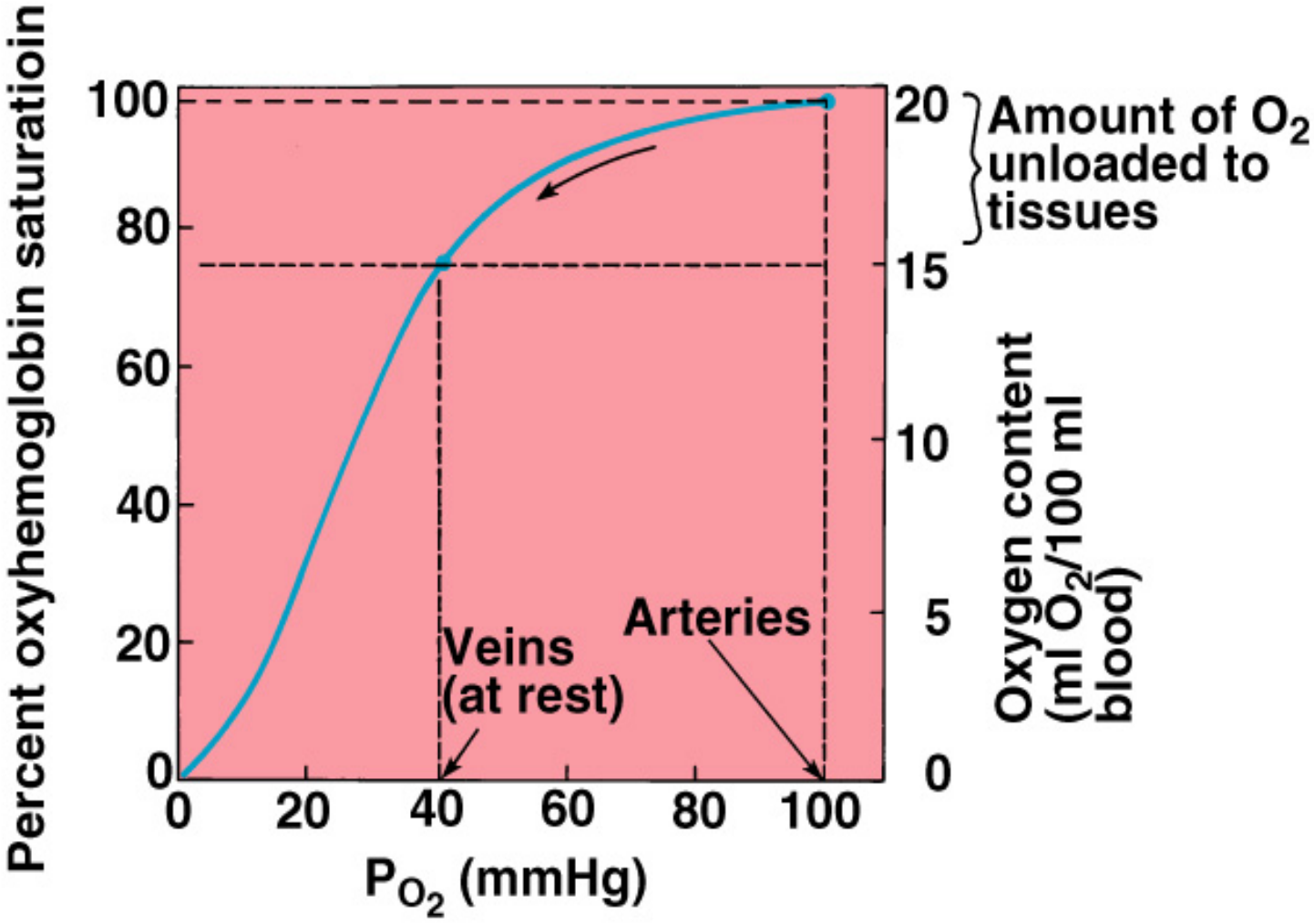

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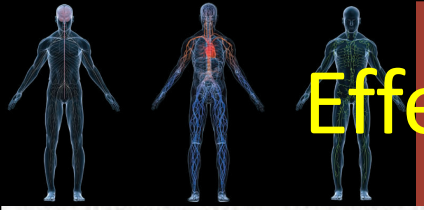

Effect of 2,3 DPG on O_2 Transport

- Anemia:
  - When RBCs or blood [hemoglobin] falls, each RBC produces greater amount of 2,3 DPG.
    - Since RBC lacks both nucleus and mitochondria, it produces ATP through anaerobic metabolismm, which makes enough 2,3,DPG available
    - Glucose $\rightarrow$ G-6-P $\rightarrow$ 1,3 DPG (2,3 DPG) $\rightarrow\rightarrow$ G-3-P $\rightarrow\rightarrow$
- Fetal hemoglobin (HbF):
  - Has 2 γ-chains in place of the β-chains… γ-chain does not bind 2,3,DPG…therefore, HbF has higher affinity towards O_2…make sense…mother's placenta PO2 is low (<40 mmHg)

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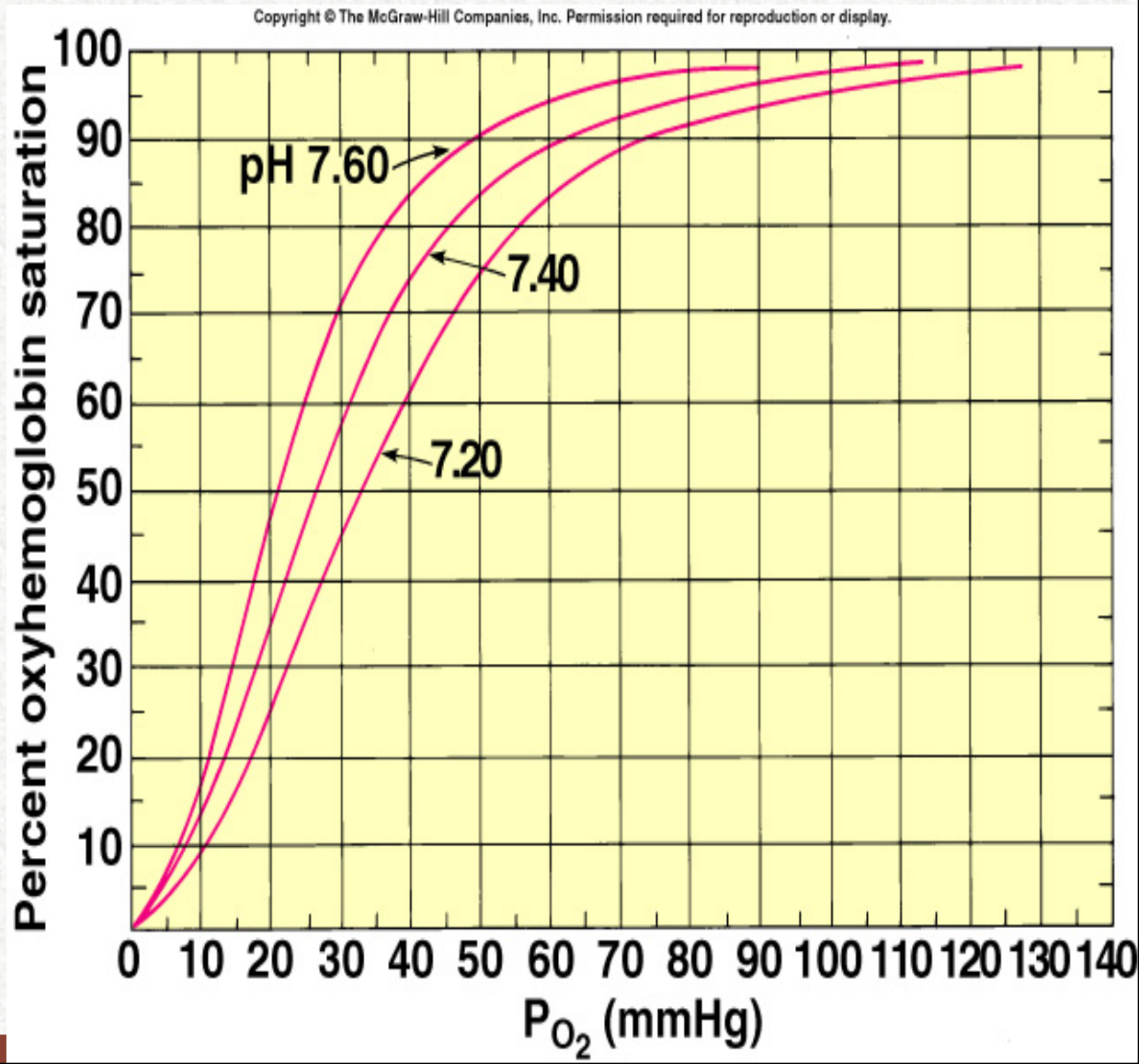
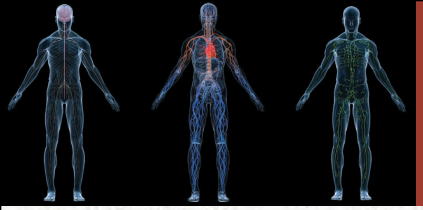
Effects of pH and Temperature

- The loading and unloading of O_2 influenced by the affinity of hemoglobin for O_2.

Affinity is decreased by:

- ↓blood pH
- ↑temperature
- ↑ 2,3-DPG
- ↑ PCO2
  - All Shift the curve to the right.





Values to remember

PO_2	O_2 Sat (%)	
10	25	
20	35	
25	**50**	**P_{50}**
30	60	
40	**75**	**Venous**
50	85	
60	**90**	**Respiratory center stimulation**
80	96	
100	**98**	**Almost Fully saturated**

Remember this rule…it is close enough!

4,5, 6 7-8-9

Po_2 (mmHg)	40	50	60
%Sat	70	80	90

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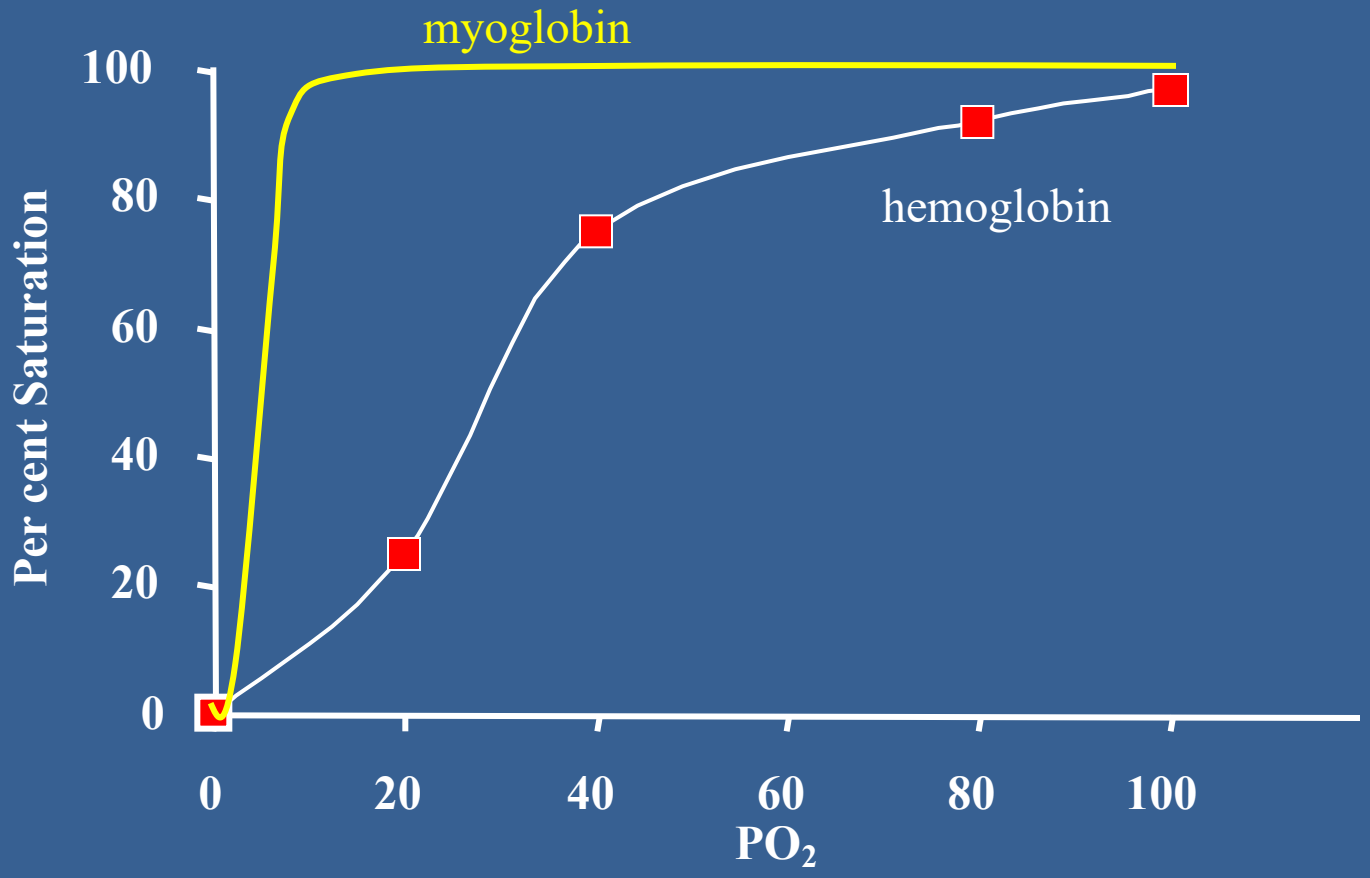
Dissociation Curve



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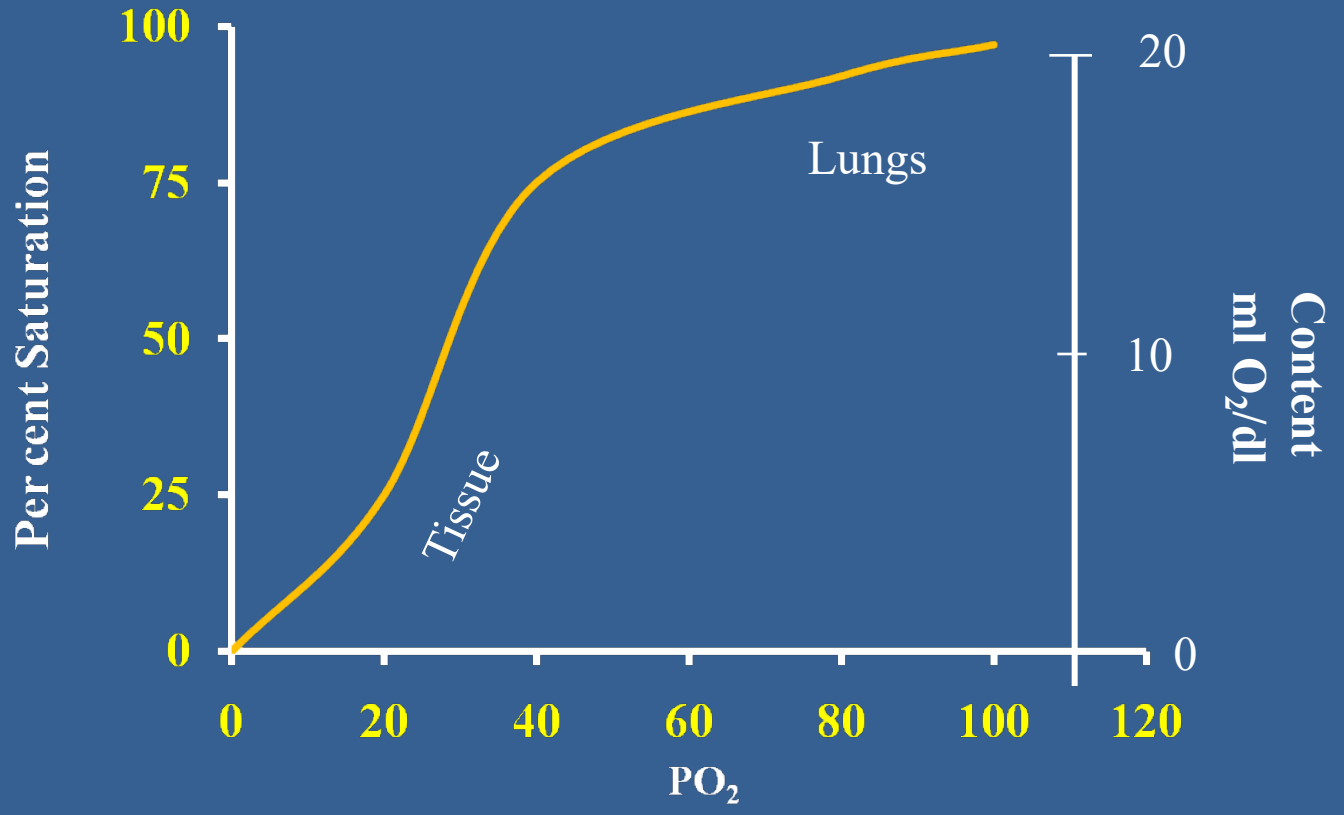
Hemoglobin Dissociation Curve



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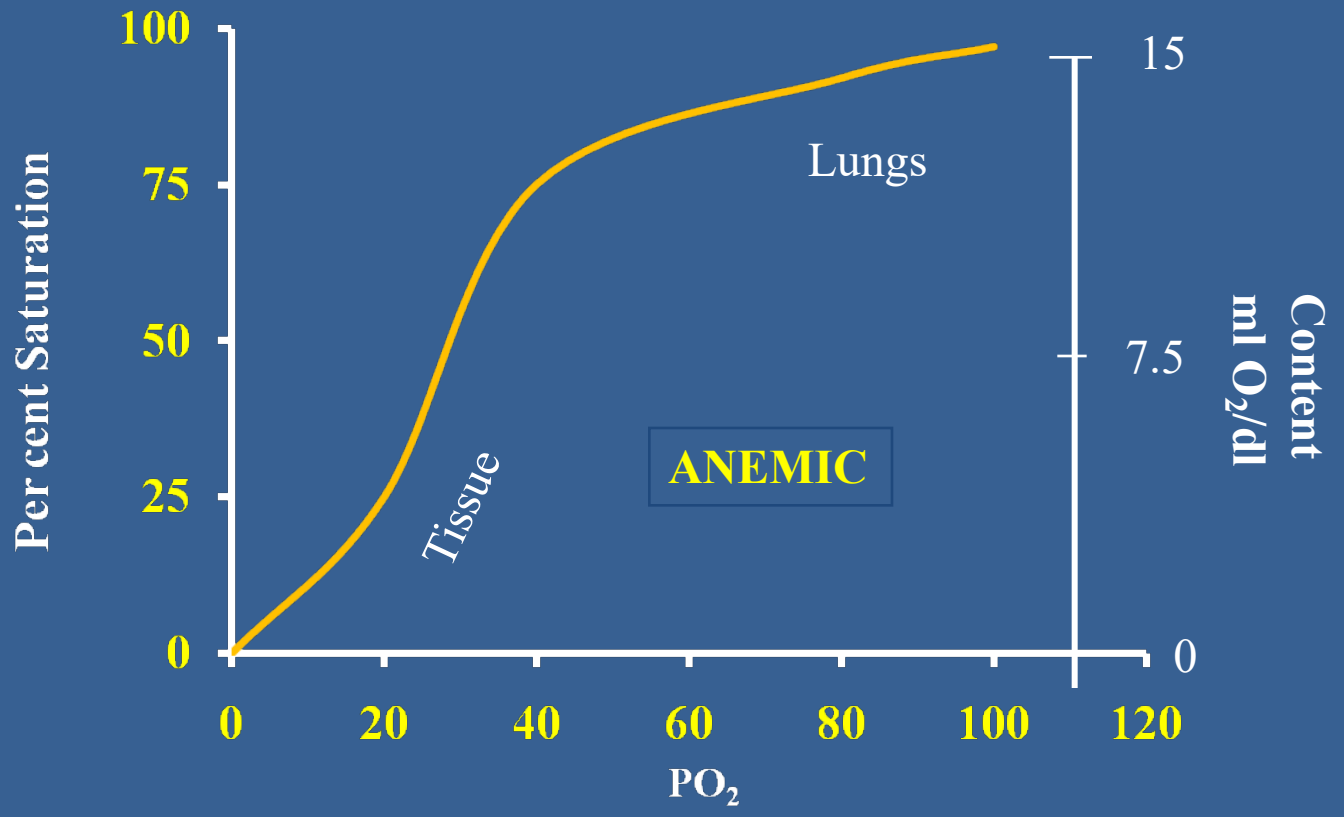
Hemoglobin Dissociation Curve



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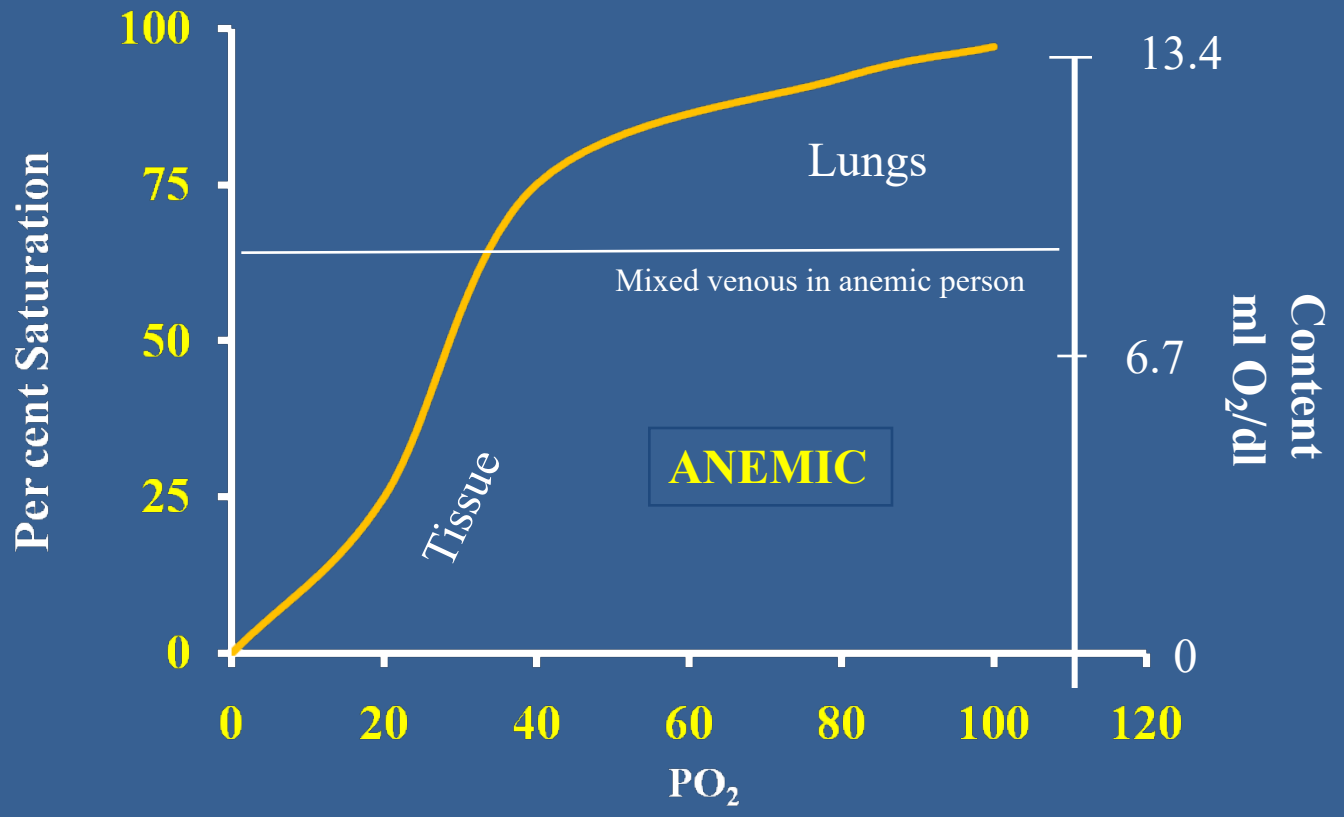
Hemoglobin Dissociation Curve



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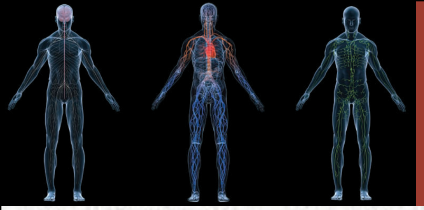

Shifts of Dissociation Curve

- Right shift occurs at tissue level…Bohr's effect
  - ↑$PaCO_2$ or ↑ arterial H^+→ ↓ affinity for oxygen or increase O_2 release…this occur at the tissue level
- Left shift at lungs…Haldane's effect is the reverse Bohr's effect
  - loss of carbon dioxide at lungs → ↑affinity of Hb towards oxygen

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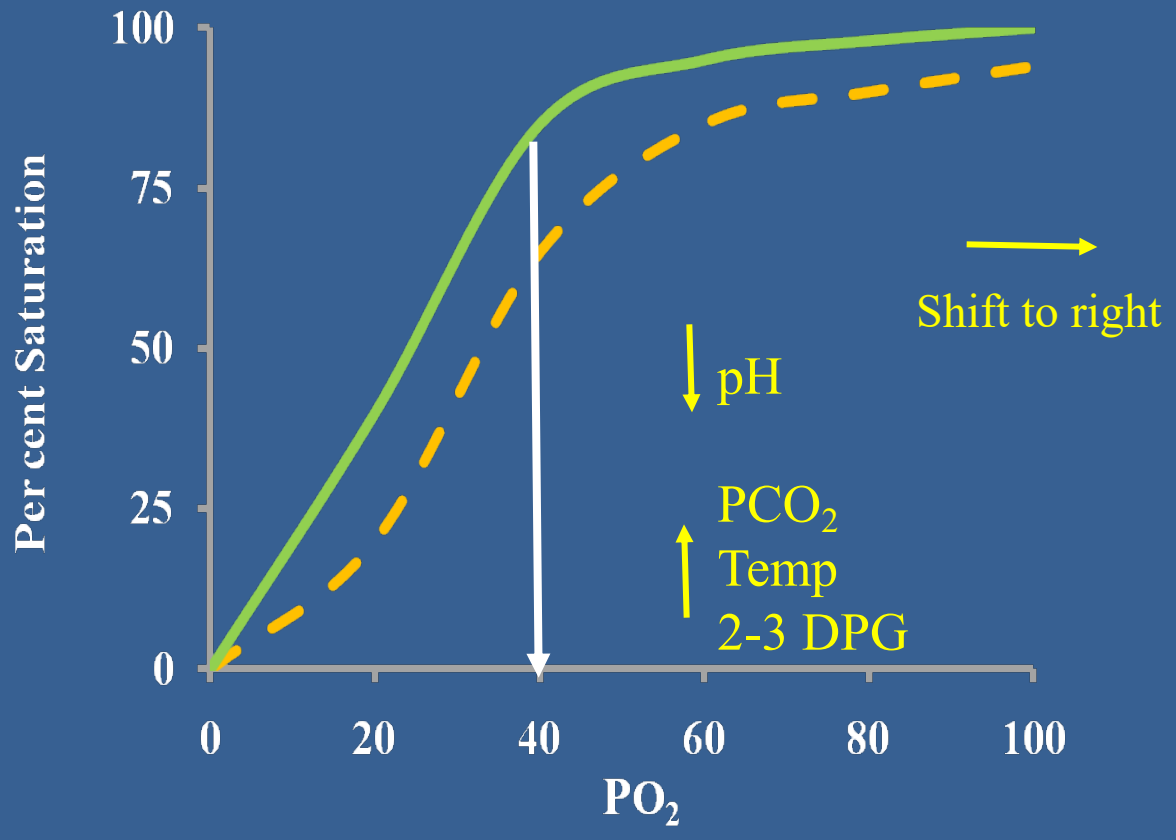
Right Shift of Dissociation Curve



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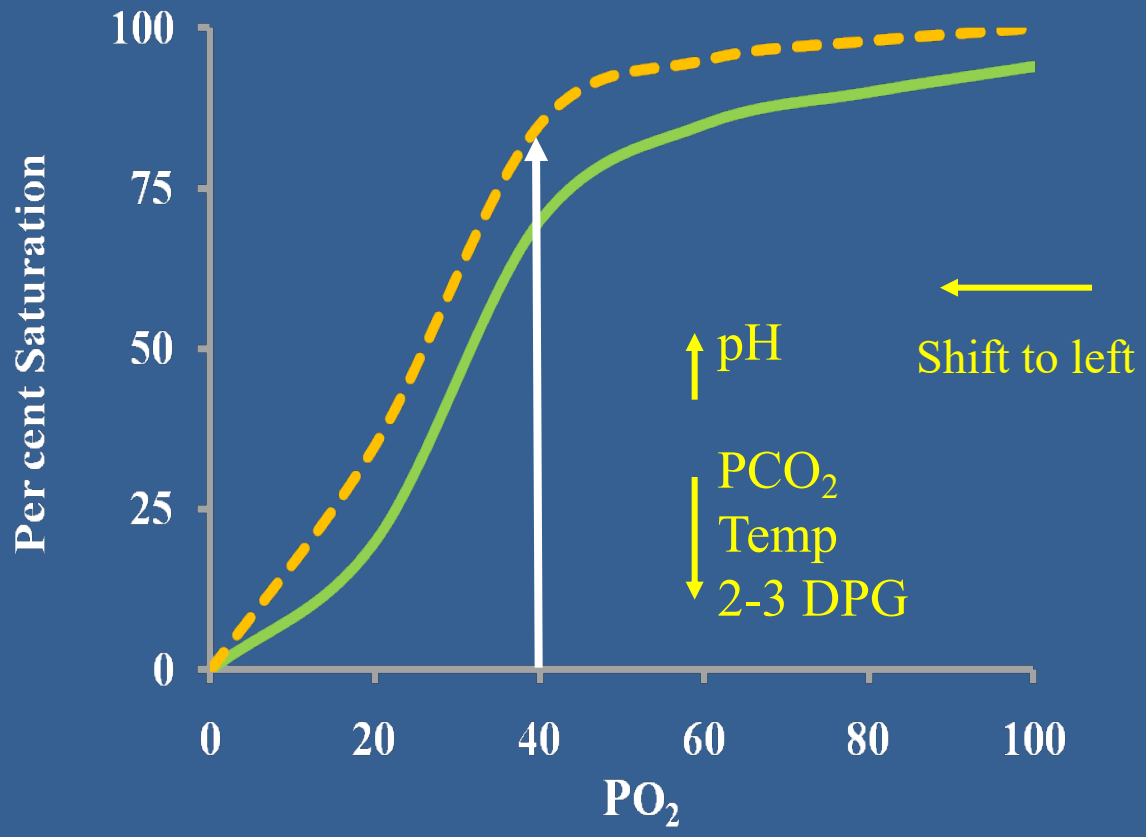
Left Shift of Dissociation Curve
Bohr's effect



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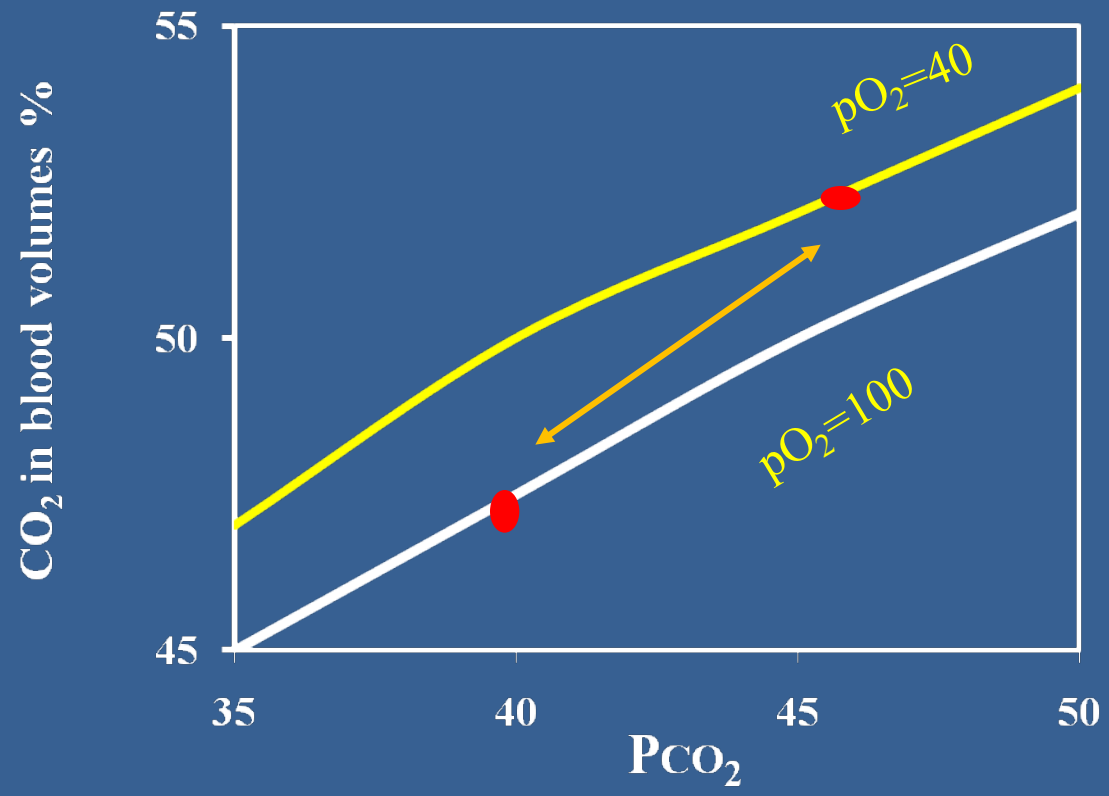
Haldane Effect

Venous 52 vol%

Arterial 48 vol%



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Fetal and Maternal Hemoglobin

- Fetal hemoglobin has a higher affinity for oxygen than adult hemoglobin
- Hb-F can carry up to 30% more oxygen
- Maternal blood's oxygen readily transferred to fetal blood

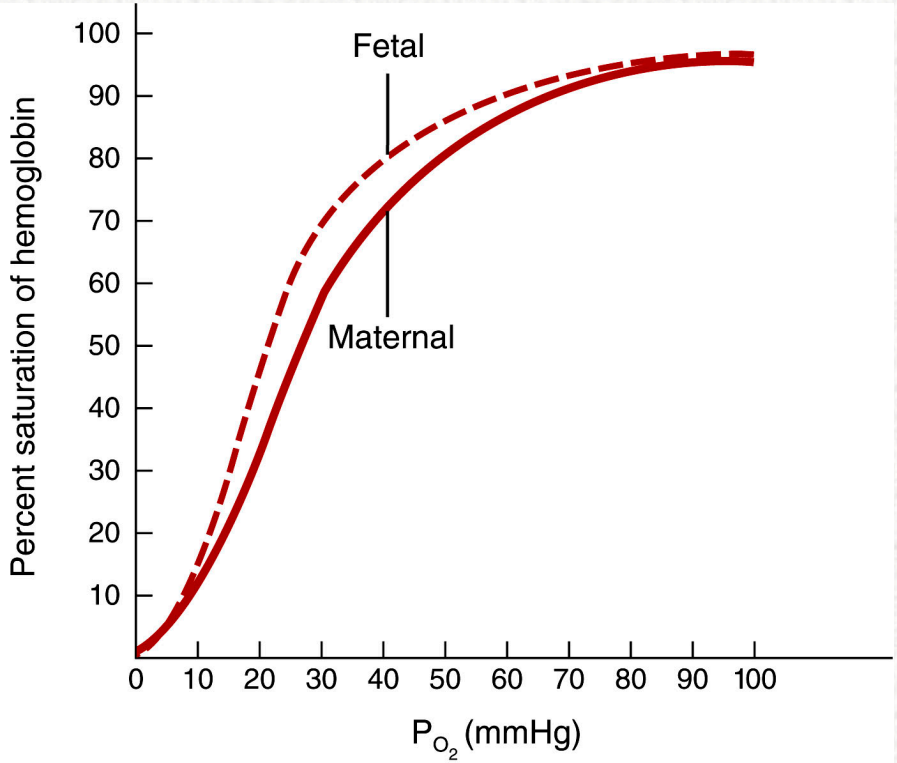

Figure 23.22 Tortora - PAP 12/e
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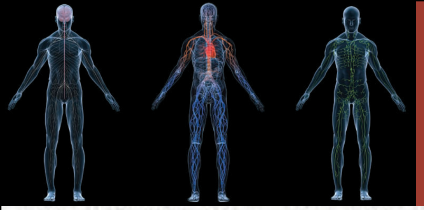

Hemoglobin Dissociation Curve

- Alveoli
  - Over wide range hemoglobin will be highly saturated
  - example: PO_2 of 60 mmHg correspond to 90% saturation
- Tissue
  - Normal: consume 5 ml O_2/100 ml blood (P_iO_2 is 40 mmHg)
  - During exercise: 15 ml of O_2 /100 ml blood (P_iO_2 is only 20 mmHg)

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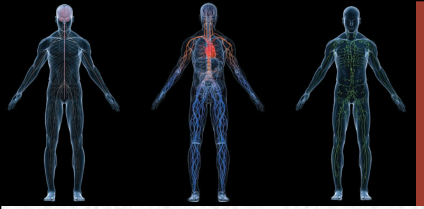

Question

A person has a hemoglobin concentration of 10 gm/dl. The arterial oxygen content is 6.5 ml O_2/dl. What is the saturation?

A. 25%

B. 50%

C. 75%

D 100%

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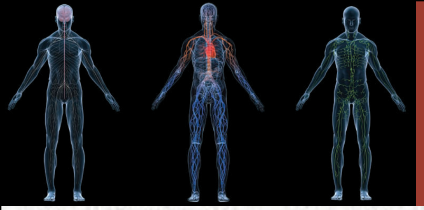

Calculations

- Calculate % saturation
  - Patient has Hb of 10 gm/dl
  - Venous oxygen content is 6.5 ml O_2/dl
- Calculate oxygen content
  - Patient has saturation of 60%
  - Patient has Hb of 15 gm/dl

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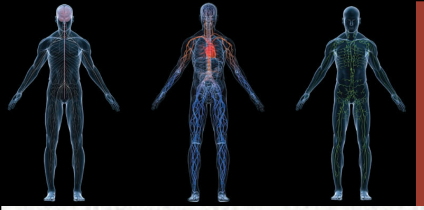

Calculations

- Calculate % saturation
  - 10 gm/dl * 1.34 ml O_2/gm Hb= 13.4 ml O_2/dl
    - This is max oxygen carrying capacity
  - (6.5 ml O_2/dl) / (13.4 ml O_2/dl) = ~50%

- Calculate oxygen content
  - 15 gm/dl * 1.34 ml O_2/dl = 20 ml O_2/dl
    - This is max oxygen carrying capacity
  - 20 ml O_2/dl * 60% saturation = 12 ml O_2/dl

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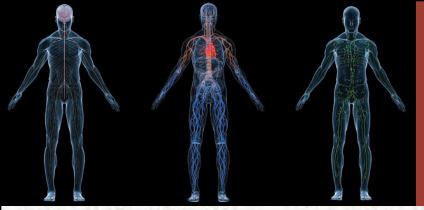

Calculations

- Assume Hb is 10 gm/dl
- 100% saturation give a content of 13.4 ml/dl blood
- At rest body uses 5 ml O_2/dl
- This leaves a mixed venous content of 8.4 ml/dl
- Saturation is now 8.4/13.4 = 63%

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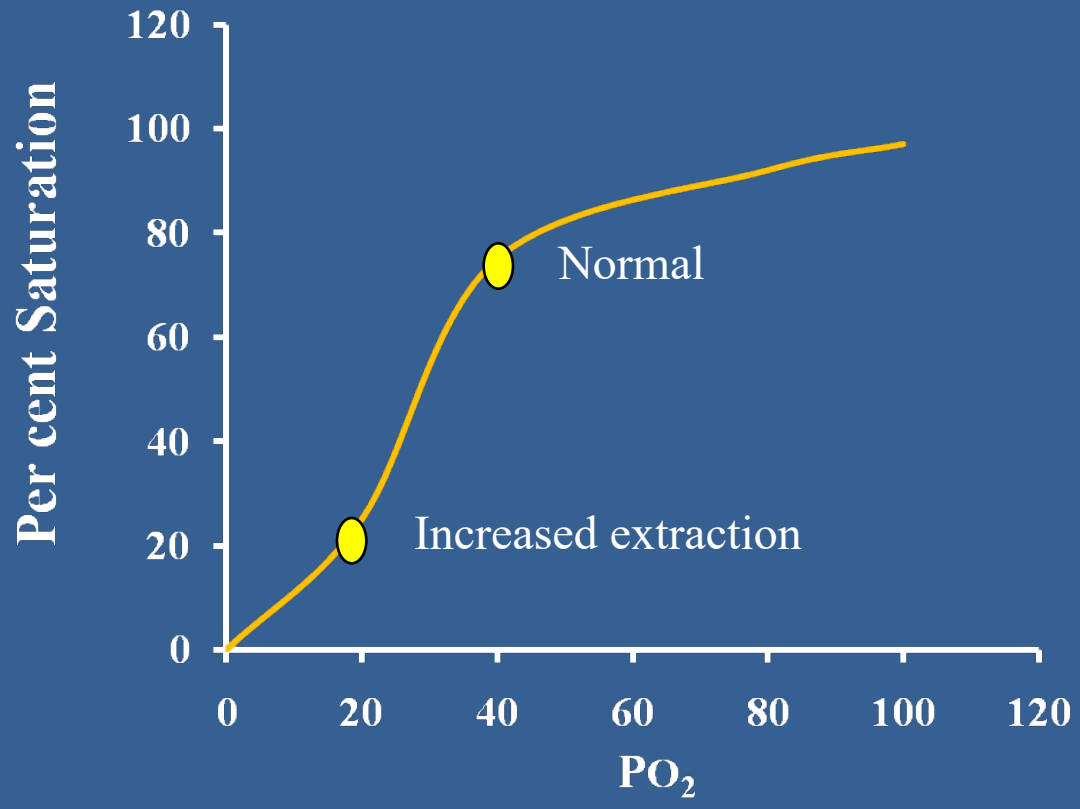
Increased Oxygen Extraction



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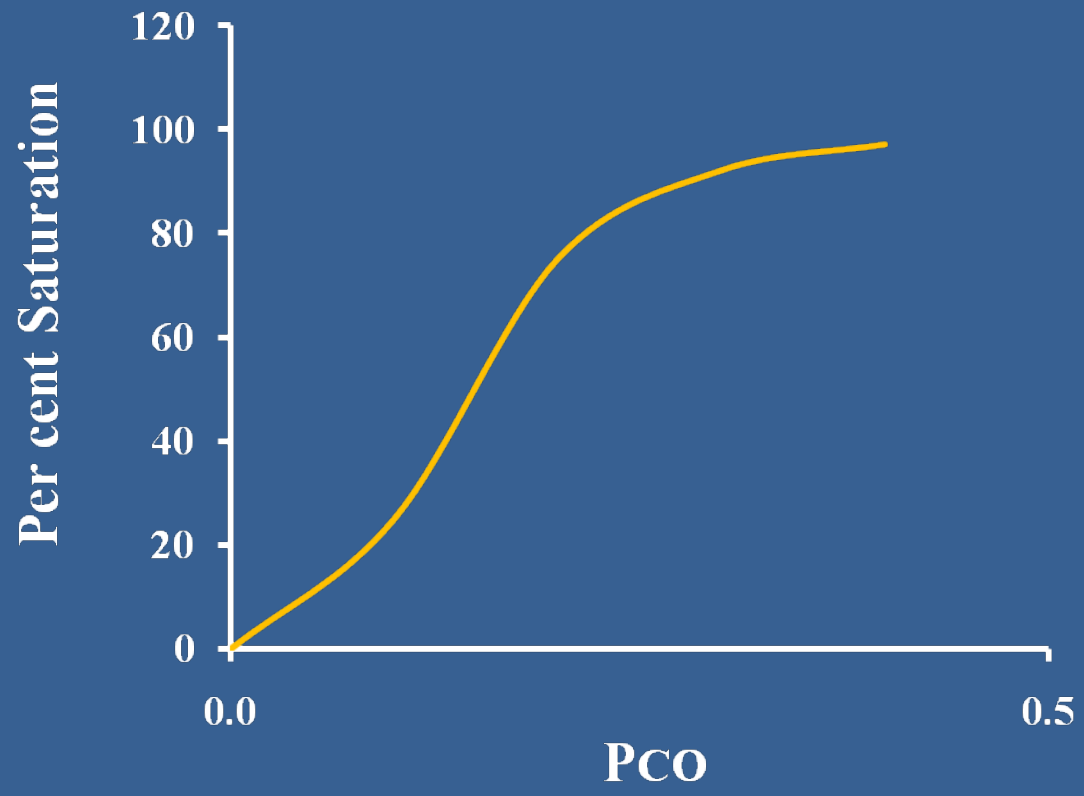
Carbon Monoxide Dissociation Curve



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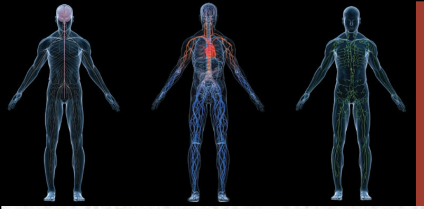

Question

Which of the following is least important for the transport of carbon dioxide?

a. hydrogen ions bound to hemoglobin

b. carbonic anhydrase

c. CO_2 dissolved in plasma

d. CO_2 bound to plasma proteins

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Inherited Defects in Hemoglobin Structure and Function

- Sickle-cell anemia:
  - Hemoglobin S differs in that **valine is substituted for glutamic acid on position 6 of the β chains**.
    - Cross links form a "paracrystalline gel" within the RBCs.
      - Makes the RBCs less flexible and more fragile.
- Thalassemia:
  - Decreased synthesis of α or β chains, increased synthesis of γ chains.

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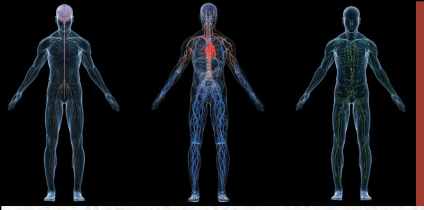
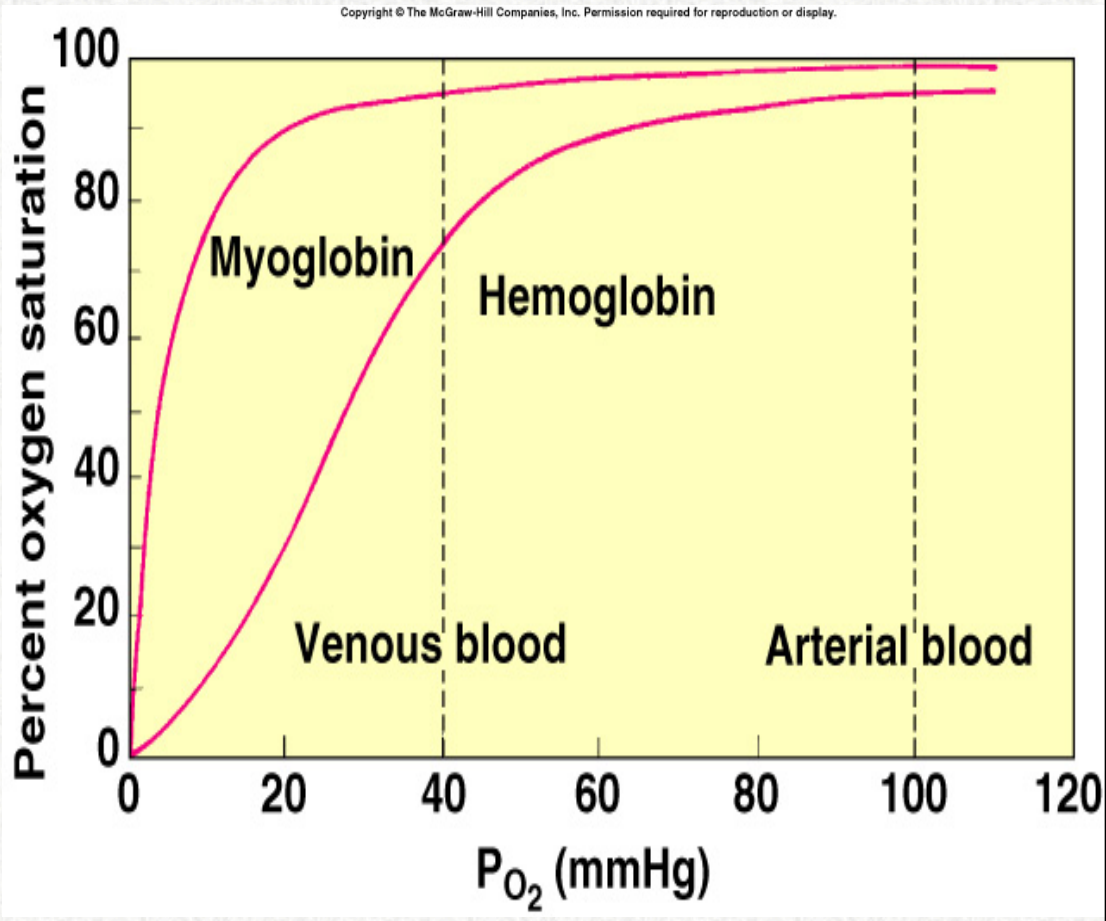


Muscle Myoglobin

- Red pigment found exclusively in striated muscle.
  - Slow-twitch skeletal fibers and cardiac muscle cells are rich in myoglobin.
    - Have a higher affinity for 0_2 than hemoglobin.
  - May act as a "go-between" in the transfer of 0_2 from blood to the mitochondria within muscle cells.



- May also have an O_2 storage function in cardiac muscles.

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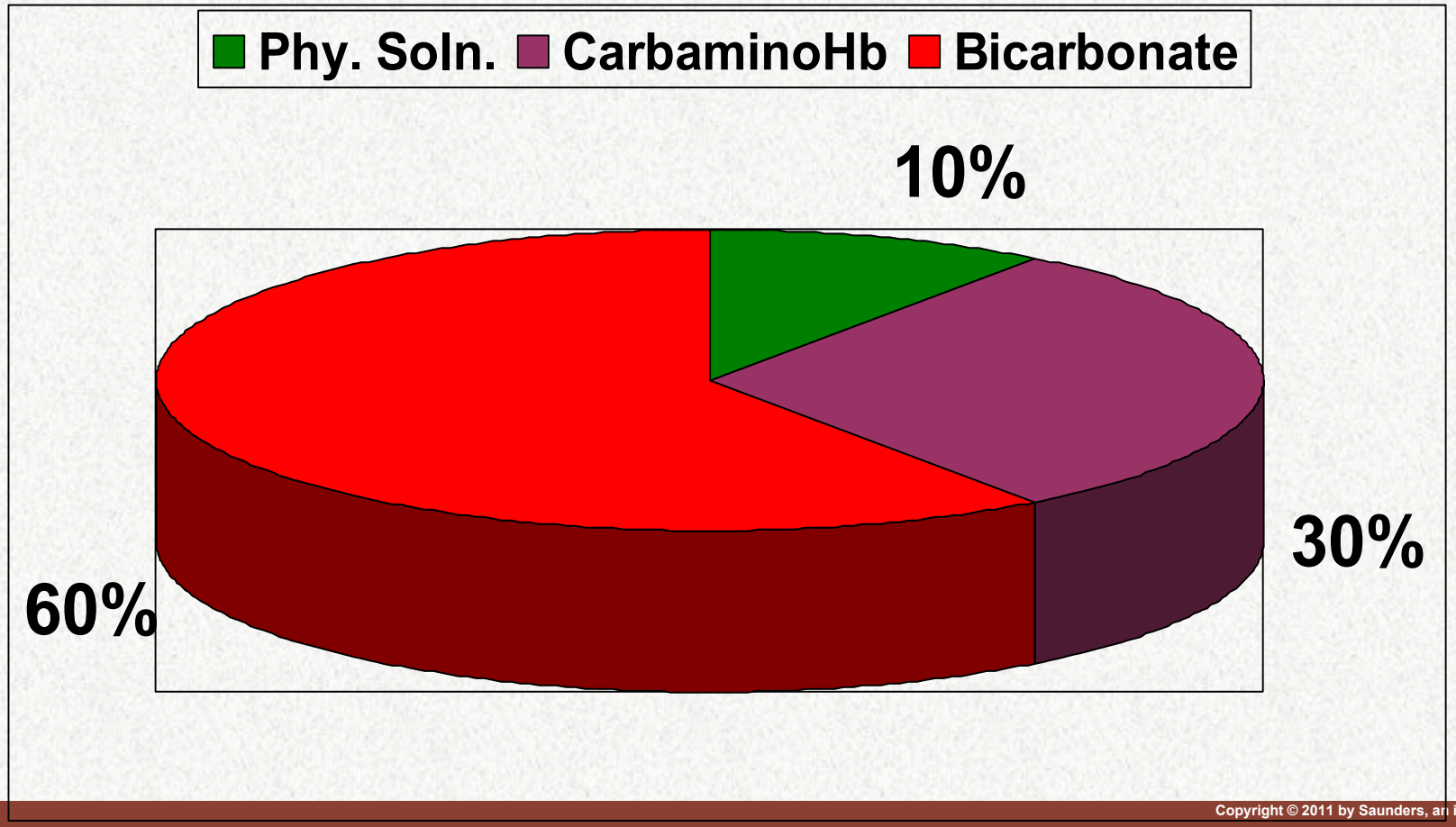
Carbon Dioxide in Blood

Transported from the body cells back to the lungs (Tidal CO_2) as (the 4 ml):



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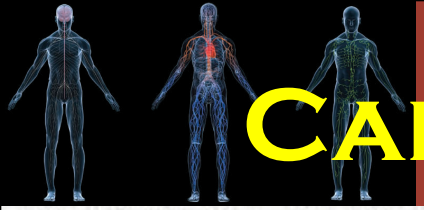

Carbon Dioxide in Blood

Fate of CO_2 in blood

In plasma

1. Dissolved
2. Formation of carbamino compounds with plasma protein
3. Hydration, H^+ buffered, HCO_3^- in plasma

In red blood cells

1. Dissolved
2. Formation of carbamino-Hb
3. Hydration, H^+ buffered, 70% of HCO_3^- enters the plasma
4. Cl^- shifts into cells; mosm/L in cells increases

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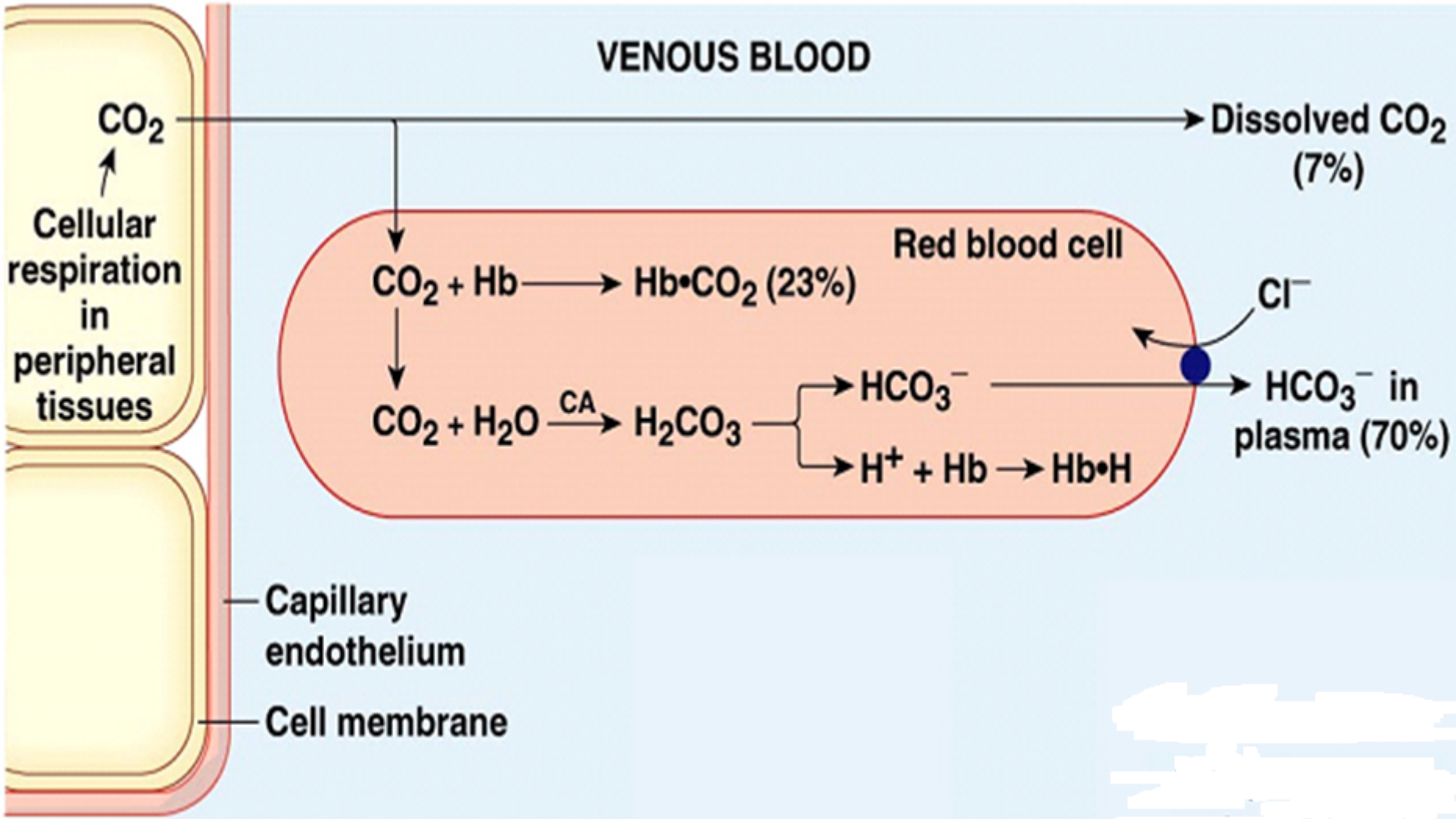
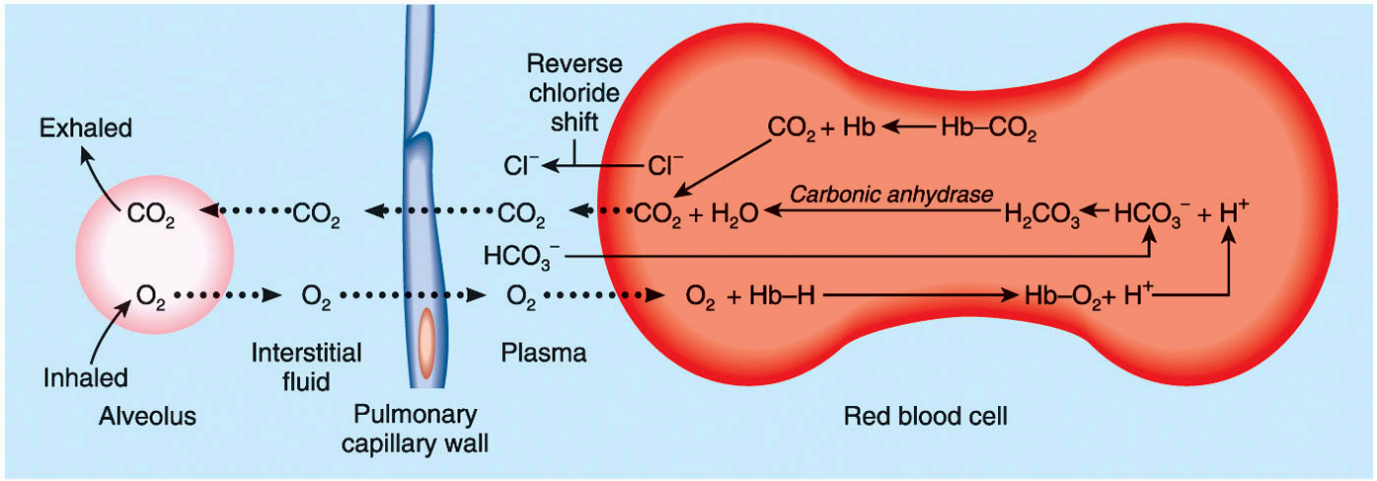
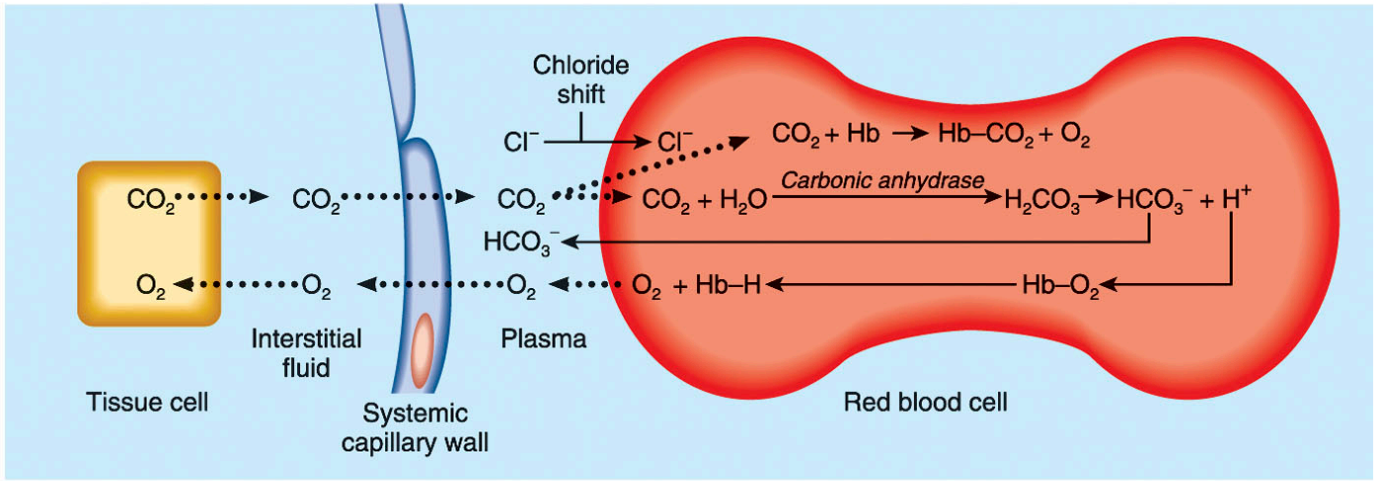
Carbon dioxide in blood





(a) Exchange of O_2 and CO_2 in pulmonary capillaries (external respiration)



(b) Exchange of O_2 and CO_2 in systemic capillaries (internal respiration)

Figure 23.23 Tortora - PAP 12/e

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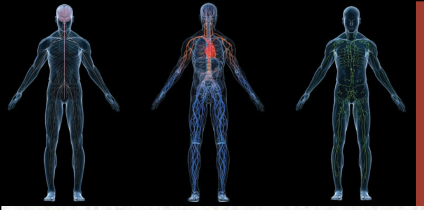

$C0_2$ Transport

- CO_2 transported in the blood (the 4 ml):
  - $HC0_3^-$ (60%).
  - Dissolved $C0_2$ (10%).
  - Carbaminohemoglobin (30%).

$$H_20 + CO_2 \overset{CA}{\Longleftrightarrow} H_2CO_3$$

High $PC0_2$

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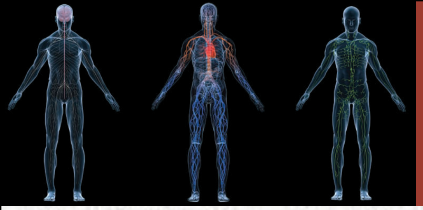

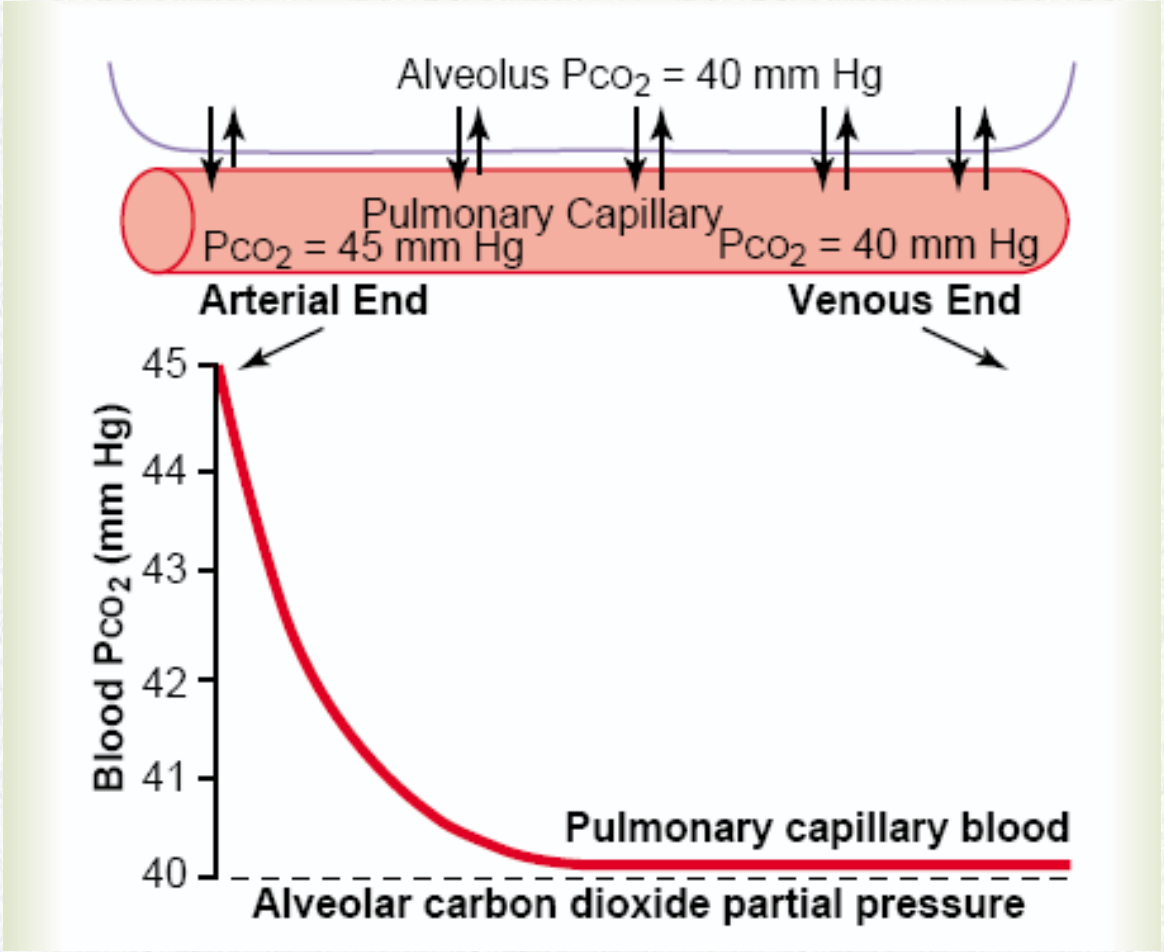

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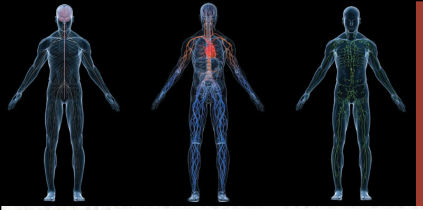

CO_2 TRANSPORT

	Arterial	Venous	A-V difference
Bicarbonate	43.2 (90%) 22.73 mM/l	45.6 (88%) 24 mM/l	2.4 (60 %)
$HbCO_2$	2.4(5%)	3.6 (7 %)	1.2 (30%)
Dissolved CO_2	2.4 (5%)	2.8 (5%)	0.4 (10%)
Total	48 (100%)	52 (100%)	4 (100%)

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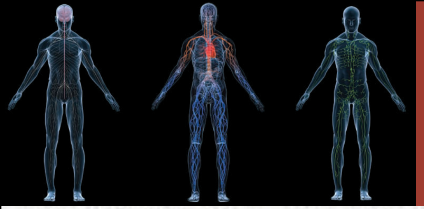

Transport of Carbon Dioxide

- Dissolved
  - solubility is 20-times of oxygen
  - venous blood: 2.7 ml/100 ml blood
  - arterial blood: 2.4 ml/100 ml blood
  - transported : 0.3 ml/100 ml blood
  - 7% total

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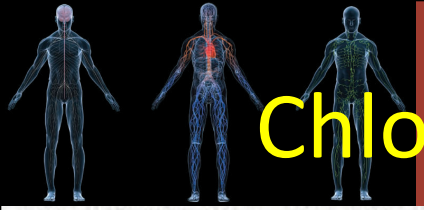

Chloride Shift at Systemic Capillaries

- **$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$**
- At the tissues, CO_2 diffuses into the RBC; shifts the reaction to the right.
  - Increased [HCO_3^-] produced in RBC:
    - HCO_3^- diffuses into the blood.
  - RBC becomes more +.
    - Cl^- attracted in (Cl^- shift).
  - H^+ released buffered by combining with deoxyhemoglobin.
- $HbCO_2$ formed.
  - Unloading of O_2.

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Carbon Dioxide Transport and Chloride Shift

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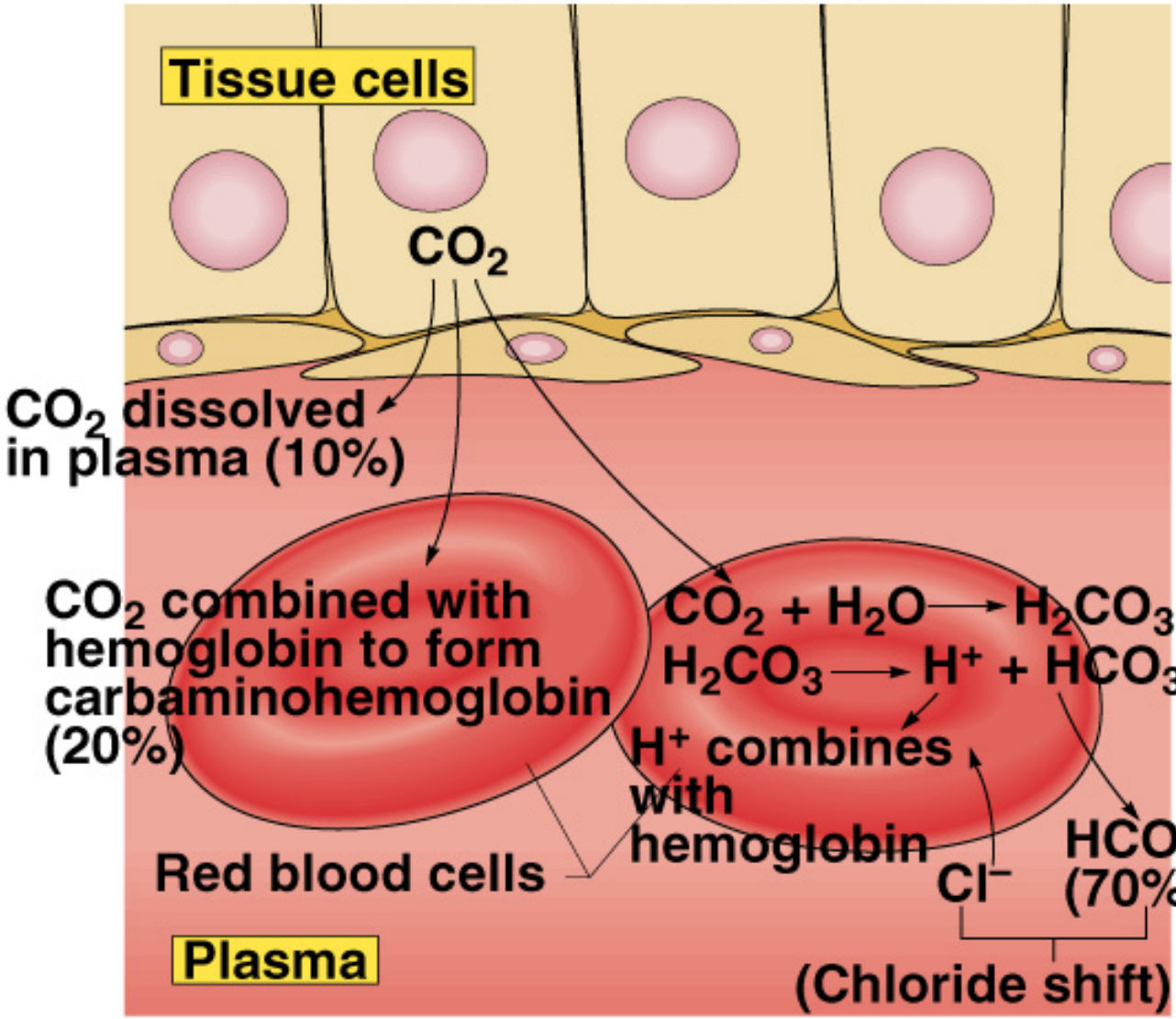

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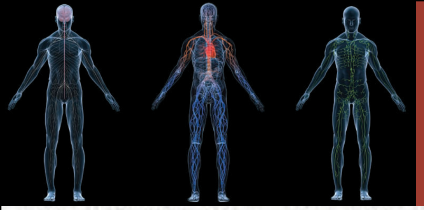

At Pulmonary Capillaries

- $H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$
- At the alveoli, CO_2 diffuses into the alveoli; reaction shifts to the left.
- Decreased [$HC0_3^-$] in RBC, $HC0_3^-$ diffuses into the RBC.
  - RBC becomes more -.
    - Cl^- diffuses out (reverse Cl^- shift).
- Deoxyhemoglobin converted to oxyhemoglobin.
  - Has weak affinity for H^+.
- Gives off $HbC0_2$.

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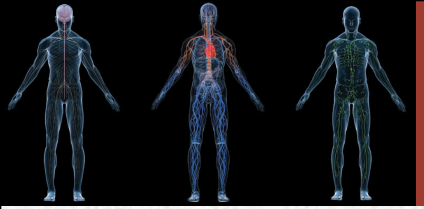

Increased Oxygen Delivery to Tissue

- Two means by which oxygen delivery to tissue can be increased. Name them….
  - 1:
  - 2:

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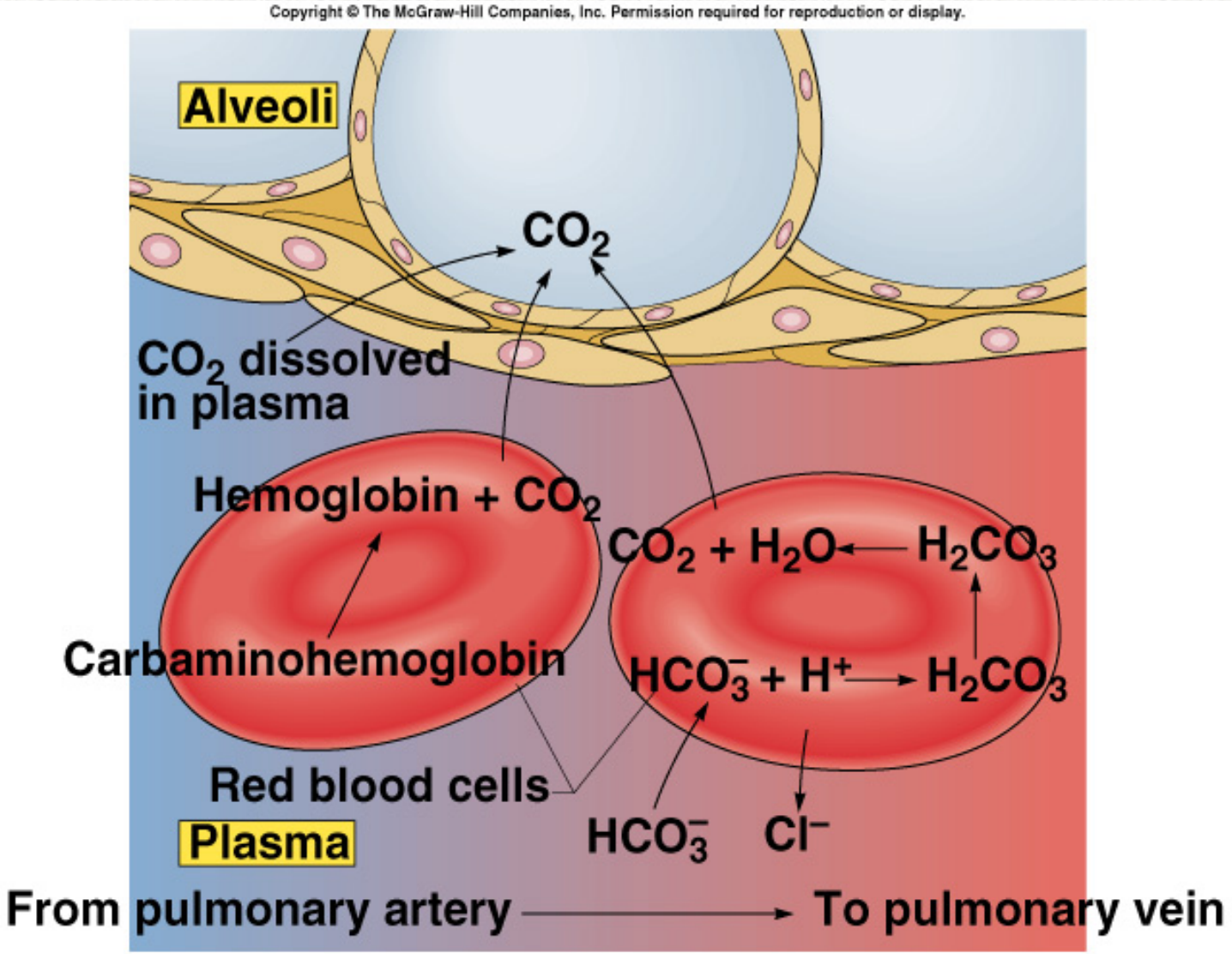
Reverse Chloride Shift in Lungs



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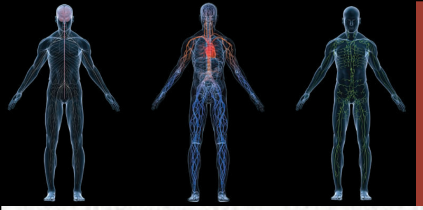
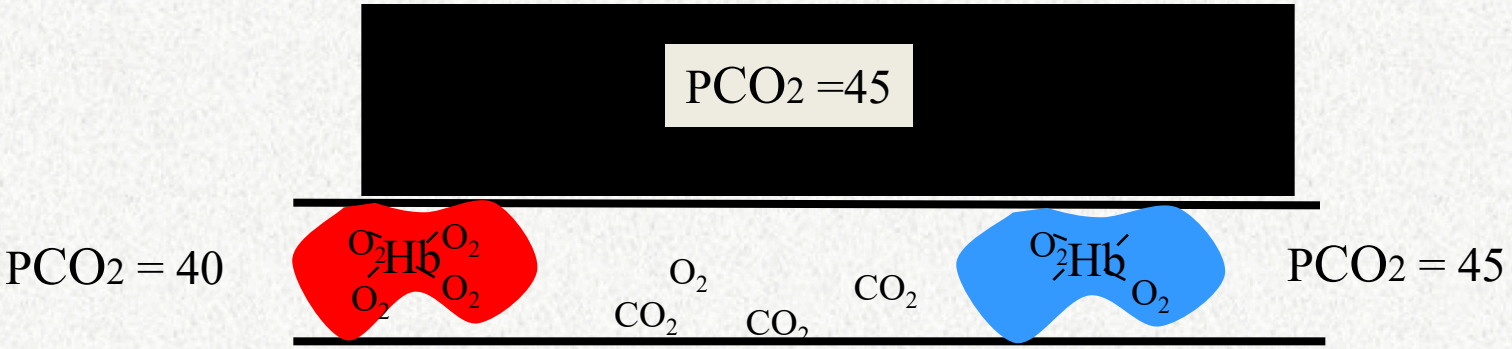
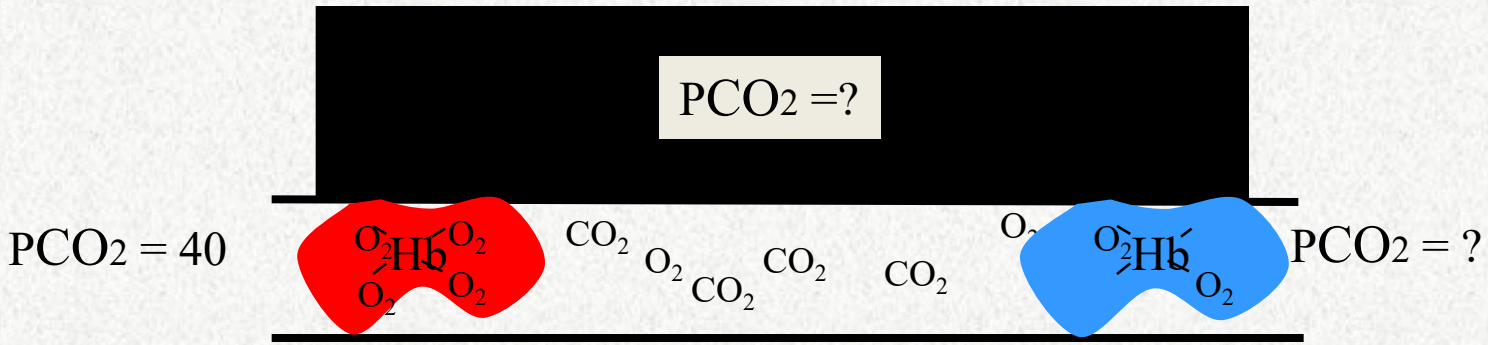


Blood and Muscle PCO_2



Increased Metabolism and **normal** blood flow



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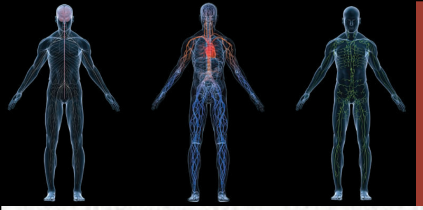
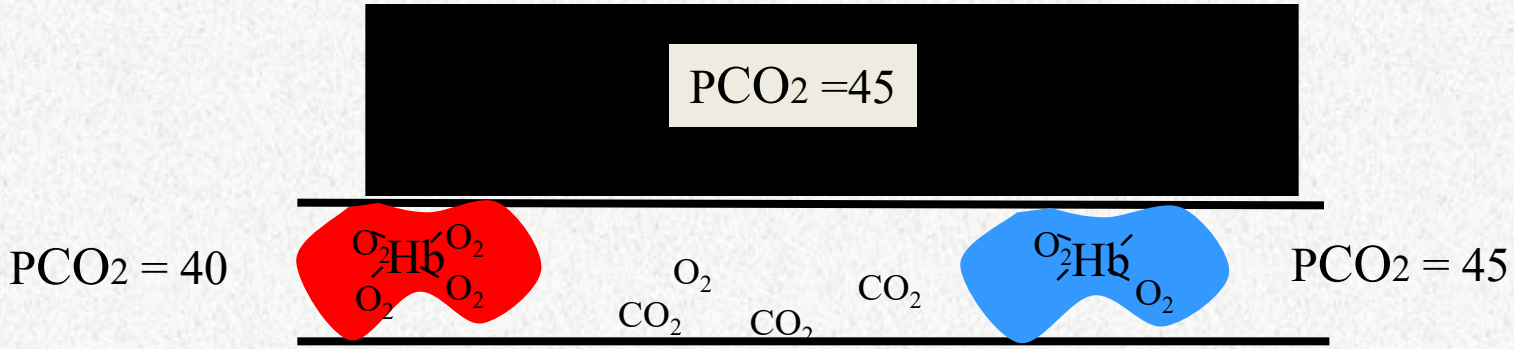
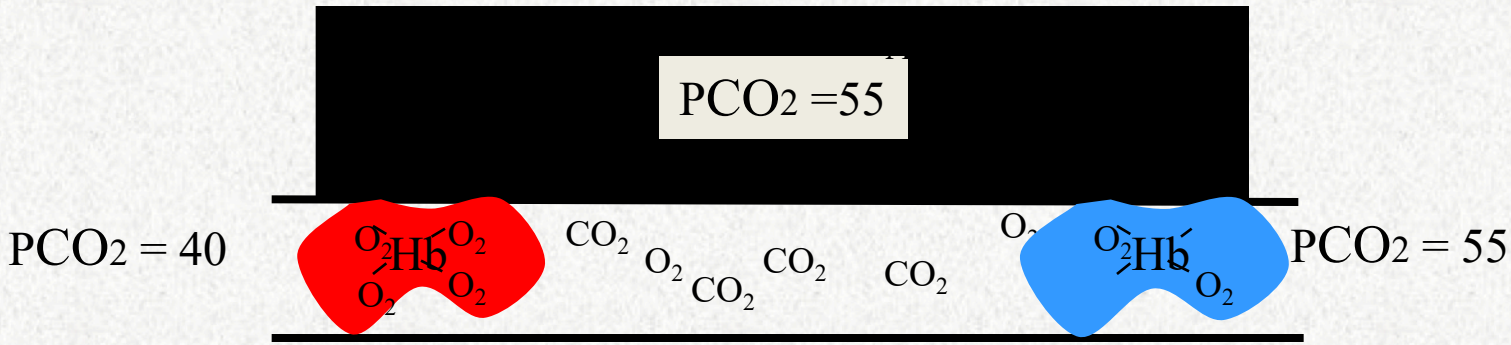


Blood and Muscle PCO_2



Increased Metabolism and normal blood flow



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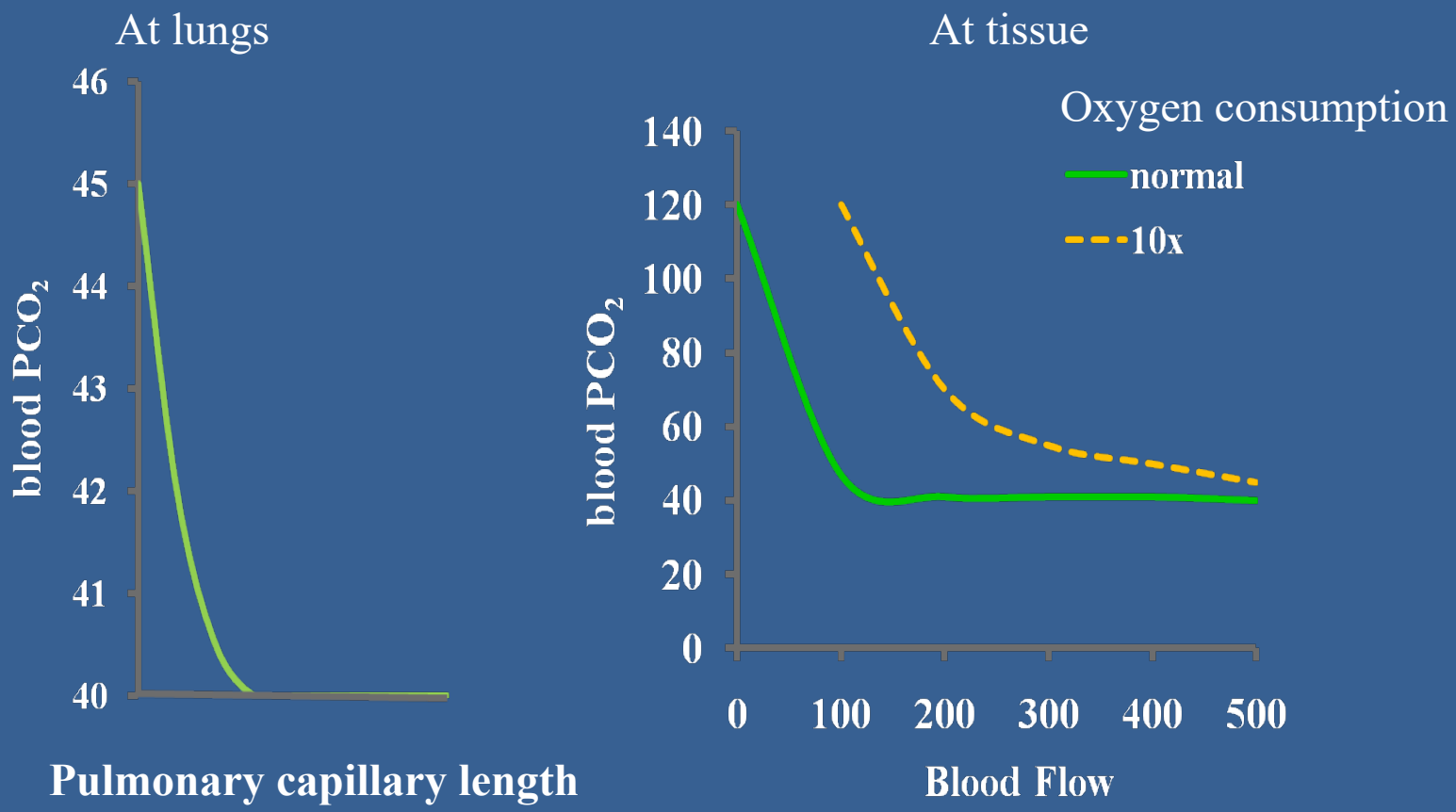
Diffusion of Carbon Dioxide



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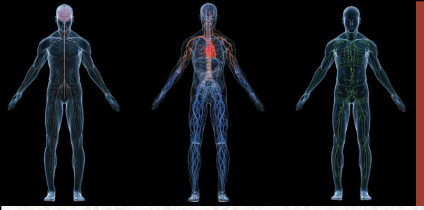
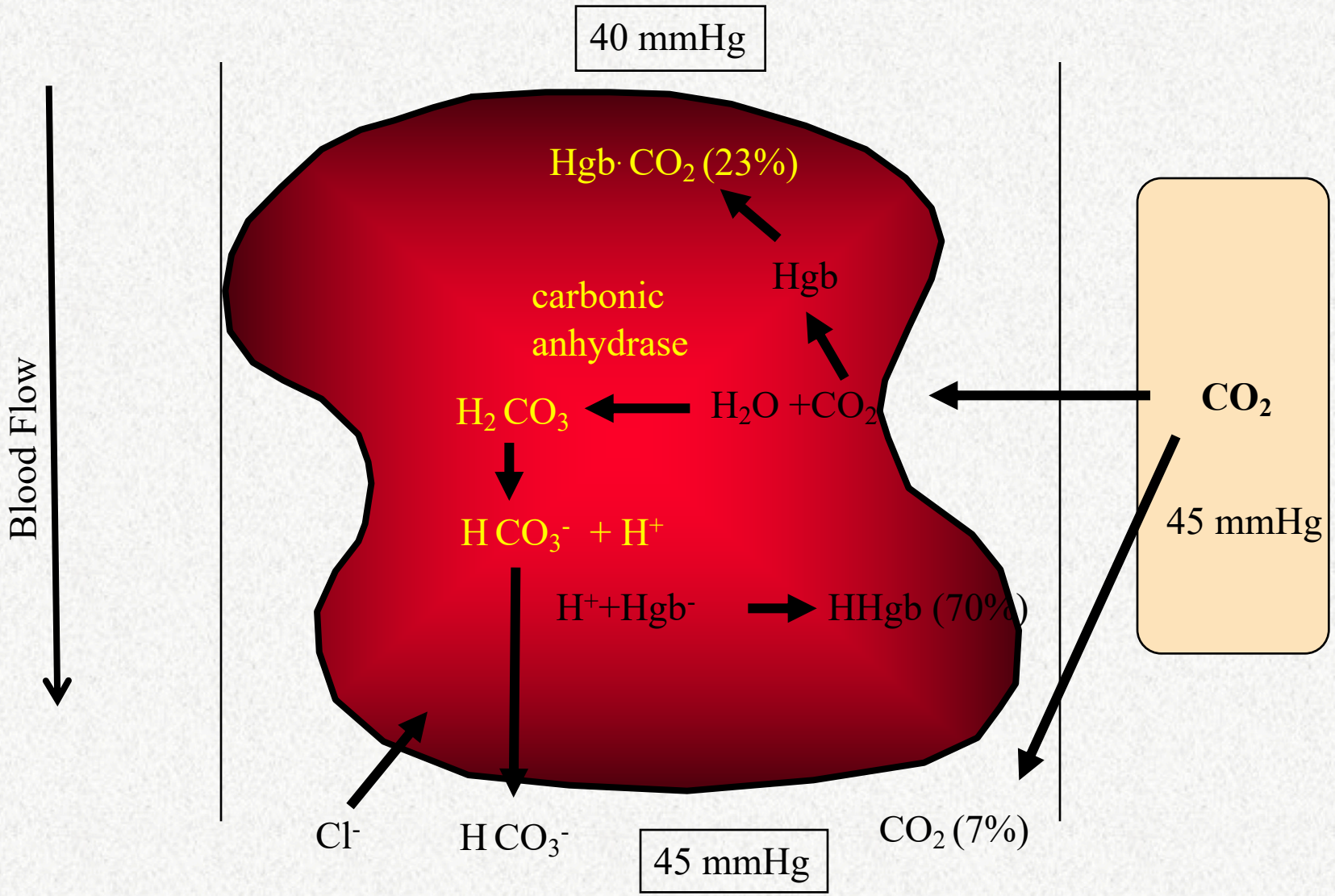
Transport of Carbon Dioxide at Tissue





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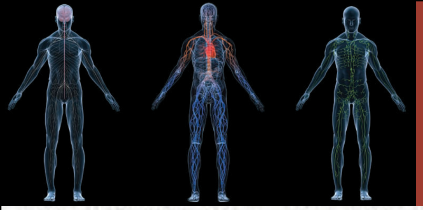
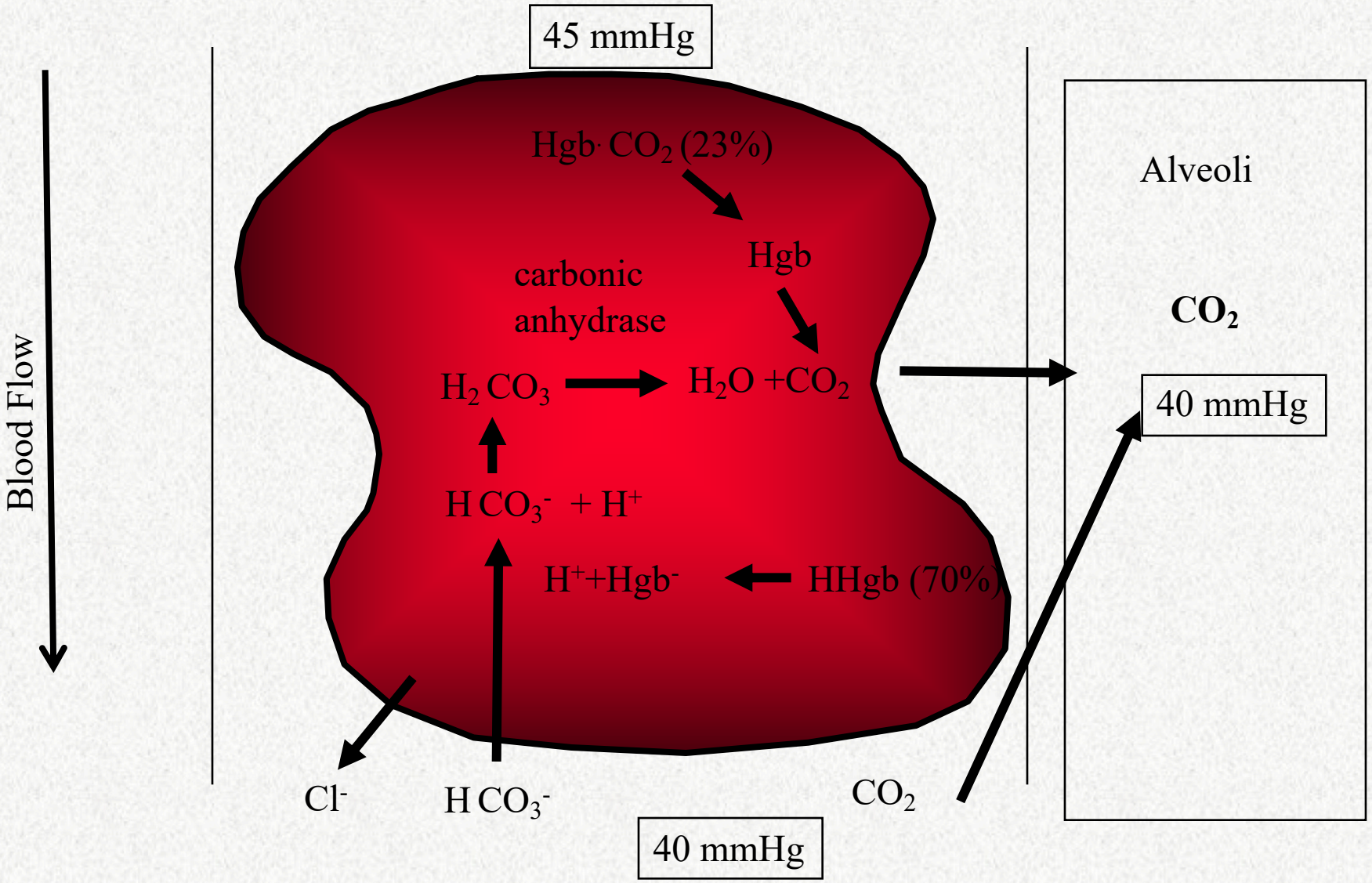


Transport of Carbon Dioxide at Lung



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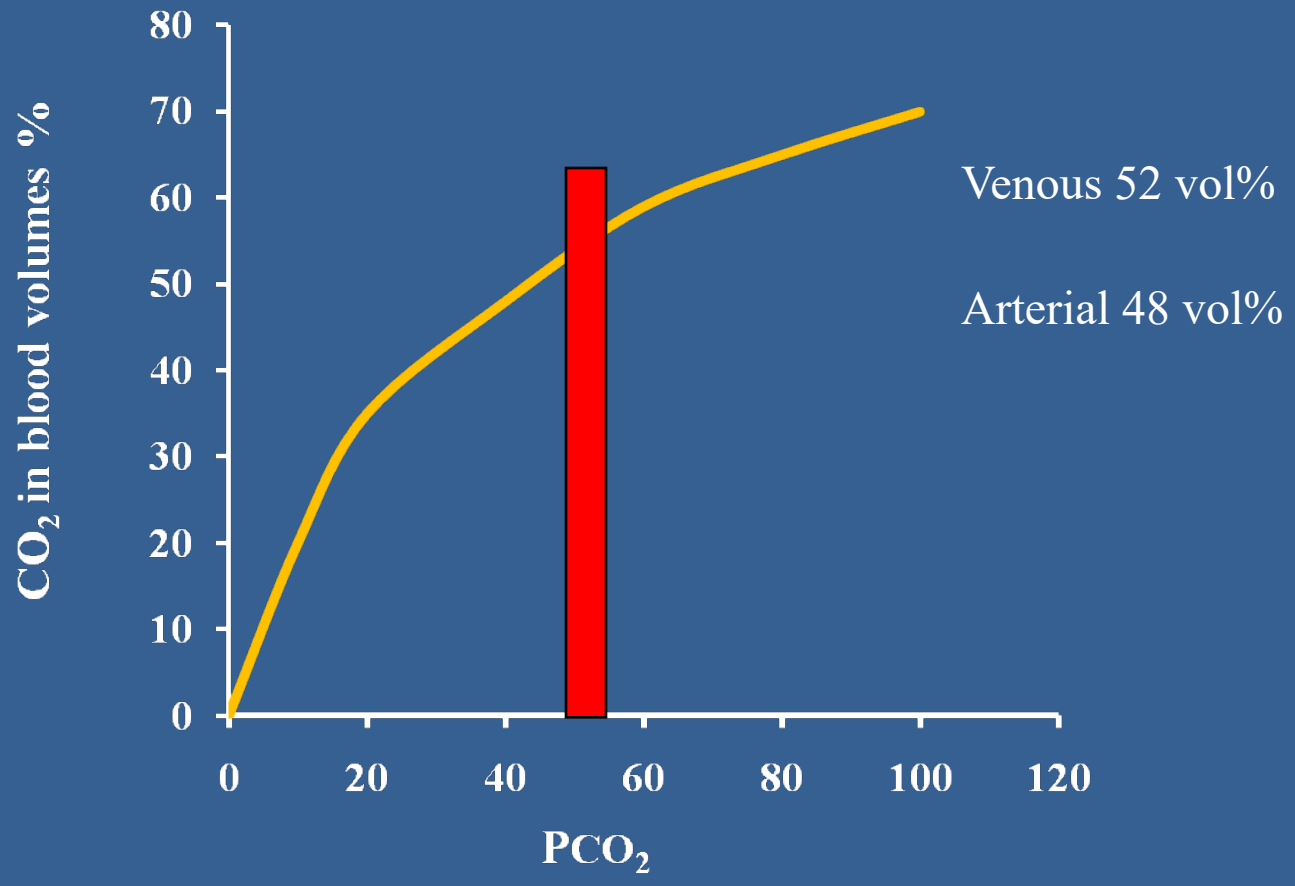
Carbon Dioxide Dissociation Curve



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