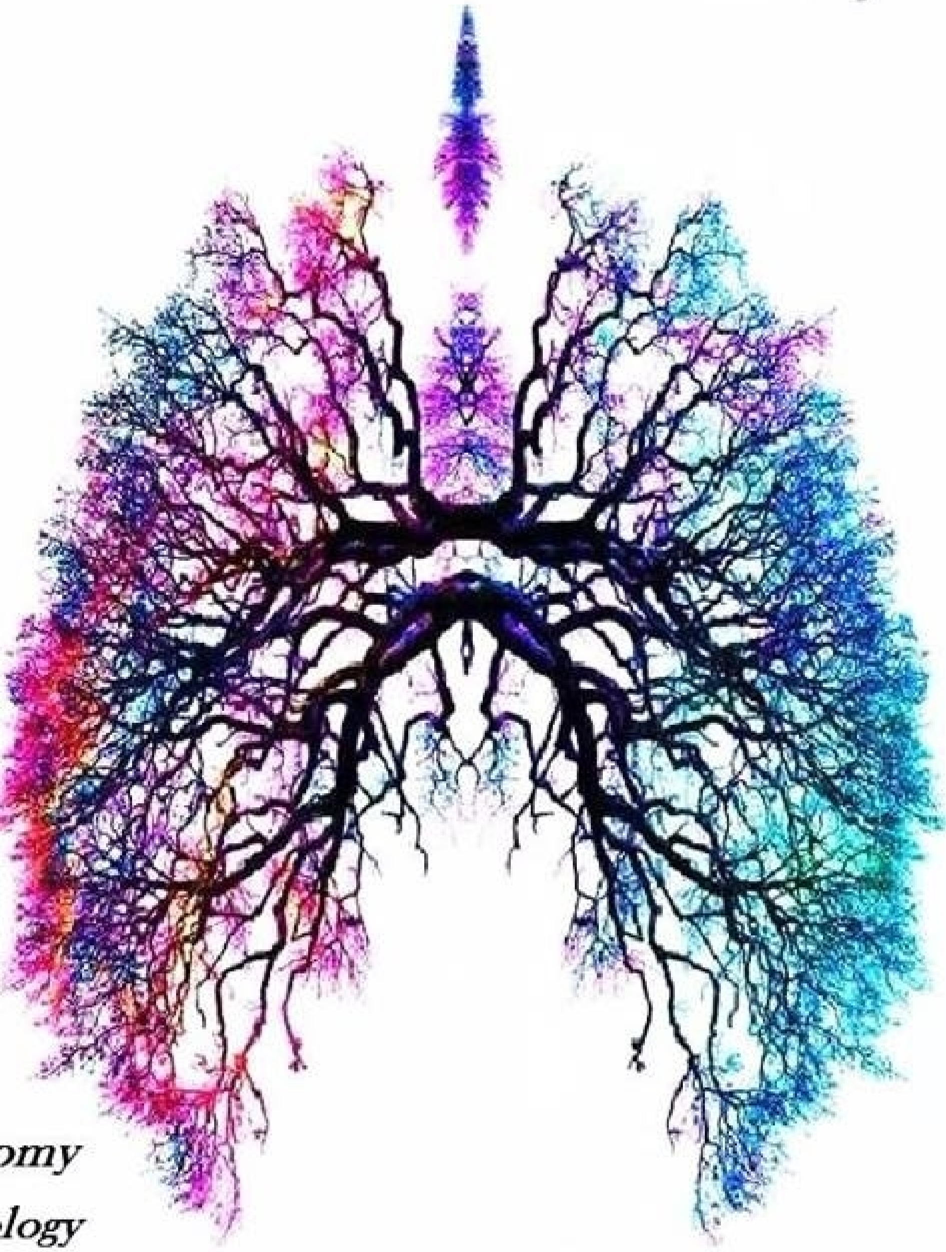
RESPIRATORY SYSTEM

Cover by: Aseil Khatib



- ○ Anatomy
- ○ Pathology
- ● Physiology
- ○ Pharmacology
- ○ Microbiology
- ○ PBL

Dr Name: Dr. Yanal Shafagoj
Lecture # 1

Sheet ☐
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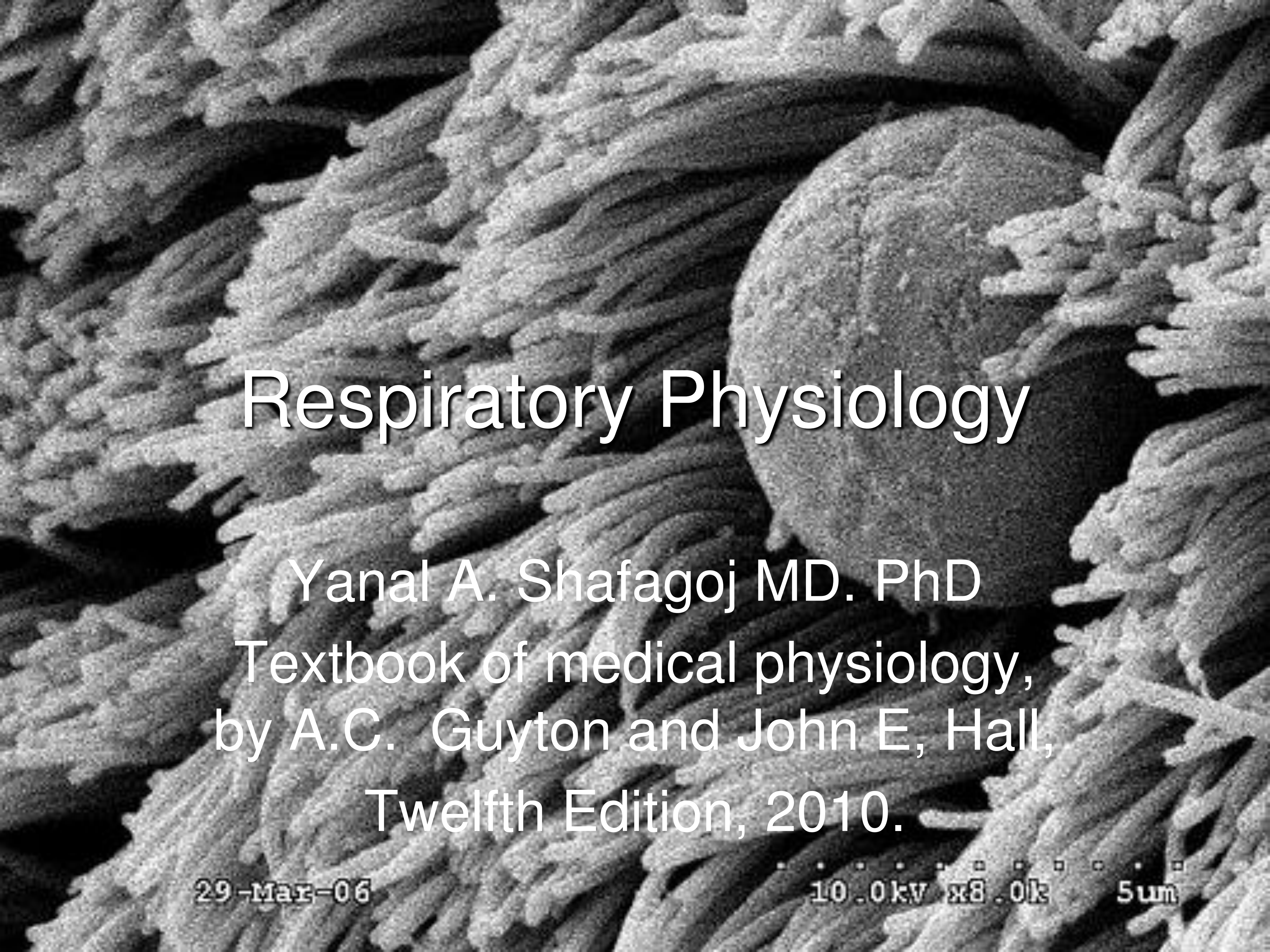
Other ☐

Respiratory Physiology

Yanal A. Shafagoj MD. PhD

Textbook of medical physiology,
by A.C. Guyton and John E, Hall,
Twelfth Edition, 2010.



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

- What are the Potential Causes of Hypoxia
  - inadequate oxygenation of lungs
    - atmosphere
    - decrease muscle activity
  - pulmonary disease
  - inadequate transport
    - anemia, abnormal hemoglobin
    - blood flow
  - inadequate usage
    - cyanide

Introduction

- Respiration is the process by which the body takes in and utilizes oxygen and gets rid of CO_2.
- ***Three determinants of respiration***
- Respiration depends on three things: the lungs, the blood, and the tissues.

- ***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 system), 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.
- **<u>Hypoxia can therefore result from a fault at any point along this lungs-blood-tissue chain.</u>**

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….Homeostasis of O2, CO2, pH

One more time: To achieve these goals:

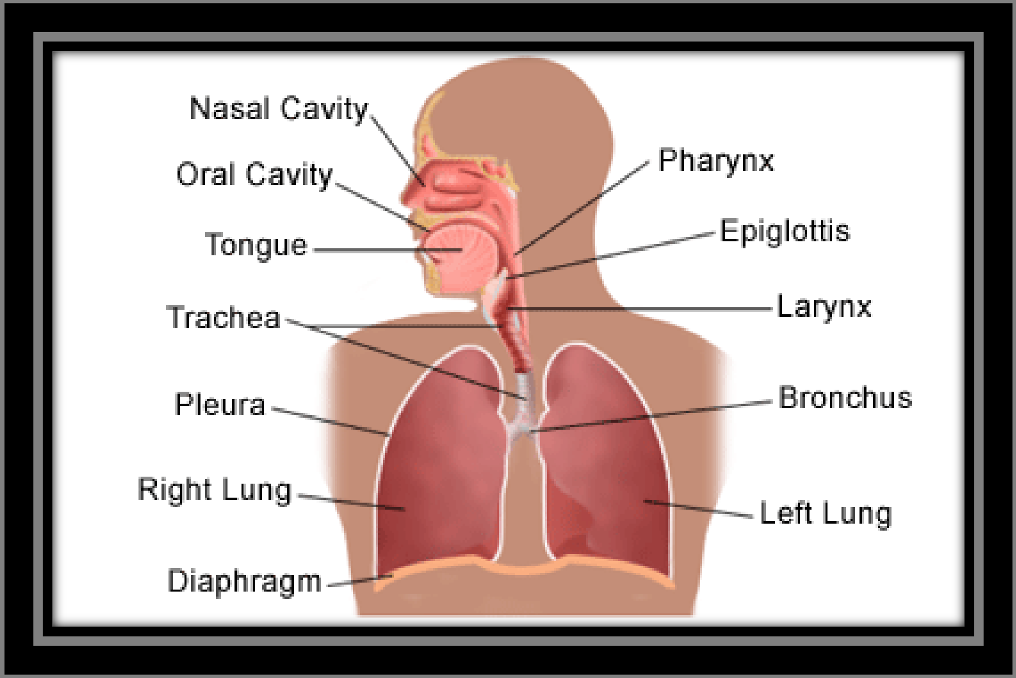
respiration can be divided into four major functions:

(1) *Pulmonary ventilation*

(2) *Diffusion*

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

(4) *Regulation of ventilation*.



Lecture Outline

- **Basics of the Respiratory System**
  - Function & Structure
- Gas Laws
- Ventilation

The lungs have several metabolic and endocrine functions

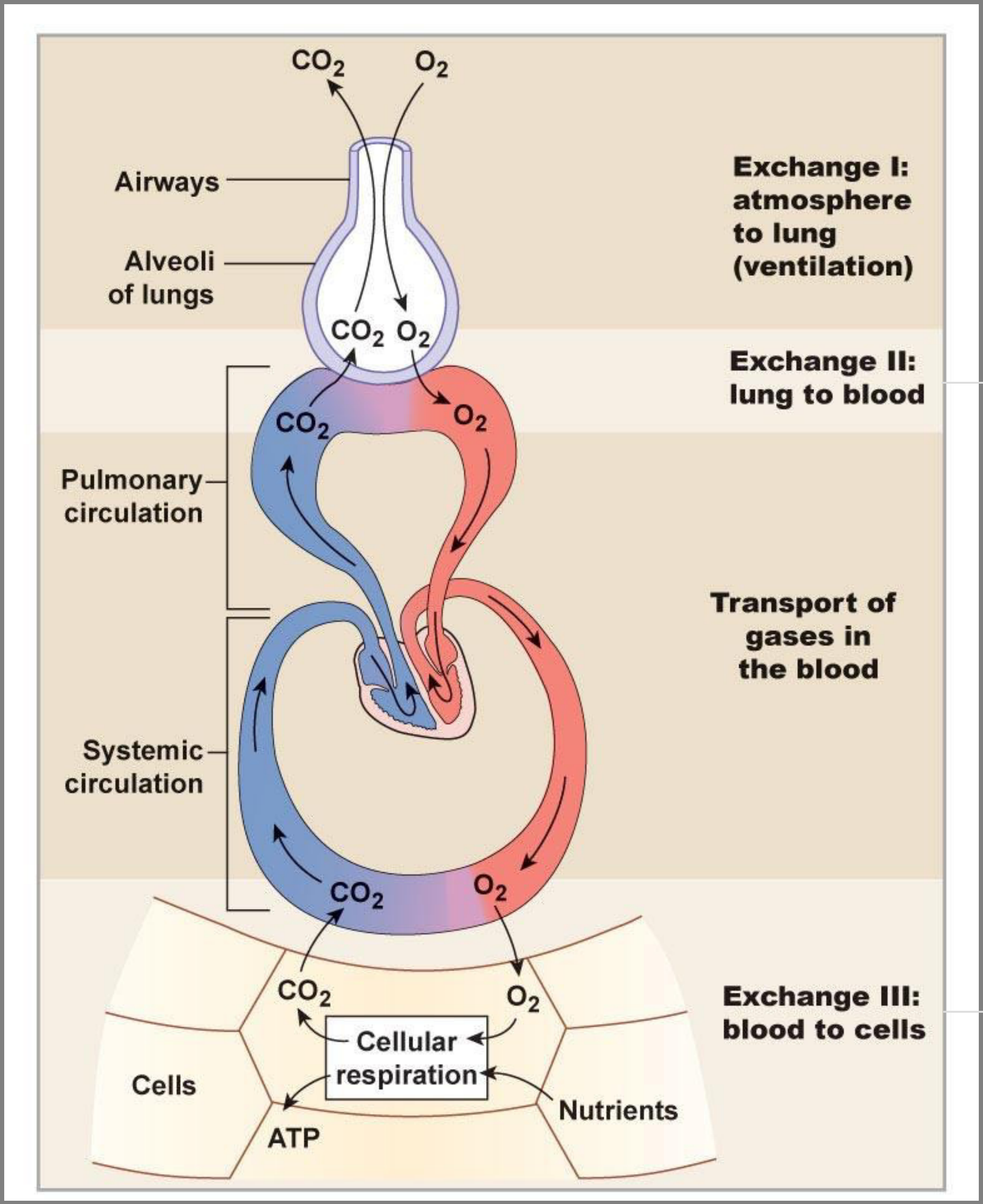
- Exchange of gases
- Directionality depends on gradients “Pressure difference “!
  - Atmosphere to blood - Blood to tissues
- Excretion of some volatile waste products e.g. acetone and alcohol.
- Helps blood and lymph flow (venous return)
- Regulation of body temperature by evaporation of water from the respiratory passages to help heat loss from the body
- Regulation of pH…Acid-base balance which dependents on rate of CO2 release
- BP regulation by conerting AI to AII
- Protection…..Vocalization etc
- Plus other things you learn them from your lecture outline

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 in ATP synthesis

Schematic View of Respiration



→ External Respiration

→ Internal Respiration

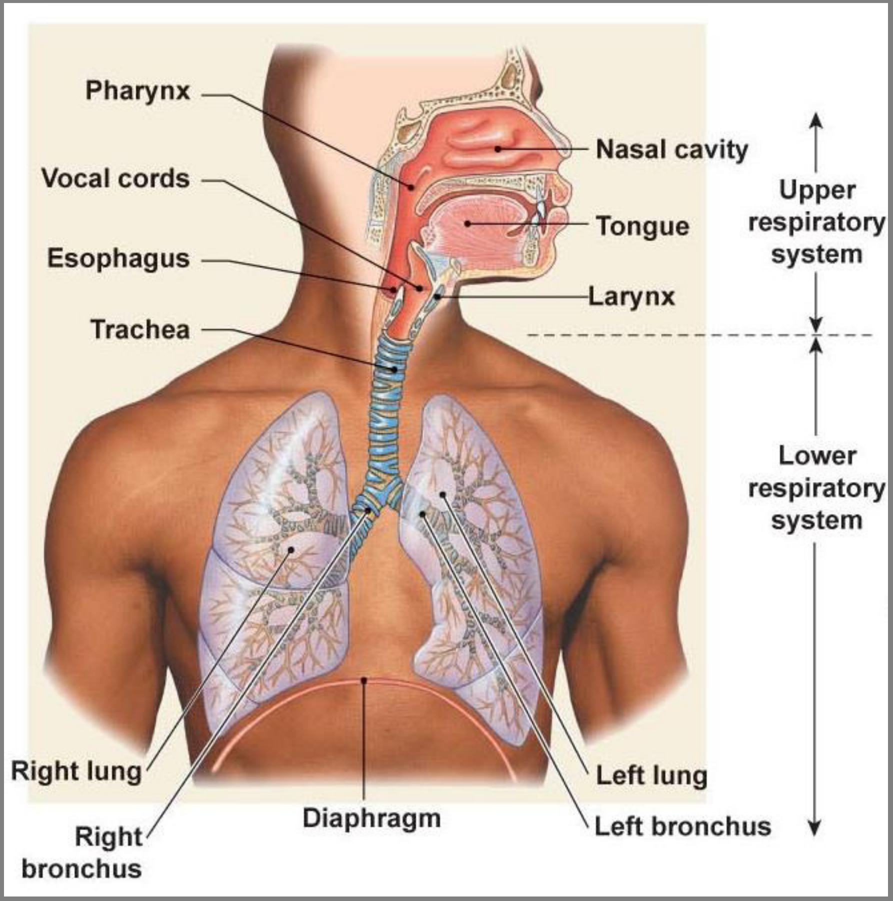
Partial Pressures of Gases in Inspired Air and Alveolar Air

	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

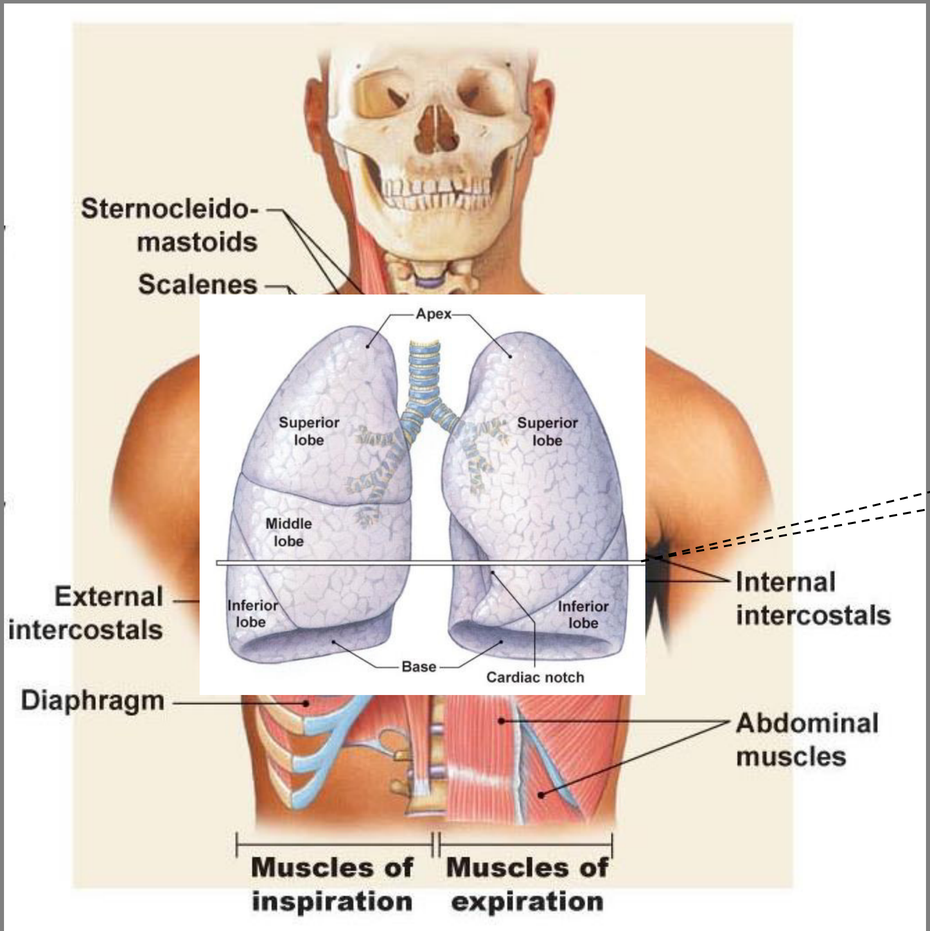
- What structural aspects must be considered in the process of respiration?
  - The conducting zone
  - The respiratory zone
  - The structures involved with ventilation
    - Skeletal & musculature
    - Pleural membranes
    - Neural pathways
- All divided into
  - Upper respiratory tract
    - Entrance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

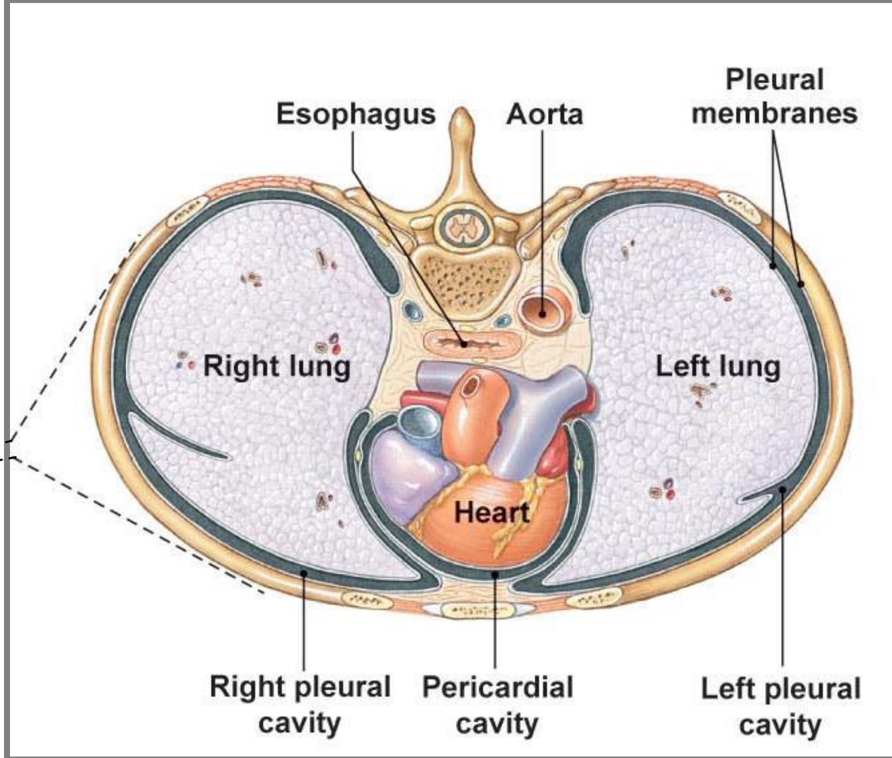


Basics of the Respiratory System

Functional Anatomy

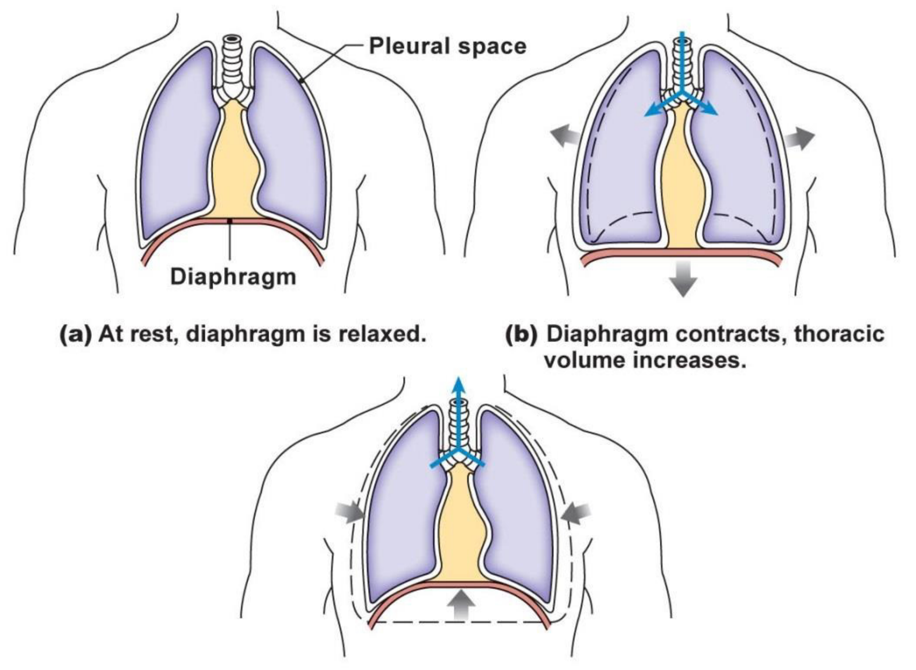
- Bones, Muscles & Membranes





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



(a) At rest, diaphragm is relaxed. **(b)** Diaphragm contracts, thoracic volume increases. **(c)** Diaphragm relaxes, thoracic volume decreases.

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 call it branch or division)…we have 23 generations or branches or divisions
  - similar to the vascular component
  - larger airway = high velocity
    - small cross-sectional area
  - smaller airway = low velocity
    - large cross-sectional area

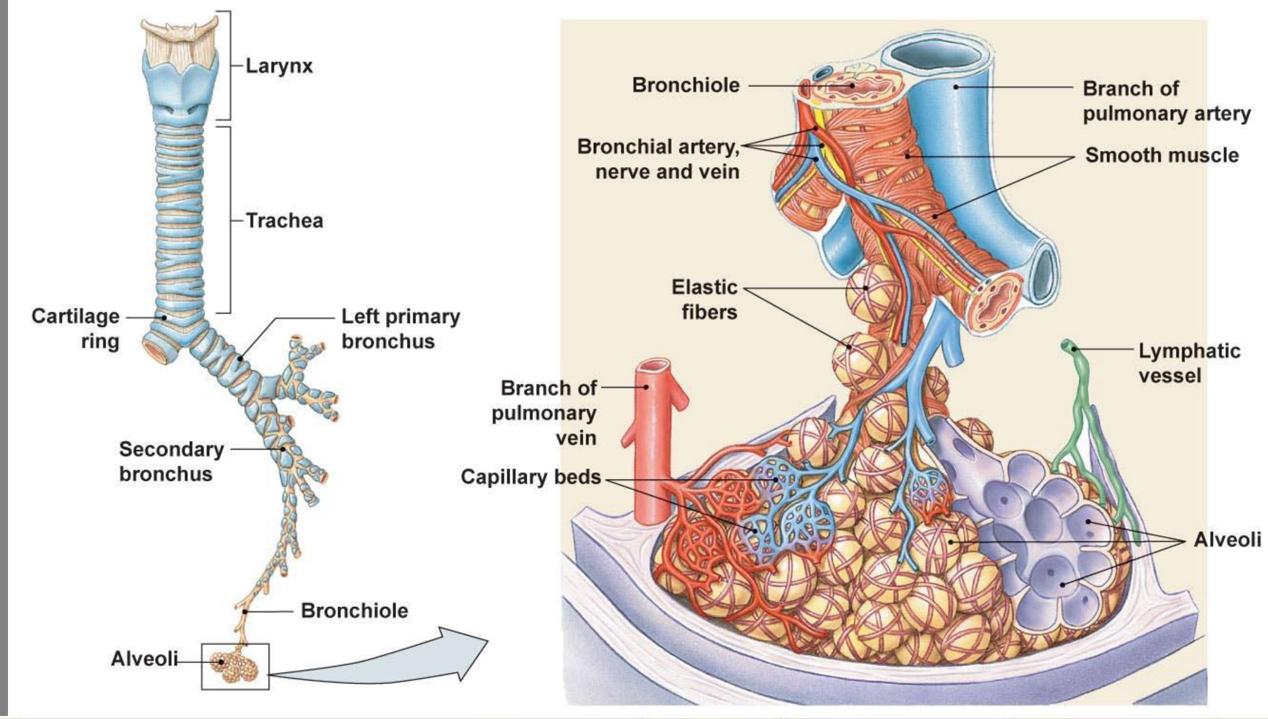
Basics of the Respiratory System

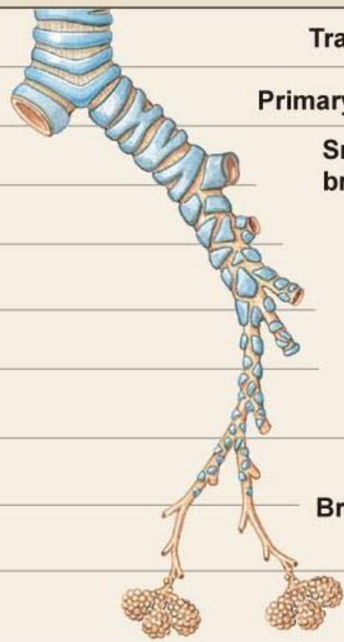
Functional Anatomy

- 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 (Trachea through Terminal bronchioles)

exchange portion…last 7 generations (Respiratory bronchioles and Alveolar ducts)

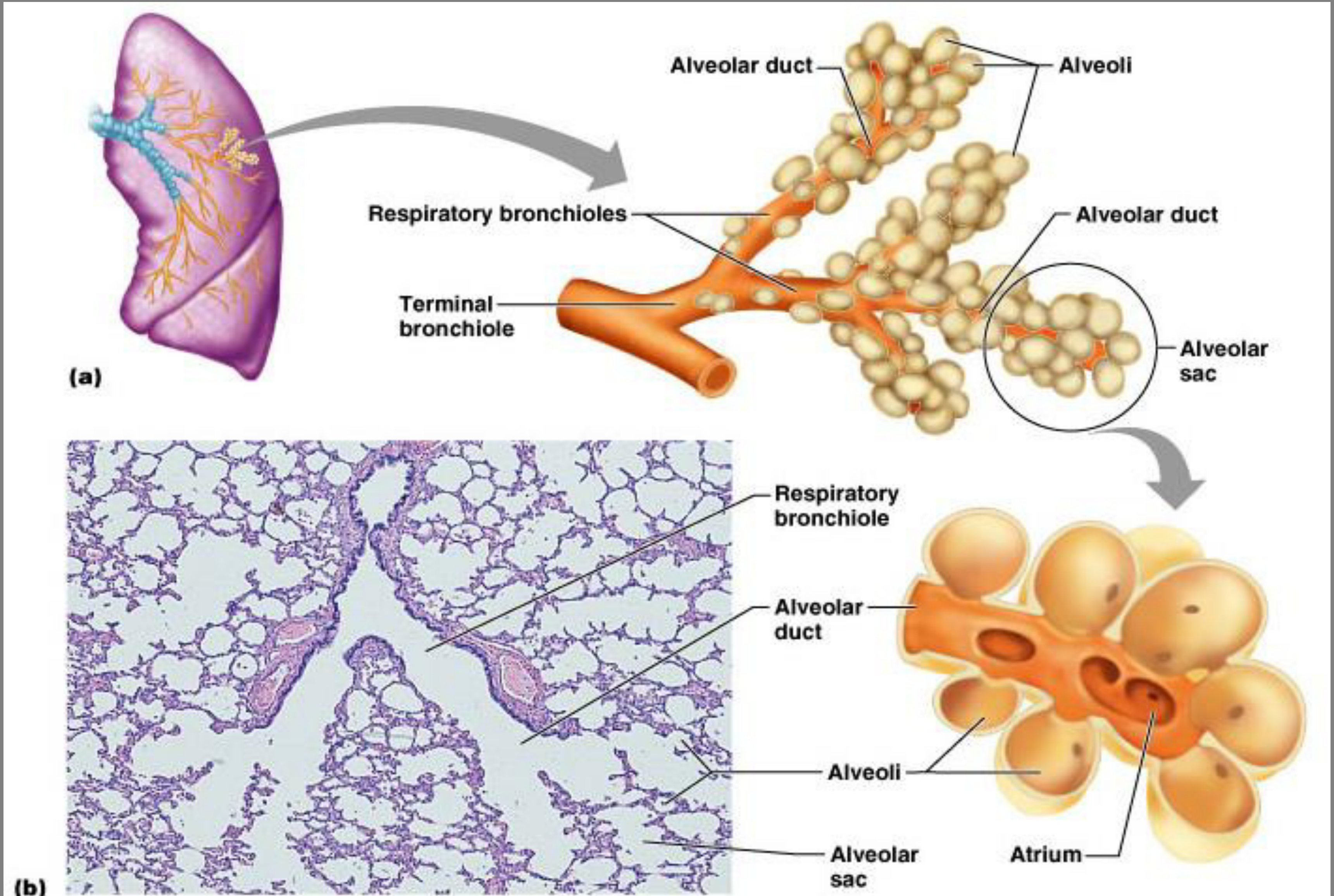




	Name	Division	Diameter (mm)	How many?	Cross-sectional area (cm^2)
Conducting system	Trachea	0	15-22	1	2.5
	Primary bronchi	1	10-15	2	↓
	Smaller bronchi ↓	2	1-10	4 ↓	
		3			
		4			
		5			
		6-11		1×10^4	
	Bronchioles	12-23	0.5-1	2×10^4 ↓ 8×10^7	100 ↓ 5×10^3
Exchange surface	Alveoli	24	0.3	$3\text{-}6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

Cartilage and protection

- The first 10 generations have cartilage and thus have support and therefore are somehow not collapsible structures
- 12th to 16th are called bronchioles (diameter < 1 mm) lack cartilage….and thus collapsible
- From 0-16 is the conductive zone
- From 17-23 is the respiratory zone
- Some times 17th -19th are called Transitional zone
- 20th to 22nd 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)

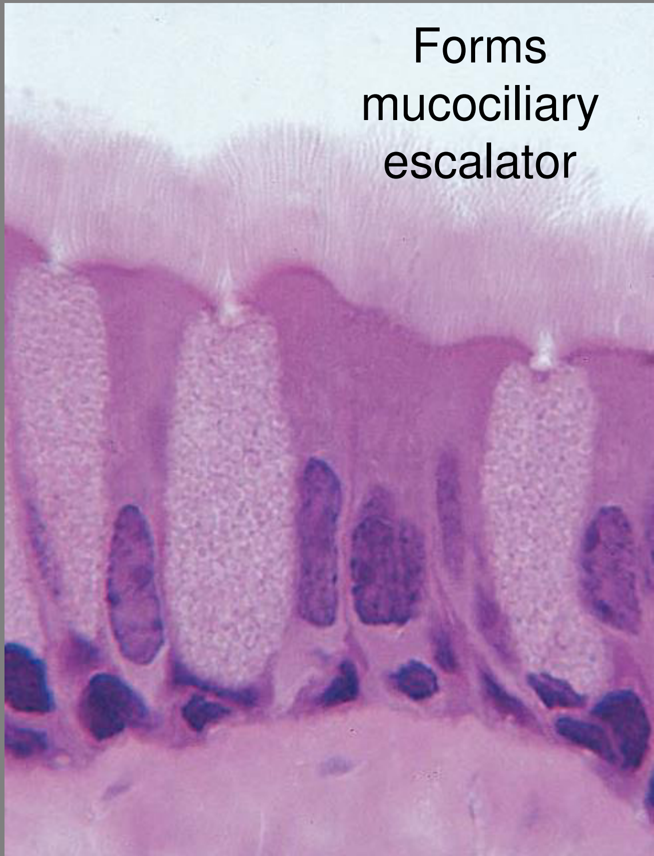
Basics of the Respiratory System

Functional Anatomy

- Anatomic Dead space : Definition…Function
-
  - Warm
  - Humidify
  - Filter
  - Vocalize

Raises incoming air to 37 Celsius

Raises incoming air to 100% humidity



Basics of the Respiratory System
Functional Anatomy

- What is the function of the respiratory zone?
  - Exchange of gases …. Due to
    - Huge surface area = type I alveolar cells (simple squamous
    - epithelium) alveolar surface area is 50-100 m^2
    - The surface area of the alveoli available for diffusion is about the size of a tennis court
    - Associated network of pulmonary capillaries
      - 80-90% of the space between alveoli is filled with blood in pulmonary capillary networks
    - Exchange distance is approx 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
  - 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   for practical purposes we will consider PCO≈ zero mmHg
    - Water vapor, krypton, argon, …. Make up the rest
- A few laws to remember
  - Dalton's law…the partial pressure law
  - Fick's Laws of Diffusion…Ohm's law
  - Boyle's Law: volume versus pressure
  - Ideal Gas Law…conversion between units

- **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	---	---	40	40	46	27
PH_2O	---	47	47	47	47	47
PN_2	600	563 →	571	571	571	566
Total P	**760**	**760**	**760**	**760**	**704**	**760**

Po_2 IN THE ALVEOLI

$$P_AO_2 = P_IO_2 - (PCO_2/R)$$

$$PO_2 = 149 - (40/0.8) = 99$$

R is respiratory exchange ratio ~0.8

Remember in a normal person alveolar PO_2 = arterial PO_2, and alveolar PCO_2 = arterial PCO_2 .

Respiratory Physiology
Gas Laws

- Dalton's Law
  - Law of Partial Pressures
    - "each gas in a mixture of gases 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 the 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
        - » P_{O_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.

$$P_{atm} = P_{H_2O} + P_{O_2} + P_{N_2}$$

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

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**

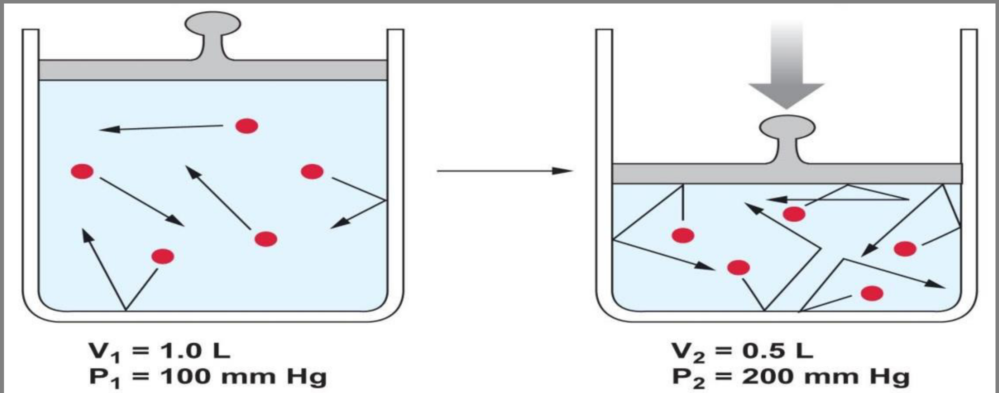
- **Diffusion Coefficient = Solubility/(Molecular weight)$^{1/2}$**

- Since it is the square root of MW, its effect is small

Respiratory Physiology

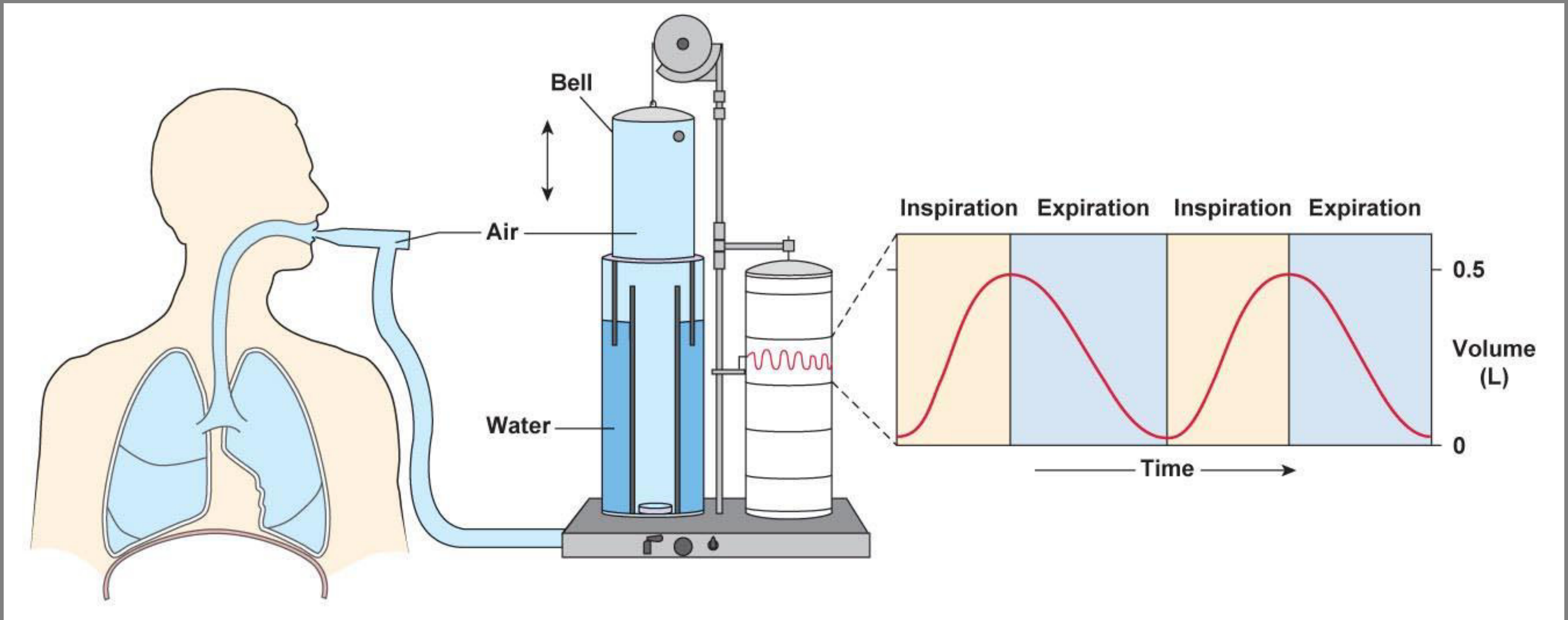
Gas Laws

- 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"
    - $P_1V_1 = P_2V_2$



Respiratory Physiology
Gas Laws

- How does Boyle's Law work in us?
  - As the thoracic cavity (container) expands the volume must up 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
- Do we care? It helps you to covert PCO2 (mmHg) to [CO2] in mMole/l later when you consider acid-base disturbance.

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 in equilibrium with that liquid.

OR

the solubility of a gas in a liquid at a particular temperature is proportional to the pressure *of that gas* above the liquid.

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

Using this law you can predict how much O2 and CO2 are available in dissolved form

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.
- [Gas] dissolved in a fluid depends directly on its partial pressure in the gas mixture.

Ventilation

- Cause of Inspiration?
  - 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?

Mechanics of Breathing

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

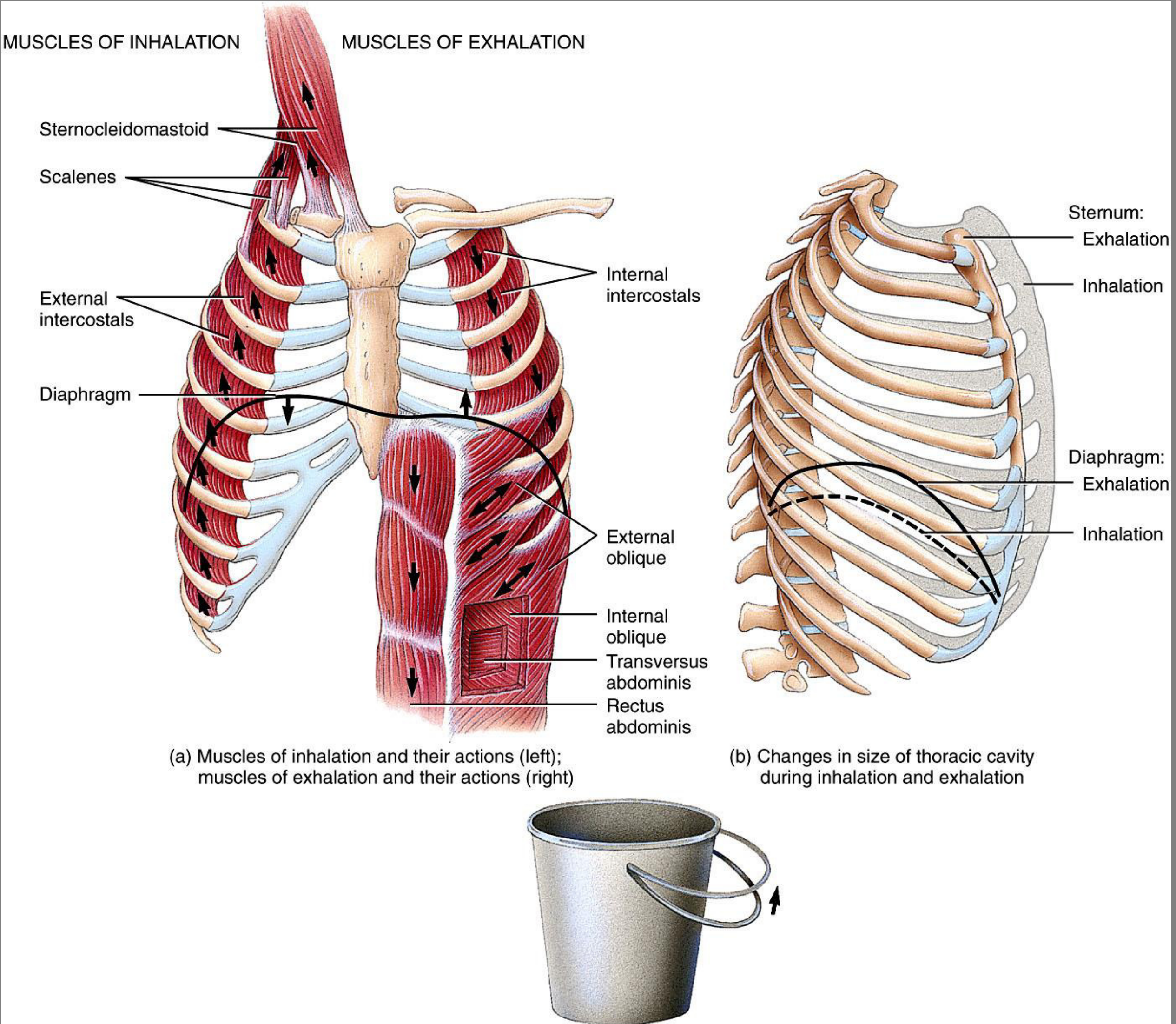
Always remember Ohm's law:

Flow = pressure difference / 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
- 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.
- Boyle's law: The pressure and the volume of a gas are

Inhalation

- Inhalation is active – 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 intercostals
    - Contraction elevates ribs
    - 25% of air entering lungs during normal quiet breathing
  - Accessory muscles for deep, forceful inhalation
- When thorax expands, parietal and visceral pleurae adhere tightly due to subatmospheric pressure and surface tension – pulled along with expanding thorax
- As lung volume increases, alveolar (intrapulmonic) pressure drops



(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

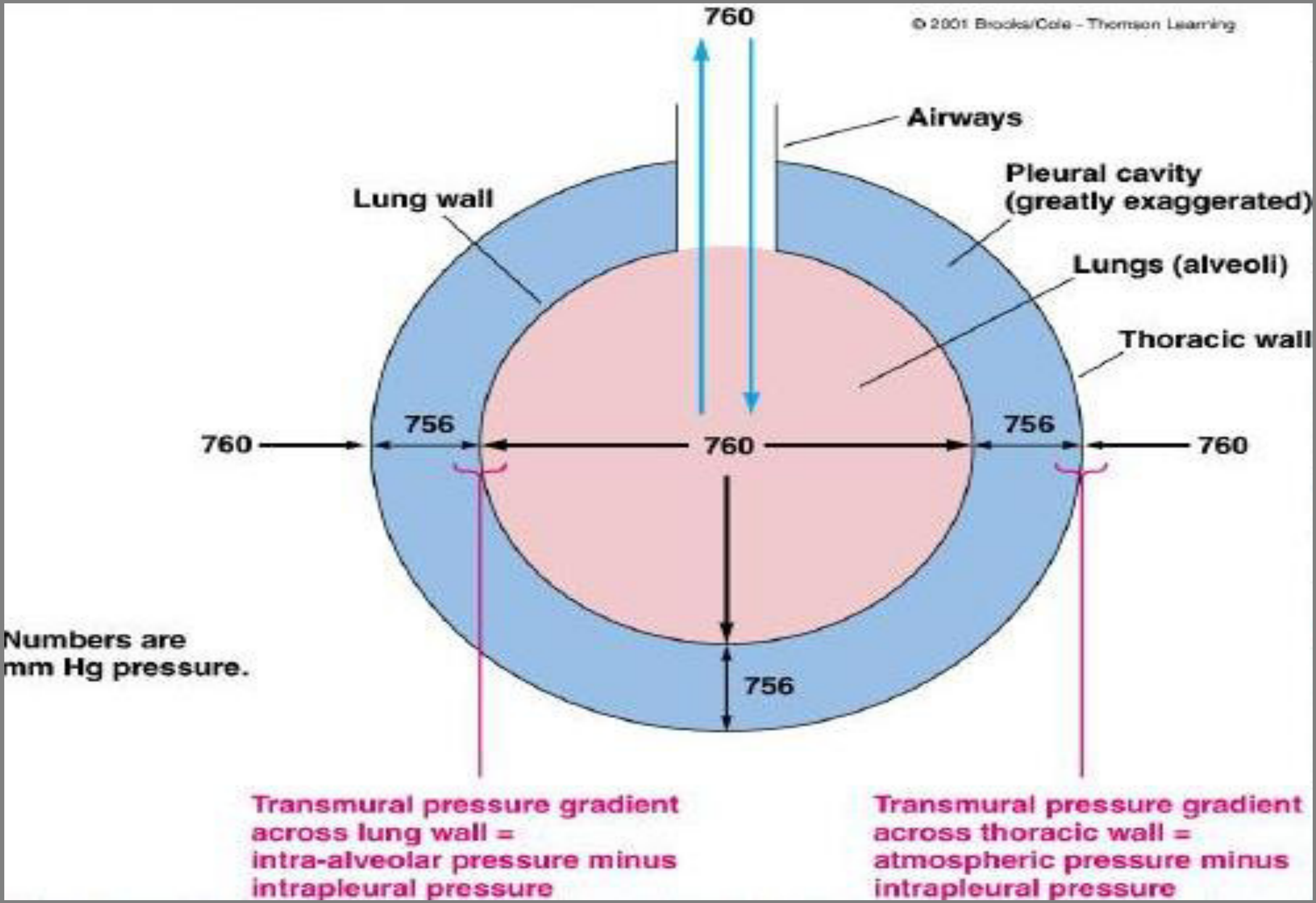
(c) During inhalation, the ribs move upward and outward like the handle on a bucket

Figure 23.13 Tortora - PAP 12/e

Ventilation

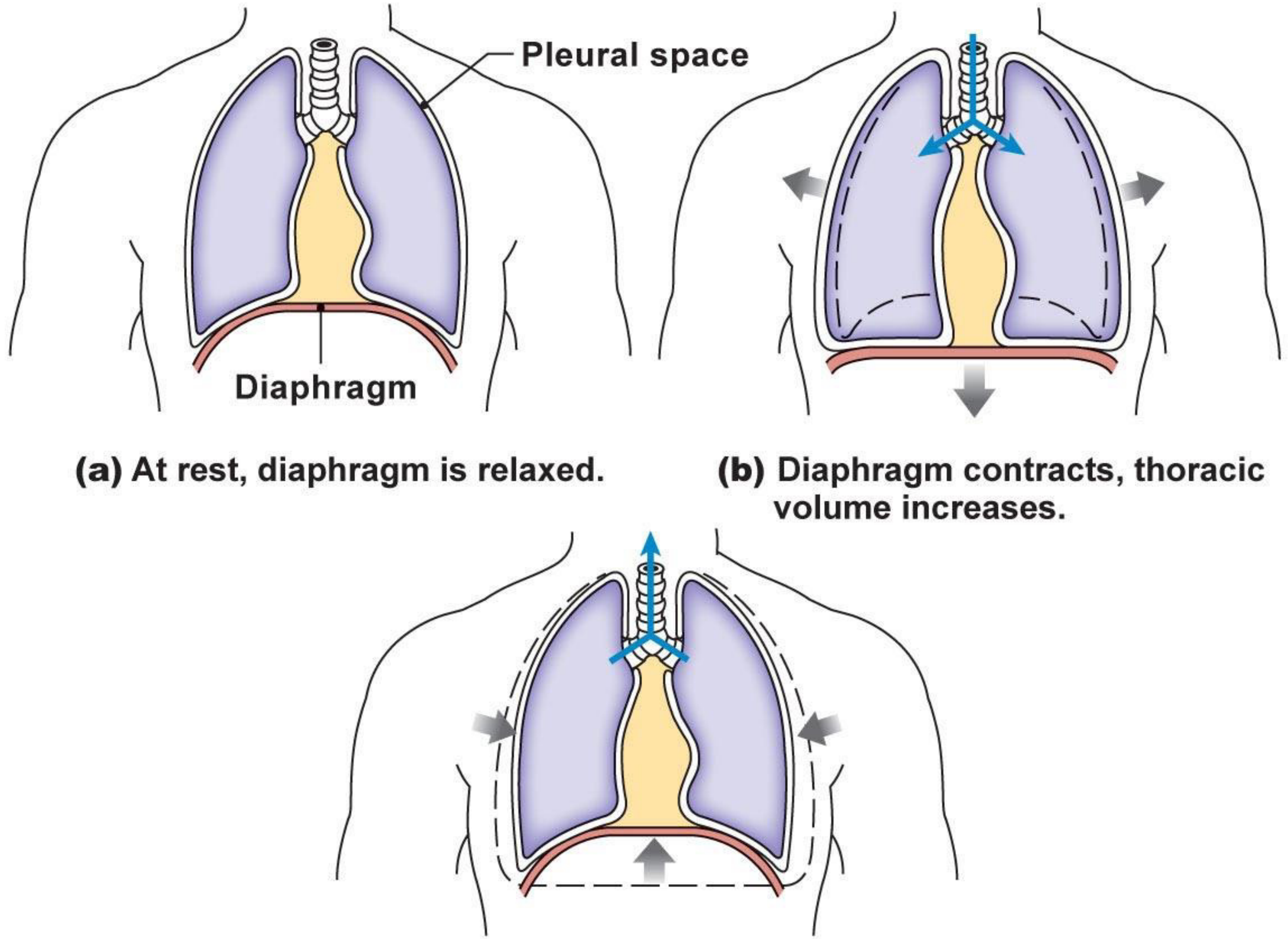
- Inspiration
  - Occurs as alveolar pressure drops below atmospheric pressure..-ve pressure breathing
    - For convenience atmospheric pressure = 0 mm Hg
      - A negative value (-) indicates pressure below atmospheric P
      - A positive (+) value indicates pressure above atmospheric P
    - At the start of inspiration (time = 0),
      - atmospheric pressure = alveolar pressure
        - » No net movement of gases! No driving force (Ohm's)
    - 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
      - 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?

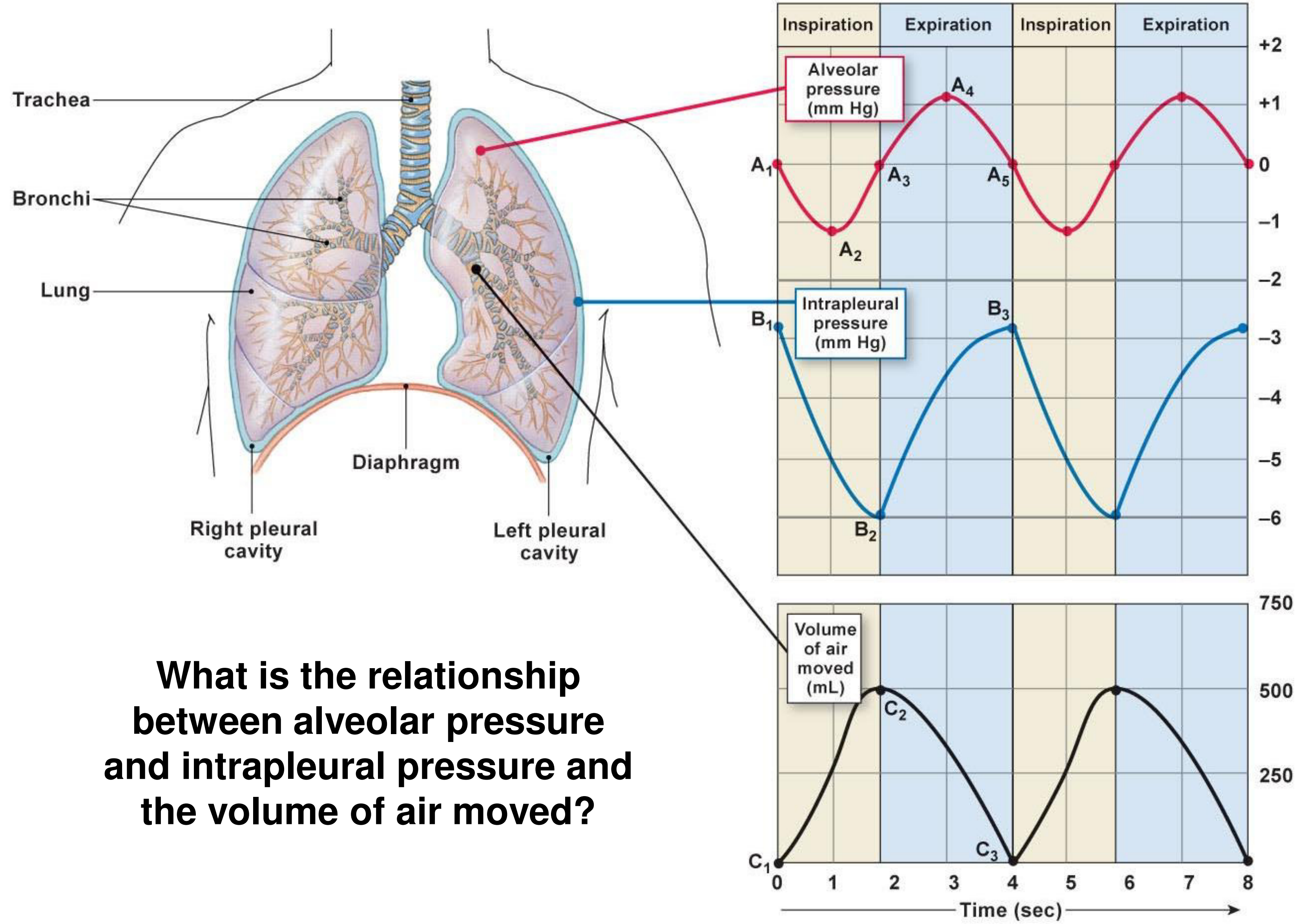


(a) At rest, diaphragm is relaxed.

(b) Diaphragm contracts, thoracic volume increases.

(c) Diaphragm relaxes, thoracic volume decreases.

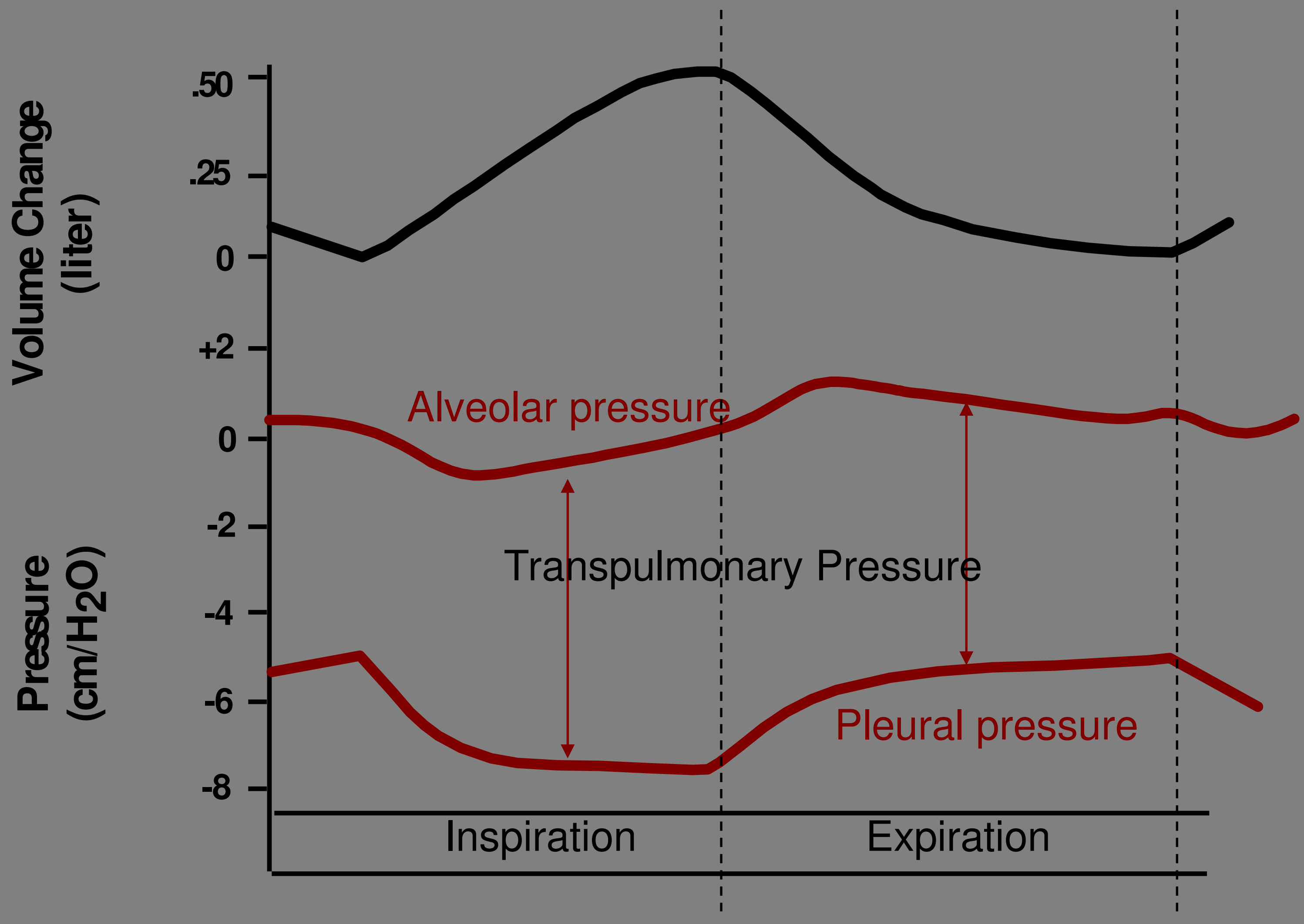
Ventilation



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 2-4 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 4 seconds
      - Atmospheric pressure once again equals alveolar pressure and there is no net movement

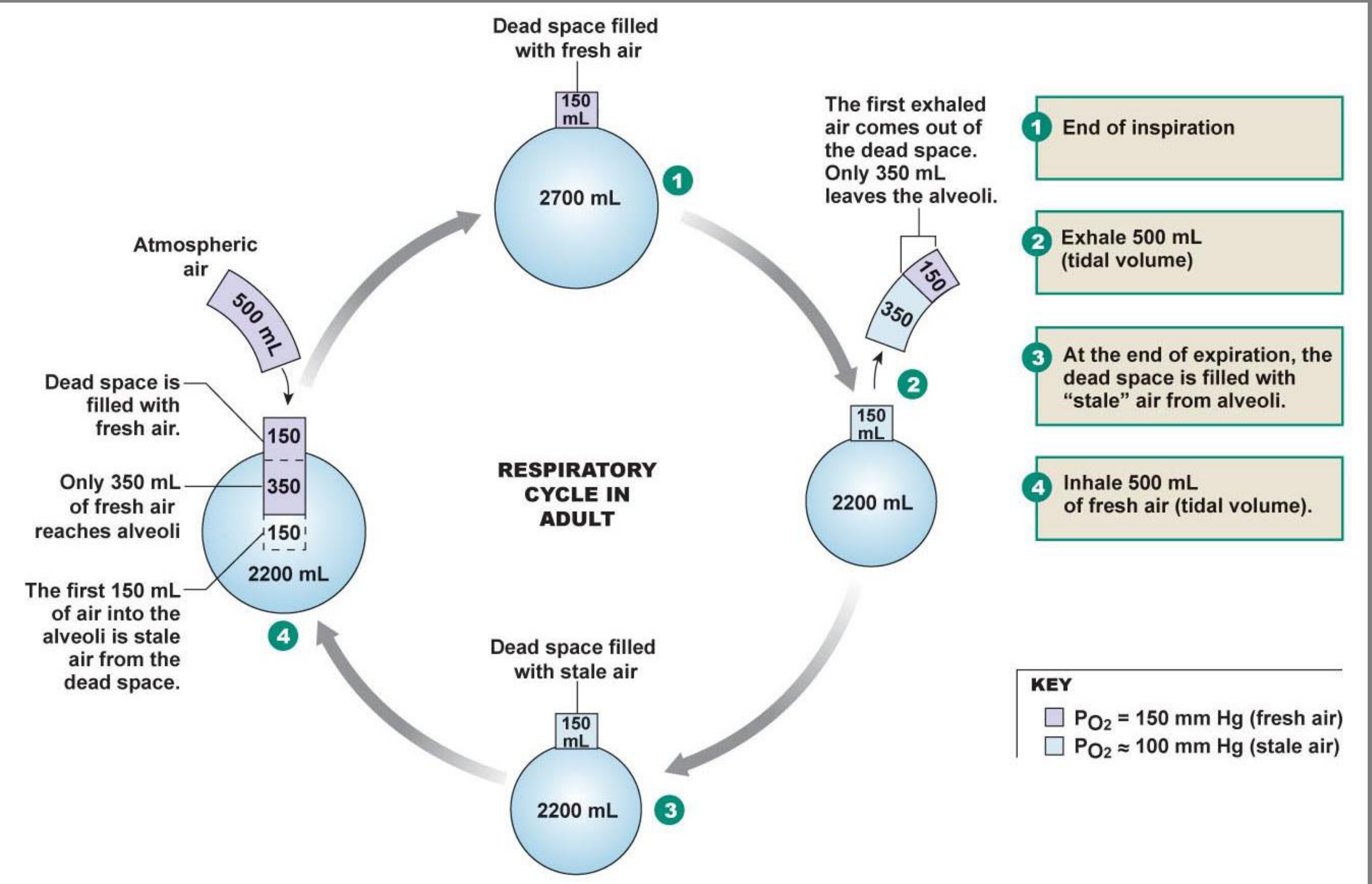

Volume Change (liter)
.50
.25
0
+2
0
-2
-4
-6
-8
Pressure (cm/H2O)
Alveolar pressure
Transpulmonary Pressure
Pleural pressure
Inspiration
Expiration

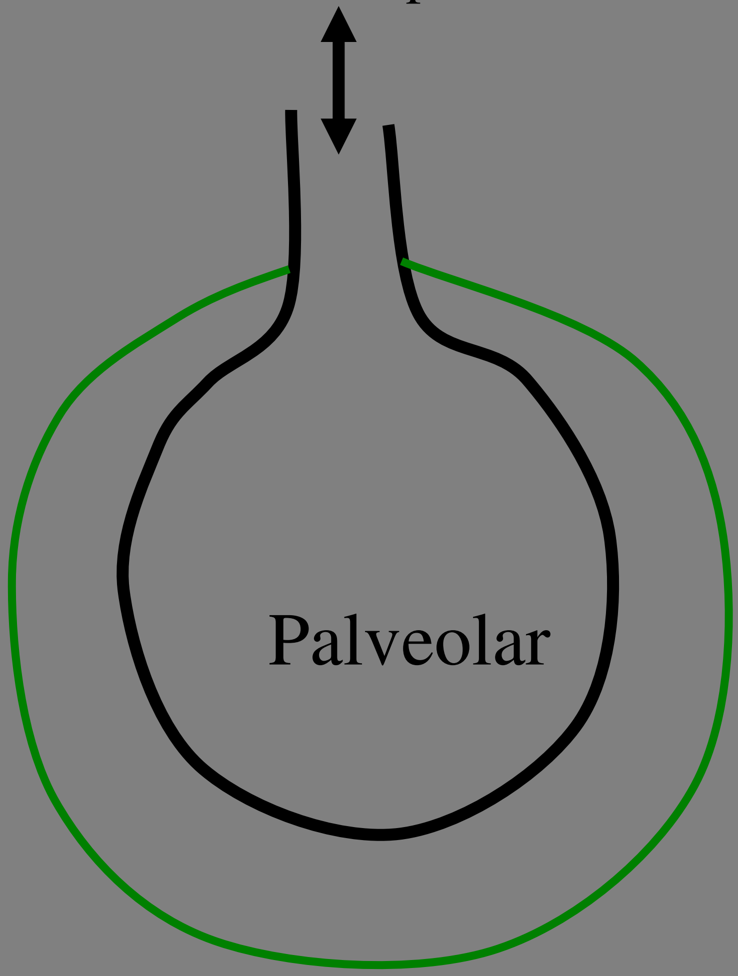
Ventilation

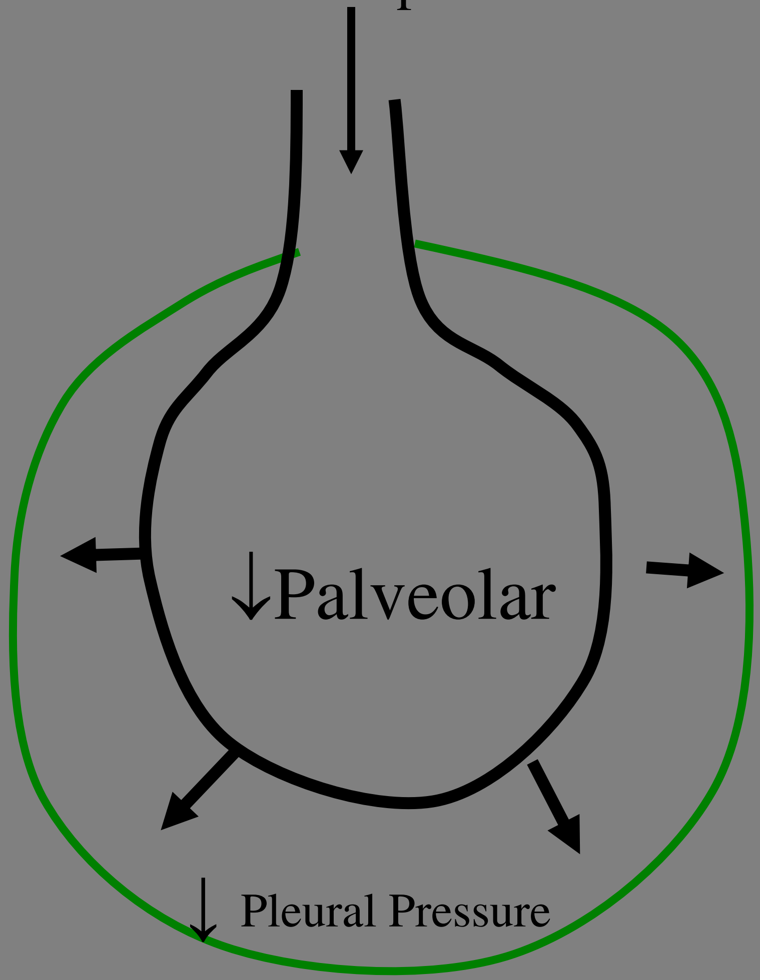
- What are the different respiratory patterns?
  - Quiet breathing (relaxed)
  - Forced inspirations & expirations
- Respiratory volumes follow these respiratory patterns…
- HYPERVENTILATION is when alveolar ventilation is more than CO_2 production $\rightarrow$ decrease PaCO2
- HYPOVENTILATION is when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



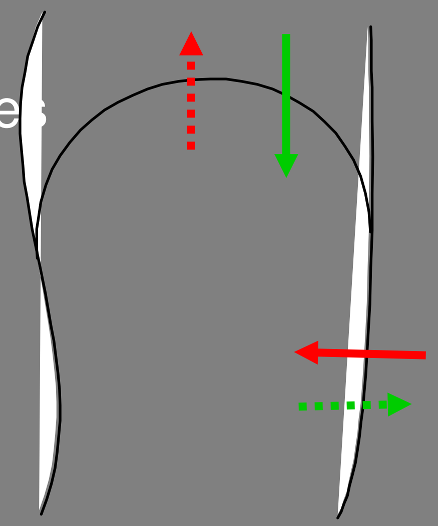



Rest

Inhalation

Mechanics Of Respiration

- Expiration
  - Active
    - Abdominals
    - decrease chest volumes

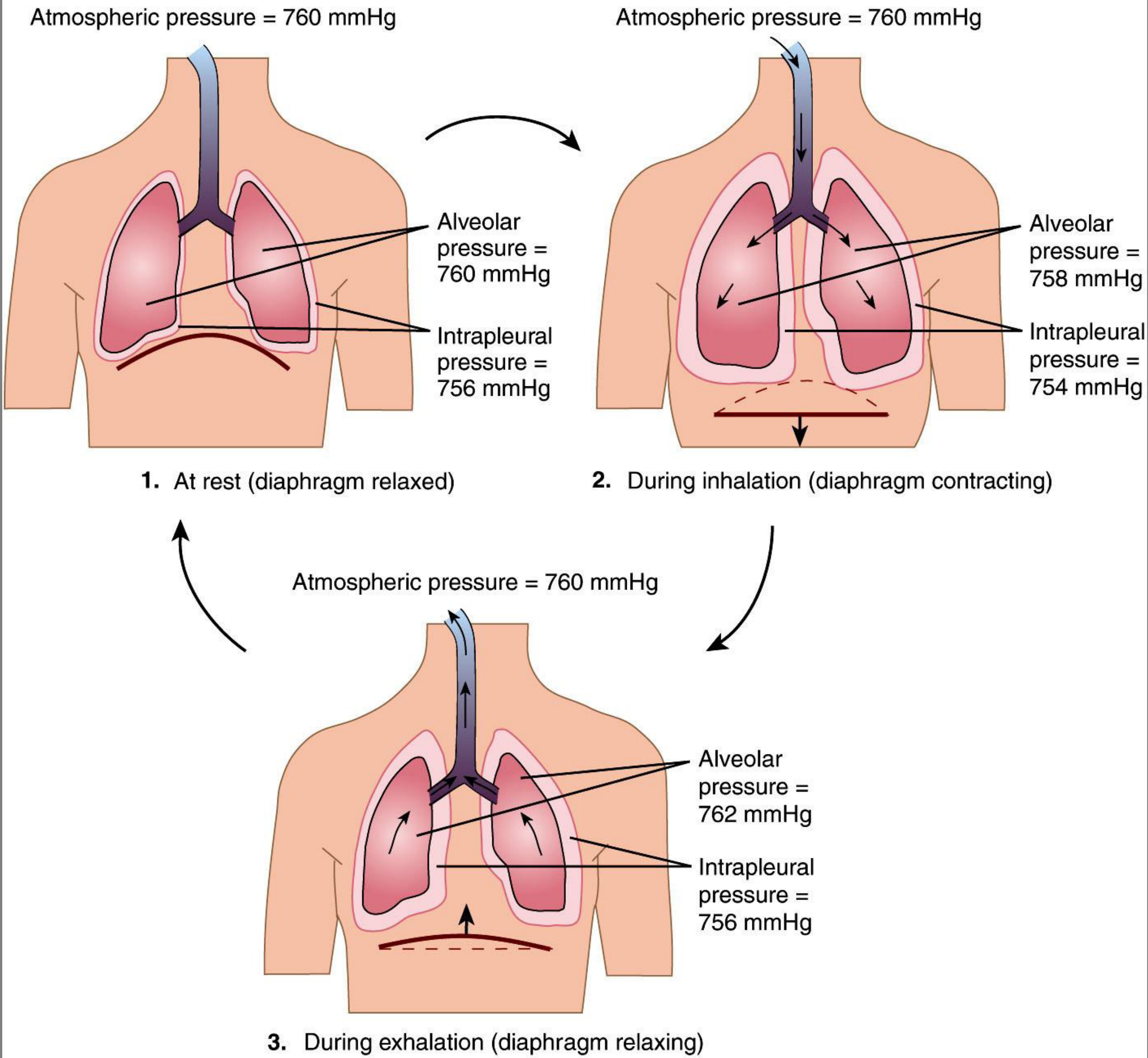


Active exhalation abdominal compression

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


Atmospheric pressure = 760 mmHg
Alveolar pressure = 760 mmHg
Intrapleural pressure = 756 mmHg
1. At rest (diaphragm relaxed)
Atmospheric pressure = 760 mmHg
Alveolar pressure = 758 mmHg
Intrapleural pressure = 754 mmHg
2. During inhalation (diaphragm contracting)
Atmospheric pressure = 760 mmHg
Alveolar pressure = 762 mmHg
Intrapleural pressure = 756 mmHg
3. During exhalation (diaphragm relaxing)

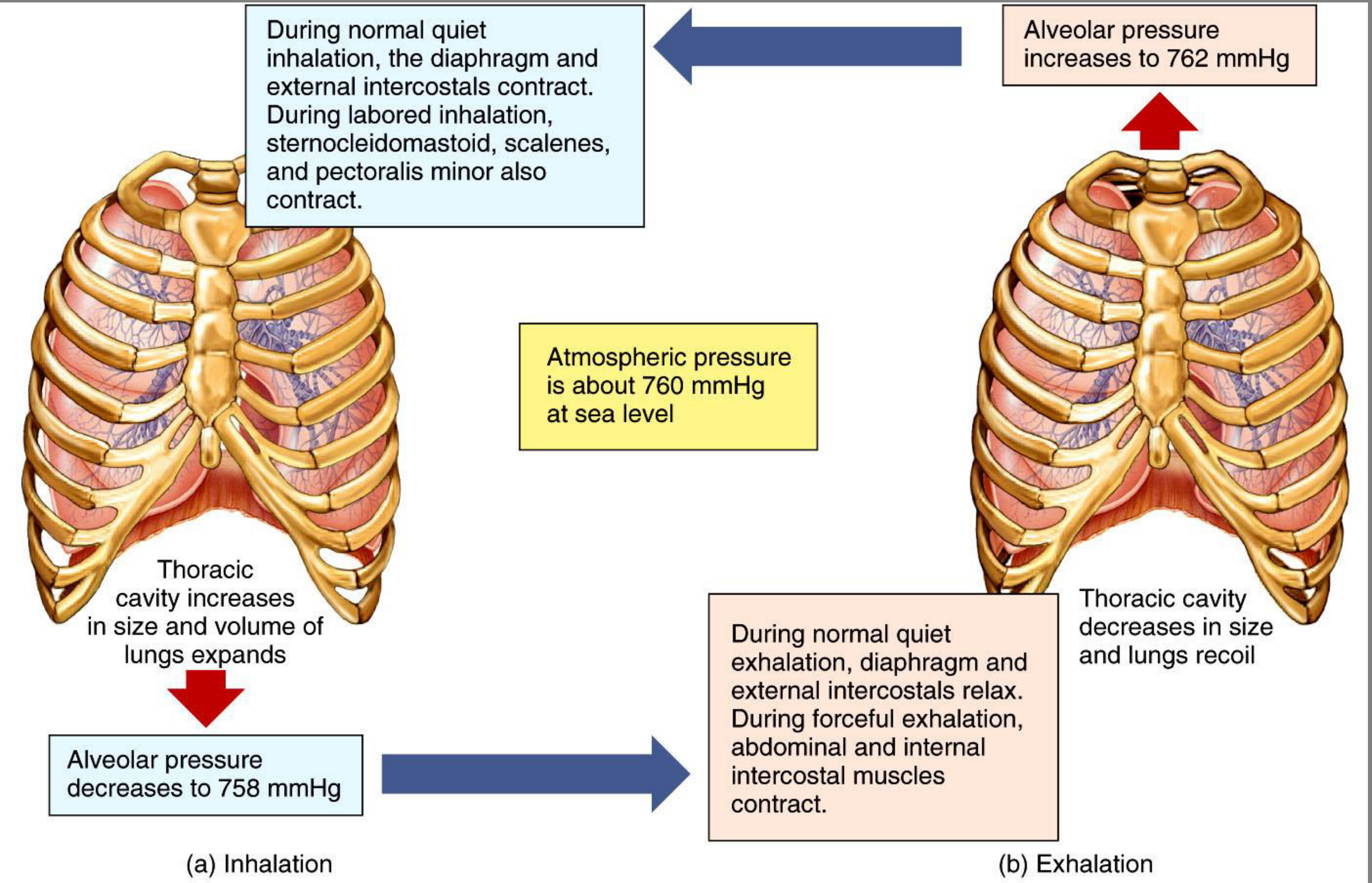


Figure 23.15 Tortora - PAP 12/e

Ventilation

- Things to consider
  - airway diameter (Lecture 3-4)
  - surfactant effect (Lecture 5)

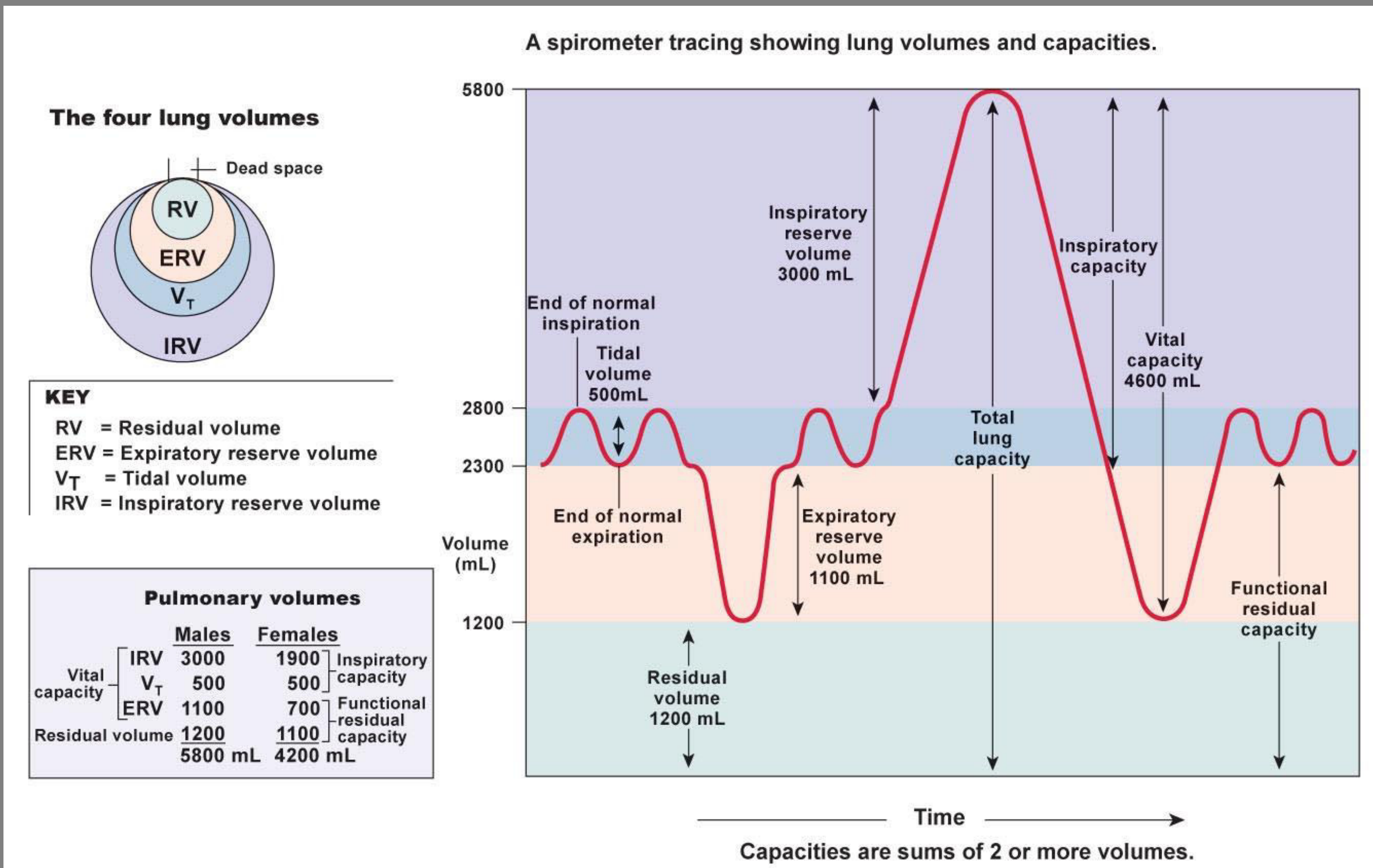
  - Minute volume respiration (ventilation rate times tidal volume) & anatomical dead space
    - Leading to a more accurate idea of alveolar ventilation rates

  - Changes in ventilation patterns

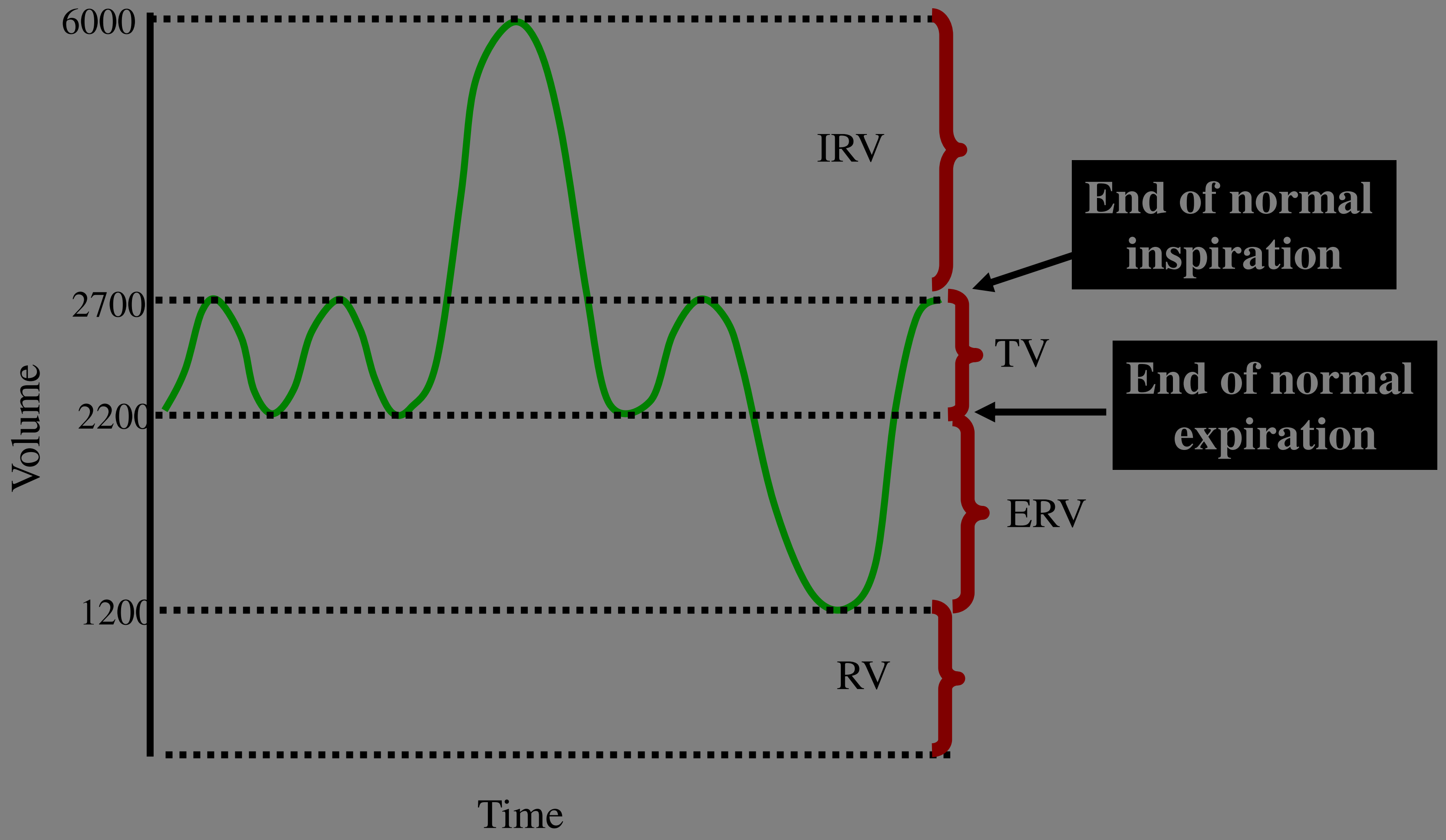
PFT

- Lung Volumes and Capacities
- **In lecture 1+2 we will discuss lung volumes and capacities. Other tests will be discussed in lecture 3-4. Diffusing Capacity of the Lung for Carbon Monoxide will be discussed with Gas Exchange lecture**

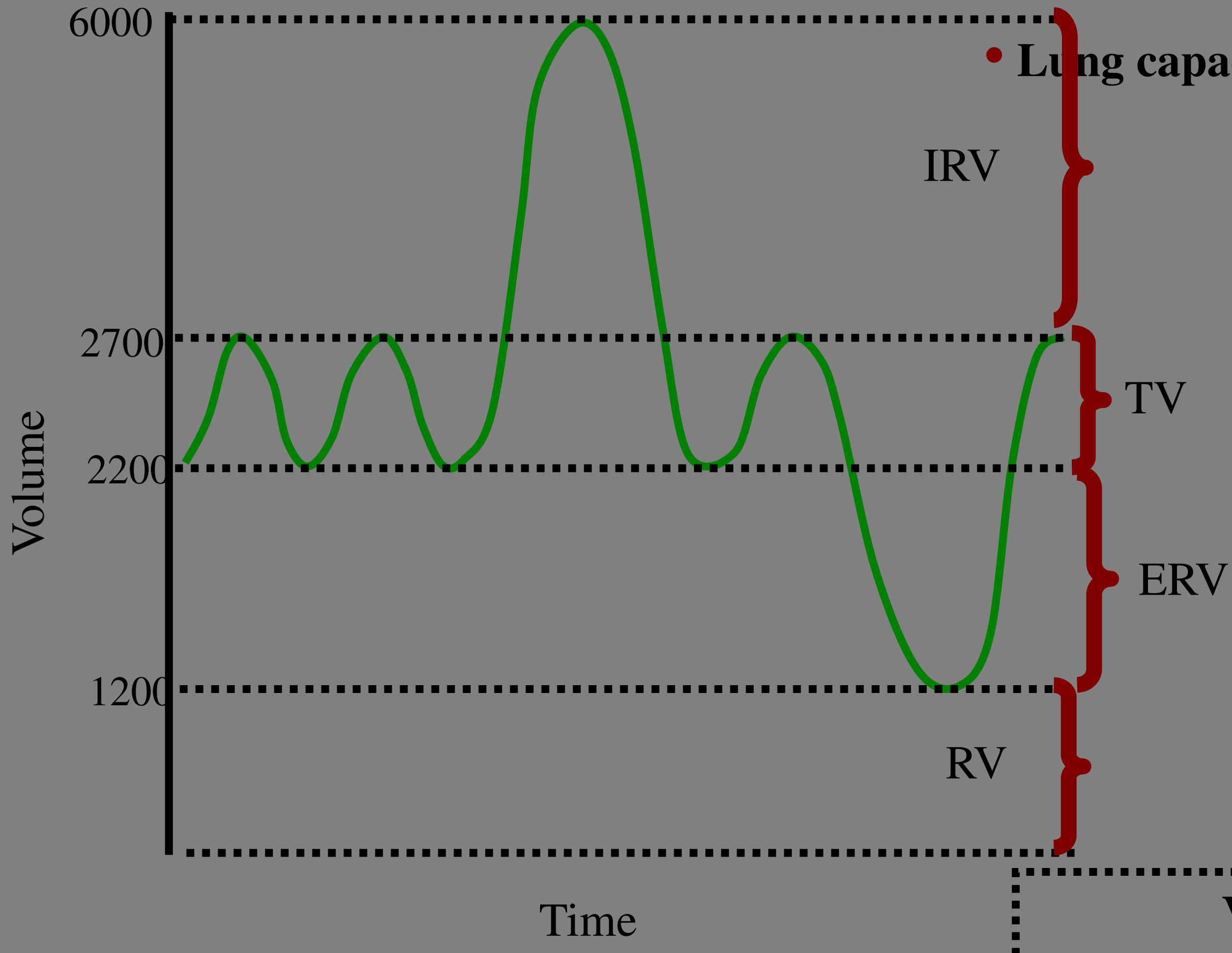
Ventilation



Lung Volumes



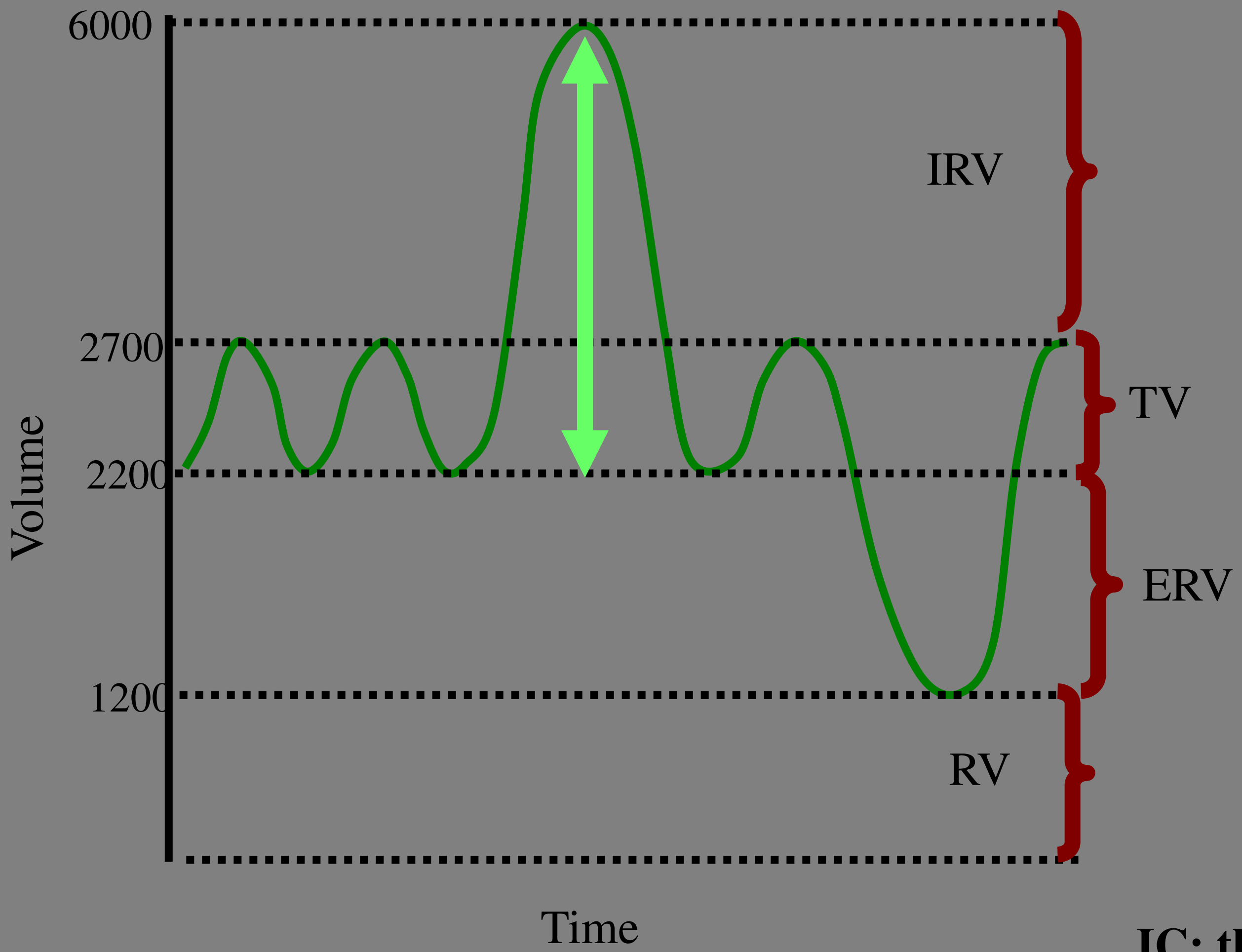
Lung Capacities



- 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

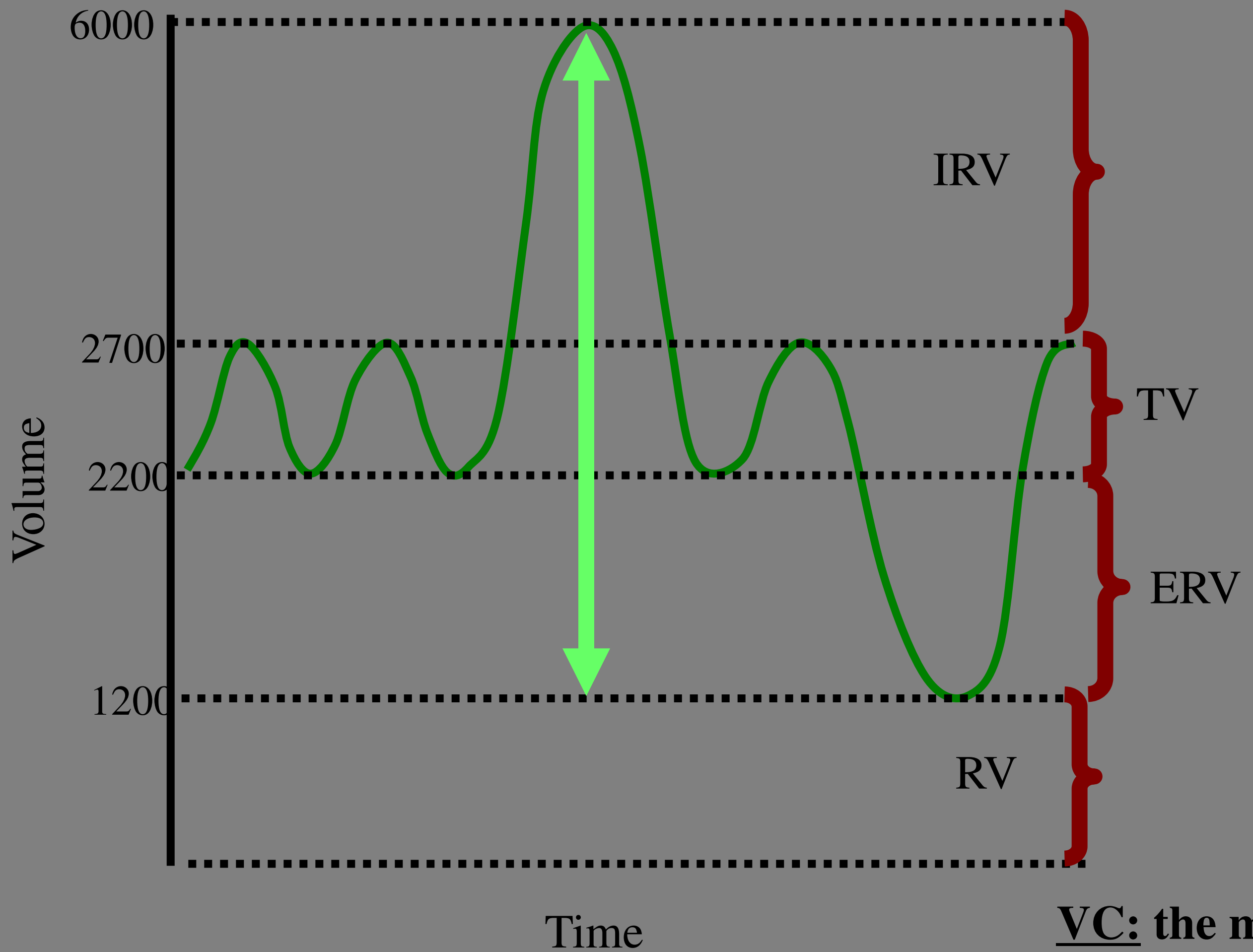
Lung Capacities: Inspiratory Capacity (IC)



$IC = V_T + IRV$

<u>IC:</u> the maximum amount of air that can be inspired following a normal expiration

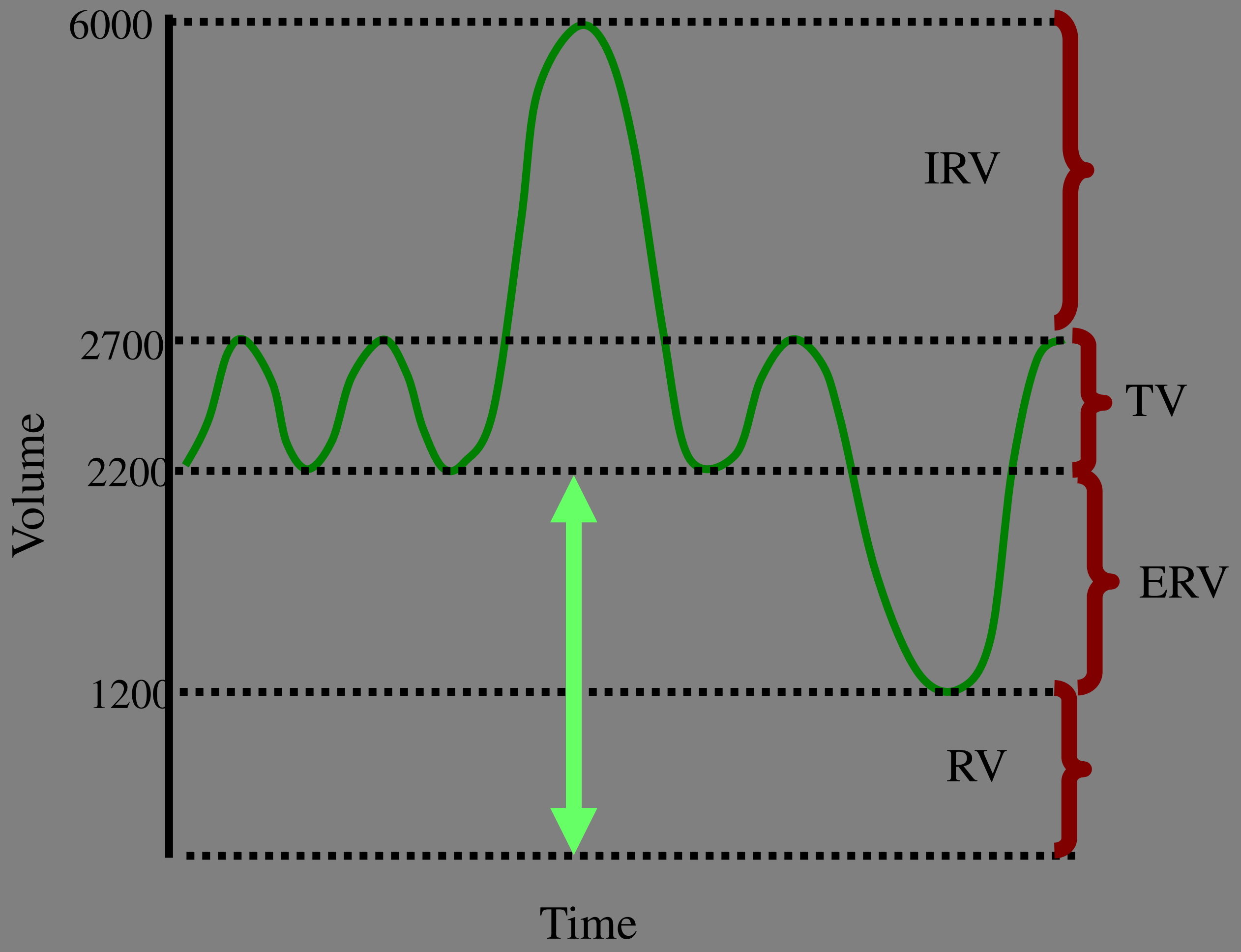
Lung Capacities: Vital Capacity (VC)



VC = IRV + V_T + ERV

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

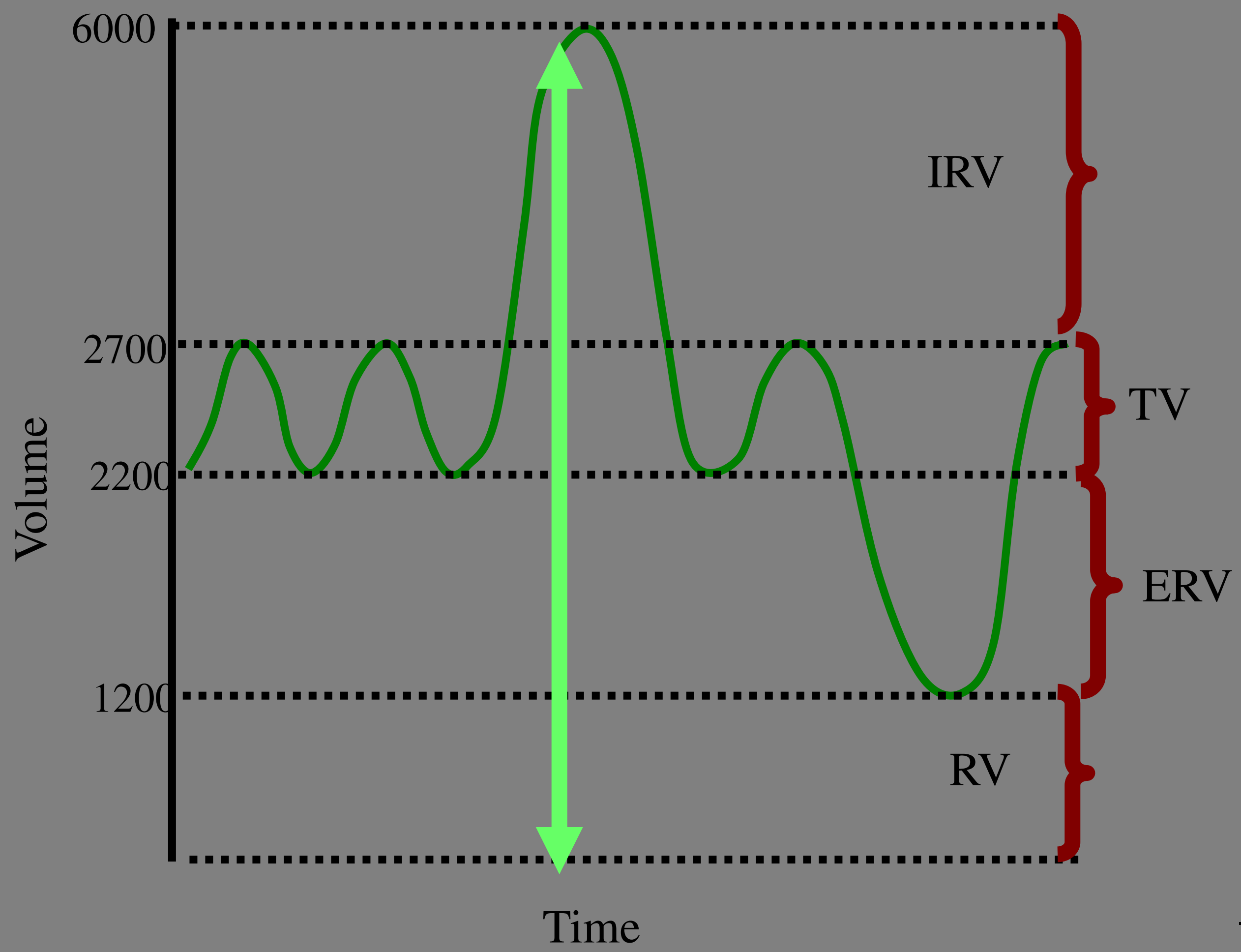
Lung Capacities: Functional Residual Capacity (FRC)



FRC = ERV + RV

<u>FRC:</u> the amount of air remaining in the lungs following a normal expiration.

Lung Capacities: Total Lung Capacity (TLC)



$TLC = IRV + V_T + ERV + RV$

<u>TLC:</u> the amount of air in the lungs at the end of a maximal <u>inspiration</u>.

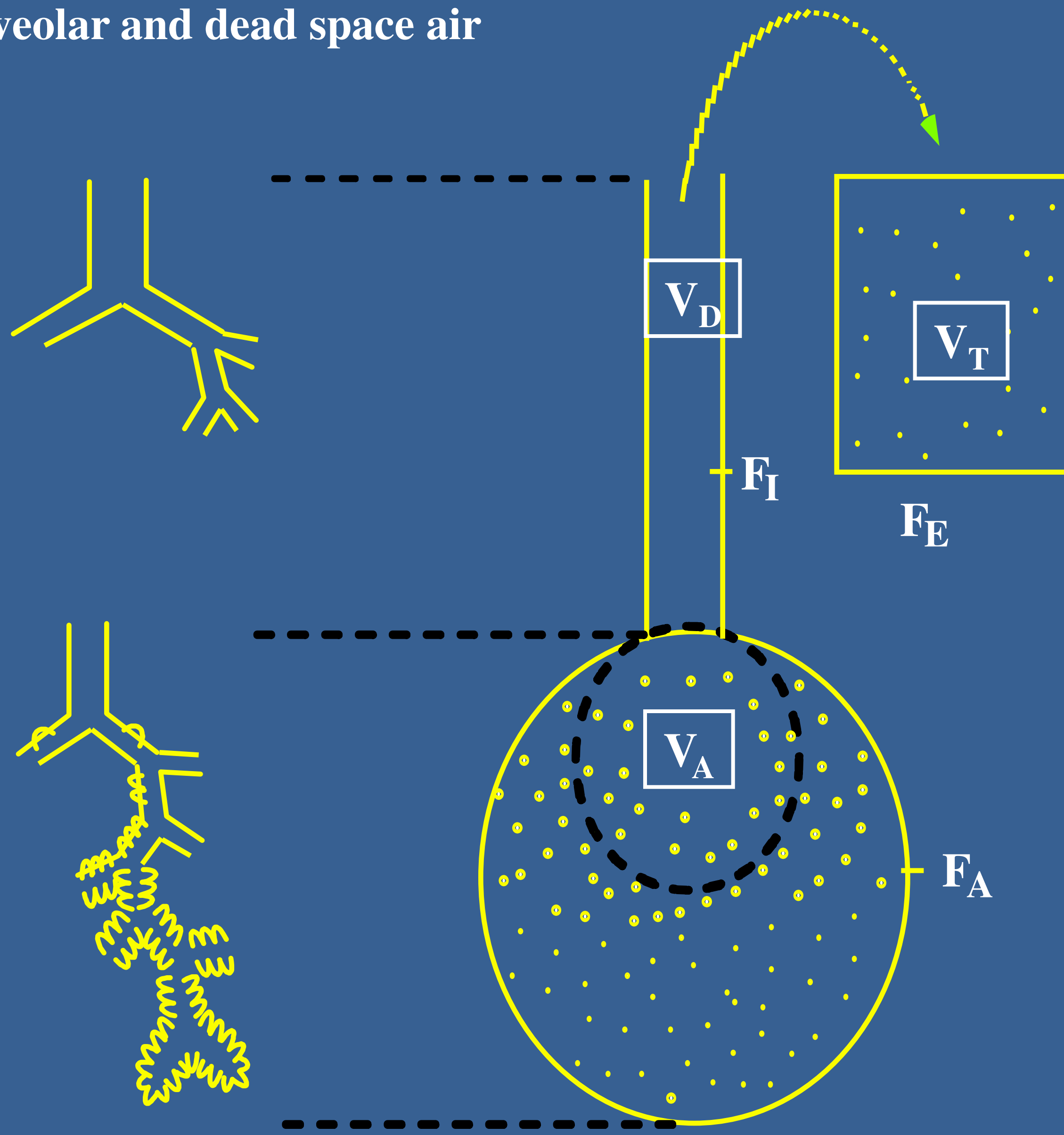
Minute and Alveolar Ventilation

- Minute ventilation: 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 ≈ 75 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

TIMED VOLUMES

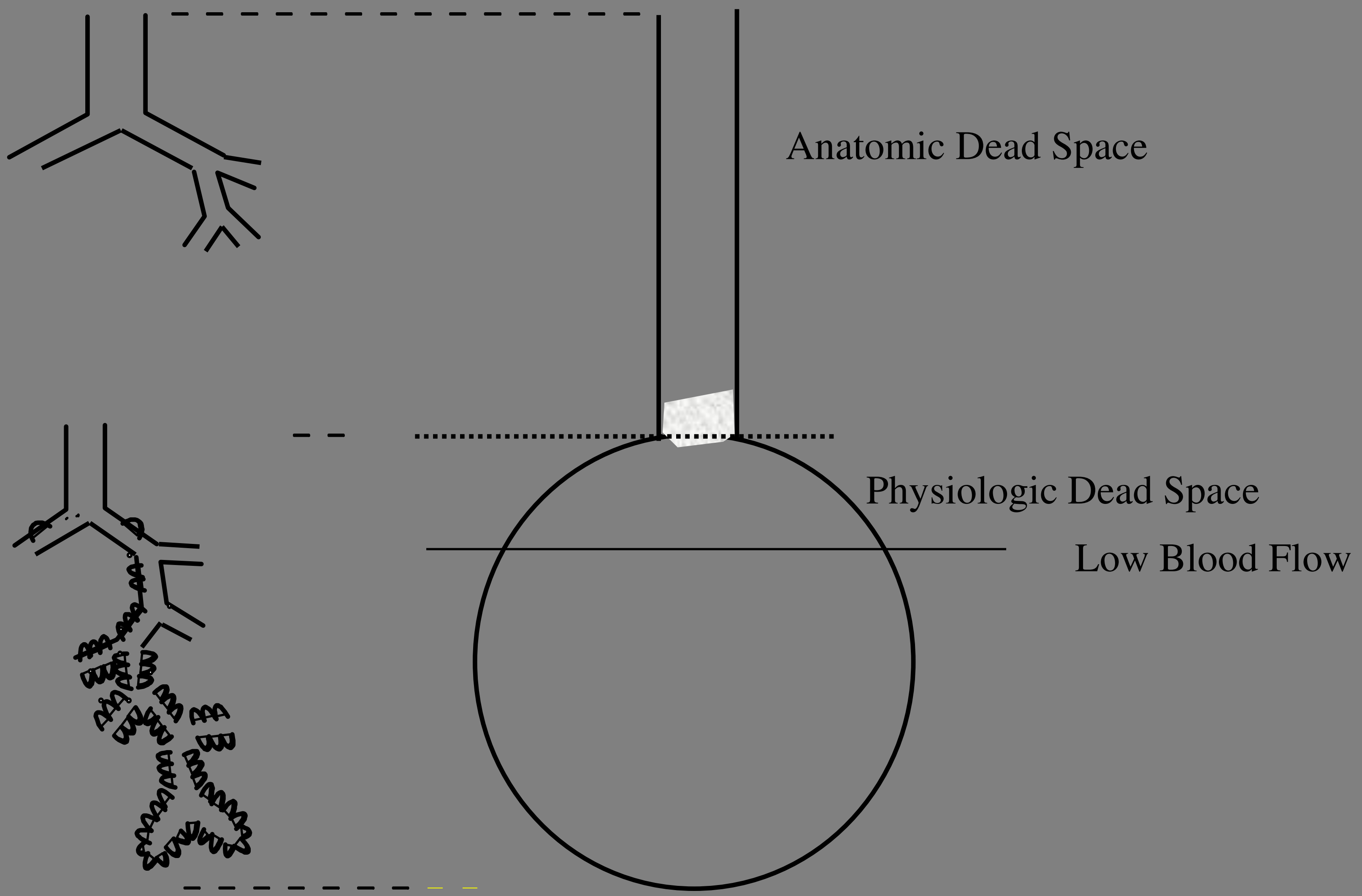
- Minute Respiratory Volume
  - Tidal volume * respiratory rate
- Alveolar Ventilation
  - (Tidal volume-dead space)*resp rate
  - ADS Ventilation =ADSV *RR.

Expired air has alveolar and dead space air

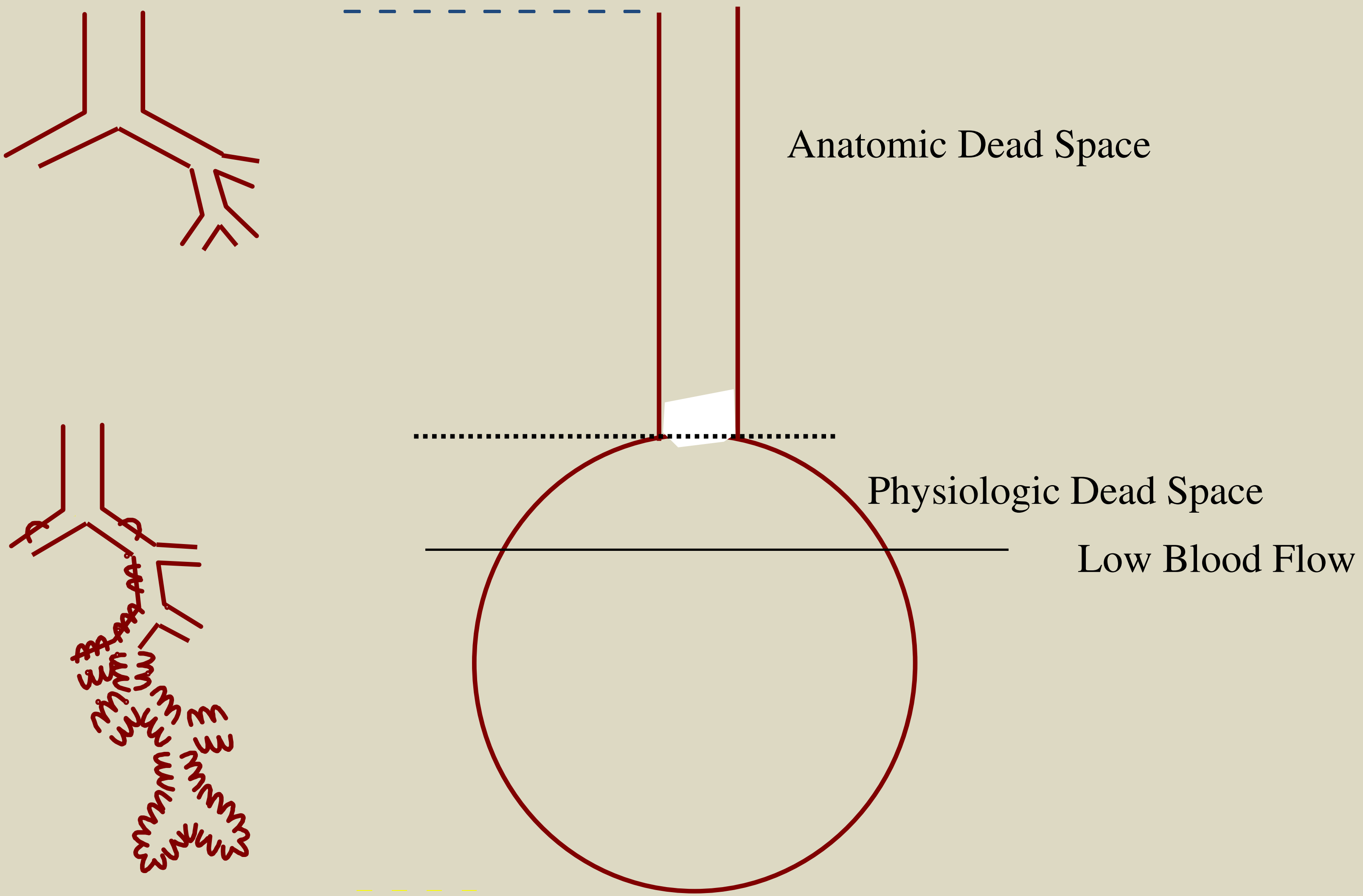


DEAD SPACE

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


Anatomic Dead Space
Physiologic Dead Space
Low Blood Flow

$$V_D = VT\left[\frac{PaCO2 - PECO2}{PaCO2}\right]$$


Anatomic Dead Space
Physiologic Dead Space
Low Blood Flow

Next Time…

- Airway Resistance Lecture 3-4
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