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 CO_2 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:

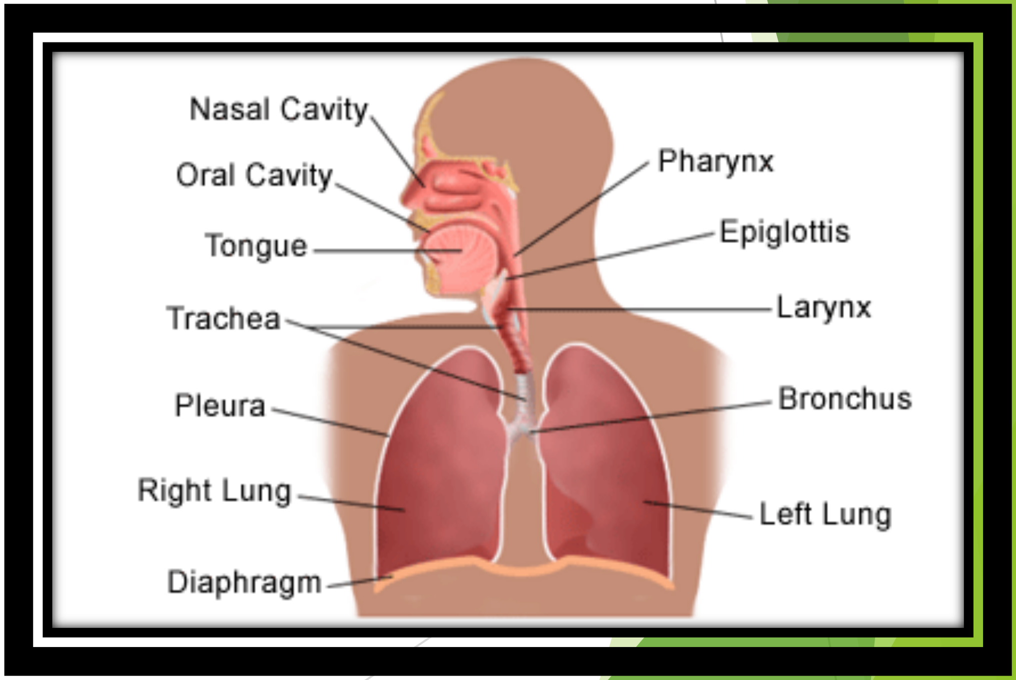
respiration can be divided into four major functions:

(1) *Pulmonary ventilation*

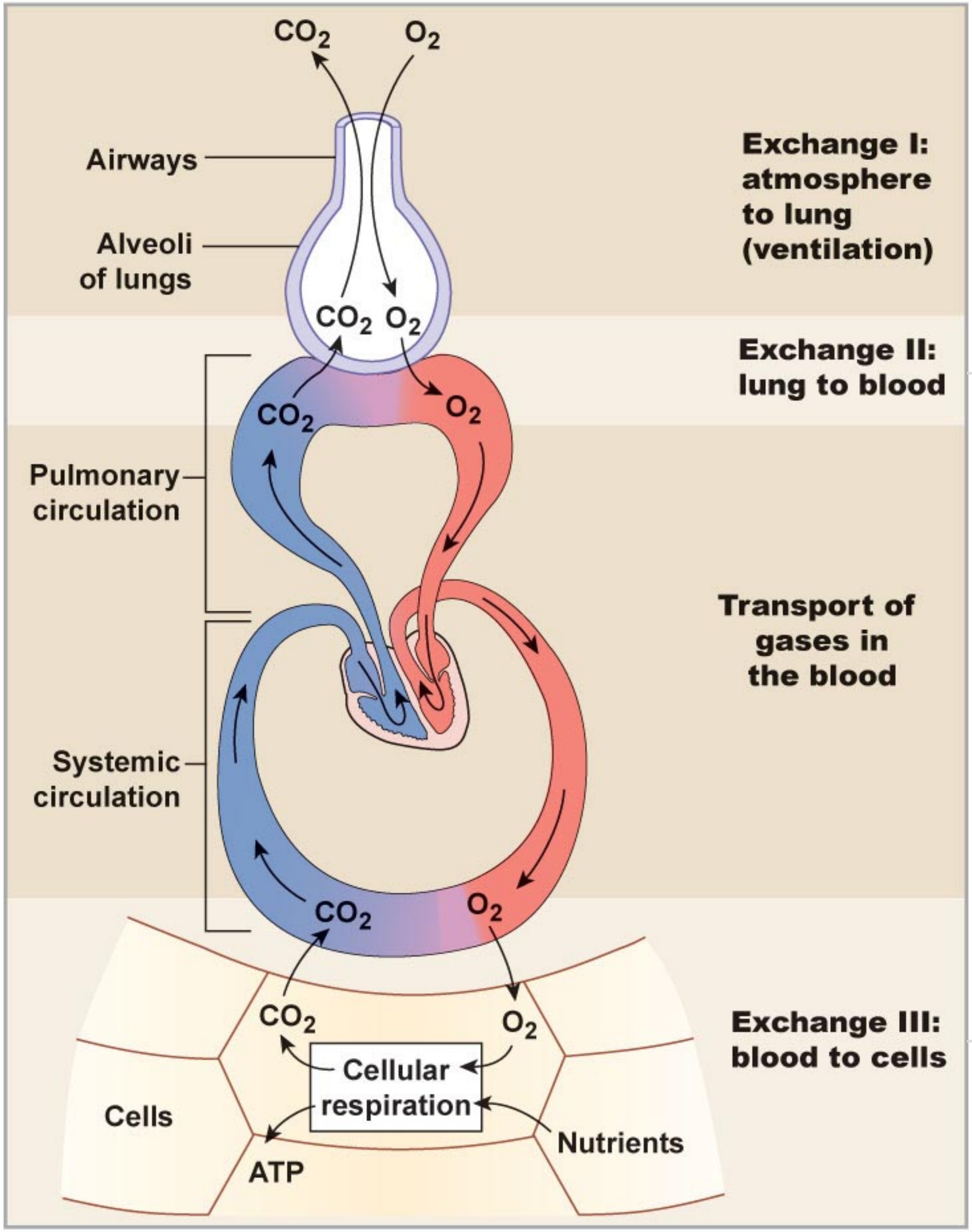
(2) *Diffusion*

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

(4) *Regulation of ventilation*.



Schematic View of Respiration



External Respiration

Internal Respiration

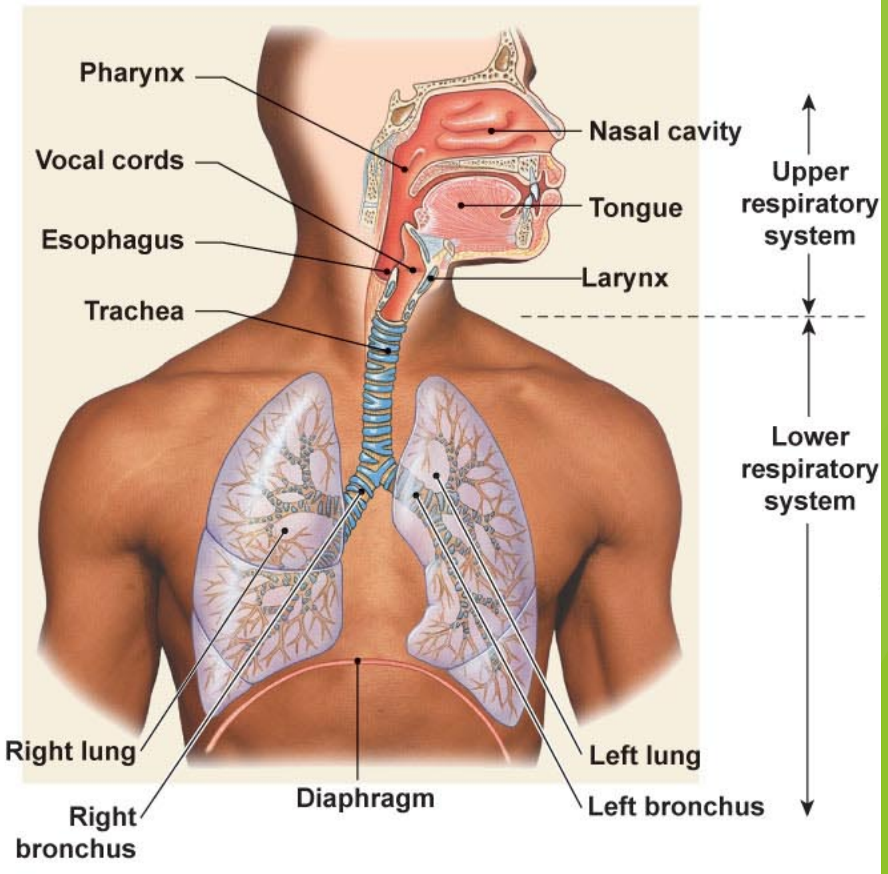
Partial Pressures of Gases in Inspired Air and Alveolar Air

	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

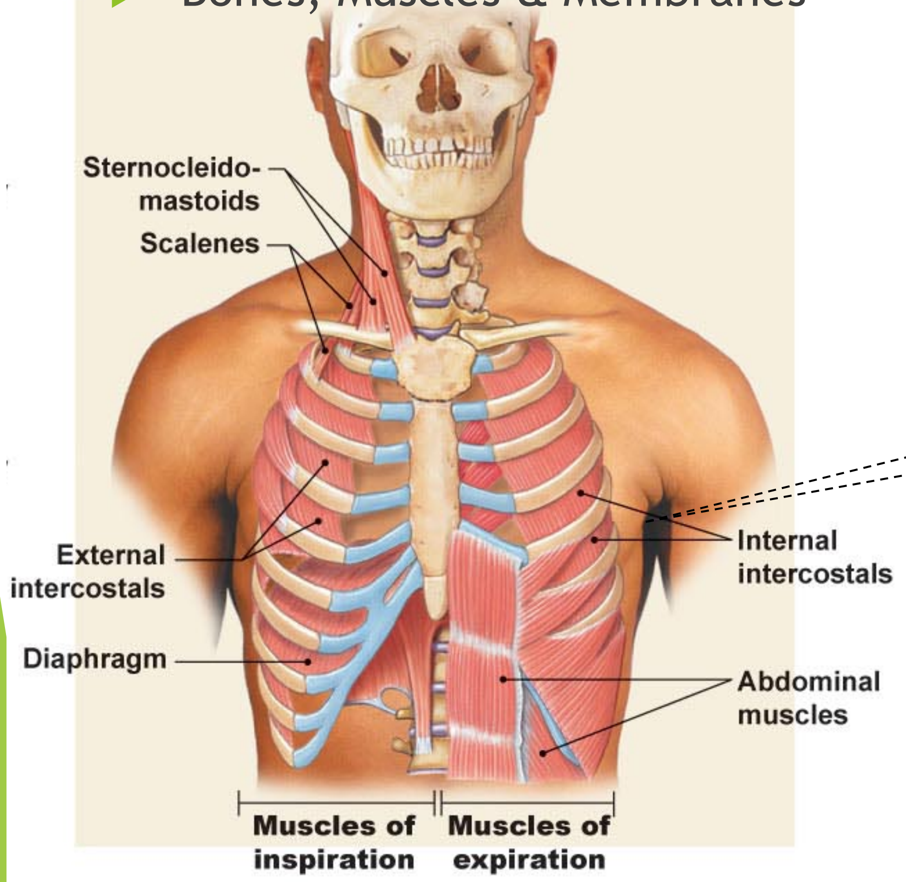
- What structural aspects must be process of respiration?
  - The conducting zone
  - The respiratory zone
  - The structures involved with ventilation
    - Skeletal & musculature
    - Pleural membranes
    - Neural pathways
- All divided into
  - Upper respiratory tract
    - Entrance to larynx
 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

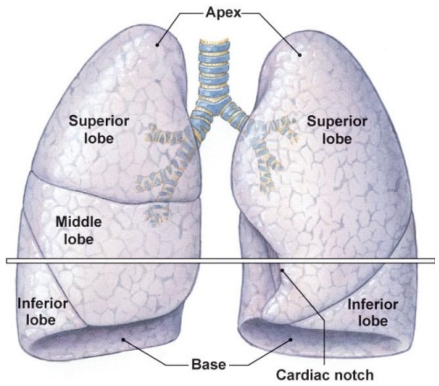


Basics of the Respiratory System

Functional Anatomy

- Bones, Muscles & Membranes

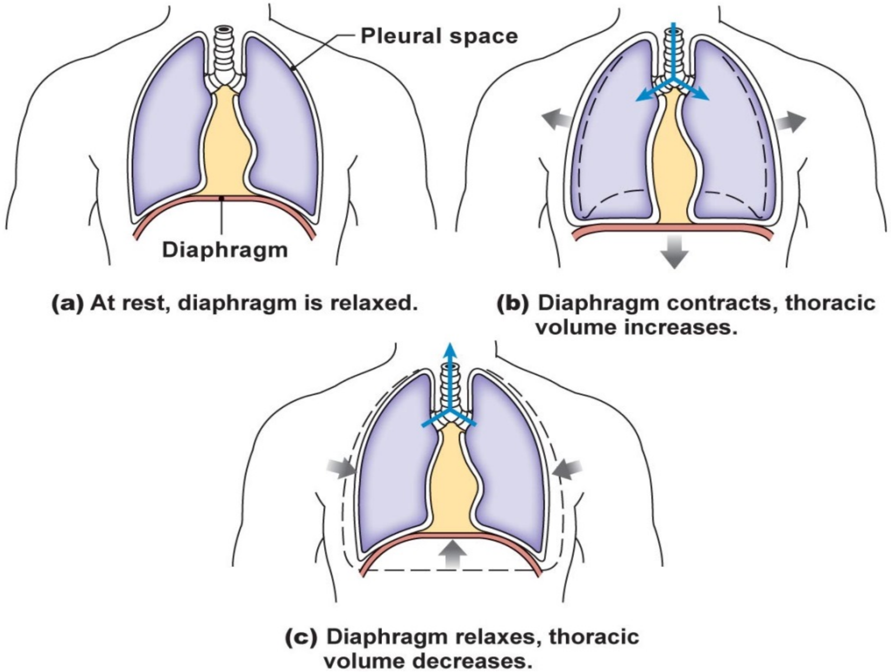




Basics of the Respiratory System

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

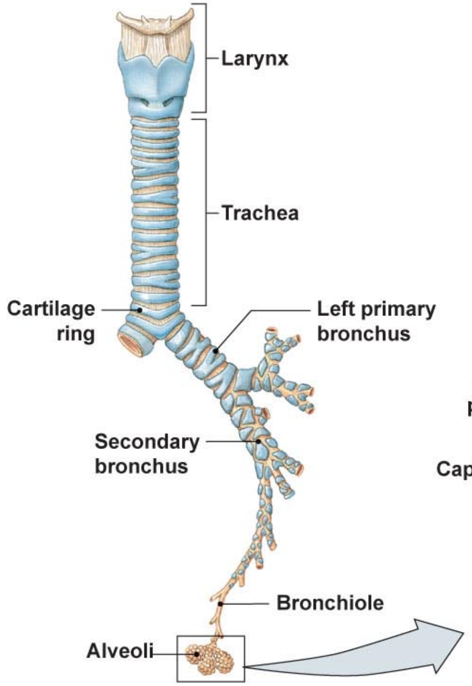
Basics of the Respiratory System

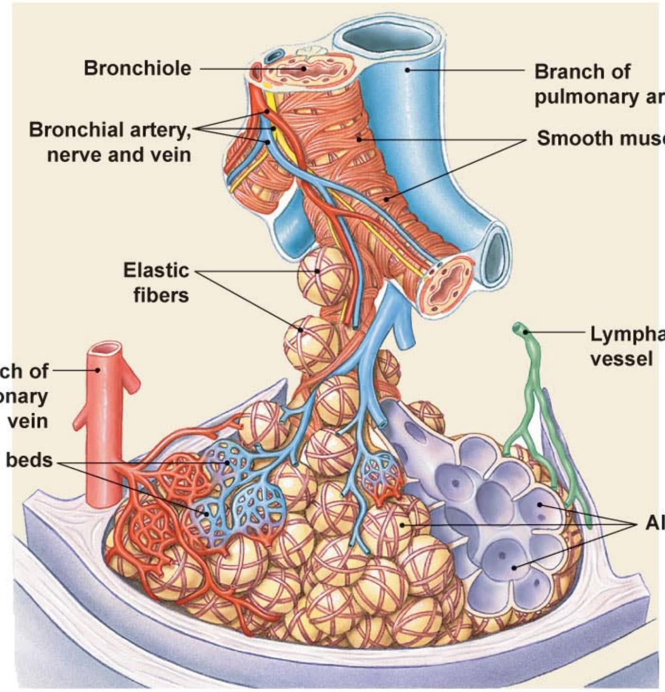
Functional Anatomy

- 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

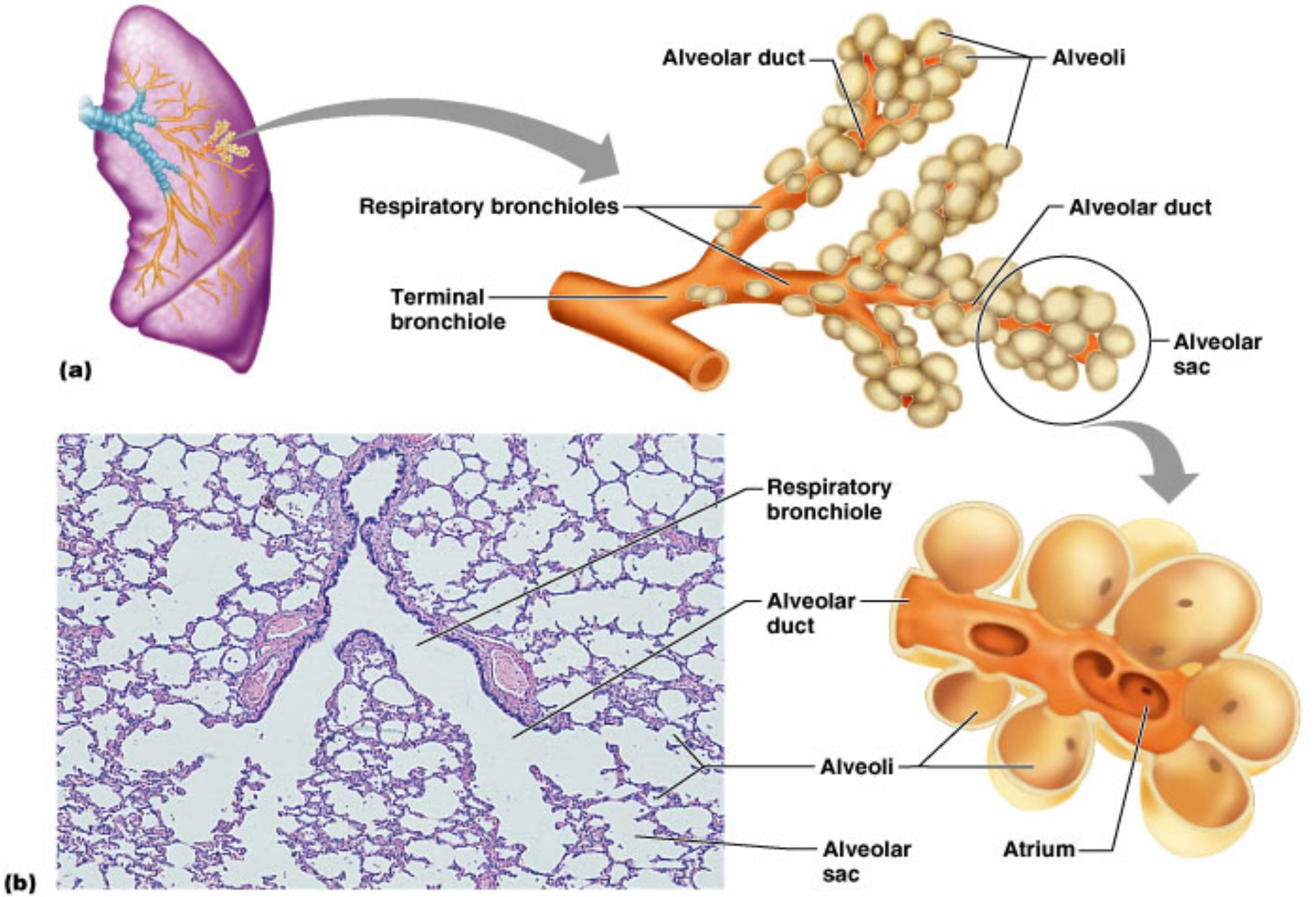




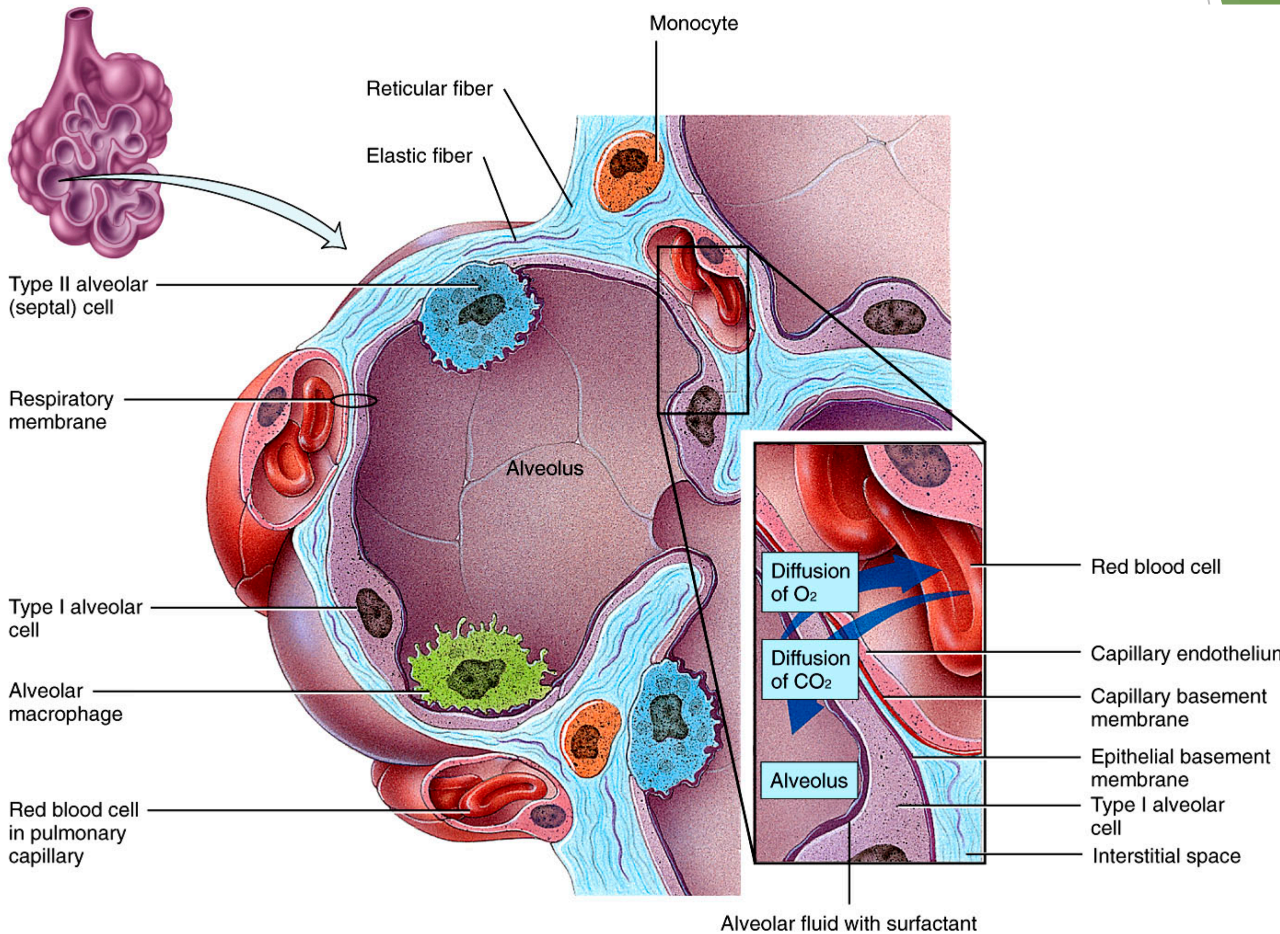
	Name	Division	Diameter (mm)	How many?	Cross-sectional area (cm^2)
Conducting system	Trachea	0	15-22	1	2.5
	Primary bronchi	1	10-15	2	
	Smaller bronchi	2	1-10	4	
		3			
		4			
		5			
		6-11		1×10^4	
	Bronchioles	12-23	0.5-1	2×10^4 – 8×10^7	100 – 5×10^3
Exchange surface	Alveoli	24	0.3	$3\text{-}6 \times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

Cartilage and its 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 are collapsible
- From 0-16 is the conductive zone…ADS (2 ml/kg BW)
- 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)

Components of Alveolus



(a) Section through an alveolus showing its cellular components

(b) Details of respiratory membrane

Figure 23.11ab Tortora - PAP 12/e

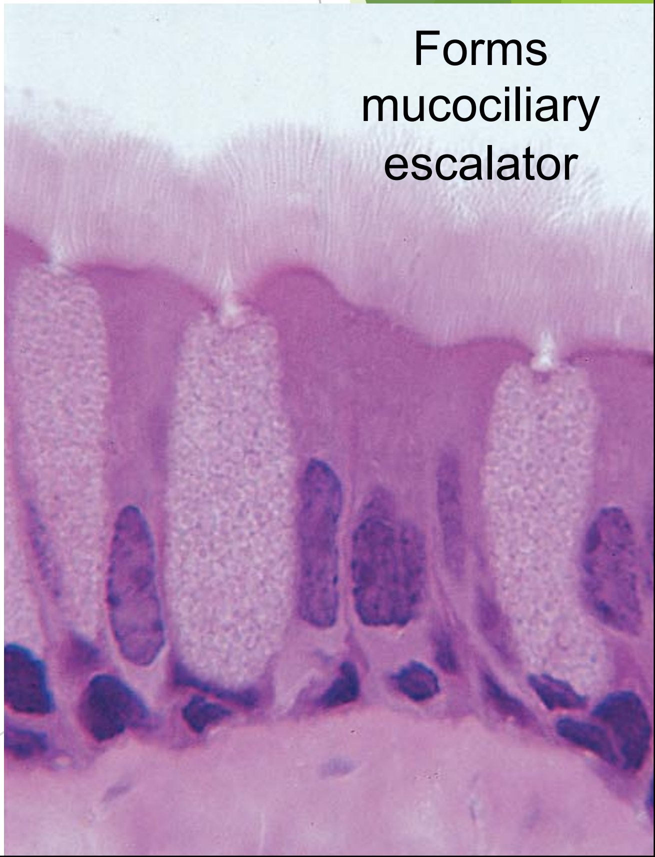
Basics of the Respiratory System

Functional Anatomy

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

Raises incoming air to 37 Celsius

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



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) **<u>Alveolar macrophage</u>** 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 $\rightarrow$	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!

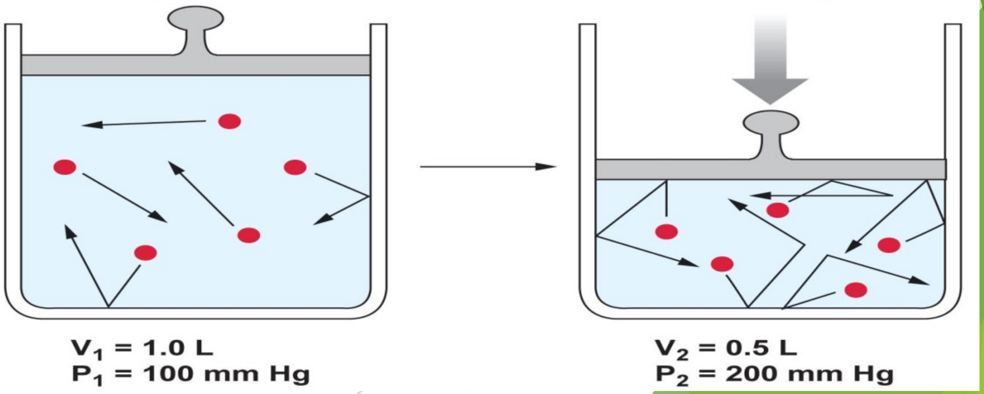
Fick's Law

- **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

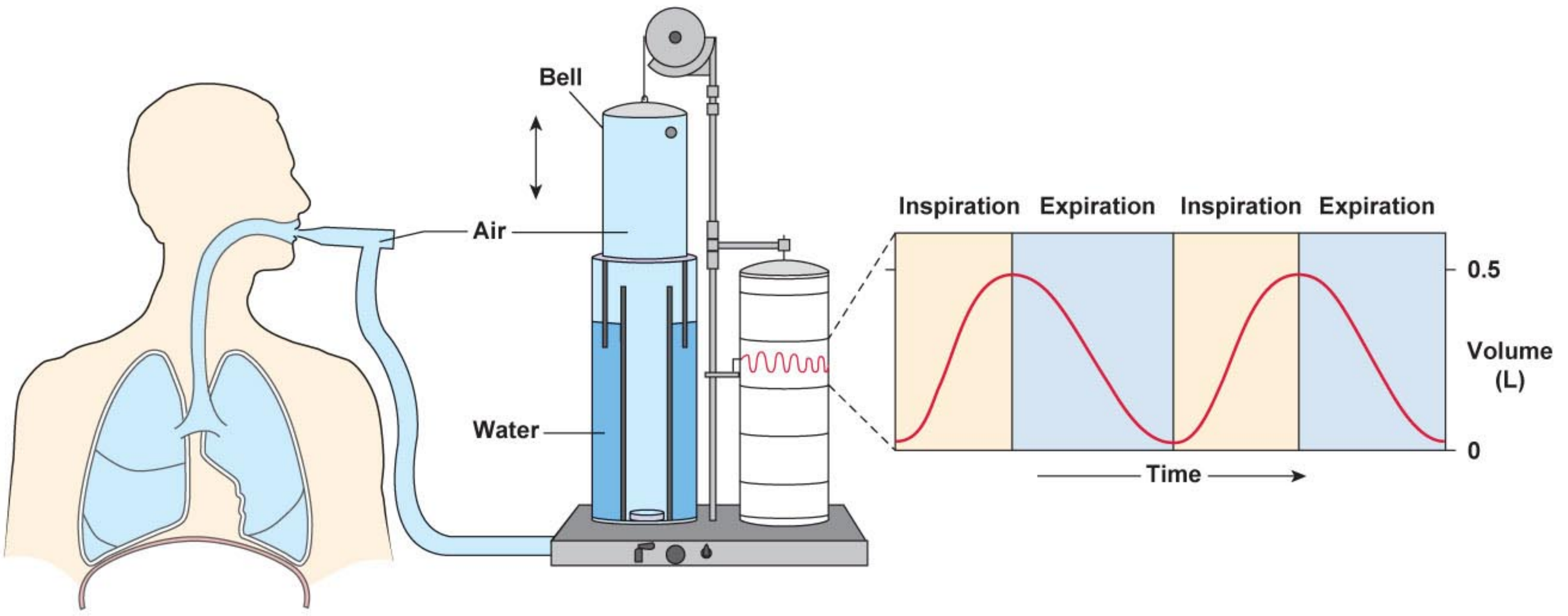
- Boyle's Law
  - Describes the relationship between pressure and volume…this law helps you to understand how we breath in and out.
    - "the pressure and volume of a gas in a system are inversely related if the temperature is kept constant
    - $P_1V_1 = P_2V_2$



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.

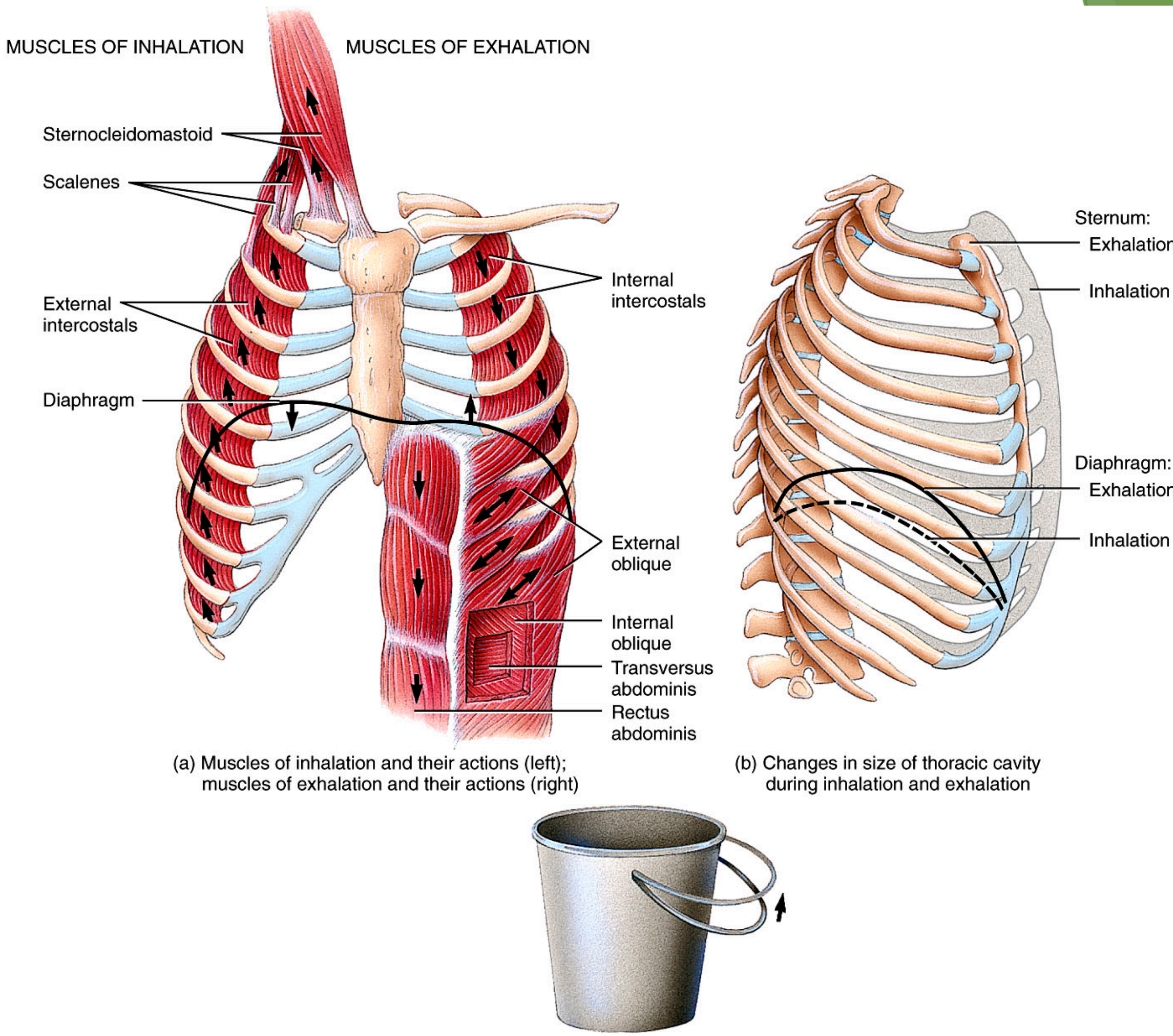
Always remember Ohm's law: Flow is directly proportional to the driving force and inversely proportional to the resistance

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



(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

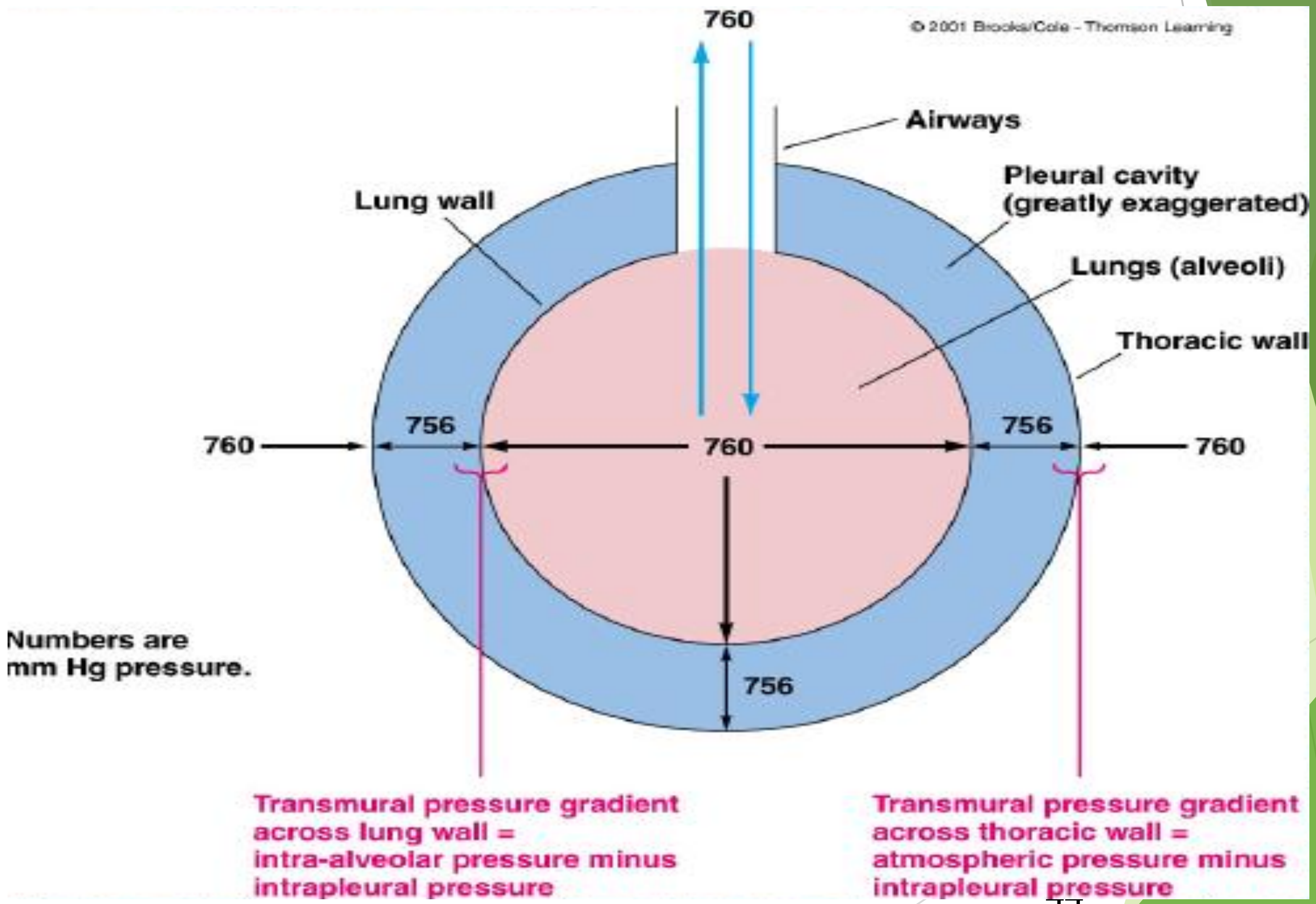
(c) During inhalation, the ribs move upward and outward like the handle on a bucket

Figure 23.13 Tortora - PAP 12/e

Ventilation

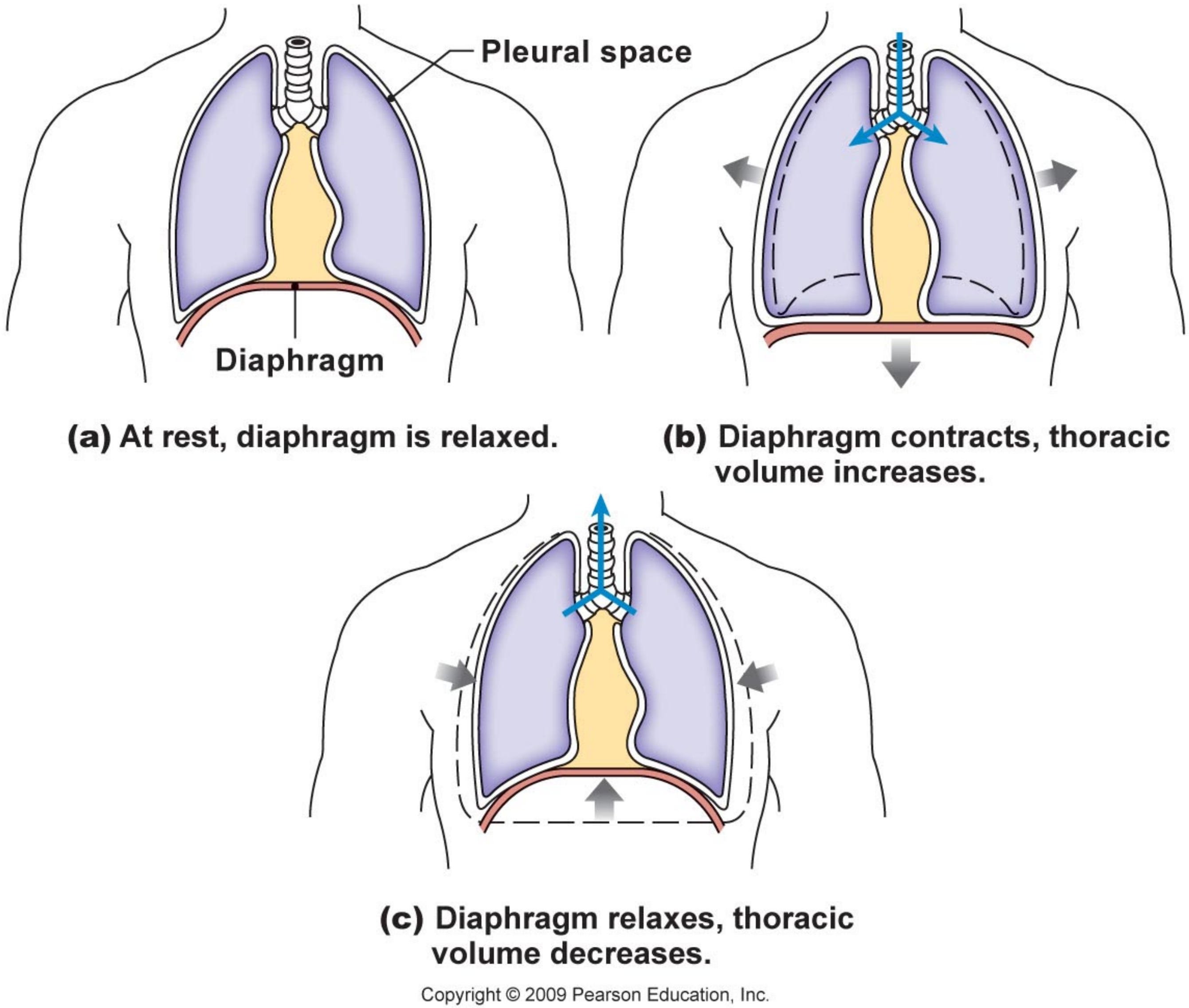
- Inspiration
  - Occurs as alveolar pressure drops below atmospheric pressure… becomes less than atmospheric and thus we call this pattern as: **negative pressure breathing**
    - For convenience atmospheric pressure = 0 mm Hg
      - A negative value (-) indicates pressure below atmospheric P
      - 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

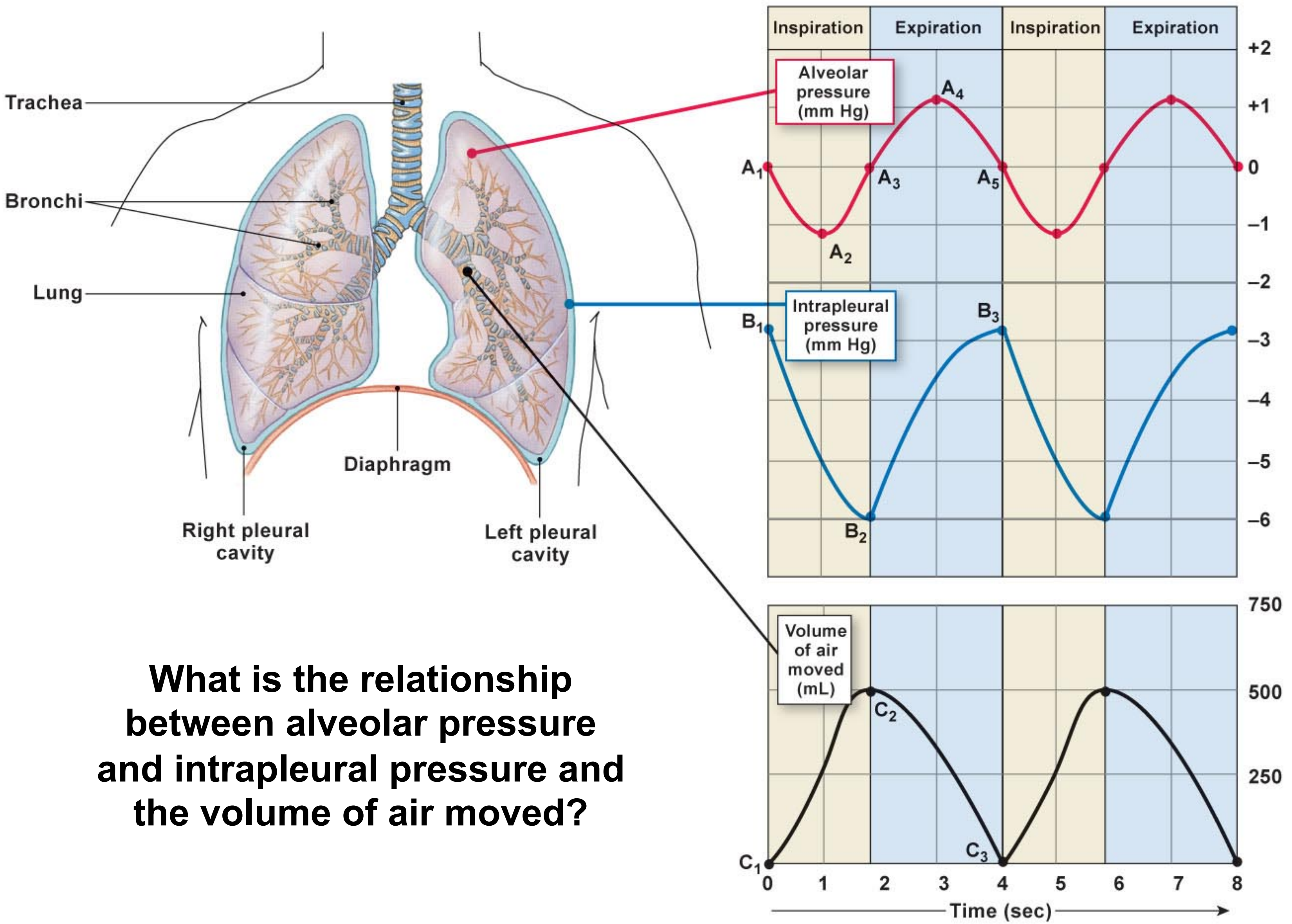


Ventilation

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



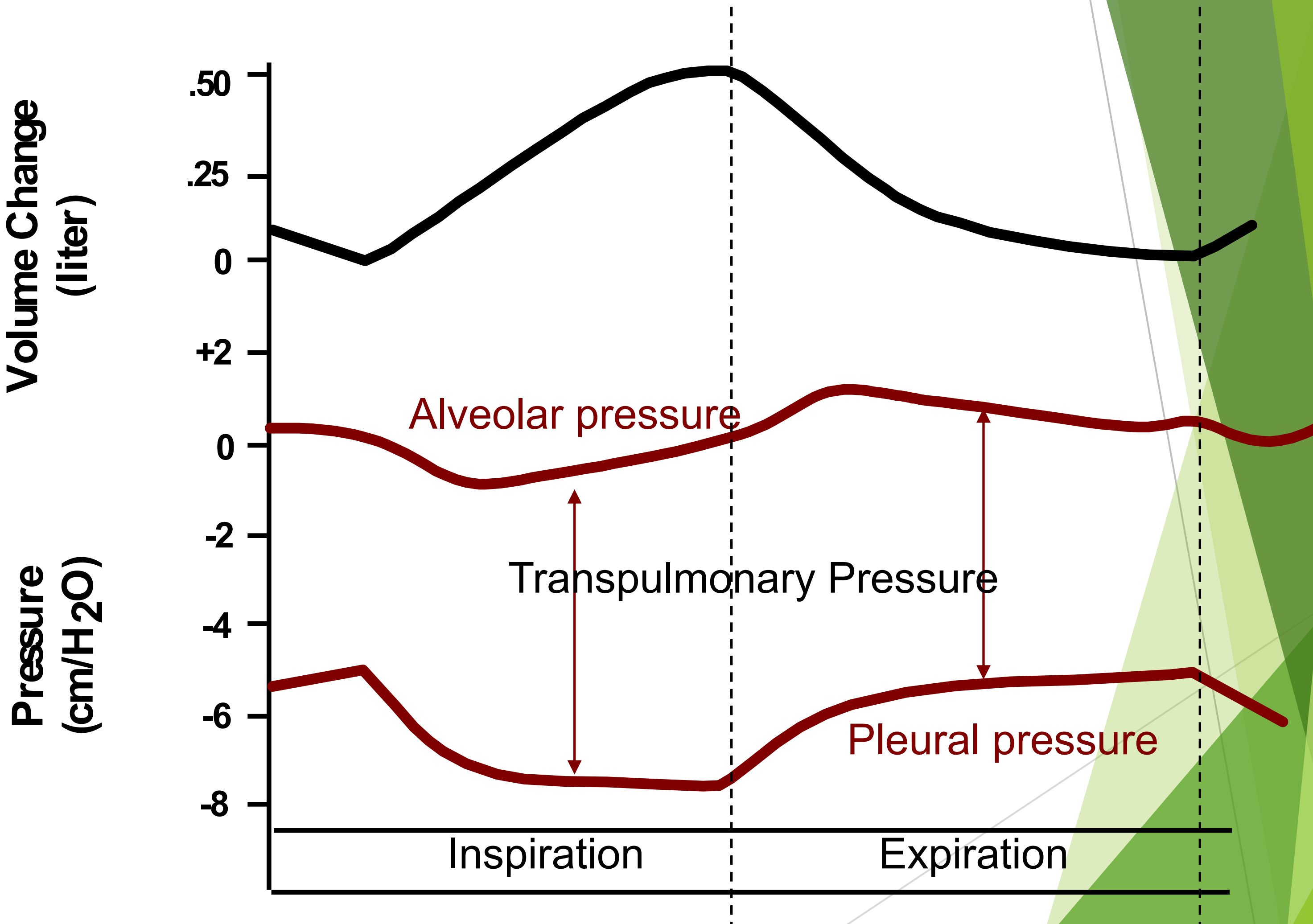
Ventilation



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



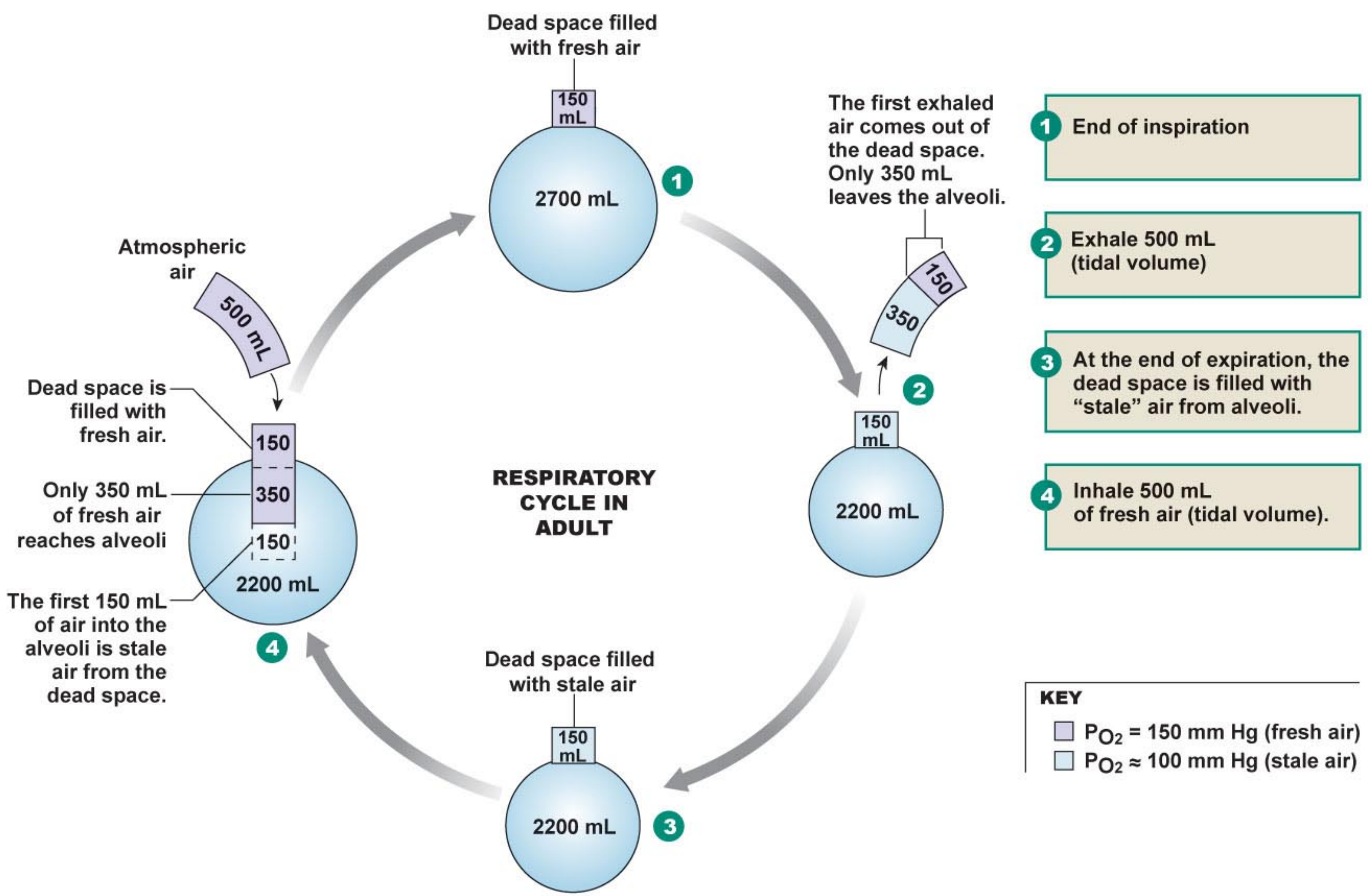
Volume Change (liter)
.50
.25
0
+2
0
-2
-4
-6
-8
Pressure (cm/H2O)
Alveolar pressure
Transpulmonary Pressure
Pleural pressure
Inspiration
Expiration

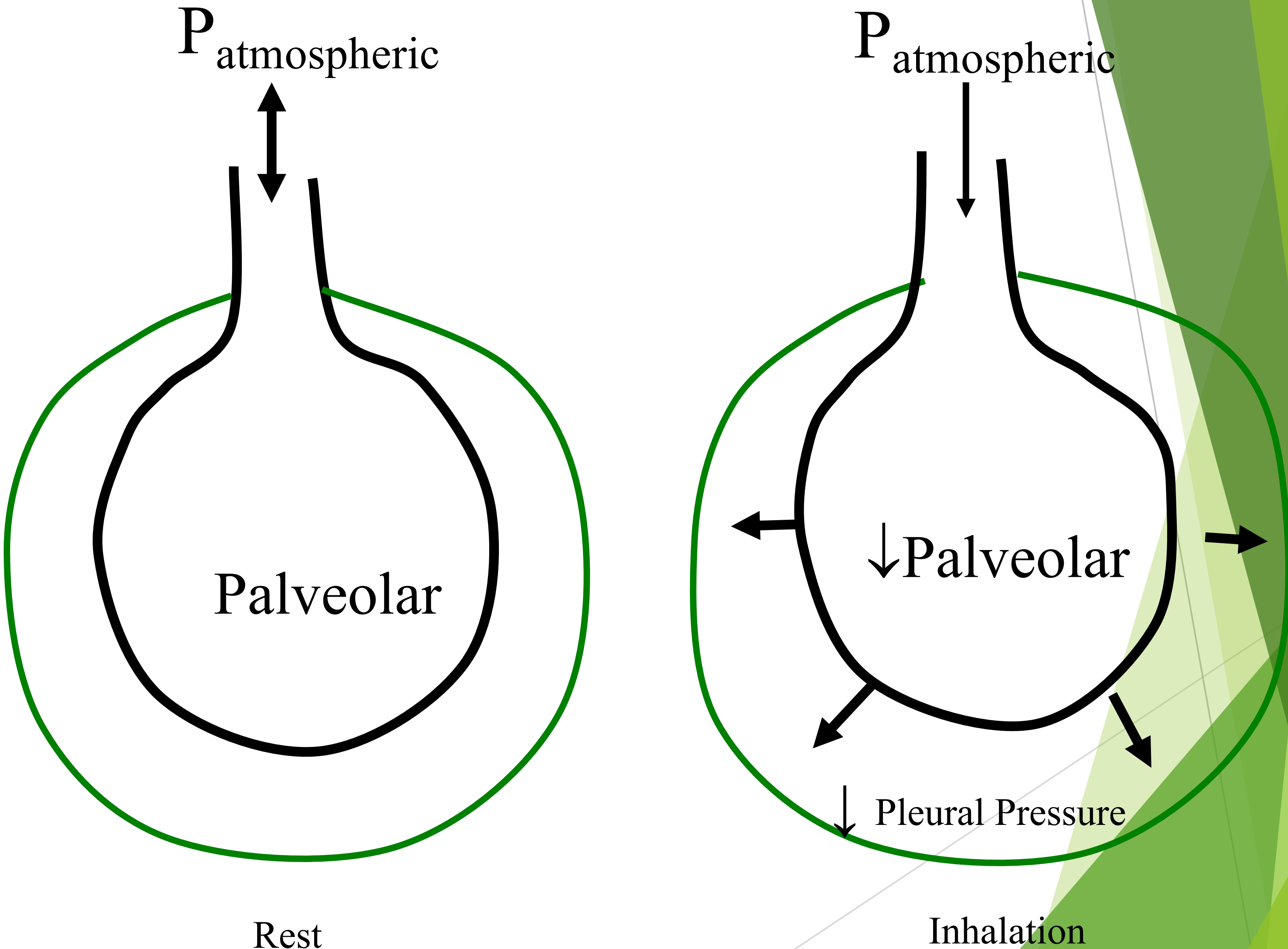
Ventilation

- 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 → decrease $PaCO_2$
- HYPOVENTILATION is when alveolar ventilation is LESS than CO2 production → increase PaCO2

Ventilation

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

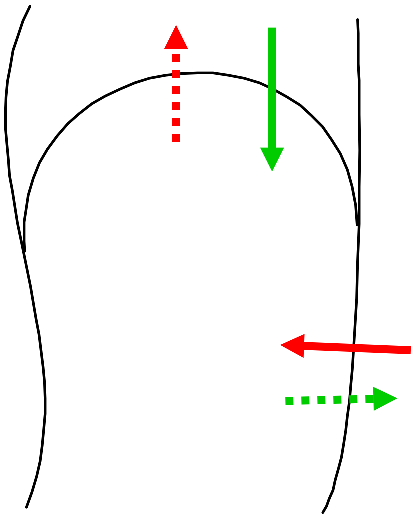




$P_{atmospheric}$
Palveolar
Rest
$P_{atmospheric}$
↓Palveolar
↓ Pleural Pressure
Inhalation

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

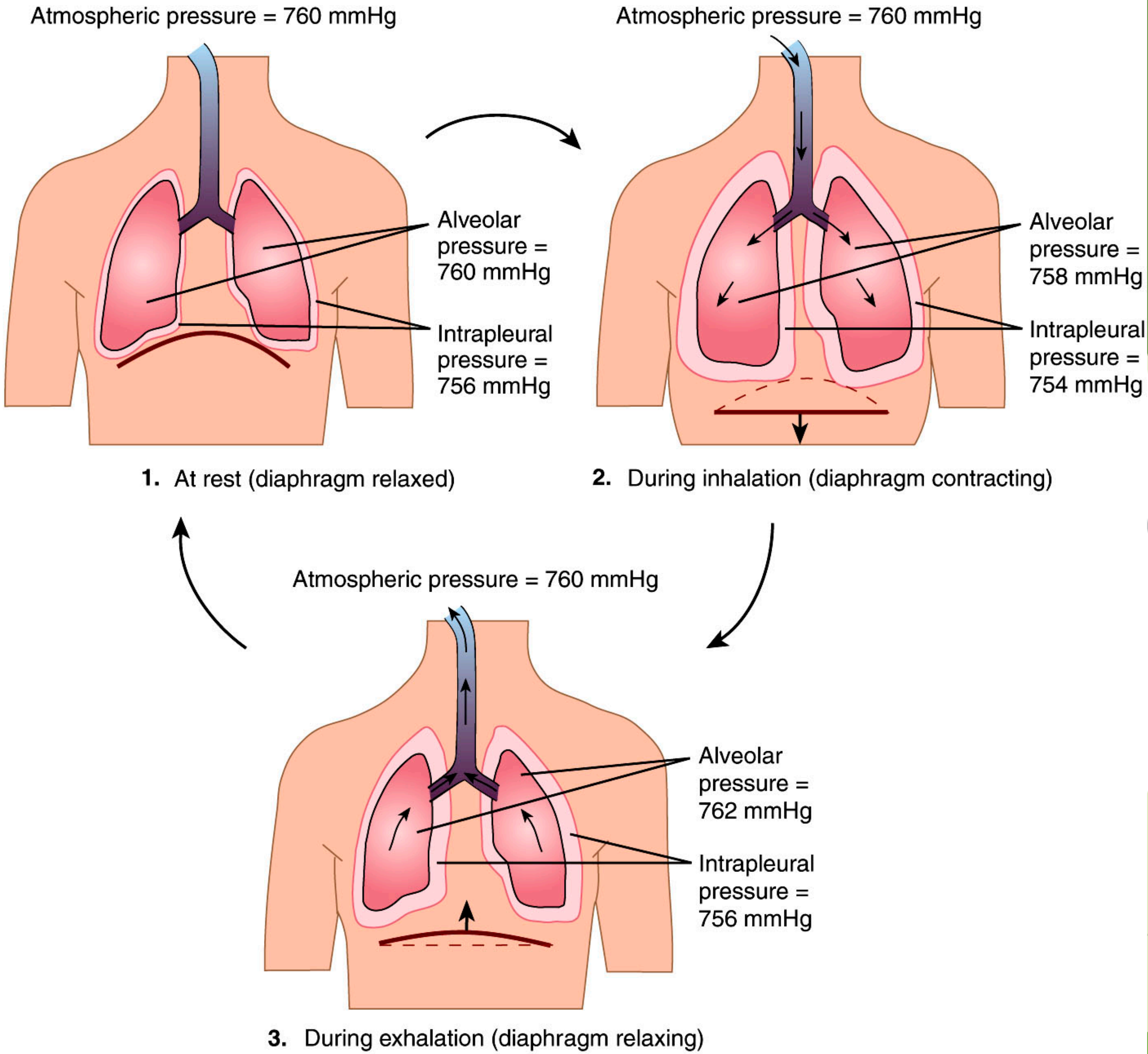


Figure 23.14 Tortora - PAP 12/e

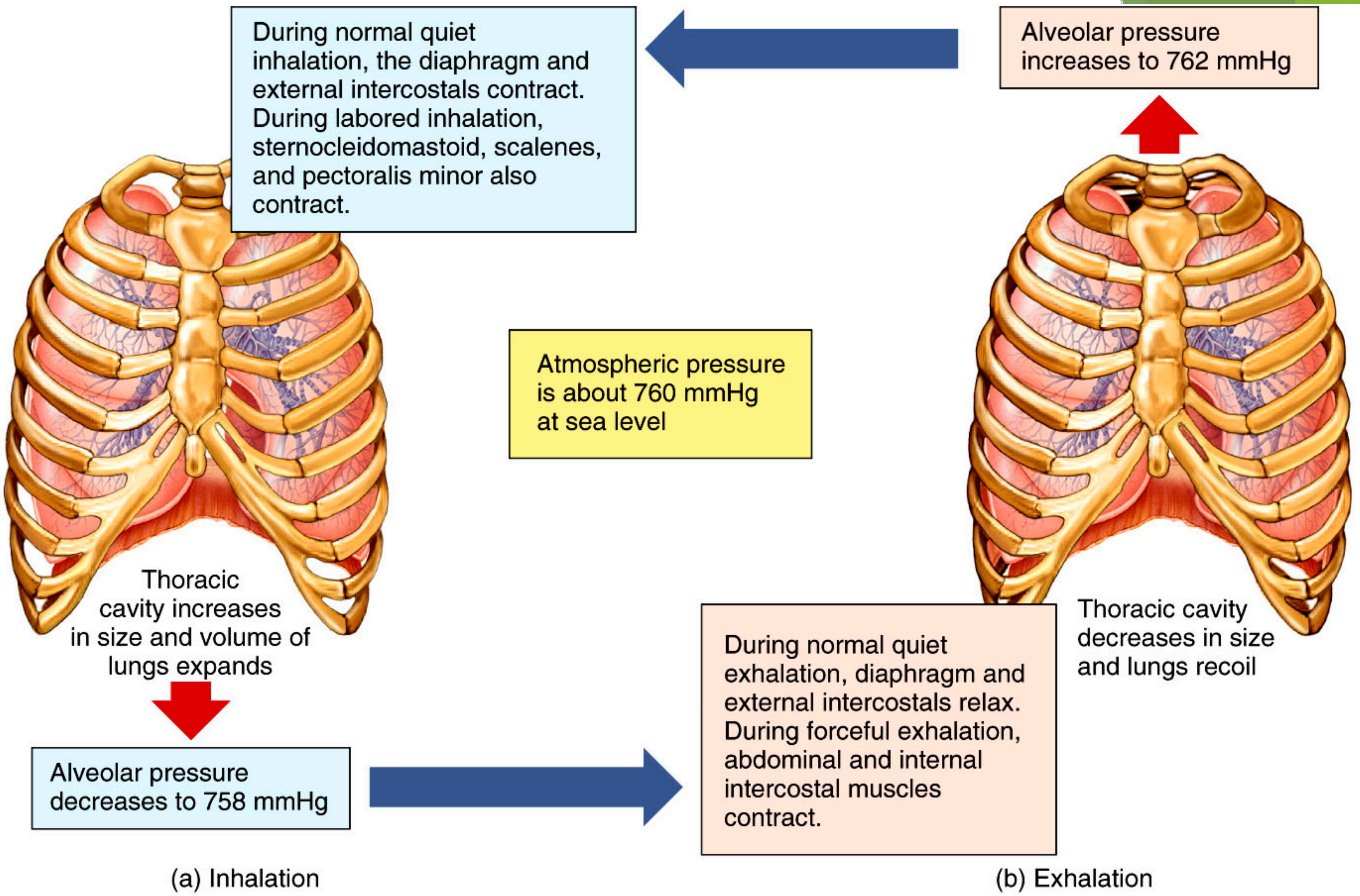


Figure 23.15 Tortora - PAP 12/e

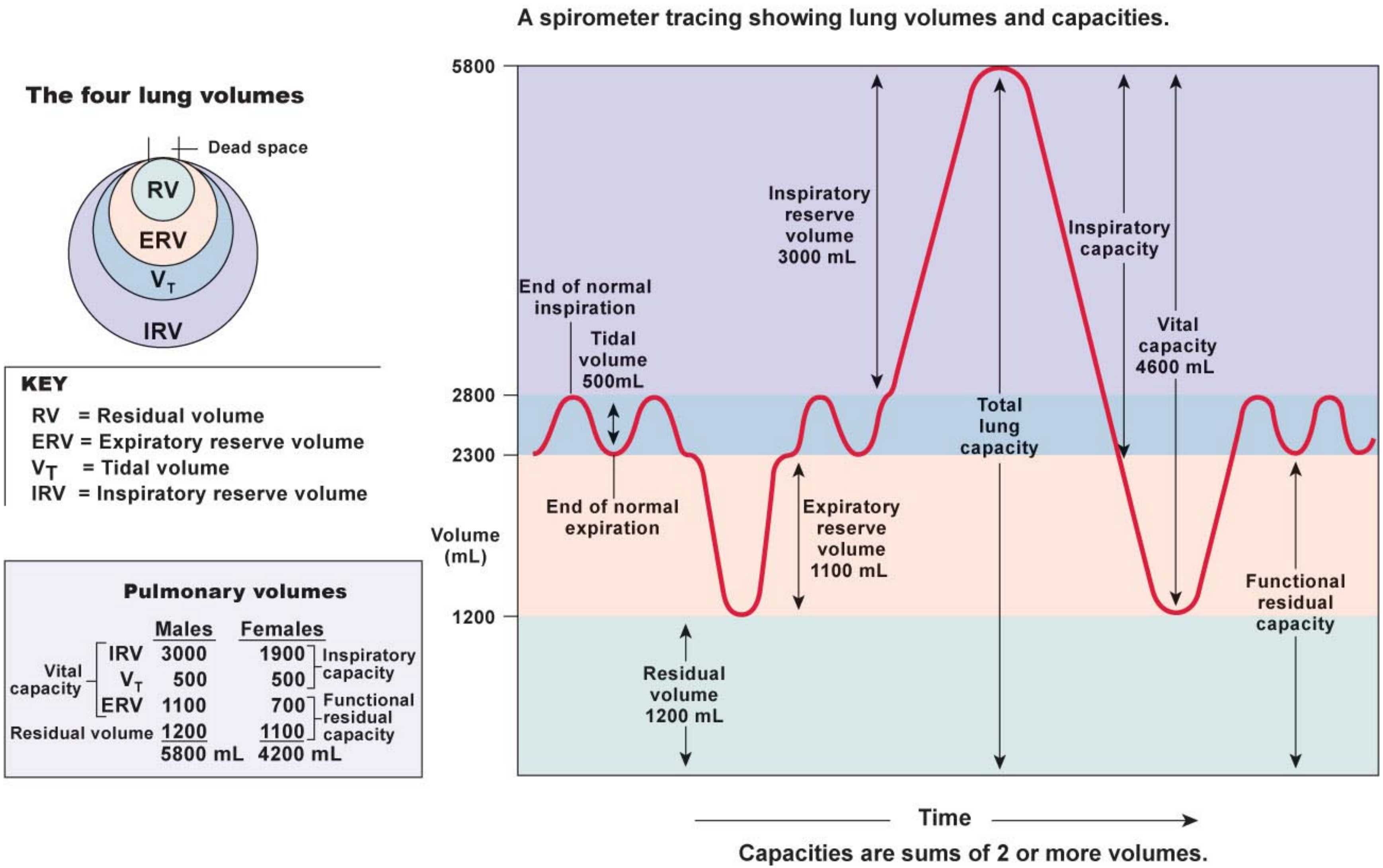
Respiratory Minute ventilation

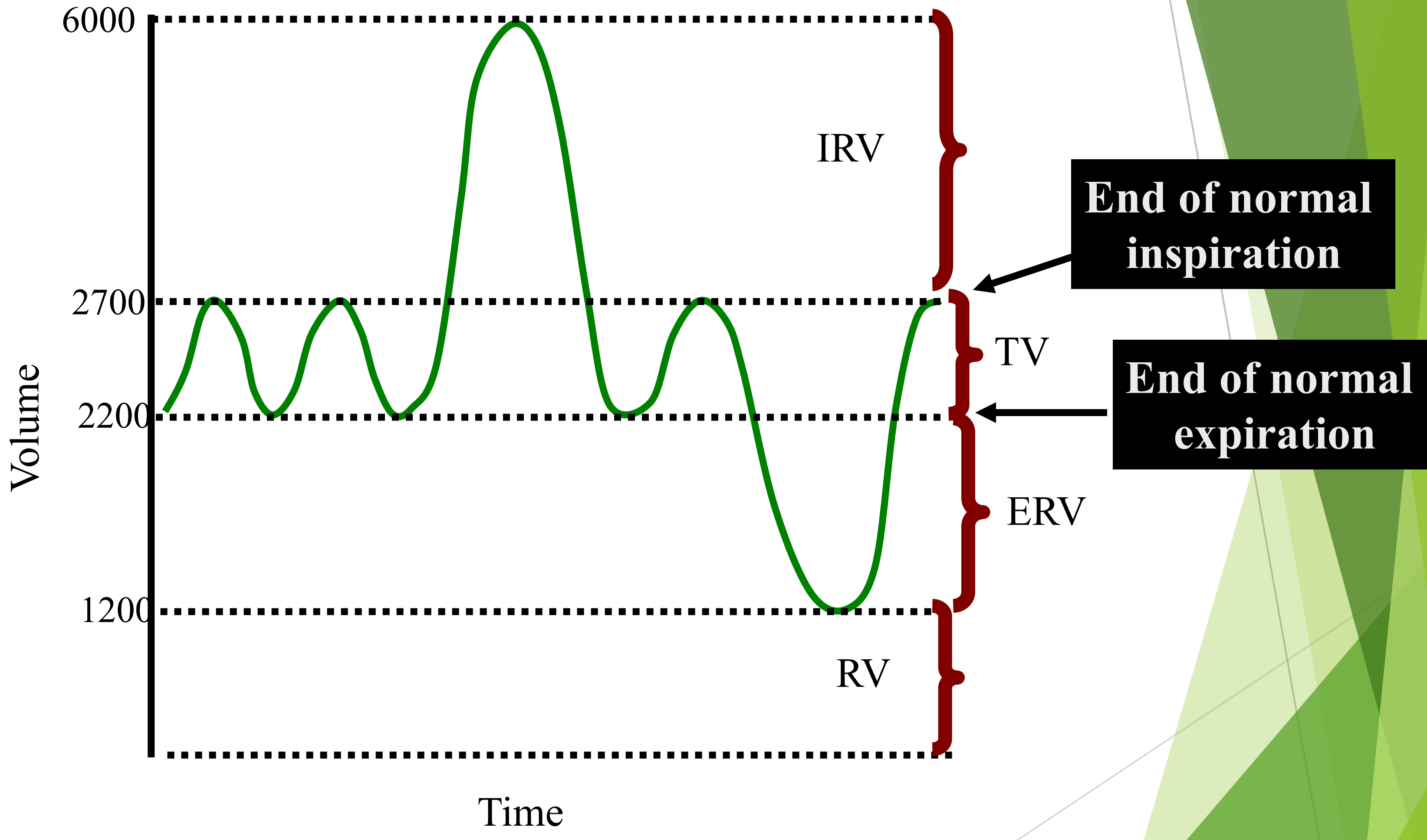
- Respiratory Minute ventilation RMV (respiratory rate times tidal volume 0.5 L * 12=6L/min). if you remember how the cardiac output is calculated then it is easy for you to understand
- RMV: Q=HR * SV… it is the same principle
- $RMV = RR * V_T$
- Anatomical dead space ventilation and alveolar ventilation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

PFT Pulmonary Function Tests

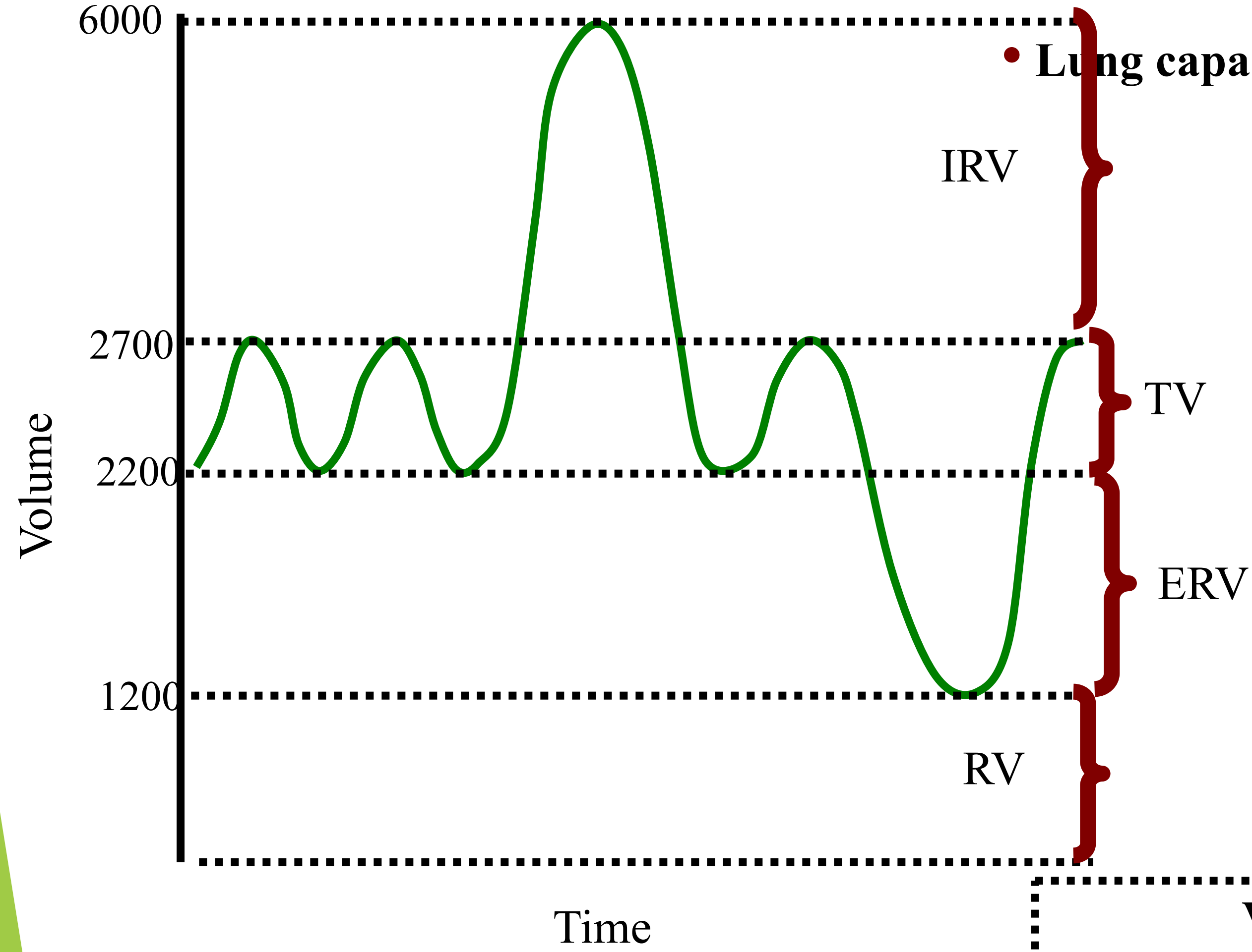
- **<u>Lung Volumes and Capacities</u>**
- **Other tests will be discussed too. Diffusing Capacity of the Lung for Carbon Monoxide will be also discussed, but with Gas Exchange lecture**

Ventilation e-learning



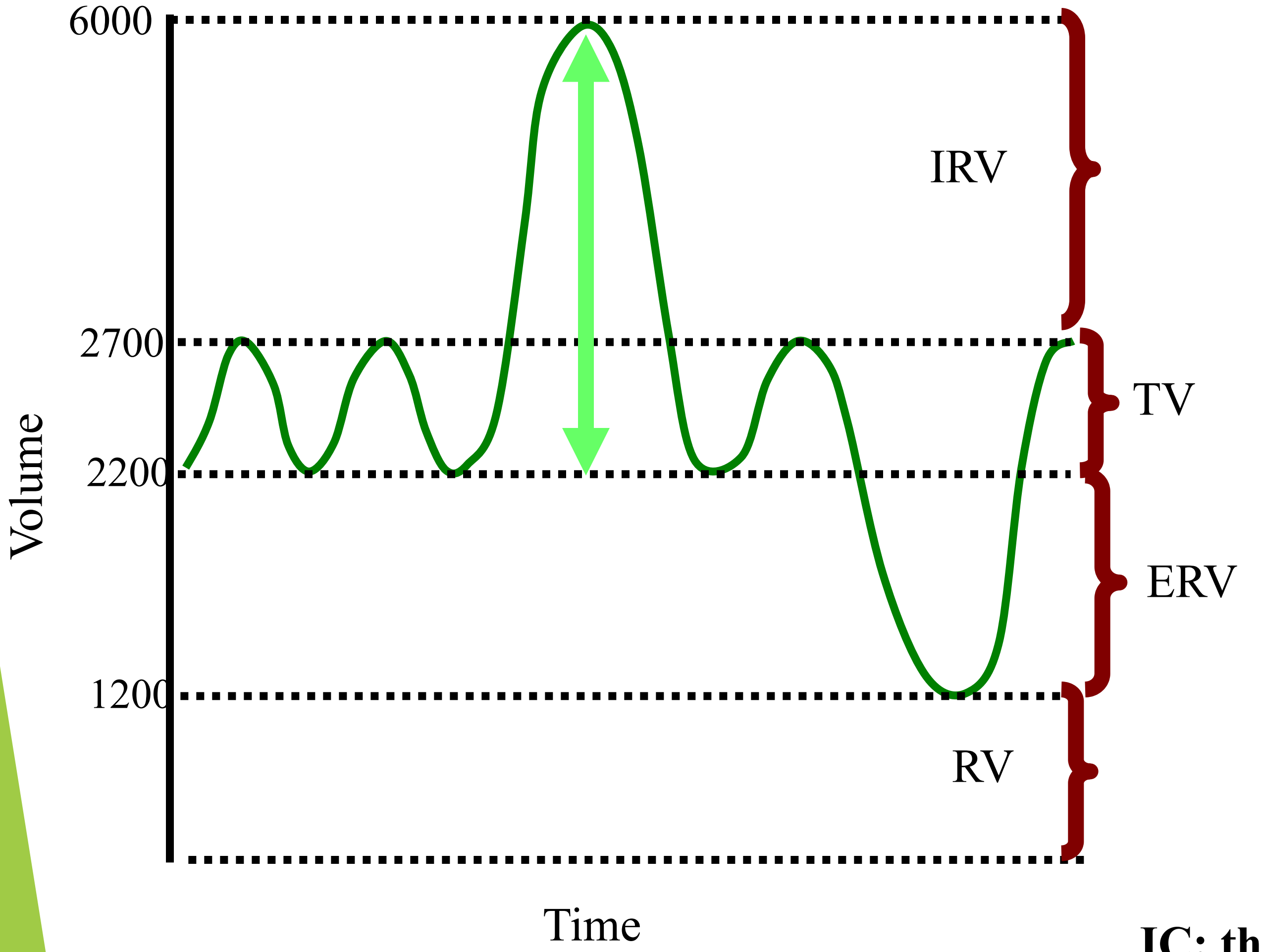

6000
2700
2200
1200
Volume
Time
IRV
TV
ERV
RV
End of normal inspiration
End of normal expiration

- 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

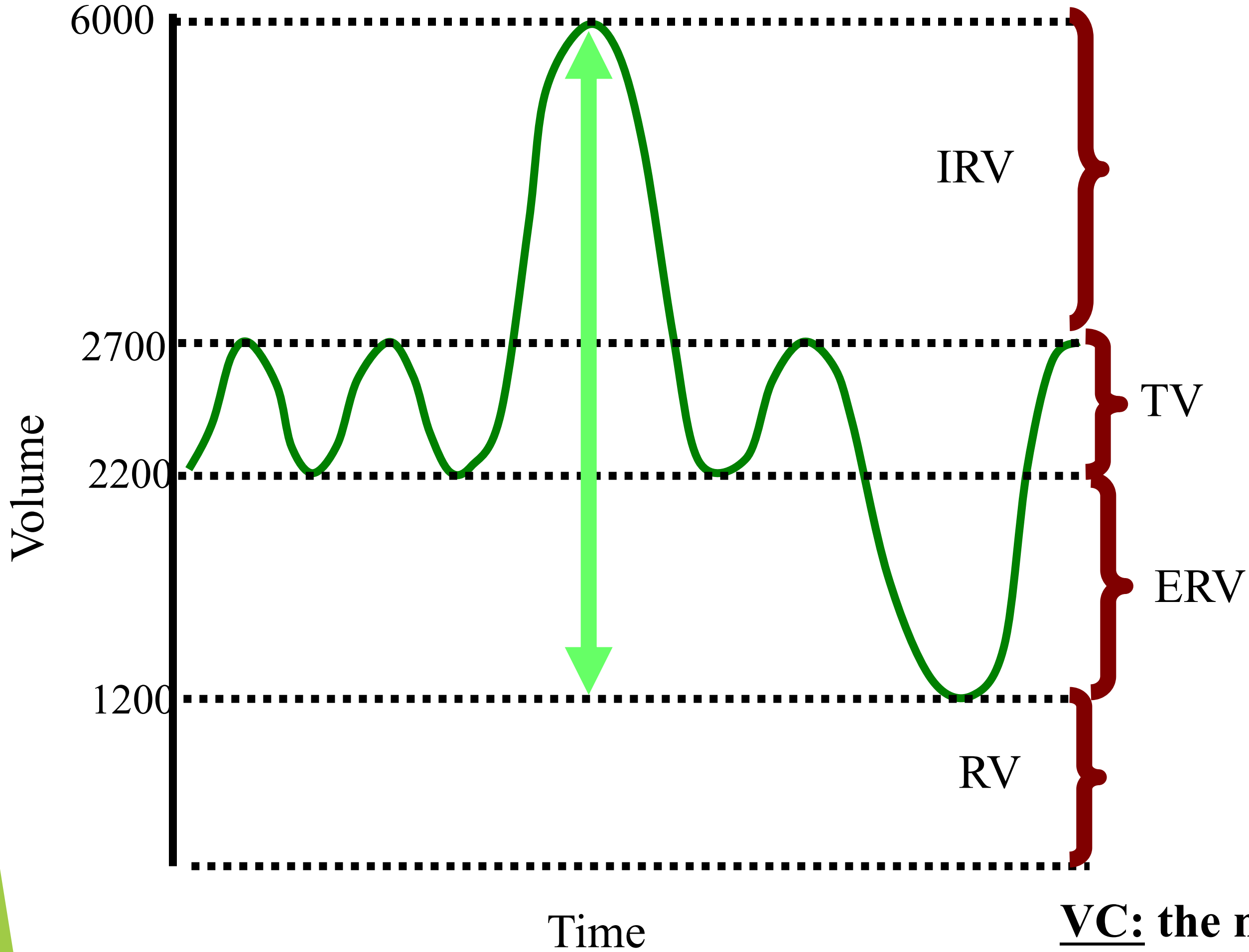
apacity (IC)



$IC = V_T + IRV$

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

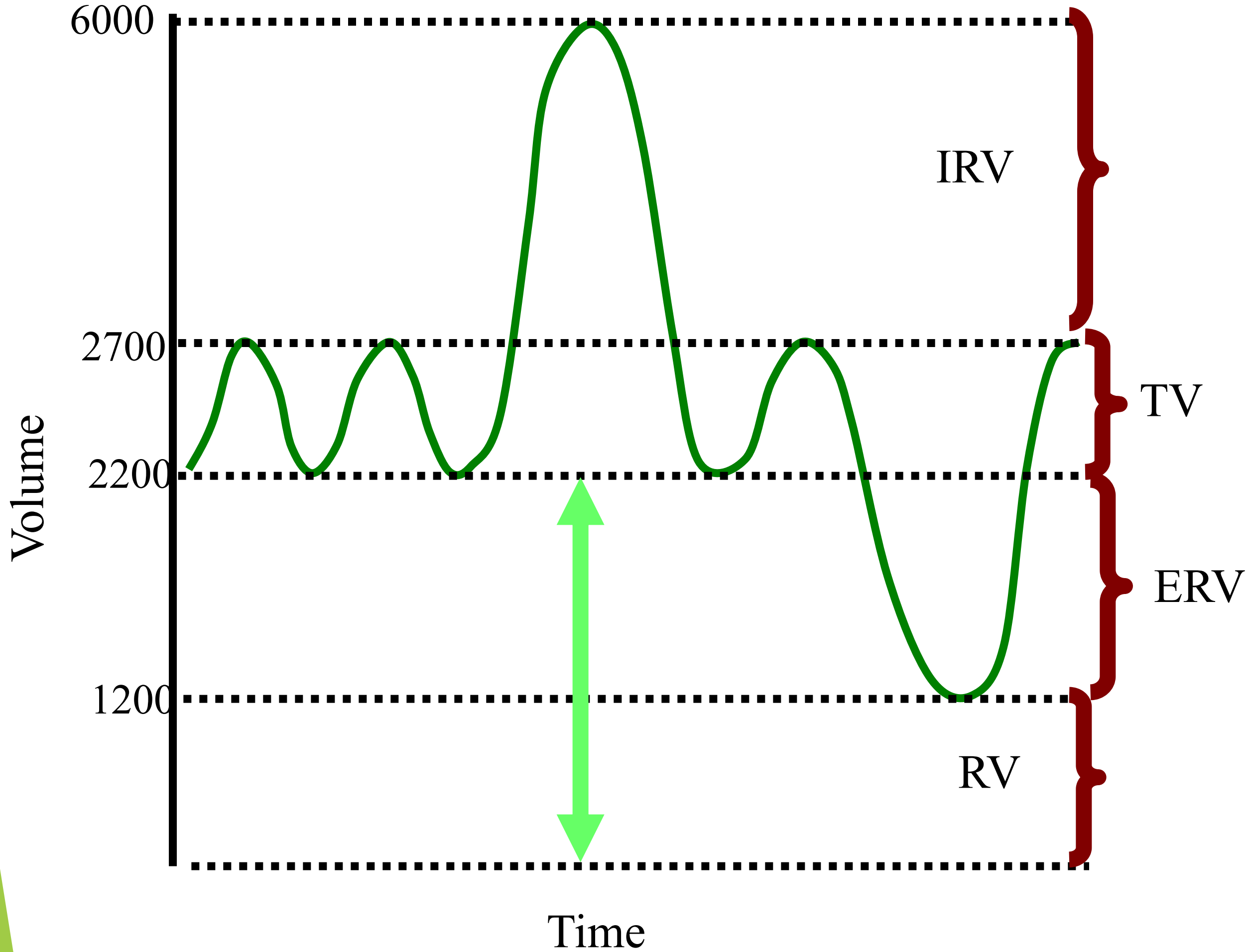
y (VC)



$VC = IRV + V_T + ERV$

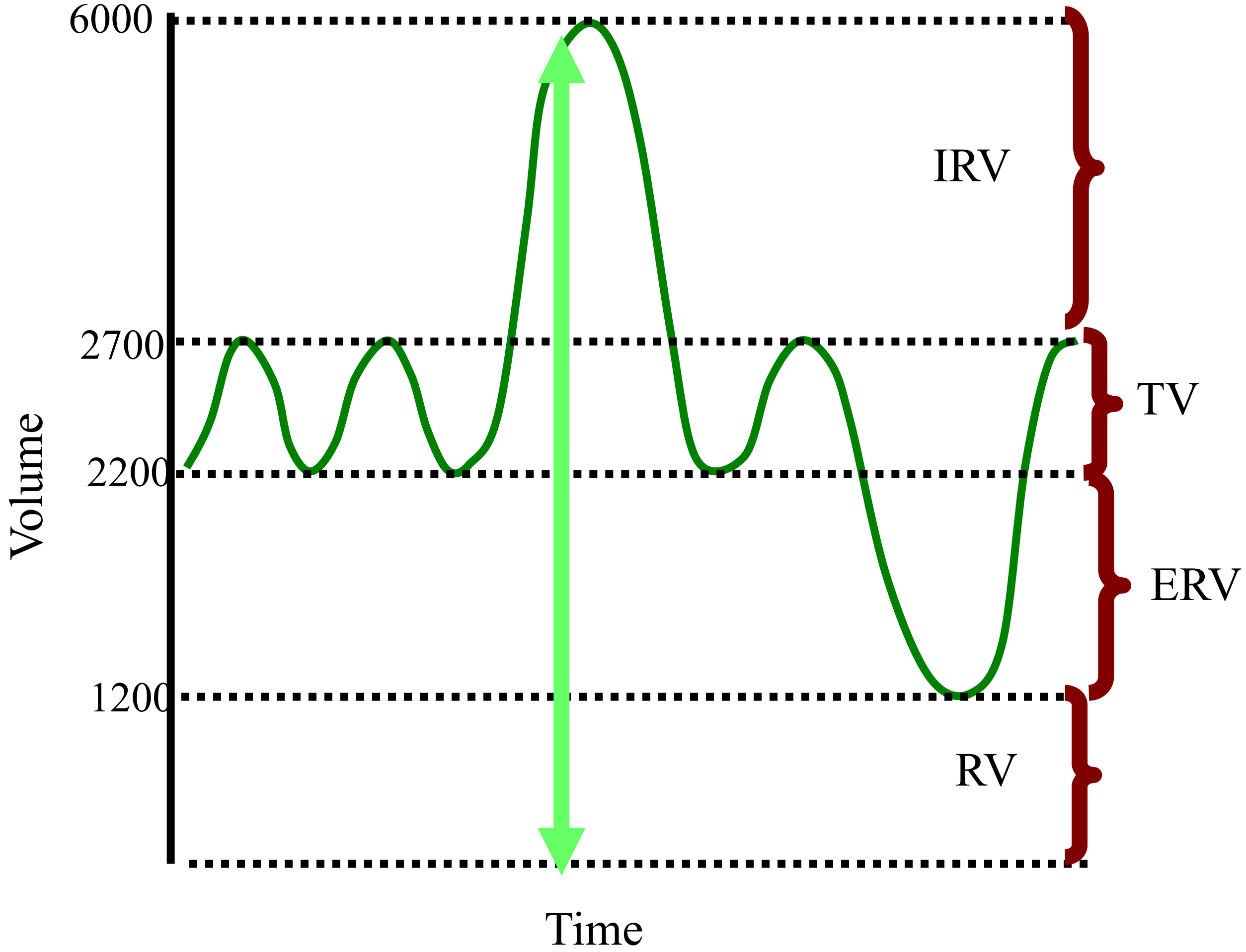
<u>VC</u>: the maximum amount of air that can be expired following a maximal inspiration

al



FRC = ERV + RV

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



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>.

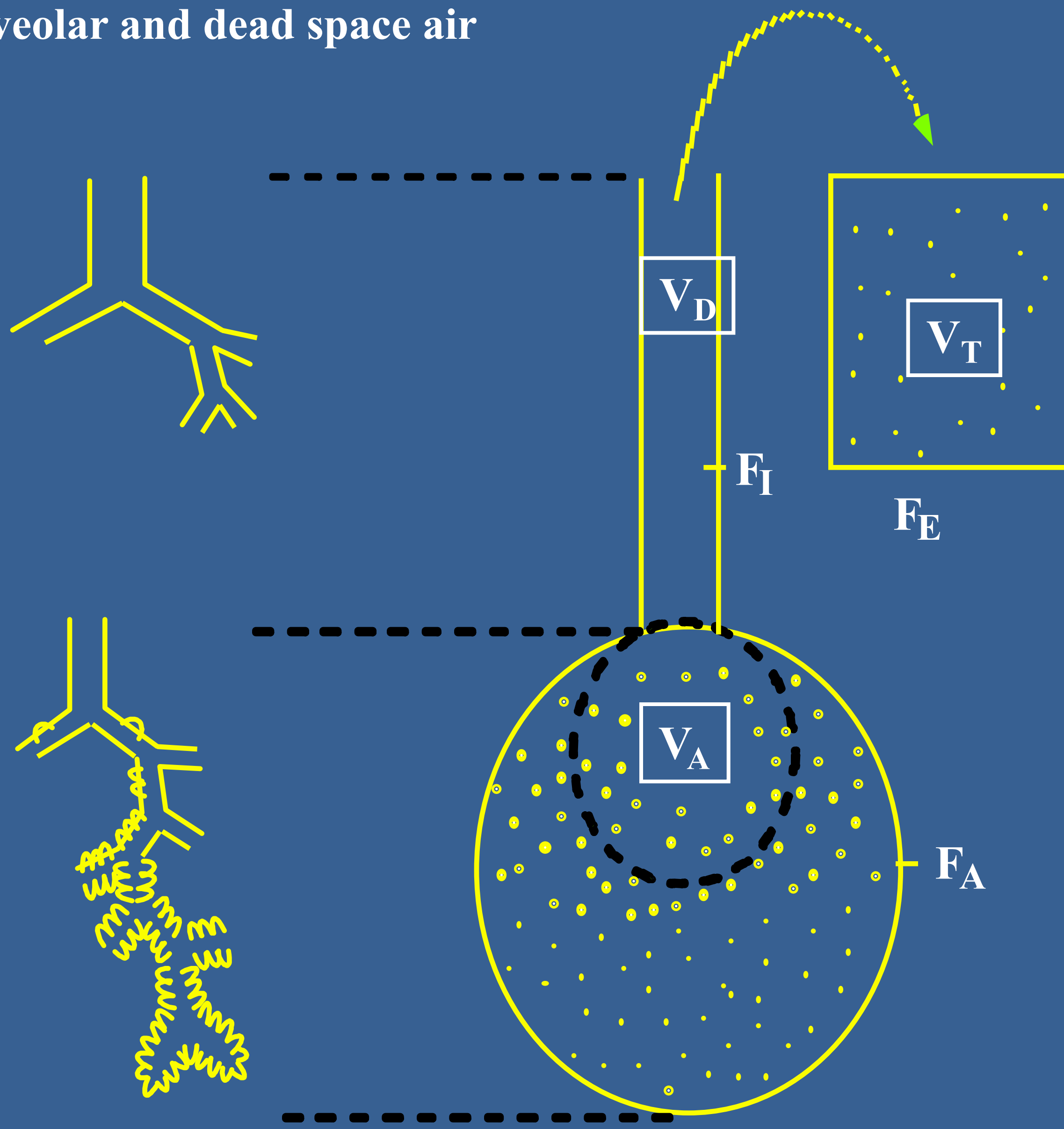
ation

- 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

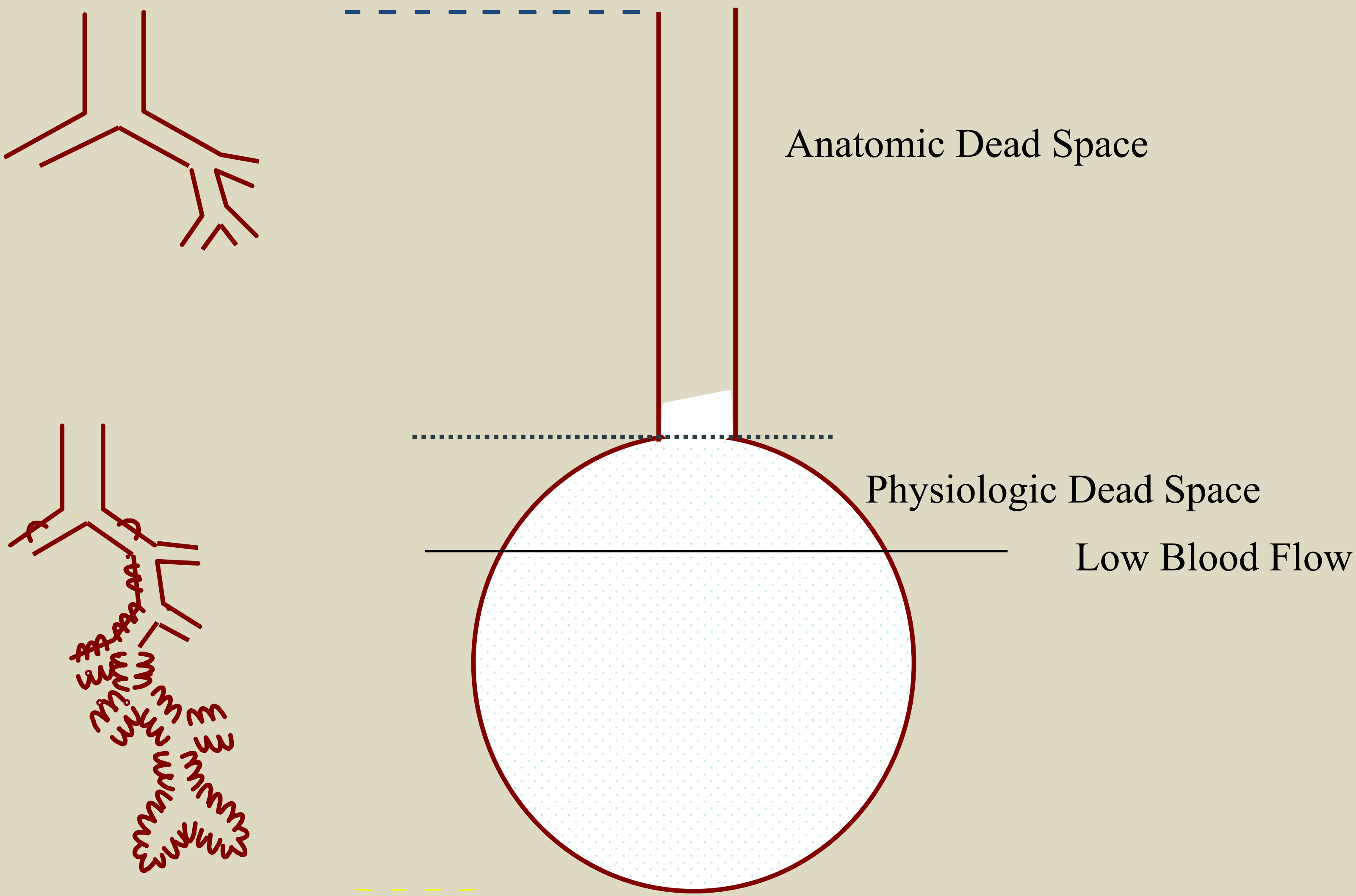
- Anatomic dead space: Part of respiratory system where gas exchange does not take place ≈ 150 ml in an adult (2 ml/kg)
  - Physiological dead space=ADS + alveolar wasted volume
- Alveolar ventilation: How much air per minute enters the parts of the respiratory system in which gas exchange takes place

Expired air has alveolar and dead space air

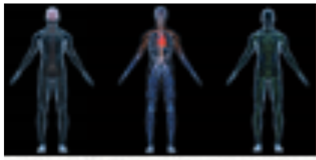


- ANATOMICAL: *Anatomical dead space is the volume of air that does not participate in gas exchange*
  - 150 ml (or 2 ml/Kg body weight)
- PHYSIOLOGICAL
  - Depends on ventilation-perfusion ratio (V/Q)
  - **Physiologic Dead Space = Anatomic Dead Space + alveolar dead space**

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

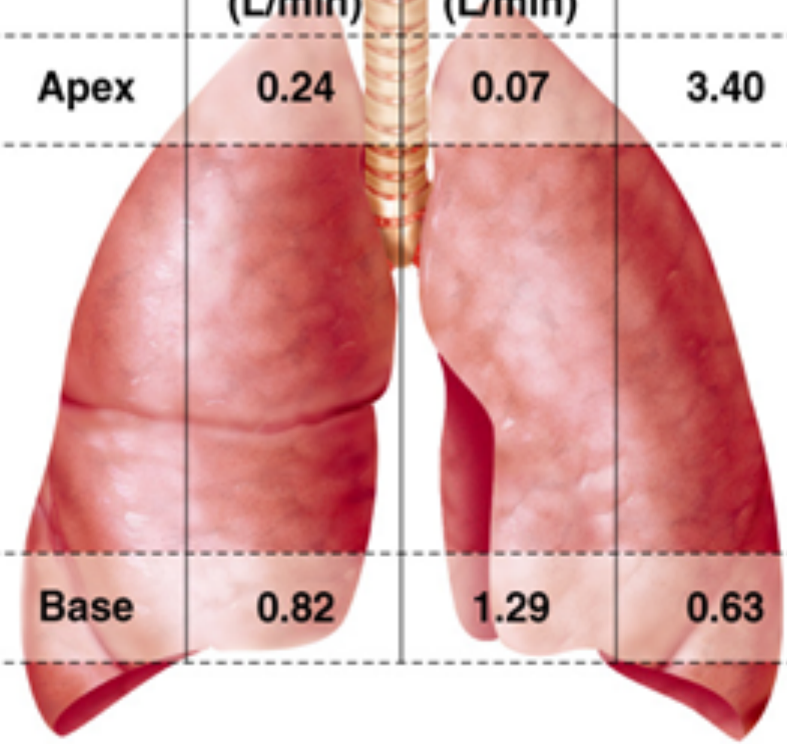

Anatomic Dead Space
Physiologic Dead Space
Low Blood Flow

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).



	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
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