

**ADDIS ABABA UNIVERSITY
SCHOOL OF MEDICINE
PHYSIOLOGY DEPARTMENT**

RESPIRATORY PHYSIOLOGY

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Chapter outline

- Introduction:
 - General overview of respiratory system
 - functions of the system: Respiratory and non-respiratory functions
 - Phases of respiration: external and internal
- Overview of Physiologic anatomy of respiration
- ANS innervations of respiratory tract
- Circulation: pulmonary and bronchial circulations
- Zones of the lung, Pulmonary blood flow and its distribution
- Pulmonary ventilation-perfusion ratio, mismatch and its regulation
- Pulmonary capillary dynamics

- Mechanics of pulmonary ventilation
- Pressure systems of respiration
 - Pleural, alveolar and transpulmonary pressures
- Pressure changes in respiratory cycle
- Lung compliance
- Surfactant, surface tension and Respiratory distress syndrome
- Work of breathing:
 - Compliance work, tissue resistance work and, airway resistance work
- Lung volumes and capacities
- Pulmonary and alveolar ventilation
- Physical principles of Gas exchange
 - Partial pressure
 - Gas laws
 - Gas exchange at pulmonary bed
 - Gas exchange at tissue bed

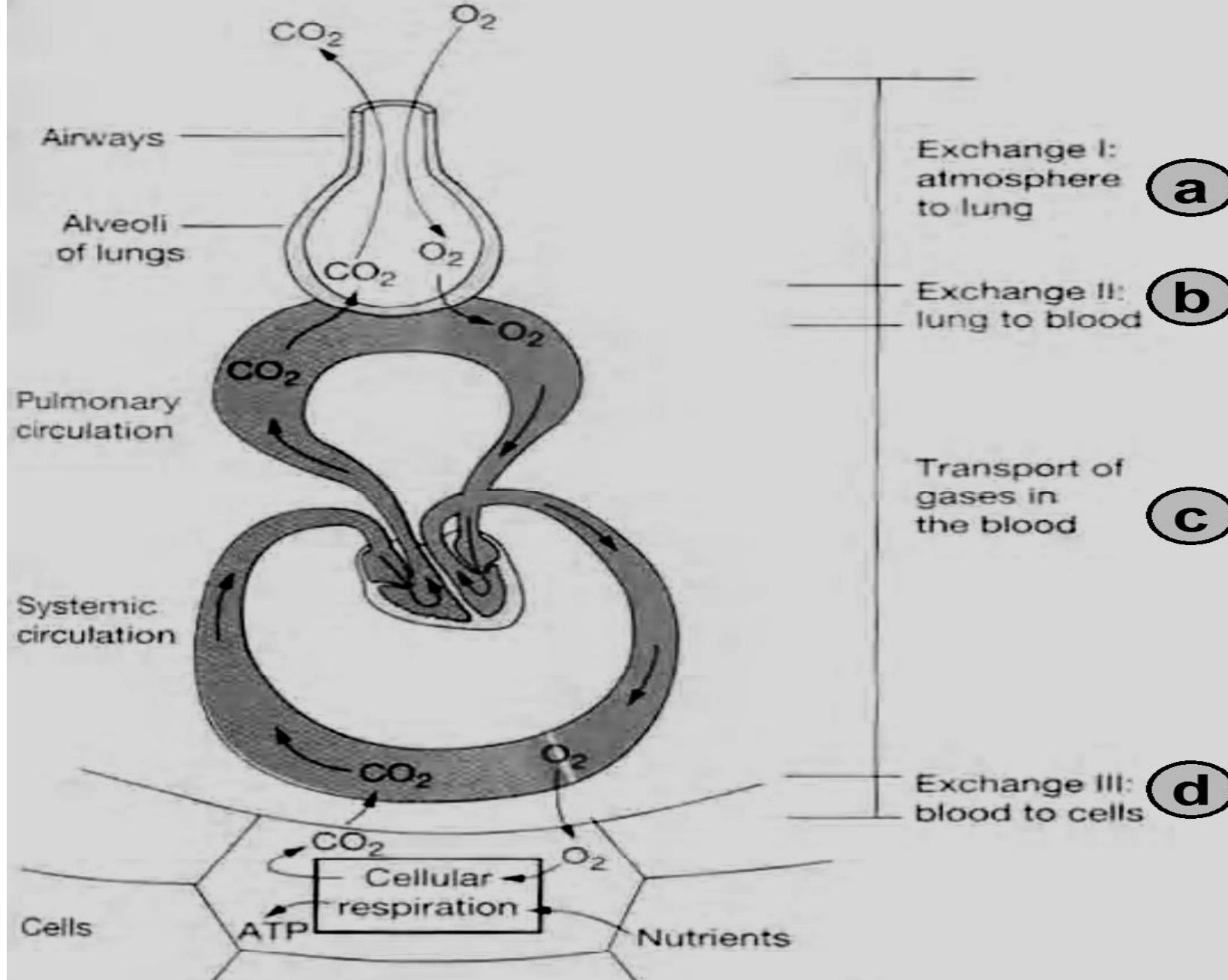
- Respiratory membrane/ **blood-air barrier**
- Factors affecting rate of diffusion of gas through the membrane:
Fick's Law
- Transport of oxygen and carbon dioxide in the blood
 - Hemoglobin saturation
 - Oxygen-hemoglobin dissociation (saturation) curve
 - Factors that affect the Ox-Hemoglobin dissociation curve
 - Bohr effect and Haldane effect
- Carbon monoxide poisoning
- Control of Respiration
 - Neural control: Medulary and pontine respiratory centers
 - Chemical control : Central and peripheral chemoreceptors

- Forms of hypoxia:
 - hypoxic, anemic, histotoxic & stagnant hypoxias
- Treatment of hypoxia: oxygen therapy (**+ways O₂ supplementation**)
- hypercapnea
- Fetal gas exchange

General over view

- **Respiration** - is the exchange of gases b/n atmosphere and body
 - The functions of the respiratory system:
 - Respiratory and non-respiratory functions:
- A. **Respiratory function** - is maintaining appropriate gas exchange
- to obtain oxygen for use by body's cells &
 - To eliminate CO₂ that the cells produce

- Such respiratory functions involve 4 stages:
 - Pulmonary ventilation
 - Inflow and outflow of air between atm & lung alveoli
 - Alveolar ventilation
 - Diffusion of O₂ & CO₂ b/n alveoli & pulmonary capillary blood
 - Transport of such gases in the blood
 - Exchange in tissue bed- b/n systemic capillaries & cells



B. Non respiratory functions of respiratory system

1. A means for water & heat loss
2. Enhances venous return:- the negative pleural pressure
3. Maintenance of normal - acid base balance
 - by altering the amount of H+-generating CO₂
4. It enables vocalization: speech, singing,
5. Defense against foreign matter
 - Eg. by alveolar macrophages, dendritic cells -act as APCs
 - NK cells - contain hydrolytic enzymes, secrete interferon & TNF
 - Destroy virus, virus infected cells & malignant cells (prevent cancer)
 - First line defense against viruses

6) The lungs convert angiotensin I \Rightarrow angiotensin II

- By producing angiotensin converting enzyme = ACE
 - ACE is produced in pulmonary capillary
- Angio II (RAS system) is important in controlling:
 - $[Na^+]$ & $[K^+]$ in ECF
 - Vasoconstriction - it is Potent vasoconstrictor
 - ADH release
 - BP regulation and many more

7. Olfaction

- The nose serves as organ of smell
 - Olfactory receptors are in the mucus membrane lining the upper nostril

Phases of respiration - are 2 :

1. External respiration

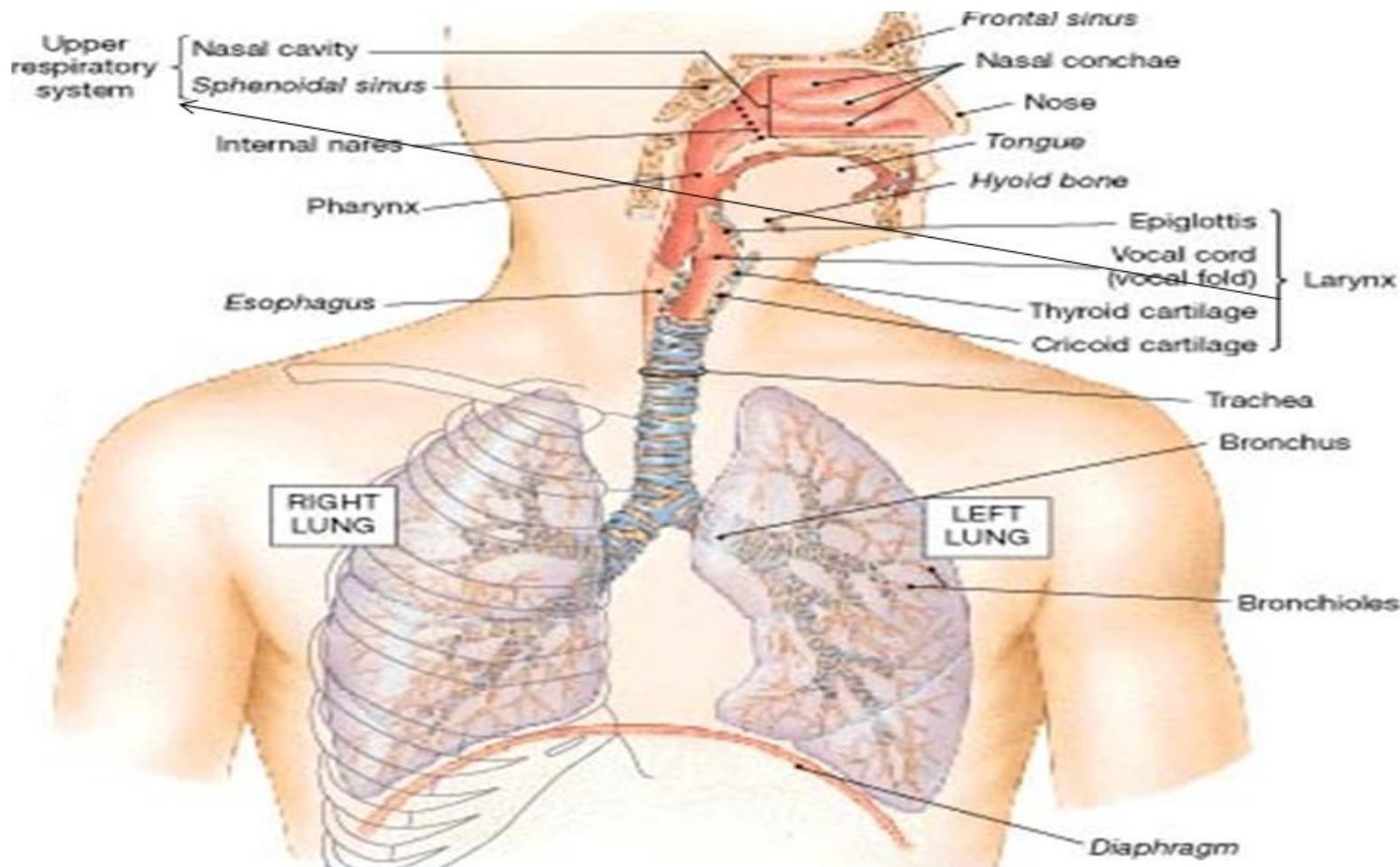
- inhalation of gas (O_2) from atm into the pulmonary capillary beds &
- exhalation of CO_2 from pulmonary capillary to the atmosphere.
- Includes:
 - Pulmonary ventilation = exchange I
 - Between atm and lung
 - Alveolar ventilation = exchange II
 - Between alveoli and pulmonary blood

2. Internal (Cellular) respiration-between systemic capillaries & cells

- O_2 is utilized for metabolic activities &
- CO_2 produced as a result of metabolic activities
⇒ carried out from the cells

Physiologic anatomy of respiratory system

- Pathway of air: nasal cavities (or oral cavity) → pharynx → larynx → trachea → primary bronchi (Rt & Lt) → secondary (lobar) bronchi → tertiary (segmental) bronchi → bronchioles (terminal → respiratory) → alveolar ducts → alveolar sac → alveoli



Main anatomical components

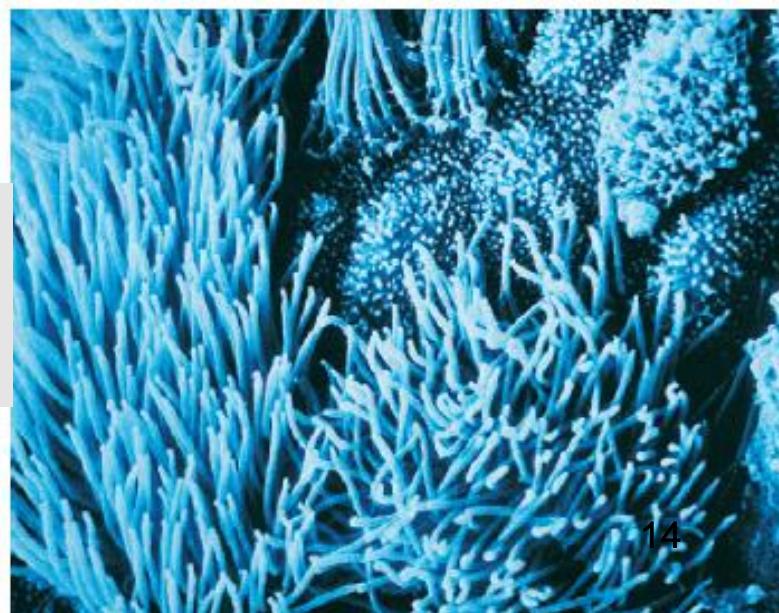
The nose and the nasal cavity: conditioning of air

- The primary passageway for air entering the respiratory system
- Nasal mucosa has a rich blood supply and secretions
 - Warming and humidifying the incoming air due to high blood supply
- Nasal cavity [up to T bronchioles] contain epithelial cell lining
 - each epithelium contains 200 -300 cilia
 - Beat 10-20x/sec, Move mucus at rate of 2 cm/min
 - goblet cells inside the epithelial lining \Rightarrow secrete mucus

- **The mucus & cilia form muco-ciliary layer/Blanket**
 - important to trap dusts, smokes, pollen, bacteria, toxins
 - Particulates sticking to mucus is moved by cilia to pharynx
 - thus, air born particles become filtered out → keep lungs clean
 - The epithelial lining also used to humidify (moisten) & warm the air
 - due to high supply of capillary blood in the nasal cavity.
-
- ◊ *Oral breathing lacks such advantages!*
 - Ciliary activity can be reduced by smoking, hypoxia leading to lung infection.

Fig.

A scanning electron micrograph of cilia in a bronchial wall. The cilia that project from the tops of the epithelial cells help to cleanse the lung by moving trapped particles.



NB: Ciliary activity can be reduced by smoking, hypoxia, leading to lung infection.

The trachea

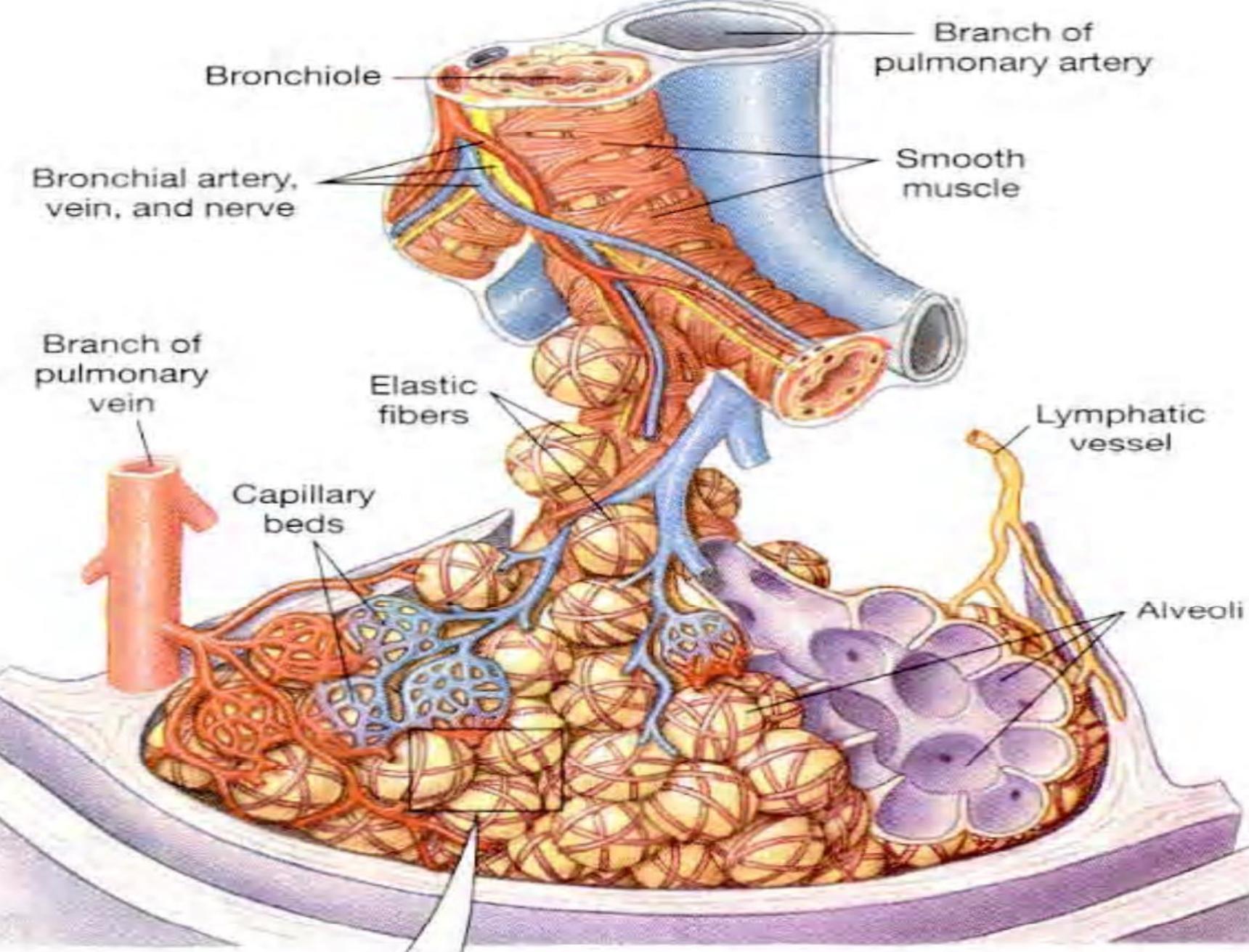
- Surrounded by C - shaped cartilages
 - Such cartilages extend anterior five-sixth of trachea
 - Protect the tracheal wall and prevent it from collapse
 - Keep the trachea open to allow easy passage of air
 - No cartilage at the back side of trachea. What is advantage?
 - Since esophagus is behind the trachea,
 - allows easy peristaltic movement of esophagus during deglutition of a bolus
- Trachea bifurcates in to two primary bronchi: Rt and Lt bronchi
 - Bronchi has less extensive curved cartilages
 - 1° bronchi branch to 2° then to 3° bronchi \Rightarrow bronchioles

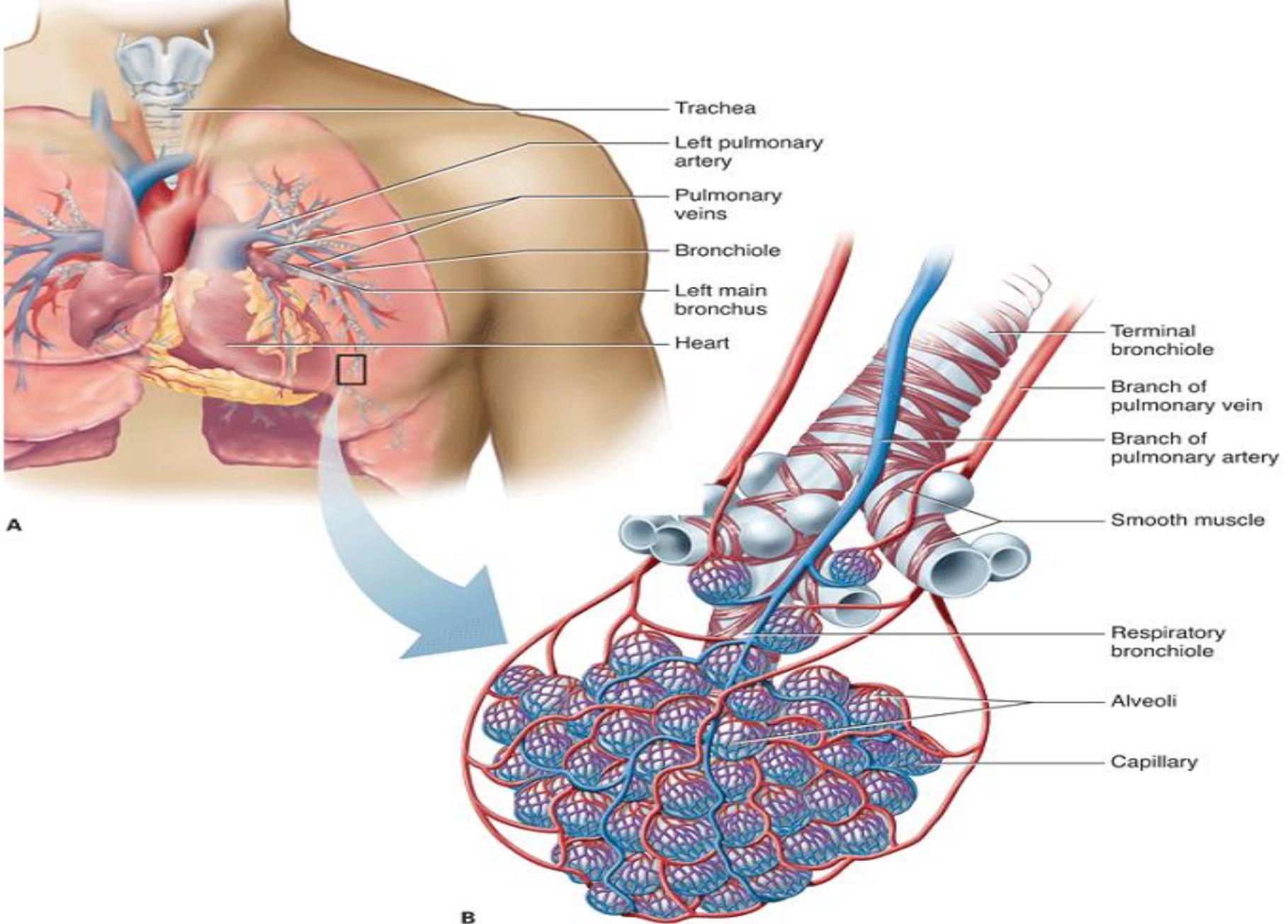
Bronchioles

- The walls lack cartilaginous supports
 - but dominated by smooth muscle tissue
- The ANS regulates the activity of smooth muscle layer
 - alter the diameter of the bronchioles
- Sympathetic activation via Beta2-adrenergic receptors
→ enlargement of the airway diameter ⇒ **BRONCHODILATION**
- Parasympathetic stimulation via muscarinic receptors
→ a reduction of airways diameter ⇒ **BRONCHOCONSTRICITION**

Alveolus

- A one cell layer thick diffusion barrier to respiration
- each alveolus has an average diameter of about 0.2 mm
 - This extremely thin alveolar wall is important for gas diffusion
- No muscle around the alveoli
- There are about 300 million alveoli in the two lungs
- between the alveoli is an almost solid network of interconnecting capillaries,
- Capillaries cover —90% of the alveolar surface





- The alveoli are lined by two types of epithelial cells.
 - **Type I cells** - are the primary lining cells of the alveoli,
 - account approximately 95% of the alveolar epithelial surface area
 - involved in gas exchange
 - **Type II cells (granular pneumocytes)**
 - A primary function of these cells is to secrete surfactant
 - make up approximately 5% of the surface area
 - The alveoli also contain other specialized cells, including :
 - pulmonary alveolar macrophages ,
 - lymphocytes, plasma cells, mast cells.
- **The mast cells contain heparin, histamine, and various proteases that participate in allergic reactions**

- Anatomically, the air passages of the respiratory system are divided into 2 parts:
- *Upper respiratory tract*
 - nose, nasal cavity, paranasal sinuses, pharynx, and larynx
- *Lower respiratory tract*
 - trachea,
 - 1^o, 2^o, & 3^o bronchi (10 generation of 3^o bronchi in Rt lung and 8 generation in Lt lung)
 - terminal & respiratory bronchioles (with several generations),
 - alveolar ducts and alveoli of the lungs

- Physiologically, respiratory tract can be divided into 2 zones:

1. The conducting zone

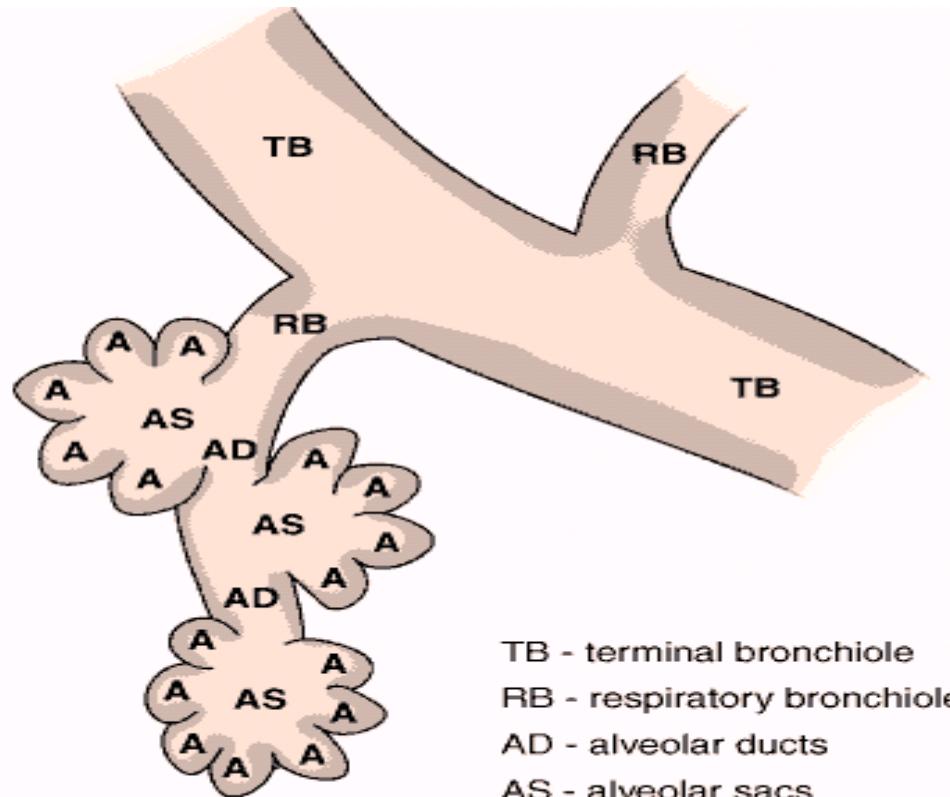
- only passage of air, no exchange because walls are thick
- from the **nasal cavity up to the terminal bronchioles**
 - Filters, warms, and humidifies the incoming air

2. The respiratory zone - involved in gas exchange, walls are thin

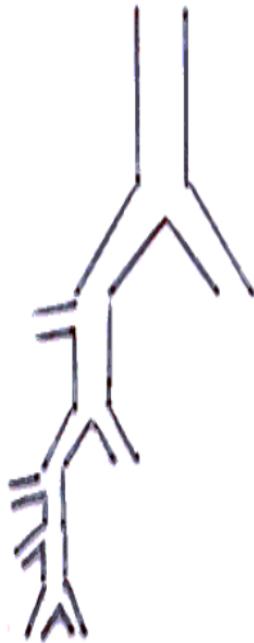
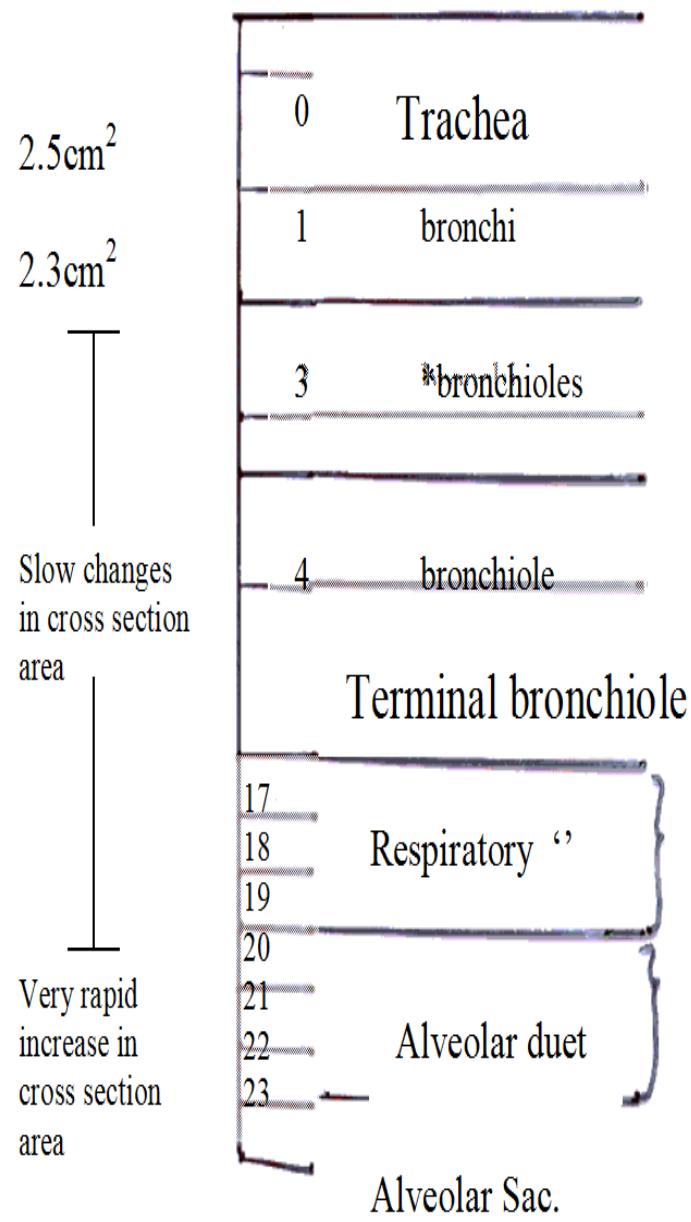
- Respiratory bronchioles, alveolar ducts, sacs, & alveoli
 - There are about 300 million alveoli in the two lungs
 - Huge number increases surface area for gas exchange

Diffusion of Gases Through the Respiratory Membrane

- The respiratory unit
 - a unit where gas exchange takes place
 - between external air and the pulmonary blood
- .
- It is composed of :
 - respiratory bronchiole,
 - alveolar ducts,
 - atria (alveolar sacs), and
 - alveoli (300 M in two lungs)



The human air ways



Gas exchange

Conductive zone

Transition & respiratory

Functions

1. *Conduits for air travel to and from the lungs.*

2. *Conditioning the inspired air (cleansed, moistened, and warmed)*

- In the lung there are two types of circulation:
 1. **pulmonary circulation** - for oxygenation of blood
- Deoxygenated blood from Rt atrium → Rt ventricle → pulmonary artery
→ lung (oxygenation) → Lt atrium
- 2. **Bronchial circulation**: contain 1-2% of cardiac output
- Oxygenated blood from Lt ventricle → aorta → bronchial artery
→ supplies O₂ to surrounding tissues of the lung
 - => Bronchial blood become deoxygenated
- → some of the deoxygenated blood meets the pulmonary vein containing oxygenated blood
 - => the purity of pulmonary blood or PO₂ is reduced
 - Thus part of the bronchial blood does not involve in gas exchange &
 - Lt ventricular CO is 1 to 2% greater than Rt ventricular CO

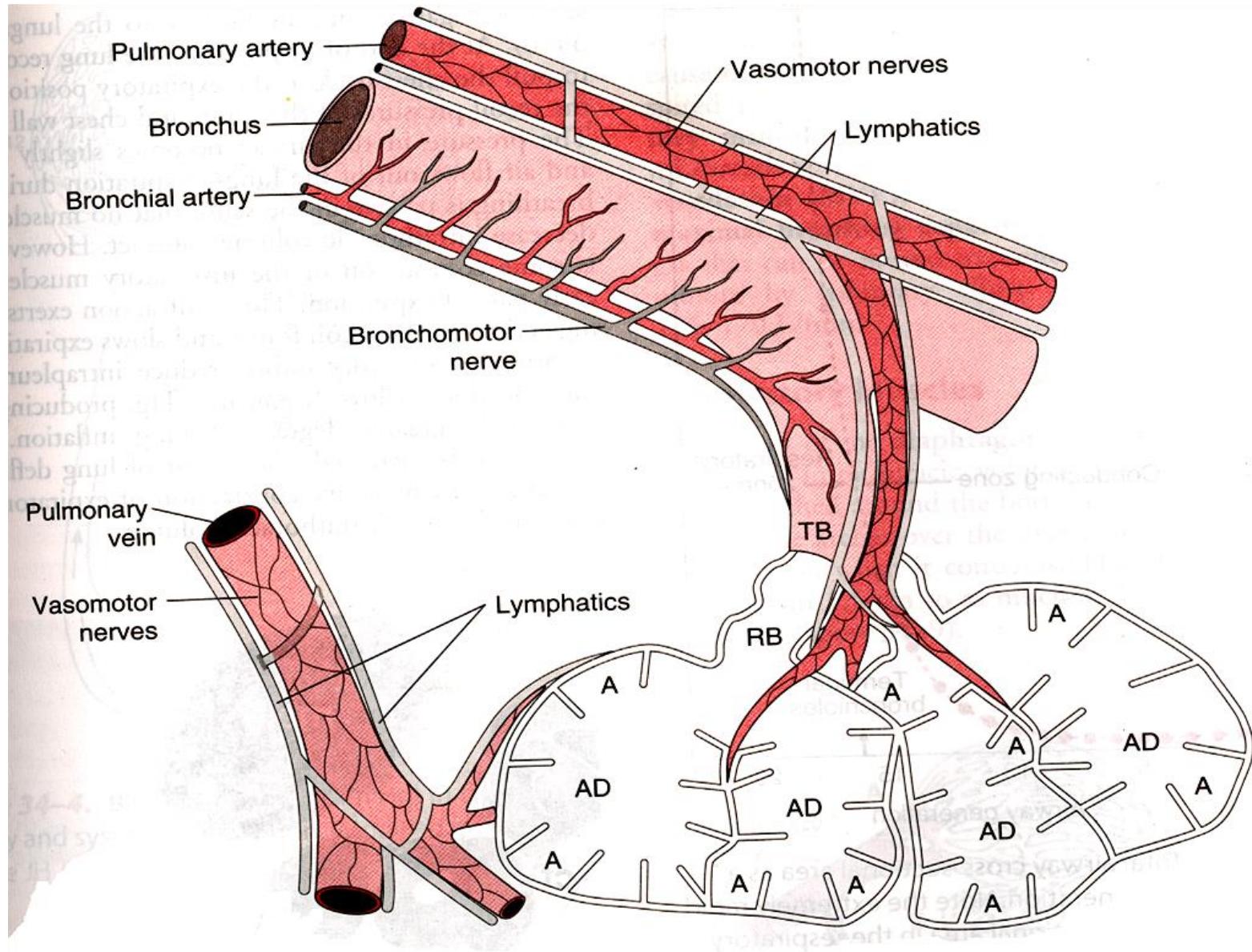


Fig.3a. Structure of the Lung: A, Alveolus; AD, Alveolar Duct;
Respiratory bronchiole; TB, Terminal Bronchiole.

Blood flow through the lung and its distribution

- BF via the lung is essentially equal to CO
 - Factors that control CO regulate pulmonary BF
 - specially the peripheral factors are more important
 - Usually pulmonary vessels are passive, distensible:
 - enlarge with ↑ in pressure and narrow with ↓ in pressure
 - For adequate aeration of the blood to occur, blood should be distributed to the segment of lung where alveoli is best oxygenated.
 - how is this achieved?

ANSWER:

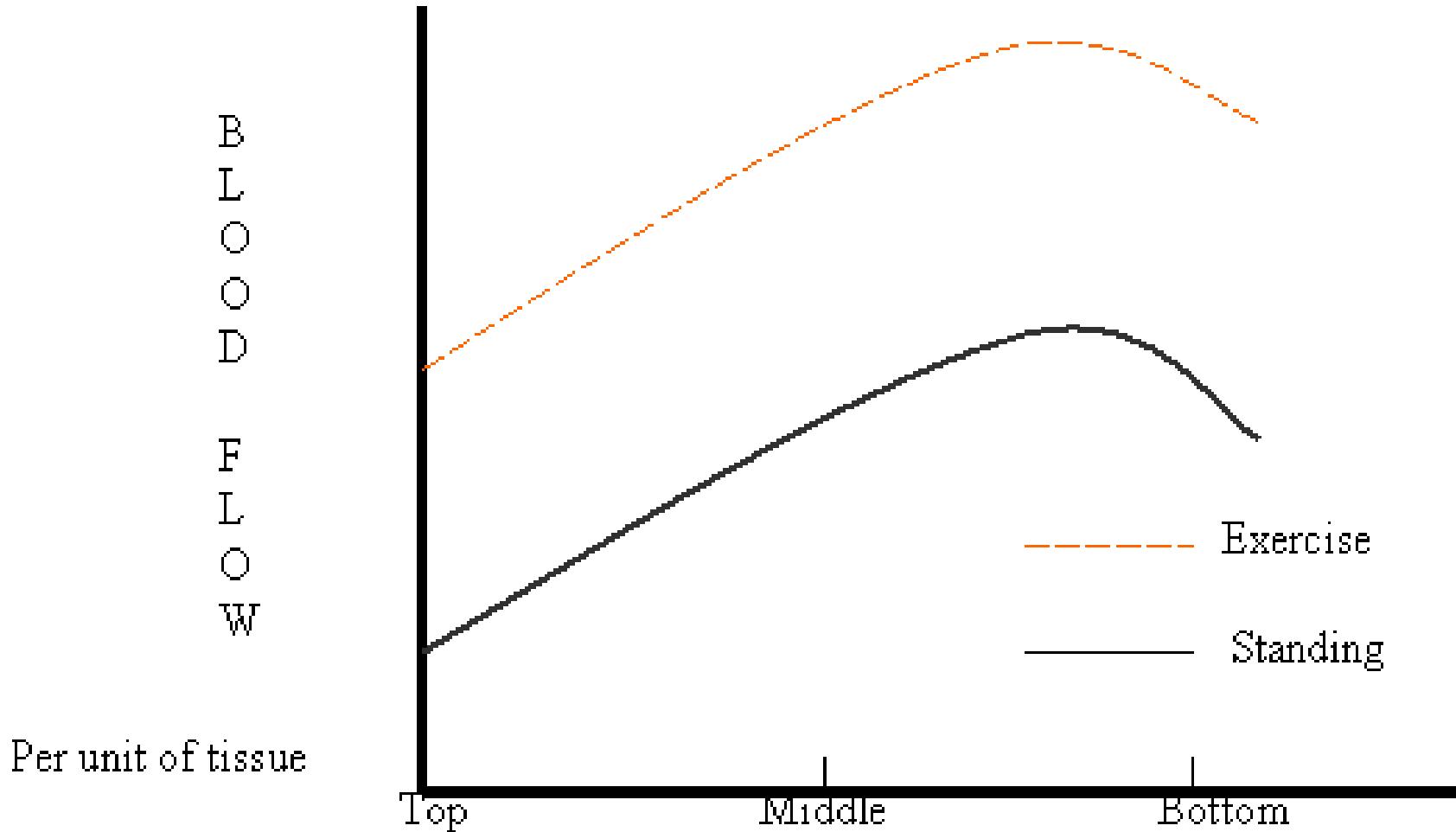
- Blood is redistributed to a well ventilated areas of the lung
 - when alveolar PO_2 falls below 70% normal (<73mmHg),
 - ↓
 - the adjacent blood vessels constrict during the coming 3-10 min
 - **The vascular resistance increases more than 5x at extremely low O₂ levels**
 - This leads to the redistribution of blood in to well-ventilated alveoli
 - ↳ important to correct ventilation-perfusion mismatch
- This effect is opposite to that in systemic vasculatures which dilate in response to low O₂ level

Effect of hydrostatic pressure on regional BF to the lung

- In normal upright adult:
 - The lowest pt in the lung is 30 cm below the highest pt
 - This represents 23mmHg pressure difference
 - 15mmHg is above heart level & 8mmHg below the heart
 - The pulmonary ABP in the top portion of the lung is about 15mmHg < P at heart level, &
 - the P in the base of the lungs is 8mmHg > P at heart level
- At rest, there is lower blood flow in the top of the lung
 - but about 5x these much flow in the bottom of the lungs

Blood flow at different levels in the lung

- differential BF in standing position is due to the effect of gravity which increases the hydrostatic Pressure (0.77mmHg/cm away from Heart level)



Zones of the lung & blood flow

Zone 1 - zone of no BF

- no blood flow during all portion of cardiac cycle
 - Because alveolar air pressure $>$ pulmonary capillary pressure

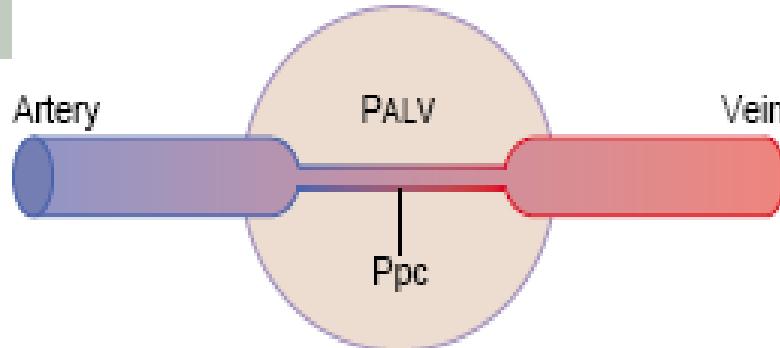
Zone 2 - zone of intermittent systolic blood flow

- because SBP $>$ alveolar air pressure

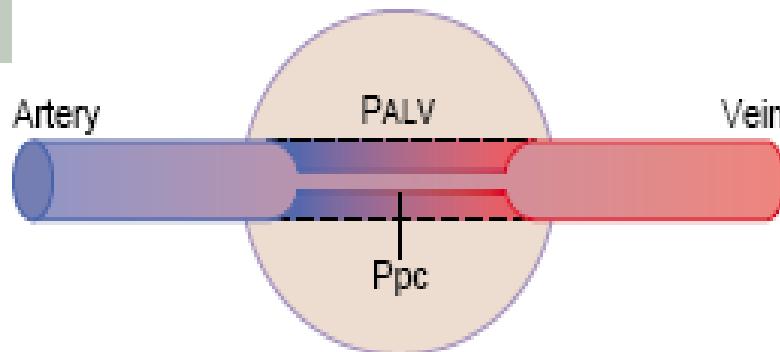
Zone 3 - found in the lower areas of the lung

- zone of continuous blood flow
- because alveolar Ppc (both SBP & DBP) remains greater than the alveolar air pressure
- When alveolar pressure $>$ Ppc \Rightarrow the capillaries close and no BF
- Normally lungs have 2 zones: zone 2 in apex & zone 3 in lower area

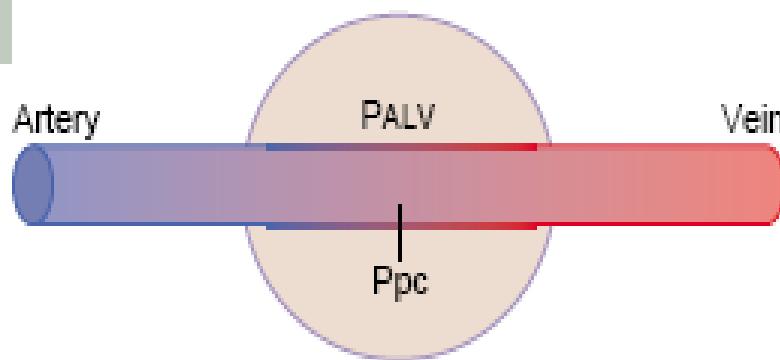
ZONE 1



ZONE 2



ZONE 3



Mechanics of BF in 3 zones of the lung:

zone 1, no flow—alveolar air pressure (PALV) > pulmonary capillary pressure (Ppc);

zone 2, intermittent flow—SBP rises higher than PALV, but DBP falls below PALV; and

zone 3, continuous flow—Ppc remain greater than PALV at all times.

PULMONARY VENTILATION-PERFUSION RATIO

- is expressed as V_A/Q
- in upright position, in the upper part of the lung blood flow decreased more considerably than ventilation



V_A/Q is 2.5x the ideal value (\uparrow physiologic dead space)

- in the bottom of the lung \rightarrow low V_A in relation to Q ,



V_A/Q is 0.6x the ideal value (physiologic shunt that means blood fails to be oxygenated)

When ever $V_A/Q < \text{normal}$, there is inadequate V_A to provide the O₂ needed to fully O₂nate pulmonary blood

The fraction of pulmonary blood not O₂ated is shunted blood

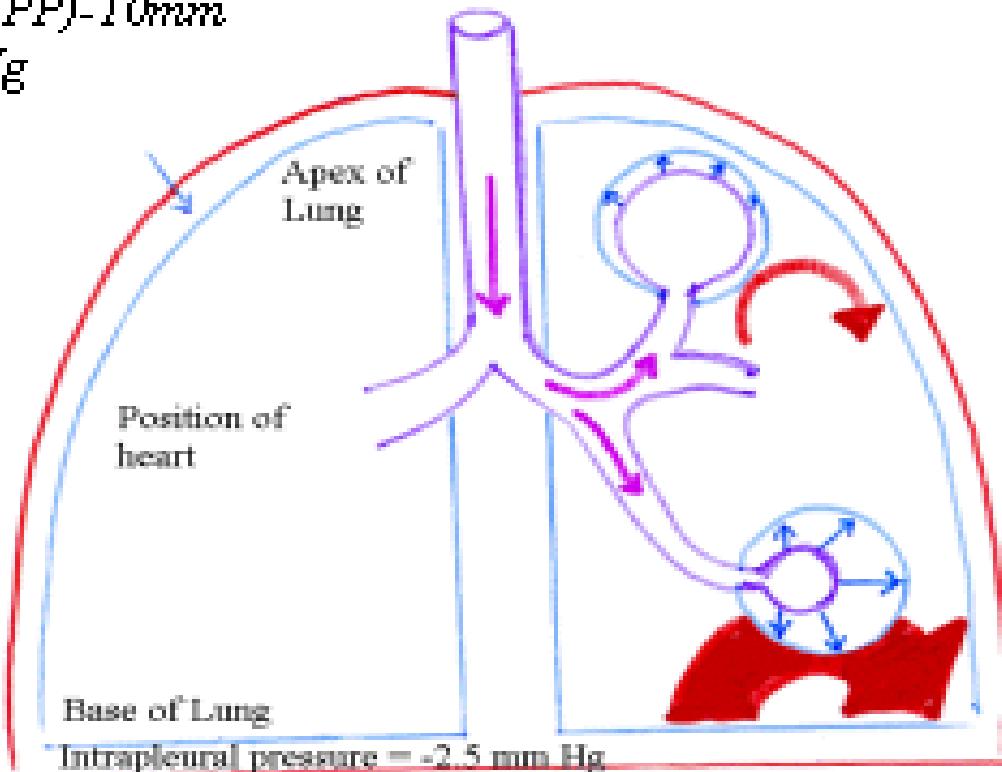
Total amount of shunted blood per minute is **physiologic shunt**

Anatomic (Rt to Lt) Vs Physiologic shunt (pneumonia, ARDS) 33

VENTILATION-PERFUSION RELATIONSHIP IN THE LUNG (V/Q)

Alveoli at base receive greater fraction of total lung ventilation and perfusion

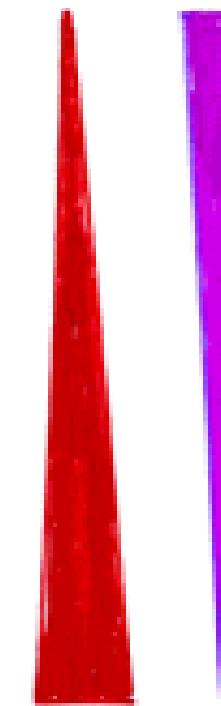
Intrapleural
pressure
(IPP)-10mm
Hg



Gradient of
Ventilation



Gradient of blood flow



Gradient of ventilation
/perfusion

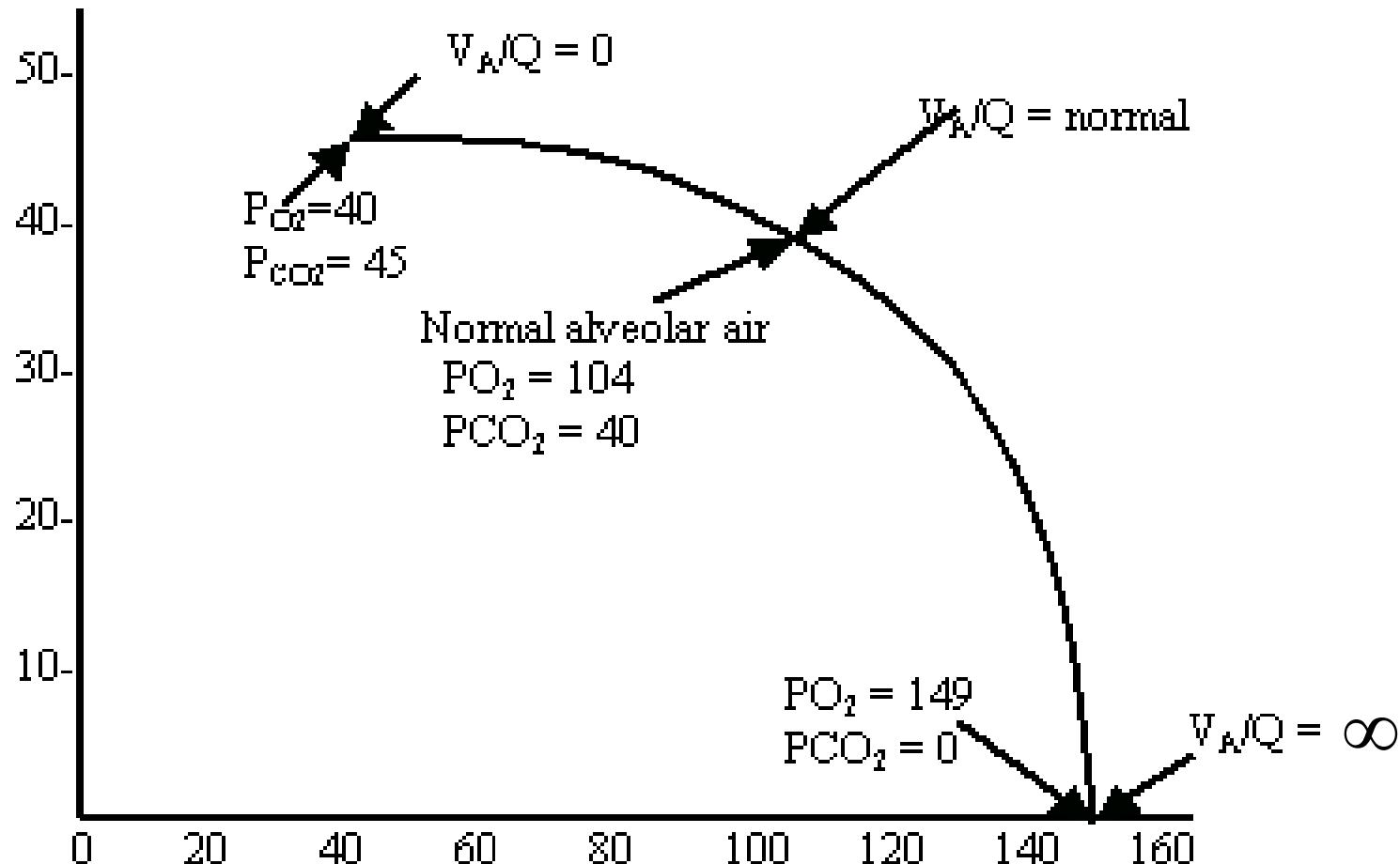
The ratio of V/Q decreases from the apex to base

Effects of V_A/Q mismatch on alveolar PO₂ & PCO₂

- When $V_A/Q = 0$
 - No ventilation
 - The level of O₂ & CO₂ is in equilibrium with blood level
 - PO₂ = 40mmHg & PCO₂ = 45mmHg
 - Because gases diffuse b/n blood & the alveolar air
- When $V_A/Q = \text{normal}$
 - Exchange of O₂ & CO₂ through respiratory membrane is optimum
 - Alveolar PO₂ = 104mmHg & Alveolar PCO₂ = 40mmHg
- When $V_A/Q = \infty$
 - No capillary blood to carry O₂ away or to bring CO₂ to alveoli
 - Alveolar level of gases is in equilibrium with humidified inspired air
 - PO₂ = 149mmHg = PO₂ in inspired humid air
 - PCO₂ = 0 = PCO₂ in inspired humid air

V_A/Q mismatch

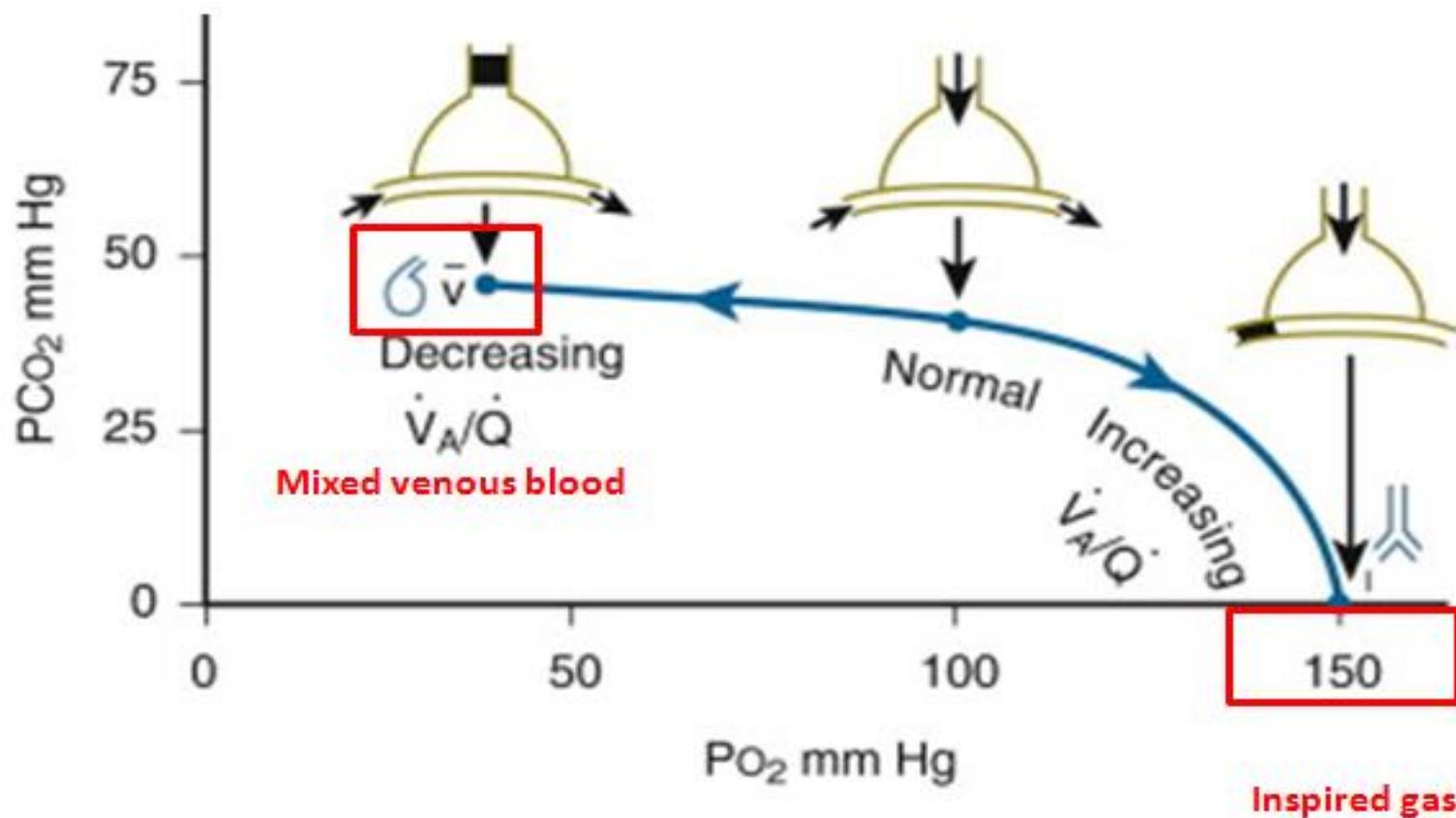
PCO_2



NORMAL PO_2 - PCO_2 , V_A/Q DIAGRAM

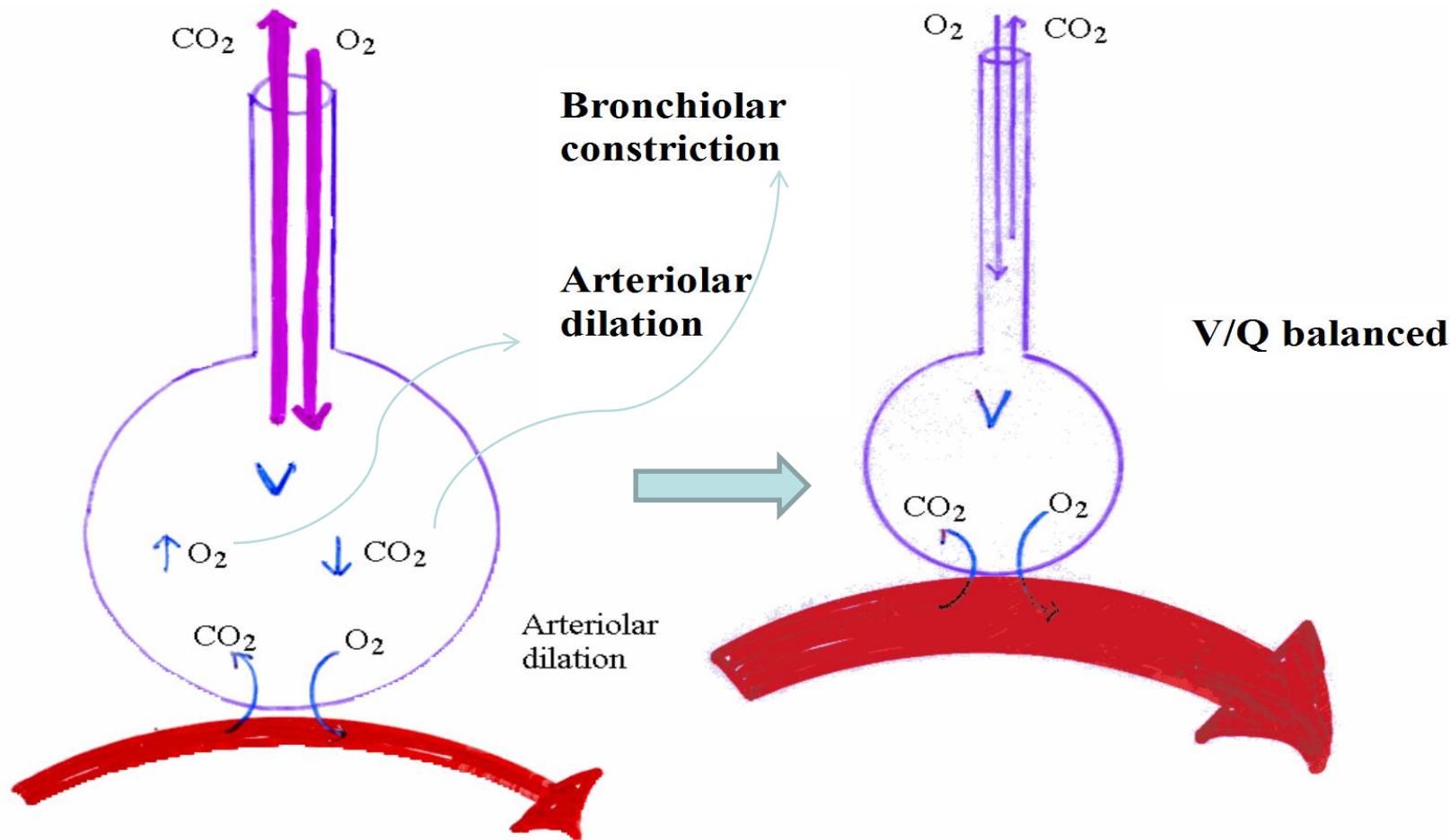
PO_2

- V/Q mismatch refers to imbalance of BF and ventilation.
- Most common cause of hypoxemia in lung disease
- Common causes of hypoxemia due to V/Q mismatch: obstructive lung diseases, pulmonary vascular diseases, and interstitial diseases.

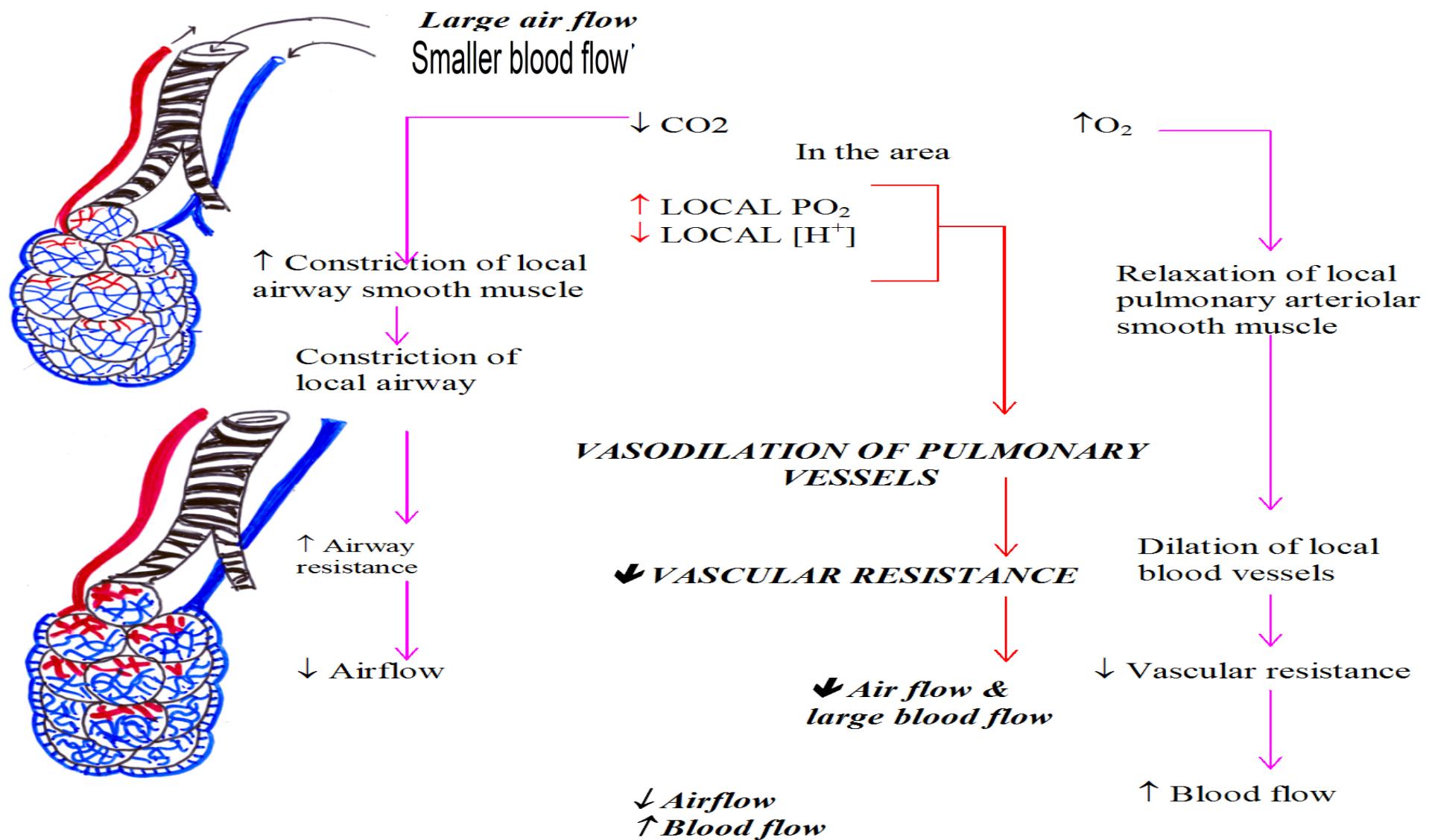


REGULATION OF VENTILATION-PERFUSION MISMATCH

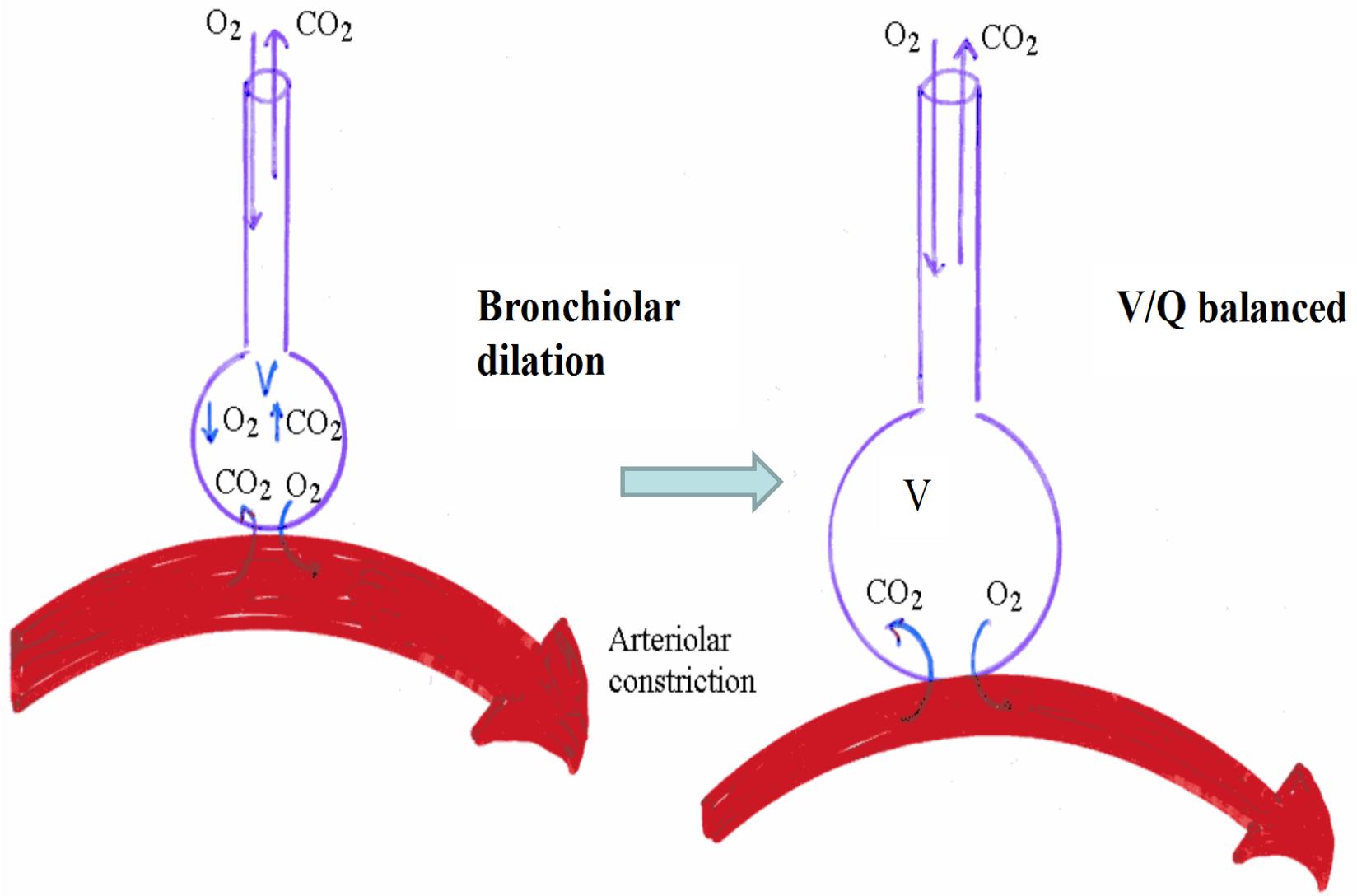
- A. When ventilation overbalances perfusion($V > Q$)



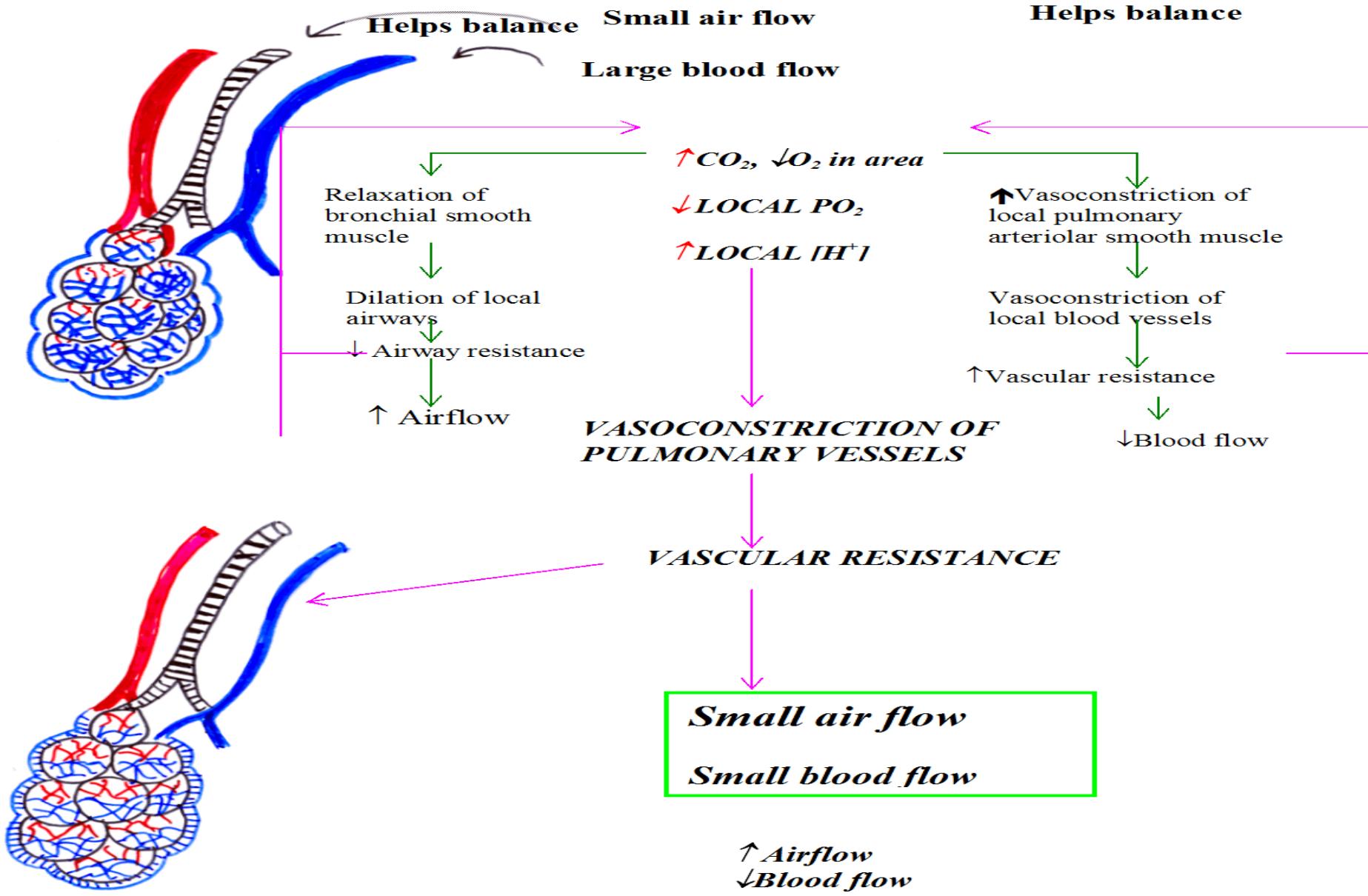
- LOCAL MATCHING OF VENTILLATION AND PERfusion (V>Q)



- B. When Perfusion overbalances ventilation ($Q > V$)

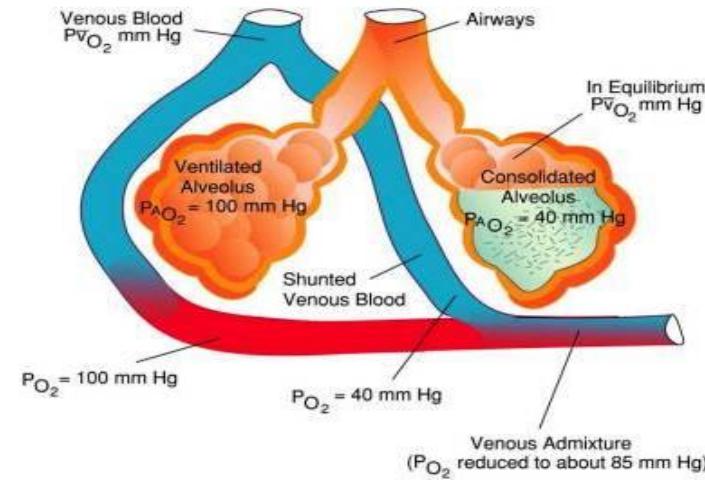
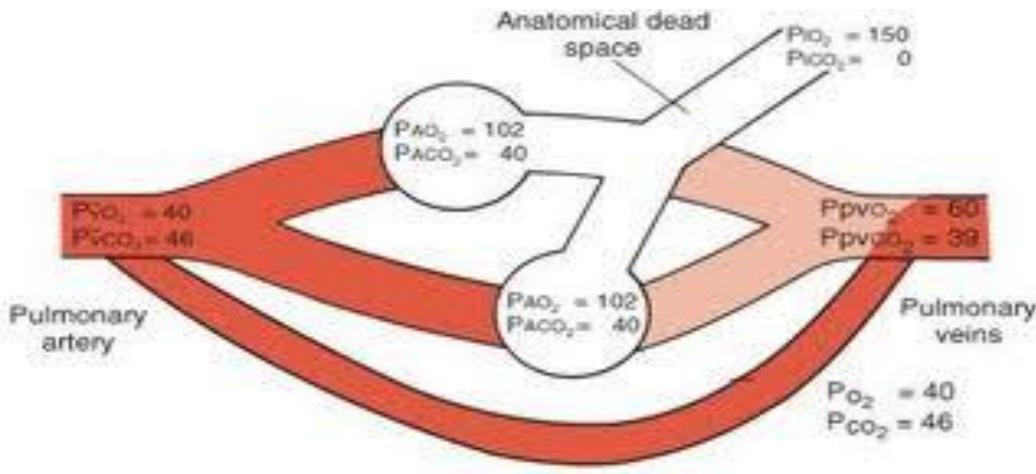


LOCAL MATCHING OF VENTILLATION AND PERFUSION



Right-to-left shunt

- Exists when blood passes from Rt to Lt heart without being oxygenated.
- **Shunt responds poorly to 100% oxygen**
 - **Bypass alveoli, never exposed to higher PAO₂**
- There are two types of right-to-left shunts:
 - **Anatomic shunts exist when the alveoli are bypassed.**
 - Eg: intracardiac shunts, pulmonary AVMs, and hepatopulmonary syndrome.
 - **Physiologic shunts exist when non-ventilated alveoli are perfused.**
 - Eg: atelectasis and diseases with alveolar filling (eg, pneumonia, ARDS).



PULMONARY CAPILARY DYNAMICS

- blood passes in the pul capillaries in ~0.8 sec (\downarrow es to 0.3 sec in high CO)
- Pulmonary vs. Systemic capillary pressure

Pulmonary capillary

1-low pressure; 7mmHg

2-Low interstitial fluid pressure -8mmHg

3-Leaky to protein

4. colloid osmotic pressure of pul interstitial fluid is ~14 mm Hg,

5-pulmonary edema- w/n the pressure rises above 28mmHg

- ✓ (7- 27mmHg = safety factor, controlled by pulmonary lymphatic in chronic cases).
- ✓ If pressure rises above safety factor rapidly, rapid death within hrs (can be in 20-30min)

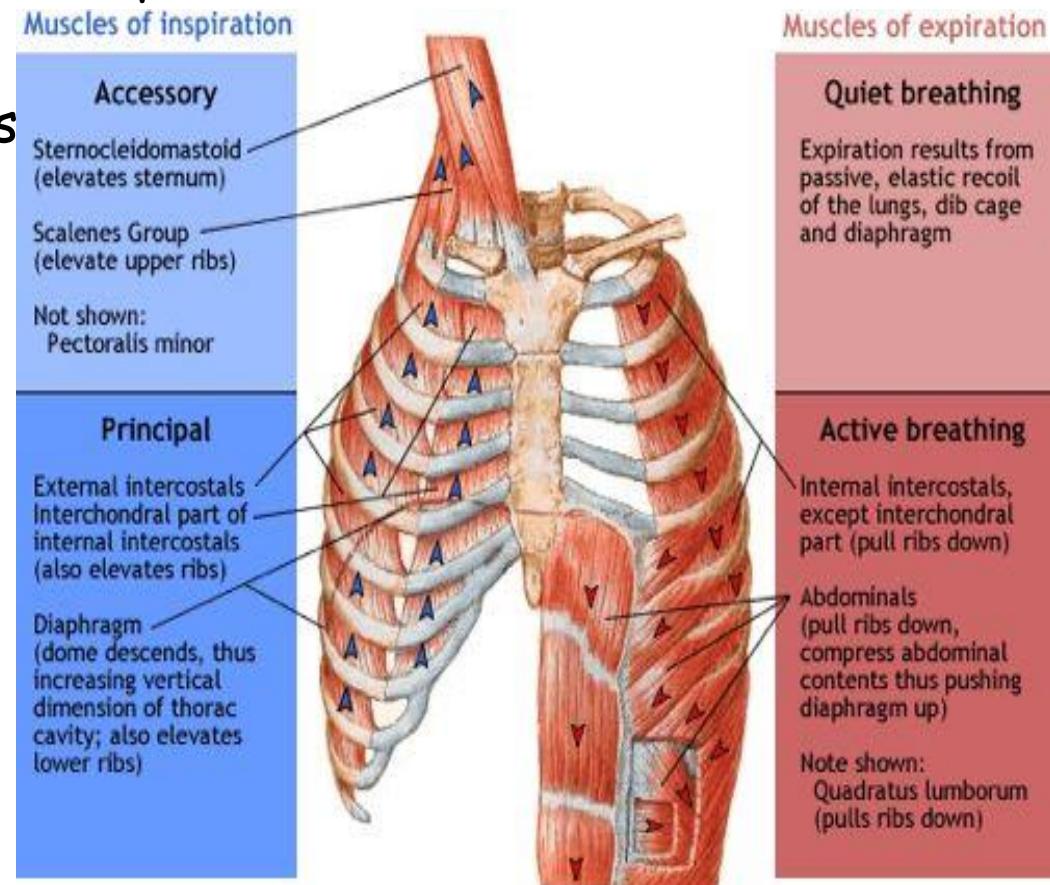
- ❖ Pulmonary hypertension (PH)- elevated pulmonary artery pressure (>25mmHg)
 - results in right heart failure (cor pulmonale).

Mechanics of Pulmonary Ventilation

- Involves inspiration and expiration
- Under the principle of Boyle's law : $P \propto 1/V$, ie: $\uparrow P \Rightarrow \downarrow V$
- Gases diffuse from area of high to low Pressure
- **Inpiration:**
- the most fundamental muscles of inspiration:
 - Diaphragm and
 - external intercostal muscles

The 3 accessory muscles, contract during inspiration:

- a. sternocleidomastoid muscles
 - lift the sternum upward,
- b. Anterior serrati - lift many of the ribs
- c. The scalene - lifts the first two ribs



- Inspiration involves contraction of inspiratory muscles:
 - **Contraction of external intercostal muscles**
 - ↓
 - elevation of ribs & sternum
 - Ribs and sternum move outward & upward
 - ↓
 - increased front- to-back dimension of thoracic cavity
 - ↓
 - lowers air pressure in lungs → air moves from atm into lungs.

- Contraction of diaphragm → diaphragm moves downward
 - → increases vertical dimension of thoracic cavity
 - ↓ ↓
 - lowers air pressure in lungs
 - ↓
 - air moves from atmosphere into the lungs
- There is also contraction of accessory inspiratory muscles
 - Augment the effects of fundamental inspiratory muscles

NB:

- ❖ Diaphragm: innervated by Phrenic nerves arising from C3-5
- ❖ Intercostals: innervated by intercostal nerves from thoracic segments

Active



Nerve impulse



Contraction of:

-diaphragm

-external

intercostals

-accessory muscles

Contraction of Diaphragm



↑Vertical dimension of thorax by its descent (1.5 cm up to 7cm)



Contributes 70% of TV

Contraction of External intercostals



↑A-P dimension of thorax



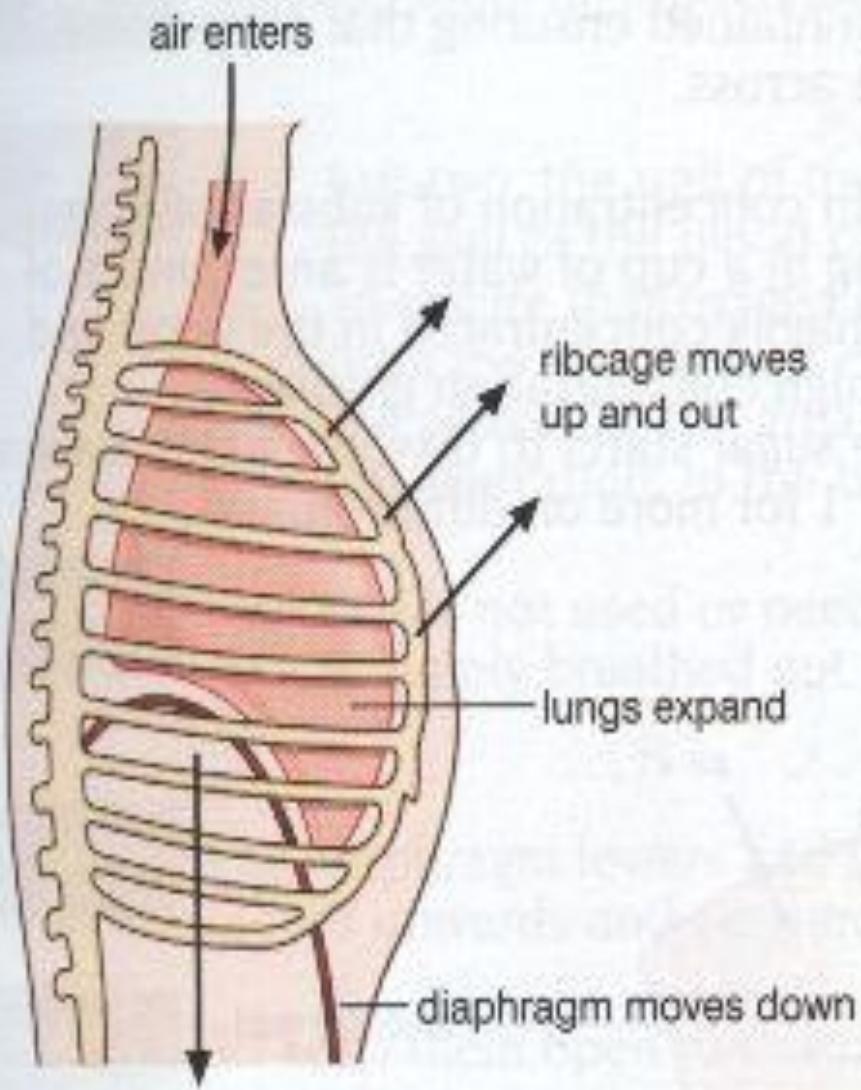
Contributes 30% of TV

Accessory muscles are involved when $TV > 800$ ml/breath during inspiration

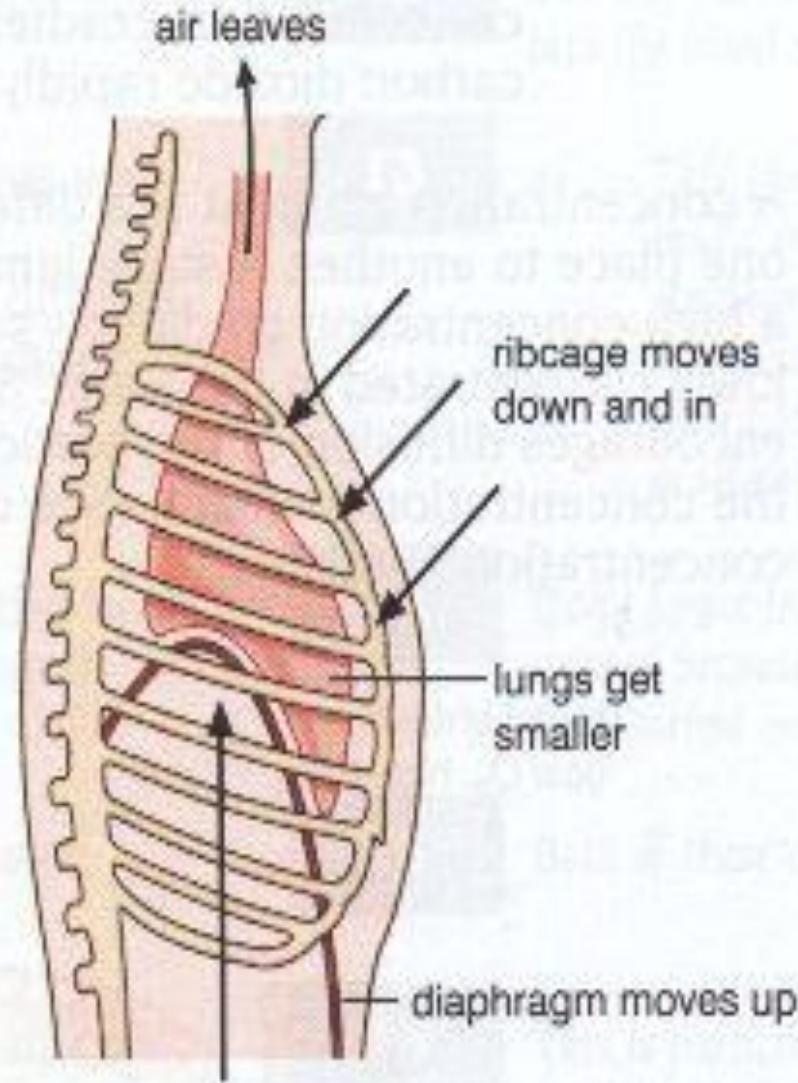
Expiration:

- Expiratory muscles are abdominal & internal intercostal muscles
 - **Abdominal muscles-the most important muscles of expiration**
 - ↓ ↓
 - their contractions push the abdominal contents upward against bottom of diaphragm
 - ↓
 - diaphragm relax (move upward)
 - ↓
 - ↓ the volume of thoracic cavity (\uparrow pressure in lungs)
 - ↓
 - air is exhaled

- contraction of internal intercostal muscles
 - return ribs, & sternum to resting position
 - restores thoracic cavity to pre-inspiratory volume
→ ↑ pressure in lungs → air is exhaled
- The muscles of expiration are come into action during forced expiration
 - Eg. During blowing out, coughing, straining during defecation, exercise etc



Inhalation



Exhalation

Movement of Air In and Out of the Lungs in respiratory cycle

- Caused by the changes in pressures of the lung & atm
 - The lung is an elastic structure
- The lung "floats" in the thoracic cavity,
 - surrounded by a thin layer of *pleural fluid* (10-20ml)
 - fluid in the thin space b/n the lung pleura and the chest wall pleura
 - Fluid in the space b/n visceral pleura & parietal pleura
 - the fluid lubricates movement of the lungs within the cavity
- .

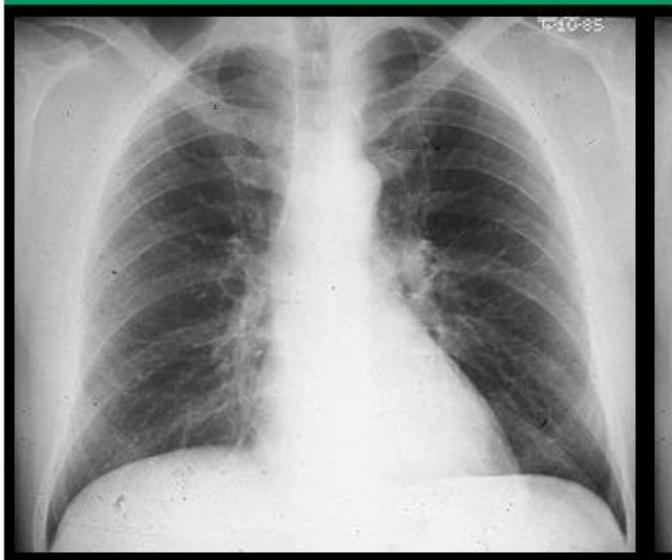
Units of Pressure

- **1 atm = 760mm Hg**
- In respiratory physiology, Pressure is usually given in cm H₂O.
 - ❖ 1 cm H₂O = 0.74 mm Hg
 - ❖ (1 mm Hg = 1.36 cm H₂O)
- **Intrapleural Pressure (Pip)**
- Represents the pressure in the thin film of fluid between the lung and the chest wall.
 - Subatm pressures (-) act as a force to expand the lung, and
 - positive pressures (+) act as a force to collapse the lung.

- During normal restful breathing, Pip is always subatm (-)
 - thus acts as a force to expand the lung.
- The normal values of Pip in quiet breathing:
 - During inspiration : about -6mm Hg ($760 - 6 = 754$ mm Hg)
 - Required to hold the lung and airways open
 - During expiration: about -3mm Hg ($760 - 3 = 757$ mm Hg)

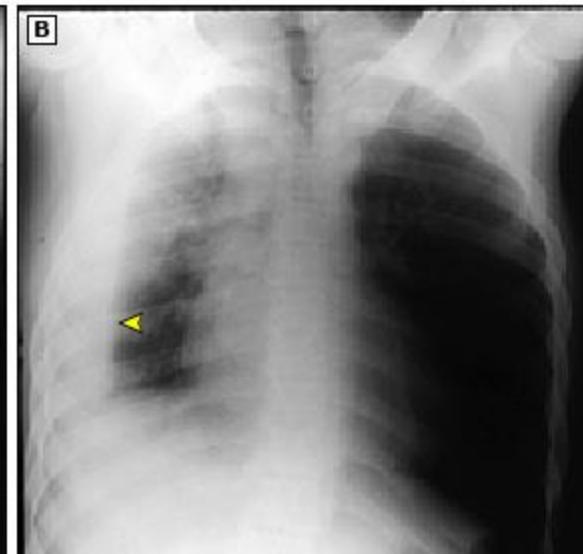
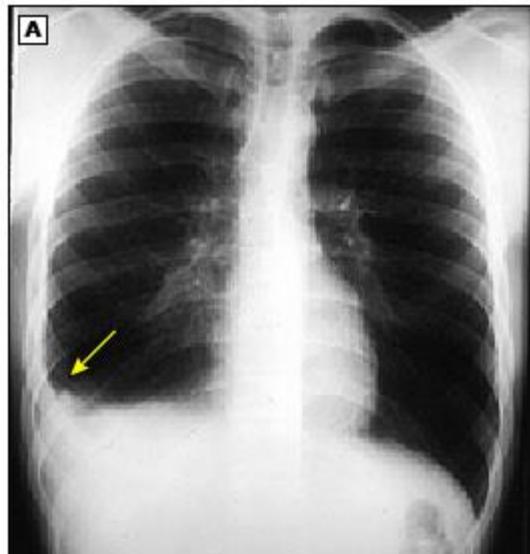
- **Significance of Pip:**
 - Prevents lung collapse
 - Dilates large veins & vena cava
 - because of the -ve pressure in the thoracic region
 - Acts like suction pump to pull the venous blood from lower parts of the body towards the heart against gravity
 - **Thus, Pip is responsible for VR or respiratory pump for VR**
- Pip is Positive in Valsalva maneuver, Pathologic conditions :
 - Air or fluid in the pleural cavity will increase Pip
 - **Pneumothorax**- when air accumulates in the pleural cavity
 - **Hydrothorax**- when water accumulates in the pleural cavity
 - **Haemothorax** - when blood accumulates
 - **Pyothorax**- when pus accumulates in the cavity (empyema)

Normal chest radiograph



Posteroanterior view of a normal chest radiograph.

Courtesy of Carol M Black, MD.



Panel A shows blunting of the right costophrenic sulcus (arrow) on an upright CXR due to the presence of a pleural effusion. Panel B shows a right lateral decubitus CXR from the same patient, and reveals layering of pleural effusion (arrowhead).

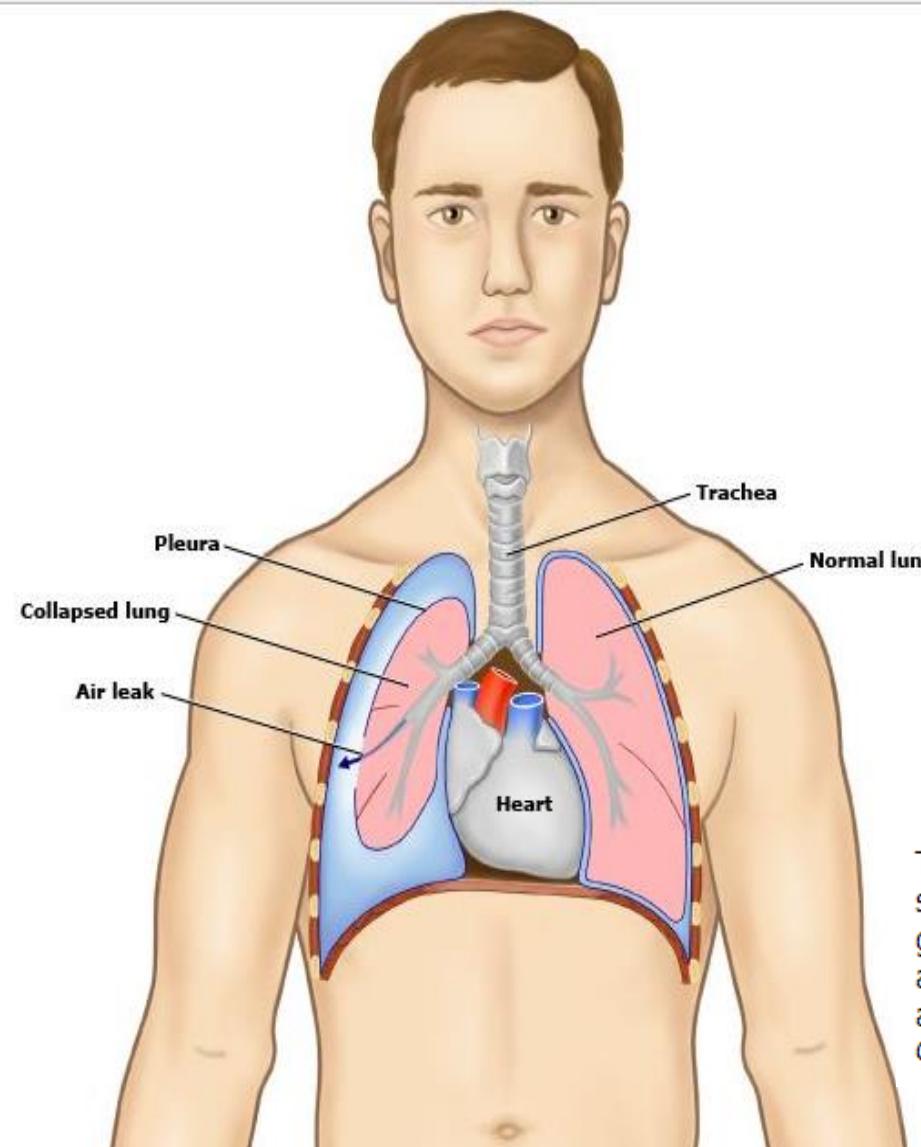
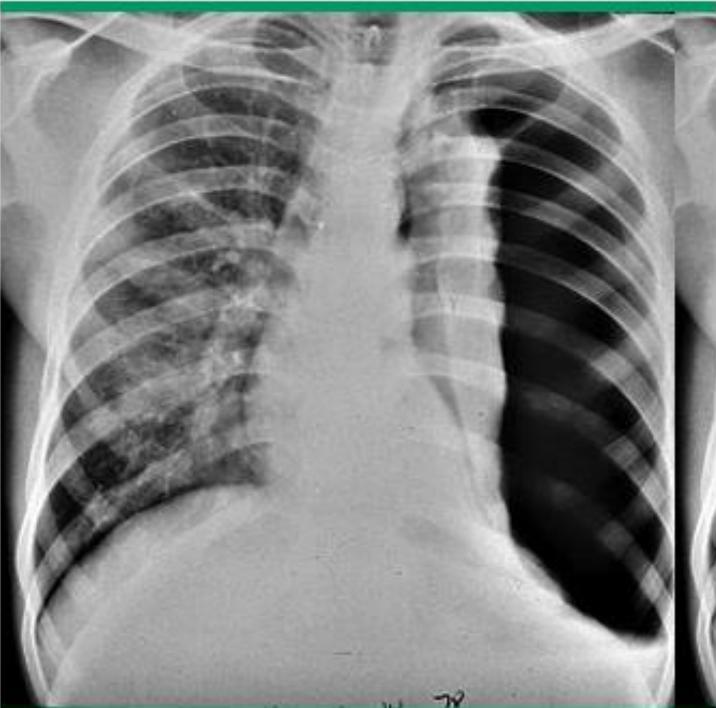
Hepatic hydrothorax



Large right sided pleural effusion forming typical meniscoid arc (arrow) in patient with advanced liver cirrhosis.

Courtesy of Paul Stark, MD.

Chest radiograph of a tension pneumothorax



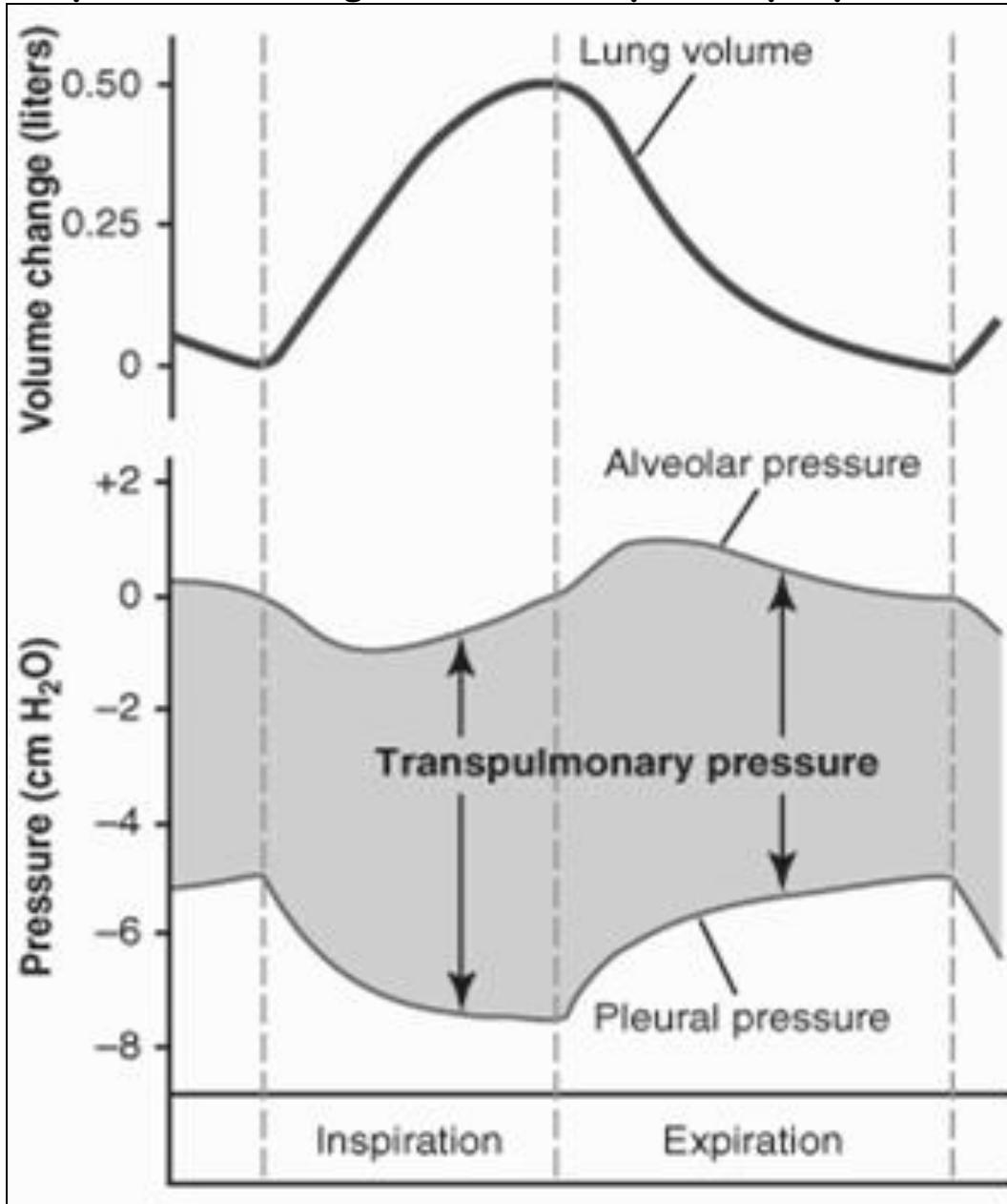
Tension pneumothorax due to extensive tuberculosis in the subjacent left lung. Chest radiograph shows a large collection of gas in the left hemithorax with inversion of the left hemidiaphragm and cardiomedastinal shift to the right. The left intercostal spaces are wider than the right ones.
Courtesy of Paul Stark, MD.

The lungs sit in the chest, inside the ribcage. They are covered with a thin membrane called the "pleura." The windpipe (or trachea) branches into smaller airways. In this drawing, 1 lung is normal, and 1 has collapsed because air has leaked out of it. The air that has leaked out of the lung (shown in blue) has filled the space outside of the lung.

Alveolar and pleural pressure changes in the Respiratory Cycle

- 1. During inspiration, alveolar pressure < atm pressure
- 2. During expiration, alveolar pressure > atm pressure
- 3. At the end of inspiration & expiration, alveolar P = atm P
 - because alveoli are in direct communication with atm
 - air flows down its pressure gradient until the two pressures equilibrate
- 4. Through out the respiratory cycle:
 - the pleural pressure < alveolar pressure \Rightarrow to prevent lung collapse
 - If pleural p > atm P \Rightarrow the lung collapses to a lesser or greater extent
 - b/c of the P exerted on the exterior surface of the lung

pressure changes in the Respiratory Cycle

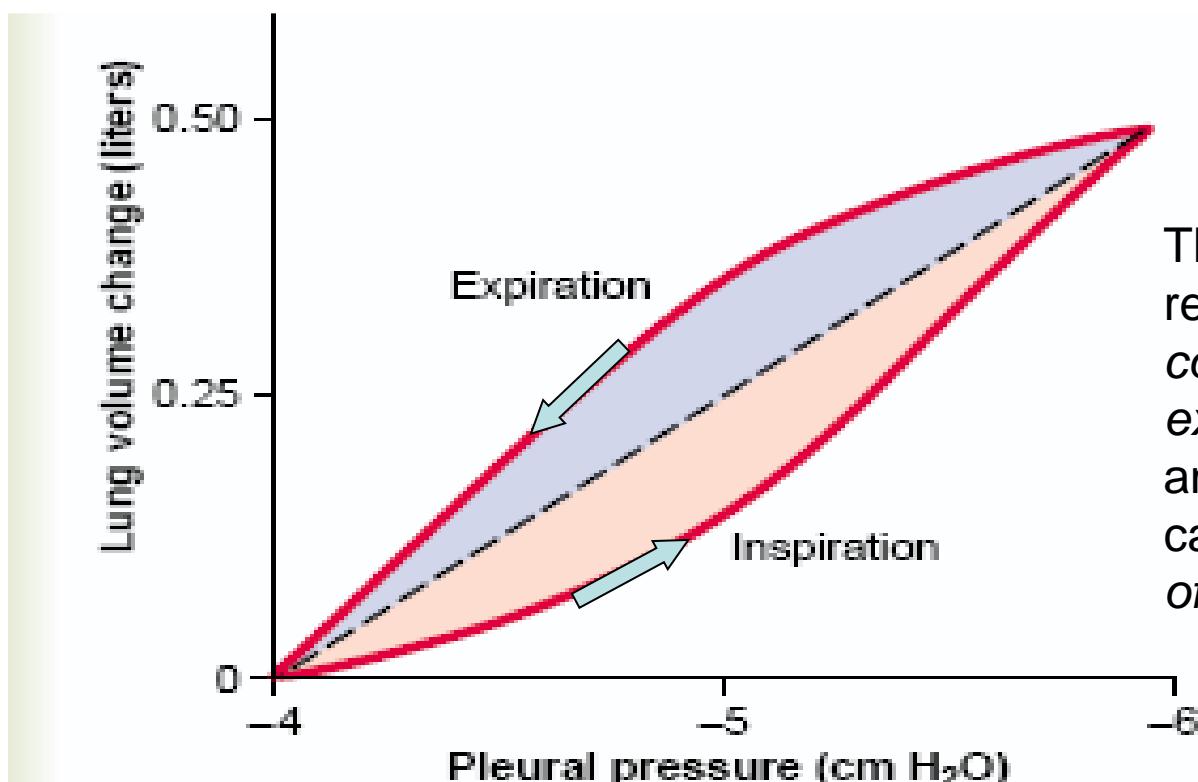


Lung Compliance

- The **ease** with which the lungs distend
- **Stretchability** of the lung tissue and chest wall
- The extent to which the lungs can expand for each unit increase in transpulmonary pressure (if enough time is allowed)
 - transpulmonary pressure is the difference b/n P_{ALV} & P_{ip}
- is the change in lung volume (tidal volume) divided by the change in surrounding pressure.
- This is stated in the following formula:

$$\text{Compliance} = \Delta V / \Delta P$$

- Total compliance of the two lungs in normal adult is about 200ml of air per a cm of H₂O transpulmonary pressure
 - Every time the Ptp increases 1cm H₂O, the lung volume, after 10 to 20 sec, will expand 200ml



The two curves are called, respectively, the *inspiratory compliance curve* and the *expiratory compliance curve*, and the entire diagram is called the *compliance diagram of the lungs*.

- Problem, If:
 - Tidal volume = 0.6 liters
 - Intrapleural pressure before inspiration = -5 cm H₂O
 - Intrapleural pressure after inspiration = -8 cm H₂O
 - Lung compliance = $0.6\text{L}/3\text{cm H}_2\text{O} = 0.200 \text{ liters/cm H}_2\text{O}$
- This simply means that for every 1 cm H₂O surrounding pressure changes, 200 ml of air flows in or out of the respiratory system.
- It flows into the system if surrounding pressure becomes more negative
 - (e.g., -5 to -6 cm H₂O) or
- out of the system if surrounding pressure becomes more positive
 - (e.g., -5 to -4 cm H₂O).

- Increased compliance



- means more air will flow for a given change in pressure.

- Eg. emphysema

- With emphysema, it is easier to inhale, as there is less resistance, but it is harder to exhale.

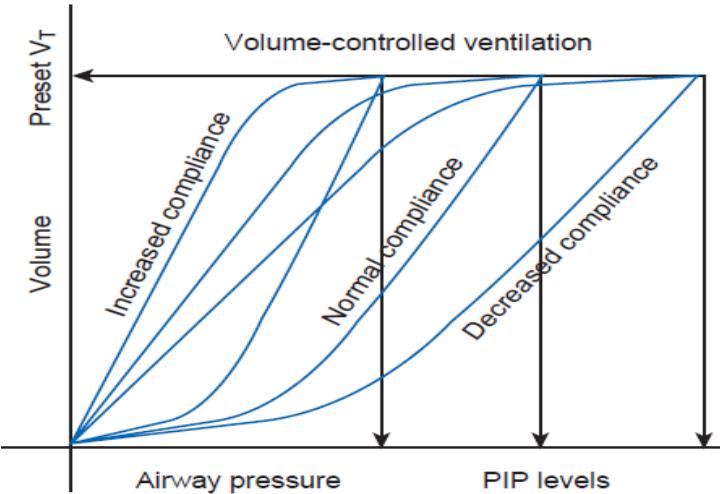
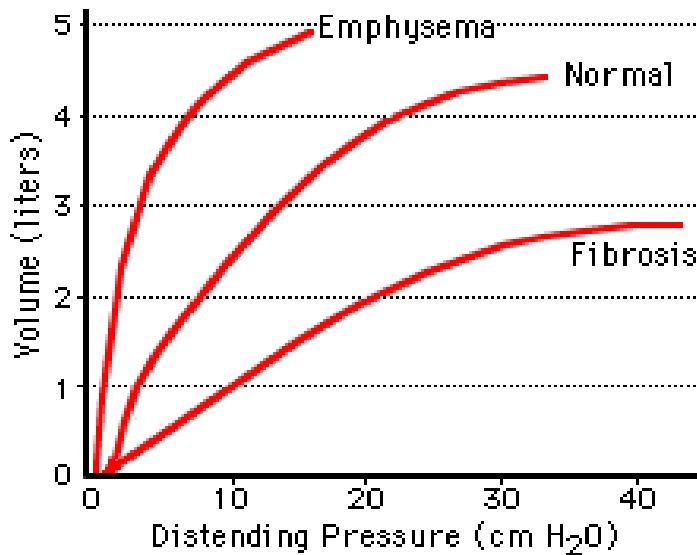
- Reduced compliance



- means less air will flow for a given change in pressure.

- Eg. Pulmonary Fibrosis (a formation of excess tissue that inhibits stretch);

- Ca, Tb, Asbestosis, Silicosis, Pulmonary edema, Kyphosis...



Reading Assignment

What are forces that determine the compliance characteristics of the lungs?

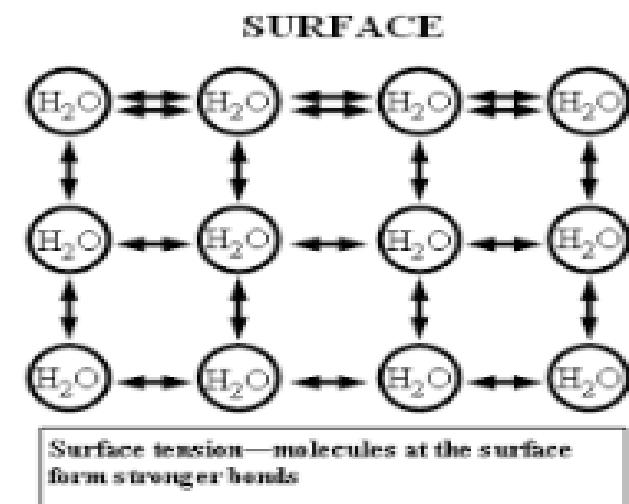
Compare compliance of saline filled Vs air filled lungs

Surface tension of water molecules and Surfactant

- Surface tension of water molecules
 - Water molecule in interface with air have strong attraction for one another.
 - Hence there is a tight contractile membrane of water molecules around the surface in a droplet

• Surface tension in alveoli

- is created by water molecules surrounding the wall of alveoli.



- Adjacent water molecules cause attractive forces that are much more stronger than those b/n liquid and gas

$$\text{pressure} = \frac{(2 \times \text{surface tension})}{\text{radius}}$$

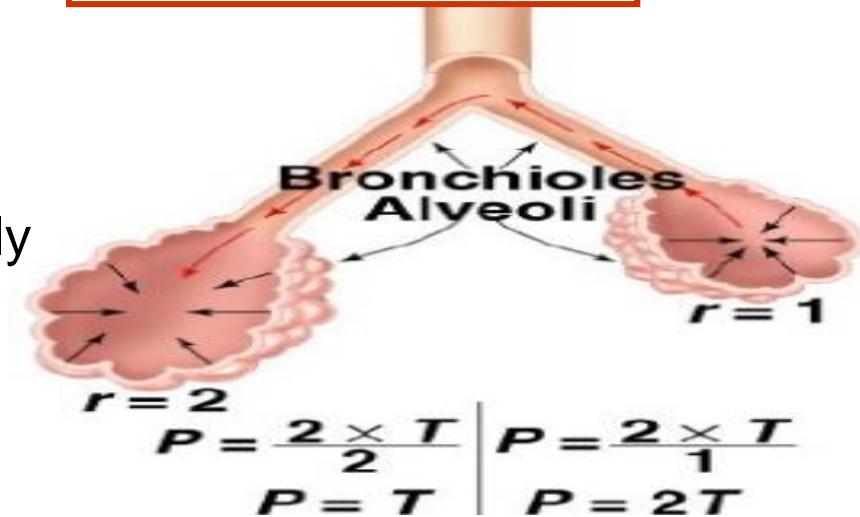
The collapse pressure created can be predicted by **law of La Place**:

➤ The pressure to collapse alveoli is directly proportional to surface tension and inversely proportional to radius

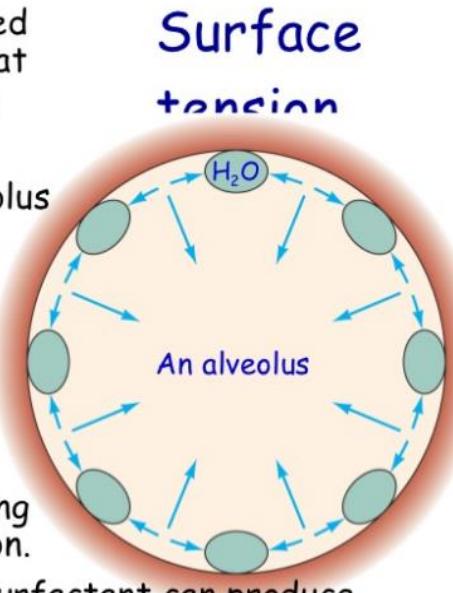
➤ **The higher the surface tension, the more pressure required to inflate (less pressure to collapse)**

➤ the Smaller the radius of alveoli the higher the collapse pressure

✓ Eg. premature babies have risk of **RDS**



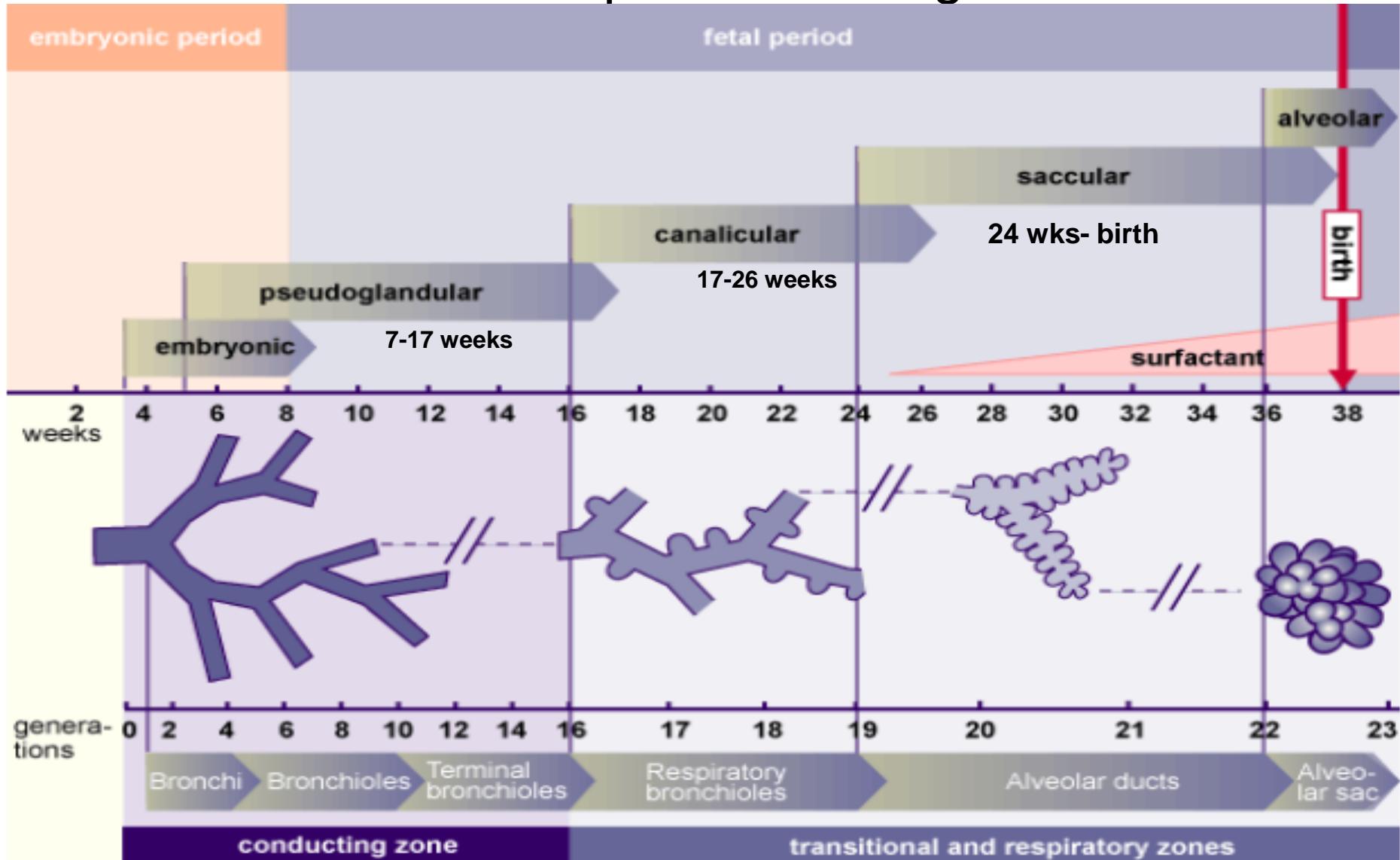
- This tension is determined by the thin liquid film that lines the outside of each alveolus.
- This film allows the alveolus to resist expansion.
- This film also squeezes the alveolus, producing recoil.
- A coating of pulmonary surfactant prevents the alveoli from collapsing from this surface tension.
- Insufficient pulmonary surfactant can produce newborn respiratory distress syndrome.



Surfactant and Its Effect on Surface Tension

- Surfactant - a substance that greatly reduces the surface tension of water \Rightarrow prevent lung collapse.
increases pulmonary compliance
- Secreted by special surfactant-secreting epithelial cells
 - Such cells are type II alveolar epithelial cells/peumocytes
- is a complex mixture of several phospholipids, proteins, & ions
 - The most important components are:
 - phospholipid: dipalmitoylphosphatidylcholine
 - » is most responsible for the action
 - surfactant apoprotein, & Ca^{++}

Development of Lung



Respiratory Distress Syndrome (RDS)

- also called hyaline membrane disease

- A deficiency of surfactant in premature infants.
 - Infants born before their surfactant is fully functional
- The fetus makes respiratory movement in utero
 - But the lungs remain collapsed until birth
- The infant makes strong inspiratory movement just after birth
 - ↓
 - The lungs expand
 - ↗ The surfactant keeps them from collapse again
- Lung washings from infants with RDS have a very high surface tension
- Premature birth & maternal diabetes are among risk factors.

- **Clinical manifestations**
 - **Respiratory distress: Grunting, flaring, retraction, tachypnea**
 - **Cyanosis**
 - **Auscultation:- markedly decreased air entry bilaterally**
- **Onset of recovery is at 72 hrs.**

- **Risk factors:**
 - Low gestational age,
 - Low birth weight,
 - Maternal diabetes,
 - Perinatal asphyxia,
 - Elective caesarian section
- Mostly occur in babies born before 37 weeks of gestation.
- Incidence is inversely related to gestational age and birth weight.
- Uncommon in full term babies.
- The incidence based on gestational age is as follows:
 - Less than 28 weeks 60 – 80%,
 - 32-36 weeks 15-35% in
 - >37 weeks 5%.

• Prevention

- Prevention of preterm delivery
- Antenatal corticosteroids (at least 24-48hrs before delivery) given to pregnant women < 34wks of GA

• Management

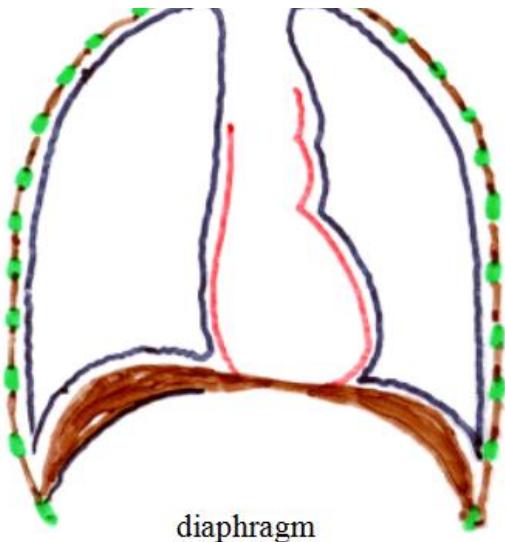
- Nasal CPAP with continuous monitoring
- Fluid and metabolic management
- **Surfactant administration**

• Complication and Prognosis

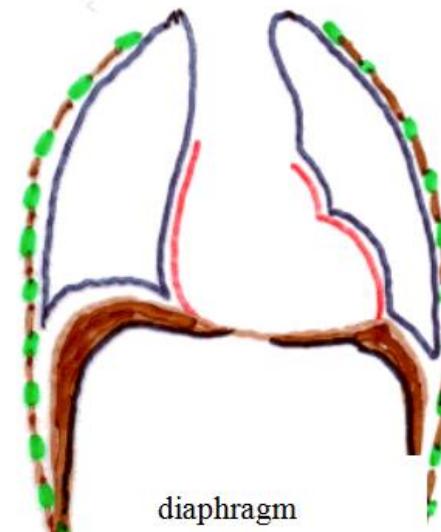
- Air leaks (pneumothorax, pneumomediastinum)
- Intracranial bleeding, pulmonary hemorrhage
- Bronchopulmonary dysplasia
- Retinopathy of prematurity

WORK OF BREATHING - work done to cause inspiration

INSPIRATION



EXPIRATION



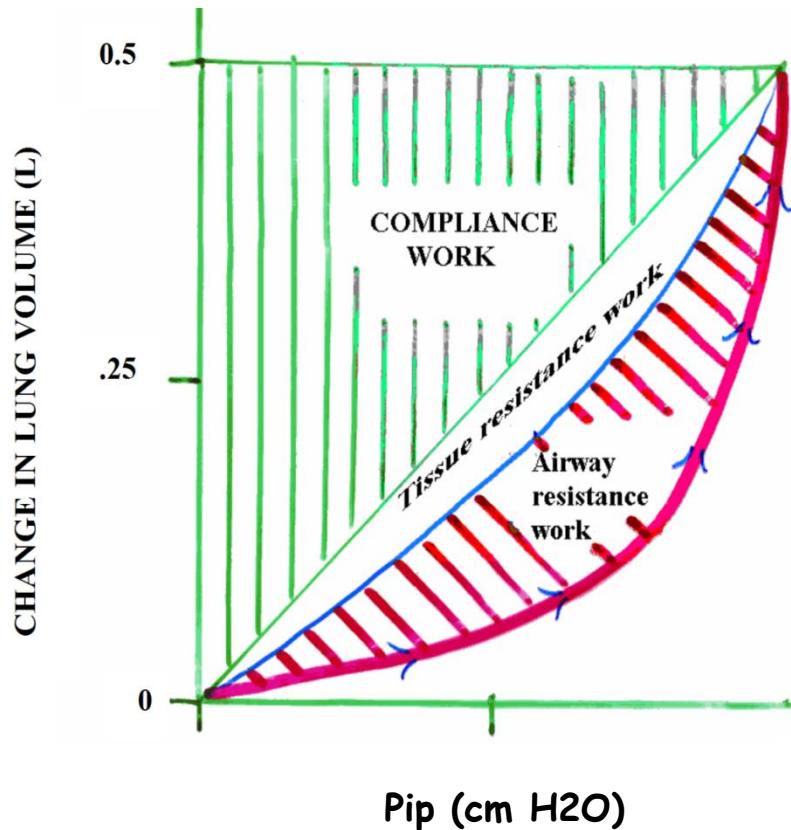
Thorax and lungs in maximal inspiration and expiration

During normal quiet breathing

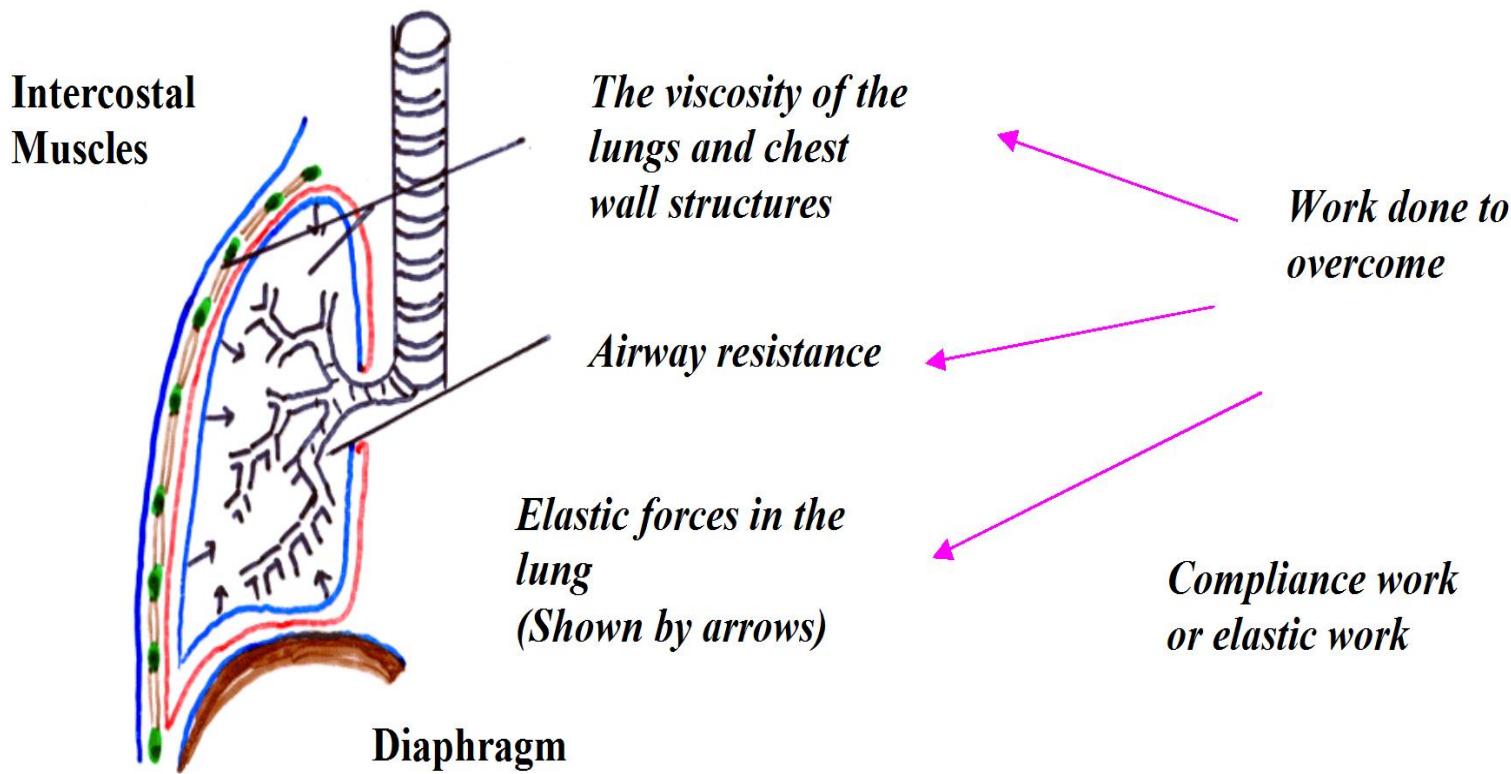
Respiratory muscles contract during inspiration
- Muscles perform ‘work’ to cause inspiration

Expiration is a passive process caused by elastic recoil of the lungs and chest wall structures.
- Muscles do not ‘work’ to cause expiration

- The 3 different types of work done during inspiration:
- 1. compliance work
 - to expand the lung against the lung & chest elastic forces
 - 65% of total work of quiet breathing
- 2. airway resistance work
 - to overcome airway resistance to move air into the lungs
 - 28% of total work of quiet breathing
- 3. tissue resistance work
 - to overcome the viscosity of lung & chest wall structure
 - 7% of total work of quiet breathing



The “work” inspiration: 3 types of work



- ✓ During quiet respiration ➔ energy requirement for pulmonary ventilation is 3 to 5% of the total energy expended by the body
- ✓ During heavy exercise ➔ it can increase as much as 50-fold, especially if the person has ↑ airway resistance or ↓ pulmonary compliance.

- During normal quiet breathing most of the work done by the muscles is used to expand the lungs against the elastic forces.
- During heavy breathing :
 - when air flows in the respiratory passage ways at high velocity,
 ↓
 - most of the work is used to overcome airway resistance.
- In pulmonary diseases the breathing work is increased:
 - In obstructive airways disease, airway resistance work is increased
 - In pulmonary fibrosis, compliance work is increased.

Lung Volumes and capacities: - measured by Spirometer

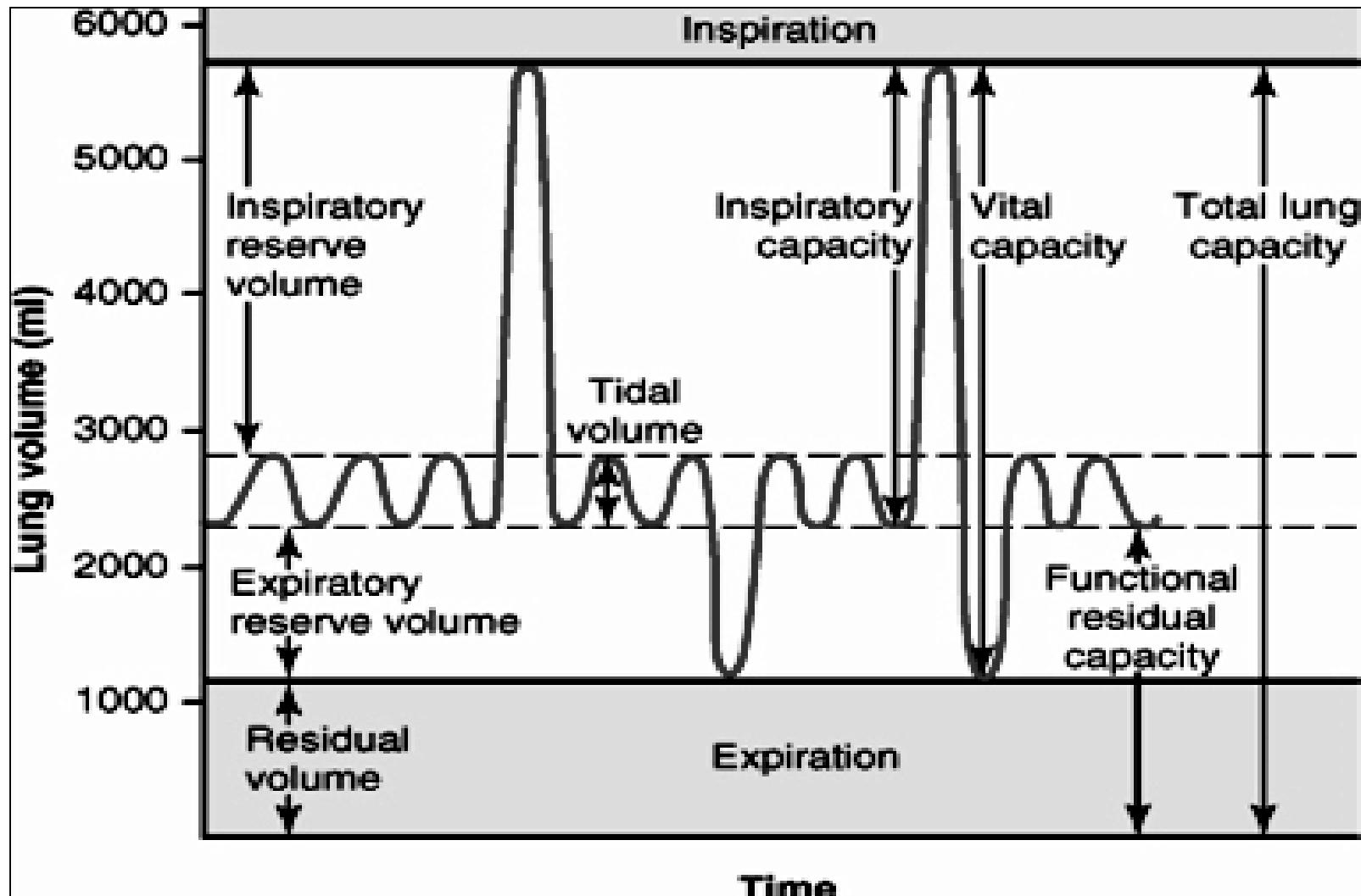
- The tracing is spirogram, the method is spirometry
- Lung volume - amount of air inspired or expired,
 - it is single entity
- lung capacity -is the Σ of two or more lung volumes
- There are four pulmonary lung volumes:
 - when added together = the maximum V of air the lung can hold

- There are four pulmonary lung volumes:
 - Tidal Volume (TV) = 500ml
 - the V of air inspired or expired during quiet breathing
 - Inspiratory reserve volume (IRV) = 3000ml
 - The V of air a person can inspire above TV
 - Expiratory reserve volume (ERV) = 1100ml
 - the V of air that a person can exhale below TV
 - Residual volume (RV) = 1200ml
 - the V of air left in the lung after max expiratory effort
- ❖ when added together = the maximum V of air in the lung

Pulmonary Capacities - 4 types

- The inspiratory capacity, IC
 - V of air a person can inspire above the resting expiratory volume
 - $IC = TV + IRV$ & is about 3500ml
- The functional residual capacity, FRC
 - the V of air that remains in the lungs at the end of normal expiration
 - $FRC = ERV + RV$ & is about 2300 ml
- The vital capacity , VC
 - the max V of air a person can expire after deep inspiration
 - $VC = IRV + TV + ERV$ & is about 4,500ml
- The total lung capacity, TLC
 - max V of air the lungs can hold with the greatest possible effort
 - $TLC = VC + RV \Rightarrow TLC = IRV + TV + ERV + RV$ & is about 5800 ml

Lung volumes and capacities



- All lung volumes & capacities are:
 - 20-25% less in women than men
 - higher in large and athletic than small people

Measurement of lung volumes.

- Most are measured with spirometer
 - Subject sits and breathes into and out of the spirometer displacing a bell.
 - Volume displaced are recorded on calibrated paper
 - Note that FRC and RV can't be measured by spirometer alone
 - can be by: Helium dilution method, Nitrogen washout method, Plethysmography
 -

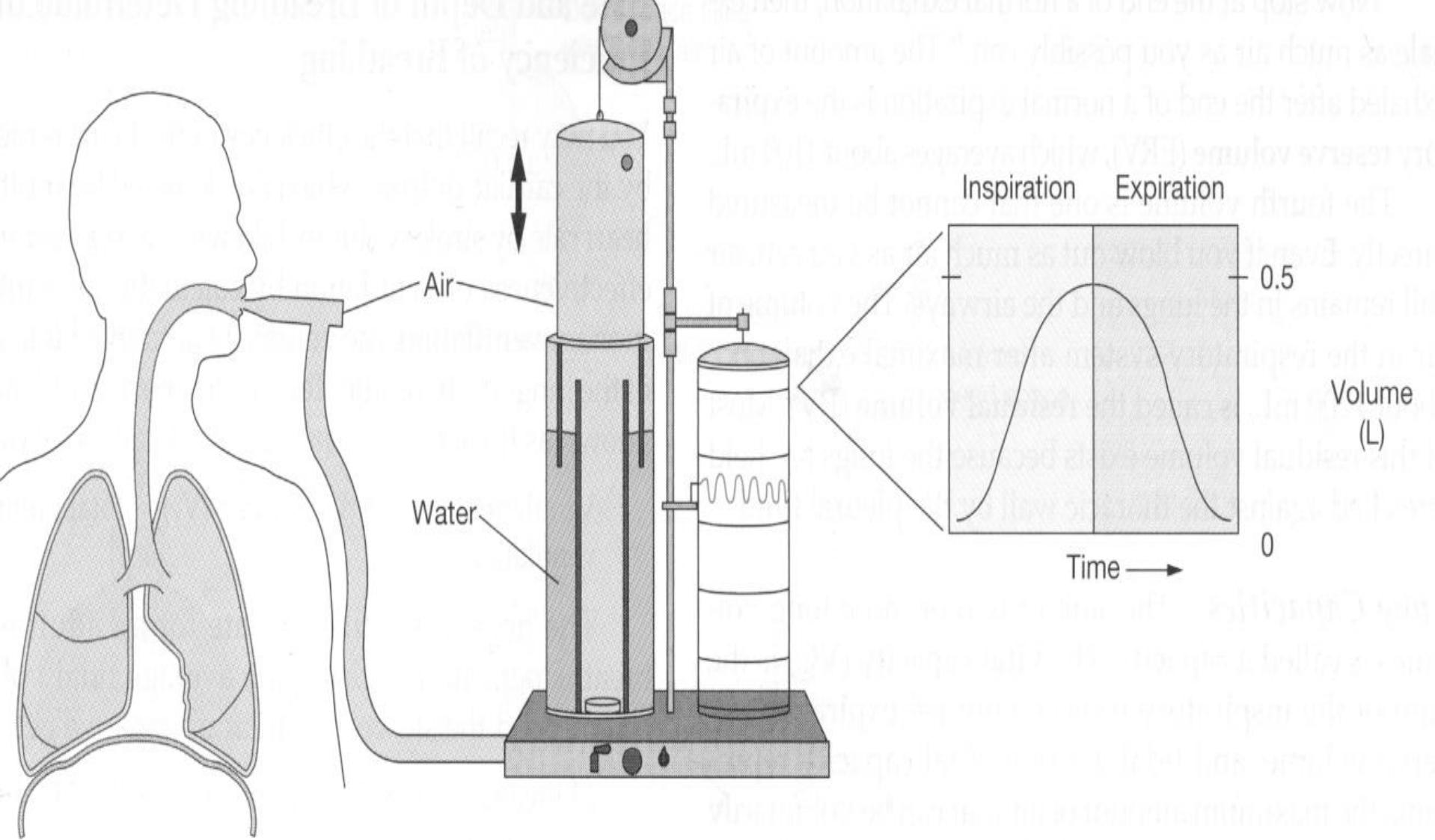


Figure. Measurement of lung volumes and capacities

Spirometer

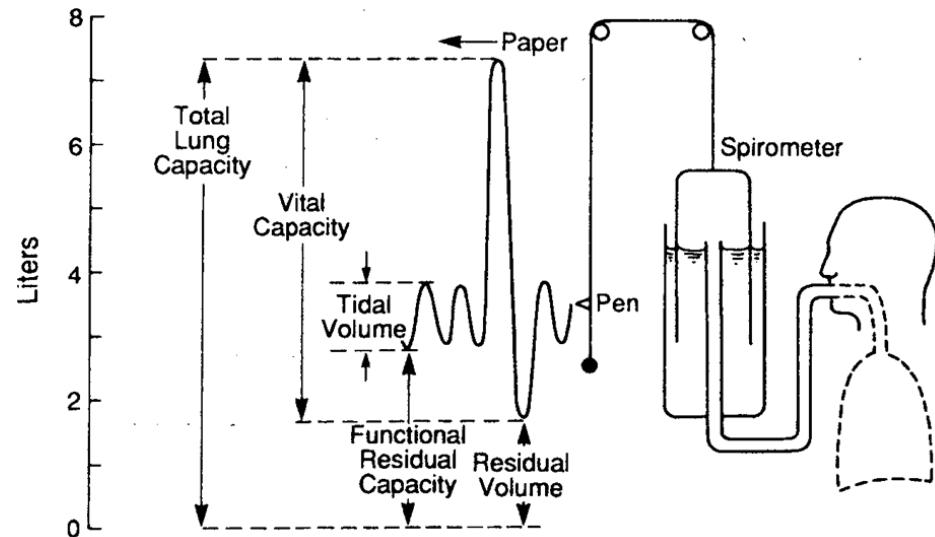
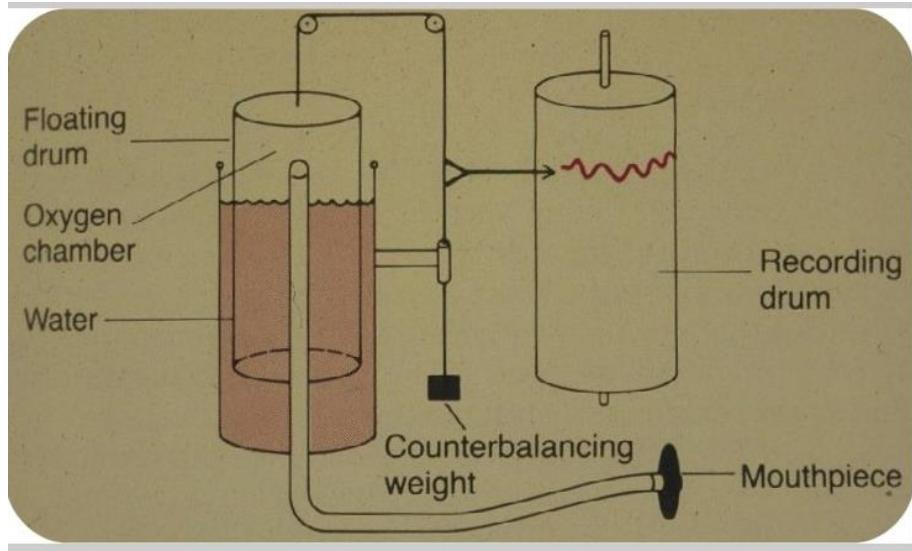
- device that measures various aspects of lung function.
 - the amount of air inhaled or exhaled and the rate at which the air is moved into or out of the lungs.
- Two essential aspects of PFT can be assessed by spirometry:
 - 1. What is the size of lung volume inspired or expired?
 - 2. What is the time it takes to exhale this volume, or what is the flow rate during exhalation?
- **Why spirometry**
 - Distinguish between obstructive and restrictive lung diseases
 - Differentiate Asthma from COPD
 - Assess response to therapy
 - Assess index of disease severity
 - Monitor disease progression and prognosis in COPD
 - Form pre-operative assessment/ Assess risk for surgical procedures

Types of Spirometers

A. Volume Spirometers

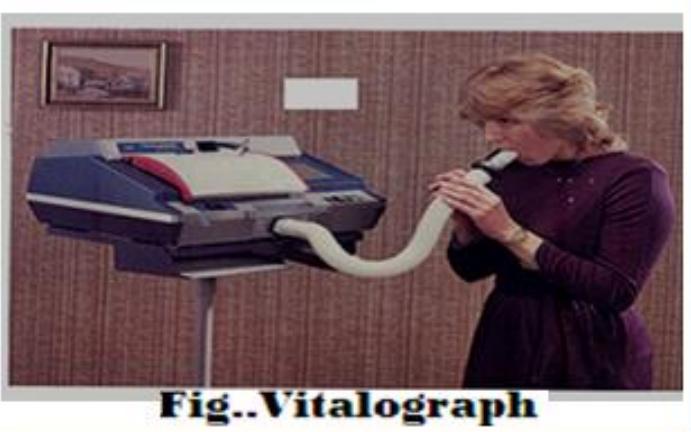
- are **volume-time** sensing spirometers.
 - record the amount of air exhaled or inhaled in a certain amount of time.
 - used in recording timed FVC and its component volumes- FEV1, ...
 - FVC: volume of air expired as forcefully and rapidly as possible after maximal inspiration.
 - ❖ Can be wet spirometer or dry spirometer
 - ❖ Wet spirometers- use a volume displacement spirometers with a water-seal
 - ❖ Volumes and capacities measured using this method: TV, IRV, ERV, VC, and IC

- FVC and FEV₁ are useful indices of disease.
 - FEV₁ is a Volume of air that can be forcibly expired in 1sec
- Ratio of FEV₁ to FVC (FEV₁/FVC) is used to differentiate among pulmonary diseases.
- In normal person, FEV₁/FVC ≥ 0.8 (80%), meaning 80% of VC can be forcibly expired in 1 second.
- In restrictive lung diseases (e.g. fibrosis), both FEV₁ and FVC are reduced,
 - **but ratio of FEV₁/FVC may not change or even may increase.**
- In obstructive lung disease (e.g. asthma), FEV₁ is reduced more than FVC and ratio of FEV₁/FVC is decreased.



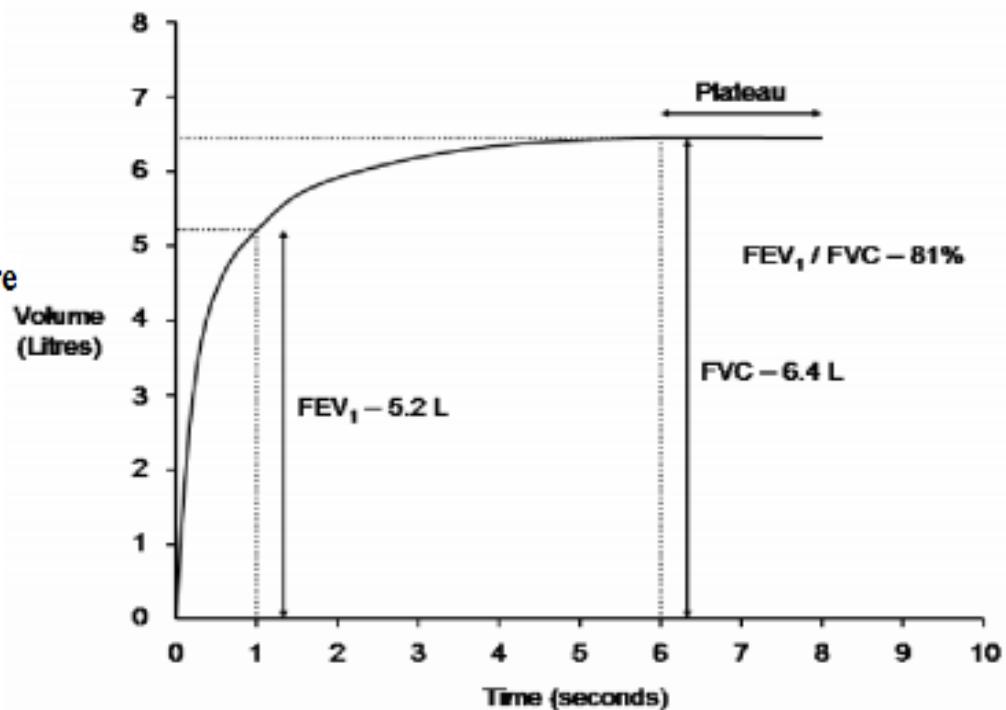
Subject sits and breathes into and out of the spirometer displacing a bell.
Volume displaced are recorded on calibrated paper

The subject breathes into a mouthpiece, the air moves a a plastic bell, or a plastic diaphragm that in turn moves a pen writing on a moving drum with a graph paper.

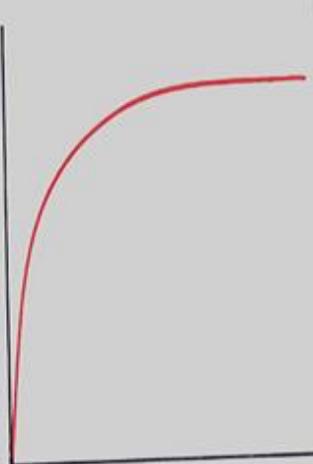


A simple vitalograph test can be performed to show pattern of tracings of expiratory spirometers in normal and disease conditions (obstructive and restrictive) showing volume-time curves and flow-volume curves

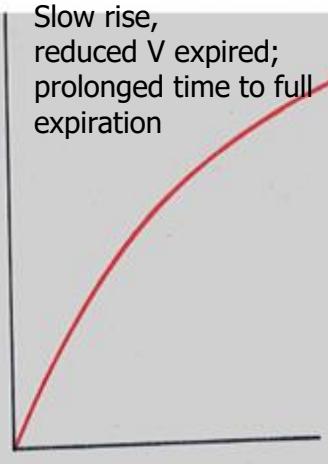
FVC and FEV₁ on a normal volume-time curve



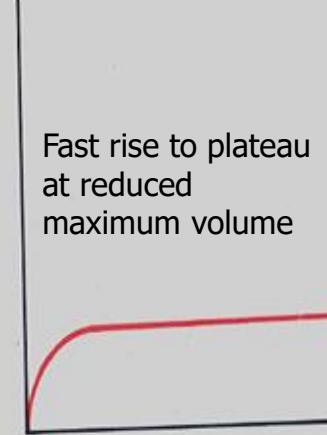
COMPARISON OF VOLUME-TIME AND FLOW-VOLUME CURVES



NORMAL



OBSTRUCTIVE



RESTRICTIVE

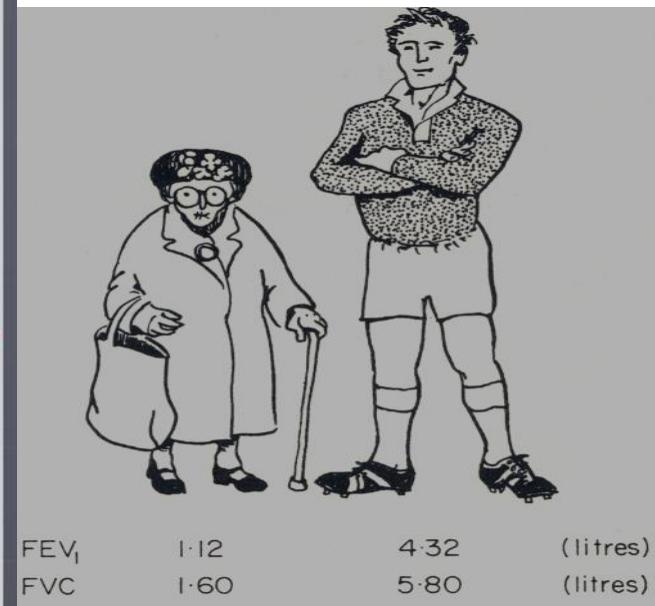
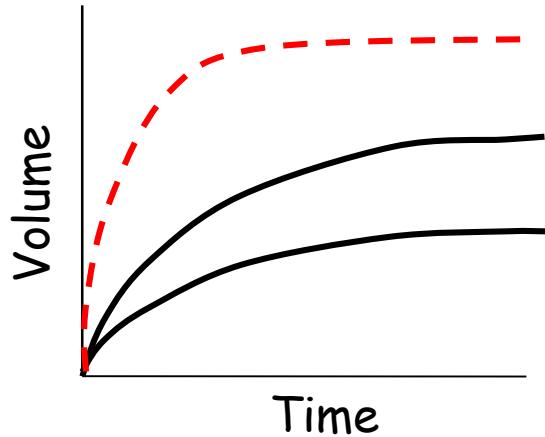


Fig. Normal, Obstructive and Restrictive patterns of airways condition recorded by a dry spirometer (vitalograph).

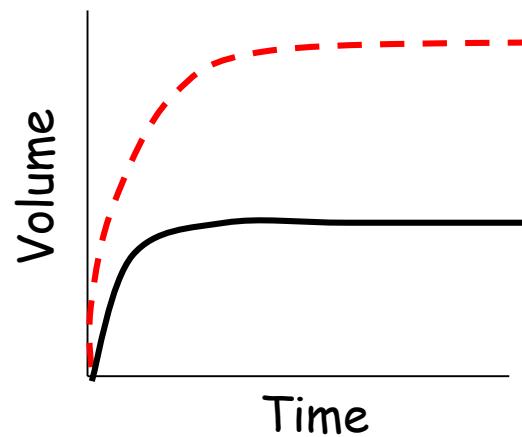
Fig. Normal values.

Spirometry: Abnormal Patterns

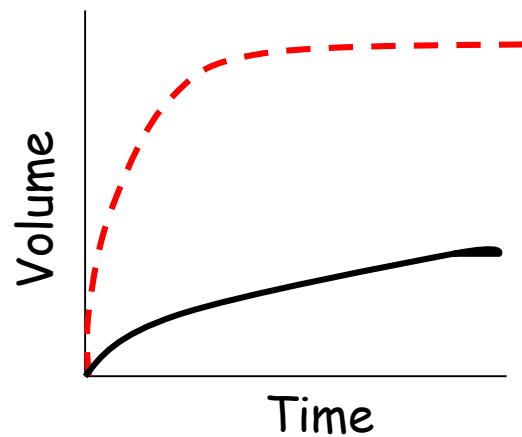
Obstructive



Restrictive



Mixed



Slow rise, reduced volume expired; prolonged time to full expiration

Fast rise to plateau at reduced maximum volume

Slow rise to reduced maximum volume; measure static lung volumes and full PFT's to confirm

B. Flow-volume spirometers

- Record how fast the air flows in or out as volume of air inhaled or exhaled increases.
- After the starting point the curve rapidly mounts to a peak (PEF).
- Tend to be lighter and more portable

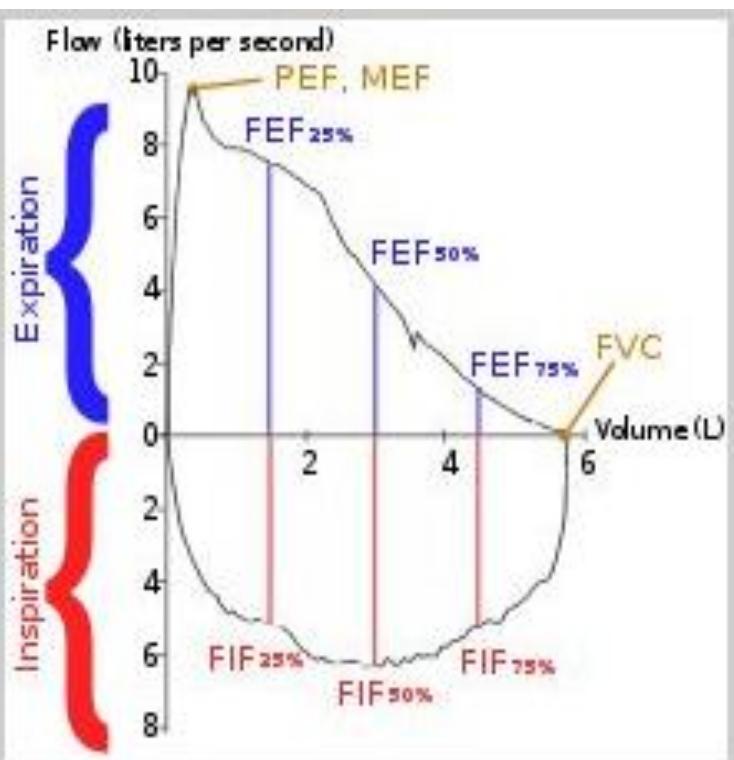


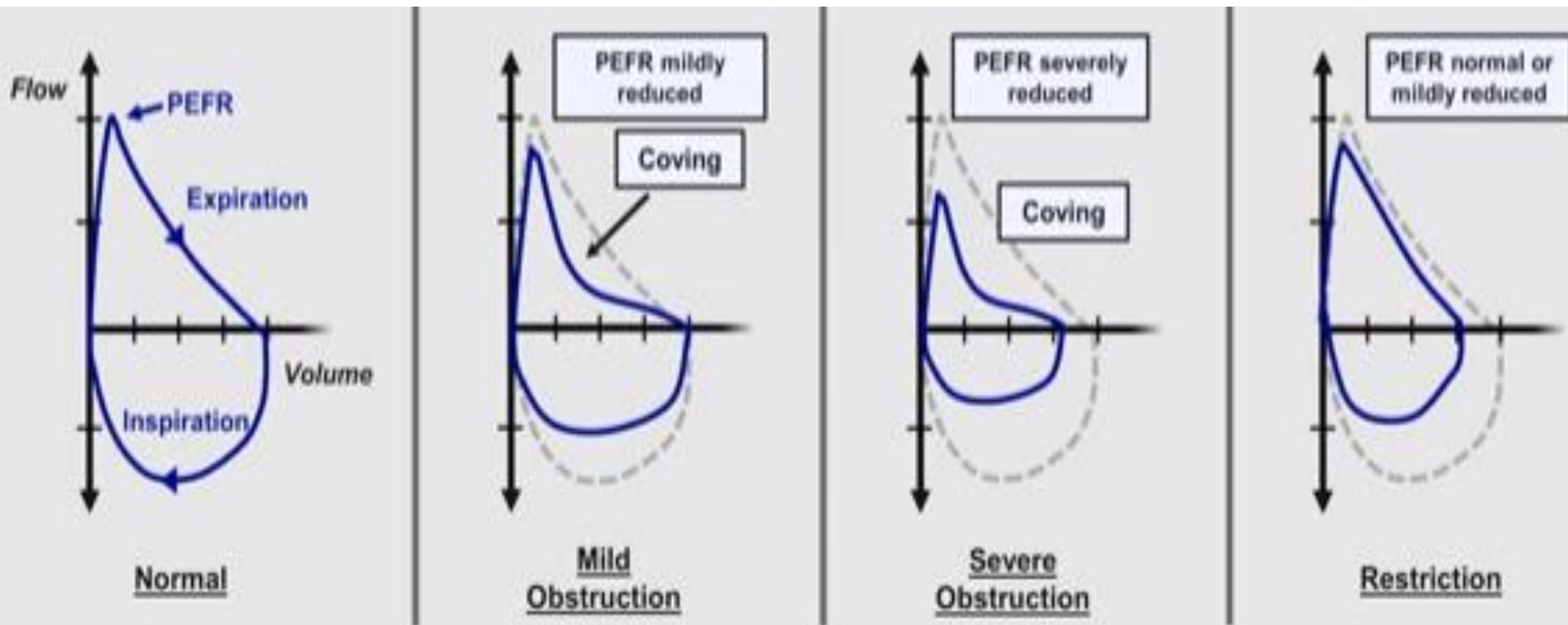
Fig..Digital spirometer used to measure flow rate-volume and volume-time

- ✓ A normal Flow-Volume loop begins on X-axis (Volume axis)
- ✓ At the start of test both flow and volume are equal to zero. After the starting point the curve rapidly mounts to a peak: **Peak Expiratory Flow**
- ✓ After the PEF the curve descends as more air is expired. A normal F/V loop descends in a **straight or a convex line from top (PEF) to bottom (FVC)**.
- ✓ The forced inspiration that follows the forced expiration has roughly the same morphology, but the PIF is not as distinct as PEF.

Fig. Flow-volume curve

PFT in obstruction and restriction:

Flow-volume spirometers



- Spirometry is a useful tool in diagnosing respiratory-disease states.
 - 2 broad types of respiratory dysfunction during spirometry:
 - **obstructive air ways,**
 - Any abnormal respiratory condition which makes it difficult to push the air out
 - is characterized by an increase in airway resistance
 - decrease in expiratory flow rates.
 - Eg. Chronic asthma, chronic bronchitis, emphysema
 - **restrictive (or constrictive) lung disease**
 - Any abnormal respiratory condition which makes it difficult to inspire
 - decreases all lung volumes.
 - Eg. Diaphragmatic paralysis, spinal cord disease, fibrosis.....

Table VI-1-1. Summary of Obstructive versus Restrictive Pattern

Variable	Obstructive Pattern e.g., Emphysema	Restrictive Pattern e.g., Fibrosis
Total lung capacity	↑↑	↓
FEV ₁	↓↓	↓↓
Forced vital capacity	↓↓	↓↓
FEV ₁ /FVC	↓↓	↑↑ or normal
Peak flow	↓↓	↓↓
Functional residual capacity	↑↑	↓↓
Residual volume	↑↑	↓↓

Forced vital capacity always decreases when pulmonary function is compromised.

A decrease in FEV₁/FVC ratio is evidence of an obstructive rather than a restrictive pattern.

- **COPD** - a disease state characterized by airflow limitation that is **not reversible**

- **Emphysema** - chara by destruction and enlargement of the lung alveoli
- **Chronic bronchitis** - condition with chronic cough and phlegm

- COPD **4th** leading cause of death in US
- **3rd** most common cause of death worldwide by 2020.



• Risk Factors

- ✓ **Cigarette Smoking**
- ✓ **Passive, or 2nd-Hand Smoking**
- ✓ Airway Responsiveness
- ✓ Respiratory Infections
- ✓ Genetic α_1 Antitrypsin defic

❖ Clinical Presentation

- ✓ cough, sputum production, and exertional dyspnea
- ✓ symptoms for Mons or yrs before seeking medical attention
- ✓ worsening dyspnea on exertion- principal feature of advanced COPD
- ❖ **Copr pulmonale → death**

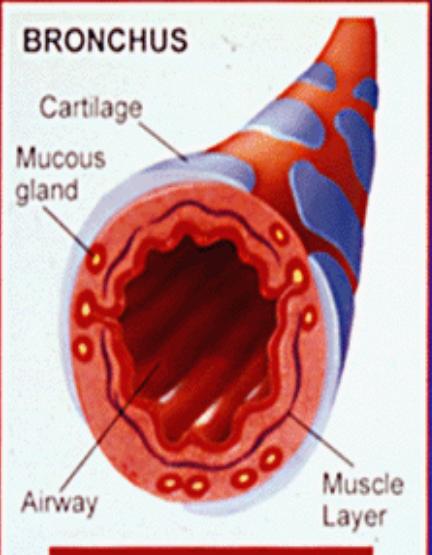
Figure 1. GOLD SPIROMETRIC CRITERIA FOR COPD SEVERITY¹

I: Mild COPD	<ul style="list-style-type: none"> • $FEV_1/FVC < 0.7$ • $FEV_1 \geq 80\% \text{ predicted}$ 	At this stage, the patient may not be aware that their lung function is abnormal.
II: Moderate COPD	<ul style="list-style-type: none"> • $FEV_1/FVC < 0.7$ • $50\% \leq FEV_1 < 80\% \text{ predicted}$ 	Symptoms usually progress at this stage, with shortness of breath typically developing on exertion.
III: Severe COPD	<ul style="list-style-type: none"> • $FEV_1/FVC < 0.7$ • $30\% \leq FEV_1 < 50\% \text{ predicted}$ 	Shortness of breath typically worsens at this stage and often limits patients' daily activities. Exacerbations are especially seen beginning at this stage.
IV: Very Severe COPD	<ul style="list-style-type: none"> • $FEV_1/FVC < 0.7$ • $FEV_1 < 30\% \text{ predicted or } FEV_1 < 50\% \text{ predicted plus chronic respiratory failure}$ 	At this stage, quality of life is very appreciably impaired and exacerbations may be life-threatening.

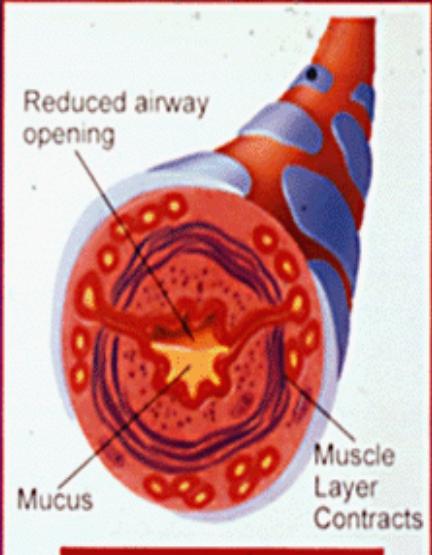
Bronchial Asthma- over view

- Asthma is an airway disease characterized by ;
 - chronic inflammation of airways,
 - hyper-responsiveness, with exposure to wide variety of stimuli, and
 - reversible airways obstruction with variable airflow limitation.
- is a chronic disease, with episodic acute exacerbations interspersed with symptom-free periods.
- **The triads: intermittent dyspnea, cough, and wheezing**
- Symptoms may be worse at night, and patients typically awake in the early morning hours.

Airway Pathology in Asthma

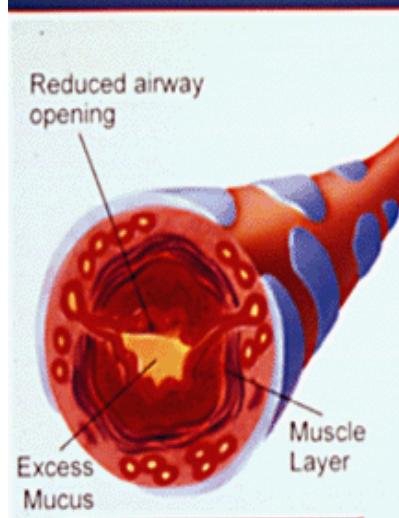


Normal

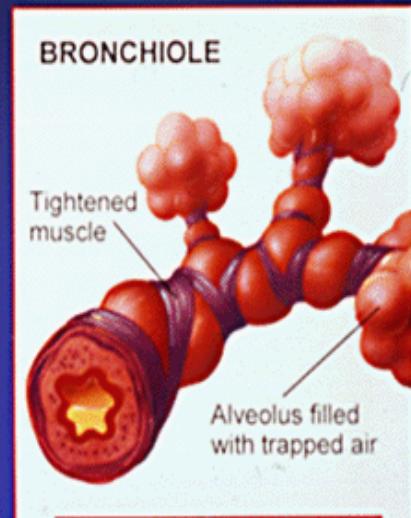


Asthma

Role of Inflammation and Bronchoconstriction in Asthma

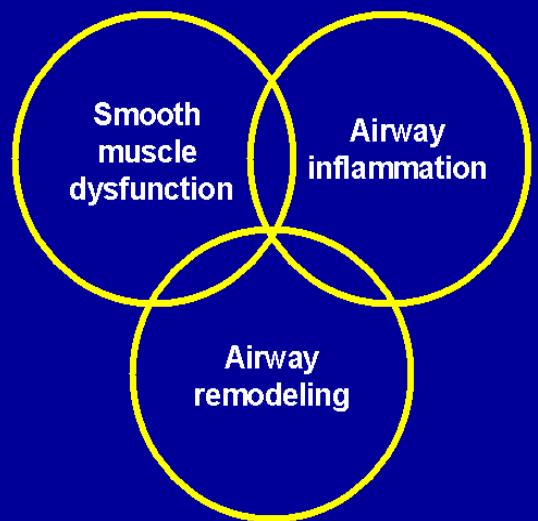


Inflammation



Bronchoconstriction

Asthma Pathophysiology



Smooth muscle dysfunction

- Bronchial hyperreactivity
- Hyperplasia/hypertrophy
- Inflammatory mediator release

Airway remodeling

- Cellular proliferation
 - Smooth muscle cells
 - Mucous glands
- Increased matrix protein deposition
- Basement membrane thickening
- Angiogenesis

Categories/Classification of asthma

1. *Allergic/ atopic/extrinsic asthma:*

- Often personal/family history of allergy: rhinitis, urticaria, and eczema;
- with positive skin tests, and increased serum IgE level
- its onset is early in life**

2. *Idiosyncratic/ nonatopic/ intrinsic asthma(10 %) :*

- no personal or family history, negative skin tests, and normal IgE,
- adult-onset asthma, may have nasal polyps, and aspirin-sensitivity.
- They usually have more severe, persistent asthma.

3. **Mixed group etiology:** have features of each preceding categories .

Diagnosis of asthma

- Usually clinical,
- Can be confirmed by objective measurements of lung function.
 - Spirometry: airflow limitation with reduced FEV₁, FEV₁/FVC, and PEF.
 - **Reversibility is demonstrated by**
 - >12% and 200-mL increase in FEV₁ 15 min after inhaled SABA or
 - in some pts 2-4 wks trial of OCS (prednisone or prednisolone 30-40 mg daily).
- COPD is usually easy to differentiate from asthma:
 - less variability, never completely remit, & less or no reversibility to bronchodilators

CLASSIFICATION	DAYS WITH SYMPTOMS	NIGHTS WITH SYMPTOMS	FEV ₁ or PEF ^[*] % Predicted Normal	PEF Variability (%)
Severe persistent	Continual	Frequent	≤60	>30
Moderate persistent	Daily	>1/wk	60 < x < 80	>30
Mild persistent	>2/wk, but <1 time/day	>2/mo	≥80	20–30
Mild intermittent	≤2/wk	<2/mo	≥80	<20

Classification of chronic Asthma by Severity

Management Principles

I. SUPPORTIVE: Fluid, O₂

II. BRONCHODILATOR THERAPIES- 3 classes of bronchodilators in current use:

- **β 2 -adrenergic agonists**- far the most effective than the next two.
 - Short-acting β 2 -agonists (SABAs): Salbutamol **albuterol, terbutaline ...**
 - Long-acting β 2 -agonists (LABAs) : **salmeterol, formoterol ...**
- **Anticholinergics** - Muscarinic receptor antagonists Eg. **ipratropium bromide**,
 - prevent cholinergic nerve-induced bronchoconstriction and mucus secretion.
 - much less effective than β 2 -agonists in asthma therapy
 - S/E: dry mouth; urinary retention
- **Theophylline: Aminophylline**
 - bronchodilator effect is due to inhibition of **phosphodiesterases** in airway smooth-muscles
 - Probably at lower doses has **anti-inflammatory effects**,
 - S/Es: headache, nervousness, dizziness, cardiac Arrhythmias
- ❖ Bronchodilators are mainly to reverse the bronchoconstriction of asthma
 - ✓ has little or no effect on the underlying inflammatory process.
 - ✓ Thus, not sufficient to control asthma in patients with persistent symptoms

III. CONTROLLER THERAPIES

- **Inhaled Corticosteroids** Eg. **Fluticasone, Beclomethasone, Budesonide...**
 - are by far the most effective controllers for asthma.

Mode of Action

- **Anti-inflammatory** agents
- reducing inflammatory cell numbers and their activation in the airways.
- ICS reduce
 - eosinophils in the airways and sputum, and
 - numbers of activated T lymphocytes and
 - surface mast cells in the airway mucosa.

Systemic Corticosteroids–

- Iv: Hydrocortisone or methylprednisolone
- OCSs - are as effective as and easier to admin:
eg. Prednisolone, prednisone

Stepwise approach to chronic asthma therapy according to the severity of asthma and ability to control symptoms

Short-acting β_2 -agonist as required for symptom relief				
Mild intermittent	Mild persistent	Moderate persistent	Severe persistent	Very severe persistent
ICS Low dose	LABA	ICS High dose	LABA	OCS
ICS Low dose	LABA	ICS High dose	LABA	

Pulmonary ventilation Vs Alveolar ventilation

- **Pulmonary or minute ventilation**
 - is the volume of air breathed in or out per minute
 - determined by V of air expired/breath & respiratory rate.
 - $\Rightarrow PV = TV \text{ (ml/breath)} \times \text{respiratory rate (breaths/min)}$
 - $P.V = 500\text{ml/breath} \times 12 \text{ breaths/min} = 6,000\text{ml/min}$.
 $\Rightarrow 6\text{L}$ of air breathed in & out in one minute at rest
 - A healthy young male can increase his total P.V by 25 folds,
 - \Rightarrow from 6 to 150L/min., voluntarily for a brief period of time

- Alveolar ventilation
 - is the volume of air exchanged b/n atm & alveoli in a minute or
 - the rate at which new air reaches the respiratory zone/minute
 - Calculated as alveolar Ventilation = (TV- dead space vol.) X RR
 - $AV = (500-150) \times 12 = 4200\text{ml/min}$ during quiet breathing.
- Pulmonary ventilation > alveolar ventilation
 - Because of the presence of dead space volume
 - Area of respiratory tract where there is no gas exchange

- Two types of dead space:

A. Anatomic dead space

- V of conducting passageways of the tract where there is no gas exchange
- The Volume of the nose, pharynx & tracheobronchial tree
- It is where 150ml of inspired air remains per breath

B. Alveolar dead space

- V of any ventilated alveoli that doesn't participate in gas exchange with blood

❖ physiological dead space = anatomical + alveolar dead spaces

- Under normal condition: physiol dead space = anatomical dead space
 - Because in normal condition there is no problem with alveolar areas

Effect of Increased Depth of Breathing on AV & PV

- Results in equal increase in minute and alveolar ventilation.
 - If the depth of breathing ↑ from a depth of 500 ml to a depth of 700 ml,
↓
 - the increase in minute & alveolar ventilation would be 2.4L/min.

Effect of Increased Rate of Breathing on AV & PV

- Results in a greater increase in minute than in alveolar ventilation.
- For every additional inspiration rate with a TV of 500 ml,
↓
 - ⇒ minute ventilation would increase by 500 ml,
 - ⇒ but alveolar ventilation would increase by only 350 ml (assuming dead space is 150 ml).

Reflection question

Given the following:

Tidal Volume

Rate

10/min

600ml

20/min

300ml

- Person A
- Person B
- Which person has the greater alveolar ventilation?
- Which person has the greater dead space ventilation?

Gas Exchange

- Occurs at two levels:
 - the pulmonary-capillary - b/n pulmonary capillaries & alveoli
 - tissue capillary level - b/n systemic capillaries & body cells
- involves simple diffusion of O₂ & CO₂ down *partial pressure gradients*.
 - No active transport mechanism involved

What is Partial Pressure?

- The pressure exerted independently by a particular gas within a mixture of gasses
- the air you blow into a balloon creates pressure that causes it to expand
 - The part of total pressure generated by O₂ is the PO₂
 - That generated by CO₂ is the PCO₂
- Thus, a Pg_{as} is a measure of how much of that gas is present
 - e.g. in the blood or alveoli

Gas law

- Atmospheric pressure at sea level = 760mmHg
- Percentage of gas at dry air is 78%N₂, 21%O₂, 1%inert gas, 0.04%CO₂

Daltons law of partial pressure:

- States that each gas contributes to the total pressure in direct proportion to its relative concentration
- Partial pressure of any gas can there for be calculated as:

$$P_{\text{gas}} = P_{\text{atm}} \times F_{\text{gas}}$$

- P_{gas} = partial pressure of a gas
- P_{atm} = atmospheric pressure
- F_{gas} = fractional composition (percentage) of a gas

- PN₂ at sea level =?
- FN₂ = 0.78, Patm = 760mmHg, \Rightarrow PN₂ = Patm × FN₂ = 600mmHg
- What is the partial pressure of O₂ at:
 - A. Sea level?
 - B. Mt. Everest(Patm=253mmHg)?

Henry's law

- States that concentration of gas in liquid is equal to partial pressure multiplied by solubility coefficient of the gas in particular liquid
 - $C_{\text{gas}} = [\text{gas}] = P_{\text{gas}} \times \text{solubility coefficient}$
- Used to convert the partial pressure of gas in gas phase to concentration in liquid phase (Eg in blood)

Comparison of the compositions of atmospheric air, humidified air, alveolar air and expired air.

Gases	Atmospheric air (mmHg)		Humidified air (mmHg)		Alveolar air (mmHg)		Expired air (mmHg)	
N ₂	597	78.62%	563.4	74.09%	569	74.9%	566	74.5%
O ₂	159	20.84%	149.3	19.67%	104	13.6%	120	15.7%
CO ₂	0.3	0.04%	0.3	0.04%	40	5.3%	27	3.6%
H ₂ O	3.7	0.50%	47	6.20%	47	6.20%	47	6.20%
Total	760	100%	760	100%	760	100%	760	100%

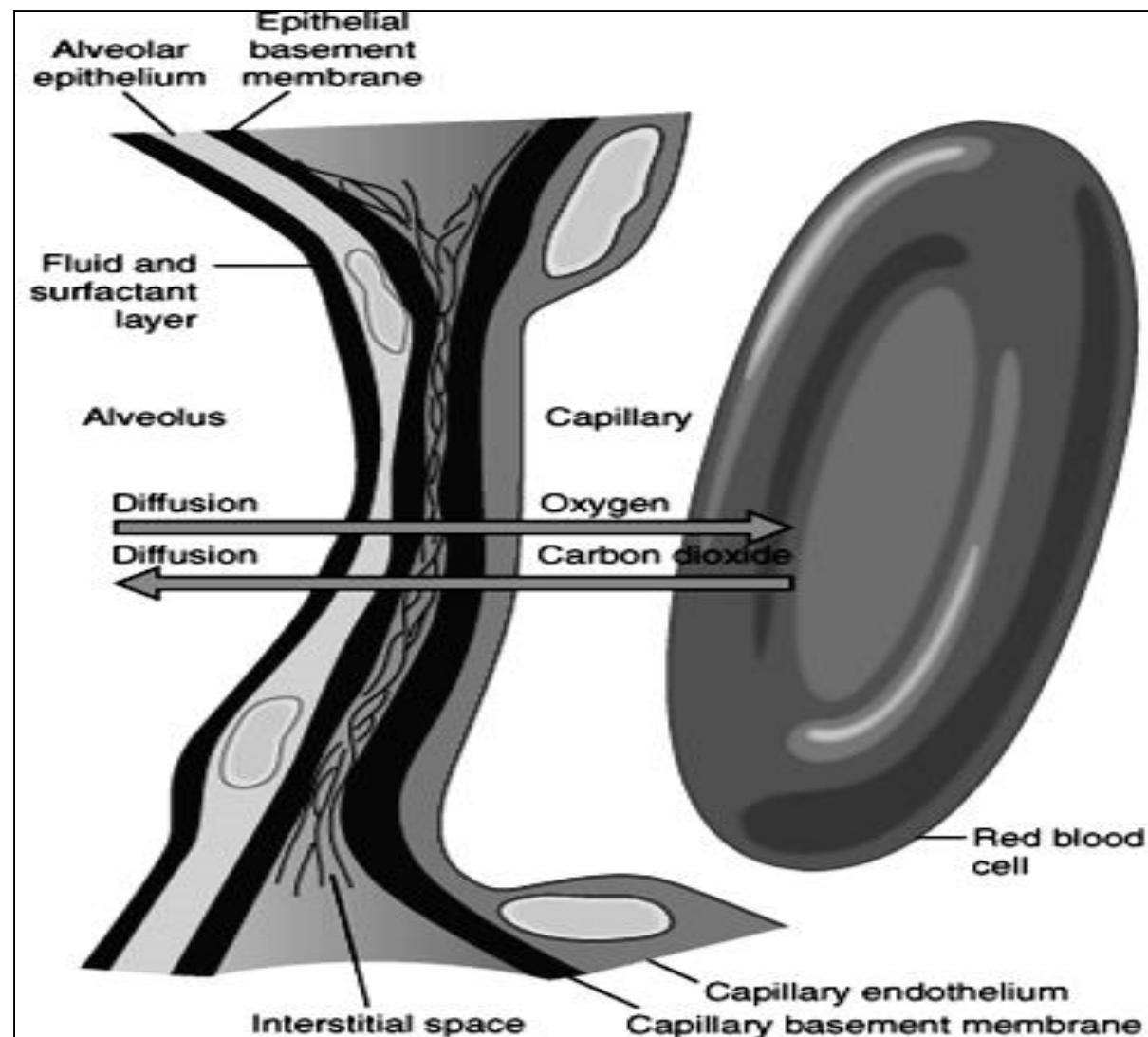
Why alveolar PO₂ & CO₂ are different from corresponding atmospheric partial pressures??

PO₂ and PCO₂ in the body (normal, resting conditions):

- In Alveoli
 - PO₂ = 104 mm Hg , PCO₂ = 40 mm Hg
- In Alveolar or pulmonary capillaries
 - Entering the alveolar capillaries
 - PO₂ = 40 mm Hg -relatively low
 - because this blood has just returned from the systemic circulation & has lost much of its O₂
 - PCO₂ = 45 mm Hg -relatively high
 - because blood returning from systemic circulation has picked up CO₂
 - Which gas diffuses where?

Gas exchange at the pulmonary capillaries

- Gases diffuse from area of high to low partial pressure
 - O₂ from alveoli to pulmonary capillaries
 - CO₂ diffuses from pulmonary capillaries to alveoli



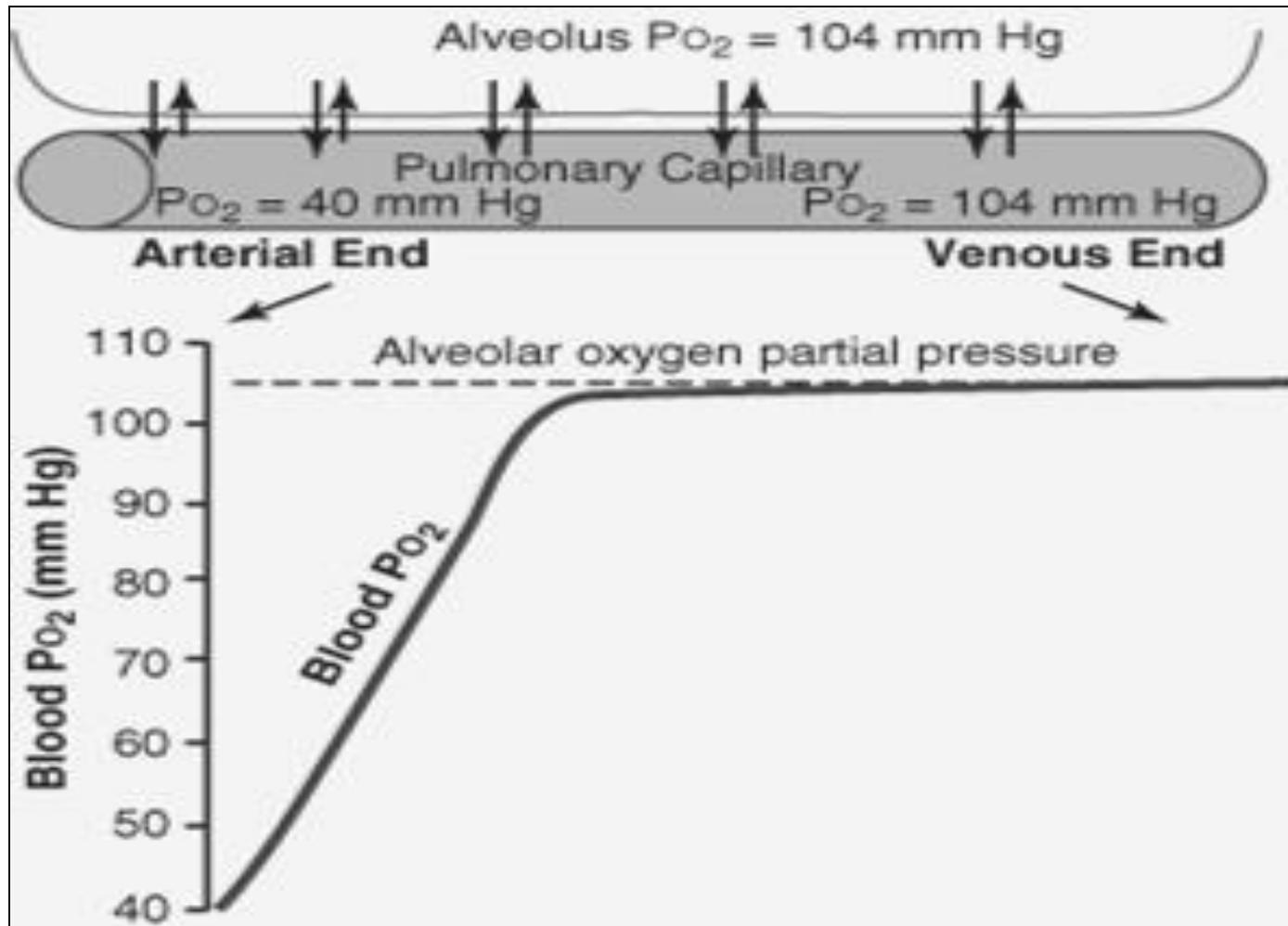
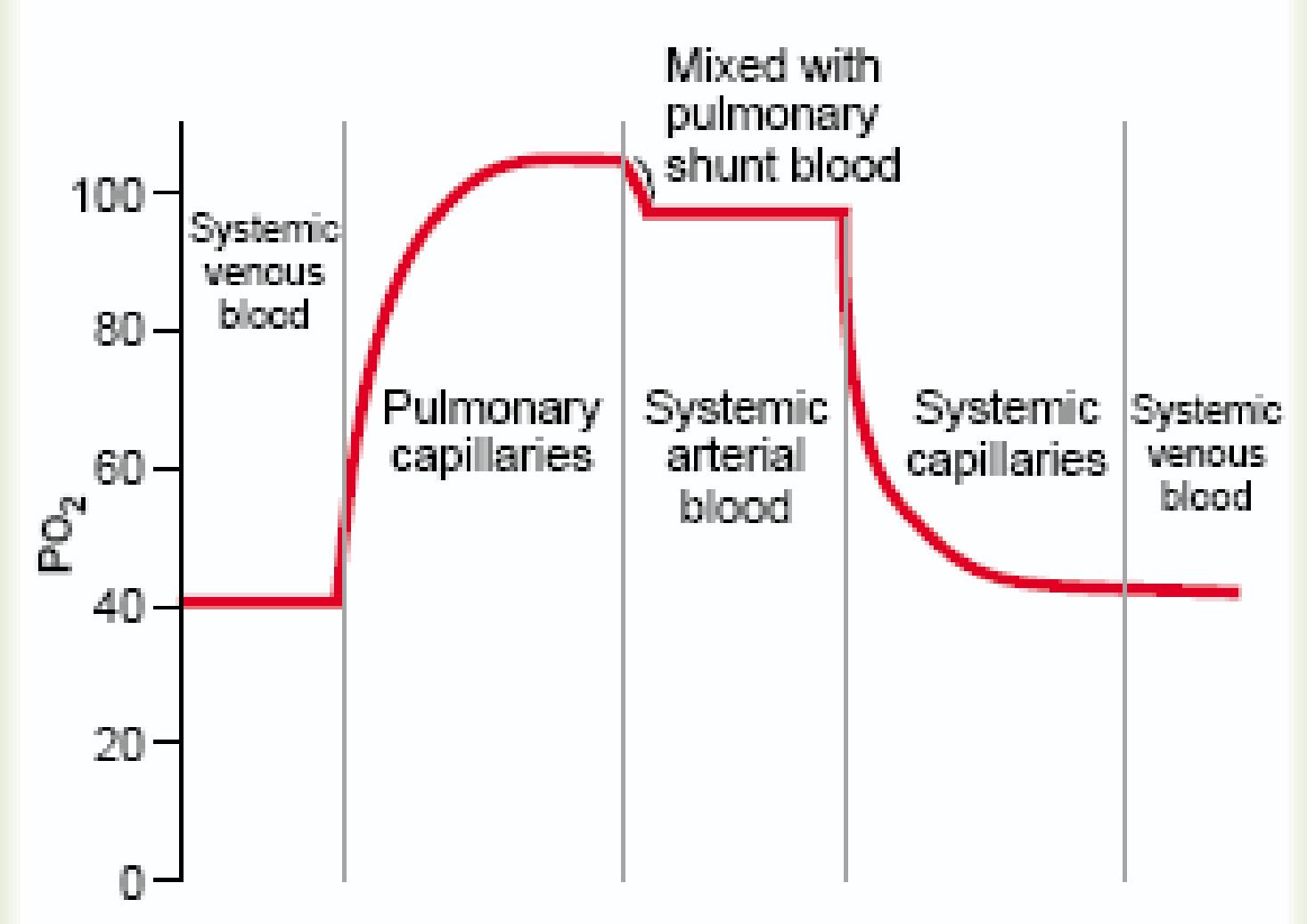
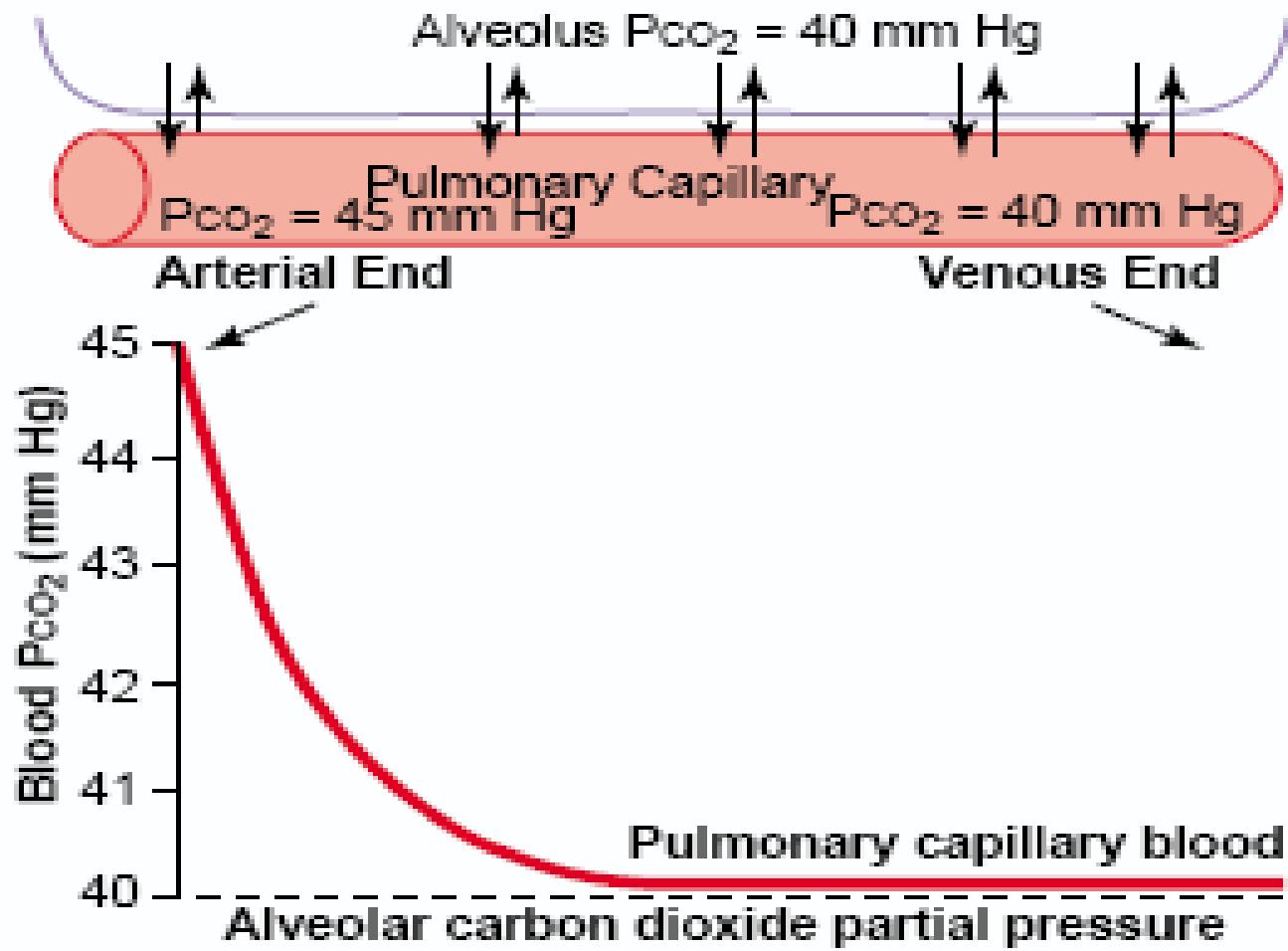


fig. Uptake of O₂ by pulmonary capillary blood

- Almost completes by the time the blood has moved a third of the distance through the capillary,



Changes in PO_2 in the pulmonary capillary blood, systemic arterial blood, and systemic capillary blood, demonstrating the effect of "venous admixture."



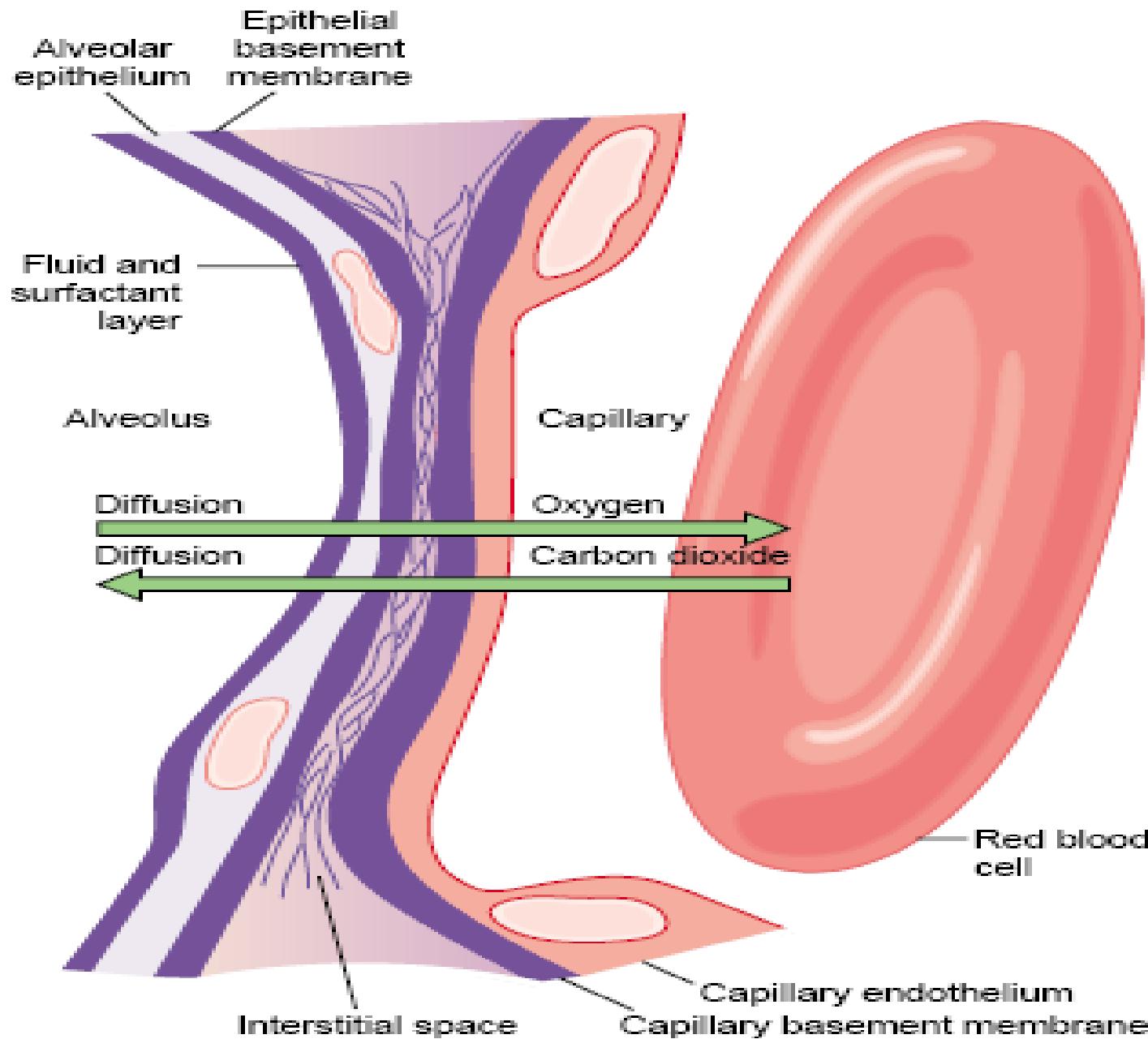
Diffusion of CO₂ from the pulmonary blood into the alveoli

Respiratory membrane/Diffusion barriers

- gas exchange between alveolar air & pulmonary blood occurs through
 - the membranes of all the terminal portions of the lungs
- All these membranes are collectively known as the respiratory membrane,
 - also called the pulmonary membrane.

- The layers of the respiratory membrane are:
 1. A layer of fluid lining the alveolus
 - contain surfactant that reduces the alveolar fluid surface tension
 2. The alveolar epithelium
 - composed of thin epithelial cells
 3. An epithelial basement membrane
 4. A thin interstitial space b/n alveolar basement & capillary membrane
 5. A capillary basement membrane
 6. The capillary endothelium

Fig. The different layers of the respiratory membrane



- Factors affecting the rate of diffusion of gas through the membrane: Fick's Law
- 1. the thickness of the membrane(diffusion distance),
 - the rate of diffusion $\propto 1/\text{thickness of the membrane}$
- 2. the surface area of the membrane,
- 3. diffusion coefficient of the gas in the membrane
 - For each gas it depends on:
 - the gas's solubility in the membrane and,
 - inversely, on the $\sqrt{\text{the gas's molecular weight}}$.
- 4. Temp

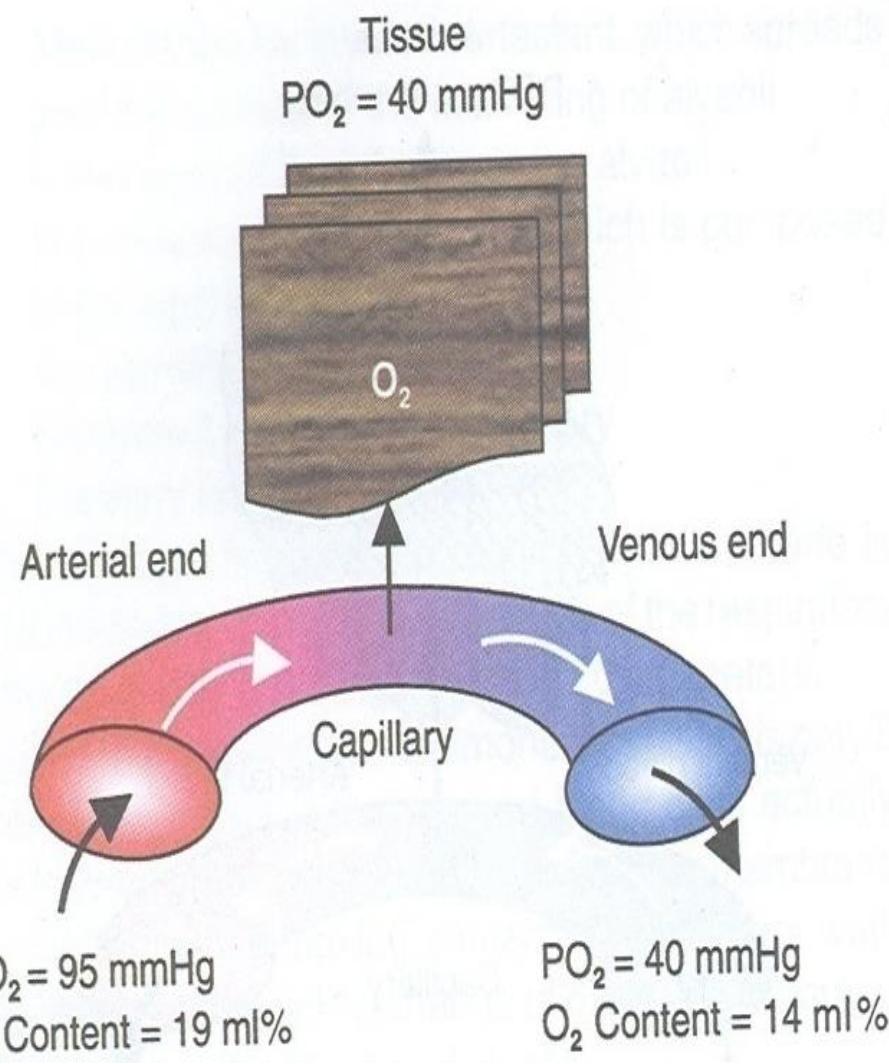
- 5. Partial pressure difference of the gas b/n the 2 sides of membrane.
 - b/n Pg_{gas} in alveoli & Pg_{gas} in the pulmonary capillary

Fick's Law of Diffusion:

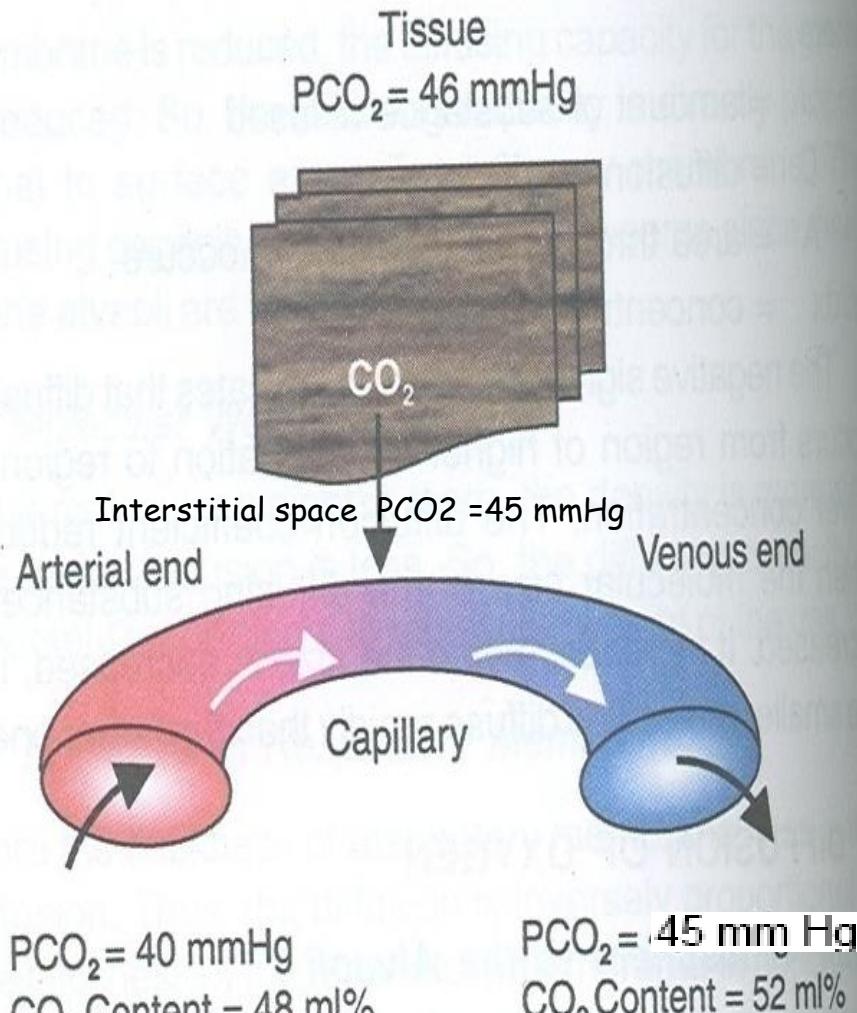
$$\frac{\text{diffusion rate}}{\text{concentration diff.} \times \text{surface area} \times T^o} \propto \frac{1}{\sqrt{\text{molecular weight} \times \text{distance}}}$$

Gas exchange at tissue bed

- Blood leaving the alveolar capillaries returns to the Lt atrium
 - is pumped by the Lt ventricle into the systemic circulation
 - This blood travels through arteries & arterioles
 - \Rightarrow into systemic or body capillaries where there is gas exchange
- As blood travels through arteries & arterioles, no gas exchange
- Gas exchange b/n systemic capillaries & cells is down Pg_{gas} gradient
 - Entering the systemic capillaries
 - PO₂ = 95 mm Hg & PCO₂ = 40 mm Hg
 - Body cells (resting conditions)
 - PO₂ = 40 mm Hg & PCO₂ = 46 mm Hg
- O₂ diffuses in to cells, CO₂ diffuses in to the systemic capillaries



A. Diffusion of O₂ from capillary to tissue



B. Diffusion of CO₂ from tissue to capillary

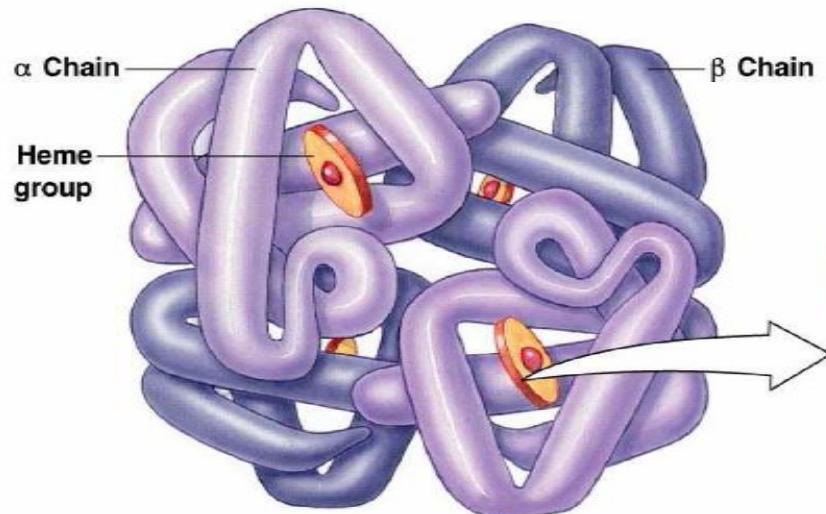
- How are O₂ & CO₂ transported in the blood?
- Oxygen transport is:
 - 1 - Bound to hemoglobin ($\approx 98\%$ of all oxygen in the blood)
 - 2 - Dissolved in the plasma ($\approx 2\%$)
- Hemoglobin saturation:
- Is the % of hemoglobin molecules carrying oxygen
- depends on PO₂ of the blood:
 - When PO₂ is high, O₂ binds with the Hb Eg. in pulmonary capillaries
 - when PO₂ is low, O₂ is released from the Hb Eg. in tissue capillaries

<i>PO₂ (mm Hg)</i>	<i>% saturation of hemoglobin</i>	<i>Dissolved oxygen(ml/dl)</i>
10	13.5	0.03
20	35	0.06
30	57	0.09
40	75	0.12
50	83.5	0.15
60	89.0	0.18
70	92.7	0.21
80	94.5	0.24
90	96.5	0.27
100	97.5	0.30

- Hemoglobin saturation depends on PO₂ of the blood

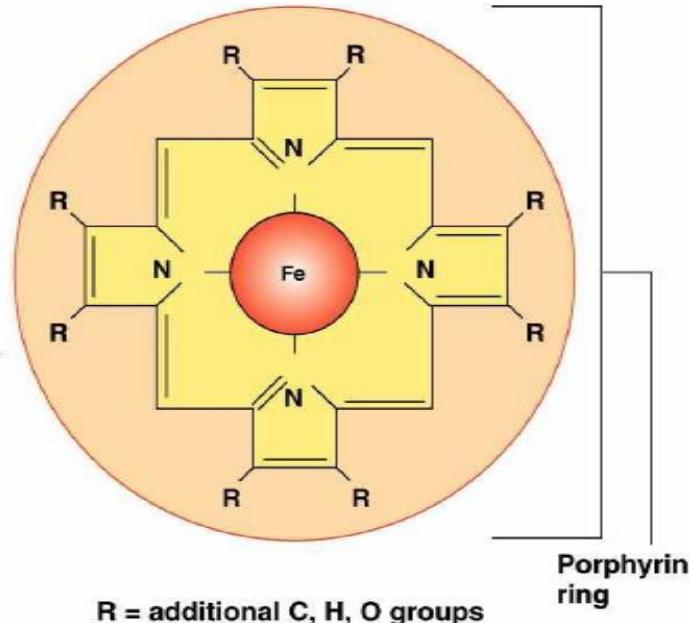
- Each molecule of hemoglobin contains 4hemes & 4globins
 - Each heme contains 1Fe which binds 1 O₂ molecule(1Hb carries 4 O₂)
- Fe is in ferrous state (Fe⁺⁺) & remain Fe⁺⁺ after combination with O₂
 - Combination with O₂ is oxygenation, not oxidation
- Methemoglobin -when Fe is in ferric state \Rightarrow methemoglobinemia
 - It is incapable of binding to O₂ \Rightarrow tissue hypoxia
 - the remaining Hb with Fe⁺⁺ has increased O₂ affinity,
 - resulting in impaired oxygen delivery to the tissues (Left-shift)
 - Normally Methemoglobin reductase in RBC reduces metHb to Hb
- 1g of Hb carries 1.34ml of O₂
 - The normal Hb content is 15g/100ml of blood
- ↓
- Total O₂ carrying capacity of pure Hb is 20ml of O₂/100 ml of blood

(a) A hemoglobin molecule is composed of four protein globin chains, each surrounding a central heme group.



In most adult hemoglobin,
there are two alpha chains
and two beta chains as shown.

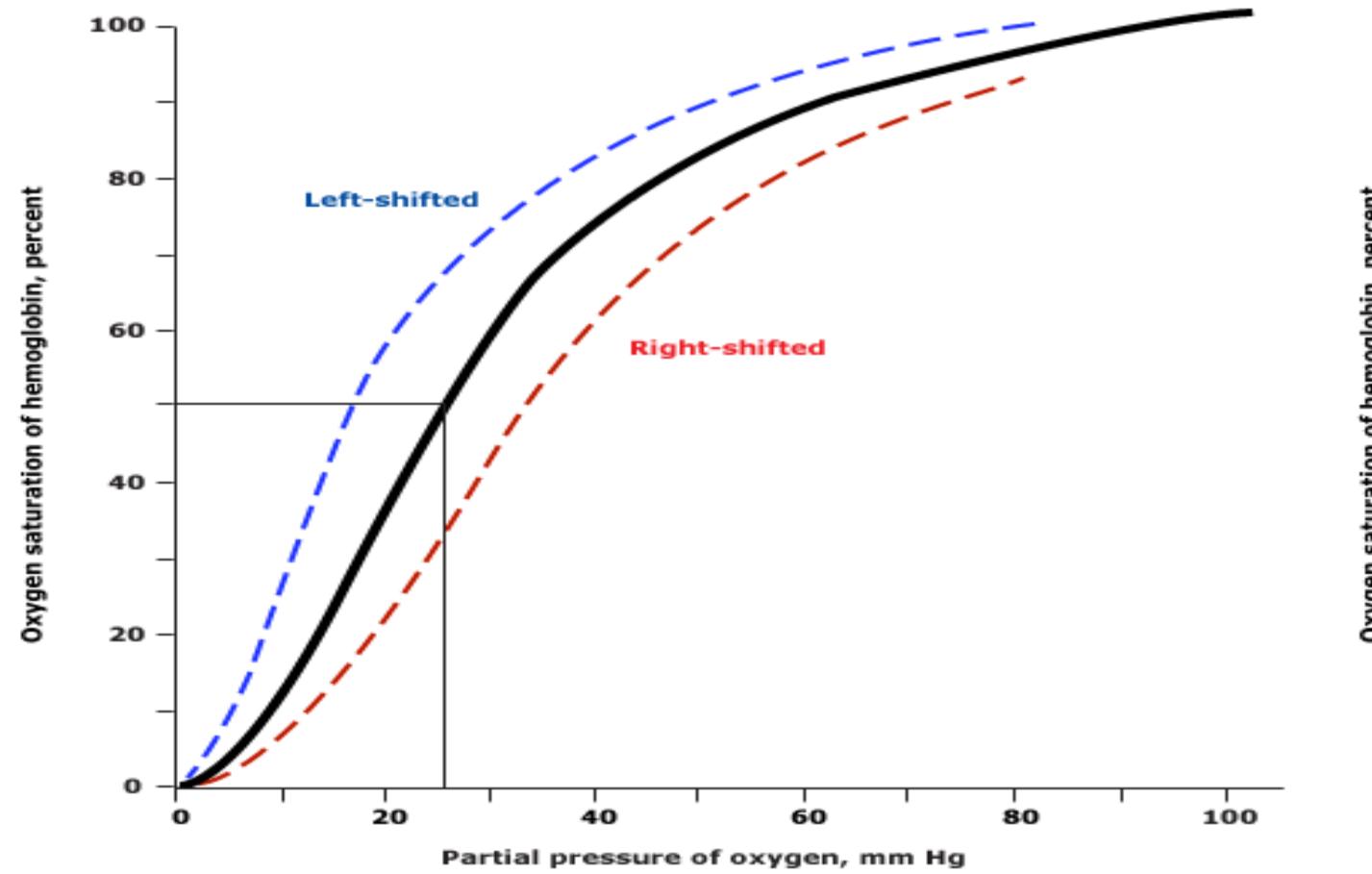
(b) Each heme group consists of a porphyrin ring with an iron atom in the center.



R = additional C, H, O groups

- ❖ O_2 reversibly combines with Hb to give oxy-haemoglobin: $O_2 + Hb = HBO_2$
 - ✓ The amount of O_2 carried by Hb increases as the paO_2 increases
 - ✓ Hb is fully saturated when all four heme of its molecule are bound to O_2
 - ✓ partially saturated when only one to three of its hemes are bound to O_2 .
- ❖ There are about 250 million Hb molecules in each RBC.
- ❖ Thalassemia refers to a spectrum of disorders characterized by reduced or absent production of one (or, rarely, two or more) of the globin chains, thus disrupting the delicate balance between alpha and non-alpha (eg, gamma or beta) globin chains.

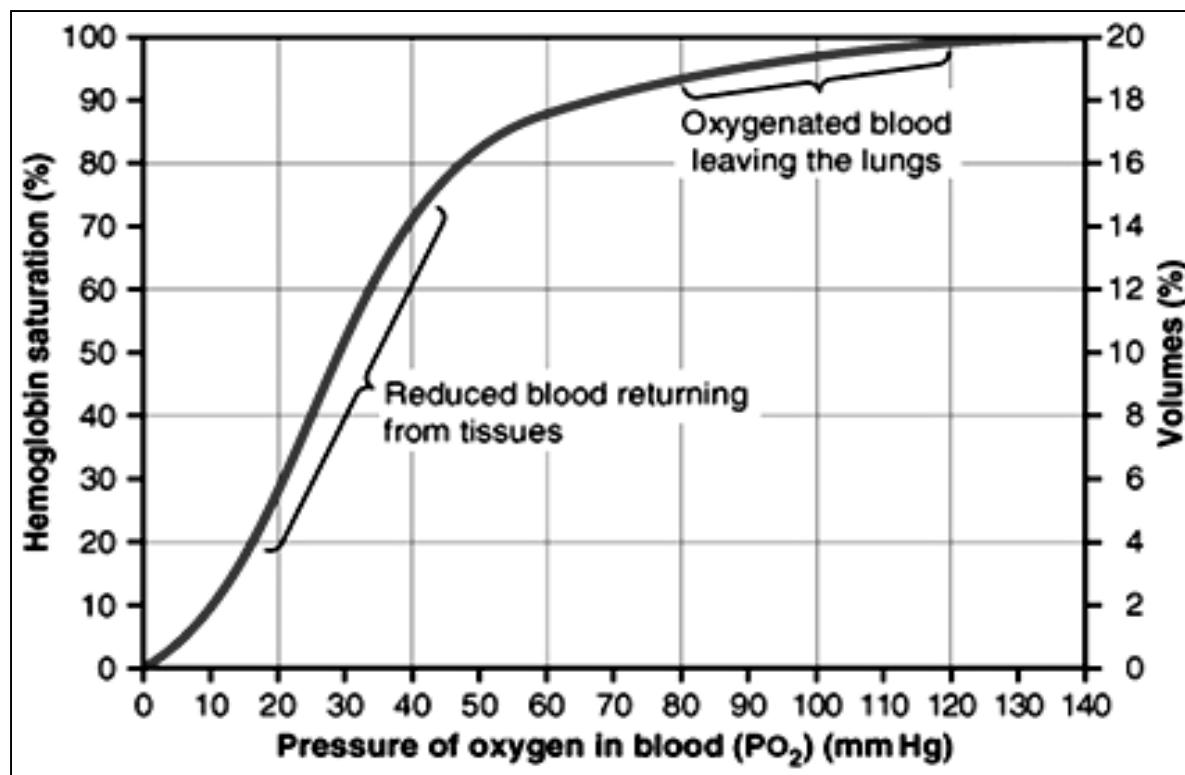
Oxyhemoglobin dissociation curve



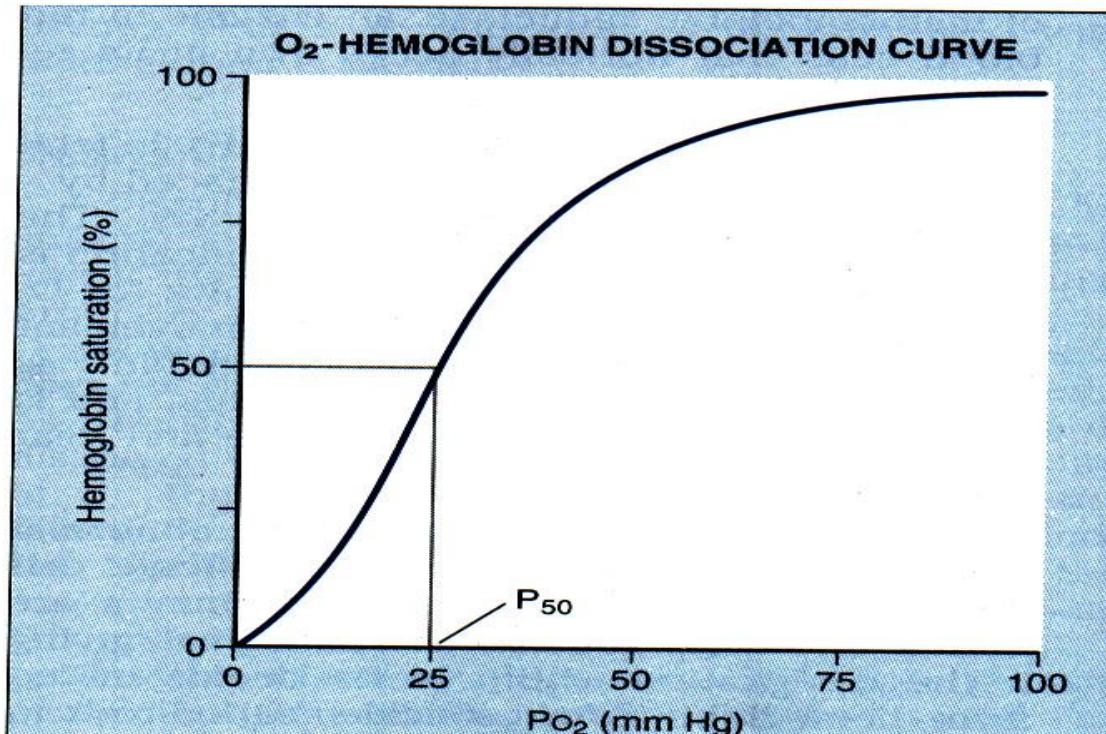
The oxyhemoglobin dissociation curve for normal adult hemoglobin (Hemoglobin A, solid line).

- ✓ Note that Hb is 50% saturated with O₂ at a partial pressure of 27 mmHg (ie, the P50 is 27 mmHg) and is 100% saturated at a pO₂ of approximately 100 mmHg.
- ✓ "left-shifted" (blue line, representing increased O₂ affinity) and "right-shifted" (red line, decreased O₂ affinity).
- ✓ The effect of right- or left-shifting of the curve is most pronounced at low oxygen partial pressures.
 - ❖ Eg, the right-shifted curve means that Hb can deliver approximately 70% of its attached O₂ at pO₂ of 27 mmHg.
 - ❖ In contrast, the left-shifted hemoglobin can deliver only about 35 percent of its attached O₂ at this pO₂.
- ✓ A high proportion of fetal hemoglobin, which has high oxygen affinity, shifts this curve to the left in newborns.

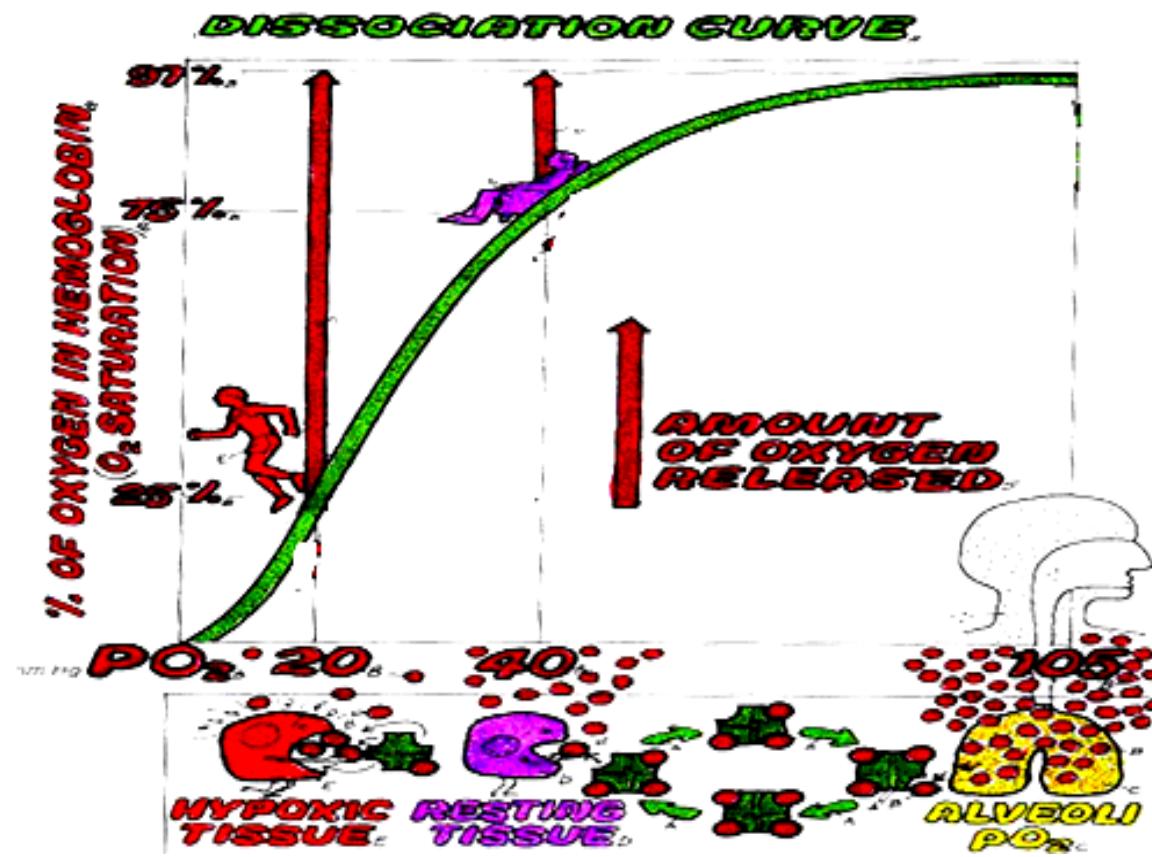
- **Oxygen-hemoglobin dissociation (saturation) curve**
- indicate the relationship between O₂ levels and Hb saturation
 - at high PO₂, Hb saturation remains rather high
 - This flat section of the dissociation curve is called the 'plateau'



- P₅₀ is the PO₂ required to achieve 50% hemoglobin saturation
 - is normally about 25 - 27 mmHg.
- If the P₅₀ is low, Hb has a higher affinity for O₂ (binds more easily)
 - the dissociation curve shifts to the left.
- A right shift (high P₅₀) indicates a lower affinity for oxygen.



- Recall that 40 mm Hg is the typical PO₂ in the body cells
 - under resting conditions, only about 25% of Hb give up O₂ in the systemic capillaries
 - When you are more active, PO₂ in active cells drop well below 40 mm Hg
 - This means the blood (Hb) 'unloads' lots of O₂ to active cells
 - cells that, of course, need more oxygen



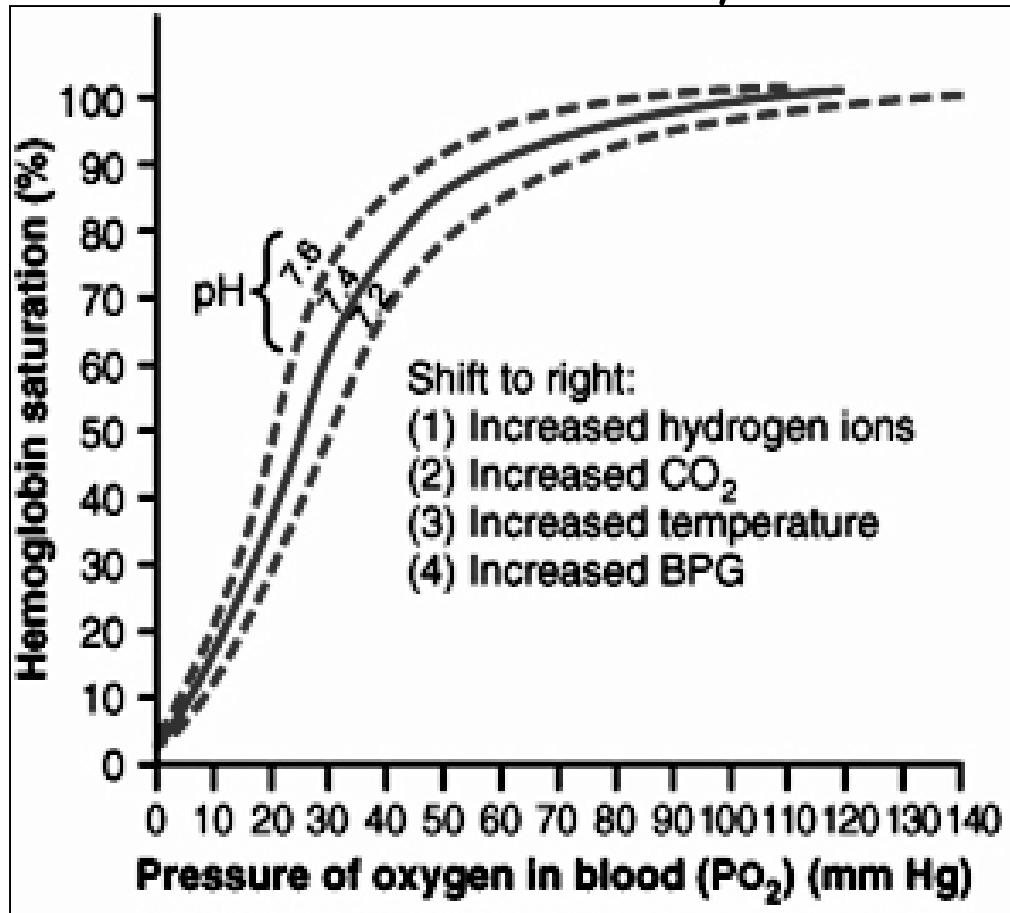
Utilization coefficient

- Is the percentage of blood that gives up its oxygen as it passes through the tissue capillaries
- normal value is 25%,
 - During strenuous exercise, it increase to 75- 85% and
 - when blood flow is extremely slow or the metabolic rate high, it approaches to 100%.

Factors that affect the Ox-Hemoglobin Dissociation Curve:

- The oxy-Hb dissociation curve 'shifts' under certain conditions.
 - Factors that can cause R_t ward shift are:
 1. increased levels of CO₂ and low O₂
 2. lower pH
 3. increased temperature
 4. more 2, 3-diphosphoglycerate - metabolic biproduct in RBC
- ❖ These factors occur when tissues become more active.
 - Eg, when a skeletal muscle starts contracting, the muscle cells use more O₂ \Rightarrow make more ATP \Rightarrow produce more CO₂
 - More ATP means releasing more heat \Rightarrow \uparrow temp in active tissues
 - More CO₂ translates into a lower pH.
$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$$

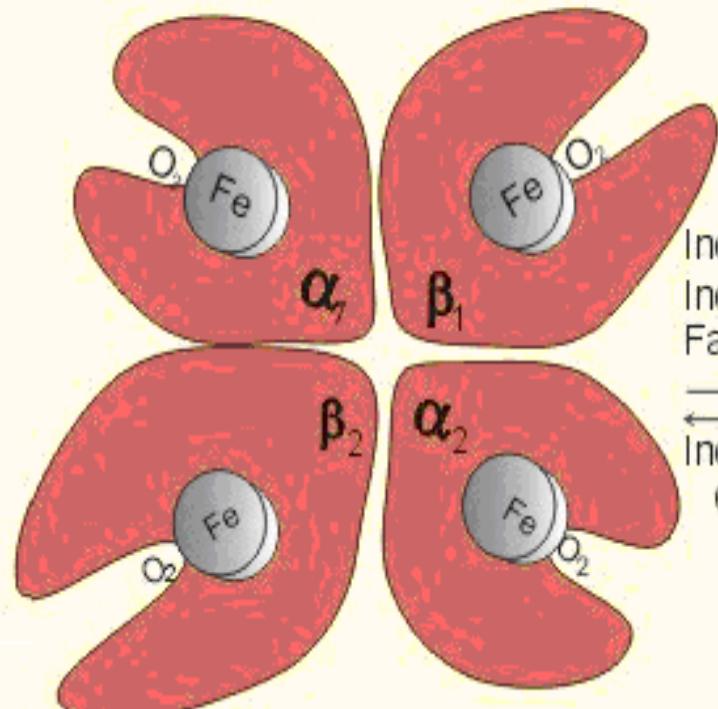
- As metabolic rate increase:
 - the curve shifts to the Rt \Rightarrow the affinity of Hb for O₂ decreases
 - More O₂ will be released at a given PO₂ in the tissues
 - The released O₂ is used by the active tissues



Oxygen Binding and Unloading

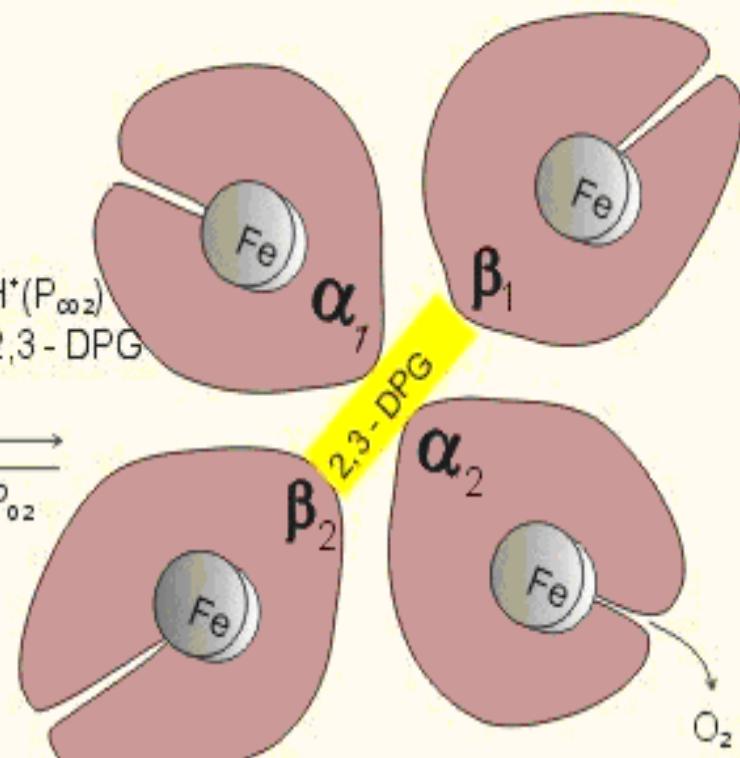
Oxyhaemoglobin

Mol weight: 64 460



Relaxed binding structure

Deoxyhaemoglobin



Tight binding structure

Increasing H⁺(P_{CO₂})
Increasing 2,3 - DPG
Falling P_{O₂}

↔

Increasing P_{O₂}
CO

2,3-DPG

The Bohr Effect - In the tissues

- As blood passes through tissues, CO₂ diffuses from the tissue cells into the blood.
- As the [CO₂]↑ ⇒ ↑H⁺ ⇒ the curve shifts to the Rt
 - Binding of CO₂ and H⁺ to oxy-Hb tend to displace O₂
 - more O₂ is released from the Hb:- important for O₂ delivery to the tissue

Haldane effect - occur in the alveoli

- as blood passes via the lung, CO₂ diffuses from blood into alveoli
 - Binding of O₂ with Hb tend to displace more CO₂
 - ↓ blood PCO₂ ⇒ shifts the O₂ dissociation curve to the Lt & upward
 - More O₂ binds to Hb and transported to the tissues
- ❖ more important in promoting CO₂ transport than Bohr effect for O₂

Carbon monoxide poisoning



- CO binds to Hb at the same site as where O₂ binds



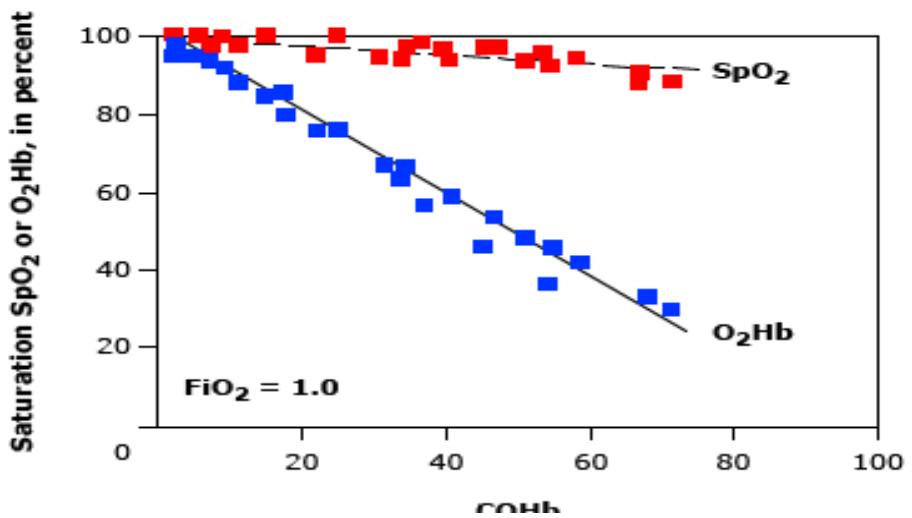
- can displace O₂ from the hemoglobin



- Decrease O₂ carrying capacity of the blood
 - CO has 250x greater binding capacity to Hb than O₂.

- Even a P_{CO} of 0.4 mmHg causes half of blood Hb to release O₂

Effect of carboxyhemoglobin on measured oxygen saturation by pulse oximetry



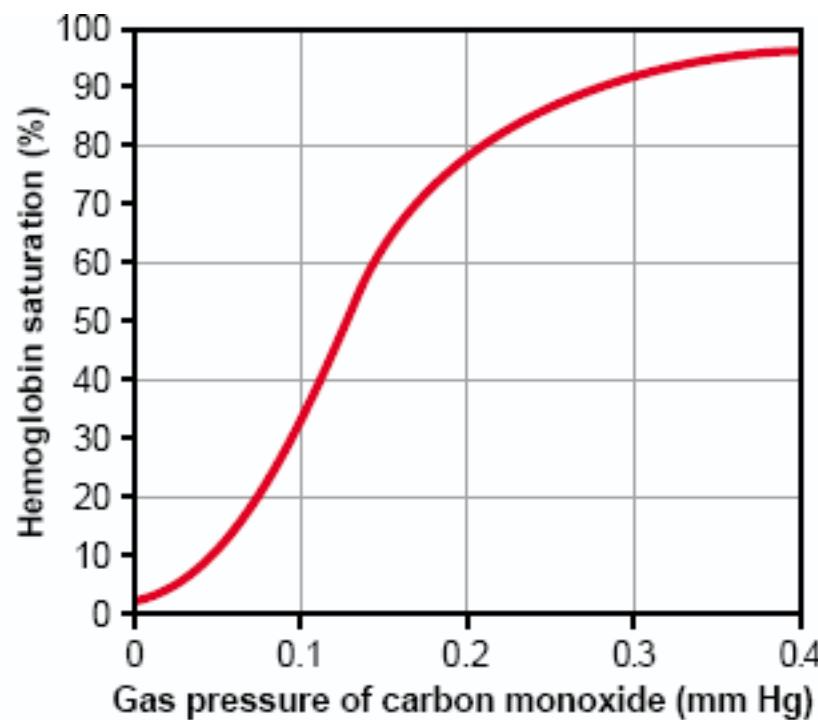
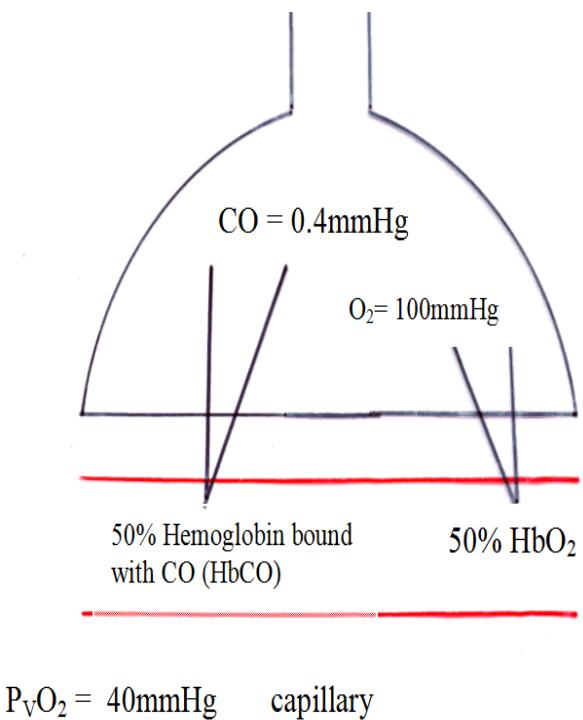
❖ The blood O₂ content is reduced but PO₂ may be normal
✓ SpO₂ consistently overestimates O₂ saturation in the presence of COHb

❖ This makes exposure to CO especially dangerous
✓ The person can be disoriented & unconscious before become aware of the danger

- **CO poisoning**

Fig. CO–Hb dissociation curve.

Note the extremely low CO pressures at which CO combines with Hb.



Acute poisoning results in

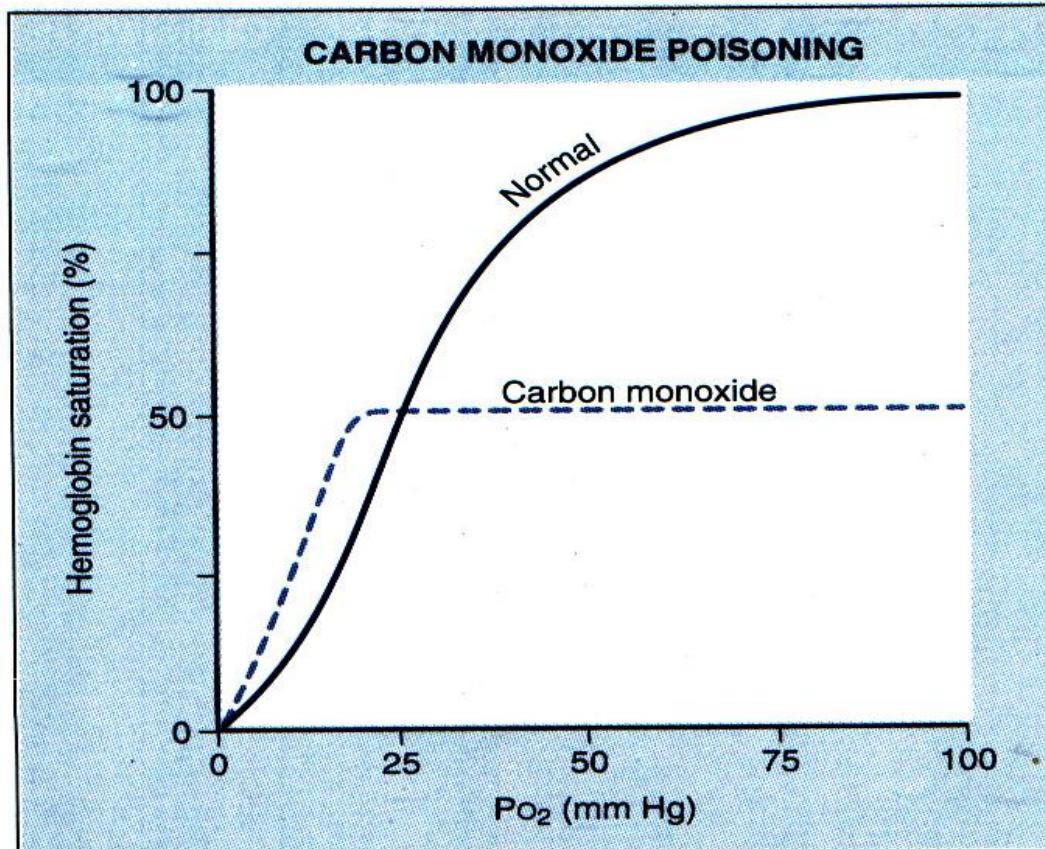
- ✓ headache, N-V, mental confusion and agitation.

Severe toxicity causes

- ✓ CVS : myocardial ischemia, ventricular arrhythmias, pulmonary edema,
- ✓ metabolic: profound lactic acidosis.
- ✓ CNS: confusion, seizures, syncope and may progress to coma, and death.

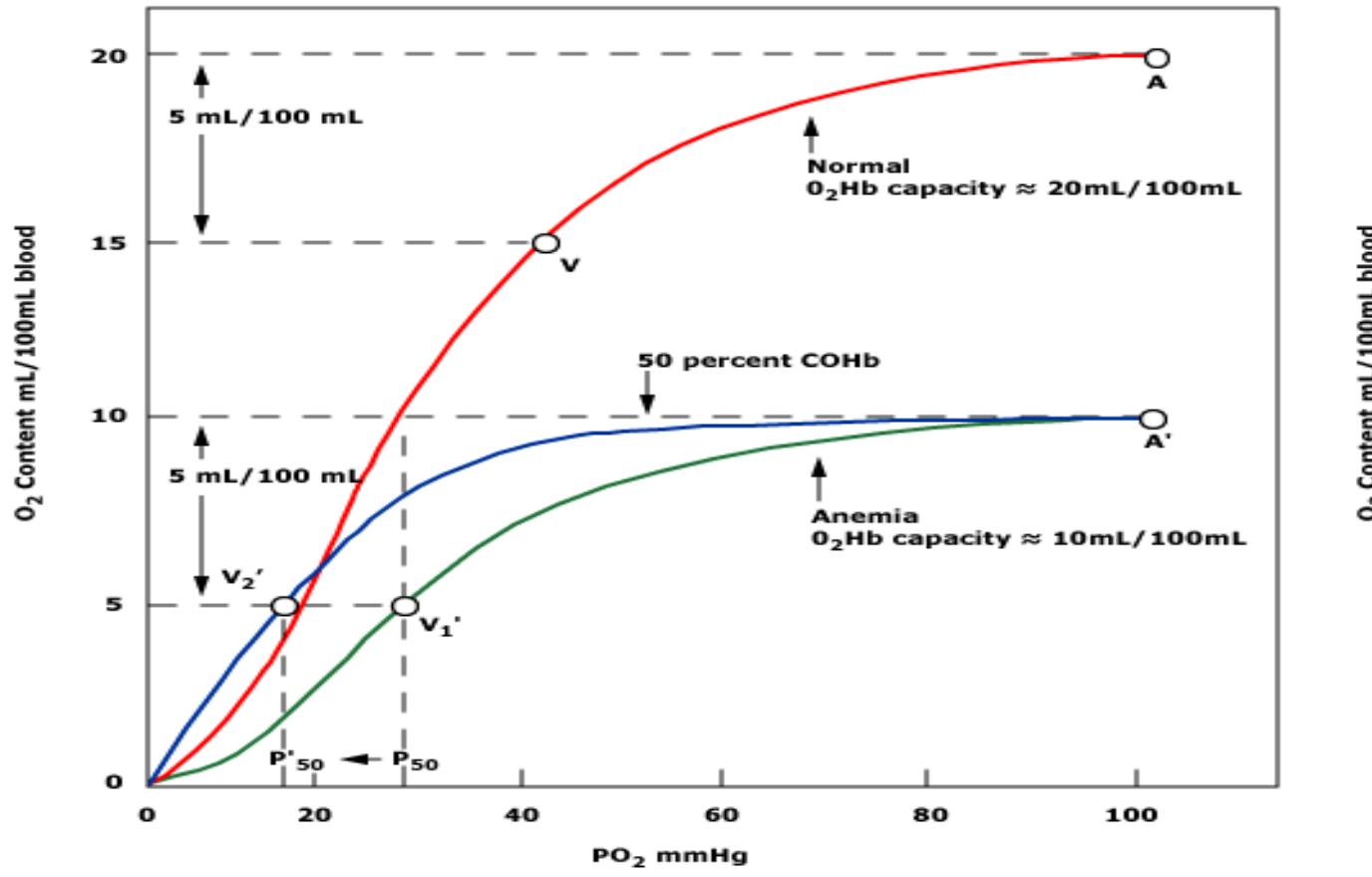
Mgt: prompt removal from the source of CO and institution of high-flow oxygen by face mask
If comatose: should be intubated without delay and mechanically ventilated with 100% O₂

- ✓ In the presence of CO, O₂ can't bind to heme group that are bound to CO
- ✓ CO also causes left shift, because heme not bound to CO have increased affinity for O₂ $\Rightarrow P_{50}$ decreased, and unloading becomes difficult.



- ❖ Once CO binds to the heme moiety of Hb,
 - ✓ an allosteric change greatly diminishes the ability of the other three O₂ binding sites to off-load O₂ to peripheral tissues.
 - ✓ This results in a deformation and left shift of the oxy-Hb curve, and compounds the impairment in tissue O₂ delivery

Fig. Effect of carbon monoxide on the oxy -Hb dissociation curve



- Red curve: the normal relationship between arterial (A) and venous (V) oxygen content.
- In general, a difference in arterial and venous oxygen content of 5 mL per 100 mL blood is expected at rest.
- Green line : the effect of a 50% decrease in Hb concentration, which decreases arterial (A') and venous (V'_1) oxygen content but does not change the partial pressure at which hemoglobin is 50% saturated (P_{50}).
- blue curve: the effect of 50% COHb, which both decreases O₂ carrying capacity (A') and impairs peripheral unloading of O₂ from Hb under conditions of low oxygen tension (V'_2), shifting P_{50} to the left (P'_{50}).
- These changes result in profound reduction in both O₂-Hb saturation and delivery of O₂ to peripheral tissues.

Transport of CO₂ in the Blood

- CO₂ - transported from the body cells back to the lungs as:
 - 1 - Bicarbonate (HCO₃⁻) - 70%
 - $\text{CO}_2 + \text{H}_2\text{O} \Rightarrow \text{H}_2\text{CO}_3 \Rightarrow \text{HCO}_3^- + \text{H}^+$
 - By action of the enzyme in RBCs called **carbonic anhydrase**
 - The HCO₃⁻ diffuses into plasma as Cl⁻ diffuse into the cell
 - This is called **Cl⁻ shift** in systemic blood & reverse Cl⁻ shift in pulmonary blood: $\Rightarrow [\text{Cl}^-]_{\text{venus RBC}} < [\text{Cl}^-]_{\text{arterial RBC}}$
 - Effected by HCO₃⁻ - Cl⁻ exchanger protein
 - The H⁺ combines with Hb in RBCs
 - 2 - **carbaminohemoglobin** - 23%
 - The amount of CO₂ carried as carbamino compounds is inversely related to the amount of O₂ bound to Hb
 - even though CO₂ & O₂ do not bind to the same site

CO_2 Dissociation Curve

- CO_2 Combines loosely with Hb to form CO_2Hb (carbamino-Hb).
 - easily be released in the alveoli
- The CO_2 curve is not sigmoid unlike that of O_2 :
 - Blood has a much greater capacity for carrying CO_2 than for O_2 (linear relationship between pCO_2 and its combination)
- ❖ The CO_2 dissociation curve is considerably steeper and linear than that of O_2 in the range of 40 to 50 mm Hg

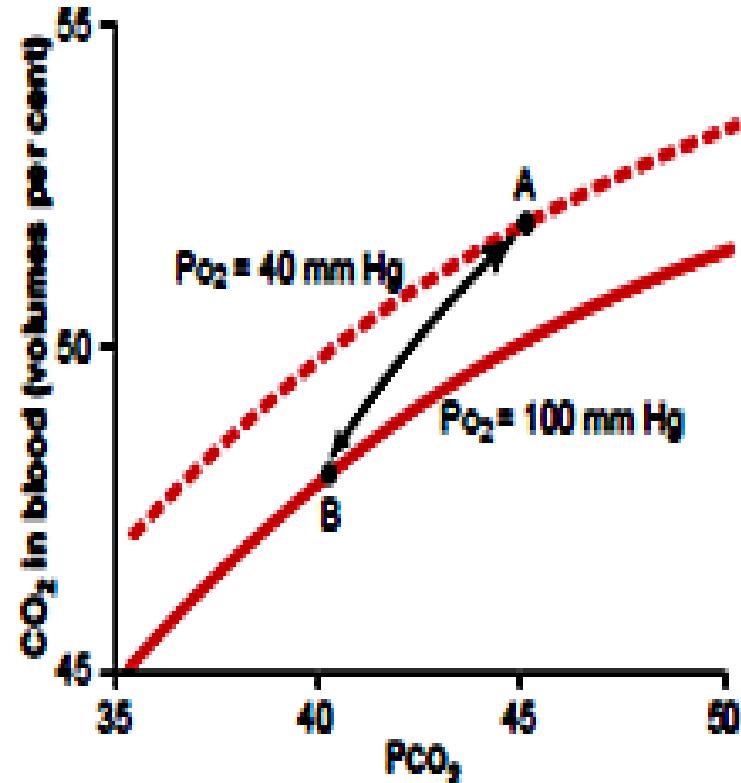


Fig. CO_2 dissociation curve

- 3 - Dissolved in the plasma - 7%
- CO_2 diffuses in to blood \Rightarrow dissolved in the plasma

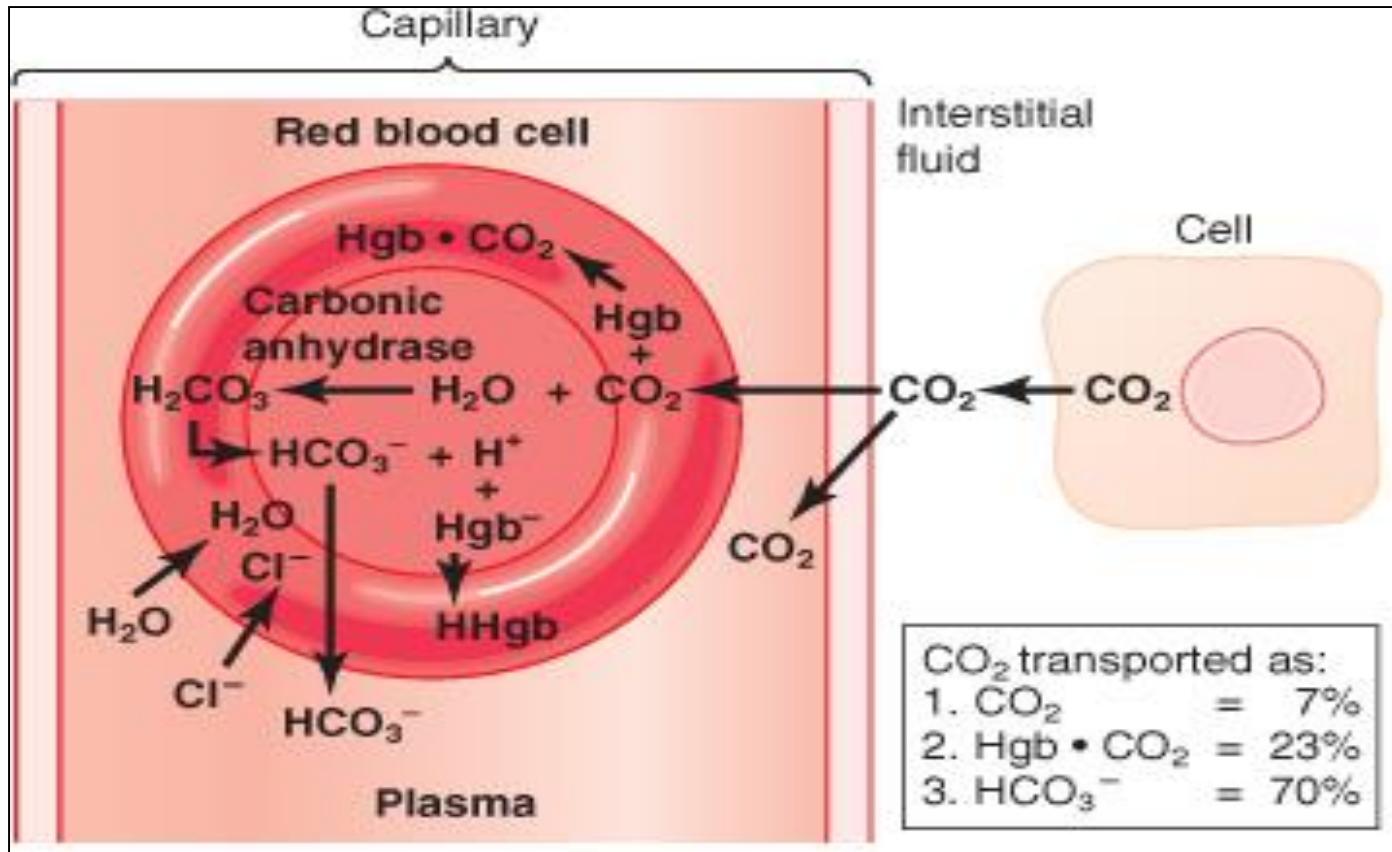
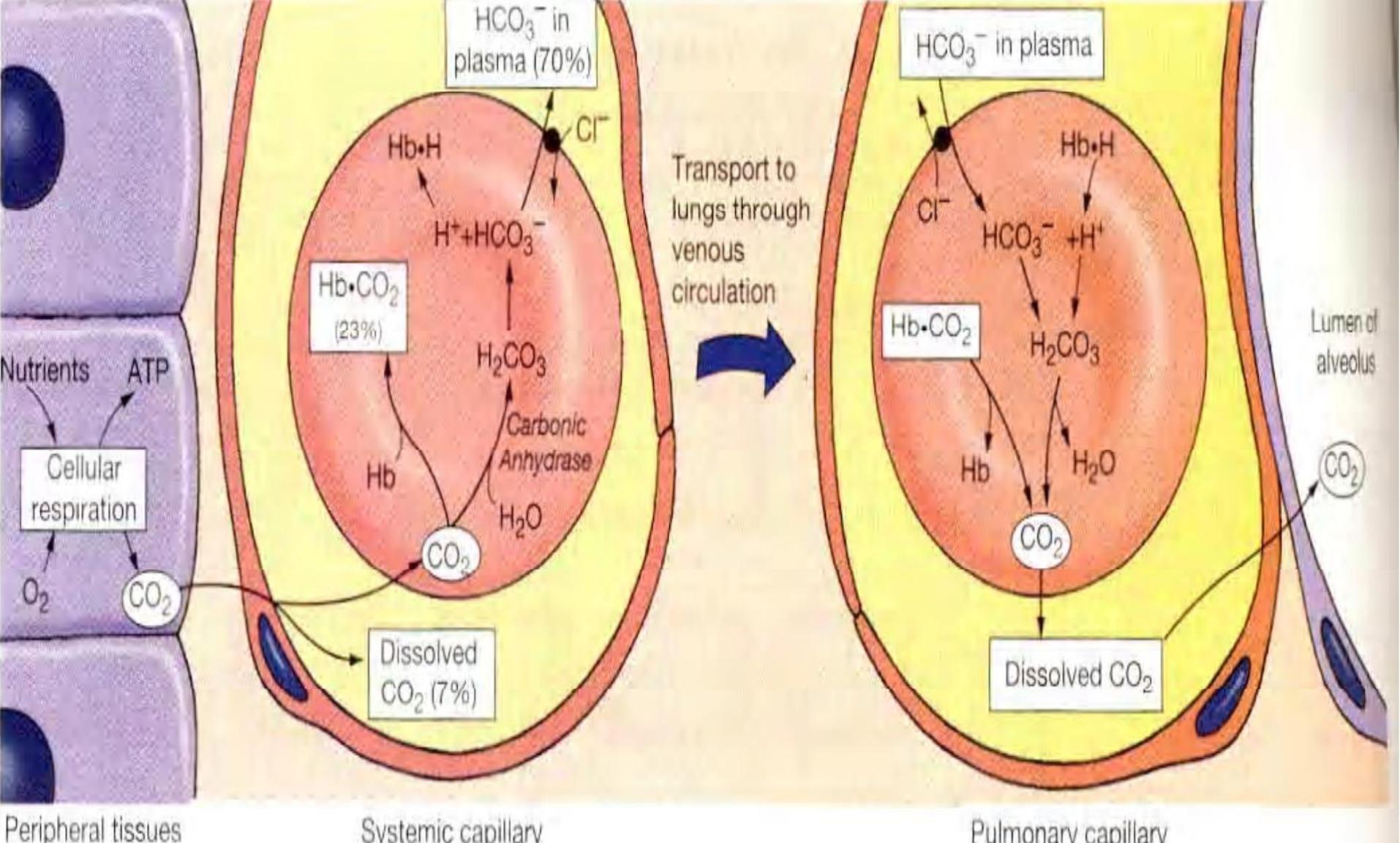


fig. Transport of Carbon Dioxide in the Blood



• Fig. Transport of CO_2 in the blood

Control of Respiration

- Your respiratory rate changes, for example:
 - when active, your respiratory rate goes up;
 - when less active, or sleeping, the rate goes down.
- Even though the respiratory muscles are voluntary, you can't consciously control them when you're sleeping.
- So, how is respiratory rate altered & how is respiration controlled when you're not consciously thinking of it?

Main parts of respiratory centers:

A. MEDULLA - this part is called medullary respiratory center.

- This center has two neuronal clusters:
- 1. **Dorsal respiratory group of neurons (DRG)**
- Most of its neurons are located in nucleus of tractus solitarius
 - This nucleus is the sensory termination of vagal & glossopharyngeal nerves
 - These nerves transmit signal from :
 - peripheral chemoreceptors, baroreceptors, & other receptors in the lung
- DRG is the center for inspiration & controls the rhythm
 - contains mainly I neurons (inspiratory neurons)
 - its descending fibers terminate on motor neurons supplying the inspiratory muscles

- These I neurons are believed to **display pacemaker activity**;
 - repetitively undergoing self induced APs similar to SA nodes of the heart.
- I neurons fire AP → motor neurons supplying inspiratory muscles fire AP
↓

Inspiratory muscles contract → inspiration starts.

 - When they cease firing APs ⇒ inspiration ends and expiration occurs
 - Expiration ends when they once again fire AP.

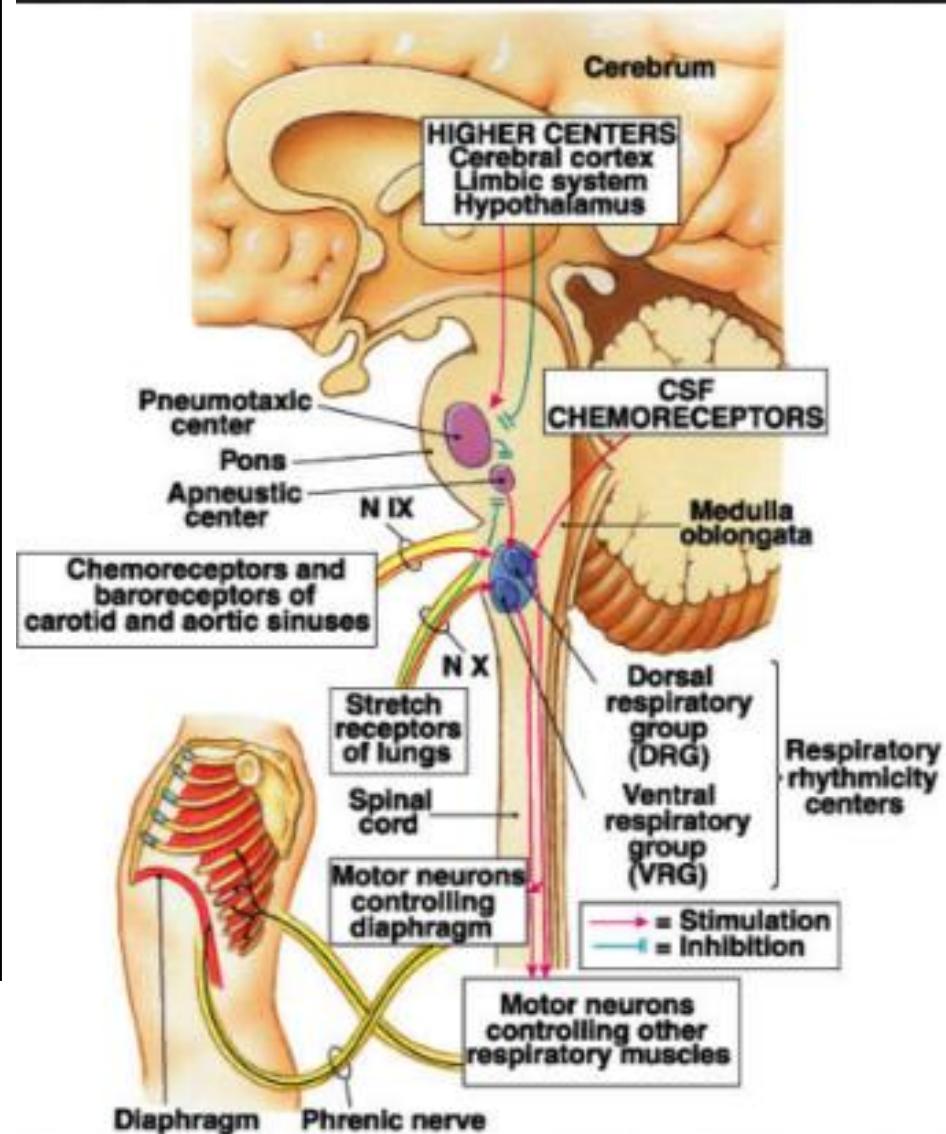
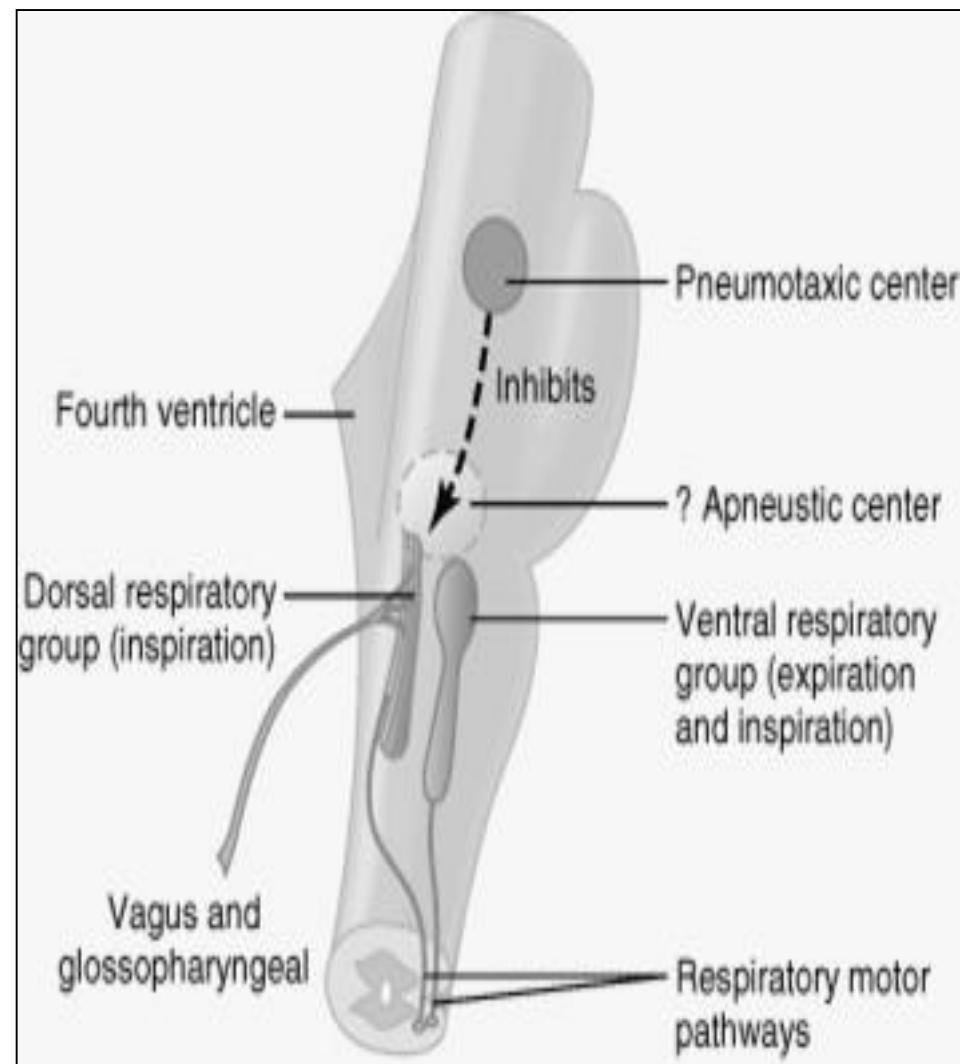
2. Ventral respiratory group of neurons (VRG)

- situated in the ventral part of medulla
- The neurons are found:
 - Rostrally in Nucleus ambiguus
 - Caudally in Nucleus retroambiguus
- It contains:
 - mainly E neurons (expiratory neurons)
 - remain inactive during normal quiet breathing
 - some I neurons

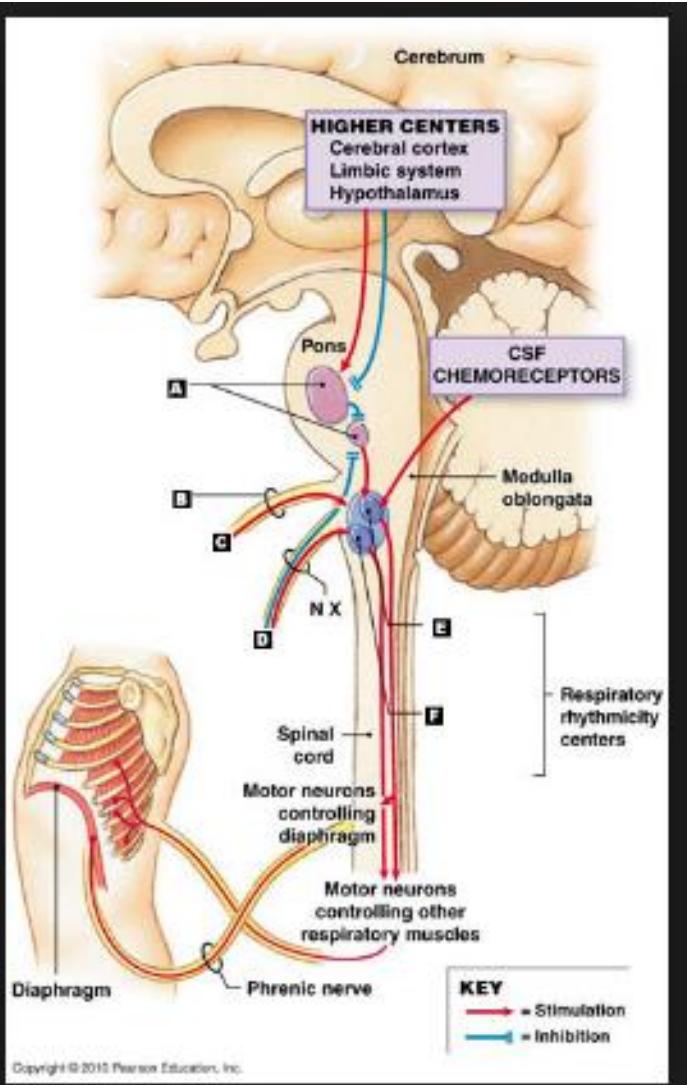
- This region is called 'overdrive' mechanism
 - Acts only during periods when demands for ventilation are increased.
- During increased ventilation:
 - the E neurons stimulate motor neurons supplying expiratory muscles
 - I neurons stimulate motor neurons supplying inspiratory muscles

B. PONS - contain 2 centers

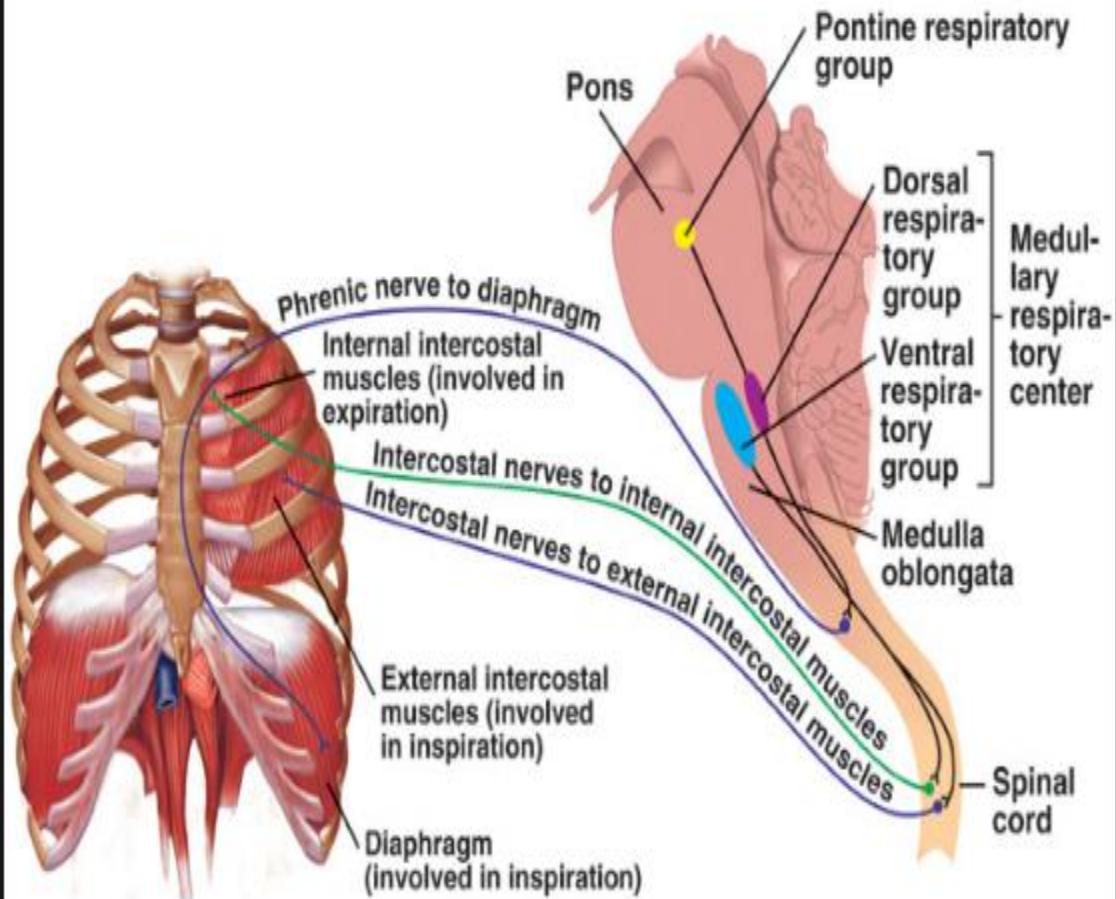
- 1. **Apneustic center**- located in lower pons
- stimulate DRG of neurons or the I neurons \Rightarrow promote inspiration
- 2. **Pneumotaxic center** - located in the upper pons
- inhibits the DRG of neurons or the I neurons
 - **This is to limit or shorten the duration of inspiration [switch off]**
 - When the signal is strong, inspiration can last in 0.5 sec
 - When the signal is weak, inspiration can last 5sec or more
- Limitation of inspiration also shortens expiration & the entire period of respiration
 - A strong pneumotaxic signal \Rightarrow can \uparrow BR to 30 to 40 breaths/minute
 - A weak signal may reduce the rate to only a few breaths/minute
- It also inhibits the apneustic center to inhibit or limit inspiration



• Fig. Centers of respiration



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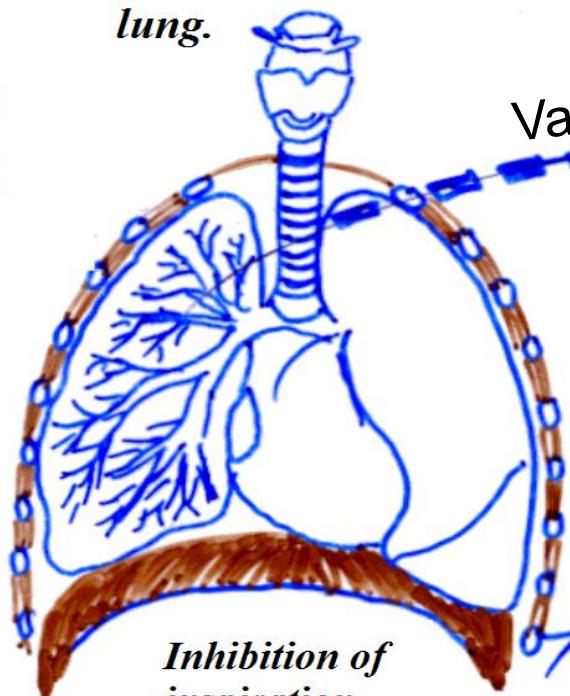


The Hering-Breuer inflation reflex - limits inspiration

- Walls of bronchi & bronchioles contain stretch receptors
 - respond to stretch of lung tissue ⇒ signal passes via vagi to DRG
- stretching of lung tissue during inspiration due to over expansion
 - ↓
 - Stretch receptors are stimulated
 - ↓
 - Impulse through vagus afferent to DRG (inhibition of DRG)
 - ↓
 - Inhibition (limiting) of inspiration, like the pneumotaxic center
 - ↓
 - inspiration stops & expiration starts
 - Prevents over inflation of the lungs

HERING – BREUER INFLATION REFLEX

*Receptors within
airway smooth
muscle stimulated by
distention of the
lung.
(TV = > IL)
as during
exercise*

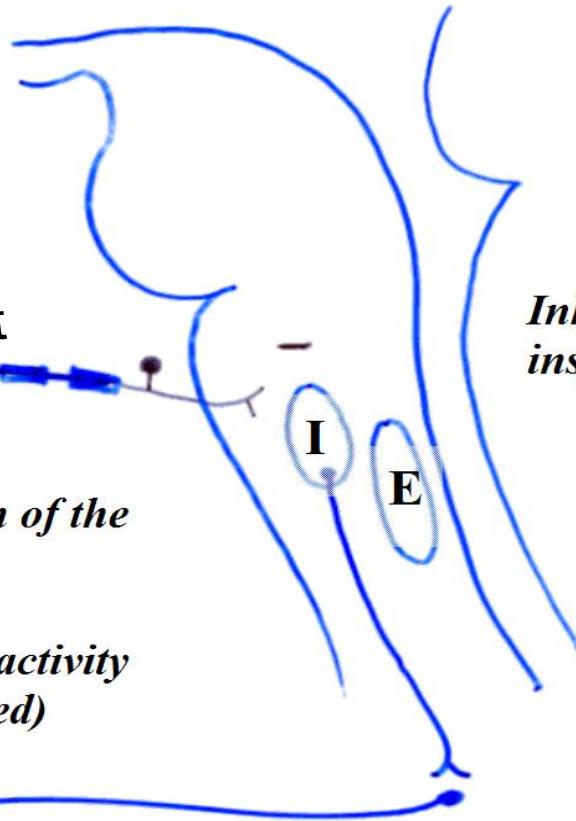


Vagus afferent

*Distention of the
lung
(receptor activity
is sustained)*

Inhibition of
inspiration

(prevents over inflation of lungs)



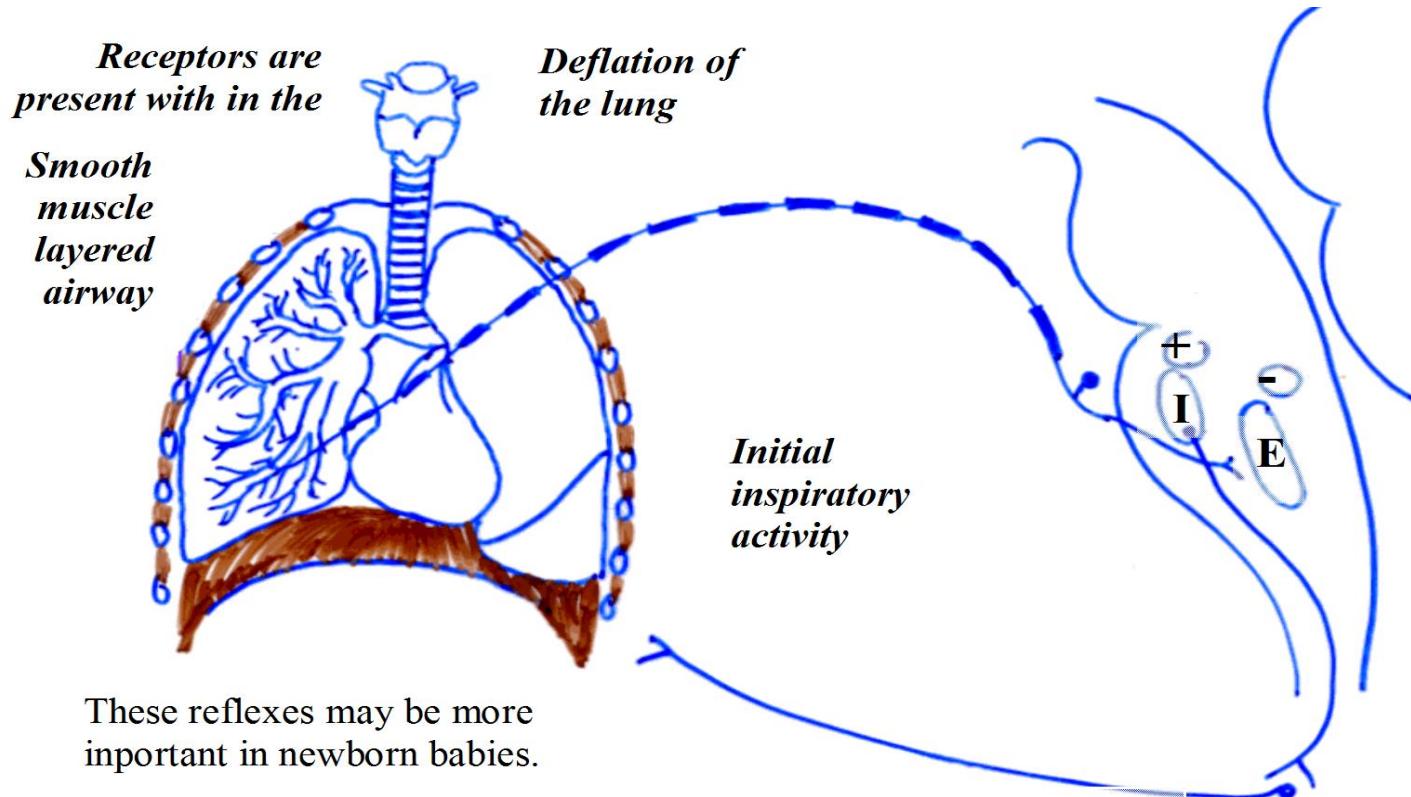
*Inhibition of
inspiration*

Increasing of
respiratory
frequency

The negative feed back from the highly stretched lungs themselves helps cut inspiration before the lungs become over inflated.

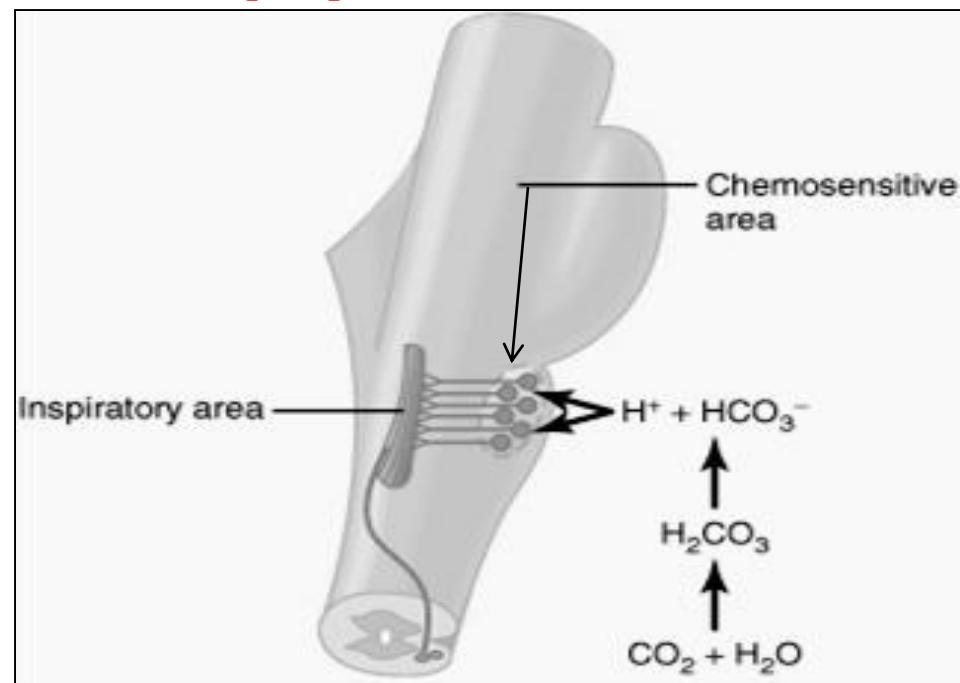
Hering-Breuer deflation reflex - the reverse of inflation reflex

- When DRG is inhibited \Rightarrow inspiration stops & expiration starts
 - \Rightarrow As the stretching of lung is abolished during expiration
 - \Rightarrow deflation of lung \Rightarrow stimulates DRG \Rightarrow promotes inspiration

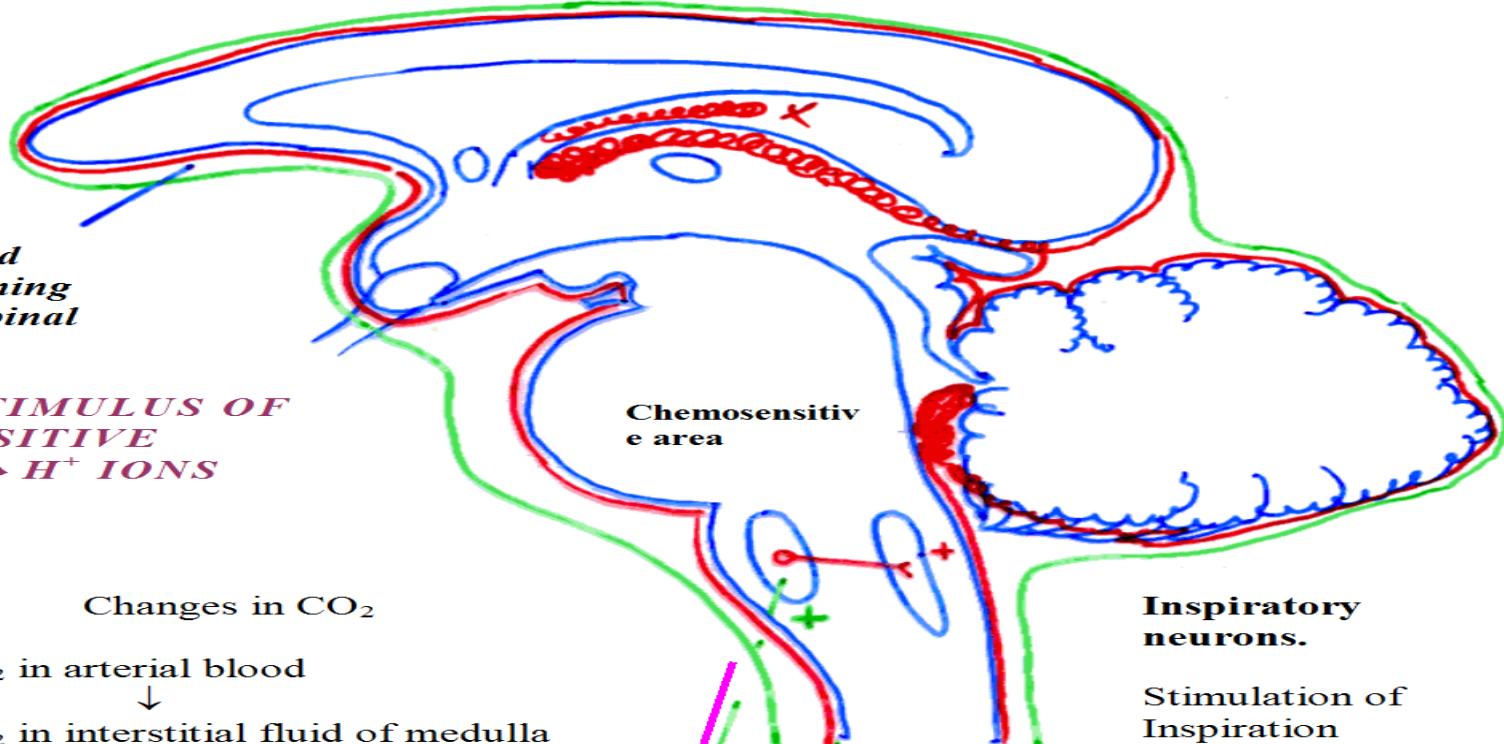


Chemical Control of Respiration

- The ultimate goal of respiration is to maintain proper concentrations of O₂, CO₂, and H⁺ ions in the tissues
- thus, respiratory activity is highly responsive to changes in each of these
 - Their changes are detected by chemoreceptors
- Two types of chemoreceptors:
 - 1. **central chemoreceptors** - located in the deeper medulla
 - Main stimulants are ↑ PCO₂ induced [H⁺]
 - H⁺ can not cross BBB and blood CSF barrier
 - Enters in the form of CO₂ and dissociate to H⁺
 - Hypoxia has no significant effect



EFFECTS OF BLOOD CO₂ ON STIMULATING THE CENTRAL CHEMORECEPTORS

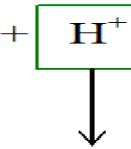


PRIMARY STIMULUS OF CHEMOSENSITIVE NEURONS → H⁺ IONS

Changes in CO₂

↑ PCO₂ in arterial blood
↓
↑ PCO₂ in interstitial fluid of medulla
↓
↑ PCO₂ in the CSF

CO₂ + H₂O → H₂CO₃ → HCO⁻₃ + H⁺
(immediate reaction)
according to the law of mass action



More H⁺ ions released into medullary chemosensitive area

The central chemoreceptors do not monitor CO₂ itself; however, they are sensitive to changes in CO₂-induced H⁺ concentration in the brain ECF that bathes them.

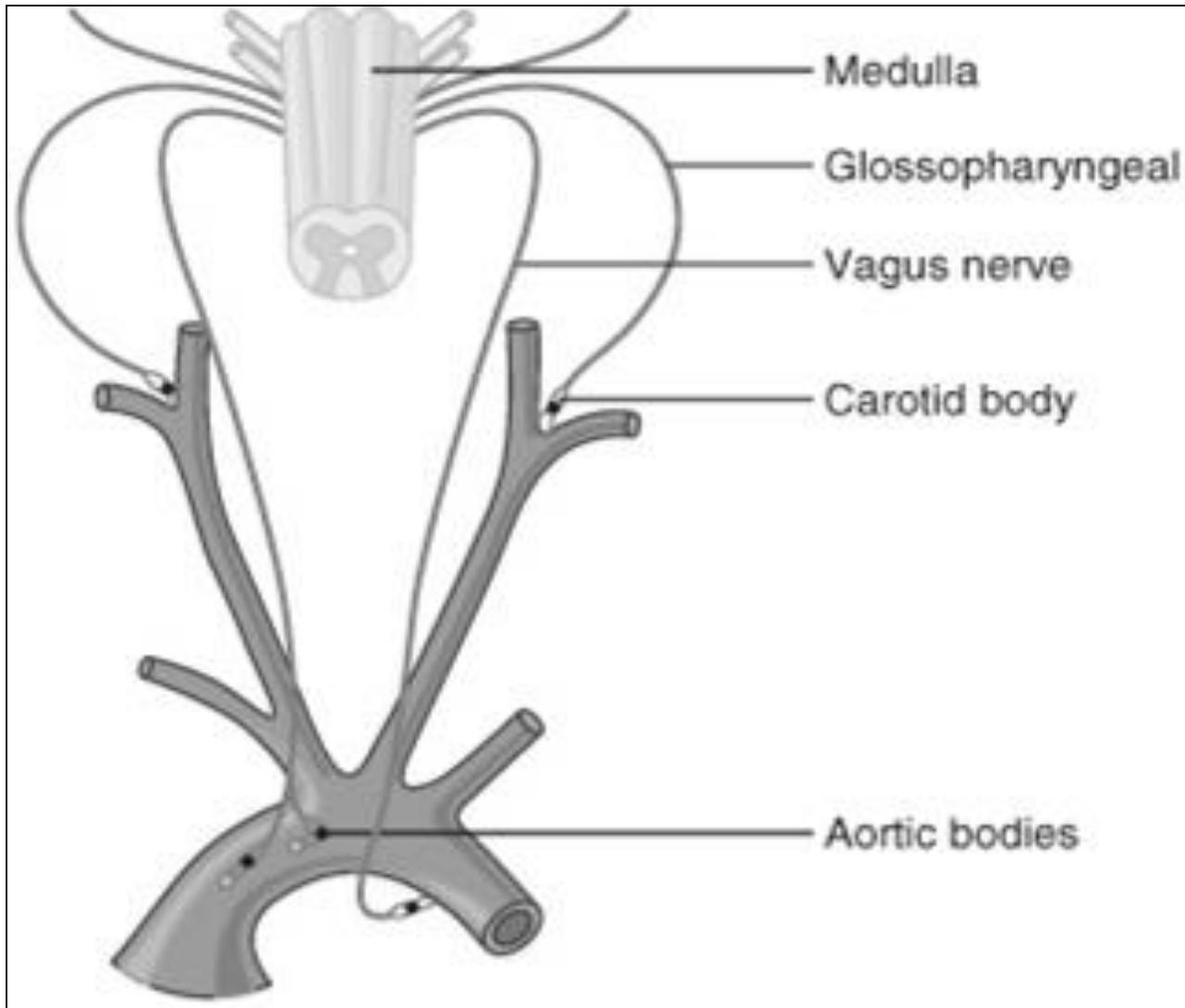
The powerful influence of the central chemoreceptors on the respiratory center is responsible for the inability to deliberately hold breath for more than about a minute.

2. peripheral chemoreceptors - located in aortic & carotid bodies

- Most chemoreceptors are in *carotid bodies*, few in *aortic bodies*
- The *carotid bodies* - in the bifurcations of common carotid arteries
 - Their afferent nerve fibers pass via glossopharyngeal nerves
⇒ to the dorsal respiratory area of the medulla

†

- The *aortic bodies* - located in aortic arch;
 - their afferent nerve fibers via the vagi
↓ ↓
to dorsal medullary respiratory area
- Potent stimulant is hypoxia
- Act mostly on inspiratory center (DRG)



- Fig. Peripheral chemoreceptors

J- receptors

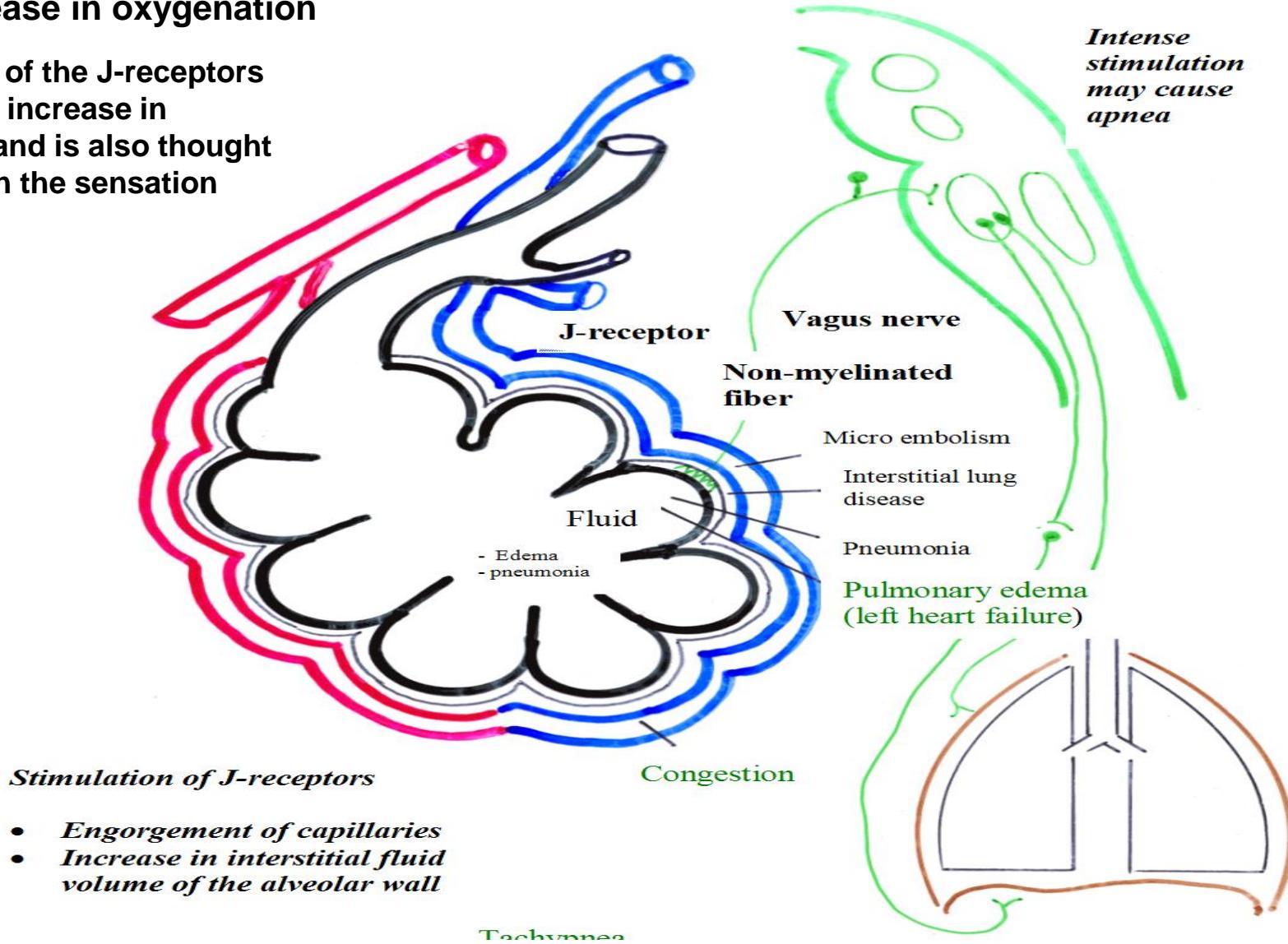
- Are sensory nerve endings of the vagus
- Located in the alveolar wall at juxta position to pulmonary capillaries
- Stimulated when pulmonary capillaries are engorged with blood or pulmonary edema (CHF)
- The stimulation of J-receptors produce a reflex response characterized by dyspnea
- Physiological function is not clearly elucidated
- However, responsible for hyperventilation in patients affected by pulmonary congestion and heart failure

J (juxtagapillary) receptors (or pulmonary C-fiber receptors)

LUNG RECEPTORS: J RECEPTORS

J-receptors respond to events which cause a decrease in oxygenation

The stimulation of the J-receptors causes a reflex increase in breathing rate, and is also thought to be involved in the sensation of dyspnea



The control of breathing during sleep

- We spend 1/3rd of our lives asleep
- Sleep results in a general depression of breathing
- Responsiveness to stimulatory effects of CO₂ and H⁺ is reduced
- **Sleep apnea** - temporary arrest of breathing during sleep
 - Loud snoring & laborious breathing soon after falling asleep
- Can be caused by:
 - 1. Obstruction of upper pharyngeal muscles = **obstructive sleep apnea**
 - Obstruction can be worsened with excessive neck fat (obesity)
 - The most common form of sleep apnea
 - 2. Impaired CNS respiratory drive = **central sleep apnea**
 - Transient cessation of CNS drive to ventilatory muscles

Terminologies

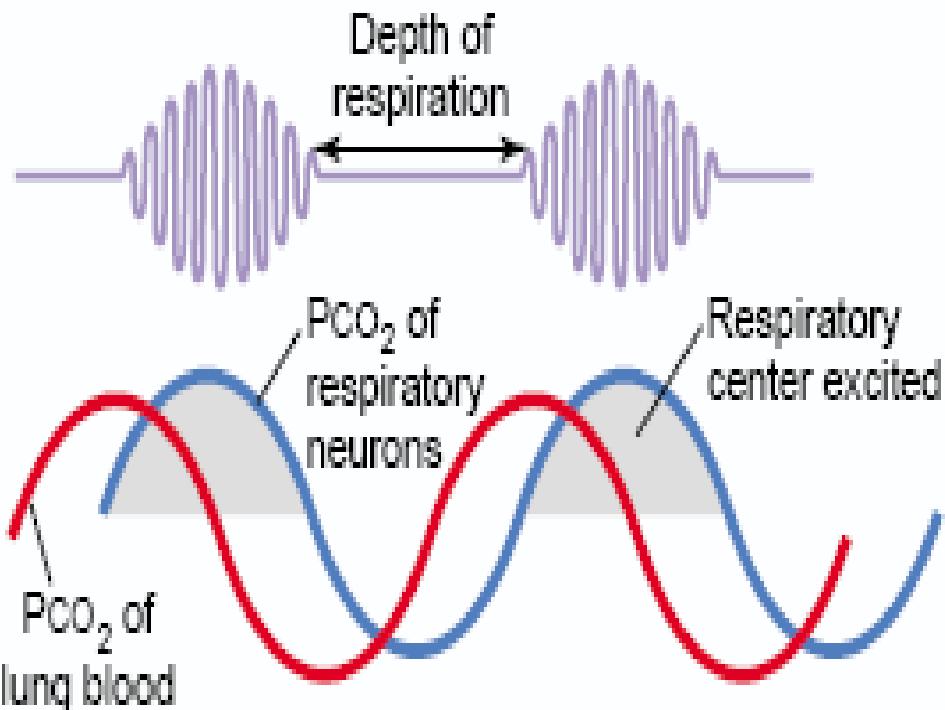
- Eupnea - normal respiration
- Terms used for some of altered patterns of respiration
- 1 **tachypnea** -increased rate of breathing
- 2. **Bradypnea** - decreased
- 3. **Polypnea** - rapid, shallow breathing; like panting in dogs
 - Only rate but not force of breathing increases significantly
- 4. **Hyperpnea** - ↑PV due to significant rise in rate or force of breathing, sometimes both with more in rate
- 5. **Apnea** - temporary arrest of breathing
- 6. **Kussmaul's breathing: rapid and deep breathing**
 - accompanied by a sigh; characteristic of acidosis (DKA)

- 6. **Hyperventilation** - ↑ in rate & force of respiration
 - Excessive ventilation → decreased PaCO₂ 35 mm Hg (hypocarbia, hypocapnea)
- 7. **hypoventilation** - Functionally inadequate ventilation
 - Produces increased PaCO₂ (hypercarbia, hypercapnia) 45 mm Hg
- 8. **dyspnea** - difficult breathing
 - **Rapid, shallow and labored breathing with shortness of breath.**
Subjective sensation of shortness of breath or difficulty breathing
 - physiologic demand for ventilation > the patient's ability to respond
- 9. **periodic breathing** -abnormal rhythm of breathing
 - Eg. **Cheyne-Stokes breathing**
 - Characterized by slowly waxing & waning breathing

 - Amplitude ↑gradually (wax)⇒ reach max ⇒↓gradually (wane)

Fig. Cheyne-Stokes breathing: the mechanism;

- **Hyperpneic period**
 - $\uparrow \text{PO}_2, \downarrow \text{PCO}_2$
 - ↓
- depression of ventilation as this blood reaches brain
 - ↓
- **Apneic period** [$\downarrow \text{PO}_2, \uparrow \text{PCO}_2$] $\Rightarrow \uparrow \text{PCO}_2 \Rightarrow \uparrow \text{H}^+$ in the brain
 - \Rightarrow stimulates ventilation
 - ↓
- **Hyperpneic period** [$\uparrow \text{PO}_2, \downarrow \text{PCO}_2$]
- The cycle repeats over and over again
- Common in patients suffering from cardiac failure
 - Blood flow is slow \Rightarrow longer delay in transporting blood from lung to brain



Hypoxia- reduced O₂ supplies to the tissues, 4 different forms:

A. Hypoxic hypoxia

- is due to poor availability of O₂ for diffusion to the pulmonary capillaries.
 - Eg. At high altitude the PO₂ is low:
 - at sea level Patm. = 760mmHg=> PO₂ = **159.5 mmHg**
 - at mount Everest Patm = 253mmHg=>PO₂= **53mmHg.**
 - At high altitude the % composition of O₂ remains the same
 - but the PO₂ changes as the atmospheric P changes
- Other reason for hypoxic hypoxia can be
 - hypoventilation, neuromuscular disorders, airway abnormalities...

HYPOXIC HYPOXIA

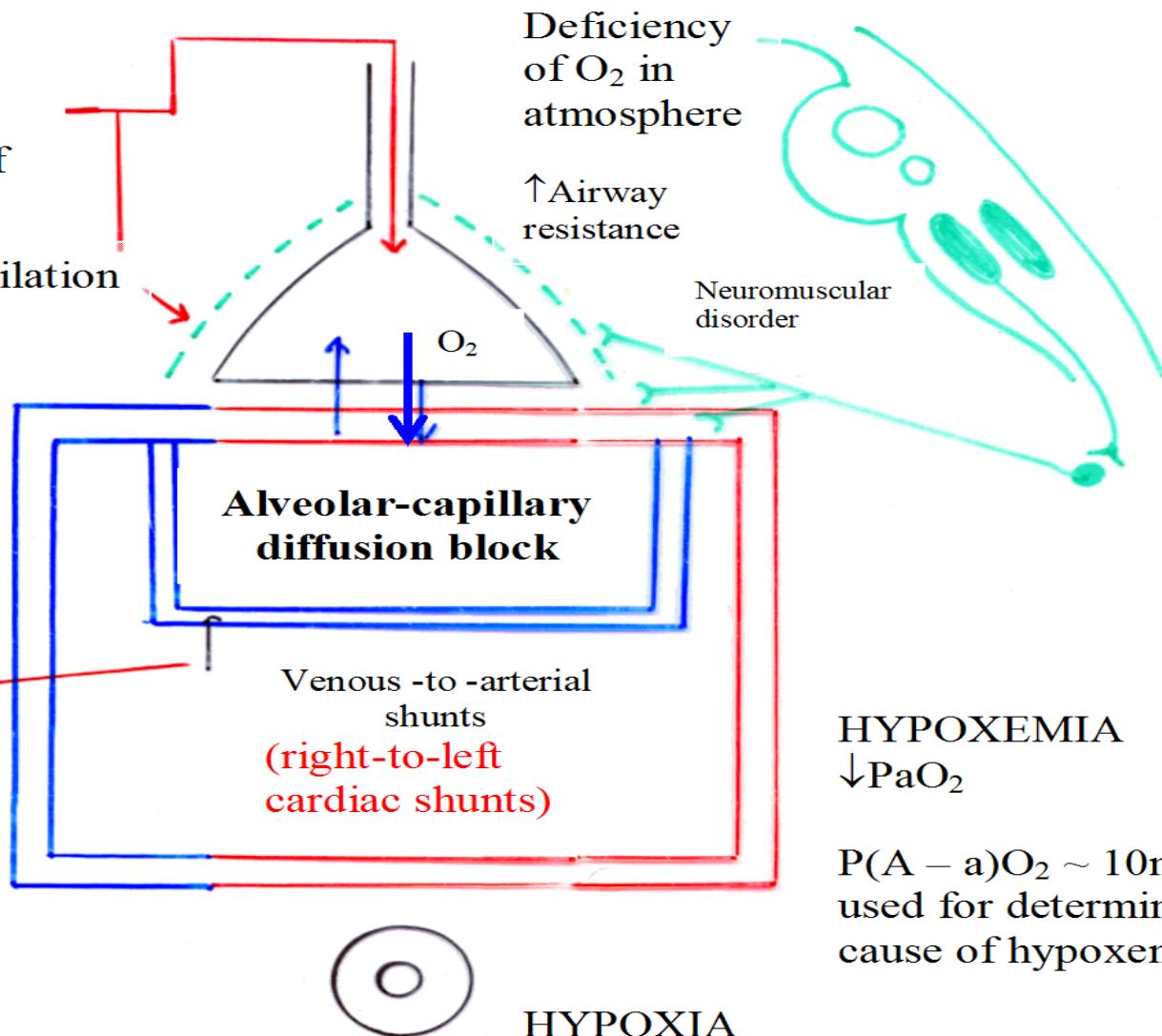
It includes all those conditions in which not enough O₂ gets to the alveoli

Causes:

Inadequate oxygenation of the lungs.

Hypoventilation

- Neuromuscular disorder
- ↑airways resistance
- ↓Lung compliance
- uneven V: P imbalance



Rt to Lt cardiac shunt

- atrial septal defects
- Ventricular septal defects
- PDA
- Tetralogy of F.

HYPOXEMIA
↓PaO₂

P(A – a)O₂ ~ 10mmHg
used for determining the cause of hypoxemia

Compensation Of hypoxic hypoxia

- stimulation of peripheral chemoreceptors by oxygen deficiency
 - ↓
Increased pulmonary ventilation, ↓PACO₂, ↓PACO₂
- stimulation of erythropoiesis.
 - ↓
↑RBC numbers, ↑Hct, ↑Hb. concentration
- Rightward shift of oxygen-hemoglobin dissociation curve by high levels of red cell 2,3-DPG

B. Anemic hypoxia

- is due to quantitative & qualitative deficiency of Hb
 - ↓
- as a result the O₂ carrying capacity of the blood is reduced.
- Cyanosis is rare, b/c it is difficult for there to be >5g of reduced hemoglobin to produce color

C. Stagnant hypoxia

- due to poor velocity of blood (sluggish circulation).
- For example:
 - ↓ CO resulting from cardiac failure, or
 - ↑ vascular obstruction
 - due to thrombosis, embolism, etc.

D. Histotoxic hypoxia

- due to lack of ability of the peripheral tissues to pick up O₂ from the feeding capillaries.
 - Cause can be poisoning eg. Cyanide, other metabolic poisons
 - ↓
 - inhibition of oxidative processes (eg. Cytochrome oxidase)



Treatment for hypoxia - Oxygen therapy

- O₂ can be administered:
 - 1. by Placing the patients head in 'tent' containing O₂
 - 2. By allowing the patient to breath O₂ from a mask (Face mask)
 - 3. By allowing the patient to breath O₂ from intranasal tube(Nasal prong)
- O₂ therapy may be the best treatment for hypoxia
- But it is not equally effective in all types of hypoxia:
 - 100% useful in hypoxic hypoxia
 - Moderately effective (70%) in anemic hypoxia
 - Usefulness is less than 50% in stagnant hypoxia
 - Not useful at all in histotoxic hypoxia



❖ The value of O₂ therapy depends on the types of hypoxia

Indications for Oxygen Therapy

- **Hypoxemia**
 - Inadequate amount of oxygen in the blood
 - $S_pO_2 < 90\%$
 - $PaO_2 < 60 \text{ mmHg}$
- Excessive work of breathing
- Excessive myocardial workload

Goal of Oxygen Therapy

- Goal of therapy is to achieve SPO_2 of $>90\%$
- For documented COPD patients (Spo_2 88–92%)-($PaO_2=55-60 \text{ mmHg}$)
- As SPO_2 normalizes the patients vital signs should improve:
 - Heart rate should return to **normal for patient**
 - Respiratory rate should decrease to **normal for patient**

MEASUREMENTS OF O₂ LEVELS IN THE BODY: *Pulse Oximetry*

- Non-invasive monitoring technique that estimates the oxygen saturation of Hgb (SaO₂)
- May be used continuously or intermittently
- Must correlate values with physical assessment findings
- Normal SaO₂ values – 95 to 100%

Pulse Oximetry



❖ ABG is more accurate than Pulse oximeter because it measures the actual concentration of O₂ in the blood in relation to other blood gases



Normal Arterial Blood Gas

Value	Normal Range	Significance
pH	7.35 – 7.45	Reflects hydrogen ion concentration <ul style="list-style-type: none">• < 7.35 = acidosis• > 7.45 = alkalosis
PaCO ₂	35 to 45 mmHg	Partial pressure of CO ₂ in arterial blood <ul style="list-style-type: none">• < 35 mmHg = hypocapnia• > 45 mmHg = hypercapnia
PaO ₂	60 – 100 mmHg	Partial pressure of O ₂ in arterial blood <ul style="list-style-type: none">• < 60 mmHg = hypoxemia
HCO ₃ ⁻	22 to 26 mEq/L	Bicarbonate concentration in plasma

Nasal Cannula

- Used for low-medium concentrations of O₂
- Simple
- Can use continuously with meals and activity
- Flow rates in excess of 5L cause drying and irritation
- Depth and rate of breathing affect amount of O₂ reaching lungs
- adults □ 6 LPM
- infants/toddlers □ 2 LPM
- children □ 3 LPM
- FIO₂ is not affected by mouth breathing
- **1lit O₂=→FIO₂ = 4%**
 - **Total FiO₂: 21%+4%→FiO₂ =25%**
- **6 lito₂=→FiO₂ = 24%**
 - **Total FiO₂: 21%+24%→FiO₂ =45%**



Simple Face Mask

- Medium to high concentration of O₂
- Client exhales through ports on sides of mask
- Should not be used for controlled O₂ levels
- O₂ flow rate- 6 to 8L
- Can cause skin breakdown; must remove to eat.
- *1 lit O₂=→FIO₂ = 6%*
- *6 lit O₂=→Fio₂ 36%*
 - *21% + 36% =→Fio₂ = 57-60%*



Cyanosis

- The term *cyanosis* means bluish discoloration of the skin, lips, nails
- Its cause is excessive amounts of deoxygenated Hb in the skin blood vessels, especially in the capillaries.
- This deoxygenated Hb has an intense dark blue-purple color that is transmitted through the skin.
- In general, definite cyanosis appears:
 - whenever the arterial blood contains $> 5 \text{ g}$ of deoxygenated Hb/100 mL of blood.

Low oxygen levels in the blood cause the lips, fingers, and toes to look blue (cyanotic) children with Tetralogy of Fallot exhibit bluish skin during episodes of crying or feeding.



"Tet spell"



- Anemic person almost never becomes cyanotic
 - because there is no enough Hb for >5 g to be deoxygenated in 100 mL of arterial blood.
- Conversely, in a person with excess red blood cells,
 - Eg. polycythemia vera,
 - the excess Hb that become deoxygenated leads frequently to cyanosis,

Hypercapnia - an excess of CO₂ in the blood

- With most lung diseases, CO₂ accumulation in the arterial blood occurs concurrently with O₂ deficit
 - b/c both O₂ & CO₂ exchange b/n lung & atm are equally affected
- Sometimes no association with hypoxia
 - Eg. Hypoxia caused by too little O₂ in the air, too little Hb, or poisoning of the oxidative enzymes
 - affect only the availability of O₂ or use of O₂ by the tissues.

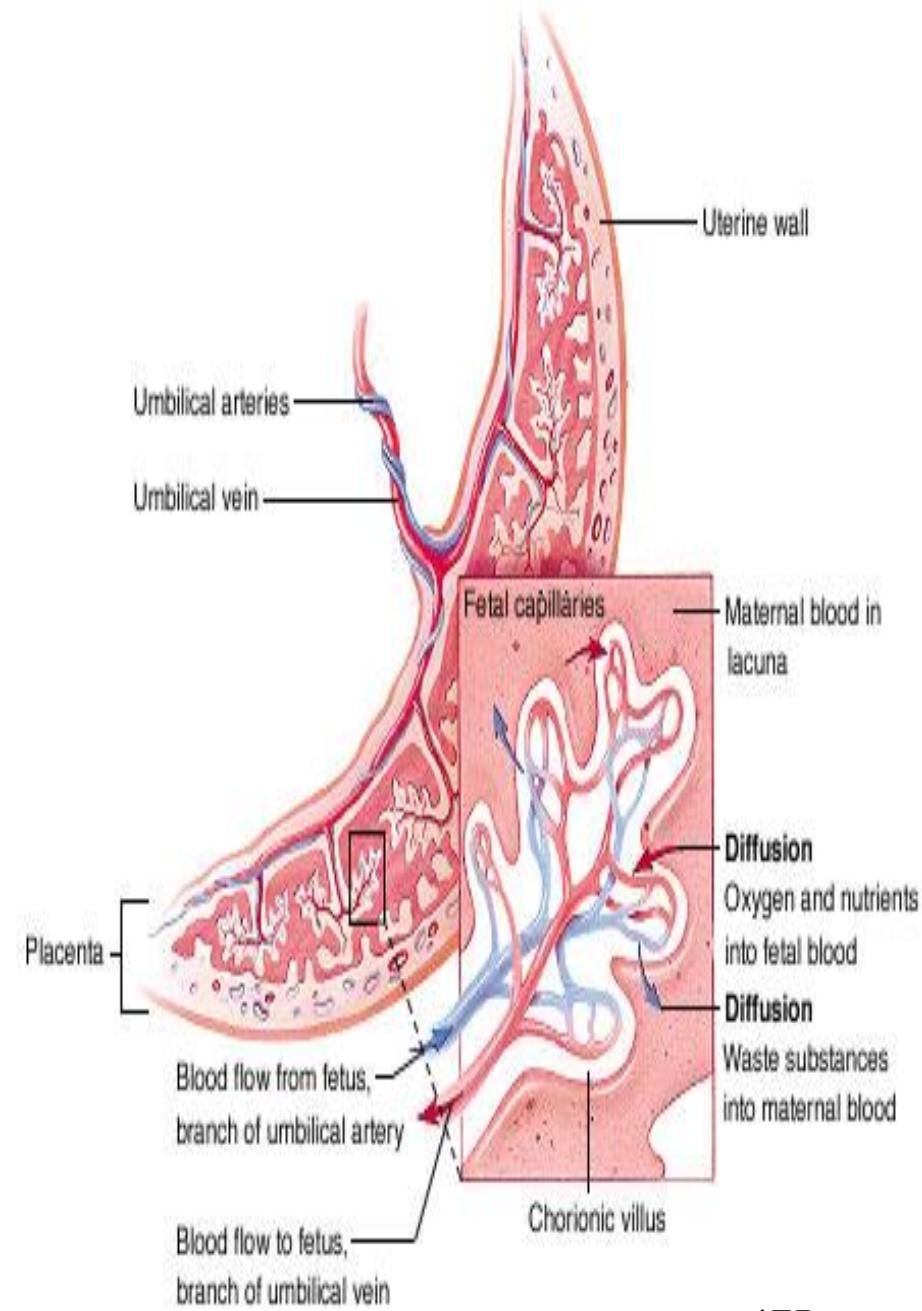
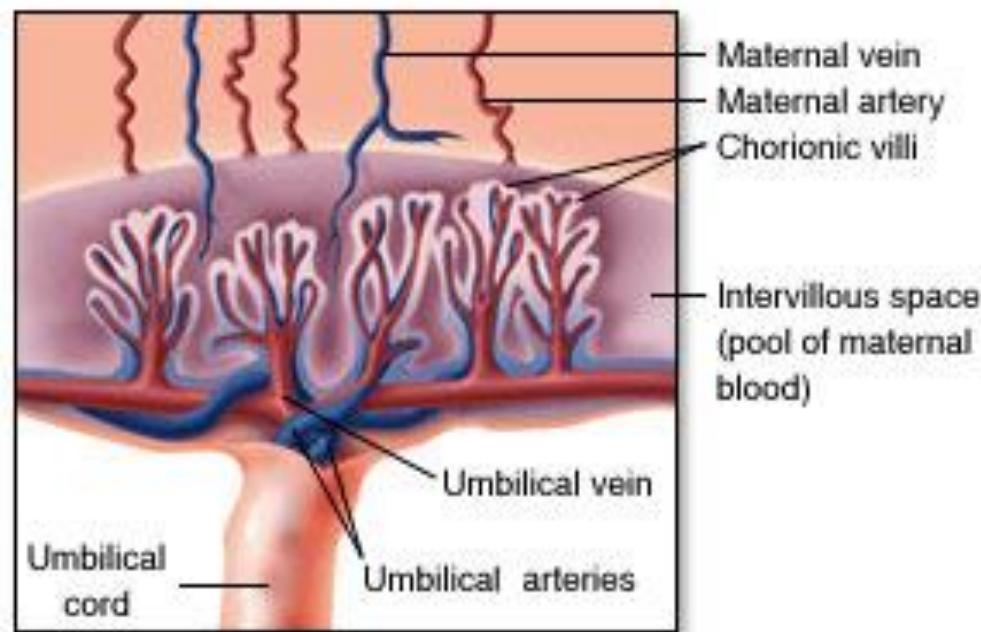
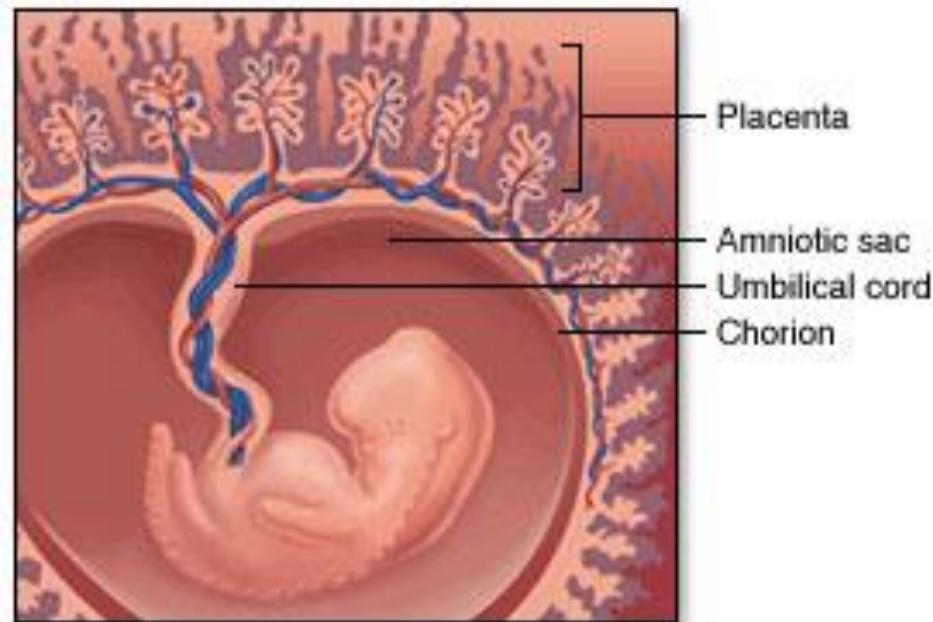
The fetal gas exchange



- Human fetus lives in watery world.
- Gas exchange occurs via placenta
- In fetal Hb, the two β chains are replaced by γ chains (γ_2, α_2)
- HbF has higher affinity for O_2 than HbA,
 - facilitating O_2 movement from mother to fetus.
 - This Hb is replaced with HbA within the first year of life

Placenta

- Is structure formed by the interdigititation of maternal & fetal tissue
- specialized for gas exchange using counter flow of blood in fetal and maternal capillaries
 - Blood does not mix



• Diffusion of O₂ Through Placental Membrane

Near the end of pregnancy:

✓ mean PO₂ of mother's blood in the placental sinuses is about 50 mm Hg

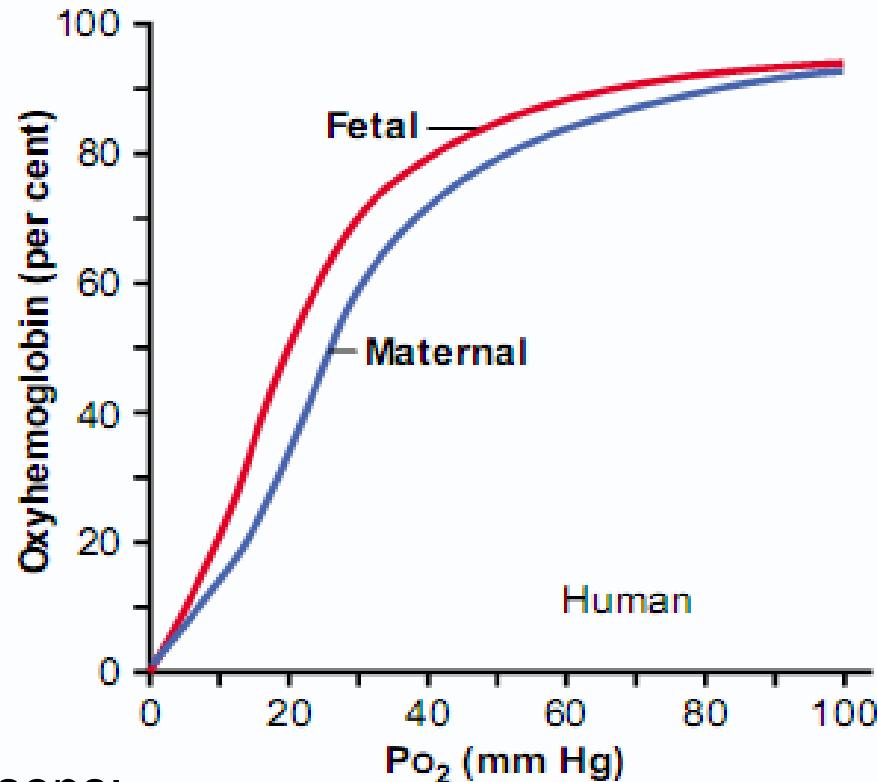
✓ mean PO₂ in the fetal blood **before** it becomes oxygenated in the placenta is about 30 mm Hg.

↓↓

✓ the mean PO₂ gradient for diffusion via placental membrane is about 20 mm Hg

✓ Yet the fetus obtain sufficient O₂: 3 reasons:

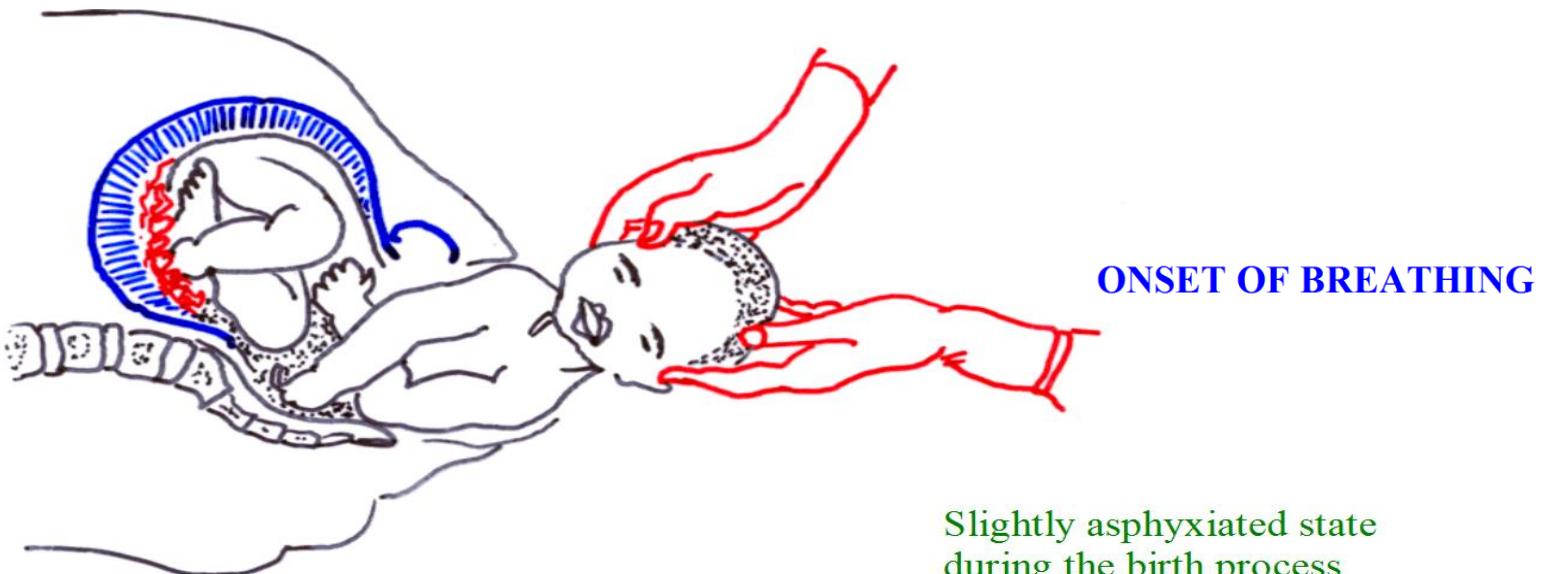
1. fetal Hb (α_2, γ_2) has high O₂ carrying cap (20 to 50% more than maternal Hb (α_2, β_2))
2. [fHb] is about 50% greater than that of the mother
3. strong Bohr effect (Hb can carry more O₂ at a low PCO₂)
 - fetal blood in the placenta has low PCO₂



- During birth, gas exchange ceases via placenta.



Drop in fetal blood pH \Rightarrow activation of breathing centers in brain
 \Rightarrow stimulate breathing muscles, and baby takes **first breath/first cry**



Loss of the placental connection with the mother and loss of metabolic support

Slightly asphyxiated state during the birth process



If breathing is delayed beyond ~5minutes, lesions develop in the thalamus, the inferior colliculi, and in other brain stem areas, thus affecting many of the motor functions of the body.

Breath Sounds

A. Normal breath sounds:

1. Bronchial breath sounds

- ✓ louder and higher in pitch,
- ✓ Expiratory phase longer than inspiratory;
- ✓ with a short silence between inspiratory and expiratory sounds.
- ✓ Over the manubrium, if heard at all
 - ❖ Abnormal if heard in the lung field anywhere else:
consolidation,

2. Broncho-vesicular sounds

- 2. Inspiratory and expiratory sounds are about equal in length,
- ✓ at times separated by a silent interval.
- ✓ Heard often in the 1st and 2nd interspaces anteriorly and b/n scapulae

3. Vesicular sound,

- ✓ soft and low pitched.
- ✓ Inspiratory sound is longer than expiratory
 - Inspiration continues without pause through expiration,
 - fade away about one third of the way through expiration.
- ✓ Heard over most of the lung fields

Characteristics of Breath Sounds

	Duration of Sounds	Intensity of Expiratory Sound	Pitch of Expiratory Sound	Locations Where Heard Normally
Vesicular*	Inspiratory sounds last longer than expiratory ones.	Soft	Relatively low	Over most of both lungs
Broncho-vesicular	Inspiratory and expiratory sounds are about equal.	Intermediate	Intermediate	Often in the 1st and 2nd interspaces anteriorly and between the scapulae
Bronchial	Expiratory sounds last longer than inspiratory ones.	Loud	Relatively high	Over the manubrium, if heard at all
Tracheal	Inspiratory and expiratory sounds are about equal.	Very loud	Relatively high	Over the trachea in the neck

If bronchovesicular or bronchial breath sounds are heard in locations distant from those listed, suspect that air-filled lung has been replaced by fluid-filled or solid lung tissue. See Table 6-5, Normal and Altered Breath and Voice Sounds (p. 240).

* The thickness of the bars indicates intensity; the steeper their incline, the higher the pitch.

B. Adventitious or added breath sounds

- **Crackles (Rales or crepitation):** pulmonary edema, early CHF, pneumonia
 - Discontinuous, intermittent, nonmusical, brief sounds
 - Heard more commonly with inspiration
 - Classified as fine or coarse
 - caused by air moving through secretions and collapsed alveoli
- **Wheeze-** Associated conditions: asthma, COPD
 - Produced when air flows through narrowed airways
 - Continuous, high pitched, musical sound, longer than crackles
 - Heard more with expiration, can be heard on inspiration
- **Rhonchi**
 - Similar to wheezes, but clear upon coughing
 - Low pitched, snoring quality, continuous, musical sounds
 - Implies obstruction of larger airways by secretions
 - Associated condition: acute bronchitis
- **Stridor:** Medical emergency requiring immediate attention
 - Intense Inspiratory musical wheeze
 - heard loudest over extra-thoracic airways; Can be heard without stethoscope
 - Suggests obstructed upper airway eg. Foreign body, croup, epiglottitis....

Adventitious Lung Sounds

DISCONTINUOUS SOUNDS (CRACKLES OR RALES) are intermittent, nonmusical, and brief—like dots in time

Fine crackles (· · · ·) are soft, high pitched, and very brief (5–10 msec).

Coarse crackles (■ ■ ■ ■) are somewhat louder, lower in pitch, and not quite so brief (20–30 msec).

CONTINUOUS SOUNDS are > 250 msec, notably longer than crackles—like dashes in time—but do not necessarily persist throughout the respiratory cycle. Unlike crackles, they are musical.

Wheezes (■■■■) are relatively high pitched (around 400 Hz or higher) and have a hissing or shrill quality.

Rhonchi (■■■■) are relatively low pitched (around 200 Hz or lower) and have a snoring quality.

Crackles may be due to abnormalities of the lungs (pneumonia, fibrosis, early congestive heart failure) or of the airways (bronchitis, bronchiectasis).

Wheezes suggest narrowed airways, as in asthma, COPD, or bronchitis.

Rhonchi suggest secretions in large airways.