RSS MODULE

Respiratory system

Objectives

- ❖ ***Describe***
  - ✓ Embryological development of tracheobronchial tree & lung
  - ✓ Tracheobronchial tree & pleura (**layers, recess, surface & applied anatomy)**
- ❖ ***Mention*** parts of respiratory system.
- ❖ **Mention** cells of respiratory epithelium
- ❖ **Describe** Histological structure of trachea, bronchi
- ❖ **Enumerate parts** of respiratory portion & lining epithelium of each part.
- ❖ **Compare** between type I pneumocyte& type II pneumocyte
- ❖ **Describe** blood air barrier, lung macrophage, pleura& fetal lung.
- ❖ **Describe**
  - ✓ Lungs (**external morphology, lobes, fissures, surface anatomy, segments& blood and nerve supply)**
  - ✓ Diaphragm (**attachments, major foramina, nerve supply& action)**
  - ✓ **Course& distribution of the two phrenic nerves**
- ❖ **Describe** functional structure of respiratory system
- ❖ **Describe** basic principles of respiratory functions tests
- ❖ **Discuss**
  - surfactant
  - Pneumothorax
  - Factors affecting diffusion of respiratory membrane
  - Hypoxia& cyanosis
  - Mention factors affecting increased barometric pressure

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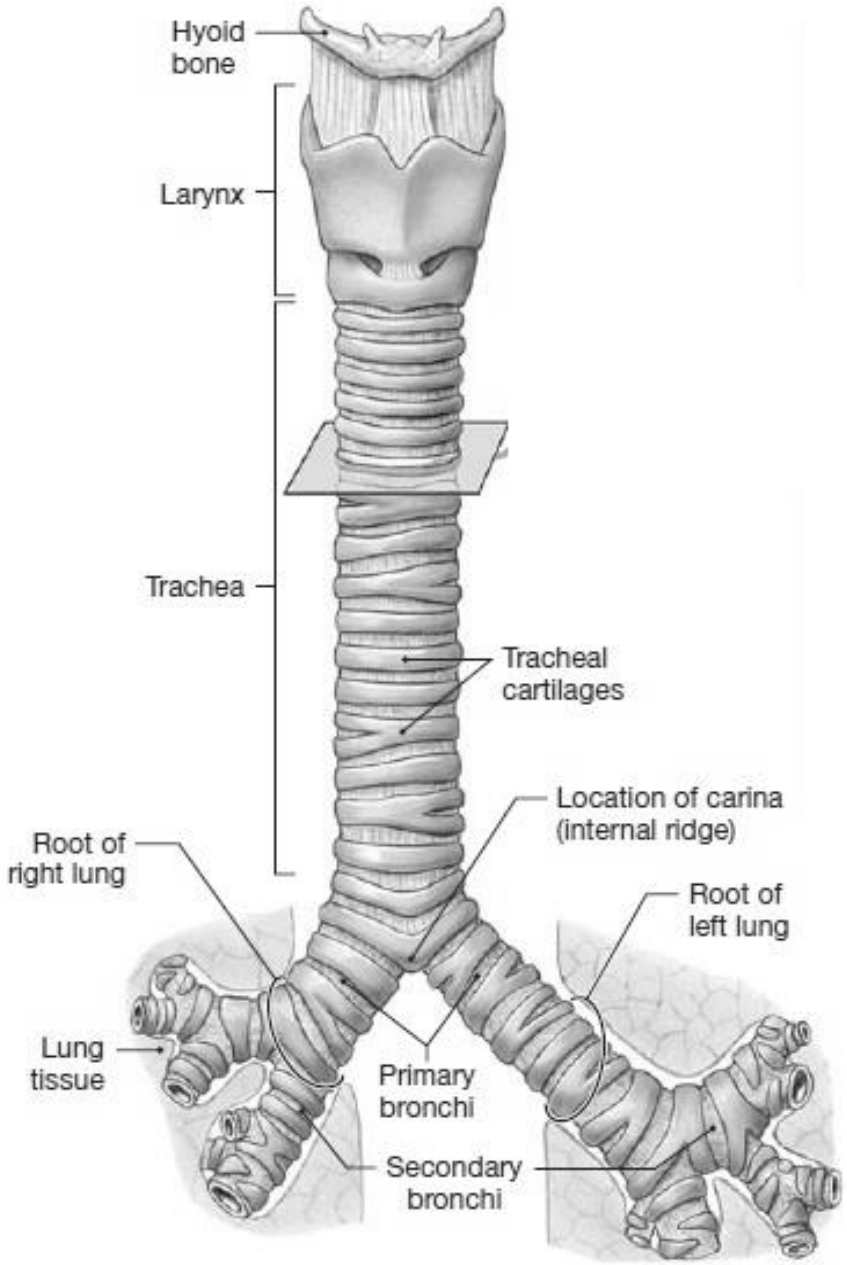


Trachea and bronchi

EMBRYOLOGICAL DEVELOPMENT OF TRACHEOBRONCHIAL TREE AND LUNGS

- The endoderm of the cranial part of foregut forms a groove, which will soon convert into a tube (laryngotracheal tube) which develops into the lining of the larynx, trachea and divides caudally into two bronchi
- The splanchnic mesoderm around will form vessels, cartilages and connective tissue of their walls. While the mesoderm of the pharyngeal arches develops into the muscles of the larynx.
- Each bronchus becomes surrounded by splanchnic mesoderm called lung buds which repeatedly divide to form the lungs. The alveoli start formation at the last trimester of pregnancy and continues after birth.

Congenital anomalies:

- Agenesis of one or both lungs
- Abnormal lobulation of the lung: due to abnormal branching. It may show a missing or extra lobes.
- Tracheoesophageal fistula: due to incomplete formation of laryngotracheal tube.
- Congenital lung cysts: due to incomplete dilatation of some bronchi

TRACHEA

- It is 12 cm long and 12 mm in diameter.
- It shows C shaped cartilages in its wall to keep it open.
- It begins at C6 vertebra and ends at T4 vertebra by dividing into 2 bronchi (Rt & Lt).

BRONCHI

Rt bronchus	Lt bronchus
Short (2.5 cm)	Long (5 cm)
Wide	Narrow
More vertical	More horizontal
Divide into 2 bronchi before entering the lung 1) Sup lobe (eparterial) bronchus 2) Rt main (middle & inf lobe or hyparterial)	Divide inside the lung

Accordingly, the foreign body is more commonly lodged in Rt than Lt bronchus.

II- Histology

Respiratory system According to function it is divided into:	
Conducting Portion	**Respiratory Portion**
(Transports air) 1. Nasal cavity 2. Pharynx 3. Larynx 4. Trachea 5. Bronchi 6. Bronchioles 7. Terminal bronchioles.	**(Gas exchange)** 1. Respiratory bronchioles 2. Alveolar ducts 3. Alveolar sacs & alveoli

Conducting Portion

This part is lined by respiratory epithelium.

❖ **The Respiratory epithelium**:

- It is **pseudostratified columnar ciliated with goblet cells**.
- It lines **most** of the **conductive portion** of respiratory system.
- It consists of **5 types** of cells.

1-Ciliated columnar cells

- The most **abundan**t type.
- Each cell has about **300 cilia**.
- Beneath the cilia, are **numerous small mitochondria** that supply ATP for ciliary beating.
- The cilia **move the mucus** and its trapped particles toward the **nasopharynx**.

2-Goblet cells

- The **next most abundant** cells.
- Form & secrete **mucous.**

3-Brush cells:

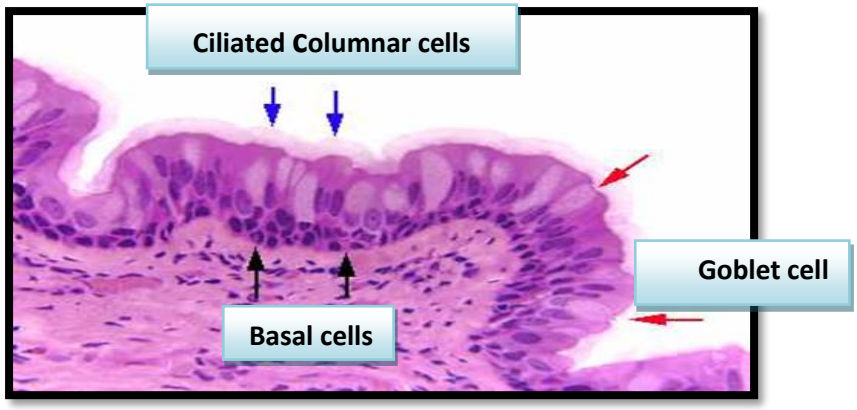
- **Columnar cells** with numerous **microvilli** on their apical surface.
- They have afferent **nerve endings** on their **basal surfaces** and are **sensory receptors**.

4-Basal (short) cells :

- **Small pyramidal** cells that lie on the basal lamina not reach to surface.
- These cells are **stem cells** that replace the other cell types.

1- **DNES cells (small granule cells):**

- **Columnar** cells with **basal dense granules**.
- Belong to the **d**iffuse **n**euro**e**ndocrine **s**ystem.
- Secrete **catecholamine** and **serotonin.**



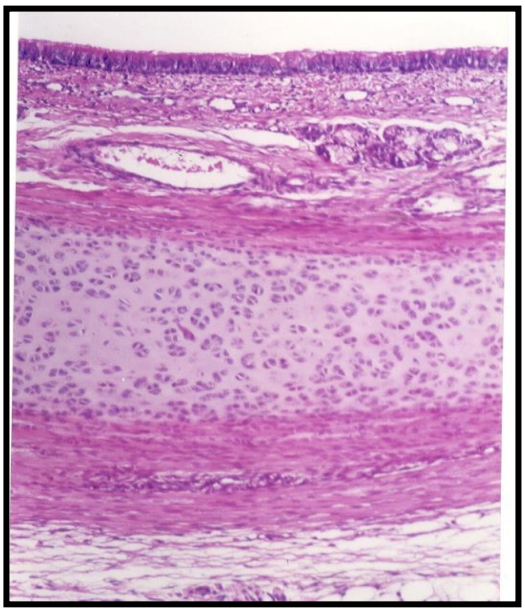
❖ Trachea and extrapulmonary (primary) bronchi:

1- Mucosa formed of:

a) The **respiratory epithelium**.

b) **The lamina propria** is a **thin** layer of **connective tissue**.

c) **Elastic membrane separating** the lamina propria from the **submucosa.**



2- The submucosa is a **connective tissue** layer containing many **seromucous glands.**

3-C-shaped hyaline cartilage: Smooth muscle extends between the open ends.

4-The adventitia: A layer of **C T**.

Extrapulmonary bronchus divides in the lung into **intrapulmonary bronchi→ primary bronchioles→ terminal bronchioles→ respiratory bronchioles→ alveolar ducts → alveoli**.

P.O.C	Extra pulmonary bronchus	Intrapulmonary bronchus
Lumen	Wide	Folded & narrow
Mucosa: • **Epithelium** • **Elastic membrane**	• pseudostratified columnar ciliated with many goblet cells • Present	• Same but with less goblet cells • **Absent**
Submucosa	Present	**Absent**
Cartilage	**C** shaped	Multiple plates
Smooth ms	Between two ends of cartilage	**Spirally** arranged under mucosa
Mucoserous glands& lymph f.	In submucosa	In **adventitia**

❖ **Primary bronchioles**

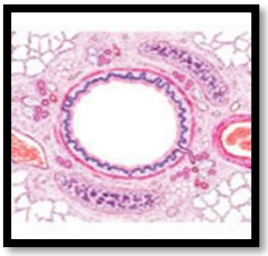
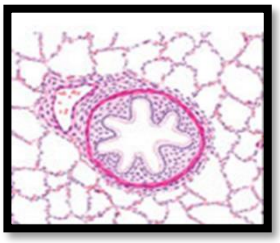
- Primary bronchioles have a diameter of **1 millimeter** (mm) or **less**.
- The wall consists of:
  1. **Mucosa:** **simple columnar ciliated** with **Clara cells**. **Cilia** gradually **decrease** as the bronchiole gets **smaller**.

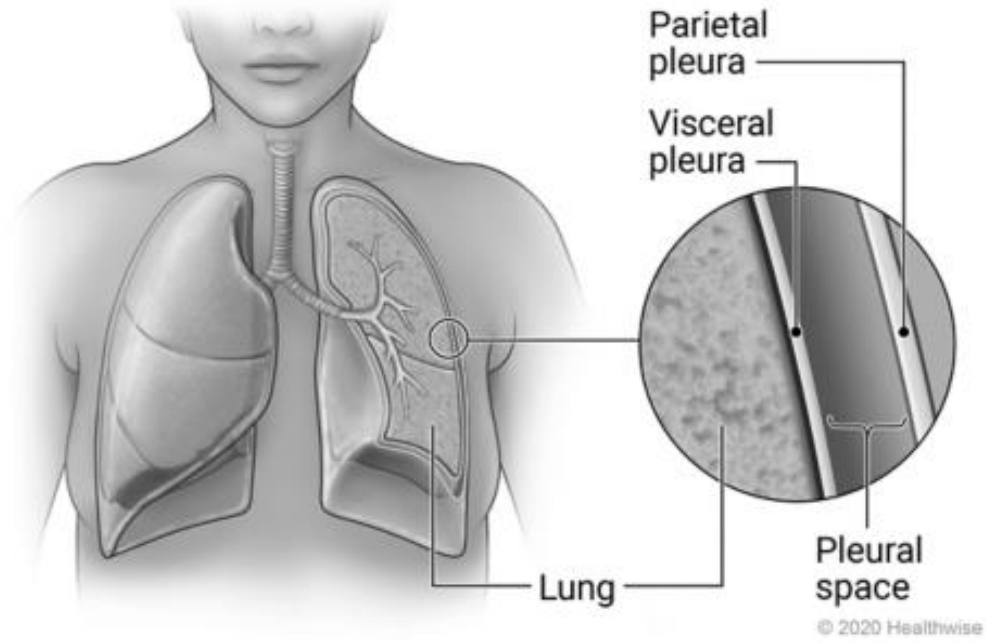
     Clara cells:
     - Tall, **dome-shaped**, **nonciliated** cells.
     - Possess numerous **secretory granules** whose contents aid in **lowering surface tension** of the **terminal bronchioles**.
     - They **metabolize** airborne **toxins**.
     - Clara cells **divide**& differentiate to **form ciliated cells**.
  2. **Musculosa:** **circularly** arranged **smooth muscle**.
  3. **Adventitia**: Connective tissue.

❖ **Terminal bronchioles**

- They have a **diameter** of **less** than **0.5 mm**.

They are lined by a **simple cubical** epithelium (**some are ciliated**) with **many Clara** cells.

P.O.C	Intrapulmonary bronchus	Bronchiole
Types		**Primary:** diameter 1mm or less **Terminal:** diameter < 0.5 mm
Mucosa: • **Epithelium**	• pseudostratified columnar ciliated • few goblet cells	• Simple columnar ciliated or cubical with Clara cells. Cilia gradually decrease as the bronchiole gets smaller &Clara cells increase. • No goblet cells
Musculosa	Spirally arranged **smooth MS**	**circularly** arranged **smooth MS**
Adventitia **-Cartilage** **-Mucoserous glands&** **-lymph follicles**	Present Present Present 	Absent Absent Absent 


Parietal pleura
Visceral pleura
Lung
Pleural space
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Pleura

LUNGS AND PLEURA

PLEURA

Definition: Each pleura is a serous sac covering the lung and lining sites of its extension.

Layers:

1) **Visceral (Pulmonary):**
   - Adherent to the lungs & follow the fissures
   - It is absent at the hilum of the lung.
   - It is supplied by bronchial vessels and autonomic Ns (insensitive to pain, touch & temperature)
2) **Parietal:**
   - It lines the sites of lung expansion,
   - It is supplied by As of thoracic walls and by somatic Ns (intercostal & phrenic Ns). Inflammation of pleura (pleurisy) is referred to thoracic and abdominal walls (intercostal Ns) and tip of shoulder (phrenic N)
   - It is subdivided into:
     a) ***Cervical Pleura:*** covers the apex of lung. It is bounded superiorly by suprapleural membrane.
     b) ***Costal Pleura:*** lines the thoracic wall.
     c) ***Mediastinal Pleura:*** covers the mediastinum.
     d) ***Diaphragmatic Pleura:*** covers the diaphragm.

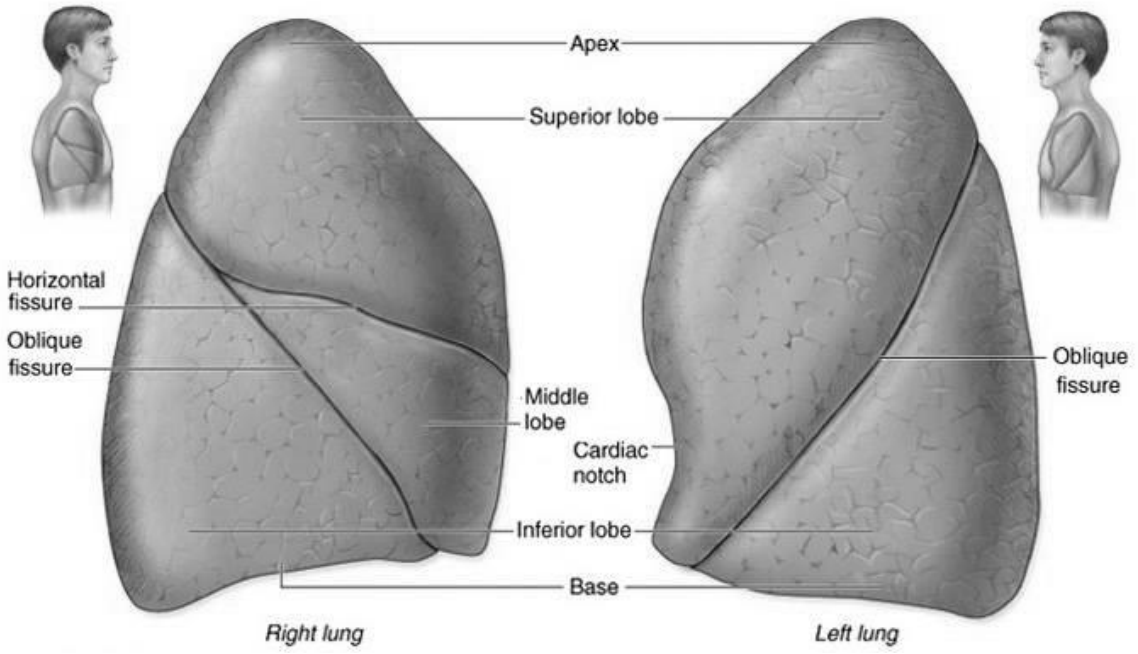
Recesses of the pleura

1) **Costomediastinal Recess:** It is the junction of costal and mediastinal pleura. It is occupied by anterior border of lungs in deep inspiration.
2) **Costodiaphragmatic Recess:** It is the junction of costal and diaphragmatic pleura. It is occupied by inferior border of lung in deep inspiration.

The pleural Cavity: a potential space, between the two layers of the pleura and contains few drops of synovial fluid.

Applied Anatomy: in some diseases, the pleural cavity may be filled by excess fluid (hydrothorax), blood (hemothorax), pus (pyothorax) or air (pneumothorax). This will collapse the lung at the same side and push the mediastinum to the opposite side. Fluids will obliterate costodiaphragmatic recess and can be drained by a needle, which should pass along the upper border of a rib to avoid injury of intercostal VAN.

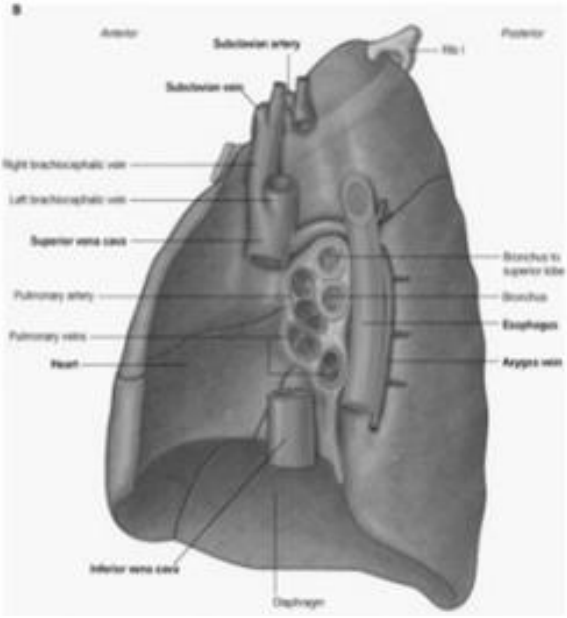
Surface anatomy: see lungs


Apex
Superior lobe
Horizontal fissure
Oblique fissure
Middle lobe
Cardiac notch
Inferior lobe
Base
Oblique fissure
Right lung
Left lung

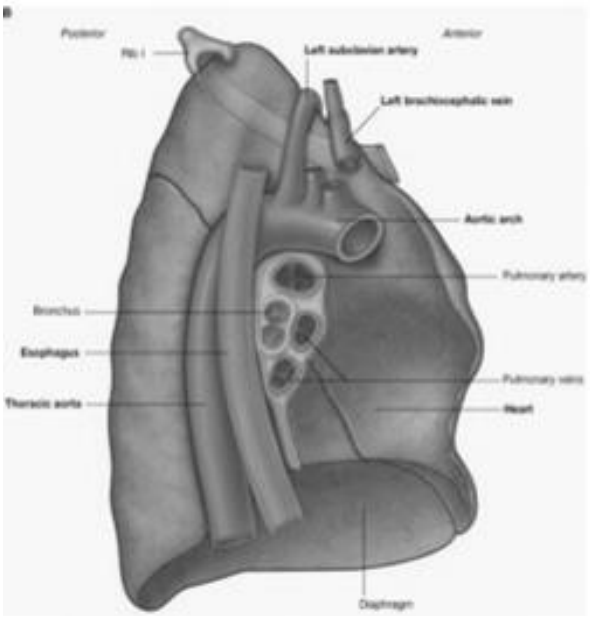
Lungs

LUNGS

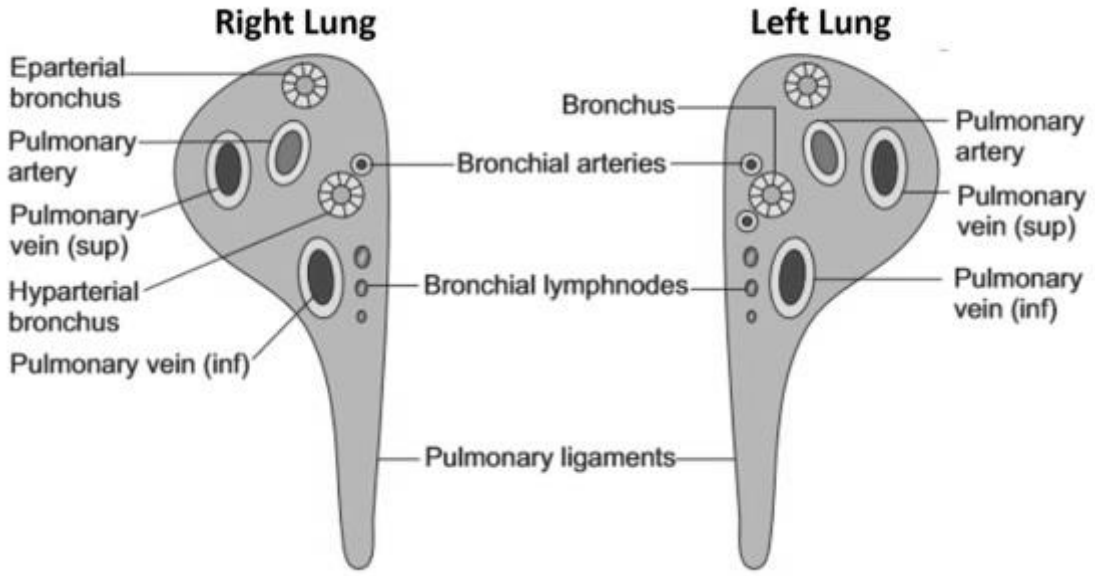
	RT	*LT*
General features	Each lung resembles 1/2 a cone, having an apex, 3 borders & 3 surfaces	
Apex	Project through thoracic inlet to the root of neck	
Borders:		
Ant	Thin, sharp & extends into costomediastinal recess	
Post	Thick, rounded at the side of vertebral column (paravertebral gutter)	
Inf	• Ant, lat & post → thin, sharp & extends into costodiaphragmatic recess • Med → rounded & related to pericardium	
Surfaces:		
Inf (base)	Concave, rests on copula of diaphragm	
Costal surface	Convex, wide & related to ribs, costal cartilages, intercostals muscles & pleura	
Medial surface		
Mediastinal part	• Related to mediastinum • Its post part shows the hilum (containing root of lung)	
Vertebral part	Related to sides of thoracic vertebrae, intervertebral discs, sympathetic chain, post intercostals Vs & root of splanchnic Ns	
Size	Larger	Smaller
Length	shorter	Taller
Width	Wider	Narrower
Ant border	Straight	Shows cardiac notch & lingula below it
Inf surface	More concave (higher copula of diaphragm due to presence of large liver below)	Less concave
Fissures	2 (oblique & transverse)	1 (oblique)
Lobes	3 (Sup, middle & inf)	2 (Sup & inf)



Mediastinal surface of Rt lung

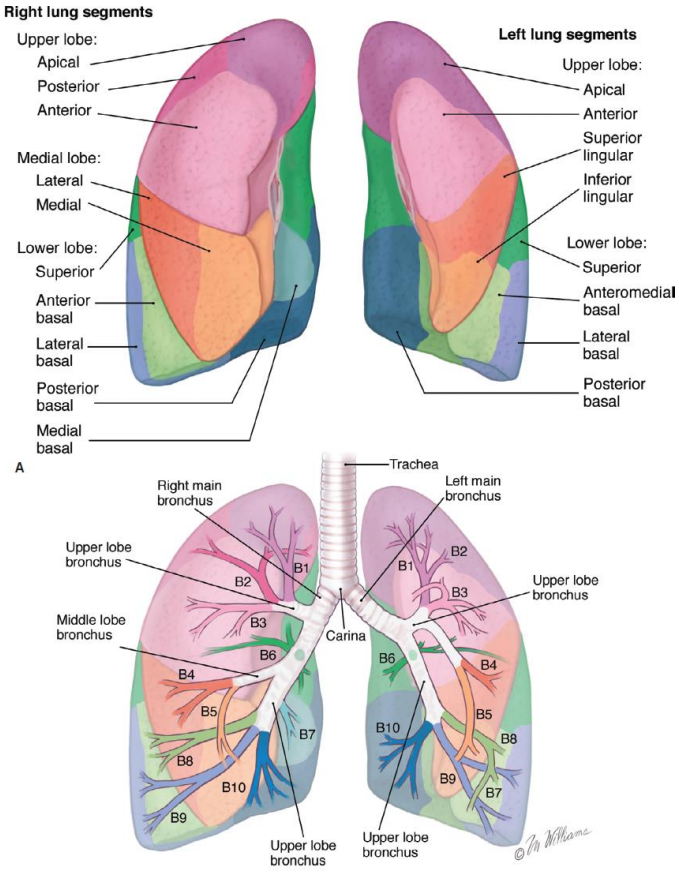


Mediastinal surface of Lt lung

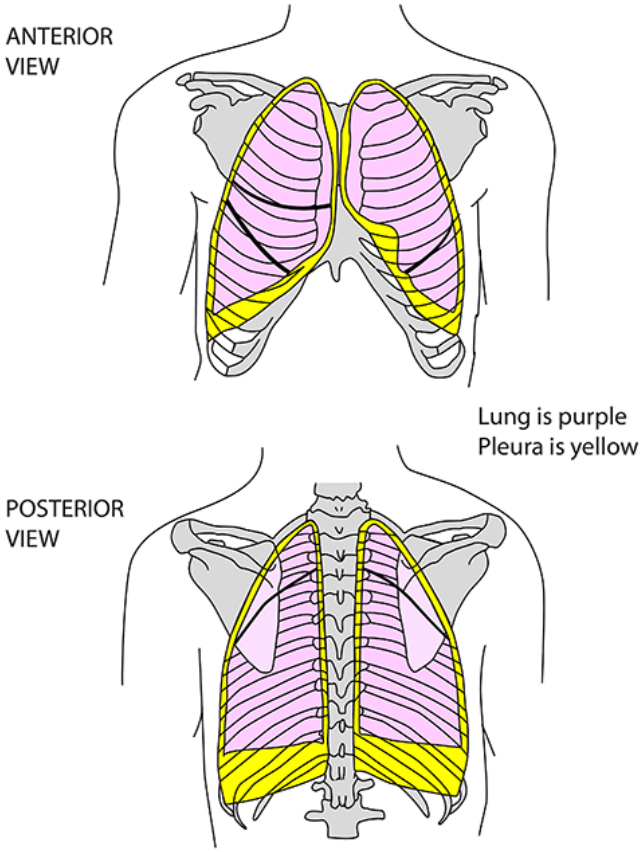


Hilum of the lungs

	RT	LT
Mediastinal surface	Shows the following impressions (both lungs shows the same impressions but for different structures. Nost of the impressions of Rt lung are venous, while most of the impressions of the Lt lung are arterial)	
Ant to hilum	• Pericardial impression (for Rt atrium & its pericardium) • Ascending aorta & thymus sup to pericardial impression	• Pericardial impression (for Lt ventricle (mainly), Lt atrium & its pericardium) • Pulmonary trunk & thymus sup to pericardial impression
Sup to hilum	• Horizontal: arch of azygous V • Vertical (above arch of azygous, from ant to post) 1) SVC (continued sup as Rt brachiocephalic V) + Rt phrenic 2) Trachea + Rt vagus 3) Esophagus	• Horizontal: arch of aorta • Vertical (above arch of aorta, from ant to post) 1) Lt common carotid A 2) Lt subclavian A + Lt vagus & Lt phrenic Ns between them 3) Esophagus + thoracic duct
Post to hilum	Azygous V + esophagus	Descending aorta
Inf to hilum	IVC	Esophagus
Phrenic N	• Along groove of Rt brachiocephalic & SVC (sup to hilum) • Then along pericardial impression (ant to hilum) • Then along IVC (inf to hilum)	• First between Lt common carotid & Lt subclavian, extending to arch of aorta (sup to hilum) • Then along pericardial impression (ant to hilum)
Hilum	Containing the root which is formed of:	
Bronchus	2; characterized by plates of cartilage 1)Sup lobe (eparterial) bronchus 2)Rt main (middle & inf lobe or hyparterial) bronchus (most post structure in the root)	• 1 main bronchus, characterized by plates of cartilage • most post structure in hilum
Bronchial vessels	Post to bronchus – 1 A – 2 Vs	Post to bronchus – 2 As – 2 Vs
Pulmonary A	• Branch of pulmonary trunk • Carries non oxygenated blood from Rt ventricle to the lung • Anterosuperior to main bronchus	
Pulmonary V	2; carry oxygenated blood from lung to Lt atrium – Sup: most ant structure in the root – Inf: most inf structure in the root	
Lymph nodes	Between the structures of the root	
Pulmonary plexus	Autonomic, for bronchial tree, lung substance & visceral pleura – Ant: ant part of root – Post: post part of root	

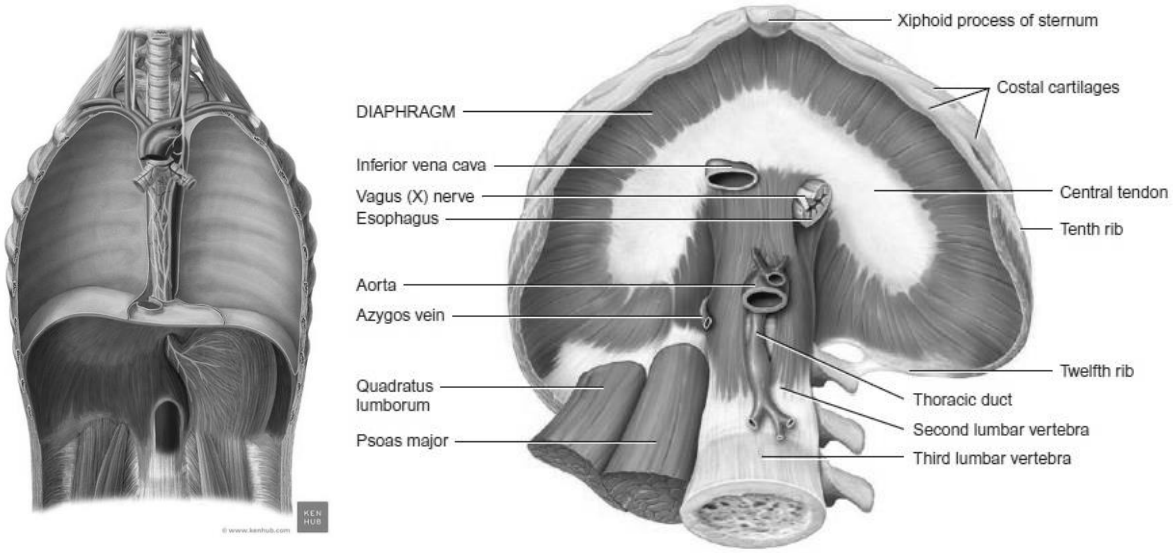


Segments of the lungs

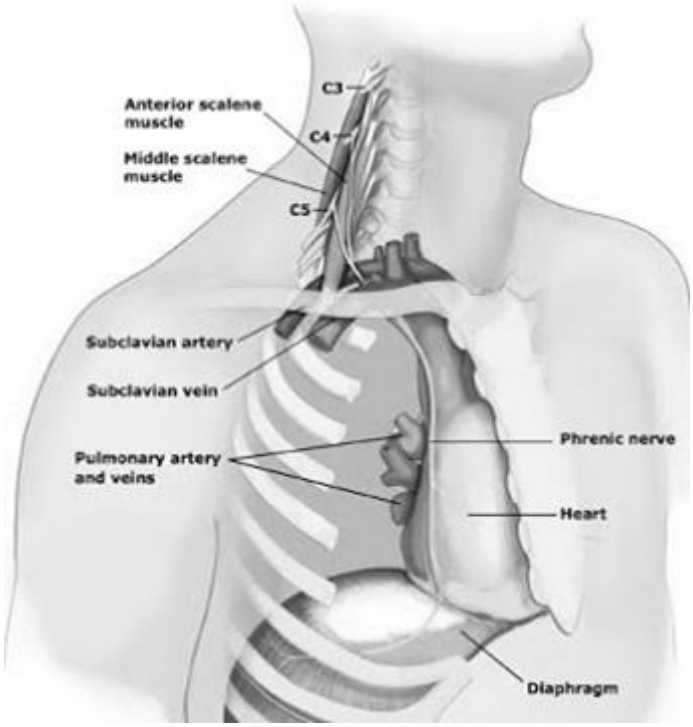


Surface anatomy of lungs and pleura

<table>
<tr><th></th><th colspan="2">RT</th><th colspan="2">LT</th></tr>
<tr><td>Segments</td><td colspan="4">Each segment contains a bronchus, branch of pulmonary A. Pulmonary V run in the intersegmental planes</td></tr>
<tr><td></td><td>Segment</td><td>Direction of bronchus</td><td>Segment</td><td>Direction of bronchus</td></tr>
<tr><td rowspan="5">Sup lobe</td><td>Apical</td><td>Sup</td><td>Apical</td><td>Sup</td></tr>
<tr><td>Post</td><td>Post & lat</td><td>Post</td><td>Post & inf</td></tr>
<tr><td>Ant</td><td>Ant & inf</td><td>Ant</td><td>Ant & inf</td></tr>
<tr><td>---</td><td>---</td><td>Sup lingular</td><td>Ant & inf</td></tr>
<tr><td>---</td><td>---</td><td>Inf lingular</td><td>Ant & inf</td></tr>
<tr><td rowspan="2">Middle lobe</td><td>Lat</td><td rowspan="2">Middle lobe bronchus passes ant & inf then divides</td><td>---</td><td>---</td></tr>
<tr><td>Med</td><td>---</td><td>---</td></tr>
<tr><td rowspan="5">Inf lobe</td><td>Apical</td><td>Post</td><td rowspan="5">As Rt lung</td><td rowspan="5">As Rt lung</td></tr>
<tr><td>Ant basal</td><td>Inf & ant</td></tr>
<tr><td>Post basal</td><td>Inf & post</td></tr>
<tr><td>Lat basal</td><td>Inf & lat</td></tr>
<tr><td>Med basal</td><td>Inf & med</td></tr>
<tr><td>Applied anatomy</td><td colspan="4">• Bronchi of middle lobe are narrow & could be occluded by lymph nodes
• Postural drainage of fluid in the lungs depends on the direction of segmental bronchi
• Segment removal could be performed as a treatment</td></tr>
<tr><td>Surface Anatomy of lungs</td><td colspan="2">⇨ 1 inch above med 1/3 of clavicle (apex)
⇨ Sternal angle near midline
⇨ 6th costal cartilage near midline
⇨ 6th rib at midclavicular line
⇨ 8th rib at midaxillary line
⇨ 10th rib near thoracic spines
⇨ To the 1st point
• Oblique fissure: from 3rd thoracic spine to 6th costal cartilage
• Transverse fissure: level of 4th costal cartilage</td><td colspan="2">⇨ 1 inch above med 1/3 of clavicle (apex)
⇨ Sternal angle near midline
⇨ 4th costal cartilage near midline
⇨ 6th costal cartilage 1 inch from sternal side
⇨ 6th rib at midclavicular line
⇨ 8th rib at midaxillary line
⇨ 10th rib near thoracic spines
⇨ To the 1st point
• Oblique fissure: from 3rd thoracic spine to 6th costal cartilage
• No transverse fissure</td></tr>
<tr><td>Surface anatomy of pleurae</td><td colspan="2">⇨ 1 inch above med 1/3 of clavicle
⇨ Sternal angle near midline
⇨ 6th costal cartilage near midline
⇨ 8th rib at midclavicular line
⇨ 10th rib at midaxillary line
⇨ 12th rib near thoracic spines
⇨ To the 1st point</td><td colspan="2">⇨ 1 inch above med 1/3 of clavicle
⇨ Sternal angle near midline
⇨ 4th costal cartilage near midline
⇨ 6th costal cartilage 1 cm from sternal side
⇨ 8th rib at midclavicular line
⇨ 10th rib at midaxillary line
⇨ 12th rib near thoracic spines
⇨ To the 1st point
Applied anatomy: intracardiac injection or needle insertion into pericardium is performed within 1 cm to the left of sternum between 4th & 6th costal cartilages</td></tr>
</table>



Diaphragm



Phrenic nerve

DIAPHRAGM

Origin	*Insertion*	*Action*	*NS*
Sternal: back of xiphoid process **Costal:** lower 6 ribs & costal cartilages **Rt crus** (stronger): L1-3 vertebrae (bodies) & intervertebral discs **Lt crus:** L1-2 vertebrae (bodies) & intervertebral discs **5 arcuate ligaments:** between the crurae, L1 transverse processes & last ribs	Central tendon	• Inspiration • Increase abdominal pressure (cough, vomiting... etc.)	Phrenic N (C3-5)

Major openings of diaphragm:

Opening	*Site*
Inf vena cava	T8, 1 inch to Rt (in central tendon)
Esophagus	T10, 1 inch to Lt
Aorta	T12 in midline

PHRENIC NERVE

Root value: C3,4,5 ventral rami

Course &Relations (revise mediastinal surface of the lungs):

- Accompanied by pericardiophrenic artery.

Lat: corresponding lung & pleura

Med (from above downwards):

Rt	Lt
• Rt brachiocephalic • SVC • Rt atrium • IVC	• Between Lt common carotid & Lt subclavian As, crossed by Lt vagus • Arch of aorta • Lt ventricle

Post: corresponding hilum of the lung

Branches:

Motor: to diaphragm (pierces it & supply it from inf surface).

Sensory: pleura, pericardium & the Rt phrenic supplies biliary system (pain due to biliary causes is referred to Rt shoulder).

Respiratory Portion (histology)

A- Respiratory bronchioles

- The **respiratory bronchioles** mark the **transition** from the **conducting** to the **respiratory** portion of the respiratory system.
- The epithelium is **simple cubical epithelium & Clara cells**
- Their **walls** are **interrupted** by **alveoli**, the sites where **gas exchange** occurs.

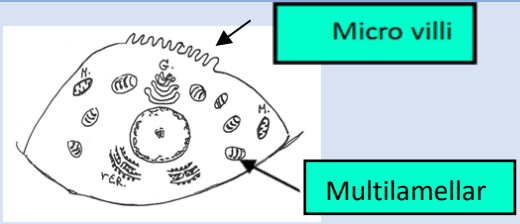
B- Alveolar ducts

- Their walls consist of **adjacent alveoli**, which are separated from one another by interalveolar septum.
- They are the **most distal portion** of the respiratory system to contain **smooth muscle**, which is present in their walls at the **openings** of adjacent alveoli.
- They are lined by **simple squamous epithelium**.

C- Alveolar sacs are expanded outpouchings of **numerous alveoli** located at the distal ends of alveolar ducts.

D- Pulmonary alveoli:

- They are **structural & functional** unit of the lung.
- There are **pores** in between **lung alveoli** that allow **communication**.
- The **alveoli** are **separated** from each other by **thin inter alveolar septum**.
- The **alveoli are lined** by two types of cells; pneumocyte type I & type II.

P.O.C	Type I Pneumocytes	Type II Pneumocytes
%	97	3
LM	• flat squamous cells • flat densely stained nuclei • Little cytoplasm	• cuboidal cells • rounded large nuclei with prominent nucleoli • Foamy cytoplasm
EM	• Few cell organelles • Tight junctions with type I and II to avoid escape of tissue fluids within the alveoli	• Apical microvilli • Rich in Golgi apparatus, rER, mitochondria • Characteristic **multilamellar bodies** (cytosomes) that contain phospholipids
Function	**gas exchange**	1. secrete **pulmonary surfactant** 2. **Stem cells** for both types
		

Clinical note:

Surfactant is only secreted late in pregnancy (9th month) so premature babies usually have respiratory distress due to deficiency in production of surfactant.

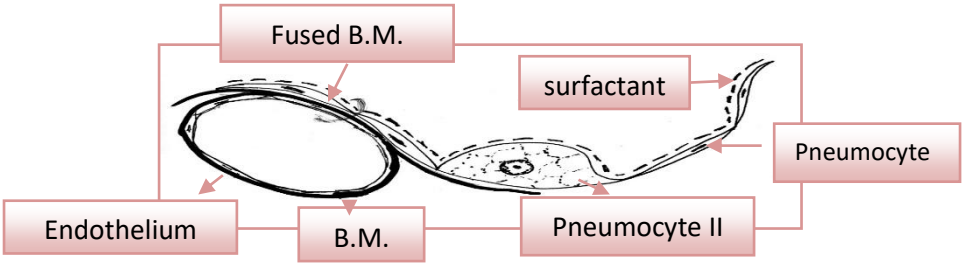
❖ **Interalveolar septum:**

Definition : It is the partition present in between the lung alveoli.

Structure: It is formed of a **thin** layer of a highly **vascular C.T**. rich in **elastic** fibers & **reticular** fibers which are important for **elasticity & support** of lung tissues.

❖ **Blood air barrier:**

Definition : It is the **wall** through which **gas exchange** occur. It is present in between **blood** in blood **capillaries** & **air** within the lung **alveoli**.



Structure:

1- Thin film of pulmonary **surfactant**.
2- Cytoplasm of pneumocyte **type I**.
3- **Fused basement membrane** of type I pneumocytes & capillary endothelium.
4- Capillary **endothelium**.

❖ **Alveolar phagocytes:**

Definition: They are **phagocytic** cells which are present **in** the cavities of lung **alveoli** or in **inter- alveolar septum**.

Function: They can **phagocytose bacteria & dust** particles (rich in **lysosomes**).

Origin: They arise from blood **monocytes**.

Staining: They are demonstrated by **vital** stain as **trypan blue**.

Fate: They may be **coughed in sputum,** or they may **die** & remain in the **interalveolar septum** or the nearby **lymph nodes**.

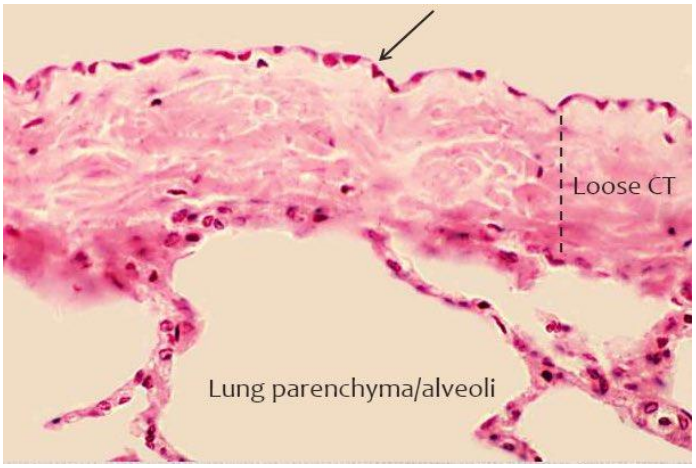
Types:

1- **Dust cells:** these cells phagocytose dust &carbon particles that appear as **black particles** within them.

1- **Heart failure cells**: they can only be seen in patient suffering from **heart failure**. Congestion of blood **capillaries** will lead to their **rupture** & escape of **RBCs** to **alveolar cavities**. **Macrophages** phagocytose **HB** & destroy it to **red** colored **haemosiderin** granules that appear within them.

Structural transitions in walls and layers of the passageways from extrapulmonary passageways to alveoli	
Layers	become thinner as passageways decrease in diameter
Epithelium	decreases in height from pseudostratified to simple squamous
Cilia & goblet cells	Decrease gradually. Goblet cells are stopped before cilia.
Lamina propria	Decrease gradually in thickness
Serous& mucous glands	Decrease gradually and stop at the junction of a bronchus with a bronchiole.
Cartilage	decreases in size, breaks up into plates, and stops at the junction of a bronchus with a bronchiole
Smooth muscle	Trachea: trachealis at the free ends of the C-shaped cartilage. Intrapulmonary bronchi: Spirally arranged. Bronchioles: circularly arranged. Alveolar ducts: only at alveolar openings Alveolar sacs and alveoli: completely absent.

The lining epithelium of the bronchial tree	
Region	**Epithelium**
Trachea& 1ry bronchi	**Respiratory epithelium** [pseudostratified col. Ciliated with goblet cells]
2nd **(Intrapulmonary)** bronchi	Respiratory with less goblet cells
Primary bronchioles **(No goblet)**	Simple columnar ciliated with Clara cells
Terminal bronchioles	Simple cubical some ciliated+ many Clara cells
Respiratory bronchiole	Simple cubical + Clara cells
Alveolar duct	Simple squamous (smooth muscle)
Alveoli	Alveolar epithelium



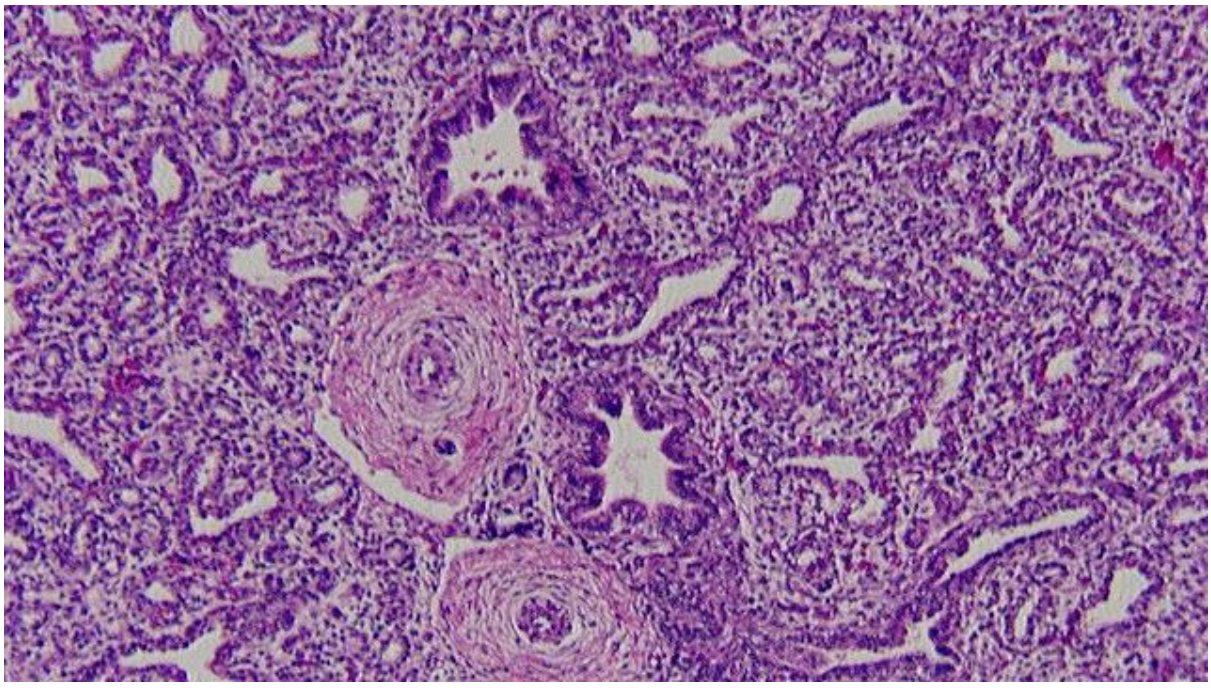
Pleura:

It is a double layered serous membrane formed of the visceral pleura (covering the lungs) and the parietal pleura (on the chest wall).

Both visceral and parietal pleurae are formed of a superficial layer of simple squamous mesothelial cells resting on a layer of connective tissue rich in collagen and elastic fibres.

Between the visceral pleura and the parietal pleura is a potential pleural space that is ordinarily filled with a thin film of serous fluid.

Foetal lung:



- **Non-functioning collapsed** in the intrauterine life.
- Clear lobes and lobules (**thick connective tissue**).
- **Like glands** because branches of bronchiolar tree are like ducts of the glands and alveoli are like acini.
- **Alveoli** are collapsed and lined by **simple cubical epithelium.**
- **Bronchi and bronchioles** are **folded.**
- **Cartilage plates** are present in the walls of the bronchi (characteristic feature of foetal lung)
- **Congested** pulmonary **blood vessels.**

Lung Functions

1) Respiration

Respiration is divided into external respiration & internal respiration

→*External respiration*

1- Pulmonary ventilation "V" 2- Pulmonary perfusion "Q"

3-Diffusion: Exchange of gases (oxygen & carbon dioxide)

4-Transport of oxygen & carbon dioxide between lungs & body tissues by blood

5-Exchange of oxygen & carbon dioxide between blood & tissues by diffusion

- Air passes from pharynx to trachea to two main bronchi
- The bronchi repeatedly subdivide within the lungs, becoming smaller and changing in structure, until the alveoli are reached after 20 generation
- The total area of alveoli in contact of capillaries = $100m^2$
- The airways contain cartilage, which gives their shape & support. They are surrounded by smooth muscle to allow change In diameter
- Stimulation of vagus & histamine leads to bronchoconstriction
- Stimulation of sympathetic leads to bronchodilation through β2 receptors

→ *Internal respiration*

- Use of oxygen within mitochondria to generate ATP by oxidative phosphorylation & production of CO2 as a waste product
- Use of oxygen within mitochondria to generate ATP by oxidative phosphorylation & production of CO_2 as a waste product

2) Non respiratory functions:

a) Regulation of acid base balance (pH): Through control of CO_2 level

b) Défense against pathogens c) H_2O & heat loss

d) Increase venous return e) Enhancing vocalization

Pulmonary Ventilation

- Air flows into or out of lungs because of pressure gradient between:

1- Alveoli 2- Atmosphere (outside air) 760 mmHg

- **Resting respiratory rate** → 12-16 cycles/min
- **Tidal Volume "TV**→ 500 cc (Volume of air inspired or expired each cycle during rest equal)
- **Pulmonary ventilation** = Respiratory rate x TV

= 12 x 500 = 6000 cc

- **Mechanics of inspiration:**
  - ↑ Vertical diameter: By Diaphragm
  - ↑ A-P diameter: By external intercostal muscles
  - ↑ Lateral diameter : By external intercostal muscles

Inspiration	Exspiration
- Air rushes in. - It is active process.	- Air forced out. - It is Passive process: Due to elastic recoil of -lung -Chest wall ant end of inspiration **Expiration becomes active: [ie expiratory muscles contract]** - **During forced expiration** - **As in conditions of bronchial obstruction eg bronchial asthma**
Increase in: 1- Thorax volume (increase all dimensions) 2- Lung volume as it follows the thoracic wall	**Decrease in:** 1- Thorax volume (decrease all dimensions due to relaxation of muscles) 2- Lung volume
Decrease in: - Intra-thoracic pressur (intrapleural): from -4 to -6 mmHg - Intra-alveolar pressure to: Become -l mmHg	**Increase in:** - Intra-thoracic pressure: To -4 mmHg - Intra-alveolar pressure: To +1 mmHg

Inspiratory muscles are:

➔ **Diaphragm:**

- Is the most important inspiratory muscle. Supplied by phrenic nerve (3^{rd} to 5^{th} cervical segment)
- When it descends: It increases the vertical diameter.
- Responsible for 75% of the change in chest volume

➔ **External intercostal muscles:**

- They run obliquely downward & forward from rib to rib
- **When contract they increases:**

1) The lateral diameter: By elevation of ribs
2) Anteroposterior diameter: By eversion of ribs

➔ **Accessory inspiratory muscles:** Contract only with deep (forced) inspiration. They are:

1) Sternomastoid ➔ lift the sternum
2) Serratus anterior ➔ lift many ribs
3) Scaleni muscles ➔ lift the first two ribs

Expiratory muscles are:

➔ **Abdominal muscles**:

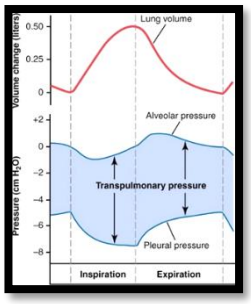
- When contract it increase intra-abdominal pressure → push diaphragm up

➔ **Internal intercostal muscles**

1- They run obliquely downward and backward from rib to rib.

2- They pull ribs downward.

Respiratory pressure



Changes in lung volume, alveolar pressure, pleural pressure & trans pulmonary pressure during normal breathing

I-Intra-Pleural Pressure (IPP)

➢ **Definition:** It is the pressure between the two layers of the pleura ie between the visceral pleura and the parietal pleura.

- Normally the intra-pleural space:

- Contains few cc of lymph for lubrication of movements
- Does not contain air.
- Normally intra-pleural pressure is: Negative

➢ **Causes of negative IPP:**

Due to: Continuous tendency of the lungs to recoil inwards **Against** Continuous tendency of chest wall to expand outwards

1- *Recoil tendency of lung Caused by*:

A- Lung elasticity

➢ It account for ⅓ of total recoil tendency elastic

➢ Lung volume at the end of normal expiration: Is 2.5 liter [while lung relaxation volume (at which, it is neither stretched nor compressed): Is one liter]. So, it tends to collapse to reach its relaxation volume.

B- Surface tension of fluid lining the alveoli

➢ It account for ⅔ of total recoil tendency of lungs.

➢ Any fluid with direct contact of air has a surface tension (intermolecular attraction between fluid surface molecules) to decrease the surface area so, alveoli tend always to collapse

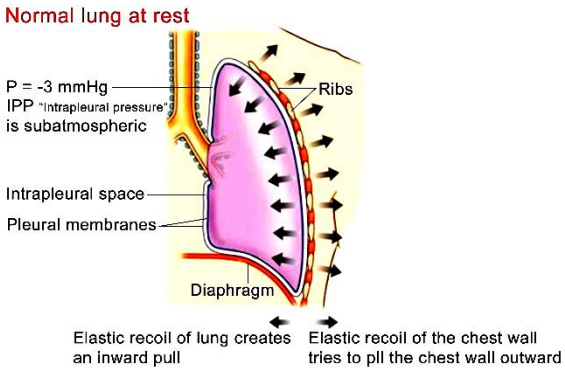
The continuous pull of the lung against the stable chest wall create negative pressure

2- Expansion tendency of chest wall

➢ At the end of normal expiration:

➢ Chest is compressed

➢ Chest volume at the end of normal expiration: Is 2.5 liter (while chest relaxation volume is 5 liter). So, the chest has a continuous tendency to expand



❖ **Measurement of IPP:** by intra-esophageal balloon connected to sensitive manometer

❖ **Normal values of IPP:**

1. **At end of normal expiration:** -4 mmHg
2. **At end of normal inspiration**: -6 mmHg
3. **With deep inspiration:** -12 mmHg

(Because with deep inspiration there is maximal expansion of lungs → maximal recoil tendency → IPP becomes more negative)

4. **During forced inspiration against closed glottis (Muller's experiment):** IPP becomes -30 to- 50 mmHg
5. **During forced expiration against closed glottis (Valsalva's experiment):** IPP becomes + 50 mmHg

❖ **Functions of IPP:**

1. It prevents lung collapse & allows for lung expansion.
2. It helps respiratory movement (pressure inside alveoli is positive while outside is negative)
3. It helps venous & lymphatic return from extra-thoracic vessels

II- Alveolar Pressure (intra-alveolar pressure)

❖ **Definition:**

It is the pressure inside the alveoli during respiratory cycle

➢ **During normal inspiration: The intra-alveolar pressure decreases:**

1. Decreases below atmospheric pressure
2. Becomes -1 mmHg less than atmospheric pressure
3. Due to expansion of chest & lungs, so air rushes in

➢ **During normal expiration: The intra-alveolar pressure increases**

1. Increases above atmospheric pressure
2. Becomes +1 mmHg more than atmospheric pressure
3. Due to elastic recoil of lung & chest, so air forces out

➢ **At end of inspiration or expiration:**

❖ The intra-alveolar pressure = 0 mmHg

III- Trans-pulmonary pressure (transmural pressure)

➢ It equals = alveolar pressure minus pleural pressure

➢ It is the distending pressure of the alveoli ie:

1- The more the negativity of the intra-pleural pressure or

2- The more the positivity of the intra-alveolar pressure.

The more the lung expansion

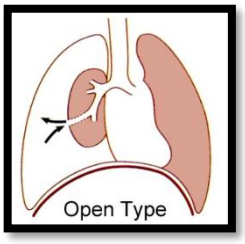
Pneumothorax "PTX

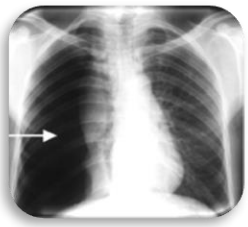
❖ **Define**→ The presence of air in the intra-pleural space.

❖ **Types**:

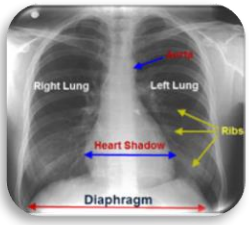
1- ***External or opened pneumothorax***:

Air is introduced from outside e.g. chest wound the negative intrapleural pressure is lost as it is equilibrated· with atmospheric pressure



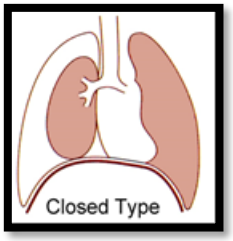


Normal X-Ray



Pneumothorax

2- Internal or closed pneumothorax:



➔ Air is introduced from Inside e.g. rupture of alveoli or damaging pleural wall by pneumonia

❖ **Effects: 1**- The lung collapse while the chest wall is expanded

2-The mediastinum shifts toward the intact side decreasing the lung volume on the normal side.

3- Decrease venous return and lymphatic return

Surfactant

❖ **Definition: I**t is a surface active agent, which means that when it spread over the surface of a fluid, it reduces its surface tension.

❖ **Chemical nature:** It is a complex nature, its components are:

1- Phospholipids: Dipalmitoyl-lecithin

2- Surfactant apoproteins→Allow rapid spread of lecithin over the fluid surface to function effectively.

3- Calcium ions (Ca++)

❖ **Origin:** It is secreted by type II alveolar epithelium

❖ **Functions:** Surfactant decreases the surface tension of fluid lining the alveoli thus:

1- Facilitates lung expansion:

✓ As it reduces surface tension of fluid lining alveoli

✓ Surfactant forms a layer between fluid lining the alveoli & the air in the alveoli.

✓ This prevents the development of a water-air interface

NB: Water-air interface has surface tension about 10 times as much as surfactant air interface.

2- **Prevents the collapse of alveoli during expiration**:

✓ As the alveolus becomes smaller during expiration, the surfactant concentration is increased reducing surface tension further.

3- **Prevents pulmonary edema** (i.e. it prevents the accumulation of fluid inside the alveolus):

NB: Surface tension in the alveoli favours the filtration of fluid from the blood into alveoli. So, surfactant decreases the surface tension of fluid lining the alveoli thus decreases filtering force preventing pulmonary edema.

❖ Surfactant deficiency:

➢ ***Causes*:**

1- ***Respiratory distress syndrome (RDS) [Hyaline membrane disease***:

✓ It may occur in premature infants (may die at birth from respiration failure)

✓ ***Due to:***

- Increase surface tension & decrease lung compliance & distensibility resulting in large regions of collapsed alveoli.
- As maturation of surfactant in lungs is increased by cortisol, which reaches high level in fetal and maternal blood only near term.

✓ **Diagnosis:**

- **Based on**: the ratio between lecithin and sphingomyelin in the amniotic fluid
- in (RDS) it is less than one (<1) at birth
- Normally, it is 2 at 35 weeks of gestation (pregnancy).

2)- ***Inhalation of 100% oxygen for a long time or at 2 atmospheric pressures of oxygen:*** *As in cardiac surgery*

3)-Heavy smokers: *Cigarette smoke inhibits surfactant secretion*

4)- Obstruction of one of main pulmonary artery

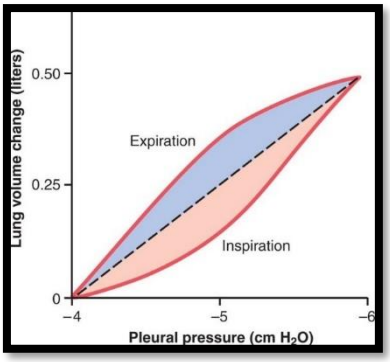
5)-Hypothyroidism

6)- Hypocorticism: *Cortisol accelerates maturation of surfactant*

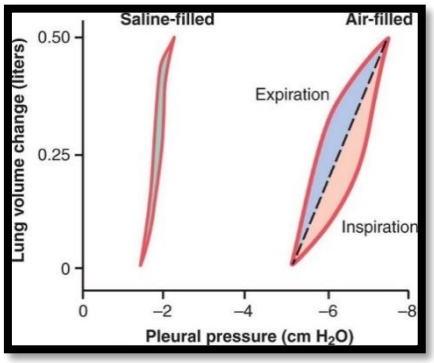
7)-Hyperinsulinism: *Insulin inhibits surfactant secretion*.

***This may explain the increased RDS in infants born to diabetic mothers*.**

Compliance



Compliance diagram in a healthy person. This diagram shows compliance of: Lungs alone



Comparison of the compliance diagrams of saline-filled and air-filled lungs when the alveolar pressure is maintained at atmospheric pressure (0 cm H2O) and pleural pressure is changed

- **Definition:** is a RATIO between change in volume to change in distending pressure (trans mural pressure)
- **Transmural pressure**= Pressure inside the lungs- pressure outside the lungs -Intra alveolar pressure (zero)
  - Intra pleural pressure (-ve)
  -Intra-pleural pressure
- **Compliance** = Change in volume / Change in Trans mural pressure
- **Compliance is an inverse of elasticity i.e**. a lung with high elasticity (increase elastic recoil tendency & tendency to collapse) has low compliance as there is difficulty in lung expansion**.**
- **Normal standard:**
- Compliance of lung alone = 0.2 liter/cm H2O
- **The compliance of both lungs = 200ml/cm H2O**
- **Compliance diagram of the lungs: Compliance of excised lung:**
- ✓ The compliance curve is made by measuring change in volume that occurs with each change of pressure during both inflation & deflation of lungs.

- ✓ It is hysteresis loop (not linear) due to change in distribution of surfactant: During lung deflation, surfactant becomes close together causing decrease in surface tension -lung become more compliant

❖ **Factors affecting lung compliance:**

A)- Decreases in →Anything affect distension of lungs

1- **Restrictive lung diseases**: As pulmonary congestion & fibrosis

3- **Respiratory distress syndrome**

B)- **Increases in→Anything changes lung elastic properties**.

1- Old age

2- **Emphysema:** Which is a pulmonary disease due to destruction of alveolar wall & elastic tissue of lung leading to → abnormal collection of air → enlargement of air spaces distal to terminal bronchi

❖ **Compliance of thoracic wall & lung together:**

➔ It is called dynamic lung compliance.

➔ It is measured in living subjects

➔ Compliance of the combined lung-thorx system is slightly greater than one half of the lung alone = 0.11 liter/cm H2O

❖ **Factors affecting chest compliance**

➔ **Decreases in**: 1-Skeletal muscle diseases 2Arthritis 3- Obesity

➔ **Increases in**: Athletes

The work of breathing

❖ **Energy needed for breathing is:**

- ✓ 5% of total energy in normal breathing
- ✓ 20% of total energy in heavy exercise.

❖ **The work of breathing** is performed by respiratory muscles during inspiration & there is kinetic energy stored in muscles & released during expiration as potential energy

❖ **The work of inspiration is divided into**:

1- Elastance work (compliance work) 65%

- ✓ It is required to: Expand lungs against elastic forces
- ✓ Leads to decrease compliance & increase work
- ✓ **The work breathing** is increased if:

I- **Increase elasticity: (Decreased is reduced) As in:**

A- Surfactant deficiency or

B- Lung fibrosis

II -**Airway resistance is increase** As in: bronchial asthma

2- *Non Elastance work*

1)- Tissue resistance work 15%

- ✓ It is required to overcome:

A)- Viscosity of lungs B)- Chest cage structure

II- Airway resistance work 20%

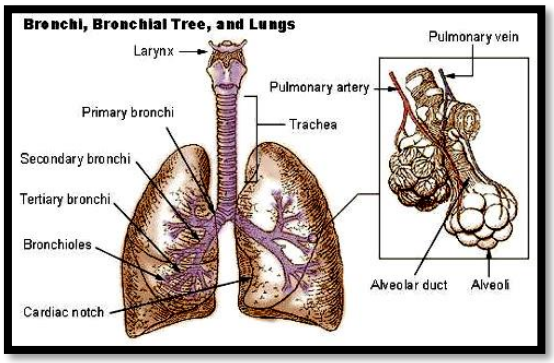
- ✓ It is required to overcome: The resistance of airflow through respiratory **Airway resistance work is inversely proportional to total cross sectional area of air passages**:

- ***Greatest resistance*** is in medium size bronchioles.
- ***Less resistance*** is in small size small bronchioles [because of their large number &large surface area]

Dead Space (DS)

❖ **Definition:**

- Air which does not share in diffusion (gas exchange) with blood
- With each respiration: 500 cc air are taken:



➔ 350 cc enter alveoli (alveolar air) & undergo gas exchange with blood

➔ While 150 cc remain in DS

❖ **Types:**

1- **Anatomical DS** (the conducting zone)

➢ Air passages from: Nose -->Pharynx to→ Trachea to→Bronchi to→ Bronchioles down → Respiratory bronchioles

➢ Because of their thick wall: Normal values: = 150 - 167 ml
= 30% of tidal volume

➢ **Vagus**: Leads to broncho constriction ie decrease dead space

➢ **Sympathetic**: Leads to broncho dilatation ie increase DS

2- **Alveolar DS**: Some alveoli not undergo gas exchange because they have no blood supply

3- **Physiological DS** (Anatomical DS + Alveolar DS)

Under normal conditions: Physiological dead space = anatomical DS because all alveoli are functioning

➢ **Significance:**

1] With each respiration: 500 cc air are taken:

- 350 cc enter alveoli (alveolar air) & undergo gas exchange with blood
- -While 150 cc remain in DS

2] It protects alveoli against damage:

- It warms, filters & moistens the inspired air
- Particles with a diameter:

❶ More than **10 microns**: Are caught in nose hairs, stick to mucus of nose

❷ **2-6 microns**: Stick to mucus of trachea & bronchi then expelled by: 1- Cough 2-Sneeze reflexes 3- Movements of cilia

❸ Less than **2 microns**: Are removed by phagocytic cells in alveoli

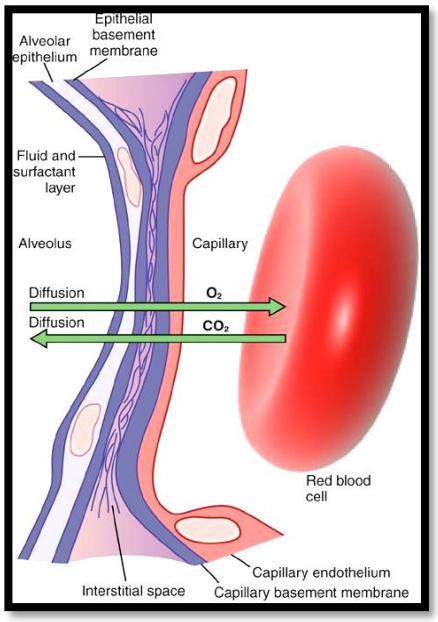
❹ Less than **0.3 microns**: Remain in air phase in the alveoli & are breathed again

➢ **Measurement:1-** Fowler method 2-Bohar method

Respiratory functions of blood

Gas exchange between alveolar air & venous blood occurs by simple diffusion.

➢ R: Rate of gas diffusion ➢ Pl- P2: Pressure difference ➢ T: Temperature ➢ A: Surface area of diffusion ➢ M: Square root of molecular size ➢ L: Length of the system ➢ S: Solubility of the gas in the medium ➢ n: Viscosity of the medium
❖ Respiratory membrane: ➢ Measures: 0.2 micron ➢ Formed of the following layers: A)- Fluid lining alveoli and surfactant B)- Alveolar epithelium C)- Epithelium of basement membrane D)- Interstitial space containing fluid E)- Capillary basement membrane F)- Capillary endothelium



Ultrastructure of the alveolar respiratory membrane, shown in cross section

❖ **Diffusion of gases**

- **Physical factors which control diffusion:**

[**A] Diffusion in gaseous media:**

- ***In a gaseous media***, the rate of gas diffusion (R) is:

1- **Directly proportional with**: A)- Pressure difference (Pl- P2)

B)- Temperature (T) c)- Surface area of diffusion(A)

2- ***Inversely proportional with:***

1] ***Square root of molecular size (M)*** : O2 has molecular weight less than CO2

2]***Length of the system***

$$R \alpha \frac{(Pl- P2)\ T\ A}{M\ L\ \sqrt{\ }}$$

2-In gaseous media: The diffusion rate of O2 is 1.2 times faster than CO2

This is because O2 (oxygen) has molecular weight (MW) less than CO2

[B**] Diffusion in aqueous media**

→ In the body, the respiratory gases diffuse through aqueous media e.g.:

1- Pulmonary membrane 2- Plasma 3- Erythrocyte wall

→ Two additional factors are considered:

1- Directly proportional with: Solubility of the gas in the medium (S)

CO_2 is 24 times more soluble in water than O_2

2- Inversely proportional with: Viscosity of the medium (n)

$$R \alpha \frac{(P1-P2)\ T\ A\ S}{\sqrt{M}\quad Ln}$$

{C} In aqueous media:

- The diffusion rate of CO2 is 20 times faster than O2

➔ This is because CO2 is 24 times more soluble in water than O2. Thus, in lung diseases (eg thickening of pulmonary membrane): Diffusion of O2 across the pulmonary membrane is affected earlier than that of CO2

❖ **Factors affecting diffusion of gas through the respiratory membrane**

[A] Diffusion rate is directly proportional to

1- Pressure gradient of gases across the respiratory membrane: i.e. between alveolar air (= arterial blood) & venous blood (= tissue)

Normally:		**Alveoli (Arterial blood)**	**Venous blood (tissue)**	**Pressure gradient**
	PO_2	100	40	60mmHg
	PCO_2	40	46	6 mmHg

So, O2 diffuses from alveoli to tissue & CO2 diffuses from tissue to alveoli

2- Surface area of pulmonary membrane:

➔ ***Normally***: It is 100 m2 (square meter)

➔ ***Increases*** in Muscular exercise due to:

1- More expansion of alveoli

2- Opening of closed capillaries

3- Dilatation of the already opened capillaries

➔ **Decreases** in:1- Old age 2- Emphysema 3- Lung collapse

3- Temperature (T)

4- Diffusion coefficient: i.e., - solubility in water

- CO2 is 24 times more soluble in water than O2

[B] Diffusion rate is inversely proportional to:

1)- **The square root of the molecular weight**

2)- **Thickness of the respiratory membrane**

➔ ***Normally***: It is 0.2 µ

➔ ***It increases with***: 1- Pulmonary edema 2- Lung fibrosis

Diffusion rate of CO2 is 20 times faster than O2

Alveolar ventilation (V_A) / pulmonary perfusion (Q) ratio

❖ ***Normally***:

① Alveolar ventilation is 4L / min.

② Pulmonary perfusion is 5L / min

So, the V/Q ratio is 0.8 [An ideal V/Q = 0.8 – 1.2 (matched V/Q)]

NB: *Both ventilation & perfusion are not equal all through the lung*:

At lung apex: The perfusion is less (so the V/Q ratio is high "3")

At lung base: The perfusion is more (so the V/Q is low "0.6")

❖ ***Causes of regional difference in lung ventilation***:

➔ ***Normally***: The intrapleural pressure at the apex of the lung is more (-ve) than at the base

- **So** trans pulmonary pressure is higher at the apex.
- **So** apical alveoli are more expanded.

So, the ventilation at the apex is high & at the base is low

❖ ***Causes of regional difference in perfusion:***

➔ (Due to the effects of gravity on pulmonary arterial pressure)

➔ **At the lung apex**: the pulmonary arterial pressure ↓↓ (< the alveolar pressure) → the capillaries nearly close At the lung base: the pulmonary arterial pressure ↑↑ → ↑↑ blood flow.

➔ **At the lung base**: the pulmonary arterial pressure ↑↑ → ↑↑ the blood flow

❖ ***Assessment of Regional ventilation & Perfusion:***

1- To test for ventilation: Xenon gas is inhaled & its distribution in lung is measured

2- To test for alveolar perfusion: Tc^{99} is injected IV & its distribution in lung is measured

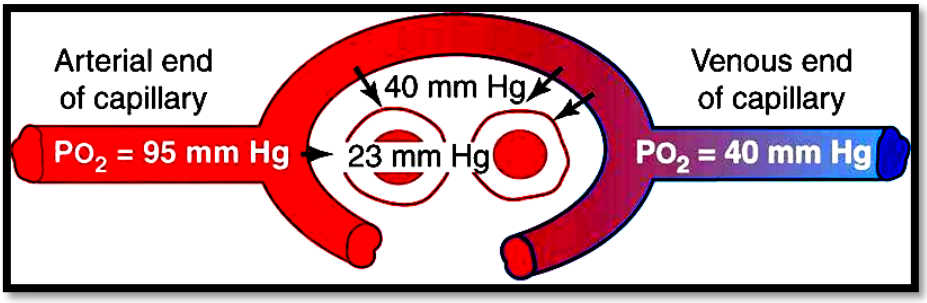
❖ ***V/Q mismatch*** :

➢ ↑ V/Q (when Perfusion ↓) eg by a Pulmonary Embolism "PE"

➢ ↓ V/Q (when ventilation ↓) eg by a emphysema.

Gas transport by the blood

A)- Oxygen (O2) transport (carriage) by blood



Diffusion of oxygen from a peripheral tissue capillary to the cells.
[(PO_2 in interstitial fluid = 40 mm Hg, and in tissue cells = 23 mm Hg]

-**Forms of O_2 transported:** O_2 is transported (carried) in blood in two forms:

1- Oxygen in physical form:

❖ ***Nature***: Free O_2 molecules dissolved in blood

❖ ***Volume:*** Normally:

➔ **0.3 ml/100 cc arterial** blood ie:

- 3 ml in one liter
- As normal blood volume is 5 liter, so O_2 in physical form is 15 ml

➔ **0.13 ml/100 cc venous** blood ie: Tissue take 0.17 ml/ 100 cc

❖ ***Importance:*** It determines:

  ➢ The O_2 tension (PO_2)

  ➢ O_2 tension; in turn determines the rate & direction of O_2 diffusion

O_2 tension (PO_2) - PO_2 in **arterial** blood = 100 mmHg - PO_2 in **venous** blood = 40 mmHg

2-Oxygen in chemical form:

❖ ***Nature:*** O2 combines with the iron of hemoglobin, while still in the ferrous state, this reaction is called oxygenation

❖ ***Volume***: Normally:

➔ **19.5 ml/ 100 cc arterial blood**

- 65 times as physical
- It depends on O2 tension
- 98% of O2 is transported in chemical combination with Hb to supply tissues.

➔ **14.5 ml/100 cc venous bloods**.

- The amount of O2 taken by tissues during rest = 19.5-14.5 = 5 ml

❖ ***Importance*:** It constitutes the main supply of O2 to the tissues

Definitions:

- **Oxygen content:** It is the volume of O_2 in ml present in **chemical combination** in l00cc blood.
- **Oxygen capacity**: It is the volume of O_2 in ml present in **chemical combination** in 100 cc blood when Hb is **fully saturated** with O_2

- **It does not** depend on **O_2 tension but on amount of Hb**:
- The adult: Contains 15 g Hb/100ml of blood

Each gm combines with 1.34 ml O_2

So O_2 capacity = 15 × 1.34 = 20 ml O_2/100 ml blood

- **% Saturation of Hb With O2**

=	O_2 content	× 100
	O_2 capacity	

In anemia: Reduction in Hb→ Decreases both O_2 content & O_2 capacity. Thus the % saturation is not affected

- **Coefficient of O2 utilization: I**t is % of O_2 in arterial blood which is taken by tissues

=	**Arterial O_2 content - Venous O_2 content**	**× 100**	
	Arterial O_2 content		
=	19.5 – 14.5	× 100 = 25%	**25% during rest**
	19.5		**75% during exercise**

It is: →**Directly proportional with**: Activity of tissues

→**Inversely proportional with**: Rate of blood flow

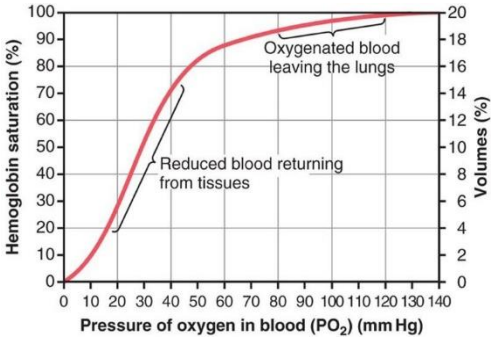
The oxygen dissociation curve

★ The oxygen dissociation curve of hemoglobin (oxyhemoglobin dissociation curve)

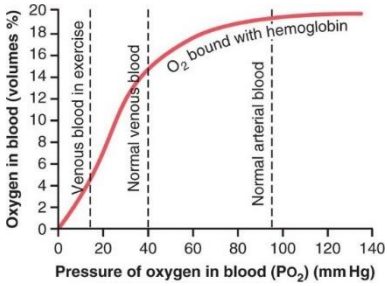
★ This curve shows the relationship between:

- **O_2 tension (PO_2)**
- **Percentage (%) saturation o**f hemoglobin with O_2 **(not O_2 content)**

Why? Because O_2 content varies from person to person according to hemoglobin content which decreases in anemia, so it will not be a universal curve.



Oxygen-hemoglobin dissociation curve



Effect of blood PO_2 on the quantity of oxygen bound with hemoglobin in each 100 milliliters of blood

➢ It is S shaped (not linear) because: hemoglobin is made of 4- subunits that load and unload O_2 with different affinities

❖ **Physiological significance of oxyhemoglobin dissociation curve**:

➔ ***At lungs (Alveoli)*** ***(****Flat or plateau part of the curve)*

- While PO_2 drops from 100 to 60 mmHg, the % of saturation drops only from 97 to 90%.
- This allows easy and nearly complete Saturation even if the O_2 tension is low (as in high altitude → allowing persons to get enough O_2 from their blood) because at high tensions of O_2, there is high affinity of Hb to O_2

➔ **At tissue (Venous)** (*Steep part of the curve)*

- While O_2 tension drops from 60 to 40 mmHg (resting venous blood), the % saturation drops from **90 to 70%**
- With exercise, O_2 tension drops to **20 mmHg** (due to increase O_2 consumption) & % of saturation drops to **30 %,** ie an extra 40% of O_2 is given to tissues.
- So, O_2 dissociation curve for Hemoglobin at tissues allows easy and rapid **Dissociation** even if the O_2 tension is not markedly lowered (as in muscular exercise) allowing tissues to take more O_2. This is because at low tensions of O_2, there is **low affinity** of Hb to O_2

❖ **Factors affecting oxyHb "Oxygen-hemoglobin" dissociation curve:**

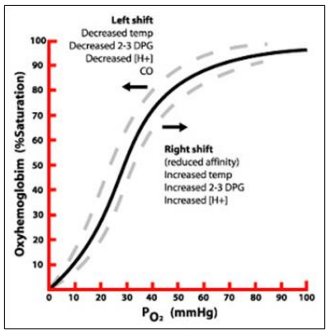
[A] Shift of the curve to the right:

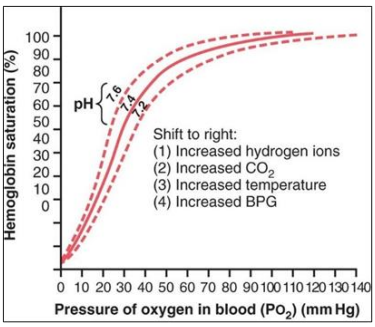
- **Decrease affinity** of Hb to O_2 ie **unloading** of Hb

1. Increase CO_2
2. Increase H^+ (low pH)
3. Increase temperature
   - Effect of CO_2 & H^+ on oxyHb dissociation curve is called **Bohr Effect** 1 & 2 & 3 occurs during muscular exercise to supply the active muscles with oxygen.
   - **Mechanism**: CO_2 & H^+ combine with sites on Hb changing its configuration & facilitating off-loading of O_2
4. Increase 2, 3-DPG: **(2, 3 diphosphoglycerate)**:
   - It is an end product of RBC metabolism. It occurs in cases of hypoxia & exercise

[B] Shift of the curve to the left:

- **Means:** *Increase affinity of Hb to O2 ie loading of Hb.*
- **Causes:** **1-** Decrease CO_2 2- Decrease H^+ (high pH) **3-** Decrease temperature 4- Decrease 2, 3 DPG 5- Carbon monoxide: It form carboxy Hb and causes shift of the remaining oxyhemoglobin to the left

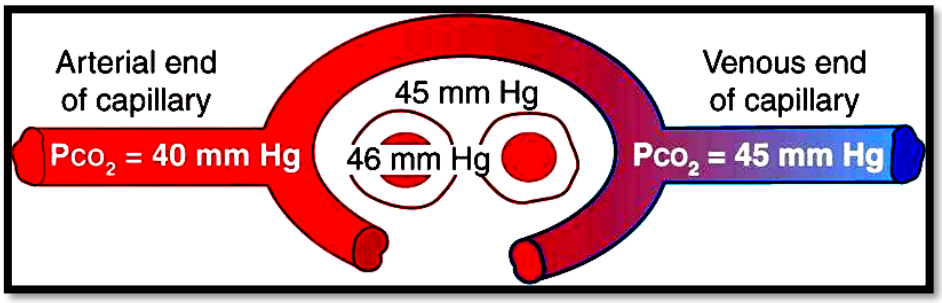




Shift of the oxygen-hemoglobin dissociation curve to the right caused by an increase in hydrogen ion concentration (decrease in pH). BPG, 2.3-biphosphoglycerate

- The position of O_2 dissociation curve can be expressed by stating Po_2 at which Hb is 50% saturated (**P50**)
- **The P50 is an inverse function of the Hb Affinity for** O_2: SO
- Hb With ↑O_2 affinity will have a dissociation curve with ↓ **P50** that lies to the left (shift to left)
- Hb With ↓O_2 affinity will have a dissociation curve with ↑**P50** that lies to the right (shift to right)
- The normal **P50** for arterial blood is 27 mmHg.

B)- Carbon dioxide (CO2) transport (carriage) by blood



Uptake of carbon dioxide by the blood in the tissue capillaries [(PCO_2) in tissue cells = 46 mm Hg, & in interstitial fluid = 45 mm Hg)]

➔ CO_2 moves down its pressure gradient from tissue → blood plasma → RBCs → lungs.

Forms of CO_2 transported: CO_2 is transported in blood in two forms:

Carbon dioxide in physical form

- **Nature**: **Soluble CO_2** [CO_2 is a more soluble gas than O_2]
- **Volume:** Normally: - **3 ml/100 cc arterial** blood
  - **3.4 ml/100 cc venous** blood

CO_2 tension (PCO_2)

- PCO_2 in **arterial** blood = 40 mmHg
- PCO_2 in **venous** blood= 46 mmHg

$CO_2 + H_2O \leftrightarrows H_2CO_3 \leftrightarrows H^+ + HCO_3$

- This reversible reaction in RBCs is 13000 times faster than in plasma because of the presence of **carbonic anhydrase enzyme** in RBCs & not in plasma

- **At tissues**: The reaction goes to the right (due to addition of CO_2)
- **At the lungs**: The reaction goes to the left (due to removal of CO_2 into air)

- **Definitions:**

➔ Venous CO2:

- Is the venous CO2/100 cc blood.
- Venous CO2 = Tidal CO2 + Total CO2
- It equals = 52 ml which are distributed as follows
  - 3.4 ml in physical form
  - 4 ml in form of **carbamino compound**
  - 44.6 ml in form of **bicarbonate**

➔ Tidal CO2

- Is the CO_2 given by tissues to each 100 ml blood
- It equals = 4 ml/100cc which are distributed as follows:
  - 0.4 (10%) in physical form
  - 1 ml (25%) in form of **carbamino compound**
  - 2.6 (65%) in form of **bicarbonate**

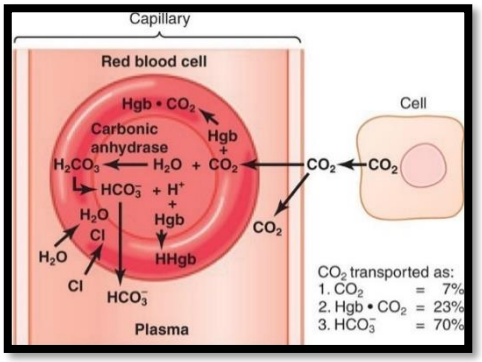
➔ Total CO_2

- Is the arterial CO_2/100cc blood.
- It equals= 48 ml/100cc which are distributed as follows:
  - 3 ml in physical form
  - 3 ml in form of **carbamino compound**

- 42 ml in form of **bicarbonate**

➔ **Buffering of the tidal CO_2:**

- The 4 ml added by the tissues should be buffered; otherwise they will decrease the pH of the blood to a dangerous level



Transport of carbon dioxide in the blood

- **They are carried as follows**:

- 0.4 ml in physical solution, so the pH of the blood will decrease from 7.4 to 7.35
- 1 ml as **carbamino compound**. The reduction of oxy-Hb to reduced Hb at the tissues allows the formation of more carbamino compound.
- 2.6 ml are buffered by Hb with resultant production of HCO3. This is done through Cl^- shift phenomenon

Chloride shift phenomenon (=Hamburger's) phenomenon or Gas exchange at tissues

➢ ***Definition***: Exchange of anions between RBCs & plasma to maintain pH constant & keep electrical equilibrium.

➢ It is responsible for carrying most of CO_2 in form of HCO_3.

➢ **The membrane of RBCs Is**:

- Permeable to anions (eg Cl^- & HCO_3^-).
- But impermeable to cations (K^+& Na^+) **EXCEPT** H^+
- However, any Na^+ enters the RBCs is immediately pumped

➢ **When blood is exposed to high CO_2 tension (at tissues), the following occurs**:

1- CO_2 enters the blood from the tissues:

- It passes through the plasma to RBCs #
- RBCs contain carbonic anhydrase (CA) enzyme:

➢ It is a protein having MW 30,000 & contain zinc

➢ This enzyme accelerates the reaction: $CO_2 + H_2O \rightarrow H_2CO_3^-$

➔This reaction occurs very slowly in plasma in absence of CA

2- The H_2CO_3 dissociates to H^+ & $H_2CO_3^-$.

3- At the same time, oxygen is given by the red cells to tissues.

4- **Reduced hemoglobin is weaker acid than oxyHb** → so, K^+ is released & combines with $H_2CO_3^-$ to form $KHCO_3$.

5- **H^+ of carbonic acid is buffered primarily** by reduced Hb (reduced Hb binds more H^+ than oxy Hb)

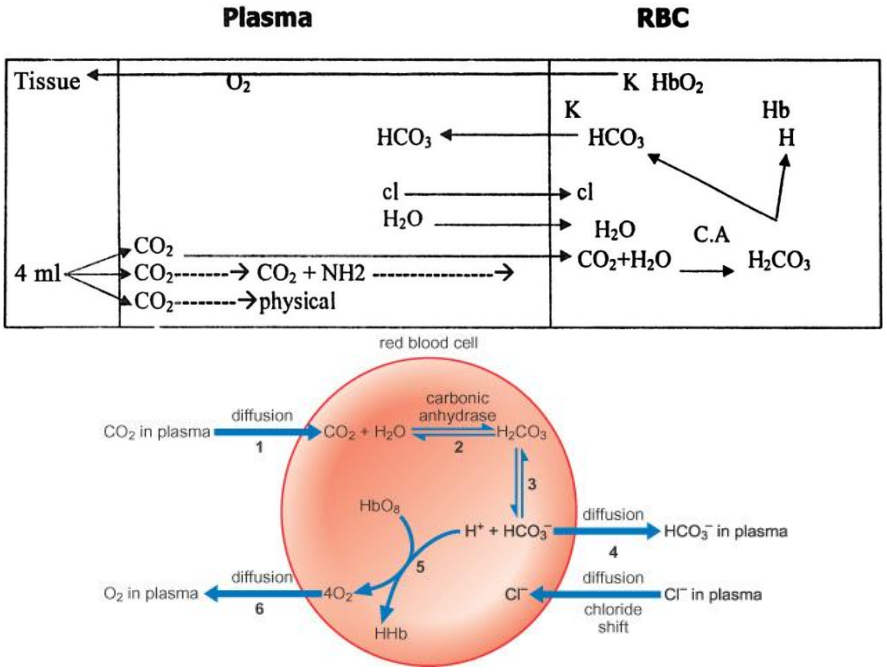
6- **At the same time**, the reduced Hb can form more carbamino compound with CO_2.

7- **According to concentration gradient**, both K^+ & $H_2CO_3^-$ try to pass to plasma, but only anions ($H_2CO_3^-$) pass. About 70% of $H_2CO_3^-$ formed in the red cells enters the plasma.

8- **According to electrostatic gradient,** Cl^- passes from plasma toRBCs.

This process continues until: $\frac{Cl^-\text{ in plasma}}{Cl^-\text{ in RBCs}} = \frac{H_2CO_3^-\text{ in RBCs}}{H_2CO_3^-\text{ in plasma}}$ (Donnan' Equilibrium)

9- **Due to increase osmotic pressure of RBCs (by Cl^-),** H_2O shifts from plasma to red cells leading to increase red cell size. Thus, the haematocrit value of venous blood is normally 3% greater than that of arterial blood



The net results are:

	RBCs	**Plasma**
HCO_3	Increase	Increase
Cl	Increase	Decrease
Cations (Na^+& K^+)	Constant	Constant
Osmotic pressure	Increase due to HCO_3 & Cl	Constant
H_2O	Diffuse from plasma to RBCs →	

	increase hematocrit	
pH	Constant	Constant

Carbon dioxide in chemical form

- **Nature**: CO2 is in form of bicarbonate & carbamino compounds.
- **Volume**: Normally: 45 ml/100 cc arterial blood:
  - 42 ml in form of bicarbonate
  - 3 ml in form of carbamino

1- Bicarbonate:

- Is the most important form of CO2
- **In RBCs**: CO2 is carried as KHCO3
- **In plasma**: CO2 is carried as NaHCO3 (which is alkali reserve).

2- **Carbamino compounds**: ie combined with protein

- **In RBCs:** CO2 is carried as carbamino-hemoglobin [combined CO2 with amine group of hemoglobin (Hb-NH-COOH)]

NB: The more the hemoglobin is deoxygenated (reduced) the more it can combine with carbon dioxide to form carbamino compounds

- **In plasma:** CO2 is carried as carbamino protein (combined CO2 with terminal amine group of plasma protein).

Control of Respiration

A. Involuntary control:

- **Respiratory centres**: Are composed of respiratory neurons
  - **Two types:**

1- I neurons:

- Discharge during inspiration
- Actively inhibited during expiration

2- E neurons:

- Discharge during expiration
- Actively inhibited during inspiration
- Located in brain stem (pons & medulla)
- Send to respiratory motor neurons via reticulospinal tract

This pathway allows spontaneous rhythmic breathing unconsciously (During day, sleep, anaesthesia)

➢ **Medullary centres: are**

1- Dorsal Respiratory Group (DRG)

➢ **Position**: Dorsomedial in medulla bilaterally

➢ **Site**: Located in: Nucleus of tractus solitaries, it is the sensory termination of 9^{th} & 10^{th} cranial nerves which are the afferent from: Chemoreceptors, Baroreceptors and Mechanoreceptors

➢ **Contains**: Inspiratory neurons only.

➢ **Function**:

➔ They are responsible for inspiratory activity during normal quiet breathing
➔ Pacemaker activity (Discharge spontaneous)

➢ **Rhythmicity**:

➔ Rhythmic inspiratory discharge.
➔ Inherent rhythmicity (Discharge spontaneous)
➔ Have inspiratory ramp signals ie:

- Their activity increases gradually for 2 sec
- Then stop for 3 sec to allow passive expiration

➢ **Receives from**:

1- Apneustic center (excitatory impulses)
2- Lung stretch receptors (inhibitory impulses along vagus

➢ **Sends to**:

1- Ventral respiratory group (VRG)
2- Inspiratory muscles: Diaphragm & External intercostal muscle

2-Ventral Respiratory Group (VRG)

➢ **Position**: Ventrolateral in medulla bilaterally
➢ **Site**: Located in: Nucleus Ambiguous (NA) & Nucleus Retro-ambiguous (NRA)
➢ **Contains**: Inspiratory (I)& Expiratory (E) neurons
➢ **Function**: Contributes to forced inspiration & expiration
➢ **Rhythmicity**: NO rhythmic inspiratory discharge
➢ **Receives from**: DRG
➢ **Sends to: 1-** Muscle of expiration (E neurons)
2-Inspiratory muscles: (I neurones)➔ Diaphragm, External intercostal muscle& Accessory inspiratory muscles

NB

Medullary centers can maintain rhythmic respiration but it will be irregular & slow.

- **Pontine centers**

A)- **Apneustic Center (APC)**

- **Site**: Located in: Lower third of pons
- **Function**:
- ➔ Stimulates the dorsal respiratory group (DRG) ie it represents the inspiratory on-switch
- ➔ Increases the duration of inspiration
- **Receives from**:

a)- Inhibitory impulses from:

1- Lung stretch receptors: Along vagus (Herring Bruer reflex)

2- Pneumotaxic center (PNC): Slower than vagus

- **Sends to:** **1-** Stimulates DRG

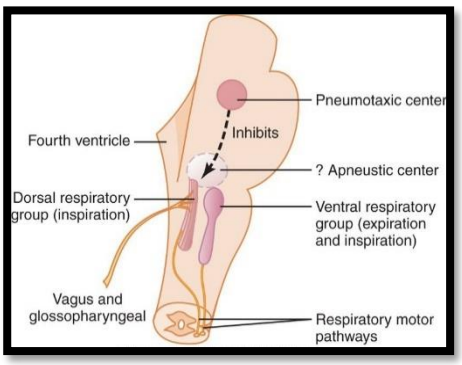
2-APC Stimulates Pneumotaxic center → Inhibits APC → stops inspiration

- **APC & PNC** act as modulating feedback control center. [APC stimulates PNC which when activated inhibit APC]

B)- Pneumotaxic Center (PNC)

- It is called nucleus parabrachialis medialis (NPBM)
- **Site**: Located in: Upper pons
- **Function**: 1- Terminates inspiration at fixed regular points by inhibiting APC ie it represents the **inspiratory off-switch** (IOS)

2-Limits the duration of inspiration



Organization of the respiratory centre

B. Voluntary control:

- Cerebral cortex send to respiratory motor neurons via:
    1. Corticospinal tract
    2. Corticobulbar tracts.

This pathway allows voluntary control of breathing during activities such as: Talking, Singing& Breath holding

- Genesis of normal rhythmic breathing (Eupnea)

1. **Apneustic centre** stimulates the medullary inspiratory neurones of DRG.
2. **Inspiratory neurones** of the DRG send impulses to the diaphragm & external intercostal muscles resulting in its contraction.
3. **This leads to expansion** of the chest and inflation of the lungs (inspiration).
4. **Inhibition of Apneustic centre** ie switch off by:

- **Signals from:** Pneumotaxic center: Apneustic center stimulates Pneumotaxic center. Pneumotaxic center in turn inhibits Apneustic center.
- **Vagus: Herring-Breuer reflex:**

➔ Vagus carries impulses from lung stretch receptors → inhibits apneustic center.

➔ It is active in animals & newly born.

- **Muscle spindles of intercostal muscles.**

5. Expiration:
    - Expiration follows passively
    - Lung stretch receptors stop to discharge their inhibitory impulses, **thus APC recovers from Inhibition & sends its impulses to DRG & the cycle repeat itself**

Regulation of Respiration

1- **Under normal resting conditions**, the adult person consumes 250 ml O2 & excretes 200 ml CO2/min. The pulmonary ventilation Is about 6 liters/min. ·

2- Respiration is regulated to ensure proper pulmonary ventilation, protect airways and lungs & maintain O2, CO2, H+ tensions in arterial blood & alveolar air constant eg muscle exercise (increase metabolism) which leads to increased CO2, and acid production and increased O2 consumption will, in turn, stimulates respiration.

3-**Regulation of respiration Involves 4 main elements which ar**e:

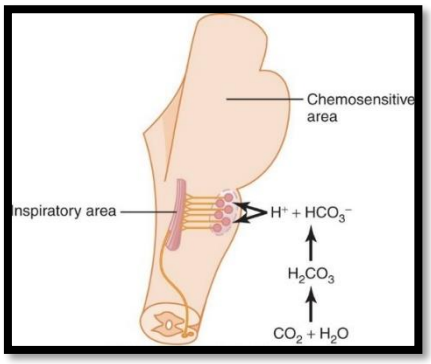
A. Sensors to detect physiologic variables in body
B. Central controller (respiratory center)
C. Effectors (respiratory muscles)
D. Negative feedback (the response affects the original stimulus)

- **There are 2 modes of Regulation of respiration:**

A- Chemical regulation

➔ It is the basic mechanism
➔ Chemical factors (PCO_2, H^+, PO_2)
➔ Chemoreceptors are of two types:
a)- Action chemoreceptors b)- Slight inhibitory chemoreceptors
➔ Respiration is **stimulated** by:
a. Increased CO_2 tension (PCO_2) of **arterial blood**
b. Increased H^+ ion concentration of **arterial blood**
c. Decreased O_2 tension (PO_2) of **arterial blood**
➔ However, changes in opposite direction have an inhibitory effect
➔ Respiratory rate is adjusted according to **metabolic rate**
➔ These **chemical factors** exert their effects on respiration by acting on: **Central chemoreceptor& Peripheral chemoreceptors**

1- **Central Chemoreceptors:**



Stimulation of the brain stem inspiratory area by signals from: the **chemosensitive area** located bilaterally in the **medulla**

➔ Lying only a fraction of a millimeter beneath the ventral medullary surface.
➔ Hydrogen ions stimulate the chemosensitive area,
➔ NB: carbon dioxide in the fluid gives rise to most of the hydrogen ion

- **Site**: They are in bilateral, **just beneath** the ventral surface of the medulla (they are separate from neurons of respiratory centre). They are protected by the blood brain barrier (BBB)

NB: BBB separates blood from CSF

➢ **Stimulus**: 1- H^+ in CSF is the only direct stimulus

NB: H^+ in blood do not cross BBB

2- CO2 have very potent indirect effect

CO2 in blood cross BBB to reach the CSF

3- In CSF (cerebrospinal fluid):

CO2+ H2O —CA→ H2CO3 —Dissociate to→ HCO3 + H+

4- H+ stimulates the central chemoreceptors (ie responding to local H+)

5- Thus, a small change in arterial PCO_2 (3%) will double ventilation

2-Peripheral chemoreceptors

➢ **Site**: They are nerve endings present

1- In Carotid bodies

- At the bifurcation of the common carotid arteries
- Send impulses along branch of glossopharyngeal nerve (Herring's nerve)

2- Aortic bodies:

- Two or more bodies in the aortic arch send impulses along vagus nerve

➢ **Stimulus**: They are stimulated:

1- Mainly by decreased O2 tension of arterial blood

- The receptors depend only on dissolved O2 (physical form)
- This is because the blood flow to the aortic and carotid bodies is high i. e 20 ml/min/gm (20 times the weight of bodies themselves)
- Therefore, the receptors are not stimulated on conditions of anemia in which the amount of dissolved O2 and accordingly O2 tension be normal
- They are stimulated when blood flow decreases markedly as in hemorrhage & hypotension

2- **By increased H+ ion concentration & CO2 tension (to a slight extent)**

❖ **Mechanism of stimulation of peripheral chemoreceptors:**

1- **Oxygen tension**:

★ Hypoxia is the most potent stimulus for peripheral chemoreceptors

★ Drop of PO2 from 100 to 60mmHg (plateau part of O2 dissociation curve) → increased is charge from peripheral chemoreceptors but not affect ventilation.

★ At PO2 = 60 mmHg → ventilation is doubled

★ At PO2 from 60 to 30 mmHg (steep part of curve) → ventilation increases 6 times
★ At PO2 20 mmHg or less → inhibition of respiratory center.

2- **CO2 tension:**

★ Peripheral chemoreceptors are less sensitive to PCO2 than central chemoreceptors
★ Denervation of carotid bodies reduce ventilatory effect of hypercapnia by 20%.

Ventilatory Response to CO2:
-CO2 excess is more effective stimulus for respiration than O2 lack
-CO2 affects both central (more Important) and peripheral chemoreceptors (discuss).
-Increase CO2 to 3% → in Inspired air will double the ventilation.
-Increase CO2 to 6% → in Inspired air will Increase ventilation 6 times
-Increase CO2 to 10% →in Inspired air will Increase the ventilation 10 times
- Increase CO2 to 20% or 50 mmHg will depress the respiratory center
-Pathways: Through central & peripheral chemoreceptors.....discuss

3- H+ concentration:

- Change in H+ concentration as in metabolic acidosis &alkalosis affect respiration eg: Metabolic acidosis→ Caused by lactic acid
- Stimulates ventilation through peripheral chemoreceptors. This lowers PCO2 & therefore H+ content returning pH to normal.

B-Non-chemical regulation

➢ **The respiratory center is influenced by various impulses reaching it from:**
- Higher centers
- Large number of sensors located in the:

1. Lungs
2. Cardiovascular system
3. Muscles Along afferent nerves
4. Tendons
5. Skin & viscera

[1] Afferent from higher centers:

(A)Cerebral cortex:

➢ ***Controlled*** - Expiration -Talking -Singing - Playing instruments

➔ excitatory and inhibitory impulses pass from cortex to respiratory centers or bypass centers and pass directly to spinal motor neurons of respiratory muscles

➢ **Voluntary hyperventilation:** Its duration is limited by CO2 level in blood.

Hyperventilation is followed by a period of apnea due to increased PO2 & decreased CO2. This is followed by few shallow breaths due to decreased PO2 i.e periodic breathing occurs

➢ **Voluntary apnea**: Is voluntary breath holding. The point at which the person is obliged to breathe again (45-60 sec) is called the breaking point

➔ It is due to increased PCO2 & decreased PO2 & increased H+.

➔ It is mainly due to Increased PCO2 which stimulate central chemoreceptors

➔ **It can be prolonged by**:

1- Hyperventilation before breath holding (prolong by 15-20 sec) to wash CO2 →decreased arterial CO2 tension
2- Breathing 100% O2 for one minute before experiment
3- Holding the breath in full inspiration This discharges inhibitory impulses to respiratory center
4- Swallowing (Deglutition) which inhibits respiration

B)- Hypothalamus:

➢ It is higher center for integration of visceral & somatic functions. It contains many centers which are related to respiration.

➢ **Parasympathetic center**: If it is stimulated (eg pain) → inhibit respiration

➢ **Sympathetic center**: If it is stimulated (eg emotions) stimulate respiration

➢ **Temperature center**: If it is stimulated (eg fever) stimulates respiration

[2] Afferent from Respiratory centers

A)- Afferents from upper respiratory passages:

➢ These reflexes (**Protection reflex**) protect alveoli from invasion by harmful irritants

	Sneezing reflex	**Cough reflex**	**Swallowing**
Stimulus	Irritation of nasal mucosa	Irritation of larynx, trachea & bronchi	Stimulation of pharyngeal mucosa
Afferent	Trigeminal nerve	Vagus nerve	Glossopharyngeal
Response	Deep inspiration followed by -forced expiration against an opened glottis	Deep inspiration followed by - forced expiration against a closed glottis which opens suddenly.	Swallowing apnea i.e. stoppage of respiration and closure of glottis

		- Contraction of abdominal muscles & rise of intra-abdominal pressure (100 mmHg)	
Results	Rush of air to outside getting rid of irritants	Rush of air to outside getting rid of foreign body or sputum from air passages	To prevent aspiration of food

B)- Afferents from lungs:

1. Lung stretch receptors:

- **Stimulus:** Lung inflation and airway distension
- **Receptors:** Stretch receptors in airway smooth muscles-slowly adapting Receptors
- **Afferent:** Vagus nerve
- **Response :**

1. Initiates Herring Breuer reflex which switch off Inspiration by inhibiting APC & DRG.
2. Not powerful in human but functions in newborns & animals
3. It is protective as it prevent lung over inflation.
4. Control rate & depth of breathing

1. Lung irritant receptors

- **Stimulus:** Mechanical eg dust particles-chemical: Exogenous eg noxious gases, cigarette or endogenous eg histamine
- **Receptors:** In mucosa of bronchi & bronchioles
- **Afferent:** Vagus nerve
- **Response:**

1. Cough to expel irritant substances
2. Bronchospasm & apnea to limit penetration of dangerous substance

2. J receptors (juxta pulmonary capillary receptors)

- **Stimulus:** Pulmonary congestion (increase pulmonary interstitial fluid pressure or capillary pressure) as in left sided heart failure
- **Receptors:** In alveolar wall close to pulmonary capillaries
- **Afferent:** Vagus nerve
- **Response**: Tachypnea (shallow rapid breathing)-dyspnea (difficult resp)

3)- **Afferent from Cardiovascular system**

(A) Arterial baroreceptors (High pressure receptors)

- **Site:** Aortic arch & carotid sinus

- **Stimulus:** Arterial blood pressure (60-180 mmHg) & pulse pressure
- **Afferent:** Vagus & glossopharyngeal nerves
- **Response:**

- Increased ABP inhibits respiration and decrease tone of abdominal muscles→ this decreases venous return, cardiac output and so, ABP return to normal.
- Proof: Injection of nor adrenaline or large dose of adrenaline leads to vasoconstriction and rise ABP which inhibits respiration (Adrenaline apnea)

(B) Atrial receptors (Low pressure receptors)

- **Site:** Right atrium & big veins opening into it
- **Stimulus:** Increased venous return & increases central venous pressure (CVP)
- **Afferent :** Vagus nerve
- **Response:**

1. Increased venous return will stimulate stretch receptors in the wall of the right atrium.
2. They send afferent Impulses along the vagus to stimulate the respiratory center.
3. This helps to increase ventilation to oxygenate the increased venous return (Harrison's reflex). This helps to increase ventilation during muscular exercise.

4)- **Afferent from chest wall receptors:**

- **Site:** Chest wall muscles & tendons
- **Stimulus:** Chest wall expansion & also tidal volume
- **Response:**

1. Inhibition of inspiration to determine tidal volume
2. In case of increase airway resistance or decrease compliance, the receptors stimulation gives rise to→ dyspnea

5)- **Afferent from proprioceptors**:

- **Site:** Skeletal muscles, tendons, joints, ligaments
- **Stimulus:** Active & passive movements during exercise
- **Response:** Increase ventilation during exercise

6)- Visceral reflexes:

(A) Swallowing &Vomiting :

- **Stimulus:** Food in pharynx
- **Receptors:** In mucosa of pharynx
- **Afferent:** Glossopharyngeal nerve
- **Response:**

1. Temporary apnea to prevent food from entering respiratory passages
2. Similar apnea occurs during straining & defecation

(B)Hiccup:

➔ It is a spasmodic contraction of the diaphragm which produces a sudden inspiration during which the glottis suddenly closes producing characteristic sound. It is due to abnormal stimulation of afferent endings in diaphragm.

➔ The afferent is the phrenic nerve. Most attacks are of short duration. It can be stopped by breath holding or inhalation of 6-7% CO2

(C)Yawning:

➔ It is a peculiar respiratory act, which leads to deep inspiration:

- To prevent collapse of under ventilated alveoli
- To increase venous return to heart
- Its physiological basis & significance are uncertain

Hypoxia

❖ **Definition:** Oxygen deficiency at tissue level

❖ **It may be due to**:

- Decrease O2 supply or.
- Decrease O2 utilization ability

❖ **Anoxia:** Complete absence of oxygen

❖ **Types:** Hypoxia is divided into four types:

1)- Hypoxic hypoxia (arterial hypoxia)

➔ In which PO2 of arterial blood is reduced

➔ This is the most common form of hypoxia seen clinically

➔ **Causes:**

1. Low oxygen tension in inspired air e.g. in: High altitudes & Mines
2. Pulmonary disorders:

A. Impaired ventilation: (hypoventilation)

- **Depression of respiratory centres** e.g. Morphine, Barbiturate& Anaesthesia
- **Obstructive lung diseases**: Bronchial asthma (acute), Emphysema (chronic) & Airway obstruction by foreign body

- **Restrictive lung diseases**:

i. Collapse (**tumor),** Compression (**pneumothorax)**, Consolidation (**pneumonia)**& Fibrosis (**TB**)

ii. Chest cage causes: Paralysis of respiratory muscles (poliomyelitis), Skeletal deformities (kyphoscoliosis)& Myopathy

B. Impaired diffusion:

- Normal rate of diffusion is 25 ml O_2/min/mmHg.
- **It decreases in**:

1. Pulmonary diseases which **decrease surface area** eg lobectomy
2. Pulmonary diseases with increase thickness of pulmonary membrane e.g.:

a. Pneumonia (alveoli filled with pus)

b. Edema (filled with lymph)-fibrosis

C. **Impaired ventilation perfusion:**

- Area with low V/Q ratio (Ventilation Perfusion ratio) result in hypoxic hypoxia eg obstructive lung diseases (emphysema) has low ventilation and normal perfusion
- So, the blood remains venous (physiological shunt)

D. Shunting of venous blood into arterial blood:

- **Congenital heart diseases** like atrial septal defect (ASD) in which there is right to left shunt & arterial po2 = venous po2

❖ **Symptoms of hypoxic hypoxia**:

1) Sudden severe hypoxia:

i. PO2 < 20 mmHg

ii. Loss of consciousness within 15 sec

iii. Death within 5 minutes

2) **Acute hypoxia**: (PO2=25-40 mmHg)

➔ symptoms like alcohol intoxication

- Drowsiness - Poor mental judgment - Euphoria - Headache
- Nausea - Vomiting

3) **Chronic hypoxia:(**40-60 mmHg: On top of mountain)

➔ symptoms like fatigue:

- Drowsiness - Headache - Nausea - Anorexia
- Dyspnea

❖ **Sign of hypoxic hypoxia: Generalized cyanosis**

2)- Anemic hypoxia (deficiency of Hb)

➔ In which PO2 of the arterial blood is normal but the amount of Hb available to carry O2 is reduced

➔ **Causes:**

1. **Quantitative (insufficient Hb):**

- In all types of anemia
- At rest hypoxia is not severe because 2, 3 DPG of RBCs is increases and causes shift to right of O2 dissociation curve decreasing affinity of Hb to O2
- At exercise, hypoxia is severing because increased O2 needs of tissues

2. **Qualitative (abnormal forms):**

1- Carbon monoxide (CO) poisoning:

- CO is a gas formed by incomplete combustion of carbon or gasoline
- **It is toxic because**:

1. CO combines with Hb to form carboxy hemoglobin at same site as O2
2. The affinity of Hb to CO is 210 times that for O2
3. Amount of carboxy Hb depends on duration of exposure and amount of CO in inspired air. CO in inspired air (0.1%) results in transformation of 50% Hb to carboxy HB. Death occurs when 70-80% of Hb is converted to COHb
4. Carobxy Hb shifts the O2 dissociation curve of the rest of oxy Hb to the left
5. Carobxy Hb breaks down very slowly

➔ **Signs**:

1. Cherry red color of carobxy-Hb in skin & mucous membrane
2. Increased cardiac output
3. NO increase in ventilation because peripheral chemoreceptors are not stimulated (arterial PO2 is normal)
4. Headache, nausea, loss of concentration

➔ **Treatment:**

1. **Termination of exposure by removal from CO atmosphere**
2. **Artificial respiration**

- ***Oxygen therapy***: Pure O2
  - 95% O2- + 5% CO2 because: CO_2 stimulates respiration Decrease affinity of Hb to O_2
  - Hyperbaric O_2: O_2 under pressure (1-3 atmosphere)

3. ***Blood transfusion***
4. ***Complete rest for several hours***

2- Met hemoglobin: (Oxidation of heme ferrous to ferric incapable to carry O_2)

❖ **Cause:** Oxidizing agents eg Drugs like nitrates or chlorates

❖ **Signs**: Dull grayish blue color in skin & mm resembling cyanosis

3- **Sulf hemoglobin**:(reduction of Hb to be incapable to carry O2)

- ❖ **Cause**: Powerful reducing agents eg Sulfur containing drugs
- ❖ **Signs:** Leaden color of sulf-Hb in skin & mm resembling cyanosisuse: Oxidizing agents eg Drugs like nitrates or chlorate

3)- Stagnant (ischemic) hypoxia (Inadequate blood flow through tissue or slow circulation)

- ➔ In which PO2 in arterial blood is normal & Hb is normal but blood flow to tissues is low
- ➔ **Causes:**

1- **Generalized**: Decreased cardiac output as in Heart failure & Shock.

- ➢ It affects mostly the brain, heart, liver & kidneys

2- **Localized**: Due to vascular obstruction of veins or arteries to a specific organ (eg atherosclerosis, thrombosis & embolism)

- ➔ **Signs**: Generalized or localized cyanosis

4)- Histotoxic hypoxia (Inhibition of tissue oxidative or cytochrome system)

- ➔ In which PO2 in arterial blood is normal, Hb is normal & blood flow is normal but due to toxic agents, tissue cells cannot utilize O2
- ➔ **Causes**:

1- **Cyanide poisoning**: Cyanide inhibits the cytochrome oxidase → cytochrome remains in the reduced form → cells cannot use (utilize) oxygen

2- **Alcohol (methylalcohol)+ narcotics:** Block dehydrogenase enzyme, so tissues cannot use oxygen

- ➔ **Treatment:**
- ❖ Methylene blue or nitrits are used to treat cyanide poisoning.
- ❖ They act by forming methemoglobin, which then react with cyanide to form nontoxic compound (cyanmethemoglobin).

❖ **Oxygen therapy in different types of hypoxia:**

1)- **O2 therapy is highly beneficial in**: Hypoxic hypoxia due to decrease:

a. Atmospheric O2 b. Hypoventilation c. Impaired diffusion

→ **It increases the amount of O2 bound to Hb as well as the dissolved O2. Also highly beneficial in CO poisoning**

2)- **O2 therapy is less beneficial in**:

a.Hypoxic hypoxia due to: AV shunt anaemic hypoxia c.Stagnant hypoxia

→ **It increases only the dissolved O2 in physical solution**

3**)- O2 therapy is not beneficial in Histotoxic hypoxia**

Cyanosis

- **Definition:** It is bluish coloration of skin & mucous membranes due to presence of excess reduced hemoglobin in blood capillary
- **Threshold:** - For cyanosis: 5 gm reduced HB/100 ml capillary blood
  - Reduced Hb has blue colour seen in:

A. Lips B. MM (Mucus membranes) C. Nail beds D. Lobule of the ear

- **Types:**

A. Generalized (or central) cyanosis
B. Localized (or peripheral) cyanosis

- **Causes of cyanosis & its relation with hypoxia:**

1) **Hypoxic hypoxia** due to decrease % saturation of Hb with O2 in arterial & venous blood
2) **Stagnant hypoxia**: due to low blood flow & extra O2 is removed from Hb.
3) **Asphyxia** eg airway obstruction, drowning

- **Cyanosis does not appear with:**

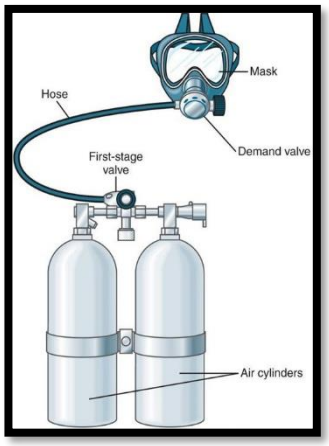
a. **Anaemic hypoxia** (because total amount of Hb is reduced & hence reduced Hb is reduced)
b. **Histotoxic hypoxia** (because there is failure of reduction of Hb)
c. **CO poisoning** (because of cherry red colour of carboxy Hb)

Effects of increased barometric pressure

Depth (feet/meters)	Atmosphere(s)
Sea level	1
33/10.1	2
66/20.1	3
100/30.5	4
133/40.5	5
166/50.6	6
200/61.0	7
300/91.4	10
400/121.9	13
500/152.4	16

Effect of sea depth on pressure

- **At sea level**, the person is exposed to pressure of one atmosphere. At this pressure, 1000 ml of Nitrogen gas are dissolved in tissues mainly in fatty tissues, nervous tissue as N_2 is five times more soluble in fat.
- **Every 10 meters of depth in sea water** (10.4 meter in fresh water), the pressure increases by one atmosphere.
- **So, at depth of 30 meter:** The diver is exposed to pressure of atmosphere & the amount of dissolved N_2 is 4000 cc. ie an extra 3000 cc N_2 are dissolved in tissues.
- Those who dig under water tunnel are also exposed to the same pressure in the chambers (caisson's) in which they work.
- The pressure of the gas, the diver breaths must be equal to pressure on his chest, otherwise he has difficulty in breathing (SCUBA device)



Open-circuit demand type of SCUBA apparatus

Problems associated with increased barometric pressure (under sea diving):

- **During Descend (compression)**

A. **CO2 toxicity**: Rare & seen only at great depths.

B. **O2 toxicity**:

- Prolonged exposure >12 hrs → oxygen toxicity develop rapidly.
- It can be avoided by using gas mixture of O2 & Inert gas (helium)

C. **Nitrogen narcosis:** Increased amount of dissolved N2 as a result of increased atmospheric pressure → lead to increase N2 in nervous tissue decreasing their excitability & anesthetic effects

- At 30 meter- euphoria
- At greater depth-- depression of CNS
- This is can be avoided by breathing gas mixture of oxygen & helium.

NB: Helium Is less soluble In body fluids than nitrogen

➢ **During Ascend (Decompression)**

❖ Decompression sickness:

1. **If the person is decompressed slowly**, the excess N2 is liberated, through lung & expired
2. **If the person is decompressed rapidly**, the excess N2 escapes from solution to form bubbles in tissues and blood.

- Bubbles in the tissues cause severe pain especially at joints
- Bubbles in the blood stream, which occur in more severe cases, obstruct arteries of the brain (cerebral) causing major paralysis, convulsions and respiratory failure
- Bubbles in coronary arteries may cause myocardial damage
- Bubbles in pulmonary vessels may cause dyspnea.

❖ **Treatment:**

1. Recompression in pressure chamber followed by slow decompression.
2. Decompression sickness may occur during rapid ascend in unpressurised airplanes

Only Nitrogen:

✓ Which can cause decompression sickness, Not CO2 because it can unite with buffers of tissues & blood

✓ Nor O2 because it is taken with hydrogen & utilized by time.