

PY-6.1 :- Functional Anatomy of Respiratory tract① Structure - function relationship of Respiratory tracta) Upper airway, conducting zone, Respiratory zone

- UPPER AIRWAY :- Nose, Paranasal sinuses, Pharynx.

- i) The respiratory system begins at the nose and ends in the distal alveolus.
- ii) The upper airways includes the structures from the nose to the vocal cords including sinuses and larynx.
- iii) The upper airways condition the inspired air bringing it to body temperature and also humidifies it.

Nose :-

- i) Filters, entraps and clears particles larger than $10\mu\text{m}$ in size.
- ii) It has surface secretory cells which produce impt Ig, Inflammatory mediators and interferons.

Paranasal sinuses :-

- i) lined by ciliated epithelium and surround nasal passages
- ii) Cilia moves the mucus from the upper airways & clears main nasal passages every 15 min
- iii) The fluid covering the surfaces is continually propelled into the nose.
- iv) The nasal cavity is only 20 ml in an adult but its surface area is $\uparrow$ due to nasal turbinates which are a series of cont ribbons of tissue

lessen the wt of skull in upright pos

Function of Sinuses

Resonance to voice

Protects brain from frontal trauma

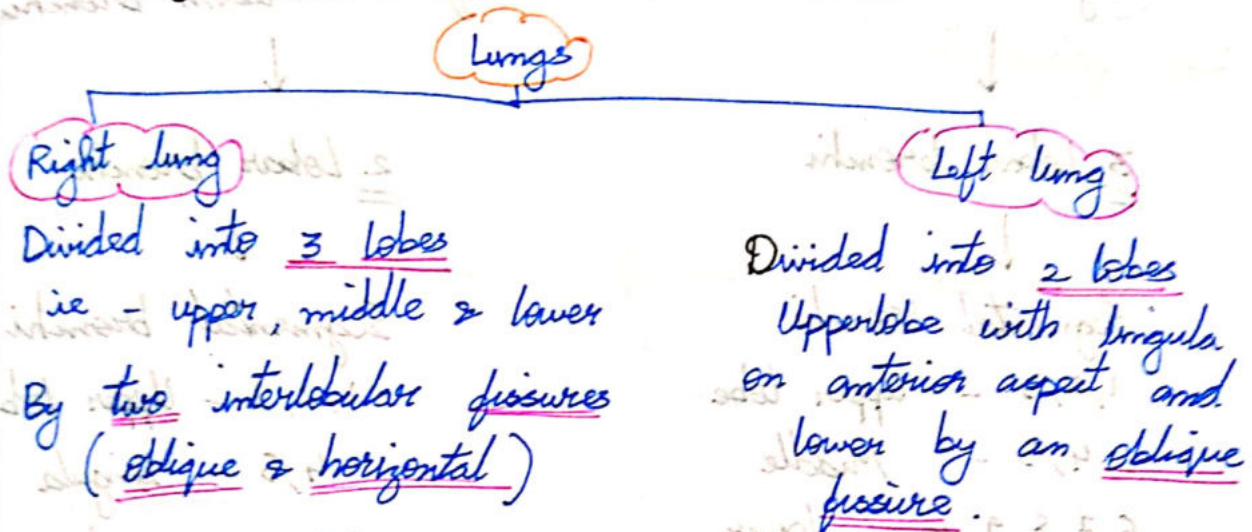
Pharynx :
 Nasopharynx
 Oropharynx
 Laryngopharynx.

- i) Nasopharynx is most anterior, lies behind the nose
- ii) In this region nose & mouth are connected by an isthmus that enables both oral & nasal breathing
- iii) Also contains Pharyngeal tonsils (adenoids) which fight infections
- iv) Connected to middle ear through eustachian tube - equalises pressure
- v) Drainage pathway of lymph B/W throat, nose and ears - common location for infections in head
- vi) Laryngopharynx helps to regulate the passage of food into esophagus and air into the lungs
- vii) Swelling of these structures - air flow resistance
- viii) The epiglottis and Arytenoid cartilages acts as hood over the vocal cords - prevent aspiration of

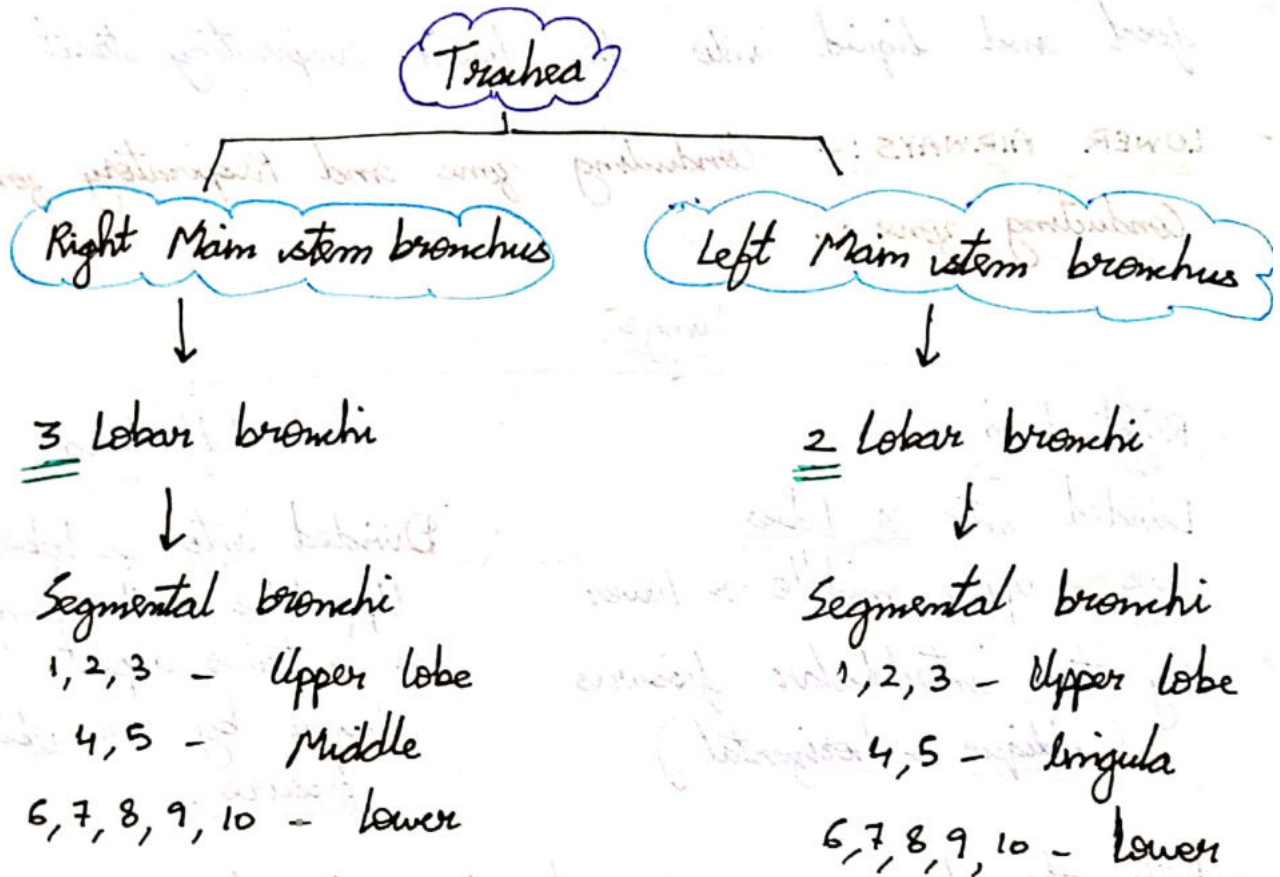
food and liquid into the lower respiratory tract

- LOWER AIRWAYS :- Conducting zone and Respiratory zone

Conducting zone :-



- i) Both the lungs are covered by visceral pleura and are enclosed by another membrane the parietal pleura
- ii) The space B/W these two pleura allows smooth gliding of lung as it expands in the chest & produces a potential space
- iii) Pneumothorax :- Air can enter the interpleural space by trauma, surgery or rupture of a group of alveoli
- iv) Fluid can also enter the space creating pleural effusion and in severe cases empyema.
- v) Conducting zone :- The trachea, bronchi and the terminal bronchioles (that do not end in alveoli) form the conducting zone or airways - conduct air towards alveoli
- Respiratory zone :- Respiratory bronchioles + Alveoli



- vi) The segmental bronchi divide further and further into smaller branches (bronchioles) until ending in Alveolus.
- vii) Beyond the segmental bronchi the airways divide in a dichotomous & asymmetric manner.
- viii) Each branching of an airway leads to $\uparrow$ in no of airways with smaller diameters, as a result the total surface area for next gen. of branches $\uparrow$.
- ix) Terminal bronchioles are the smallest airways without alveoli.
- x) Terminal bronchioles opening into a group of alveoli are called respiratory bronchioles.

- xi) The region of a lung supplied by the segmental bronchus is called a Bronchopulmonary segment - functional anatomical unit
- xii) Physiological unit / Gas exchanging unit - Respiratory unit which consists Respiratory bronchioles, alveolar ducts and alveoli

Site	Cartilage	Epithelium	Blood supply
① Bronchi	✓	Pseudostratified columnar	Bronchial
② Terminal Bronchioles	X	Cuboidal	Bronchial
③ Respiratory bronchioles	X	Cuboidal / Alveolar	Pulmonary

Respiratory zone :- Gaseous exchange

- This region is the largest vol of the lung inspite of being only 5 mm long, approx 2500 ml
- Alveoli - polygonal - 250 μ m diameter

Alveolar spaces - most of lung's volume - separated by connective tissue - interstitium - space in which fluid can accumulate

Adult - 5×10^8 alveoli

- Epithelial cells $\begin{cases} \text{Type I} \\ \text{Type II} \end{cases}$ - exist in 1:1 under normal cond.

Type I

- i) 96-98% of surface area
- ii) Primary site for gaseous exchange due to ① thin cytoplasm ② Basement membrane & capillary endothelium are fused - min dist for diffusion of gases

Type II

- i) 2-4 % of surface area
- ii) Cuboidal - corners of alveolus.
Produce pulmonary surfactant which ① surface tension of Alveoli.

- Gas exchange occurs through alveolar capillary network
- Respiratory / Alveolar barrier :- 1-2 μm thick
 ↳ Type I cell + capillary endothelial cell + their basement membrane

b) Anatomical dead space :-

- The volume occupied by conducting airways which do not participate in gas exchange
- It is $\approx 150 \text{ ml}$

② Dual circulation in lung & their importance :-

a) Pulmonary circulation :-

- The circulation to the lung is unique in having a duality

- The lung has two separate blood supplies

i) Pulmonary - for uptake of O_2 & removal of CO_2 from body

ii) Bronchial - supplies O_2 to lung.

- Pulmonary circulation begins right atrium

Right atrium [deoxygenated blood]

↓

Right ventricle

↓

Pulmonary trunk

↓

Right & Left Pulmonary arteries [only arteries that carry deoxygenated blood]

↓

Lungs

↓

Alveolar Capillary Network

- The sequential branching pattern of the pulmonary arteries follows the pattern of airway branching

- Blood is pumped under low pressure into pulmonary artery [9-24 mm Hg]

Reoxygenate blood & release CO_2

Functions of Pulmonary circulation

Aids in fluid balance in lung

Dist metabolic prod to & from lungs

- The TBV of Pulmonary circulation = 500 ml
 ↳ 10% of body circulating volume
- Approx 75 ml blood in alveolar capillary network at any time - healthy adult

Alveolar capillary network

↓
Oxygenated blood

↓
Venules & Veins

↓
Pulmonary Veins

↓
Left Atrium

- In contrast to arteries, vein & venules run distinct from airways

— Unique features of Pulmonary circulation:-

- ① Pulmonary arteries - thin walled & minimal smooth muscle
- ② They are 7x more compliant than systemic vessels and easily distensible
- ③ Blood flows through these arteries under low pressure required due to high compliant state of arteries
- ④ The vessels are normally dilated & have large diameters than similar systemic arteries
- ⑤ These factors lead to a high compliant low resistance circulatory system which aids in blood flow via the relatively weak pumping right ventricle
- ⑥ The pressure gradient differential of the pulmonary system is also lower than that of systemic system
- ⑦ During exercise the pulmonary capillary blood volume $\uparrow$ from 75 ml to 200 ml bcz of recruitment of new capillaries as the result of an $\uparrow$ in pressure and blood flow.

— Role of Alveolar & Extra Alveolar vessels:-

- Based on physio. properties the pulmonary vessels are categorised into:-

- ① Alveolar vessels
- ② Extra Alveolar
- ③ Pulmonary microcirculation

- Extra Alveolar Vessels:- Arteries, Arterioles, venules, veins

- i) Larger than their systemic counterpart
- ii) Not influenced by Alveolar pressure changes
- iii) Affected by intrapleural & interstitial pressure changes

iv) At high lung volumes, dec in pleural pressure
 (1) the caliber of intra alveolar vessels & increases.

- Alveolar vessels

- i) Alveolar capillaries reside in the intra alveolar septa
- ii) They are sensitive to changes in alveolar pressure
- iii) (1) inc in alveolar pressure $\rightarrow$ constricts capillaries.
[compresses]

b) Pulmonary microcirculation:-

Comprises small vessels that participate in liquid & solute exchange in maintenance of fluid balance in the lung.

c) Bronchial circulation:-

- It is a distinct system that provides systemic arterial blood to the trachea, upper airways, surface secretory cells, glands, nerves, visceral pleural surfaces, lymph nodes, pulmonary arteries & veins
- Perfuses the upper respiratory tract only, does not reach the terminal / Respiratory bronchioles and Alveoli
- Venous blood from bronchial capillaries has two paths

True Bronchial veins

Present in region of lung hilus
 Blood passes thru azygous, hemiazygous & intercostal veins before entering right atrium

Bronchopulmonary veins

They are formed by tributaries of Bronchial & pulmonary veins that anastomose and form vessels with an admixture of blood from both the systems
 Drains in Left Atrium

- $\frac{2}{3}^{rd}$ of total bronchial circulation returned by $\uparrow$

- It receives only 1-2% of the cardiac output
- Note:- In cystic fibrosis bronchial arteries $\uparrow$ in size i.e. hypertrophy & receive as much as 10 to 20% of cardiac output.
Erosion of these vessels with inflamed tissue due to bacterial infection - hemoptysis (coughing of blood).
- Since most of the blood in bronchial circulation empties into the left atria thru pulmonary veins, the flow into the left atria & the left ventricular output are about 1-2% greater than that of the right ventricular output.
- Pulmonary capillary resistance can be lowered by
 - ① Recruitment of capillaries
 - ② Distension of blood vessels to accommodate more blood.
- Pulmonary circulation receives almost 100% of cardiac output
- Factors regulating Pulmonary circulation:-
 - ① Pressures within pulmonary circulation
 - ② Left atrial pressure
 - ③ Cardiac output
 - ④ Pulmonary vascular resistance
 - ⑤ Alveolar pressure
 - ⑥ Reduced blood flow due to $\downarrow$ Alveolar O_2
 - ⑦ Hydrostatic pressures within the lungs

② Gaseous laws :-

① Dalton's law of Partial pressures :-

This law states that in a mixture of gases, the total pressure exerted is eq. to sum of the partial pressures of the individual component gases.

Partial pressure :- pressure exerted by each gas if it alone occupied the vol. of the mixture at the same temperature.

② Boyle's law :-

Under constant temperature the volume of a fixed mass of dry gas is inversely proportional to the pressure exerted on it.

$$P_1 V_1 = P_2 V_2$$

③ Charles' law :-

Volume occupied by a fixed mass of gas at a constant pressure is directly proportional to the absolute temperature.

$$V/T = \text{constant}$$

④ Henry's law :-

At a constant temperature the amount of gas dissolved in a liquid will be directly proportional to the partial pressure of the gas with which the liq. is in equilibrium.

⑤ Universal gas equation :-

$$PV = nRT$$

By combining Boyle's law and gas law

$n \Rightarrow$ no of gram moles of a gas

$R \Rightarrow$ universal gas constant.

④ Control of Breathing - Neural and Chemical :-

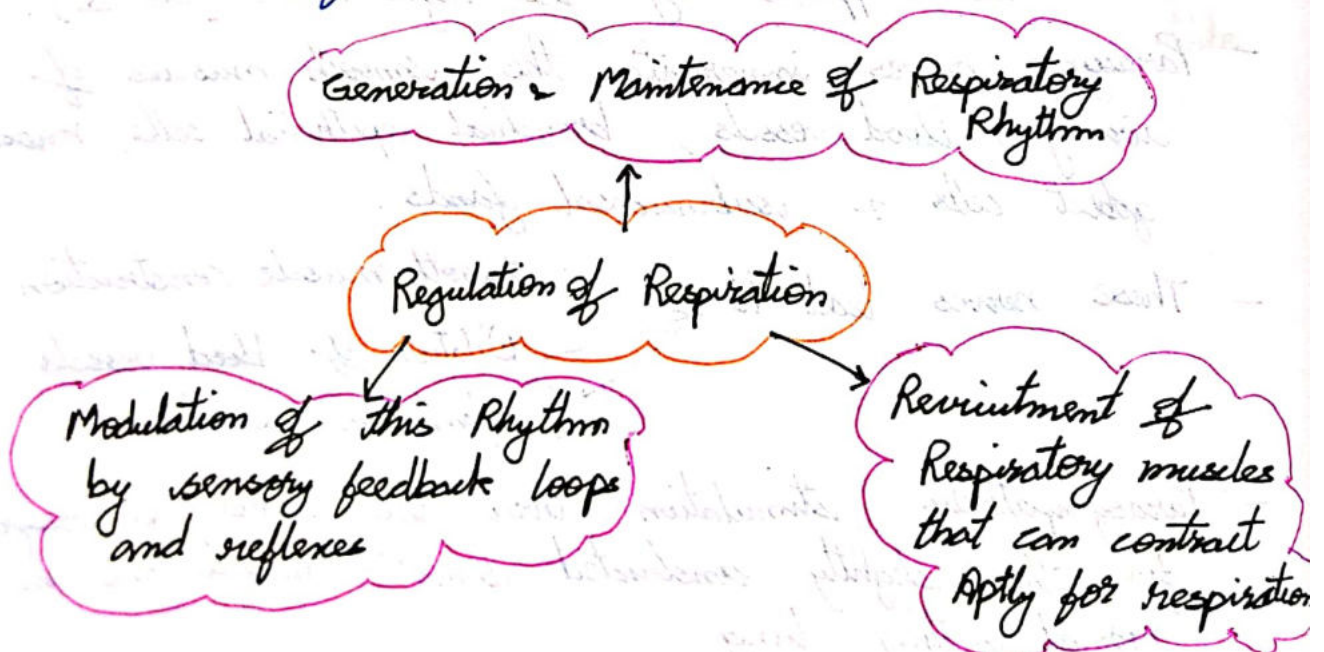
- Parasympathetic and Sympathetic innervation :-

- There is no voluntary motor innervation for lungs
- Parasympathetic nerves for the lung originate in medulla and are supplied by the Vagus Nerve (CN-X).
- Parasymp nerves innervate the smooth muscles of airways, blood vessels, bronchial epithelial cells, ~~mucosa~~ goblet cells & submucosal glands.
- These nerves lead to
 - Smooth muscle constriction
 - Dilation of blood vessels
 - ↑ glandular secretion
- Parasympathetic stimulation thru the Vagus is responsible for the slightly constricted smooth muscle tone in a normal resting lung
- Parasymp innervation is greatest in the upper airways
- Response of this system is very specific and local.
- The sympathetic NS does not ^{heavily} innervate the smooth muscle but innervates the mucous glands and blood vessels heavily.

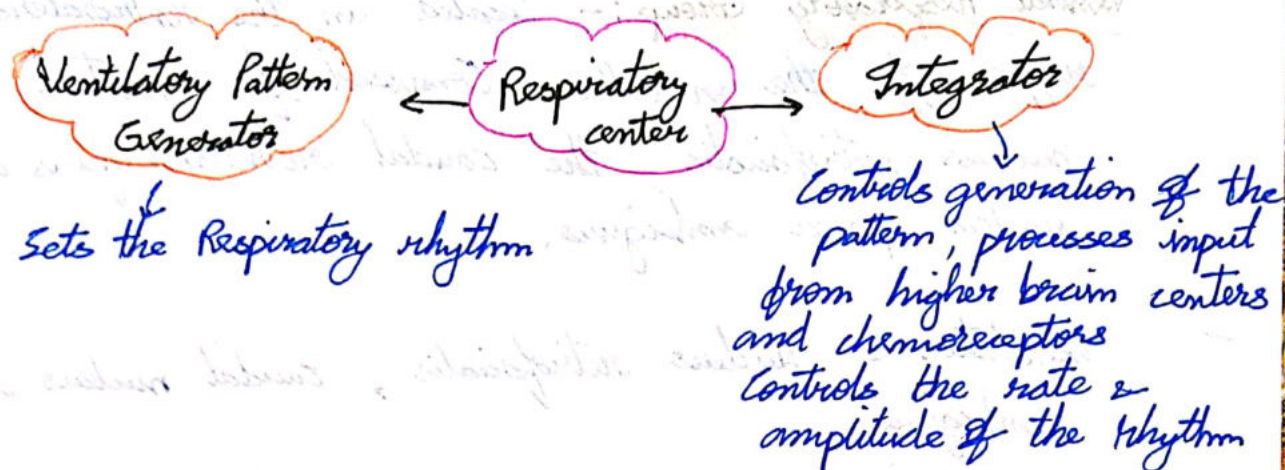
- It causes relaxation of smooth muscle, constriction of blood vessels and inhibition of glandular secretion.
- Parasymp sys $\uparrow$ the segn of mucus glycoprotein which $\uparrow$ the viscosity of mucus.
But stimulation of symp nerves mucus gland $\uparrow$ H_2O secretion.

Central Control of Respiration:-

- Breathing is an automatic, rhythmic and centrally regulated process with voluntary control.
- The Respiratory control centre is located in the medulla of brainstem



- Goals of breathing
 - Minimise work
 - Maintain PaO_2 & $Paco_2$
 - Maintain Acid base balance in brain
- Respiratory control centre includes many nuclei



- The collective output of the Respiratory centre controls the muscles of Respiration
Motor neurons of the cervical region of spinal cord controls the activity of the diaphragm through the phrenic
Those of the thoracic region control the intercostal muscles and the accessory muscles of Respiration.
- Voluntary respiration originates in motor cortex
- The motor neurons - final site of integration of the voluntary (corticospinal tract) and automatic (ventrolateral tract) control of ventilation.
- Motor neurons also innervate the upper airway through cranial Nerves - dilate the pharynx and large airways at the initiation of inspiration.
- Two distinct nuclei within the medulla - Respiratory rhythm
Dorsal respiratory group (DRG) :- located dorsomedially in the medulla - cells of Nucleus tractus solitarius
Receive afferent input from CN - IX & X
Constitute the initial intracranial processing center

located in the ventrolateral region of the medulla. Composed of Rostral nucleus retrofacialis, the caudal retroambiguus and nucleus para ambiguus.

Exhalation: - Nucleus retrofacialis, caudal nucleus retroambiguus

Inspiration: - Rostral Nucleus retroambiguus

Nucleus Para ambiguus - inspiratory & expiratory neurons that travel in vagus Nerve to laryngeal & pharyngeal muscles.

Inspiration and expiration involves three stages
Two for inspiration & one for expiration

Inspiration - Nucleus tractus solitarius
Nucleus Retroambiguus
Nucleus Paraambiguus } discharge abruptly
↓
Begin inspiration

Steady Ramp like $\uparrow$ in firing $\rightarrow$ Rest of inspiration
 $\rightarrow$ Progressive contraction of Inspiratory muscles

End of inspiration - "off switch event" - $\downarrow$ firing of neurons - marks the beginning of exhalation

Exhalation $\leftarrow$ Phase I - Paradoxical $\uparrow$ in firing of Ins neurons
Phase II - Inspiratory neuron firing stops

- Thus rhythmic breathing depends on a continuous tonic inspiratory drive from the DRG and phasic intermittent drive from cerebrum, thalamus, cranial Nerves, spinal cord ascending tracts
- Pulmonary Mechanoreceptors :-
 - a) Chest wall and Lung Reflexes :-
 - Reflexes that arise from chest wall and lungs affect ventilation and ventilatory patterns.
 - Hering Breuer inspiratory inhibitory reflex: stimulated by $\uparrow$ in lung volume, associated with $\uparrow$ in both ventilatory rate & tidal volume. It is mediated by vagal fibres. It results in cessation of breathing. It is inactive during quiet breathing and impt in New borns
 - Diving Reflex: Results from stimulation of Nasal & facial receptors with cold H_2O . It causes Apnea and bradycardia. Protects from aspirating H_2O during drowning
 - Sneeze Reflex: Receptors in nose
 - Sniff Reflex: Receptors in Nasopharynx & Pharynx (Mechanical). Results in short strong inspiratory effort bringing a substance from nasopharynx to pharynx where it can be swallowed or expectorated (spitted out)
 - Only Newborns can breathe and swallow simultaneously
 - Larynx
 - Superficial receptors - Apnea, cough, cause expiration to protect the lower tract from foreign object
 - Deep receptors - Controls muscle fibre activation

b) Sensory Receptors

i) Stretch receptors :-

i) Rapidly adapting / Irritant receptors :- stimulated by inhaled dust, noxious stimuli gases and cigarette smoke. Present in trachea and large airways. Stimulation leads to $\uparrow$ in airway resistance, reflex apnea and coughing.

ii) Slowly adapting receptors :- Mechanical stimulation and activated by lung inflation.

The $\uparrow$ in lung vol during COPD activates these receptors - delays onset of next inspiratory effort.

Info from these stretch receptors - vagus nerve (myelinated fibres)

ii) Juxta Alveolar / J receptors :-

i) Situated in lung Parenchyma respond to chemical or mech stimulation

ii) They transmit input thru unmyelinated vagal C fibres

iii) They cause dyspnea (abnormal shortness of breath) and rapid shallow ventilation - interstitial lung edema and some lung inflammatory states

iii) Somatic receptors :-

i) Respond to changes in length & tension of the respiratory muscles

ii) Provide info about lung vol & play a role in terminating inspiration

iii) Help to min chest wall distortion in newborns.

- Chemical Regulation of Respiration :-

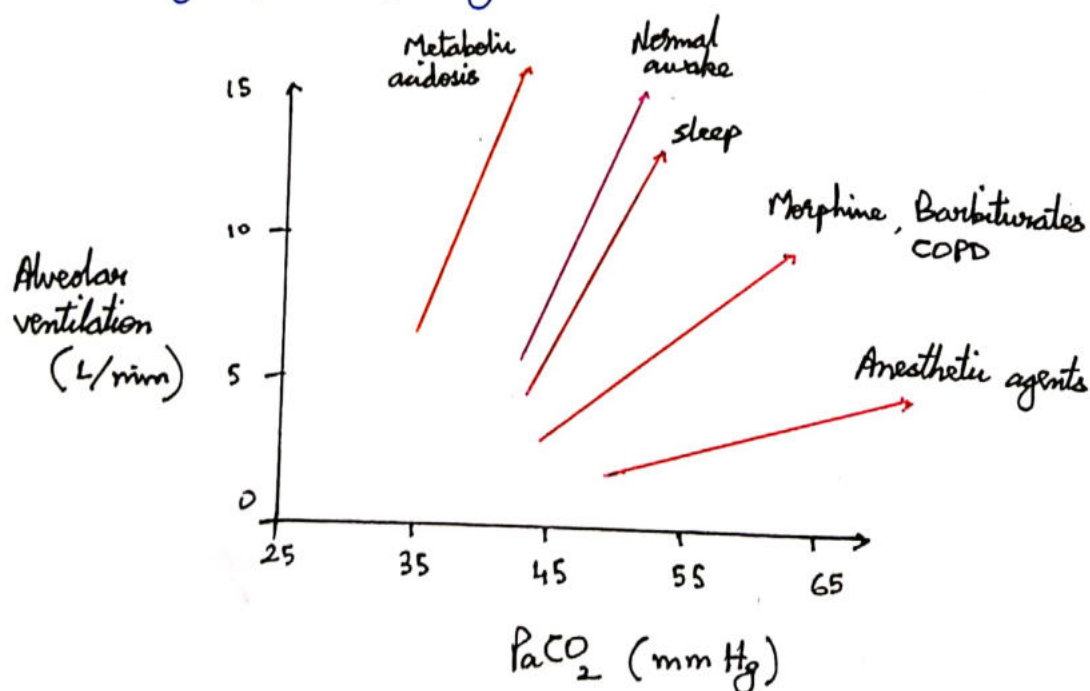
- Chem factors regulating respiration :-

- ① P_{aCO_2} - most important
- ② P_{aO_2}
- ③ PH

- Rate and depth of breathing are controlled to maintain P_{aCO_2} close to 40 mm Hg

- Ventilation rises linearly with increasing P_{aCO_2} beyond 40 mm Hg, in a normal awake person.

- This ventilatory ^{drive} in response to $\uparrow$ in P_{aCO_2} can be reduced by hyperventilation or any drugs that reduce the activity of respiratory centers.

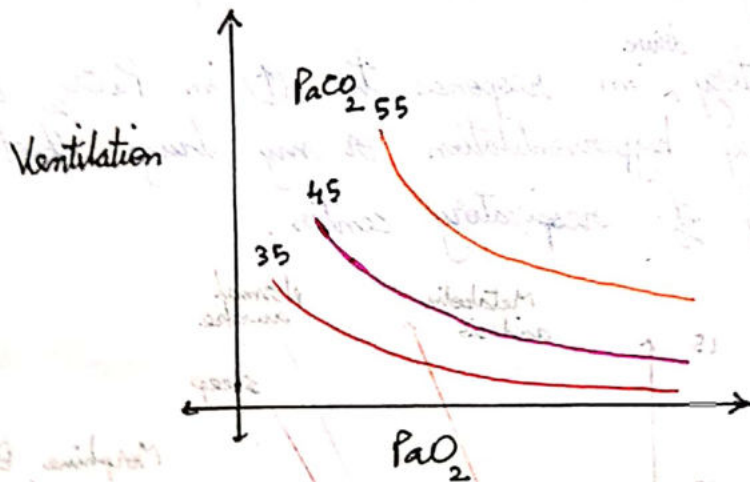


- The ventilatory drive is also suppressed during sleep

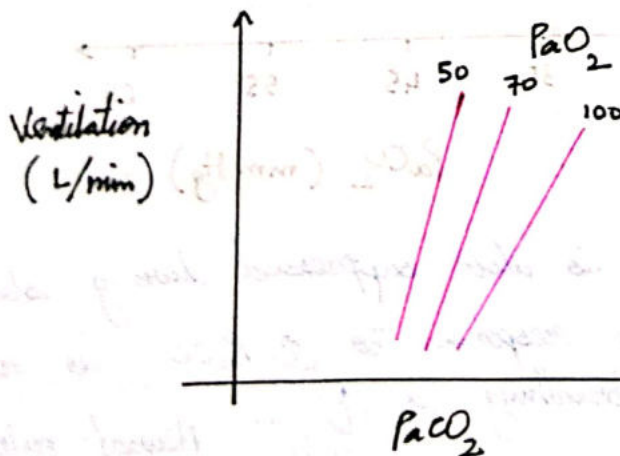
- In COPD ventilatory response to $\uparrow$ P_{aCO_2} is reduced if the work of breathing is $\uparrow$ - Neural output of Respiratory center is less effective

- The respiratory control center regulates minute ventilation, to maintain P_{aCO_2} within normal range
- When P_{aO_2} is normal ventilation $\uparrow$ by approx. 3L/min for each 1 mm Hg rise in P_{aCO_2}
- Response to P_{aCO_2} $\uparrow$ when P_{aO_2} is less
Ventilation $\uparrow$

At a given partial pressure of CO_2 (arterial) ventilation $\uparrow$ more and more as P_{aO_2} $\downarrow$



- The slope of the minute ventilation response as a function of inspired CO_2 is termed the **ventilatory response to CO_2** and is a test of CO_2 sensitivity



Chemoreceptors :- Responds to changes in $chem$ of blood

a) Central chemoreceptors :-

- located on ventrolateral surface of medulla
- Responds to P_{aCO_2} and pH of CSF (interstitial fluid of brainstem)
- Cannot respond to P_{O_2}

b) Peripheral chemoreceptor :-

- Located in Aortic and carotid bodies
- Responds to P_{aCO_2} , pH and also P_{aO_2} of arterial blood
- Can respond to changes in P_{O_2}

- The blood brain barrier is relatively impermeable to H^+ and HCO_3^- ions but it is very permeable by CO_2 . Thus the PCO_2 in CSF parallels the arterial CO_2 tension.

The pH of CSF is also slightly lower than that of arterial blood due to the ventral CO_2 prod by the cells of the brain.

For central chemoreceptors, the $\downarrow$ in pH stimulates the receptors and CO_2 in blood regulates ventilation by its effect on the pH of CSF

- Peripheral chemo - 40% of ventilatory response to P_{aCO_2}

↳ Small highly vascularised

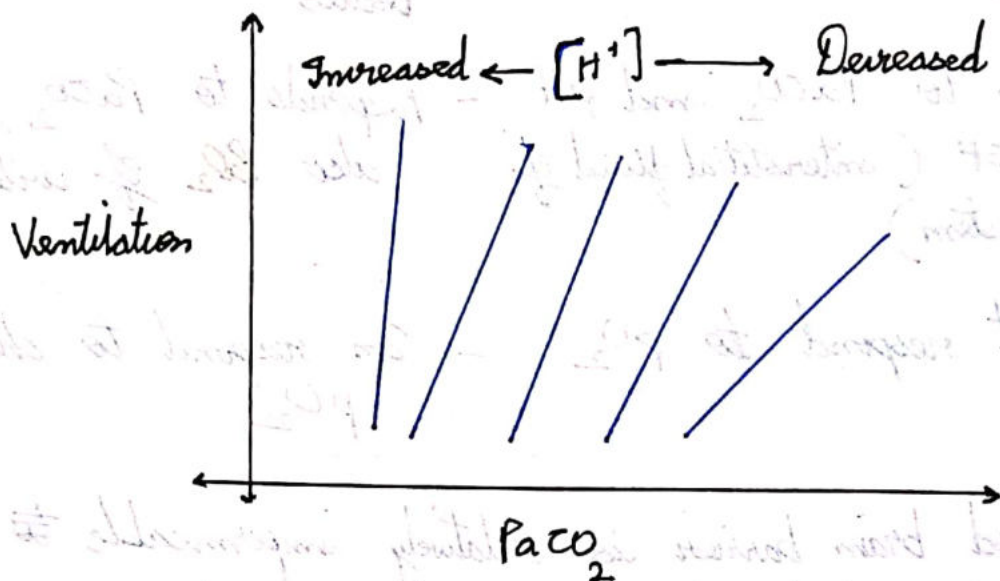
Type I cells - rich in mitochondria & endoplasmic reticulum

↓
Primarily responsible for sensing P_{aO_2} , P_{aCO_2} , pH

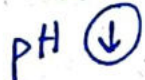
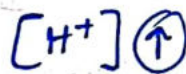
Even small $\downarrow$ in P_{aO_2} - chemoreceptor activates

Response robust - when $P_{aO_2} < 75 \text{ mmHg}$

- The ventilatory response to P_{aCO_2} is affected by the concentration of hydrogen $[H^+]$ gas in CSF and Brainstem interstitial fluid.

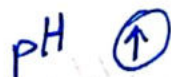
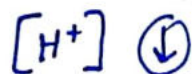


- chronic Metabolic acidosis :-



Ventilatory response to P_{aCO_2} $\uparrow$ steeper slope
lower threshold

- chronic metabolic alkalosis :-



Ventilatory response to P_{aCO_2} $\downarrow$ reduced slope
Higher threshold

⑤ Functions of Lung :- Refer guyton pg 329 to 332

a) Respiratory functions :- gaseous exchange

O_2 is taken in while CO_2 is secreted

b) Endocrine and metabolic functions of lungs :-

- Endothelial cells of the Alveoli capillary beds can metabolise various metabolic and vasoactive subs
- Angiotensin I $\rightarrow$ Angiotensin II by ACE present on endothelial cells
- Serotonin is metabolised by endothelial cells after being internalised into the cell
- Syn & secreted sub include cytokines, prostaglandins, prostacyclin, NO, and clotting factors.

PY- G.2: Mechanics of Breathing① Rde of respiratory muscles:-

- The major muscles - ① Diaphragm - Major
② External intercostals
③ Scalene muscles.
- Force of contraction - larger when stretched
shorter smaller when shortened
- Force of contraction of the respiratory muscles ↑ at larger lung volumes.
- Diaphragm - major muscle - contraction forces the abdominal contents downward forward
Inc the vertical diameter of thoracic cage
Can generate airway pressure upto 150 to 200 cm H₂O during maximal inspiration
Movt of diaphragm $\left\{ \begin{array}{l} \text{Tidal breathing} \approx 1 \text{ cm} \\ \text{Deep breathing} \approx 10 \text{ cm} \end{array} \right.$
Innervated by Phrenic Nerves [C₃ to C₅]
- The external intercostal muscles - pull the ribs upward and forward during inspiration which ↑ the antero-posterior and lateral diameters
2nd to 6th Ribs - on inspiration move upwards to acquire a more horizontal position - ↑ antero-posterior diameter - Pump handle movements
7th to 10th Ribs - swing outwards and upwards to ↑ the lateral/transverse diameter - Bucket handle movements

- Innervation of ext intercostal - Intercostal Nerves ($T_1, 2, T_{12}$)
- Paralysis of these muscles - no significant effect
 Bcoz Respiration depends primarily on the diaphragm.
 This is the reason patients with lower spinal cord injury can breathe on their own.
 When injury is above C_3 ventilator is needed.

- Accessory muscles of inspiration -
 - ① Scalene muscles
 - ② Sternocleidomastoid
 - ③ Alae Nasi

These contract only during exercise & when airway obstruction is significant. They actively pull up the subcap.
Normal breathing - Anchor sternum & ribs

- Pharyngeal muscles - muscles of inspiration - geniohyoid & mylohyoid
 ↳ Keep upper airway patent.

- Exhalation
 - Passive - normal breathing
 - Active - hyperventilation & exercise

Muscles of exhalation :-

- ① Rectus abdominis
- ② Transverse abdominis
- ③ Internal intercostal muscles
 ↳ Oppose external

- Work of breathing - Inspiratory muscles
- Respiratory muscle fatigue - major factor for respiratory failure

② Static Mechanics :-

- Mechanics :- ^{lung} study of the mech properties of the lung and chest wall (including the diaphragm, abdominal cavity and anterior abdominal muscles).

- Most lung disease affect the mech prop of lung & chest wall.

- Static mechanics :- study of mech prop of a lung whose volume is not changing with time.

- Pressures in the Respiratory system :-

- In healthy ppl lung and chest wall act and move as a single unit - changes in their respective volume equal

- Pleural space - space B/W lungs & chest wall
under normal conditions it is a potential/virtual space

- Volume changes in lungs & chest wall - driven by changes in the surrounding pressure.

- Transmural pressure :- It defined as the difference between the pressure inside and the pressure outside the surface.

It is the pressure difference across the lung and the chest wall.

- Transpulmonary / Translung pressure (P_L) :-

It is defined as a pressure diff B/W air spaces and the pressure surrounding the lungs (pleural pressure).

$$P_L = P_A - P_{PL}$$

P_A - Alveolar pressure

P_{PL} - Pleural pressure

- Transmural pressure across chest wall (P_w)
Pressure difference B/W pleural pressure and atmospheric or Barometric pressure (P_b)

$$P_w = P_{pl} - P_b$$

- Transmural pressure across Respiratory system :- (P_{rs})

$$P_{rs} = P_L + P_w$$

$$P_{rs} = P_A - P_{pl} + P_{pl} - P_b$$

$$P_{rs} = P_A - P_b$$

- Air flows into the lung when a pressure gradient is created from higher pressure to lower pressure
- No pressure gradient - no airflow
At end inspiration and end of exhalation - no airflow
No press gradient - $P_A = P_b$. Hence $(P_A - P_b = 0)$

- Before inspiration begins P_{pl} is not zero but it is negative (-3 to -5 cm H_2O) in relation to atmosphere

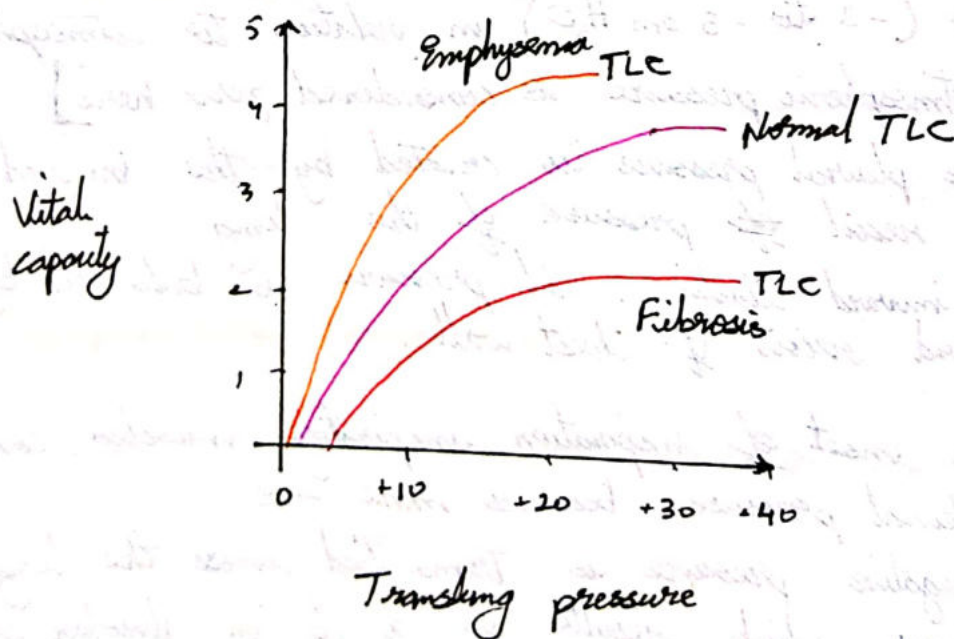
[Atmospheric pressure is considered zero here]

The -ve pleural pressure is created by the inward elastic recoil of pressure of the lung

This inward elastic recoil pressure is balanced by the outward recoil of chest wall.

- At the onset of inspiration inspiratory muscles contract the pleural pressure becomes more -ve
This negative pressure is transmitted across the lung parenchyma which results in a $\downarrow$ in alveolar pressure
As alveolar pressure $\downarrow$ below zero a gradient is created and air flows into the lungs

- When there is no longer a pressure gradient air flow stops
- $\downarrow$ in pleural pressure is greater than the transmitted $\downarrow$ in alveolar pressure
Hence transpulmonary pressure is +ve at the start of inspiration
lung vol $\uparrow$ with $\uparrow$ in Transpulmo pressure
- Transmural press across chest wall is -ve as P_{pl} is -ve
- On exhalation inspiratory muscles relax pleural pressure becomes less -ve. Air flows from Alveoli to the atmosphere
In the alveoli driving force for exhalation is sum of elastic recoil pressure and pleural pressure



- Fig 21.2 is important from Berne - pg 448

③ Static lung volumes and Capacities :-

VOLUMES :-

- a) Tidal volume (V_T) :- Volume of air that moves into or out of the lung with each quiet breath.

$$\text{Normal } V_T = 500 \text{ ml}$$

- b) Inspiratory reserve volume (IRV) :- It is the maximal volume of air that can be inspired after a normal tidal inspiration i.e. inspired after end inspiratory position.

$$\text{Normal } IRV = 2 - 3 \text{ litres}$$

- c) Expiratory reserve volume (ERV) :- It is the maximal vol of air that can be expired after a normal tidal expiration

$$\text{Normal } ERV = 750 - 1000 \text{ ml}$$

- d) Residual volume (RV) :- Air remaining in the lungs after a complete exhalation

$$\text{Normal } RV = 1.2 \text{ l}$$

CAPACITIES :- A capacity is composed of two or more volumes

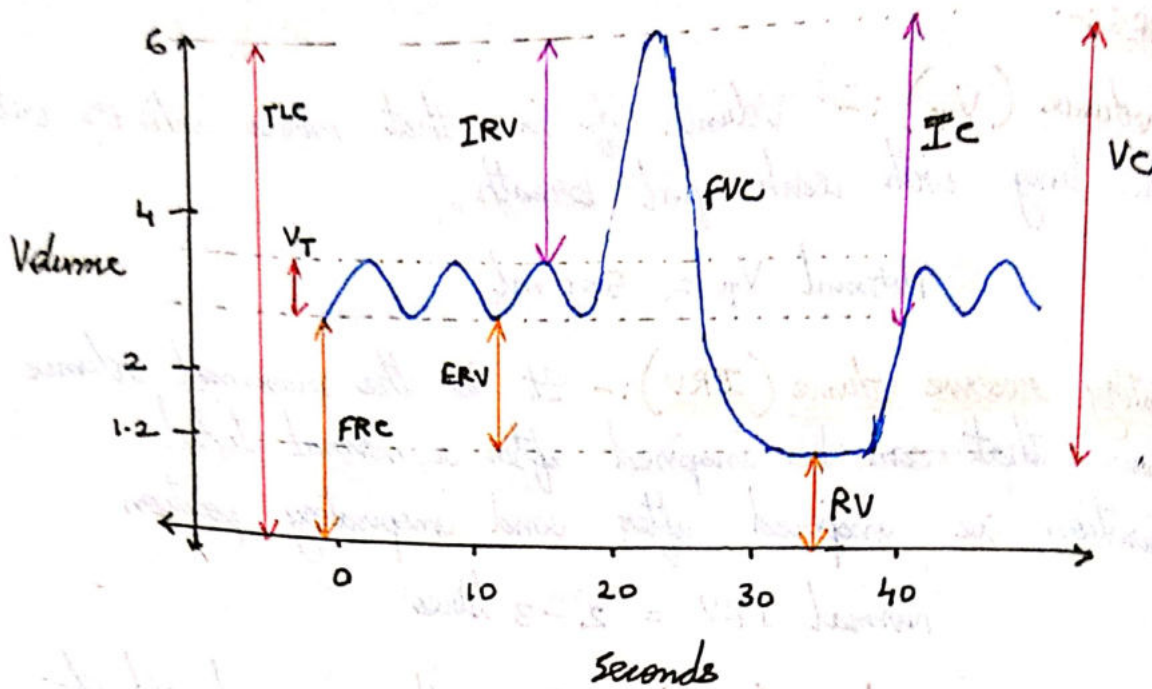
- a) Total lung capacity (TLC) :- Total vol of air contained in the lung at the point of maximal inspiration.

- b) Vital capacity (VC) :- The total vol of air exhaled air from maximal inspiration to maximal exhalation

$$TLC = VC + RV$$

- c) Functional residual capacity (FRC) :- Volume of air in the lungs at the end of exhalation during quiet breathing and is also called the resting volume of the lungs.

$$FRC = ERV + RV$$



- RV and TLC can be measured by 2 ways

① Helium dilution - old & simpler

② Body plethysmograph - New and uses Boyle's law

In normal individuals FRC measured by both methods is same.

Premature airway closure - FRC measured by plethysmograph is more.

- Lung volumes are determined by the balance B/W lung's elastic properties and properties of the muscle of chest wall

TLC is controlled by Inspiratory muscles

When vol $\uparrow$ chest wall muscles lengthen progressively

TLC occurs when chest wall muscles unable to distend the lung further.

Residual volume is controlled by expiratory muscle force

- The decrease in lung volume is also associated with an increase in outward recoil pressure of the chest wall.

RV occurs when expiratory muscle force is insufficient to further reduce chest wall volume.

When lung volume $\downarrow$ shortening of expiratory muscles occurs.

- FRC is determined by the balance B/W inward elastic recoil pressure of the lung parenchyma and outward recoil pressure of the chest wall.

FRC $\downarrow \Rightarrow$ chest wall muscles are weak
 $\text{inward recoil of lung} > \text{outward recoil of chest wall}$

FRC $\uparrow \Rightarrow$ Airway obstruction

(b) LUNG COMPLIANCE (C_L) :-

- It is a measure of elastic prop of the lungs
- It is defined as the change in lung volume resulting from a $1 \text{ cm H}_2\text{O}$ change in the distending pressure of the lung.

Units :- $\text{ml/cm H}_2\text{O}$ or $\text{l/cm H}_2\text{O}$

- When C_L is high - lung easily distended
- C_L is low - lung is stiff

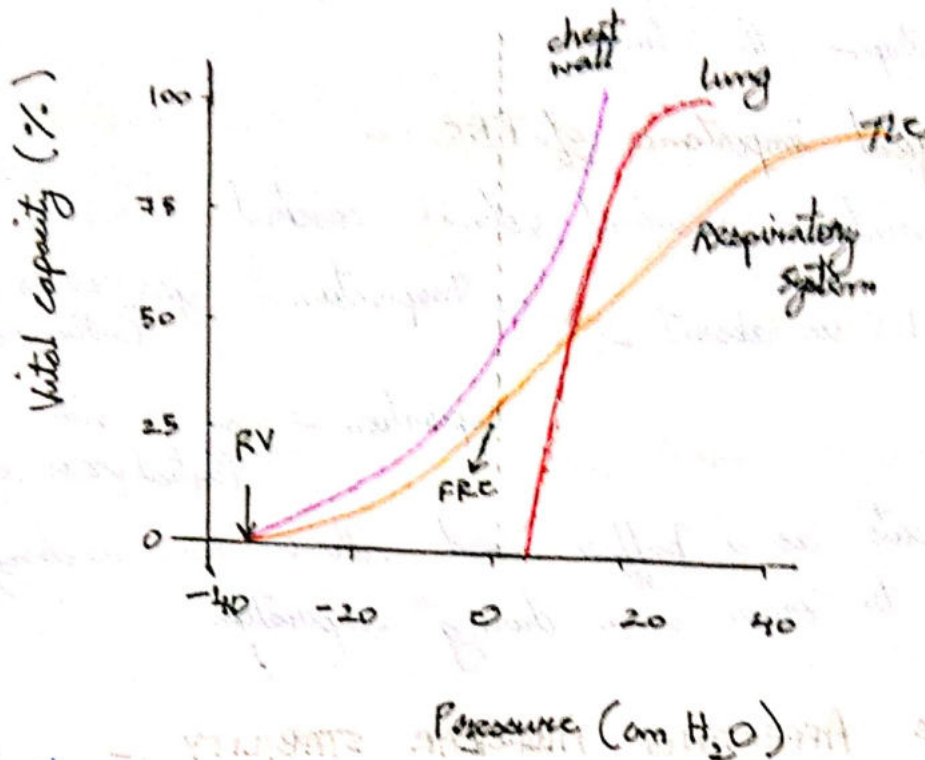
$$C_L = \Delta V / \Delta P$$

- Graphically lung compliance is the slope of the line B/w any two points on the deflation limb of the pressure volume loop curve.
- The curve demonstrates that C_L varies with lung volume.
At higher lung vol. - C_L is low
- But specific compliance does not vary with lung volumes

$$\text{specific compliance} = \frac{\text{lung compliance}}{\text{lung volume}}$$

- Normal C_L of human lung = $0.2 \text{ L/cm H}_2\text{O}$
- The change in pleural pressure (P_{Pl}) is measured as a func of the change in lung volume
ie $\Delta P_{Pl} = \Delta C_L (\Delta V)$
- Compliance of the lungs is affected by several resp disorders
 - ① Destructive eg emphysema - $C_L \uparrow$
 - ② Restrictive eg fibrosis - $C_L \downarrow$
- A lung with low compliance requires larger changes in pleural pressure to affect changes in lung volume as a result work of breathing $\uparrow$

© RELAXATION PRESSURE VOLUME CURVES :-



- At the FRC there is a balance B/W inward elastic recoil pressure of lungs and outward recoil pressure of chest wall. i.e. these forces are eq. and opposite. Hence P_{res} is zero at FRC.
- The transmural pressure across the chest wall is zero at the resting vol. of chest wall (approx 60% of TLC).
- The lungs are smallest at zero P_L but are not devoid of air b'coz of the presence of surfactant. The transmural pressure of a healthy lung flattens at elastic limits than 20 cm H₂O b'coz of the lung's.
- The lungs recoil until transpulmonary press is 0. chest wall (↑) in size until trans chest wall press is 0.

- In general P_L distends the lung and P_{el} tends to collapse the lung.

Physiological importance of FRC :-

- FRC maintains residual volume constant.
- When RV is absent
 - Inspiration - gas is in small space Partial pressure high
 - Expiration - gas is in large space Partial pressure very low
- FRC acts as a buffer and allows cont exchange of gases to occur even during expiration

© FACTORS AFFECTING ALVEOLAR STABILITY :-

- Surface tension and surfactant :-

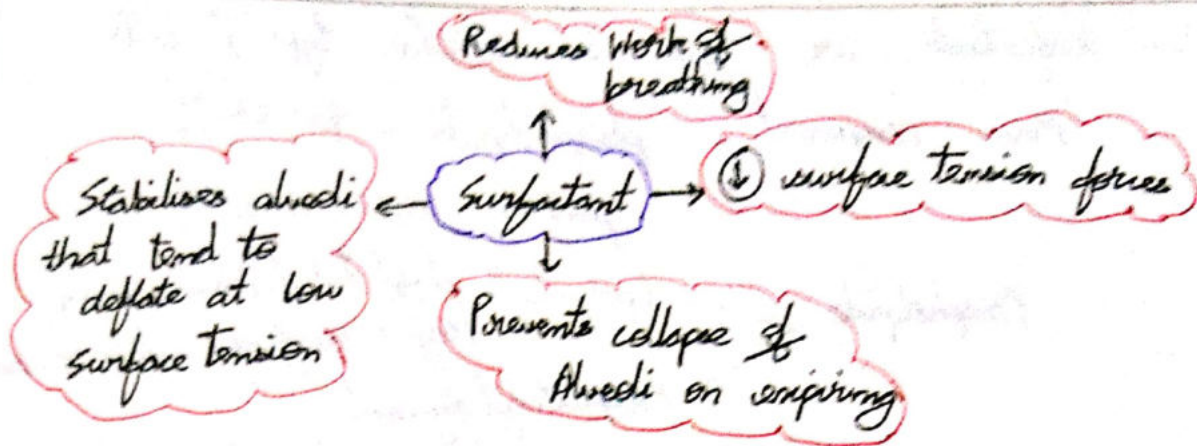
- Surface tension - Force caused by water molecules at the air liquid interface that tends to minimize surface area. - Makes inflating lungs more difficult
- It is a measure of attractive force of surface molecules per unit length of material to which they are attached

- Law of Laplace :-

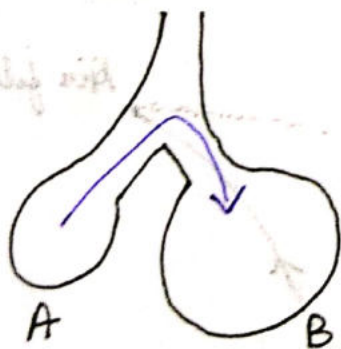
$$P_s = \frac{2T}{R}$$

where T is surface tension

- The alveoli - lined by lipid based surfactant



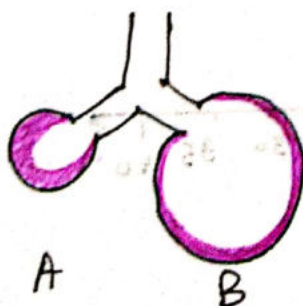
- Absence of surfactant - surface tension remains constant. More transalveolar pressure would be necessary to prod a given inc in alveolar volume at lower lung volumes than at higher lung volumes.
- In the presence of surfactant surface tension is $\uparrow$ at high lung volumes and $\downarrow$ at low lung volumes. Surface tension $\uparrow$ as alveoli become larger. Transalveolar pressure $\uparrow$ as lung vol $\uparrow$ & $P_L \uparrow$.



By Laplace law $P \propto \frac{1}{r}$ $P \propto T$
In the absence of surfactant

$$P_A > P_B$$

Air moves from A to B
resulting in collapse of A



In the presence of surfactant
T is lowered more in smaller alveoli

$$P_A \approx P_B$$

Hence alveoli are stabilised

- Surfactants are syn by alveolar type II cells.
- Main component - phospholipids - 80-85 %
 - proteins - 10-15 %

Phospholipids $\left\{ \begin{array}{l} \text{dipalmitoyl phosphatidylcholine} \\ \text{Phosphatidylglycerol} \end{array} \right.$ Major surfactant active $\downarrow$ sub

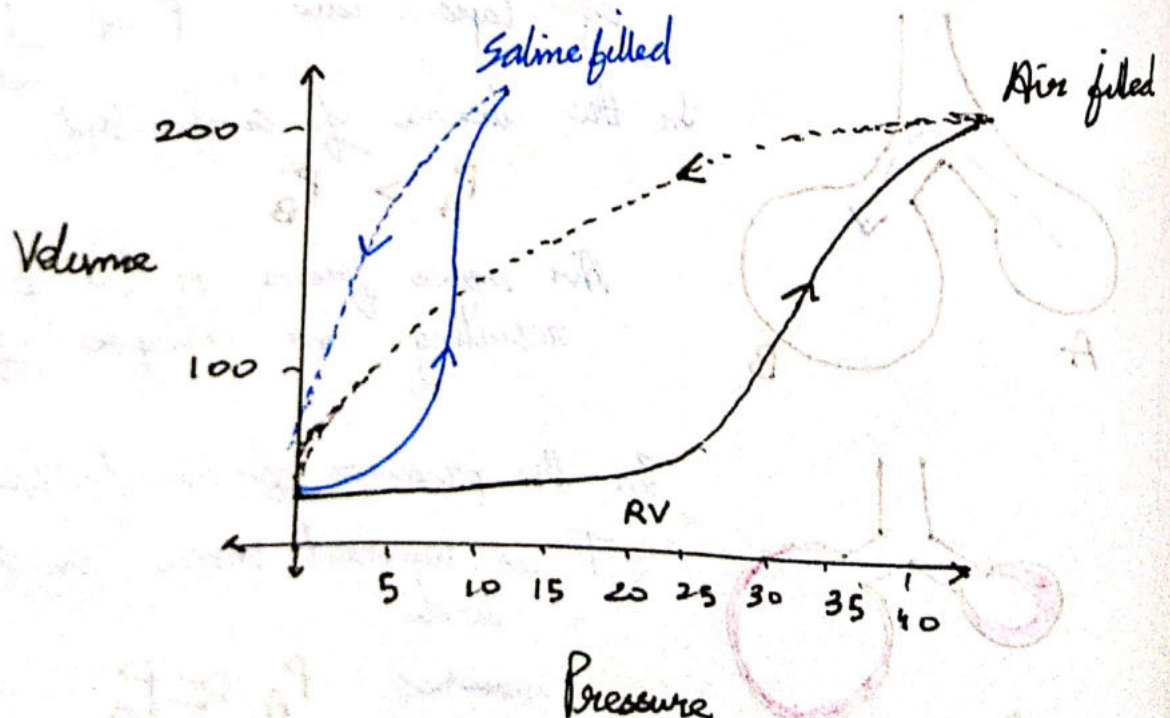
$\rightarrow$ Spreads surfactant

cholesterol - stabilisation

- Surfactant is inactivated by $\left\{ \begin{array}{l} \text{Hyponia} \\ \text{Infection} \\ \text{Edema fluid} \end{array} \right.$

(- Pressure Volume curves of Air filled & saline filled lungs :-

Lungs filled with liquid req, a low pressure to maintain a given vol than do lungs filled with air bcoz of elimination of liq air interface.



③ Dynamics Mechanics :-

Study of the properties of a lung whose volume is changing with time.

① Patterns of Airflow :-

- Gas exchange depends on two major factors
 - i) the speed at which fresh gas is brought to the alveoli
 - ii) the rapidity with which metabolic prod are removed
- The speed of airflow depends on ① Pattern of airflow
② Airway resistance
- There are 2 types of Patterns ← Laminar
← Turbulent
- Laminar Airflow :- It is parallel to the airway walls and is present at low flow rates.
- When flow rate becomes high and airways divide flow becomes unsteady & eddies develop
- Poiseuille described the pressure vol characteristics of laminar airflow

$$V = \frac{P \pi r^4}{8 \eta l}$$

Driving pressure (P) is directly proportional to flow rate (V)

$$P \propto V$$

$$\uparrow P \Rightarrow \uparrow V$$

- Flow resistance (R) = $\frac{\Delta P}{V}$
across a set of tubes

$$R = \frac{\Delta P}{V} = \frac{8\eta l}{\pi r^4}$$

Units:- cm H₂O/L.sec

- Radius of the tube - most important determinant of flow resistance

$$R \propto \frac{1}{r^4}$$

$$R \propto l$$

Resistance is inversely prop to fourth power of radius and directly prop to length of tube and viscosity of gas.

- Turbulent flow:- Gas most occurs both parallel & id to axis of the tube. It occurs at high flow rates

Pressure is directly prop to flow rate squared
Viscosity of the gas $\propto$ with $\propto$ gas density

Gas velocity is limited bcoz energy is consumed in process of prod chaotic moves

- Higher driving pressure is needed to support a given turbulent flow than to support a similar laminar flow.

- Reynold's number helps to determine whether a flow is laminar or turbulent. It is a dimensionless quantity

$$Re = \frac{2rvd}{\eta}$$

Turbulence occurs when $Re > 2000$

- High Avg velocity & large radius - turbulence
& low density gas like He in contrast is less likely to cause turbulence
- Much of the airflow in airways - both laminar & turbulent
- In the upper airways like Trachea - $Re > 2000$ even during quiet breathing
Turbulence is promoted by glottis and vocal cords
↳ by obstructing the airways
- Gas flow becomes more laminar in smaller airways even during maximal ventilation
∴ larger airways - turbulent
Smaller airways - laminar
- Breath sounds - turbulent airflow
Laminar flow is silent hence it is difficult to hear small airway disease with a stethoscope.

⑥ Airway Resistance :- (R_{aw})

- R_{aw} differs in airways of diff size
- In moving from the trachea toward the alveoli, individual airways become smaller while the number of airway branches $\uparrow$

$$R_{aw} = R_{large} + R_{med} + R_{small}$$

i) Contribution of different segments of respiratory tract to airway resistance :-

- Major site of resistance - first eight generations of airways along bronchial tree
- Smallest airways contribute very little to the overall total resistance

Reasons :- ① Airflow vel $\downarrow$ as effective cross sectional area $\uparrow$ [flow becomes laminar]

② Airway branches in each generation resist in parallel

- As airway diameter $\downarrow$ the resistance offered by each individual airway increases but the large increase in the no of parallel pathways & cross sectional areas reduces the resistance at each generation of branching.

- Normal breathing - 80% of R_{aw} at FRC occurs in airways with diameter $> 2\text{mm}$

ii) Factors that contribute to Airway Resistance :-

Normal airway resistance = $1\text{ cm H}_2\text{O/L}\cdot\text{sec}$

① Lung volume :- Most important
 ↑ lung vol ↑ caliber of the airways bcz it creates a positive transairway pressure

∴ Resistance ↓ with ↑ lung volume

Relationship B/w lung volume & conductance

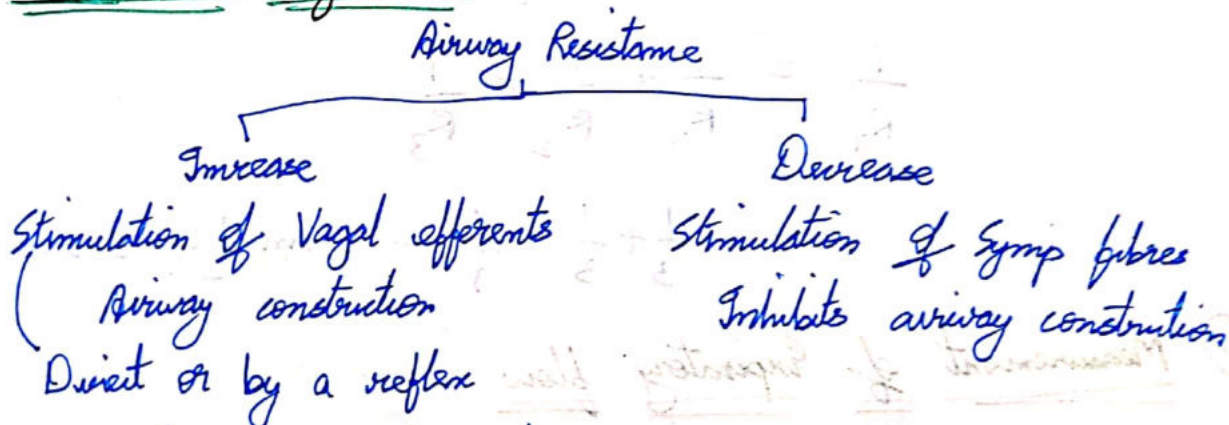
② Airway mucus, edema and contraction of bronchial smooth muscle - ↑ Raw

③ Density and viscosity of gases :-

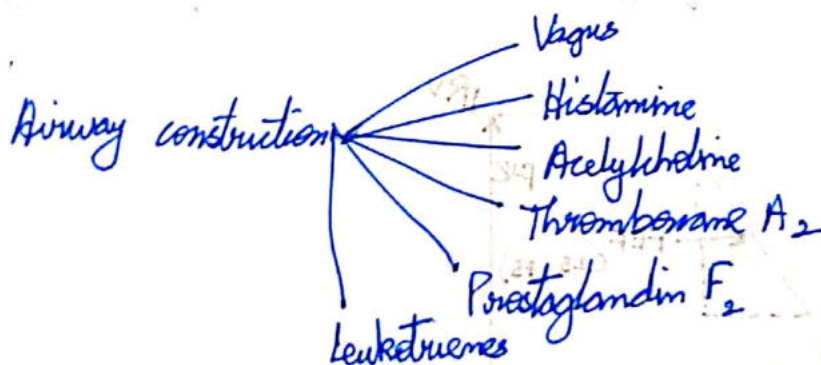
When gas density ↑ ⇒ Airway resistance ↑

Breathing a low density gas eg O_2 -He mix - ↓ airway resistance

iii) Neurohumoral regulation :-



Also ↓ Anatomical dead space



Methacholine a derivative of Acetylcholine helps to diagnose airway hypersensitivity

- One of the reason for why the small airways contribute less to total resistance is the parallel arrangement of airways in each generation.
- In series arrangement resistance gets added up

eg :- three similar tubes are arranged in series having eq R value is $3 \text{ cm H}_2\text{O}$

$$R_T = R_1 + R_2 + R_3$$

$$= 3 + 3 + 3 = 9 \text{ cm H}_2\text{O/L} \cdot \text{sec}$$

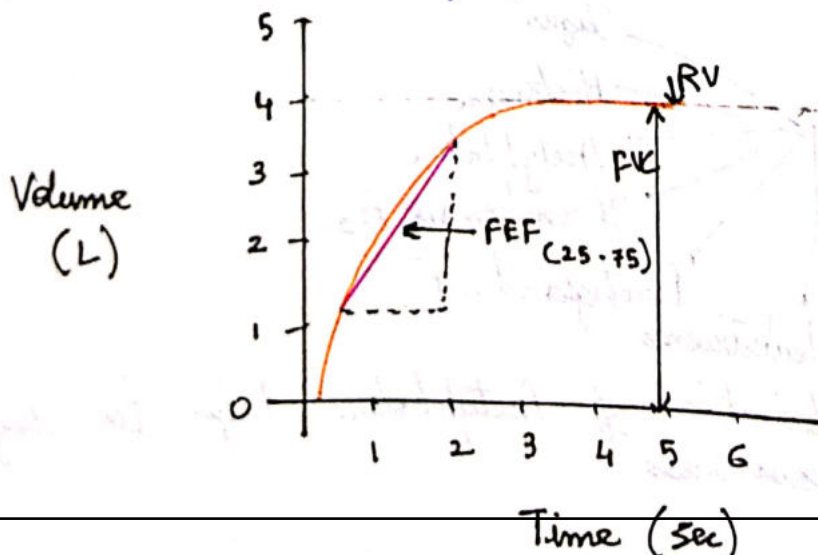
- In parallel arrangement the tot resistance is the sum of inverse of Resistances

$$\frac{1}{R_T} = \frac{1}{R_1} + \frac{1}{R_2} + \frac{1}{R_3}$$

$$= \frac{1}{3} + \frac{1}{3} + \frac{1}{3} = 1 \text{ cm H}_2\text{O/L} \cdot \text{sec}$$

(c) Measurement of Expiratory flow :-

i) Spirogram :- Volume of gas exhaled as a function of



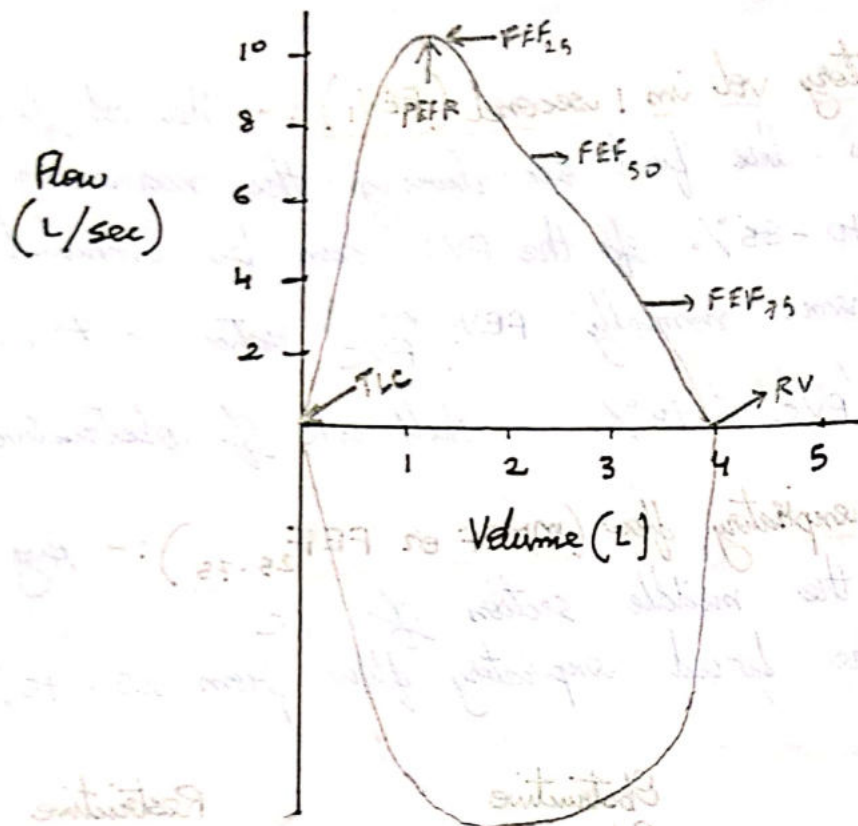
Forced Vital Capacity (FVC) :- The total volume of air ie exhaled to RV during a maximal forced exhalation from TLC

Forced expiratory vol in 1 second (FEV₁) :- The vol of air ie exhaled in the first sec during the maneuver Normally 70-85% of the FVC can be exhaled in 1st sec hence normally FEV₁/FVC ratio > 70%
If FEV₁/FVC < 70% - Hallmark of obstructive disease

Midmaximal expiratory flow (MMEF or FEF₂₅₋₇₅) :- Avg flow rate over the middle section of VC
It is the forced expiratory flow from 25-75% of VC

Parameters	Obstructive Pulmonary disease	Restrictive Pulmonary disease
FVC (L)	↓	↓
FEV ₁ (L)	↓	↓
FEV ₁ /FVC	↓	Normal ↗
PEFR (L/sec)	↓	Normal ↗
FEF ₅₀ (L/sec)	↓	Normal
FEF ₇₅ (L/sec)	↓	Normal
Slope of FV curve	↓	Normal / ↑
FEF ₂₅₋₇₅	↓	Normal / ↑

ii) Flow Volume loop :-



- A flow volume loop is created by displaying the instantaneous flow rate during a forced maneuver as a function of the vol. of gas
- Expiratory flow rate - above horizontal line
- It measures :-
 - ① FVC
 - ② PEFr :- the greatest flow rate achieved during the maneuver (forced exhalation)
 - ③ Multiple expiratory flow rates at various lung volumes.
- FEF_{50} - Instantaneous flow rate at which 50% of VC has been exhaled
- FEF_{75} - The flow rate at which 75% of VC has been exhaled.

- The flow volume loop reveals that the maximum inspiratory flow is the same or slightly greater than maximum expiratory flow.
- Factors resp for maximum inspiratory flow :-
 - ① Inspiratory muscle force $\downarrow$ as lung volume $\uparrow$ above R
 - ② Recoil pressure of lung $\uparrow$ as lung volume $\uparrow$ above RV
 - ③ Airway resistance $\downarrow$ with $\uparrow$ in lung volume.
- During exhalation maximal flow occurs early (in first 20% in the maneuver and flow rates decrease progressively
- Whereas maximal inspiratory flow occurs about halfway B/W TLC and RV.
- As effort $\uparrow$ PEFR $\uparrow$ but no amount of effort will $\uparrow$ the flow rates as lung volume $\downarrow$
- The expiratory flow rates at lower lung volumes are said to be effort independent and flow limited
- PEFR and PIFR are dependent on effort
Hence events early in the maneuver are said to be effort dependent [the first 20% of flow in expiratory flow volume loop].

(d) Dynamic Compliance :-

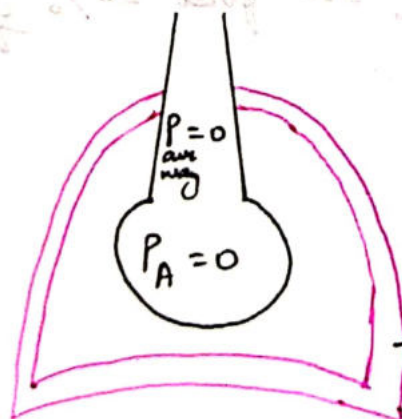
- A dynamic pressure volume curve can be created by having an individual breathe over a normal lung volume range (from FRC to FRC+1L)
- The mean dynamic compliance of lung ($\text{dyn } C_L$) is calculated as the slope of line joining the end inspiratory and end expiratory points of no flow.
- $\text{dyn } C_L < \text{static } C_L$
- Increase during exercise, sighing and yawning by $\uparrow$ tidal volume
- dynamic compliance is not significantly different from its static compliance.

(e) Flow limitation and dynamic airway compression

- Inspiratory flow is limited and effort independent
- Flow limitation occurs when airways are compressed due to a higher pressure outside the airways

Condition I:- At the start of exhalation (end inspiration)
There is no airflow

As there is no flow
 $P_{\text{airway}} = 0$



$$P_L = P_A - P_{PL} \\ = +30 \text{ cm H}_2\text{O}$$

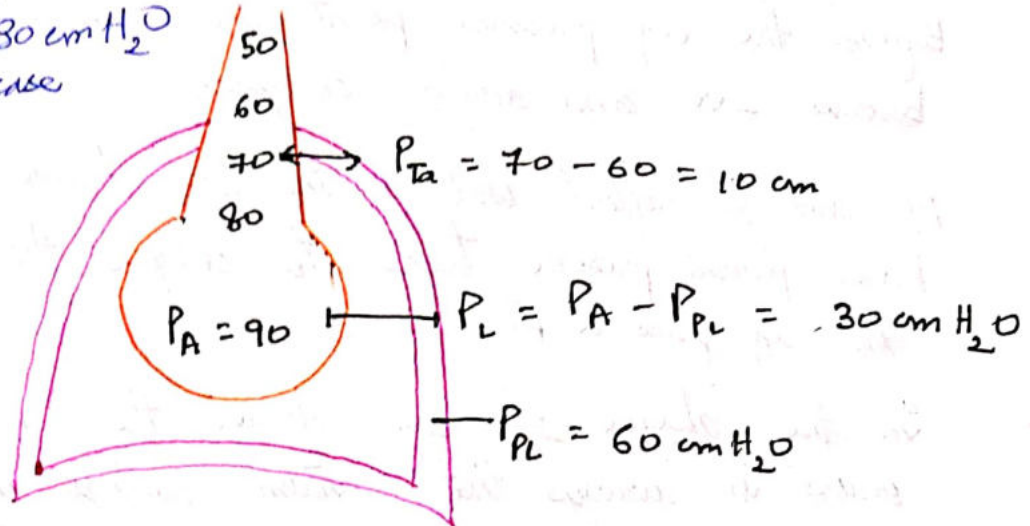
$$P_{La} = P_{\text{airway}} - P_{PL} \\ = +30 \text{ H}_2\text{O}$$

$$P_A = -30 \text{ cm H}_2\text{O}$$

The +ve P_{Ta} and P_L keep the airways open and alveoli open

Condition II: Forced exhalation - Active process
Muscles contract - Pleural pressure becomes +ve
Alveolar pressure also rises

Elastic recoil pressure = $30 \text{ cm H}_2\text{O}$ in this case



$$P_A = P_{ex} + P_{PL}$$

$$= 30 + 60 = 90$$

driving pressure for expiratory gas flow

- As gas flows out of the alveoli transmural pressure across airways decreases due to three reasons

① Expiratory flow resistance

② As the cross sectional area of the airways decreases towards the trachea, gas velocity $\uparrow$ and this acceleration further $\downarrow$ pressure

③ As lung vol $\downarrow$ elastic recoil pressure $\downarrow$

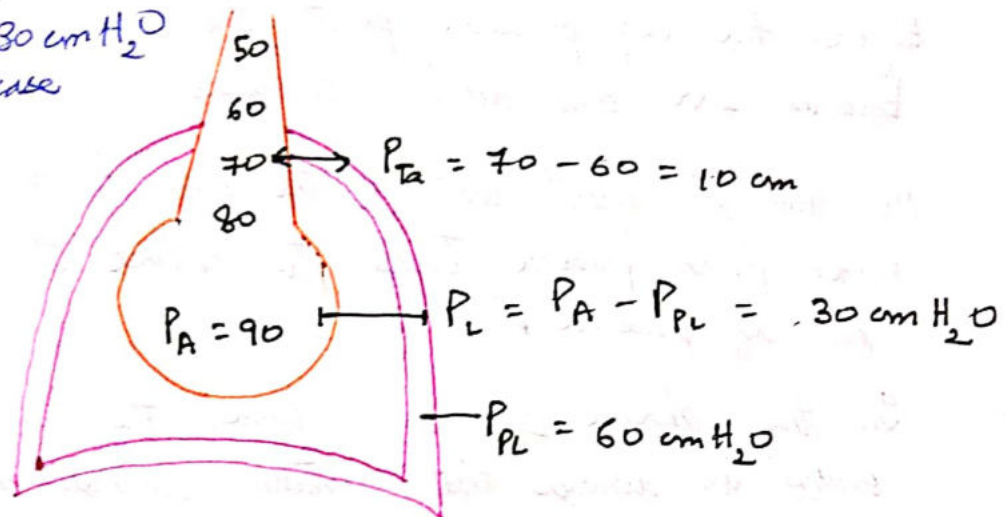
- As air moves out - driving pressure for gas flow $\downarrow$

- Equal pressure point :- A point B/w the alveoli and the mouth at which the pressure inside the airways equals the pressure that surrounds the airways

The +ve P_{Ta} and P_L keep the airways open and alveoli open

Condition II: Forced exhalation - Active process
 Muscles contract - Pleural pressure becomes +ve
 Alveolar pressure also rises

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 pressure = $30 \text{ cm H}_2\text{O}$
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driving pressure for expiratory gas flow

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① Expiratory flow resistance

② As the cross sectional area of the airways decreases towards the trachea, gas velocity $\uparrow$ and this acceleration further $\downarrow$ pressure

③ As lung vol $\downarrow$ elastic recoil pressure $\downarrow$

- As air moves out - driving pressure for gas flow $\downarrow$

- Equal pressure point :- A point B/w the alveoli and the mouth at which the pressure inside the airways equals the pressure that surrounds the airways

- Dynamic Airway Compression :- Airways towards the mouth but still inside the chest wall become compressed bcz the pressure outside is greater than pressure inside
- Beyond the eq pressure point the transairway pressure becomes -ve and airway collapses
- No amt of effort will $\uparrow$ the flow further bcz the higher pleural pressure tends to collapse the airway at the eq pressure pt.
- In the absence of lung disease the eq pressure pt occurs in airways that contain cartilage and they resist collapse
- As lung volume and elastic recoil pressure $\downarrow$ the eq pressure pt moves closer to the alveoli

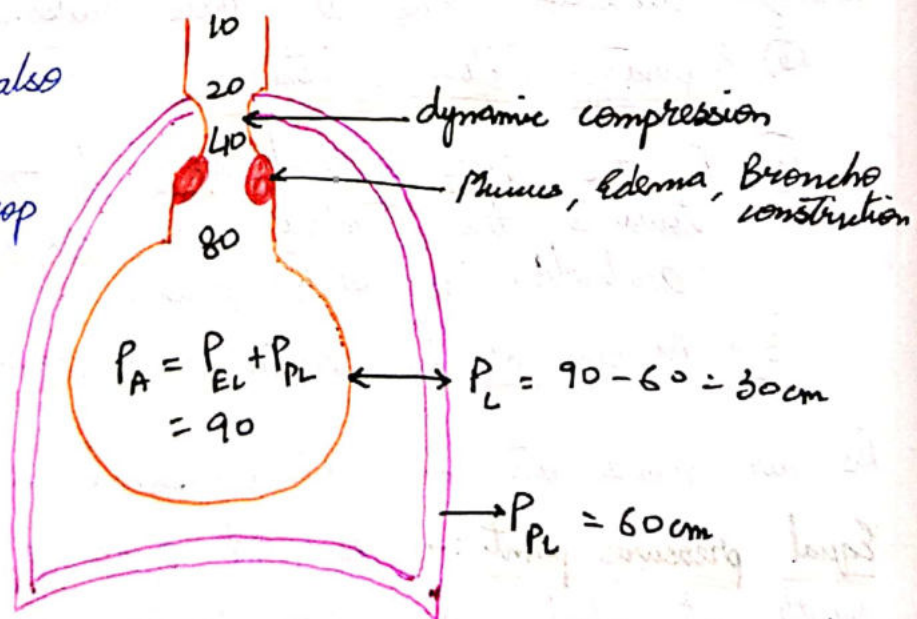
Abnormal cases :-

- ① $\uparrow$ in the airway resistance due to mucus or inflammation

P_A is normal

P_E & P_{PL} are also normal

But the resistive drop in pressure $\uparrow$ due to greater $\downarrow$ in radius of airways see to mucus etc.



Eq pressure pt now occurs in small airways devoid of cartilage resulting in premature airway closure.

② Emphysema and loss of elastic recoil :-

P_{PL} is normal

$P_A \downarrow$ due to $\downarrow$ in P_{EL}

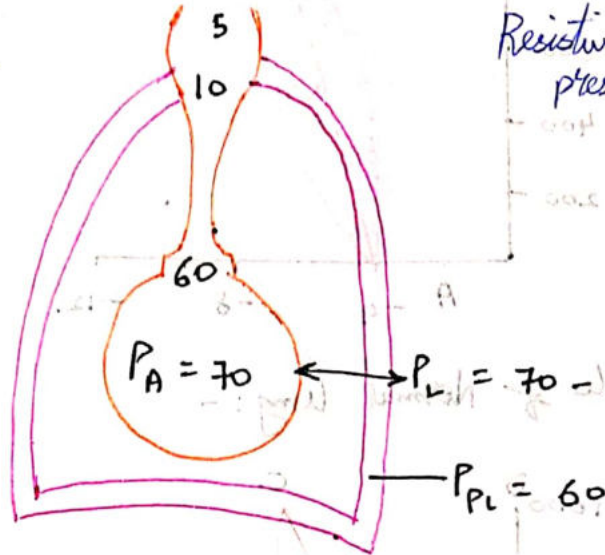
$$P_A = P_{EL} + P_{PL}$$

$$= 10 + 60$$

$$= 70 \text{ cm}$$

Again there is a Premature airway closure.

Initial driving pressure is less



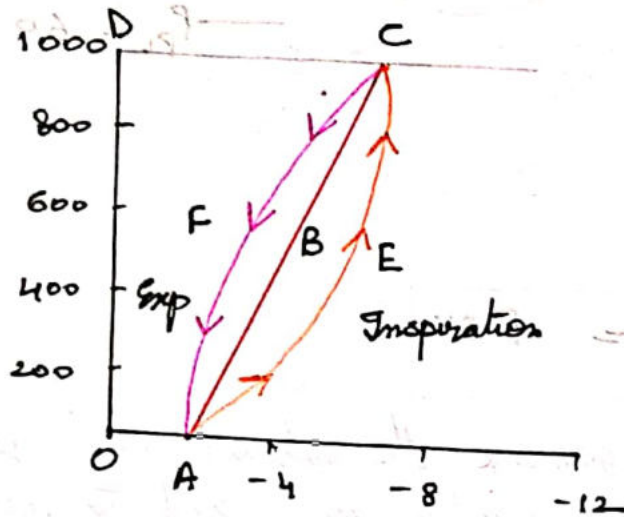
Resistive drop in pressure is normal

③ Work of Breathing

$$W = P \Delta V$$

- The work req to overcome the inherent mech prop of the lung (ie elastic and flow resistive forces) and to move both lungs and chest wall is known as work of breathing.
- Presence of disease $\rightarrow$ change in mech prop of lung or chest wall $\rightarrow$ $\uparrow$ Work of breathing.
- Respiratory fatigue $\rightarrow$ Respiratory failure major cause
- One can estimate the mech work done by measuring the volume and pressure changes during a respiratory cycle.

Respiratory cycle of Normal lung:-

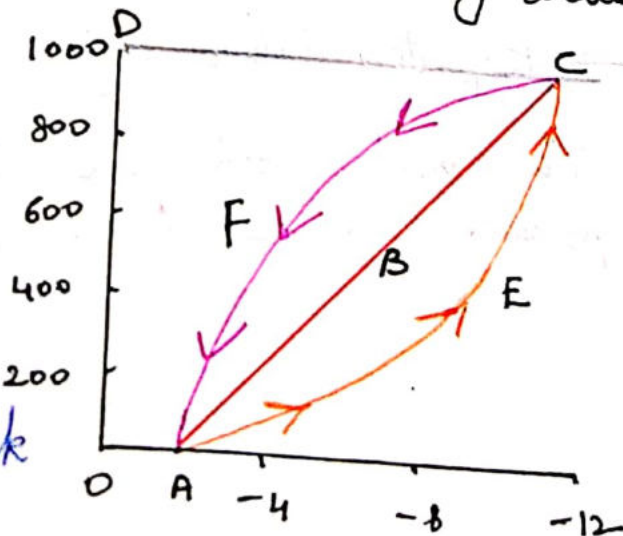


ABC - static inflation deflation curve
DAECD - Mechanical work load.

Respiratory cycle in Restrictive lung disease eg:- Pulmonary fibrosis
Compliance is ↓

The pressure volume curve is shifted to the right

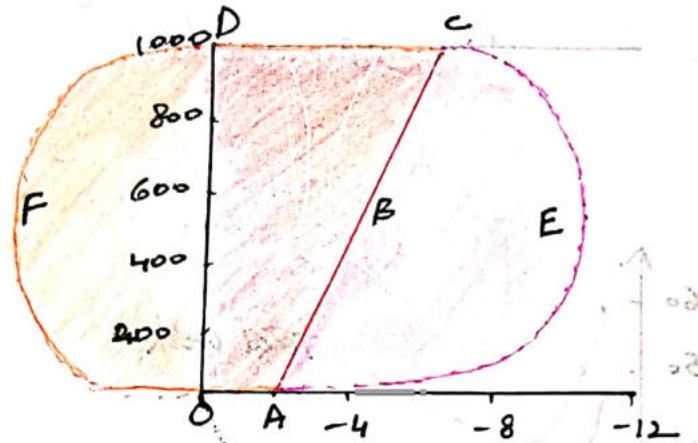
Area of DAECD
↑ Home work
is ↑



Respiratory cycle in Obs Pulmonary disease :-

eg :- Asthma, chronic bronchitis, etc

- Airway resistance is $\uparrow$



Applicable
to All
graphs

DABCD - Work to overcome elastic resistance

AECF - Work to overcome non-elastic resistance

AECB - Work ..
during inspiration

ABCF - Work to overcome non elastic resistance
during exhalation

DFO - $\uparrow$ in the work load (expiratory)

ABCF - stored elastic energy

The stored elastic energy not sufficient - Hence need more energy.

- Work of breathing $\uparrow$

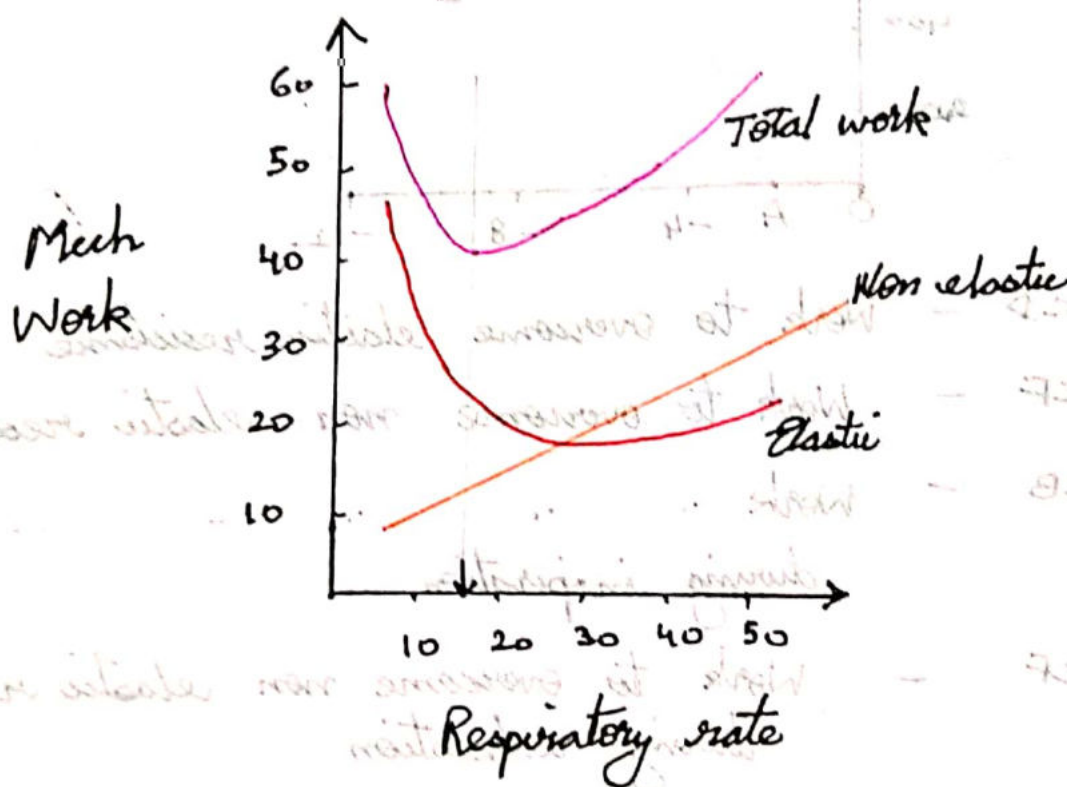
deeper breaths - more tidal vol
more elastic work to overcome

Respiratory rate $\uparrow$

more flow resistance force to
overcome

- Pulmonary fibrosis - shallow & rapid breath
 ↑ elastic work

Obstructive - More slow and deeply
 ↑ resistive work



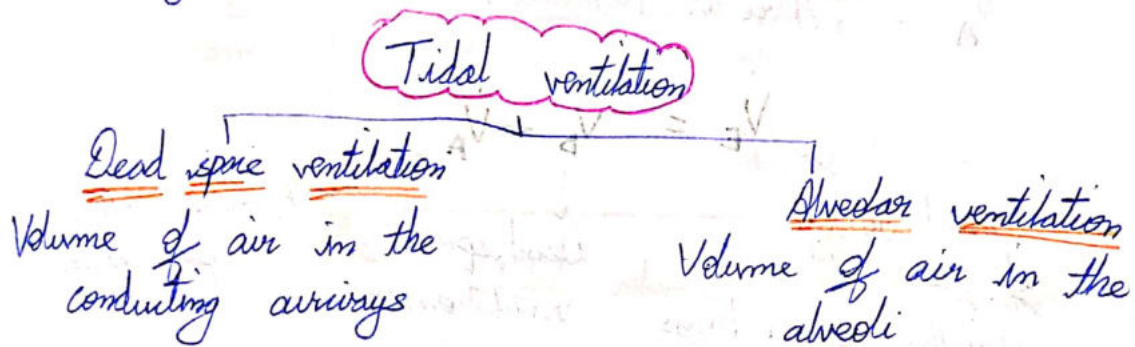
↓ - Respiratory rate at which
 Tot work is minimal

④ Ventilation and Perfusion :-

The major determinant of normal gas exchange, PO_2 & PCO_2 in blood is the V/Q ratio

VENTILATION :-

- It is the process by which air moves into and out of the lungs.



- Minute ventilation :- Volume of air that enters or leaves the lung per minute
Normal - 6 to 8 L/min

Minute / Total Ventilation = Alveolar Ventilation + dead space ventilation

$$\dot{V}_E = f \times V_T$$

$f \Rightarrow$ frequency / no of breath per min

$V_T \Rightarrow$ Tidal volume

- Tidal Volume varies with age, sex, body position and metabolic activity

- Dead space Ventilation :-

- It is the ventilation to airways that do not participate in gas exchange

- It is of two types $\begin{cases} \text{Anat} \\ \text{Physio} \end{cases}$

- Anatomical dead space ^{Volume of air that fills}
the conducting airways (V_D)

$$V_T = V_D + V_A$$

V_T = Tidal volume

V_D = dead space

V_A = Alveolar ventilation

$$\dot{V}_E = \dot{V}_D + \dot{V}_A$$

$\dot{V}_E$ → Total volume of gas in litres expelled from lungs per min
 $\dot{V}_D$ → Dead space ventilation per min
 $\dot{V}_A$ → Alveolar vent per min

- V_D/V_T ratio represents the fraction of each breath is wasted in filling the conducting airways

$$\dot{V}_D = \frac{V_D}{V_T} \times \dot{V}_E$$

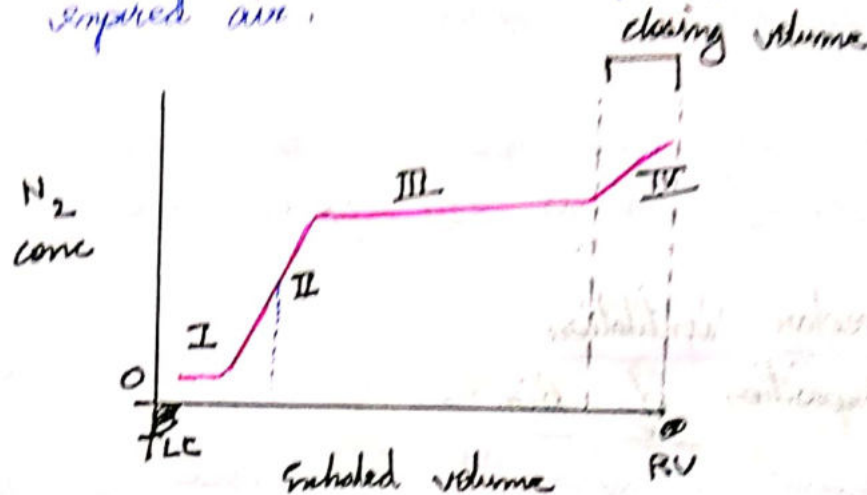
- $V_D \propto \frac{1}{V_T}$ i.e. V_D varies inversely with tidal volume

Normally V_D/V_T ratio is 20-30% of exhaled minute ventilation

- If dead space $\uparrow$ a larger V_T must be inspired to maintain normal level of blood gases. This $\uparrow$ work of breathing

- Anatomical dead space is measured by Fowler's single breath technique

Subject takes a normal breath of 100% pure O_2 and exhales 500 ml of air in a nitrogen meter. A graph is plotted b/w % of N_2 and inspired air and expired air.



- Phase I - gas that fills dead space - no N_2
- II - Mixture of dead space and alveolar
- III - Alveolar gas

The vol of dead space is the volume of gas expired from peak inspiration to midportion of phase II

- Physiological dead space:- The total vol of gas in each breath that do not participate in gas exchange.

It includes anatomical dead space and alveolar dead space [dead space due to perfused but unventilated alveoli]

- In normal healthy individual - $Physio = Anat$
But in diseased state - $Physio > Anat$

- Physio dead space by Bohr's technique

The first portion of inspired air enters alveoli

The rest remains in conducting zone

When the subject ventilates the first portion that expelled is CO_2 free air followed by CO_2 containing. Amt of CO_2 present in the volume of mixed expired is the sum of the CO_2 contributed by the volume air from dead space.

Both dead space types can be measured but they are not measured routinely in patient care.

Alveolar Ventilation

I Composition of Air:-

Ambient / Atmospheric air mainly consists of N_2 (79%), O_2 (21%) with minute quantities of CO_2 , argon, & inert gas.

Ambient air follows two principles:-

① Sum of the individual gas fractions must equal one

$$1 = F_{\text{N}_2} + F_{\text{O}_2} + F_{\text{Argon}} + \text{other gases}$$

② Sum of the partial pressures of individual gases must be eq. to atmospheric pressure [Dalton's law]

$$P_b = P_{\text{N}_2} + P_{\text{O}_2} + \text{other gases}$$

$$760 \text{ mmHg} = P_{\text{N}_2} + P_{\text{O}_2} + P_{\text{CO}_2} + P_{\text{Argon}} + \text{other}$$

Partial pressure of a gas is given by

$$\text{partial pressure} \leftarrow P_{\text{gas}} = \underset{\substack{\text{Fraction of gas} \\ \text{in air}}}{F_{\text{gas}}} \times \underset{\substack{\text{Atmospheric} \\ \text{pressure}}}{P_b}$$

- Partial pressure of O_2 is calculated as

$$P_{O_2} = F_{iO_2} \times P_b$$

$$= 0.21 \times 760$$

$$P_{O_2} = 159 \text{ mm Hg}$$

P_{O_2} - partial press of O_2

F_{iO_2} - fraction of O_2 in inspired air

P_b - barometric pressure

$\therefore$ At the onset of inspiration at the mouth the oxygen tension or P_{O_2} is 159 mm Hg / 159 torr

- F_{iO_2} does not vary at different altitudes only the barometric pressure varies. These differences in O_2 tension have profound effects on arterial blood² gas values

- As inspiration begins, the inspired air is humidified i.e. saturated with water vapour. before it reaches the trachea

- Water vapour exerts 47 mm Hg pressure. Thus partial pressures change in trachea.

$$P_{\text{trachea}} O_2 = (P_b - P_{H_2O}) \times F_{iO_2}$$

$$= (760 - 47) \times 0.21$$

$$P_{\text{trachea}} O_2 = 150 \text{ mm Hg}$$

$$P_{\text{trachea}} N_2 = (760 - 47) \times 0.79$$

$$P_{\text{trachea}} N_2 = 563 \text{ mm Hg}$$

- The total P_b remains constant and fractions of gases also remains constant
- Partial pressures of O_2 , N_2 , Water vapour remain unchanged in the airways until the air reaches the alveolus.

II Alveolar Gas Composition :-

- At the level of Alveolus respiratory gas exchange occurs
- At the end of inspiration when the glottis is open, the total P in alveolus is the same as atmospheric gas [760 mm Hg].
- Beg of gas exchange the fraction of O_2 in the alveolus (1) and fraction of CO_2 in alveolus (1)

Note :- fraction of N_2 & other gases $\Rightarrow$ As they are ~~inert~~ inert does not change

fraction of $H_2O_{(v)}$ does not change

- Beg of changes in fractions Partial pressure PO_2 & PCO_2 also change.
- PAO_2 [PO_2 in alveolus] is given by the Alveolar gas equation or ideal alveolar O_2 equation

$$PAO_2 = P_i O_2 - \frac{PA_{CO_2}}{R}$$

$$PAO_2 = [FiO_2 \times (P_b - P_{H_2O})] - \frac{PA_{CO_2}}{R}$$

- In this equation R is the respiratory exchange ratio or the Respiratory quotient

↳ It is the ratio of amount of CO_2 excreted ($\dot{V}CO_2$) to the amt of O_2 taken up ($\dot{V}O_2$) by the lungs

- R is dependent on caloric intake.

$$R = \frac{\dot{V}CO_2}{\dot{V}O_2}$$

$$R = \frac{\text{Amt Rate of } CO_2 \text{ prod}}{\text{Amt Rate of } O_2 \text{ consumption}}$$

- R varies B/W 0.7 to 1.0

0.7 $\Rightarrow$ state of exclusive fatty acid metabolism

1.0 $\Rightarrow$ state of exclusive carbohydrate metabolism

0.8 $\Rightarrow$ normal dietary conditions

Normal R value is 0.8 $\Rightarrow$ implies that quantity of O_2 taken up $>$ quantity of CO_2 released in the alveoli.

- PA_{CO_2} calculation:-

- The process of elimination of CO_2 is known as Alveolar Ventilation

- The relationship B/W CO_2 production & alveolar ventilation is given by the Alveolar CO_2 equation

$$\dot{V}CO_2 = \dot{V}_A \times FACO_2$$

① $\leftarrow FACO_2 = \frac{\dot{V}CO_2}{\dot{V}_A}$

$\dot{V}CO_2$ → Rate of CO_2 produced by the body
 $\dot{V}_A$ → Alveolar vent per min

$PACO_2 = FACO_2 \times (P_b - P_{H_2O})$

→ Atm pressure

② $\leftarrow FACO_2 = \frac{PACO_2}{(P_b - P_{H_2O})}$

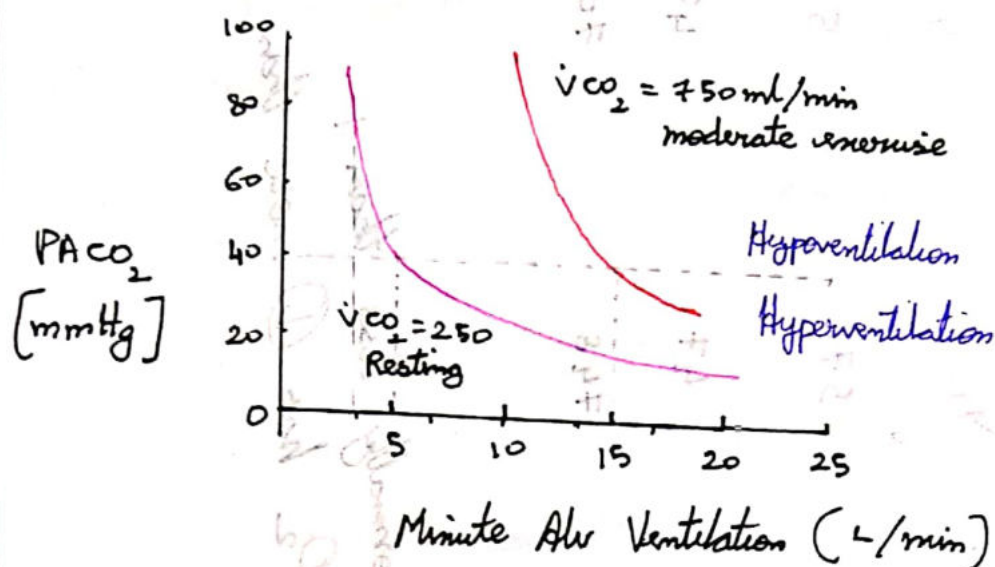
By equation ① & ② we get equation ③

③ $\leftarrow \frac{PACO_2}{(P_b - P_{H_2O})} = \frac{\dot{V}CO_2}{\dot{V}_A}$

$$PACO_2 = \frac{\dot{V}CO_2 \times (P_b - P_{H_2O})}{\dot{V}_A}$$

→ Inference from this equation :-

- ① There is an inverse relation B/w $PACO_2$ & $\dot{V}_A$ regardless of the vented CO_2
- ② At a constant $\dot{V}_A$ doubling of $\dot{V}CO_2$ causes $PACO_2$ to double.



- Alveolar ventilation is controlled to maintain $PACO_2$ at 40
- Thus at rest when $\dot{V}CO_2 \approx 250$ ml/min, alveolar ventilation of 5 L/min results in $PACO_2 = \underline{40}$ mmHg
- 50% $\downarrow$ in $\dot{V}_A \Rightarrow$ doubling of $PACO_2$
- during moderate exercise $\Rightarrow \dot{V}CO_2 = 750$ ml/min
 $\dot{V}_A \Rightarrow 15$ L/min
 $PACO_2 \Rightarrow \underline{40}$ mmHg

Arterial Gas equation :-

- In normal lungs $Paco_2$ is tightly regulated and maintained at 40 ± 2 mmHg
- Sp. chemoreceptors monitor $Paco_2$ in the brainstem and exhaled minute ventilation varies in accordance with the level of $Paco_2$
- Resp acidosis :- $pH < 7.35$ - acute $\uparrow$ in $Paco_2$
- Resp alkalosis :- $pH > 7.45$ - " $\downarrow$ " " "
- Hypercapnia - elevation in $Paco_2$ during hypoventilation
- Hypocapnia - opposite

Parameter	Ambient Air [dry]	Moist Trashed Air	Alveolar Gas $R = 0.8$	Systemic Arterial Blood	Mixed Venous Blood
P_{O_2}	159	150	102	90	40
P_{CO_2}	0	0	40	40	46
P_{N_2}	601	563	571	571	571
P_{H_2O}	0	47	47	47	47
P_{Total}	760	760	760	748	705

Note:-

P_{N_2} is $\uparrow$ in alveolar gas by 1% but R is normally less than 1.
 P_{Total} is less in venous than in arterial blood but P_{O_2} has $\downarrow$ more than P_{CO_2} has $\uparrow$.

- Distribution of Ventilation :- Ventilation is not uniformly distributed

I Affect of gravity :-

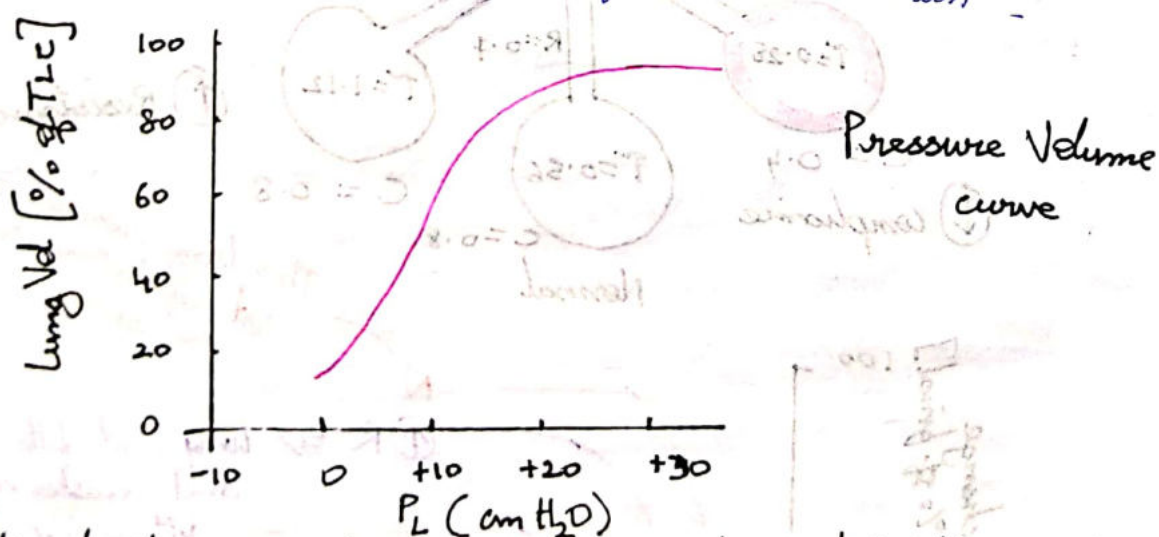
- It is more pronounced in upright position and less in supine position.

- At the apex of lungs :-

- i) Pleural press is more -ve due to gravitational pull down
- ii) P_L [translung pressure] is high
- iii) Alveoli are expanded - larger at any lung volume
The effect is greatest at RV, less at FRC and absent at TLC

iv) As a result alveoli at the apex of lung are less compliant and receive a smaller proportion of the inspired air

- whereas at the base the alveoli are more compliant and receive a large portion of the ventilation



Alveoli at the lung base are up along the steep portion of the pressure volume curve. Whereas, Alveoli at the apex are up down to the top or flat portion of the pressure volume curve.

Time constant :- www.FirstRanker.com

www.FirstRanker.com

- Ventilation in alveoli is not uniform. The reason for this is variable airway resistance or compliance. It is described quantitatively by **Time constant**

$$\tau = R \times C$$

- Alveoli with long τ fill & empty slowly.

$$\tau \propto R$$

$$\tau \propto C$$

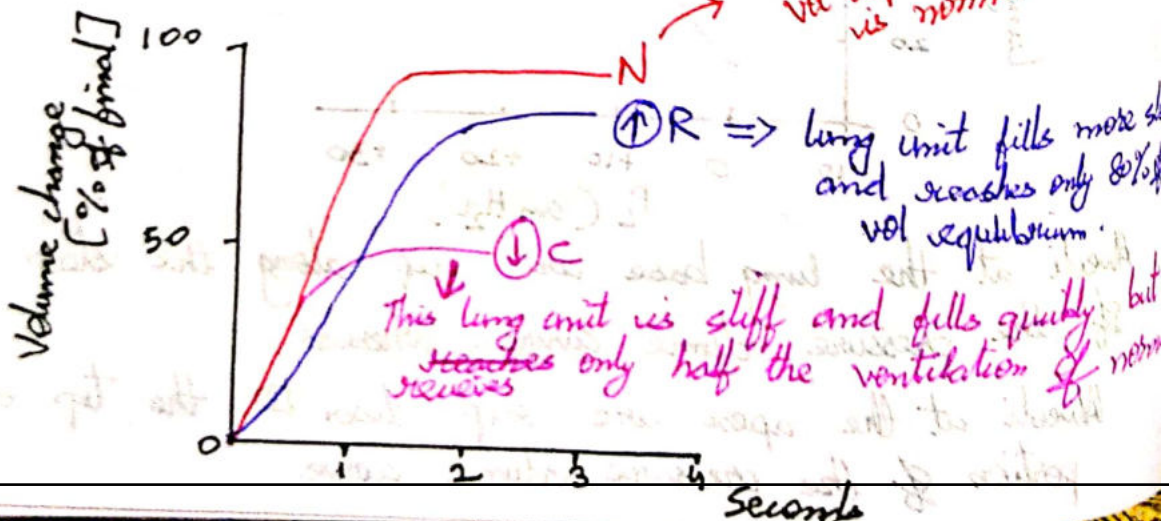
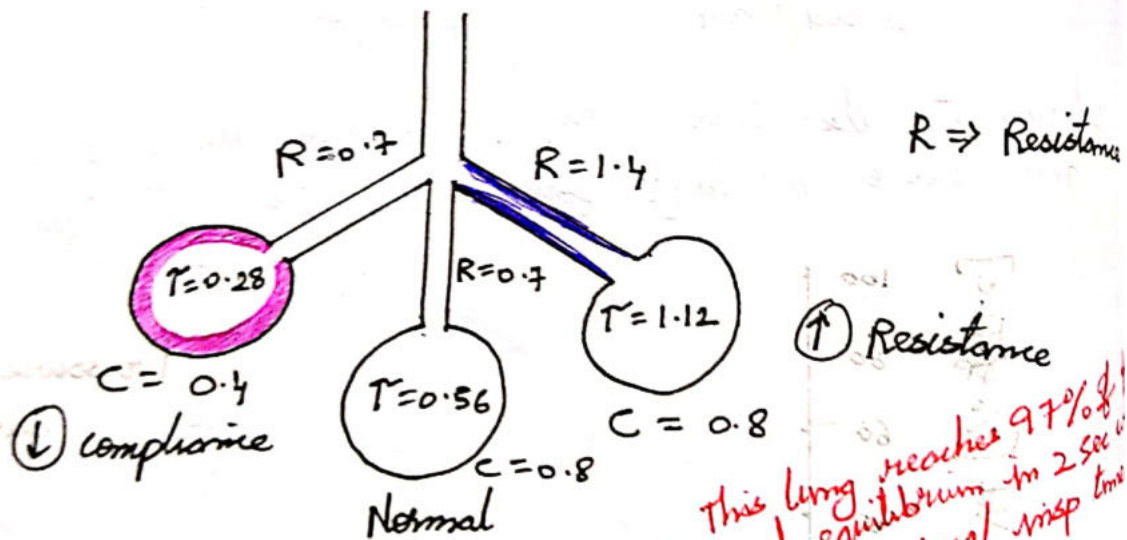
- In adults

Normal Resp rate $\Rightarrow$ 12 breaths per min

Inspiratory time $\approx$ 2 sec

Expiratory time $\approx$ 3 sec

In normal lungs this time is sufficient to approach vol equilibrium



- Adults with COPD have a very long time constant as a result of an $\uparrow$ Resistance and in the case of individuals with emphysema and $\uparrow$ Compliance.
As a result in patients with COPD there is slow resp rate.

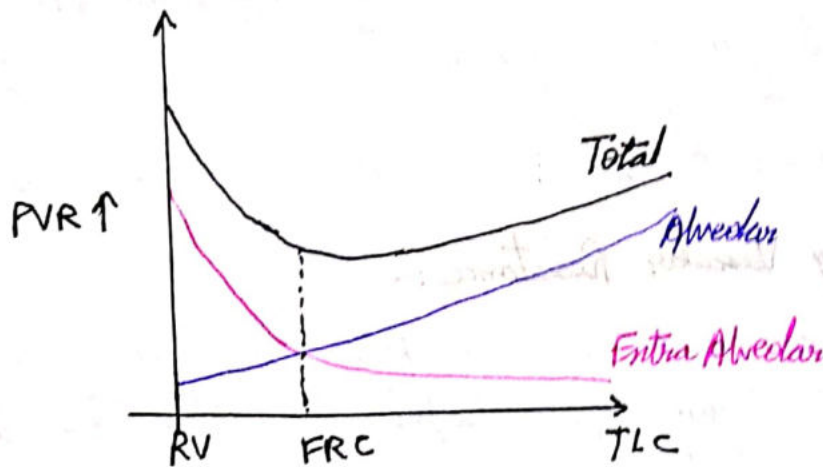
- Pulmonary Vascular Resistance :-

- PVR :- change in pressure from the pulmonary artery (P_{PA}) to the left atrium (P_{LA}) divided by flow (Q_T) which is the cardiac output
- Blood flow in the pulmonary circulation is pulsatile

$$PVR = \frac{P_{PA} - P_{LA}}{Q_T}$$

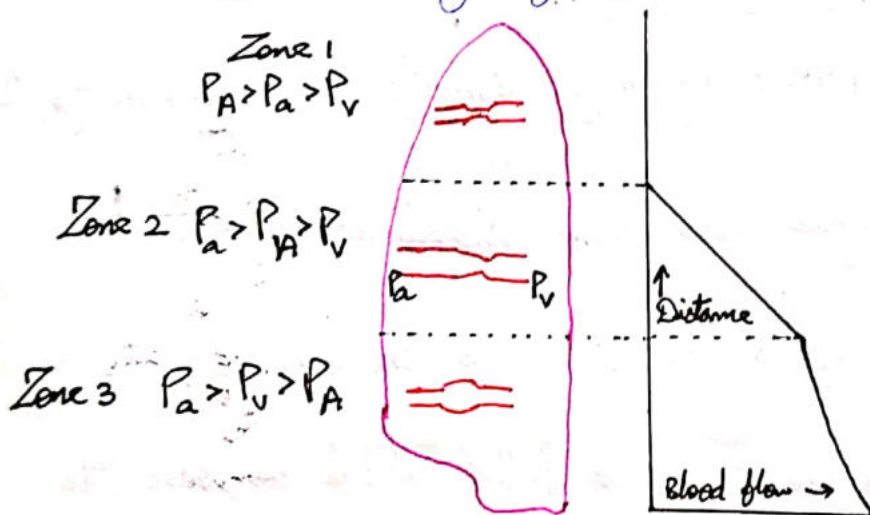
$$PVR = \frac{14 \text{ mmHg} - 8 \text{ mmHg}}{6 \text{ L/minute}} = 1.00 \text{ mmHg/L/min}$$

- PVR is 10 times less than Resistance in Systemic circulation.
- Lung volume affects PVR thru its influence on alveolar capillaries.
At end inspiration, the air filled alveoli compress the alveolar capillaries & $\uparrow$ PVR.
- Capillary beds in the lungs $\Rightarrow$ 40% of PVR
- The diameters of the larger extra alveolar vessels $\uparrow$ at end inspiration bcz of radial traction & elastic recoil & thus PVR is lower at higher lung volume.
- Total PVR in the lung is lowest at FRC



- Distribution of Pulmonary blood flow :-

- As it is a low press system pulmo circulation is affected to a large extent by gravity



- In normal upright persons at rest the vol of blood flow ↑ from apex of the lung to the base of the lung

Note :- Under conditions of stress such as exercise, the difference in the blood flow in the apex and base of the lung in upright persons becomes less, mainly bcoz of the ↑ in arterial pressure

- For every 1 cm ↑ in location of a pulmonary artery segment above the hrt there is corres ↓ in

hydrostatic pressure eq. to 0.74 mm Hg

- The effect of gravity on blood flow affects arteries and veins equally
- Due to gravity apex is poorly perfused $\rightarrow$ base is over perfused
- Perfusion zones of lung :-

Zone 1 :- $P_A > P_a > P_v$

- does not exist under normal conditions
- P_a is very low
- capillaries collapse and blood flow ceases
- Zone 1 may exist during +ve pressure mech ventilation or if $P_a \uparrow$ such as diving hemorrhage [$\downarrow$ Blood volume]

Zone 2 :- $P_a > P_A > P_v$

- Upper third of lung
- Because $P_A > P_v$, the greater P_A partially collapses the capillaries and causes a damming effect
This phenomenon is often referred as Waterfall effect

Zone 3 :- $P_a > P_v > P_A$

- High pulmonary blood flow
- Blood flow in accordance with pressure gradients -

Zone 4 :- $P_a > P_v > P_A$

collapse of extra alveolar vessels

Active Regulation of Blood flow

- Blood flow in lung is primarily controlled by passive mech but there are also certain active mech.
- **Hypoxic Vasoconstriction**:- occurs in arterioles in response to decreased PAO_2
- This response is local — shifting of blood flow from hypoxic areas to well perfused areas in an effort to enhance gas exchange
- Isolated, local hypoxia does not alter PVR; approx 20% of the vessels must be hypoxic before a change in PVR can be measured.
- High levels of inspired O_2 can dilate pulmonary vessels and ↓ PVR
- Pulmonary capillaries lack smooth muscle and thus are not affected
- In some individuals as a consequence of chronic hypoxia or collagen vascular disease or for no apparent reason, pulmonary artery vascular resistance and subsequently pulmonary artery pressures rise
[Pulmonary artery hypertension]

Ventilation / Perfusion Relationship :-

Ventilation Perfusion ratio [V/Q ratio] :- It is defined as the ratio of Ventilation to blood flow.

At the level of a single alveolus the ratio is defined as alveolar ventilation per minute ($\dot{V}_A$) divided by capillary flow $\dot{Q}_c$.

At the level of lung the ratio is defined as total alveolar ventilation divided by cardiac output.

$$V/Q = \frac{4.0 \text{ L/min}}{5.0 \text{ L/min}} = \underline{\underline{0.8}}$$

- Mismatching of Pulmonary blood flow & ventilation results in an impaired $O_2 \rightarrow CO_2$ transfer.
- In general V/Q ratios greater than 1 are not associated hypoxemia.
- A normal V/Q ratio simply means that the relationship B/W ventilation & perfusion is normal.
- Case Study :- Lobar pneumonia

$V \Rightarrow \downarrow$ in the affected lobe

$Q \Rightarrow$ perfusion normal

V/Q will be less than 1

$\downarrow$ in ventilation prod hypoxic vasoconstriction in capillaries of the affected lobe thereby reducing perfusion (Q) bringing the V/Q ratio back to normal

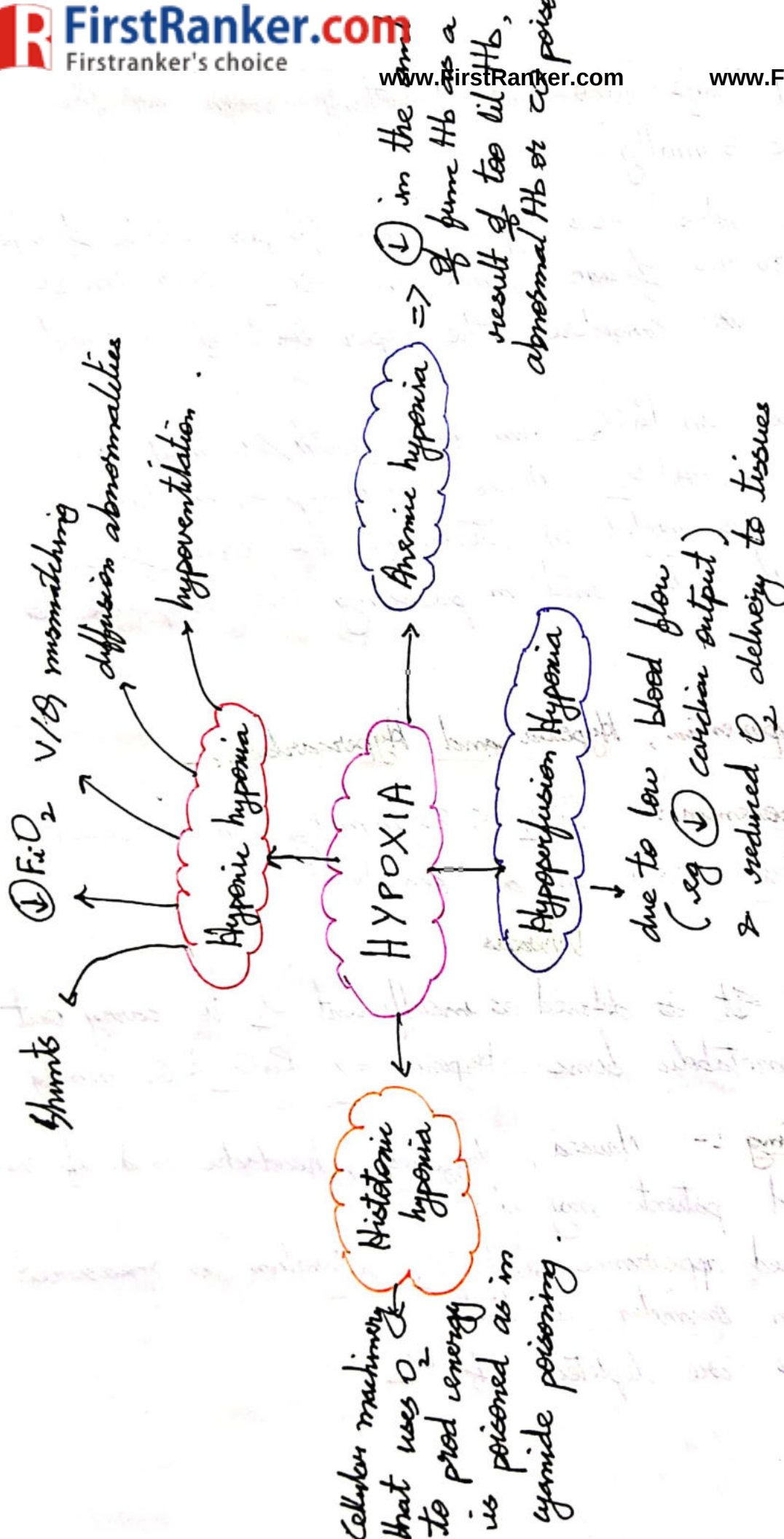
Here $V \& Q$ are $\downarrow$ but after compensation V/Q becomes normal

- Regional differences in V/Q ratios :-
- In an upright position from the apex to base both ventilation & perfusion $\uparrow$ but $\uparrow$ in ventilation is less than $\uparrow$ in perfusion.
- As a result normal V/Q ratio at the apex is much greater than 1 (V exceeds Q)
V/Q at base much less than 1 (Q exceeds V)

Apex $\Rightarrow V/Q > 1$	$V > Q$
Base $\Rightarrow V/Q < 1$	$V < Q$

- Alveolar arterial diff in O_2 :- $[AaDO_2]$
- $PACO_2 \approx PaCO_2$ are eq due to solubility prop of CO_2 but $PAO_2 \neq PaO_2$
- In normal lungs $PAO_2 > PaO_2$
- The diff B/w $PAO_2 \approx PaO_2$ is called Alveolar arterial difference for O_2
- This small difference is not caused by imperfect gas exchange but by the small no of veins that bypass the lung & empty directly into arterial circulation.
 $\hookrightarrow$ This results in venous admixture and $\downarrow$ in PaO_2
 This is also an eq of Anatomical shunt
- Approx 2-3% of cardiac output is shunted in this way.

- In normal lungs who are breathing room air the $AaDO_2 < 15 \text{ mmHg}$.
The mean value rises approx 3 mmHg per decade of life after 30 yrs of age. Hence an $AaDO_2$ lower than 25 mmHg is considered the upper limit of normal.
- Abnormalities in PaO_2 can occur with/without an elevation in $AaDO_2$. Hence relationship B/W PaO_2 & $AaDO_2$ is useful in determining the cause of an abnormal PaO_2 and in predicting the response to O_2 therapy.
- Arterial hypoxemia, Hypoxia and Hypercarbia:-
- Arterial hypoxemia:- $PaO_2 < 80 \text{ mmHg}$ in an adult who is breathing room air at sea level.
Whereas
- Hypoxia:- It is defined as insufficient O_2 to carry out normal metabolic func. Hypoxia $\Rightarrow PaO_2 < 60 \text{ mmHg}$
- CO poisoning:- Nausea, dizziness, headache and if not recognised patient may die.
Cherry red appearance and O_2 saturation as measured with an oximeter is high.
Tissues are depleted of O_2 .



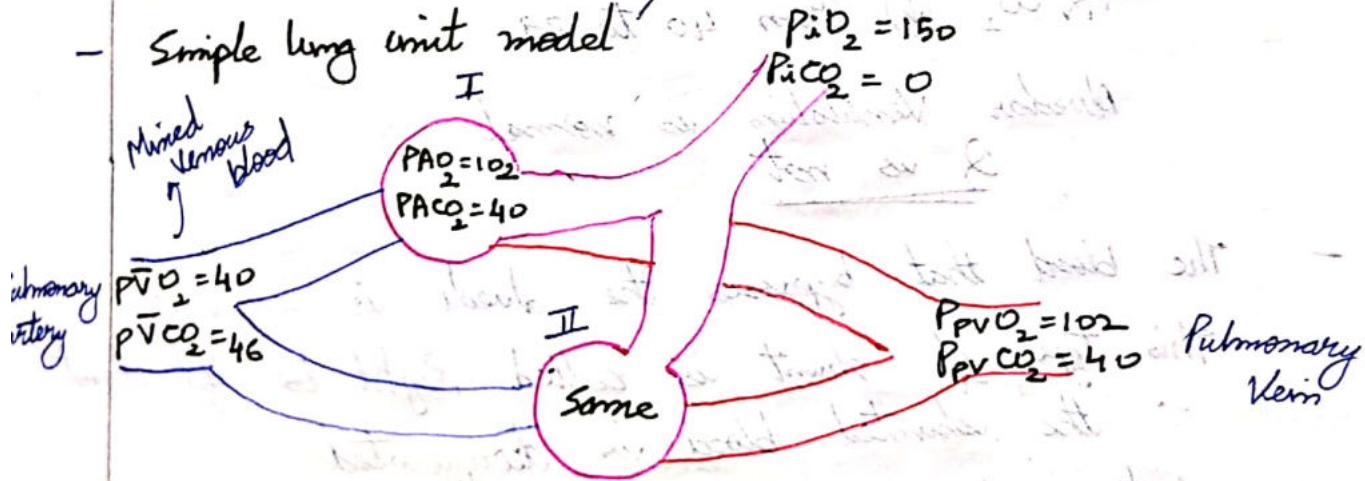
Causes of Hypoxic hypoxia :-

Cause	PaO_2	$AaDO_2$	PaO_2 response to 100% O_2
① Anat shunt	↓	↑	No change
② Physio shunt	↓	↑	↓
③ <u>Decreased FiO_2</u>	↓	N	↑
④ Low V/Q ratio	↓	↑	↑
⑤ Diffusion abnormality	↓	↑	↑
⑥ <u>Hyperventilation</u>	↓	N	↑

① ANATOMICAL SHUNTS :-

Ideal model $AaDO_2 = 0$

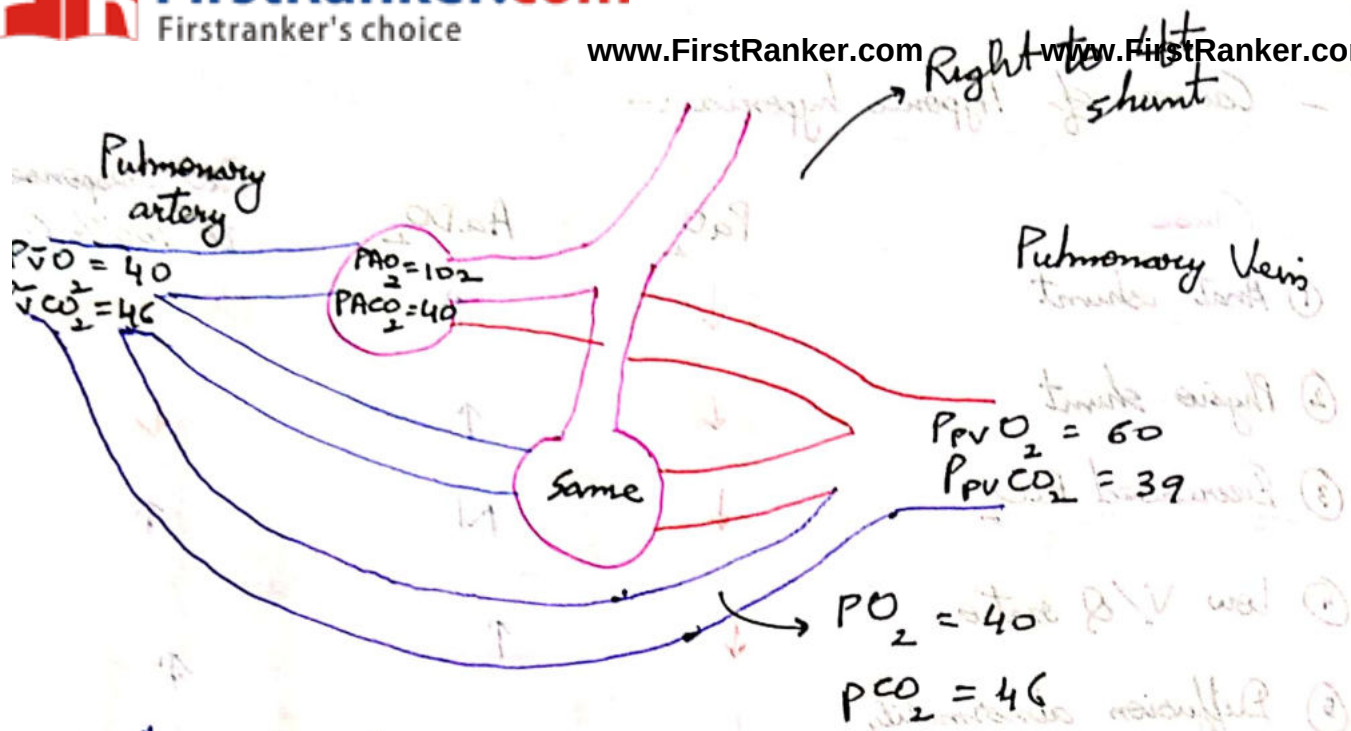
- Simple lung unit model



- In this model when ventilation is uniform half the inspired gas goes to each alveolus and when perfusion is uniform half the cardiac output goes to each alveolus.

V/Q in both I & II eq to 1

O_2 into blood
 CO_2 into alveolus } Gas exchange due to pressure gradient



- An anatomical shunt occurs when mixed venous blood bypasses the gas exchange unit & goes directly into the arterial circulation

P_{VO_2} ↓ from 102 to 60

P_{VCO_2} ↓ from 40 to 39

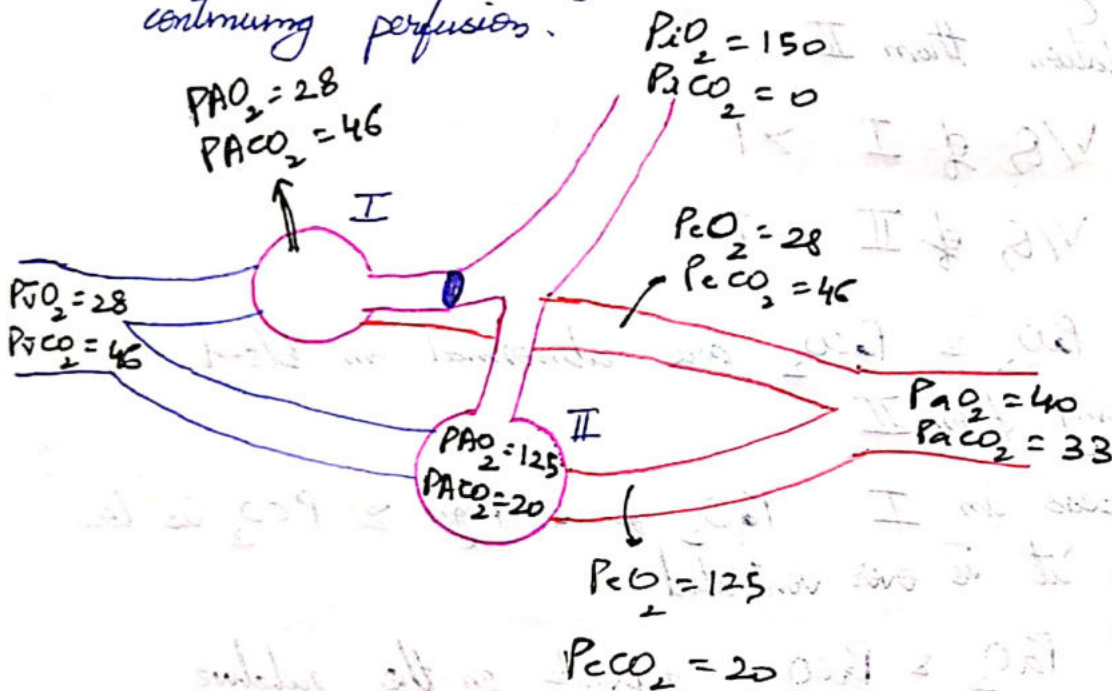
Alveolar Ventilation is normal
& is not

- The blood that bypasses the alveoli is **shunted**. This type of shunt is called **Right to Left shunt** ∴ the shunted blood is deoxygenated.
- Most Anatomical shunts dev within the heart. These shunts causing mixing of deoxygenated & oxygenated blood lead to Arterial hypoxemia.
- PaO_2 varies with the size of the shunt.
- Response to O_2 [100%] varies with the vol of blood shunted

- P_{aCO_2} does not change significantly: - central chemoreceptors respond to any elevation in CO_2 with an $\uparrow$ in ventilation and reduce to the normal range

(2) PHYSIOLOGICAL SHUNT: - Venous admixture

- When ventilation to lung units is absent in the presence of continuing perfusion.



Q is same for I & II

V of I is zero. All ventilation goes to II

$\therefore V/Q$ of I is zero

$\therefore$ The blood perfusing I will cont to remain mixed venous blood as there is no gas exchange

Atelectasis [obstruction to ventilation of a gas exchange unit] is an example where V/Q is 0

Causes

- Mucous plugs
- Pulmonary edema
- Tumours
- foreign bodies

③ Low V/Q ratio :-

- Mismatching B/W V & Q - most common cause of Arterial hypoxemia.
- When alveolar ventilation is unevenly dist B/W 2 lung units I & II such that I gets more ventilation than II
$$\frac{V}{Q} \text{ of I} > 1$$
$$\frac{V}{Q} \text{ of II} < 1$$
- Both PaO_2 & $PaCO_2$ are abnormal in blood coming from II
Whereas in I PaO_2 is high & PCO_2 is low as it is over ventilated
- Final PaO_2 & $PaCO_2$ depends on the relative contribution of each of these units to arterial blood
- $AaDO_2$ is $\uparrow$ as there is failure of compensation
- The $\uparrow$ in ventilation to a lung unit may be due to :-
 - ① Mucus obstruction
 - ② Airway edema
 - ③ Bronchospasm
 - ④ A foreign body / Tumor

④ Alveolar Hypoventilation :-

- V_A & $PaCO_2$ are inversely related
when V is halved $\Rightarrow PaCO_2$ doubles

- Ventilation insufficient to maintain normal levels of CO_2 is called hypoventilation
 - $\text{PaO}_2 \downarrow$
 - $\text{PaCO}_2 \uparrow$
- AaDO_2 is normal $\Rightarrow$ Both PArO_2 & PaO_2 are reduced due to hypoventilation. P_{50} gas exchange is normal AaDO_2 remains normal.
- Hypoventilation accompanies muscle weakness & drugs that reduce the respiratory drive.
- In the presence of hypoventilation areas of Atelectasis dev rapidly where V/Q is 0 & AaDO_2 is higher.

⑤ Diffusion Abnormalities:-

- There is diffusion disequilibrium due to incomplete diffusion and $\text{AaDO}_2 \uparrow$.
- This has been observed in individuals during exercise at high altitudes ($\geq 10,000$ feet).
- Even in individuals with an abnormal diffusion capacity diffusion disequilibrium at rest is unusual but can occur during exercise and at high alt.

- Hypocapnia:- Elevated PCO_2

- Mech of Hypocapnia
 - hypoventilation
 - $\uparrow$ dead space ventilation.

- Alveolar ventilation $\propto \frac{1}{\text{Alveolar } \text{CO}_2}$

$\therefore$ hypoventilation $\uparrow \text{PaCO}_2$

- Dead space is ∞ when pulmonary blood flow is interrupted in the presence of normal ventilation.

↳ pulmonary embolus - obstruction to blood flow

V is normal

Q is zero

$$\therefore V/Q = \infty$$

Here ventilation fails to oxygenate any of the mixed venous blood.

- Compensation by local bronchoconstriction and distribution of ventilation shifts to the areas being perfused.

Note:- PAO_2 is higher and the $PACO_2$ is lower in the apex than in the base.

PY 6.3 :- Transport of Respiratory Gases : O_2 & CO_2

The Respiratory & circulatory systems function together to transport O_2 from the lungs to tissues to sustain normal cellular activity and to transport CO_2 from the tissues to lungs for the respiration.

GAS DIFFUSION :-

- Gas most thruout the resp system occurs predominantly by diffusion.
- Resp sys & CVS have several unique features to facilitate gas diffusion :-
 - ① Large surface area for gas exchange with short distances to travel
 - ② Substantial partial pressure gradient differences
 - ③ Cases with Advantageous diffusion prop.
- Transport & delivery of O_2 & CO_2 are dependent on basic diffusion laws.
- Diffusion of Gases from Regions of Higher to lower Partial pressure in the Lungs :-
- Gas diffusion - Passive & similar in gaseous & liquid state.
- Graham's Law :- The rate of diffusion of a gas is described according to this law, the rate is directly proportional to the solubility coefficient of the gas & inversely prop to the sq root of its molecular wt.
- CO_2 diffuses approx 20 times faster than O_2 .

- Rates of O_2 diffusion from the lungs into blood and from blood into tissue are predicted by Fick's law of diffusion.

$$\dot{V}_{\text{gas}} = \frac{A \cdot D \cdot (P_1 - P_2)}{T}$$

$\swarrow$ gas diffusion $\nwarrow$ diffusion constant

$$\frac{A \cdot D}{T} = D_L - \text{diffusing capacity of lung}$$

$$\dot{V}_{\text{gas}} = D_L (P_1 - P_2)$$

$$D_L = \frac{\dot{V}}{(P_1 - P_2)}$$

- Fick's law of diffusion could be used to assess the diffusion properties of O_2 in the lungs, except that the capillary partial pressure of O_2 cannot be measured.
- True. According to Fick's law, the diffusion of a gas ($\dot{V}_{\text{gas}}$) across a sheet of tissue is directly related to the surface area (A) of the tissue, the diffusion constant (D) of the specific gas and the partial pressure difference ($P_1 - P_2$) of the gas on each side of the tissue and it is inversely related to tissue thickness (T).
- The capillary partial pressure (P_2) is essentially 0 for CO $\therefore D_L$ can be measured from the diffusion of CO ($\dot{V}_{\text{CO}}$) and the average partial pressure of CO in the alveolus that is

$$D_{LCO} = \frac{V}{P_1 - P_2} = \frac{V_{CO}}{P_{ACO}}$$

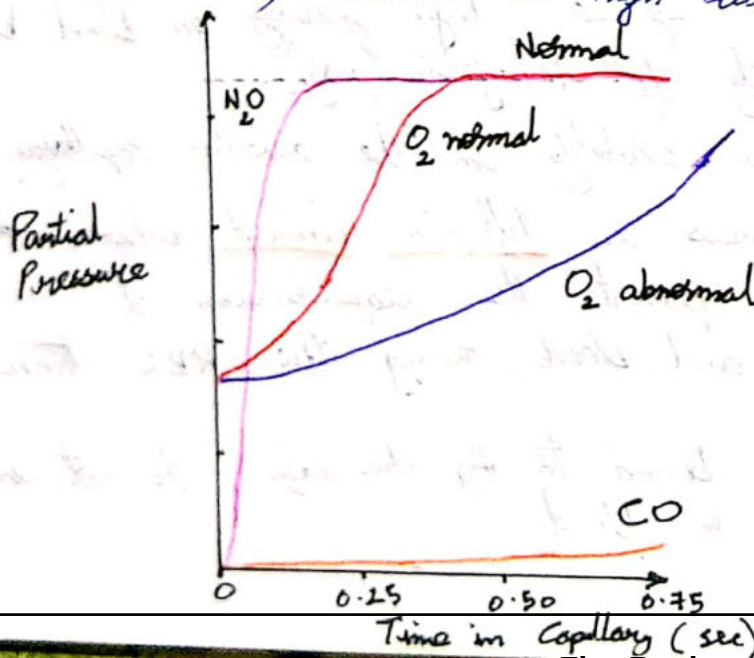
diffusion capacity of lung for CO

- Assessment of D_{LCO} has become a classic measurement of the diffusion barrier of the Alveolar capillary mem.
Useful for diagnosis of obstructive lung disease.
- O_2 & CO_2 exchange in the lung is Perfusion limited:-
 - Different gases have different solubility factors.
 - Insoluble gases:- eg Nitrous oxide & ether.
These gases do not chemically combine with proteins in blood & equilibrate rapidly B/W Alveolar gas and blood. This equilibration occurs ^{in time} less than the capillary transit time of 0.75 sec.
 - The diffusion of such gas is Perfusion limited bcoz the partial P of gas in the blood leaving the capillary has reached eq with alveolar gas and thus diffusion is limited only by the blood perfusing the capillaries.
 - Soluble gases:- eg CO - high solubility in blood bcoz of its high affinity for hemoglobin (Hgb).
But have low solubility in the alveolar capillary membrane.
Hence these gases are diffusion limited where ~~the~~
These features prevent the equilibration of CO between Alveolar gas and blood during the RBC transit time.
 - Gases that are bound to Hg chemically; do not exert a partial pressure in blood.

CO_2 and O_2 are like NO_2

low solubility in alv
capillary mem high solubility in blood

- But rate of equilibration is rapid for complete equilibration to occur during the transit time of RBC within capillary.
- Equilibration of O_2 & CO_2 usually occurs within 0.25s. Hence even after being soluble gases their diffusion is perfusion limited.
- Although CO_2 has a greater rate of diffusion in blood than O_2 does, it has a lower membrane blood solubility ratio & takes approx same time to reach equilibration in blood.
- Diffusion of O_2 & CO_2 becomes diffusion limited when capillary transit time for RBC reduced below 0.25s. This happens in case of very fit athletes during vigorous exercise, exercise at high altitude.

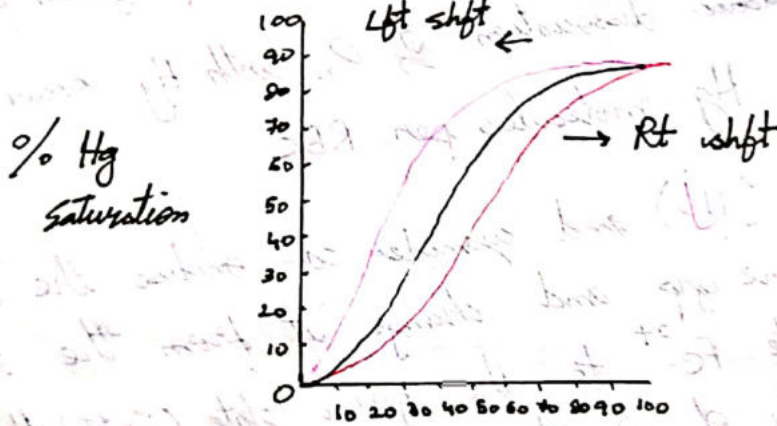
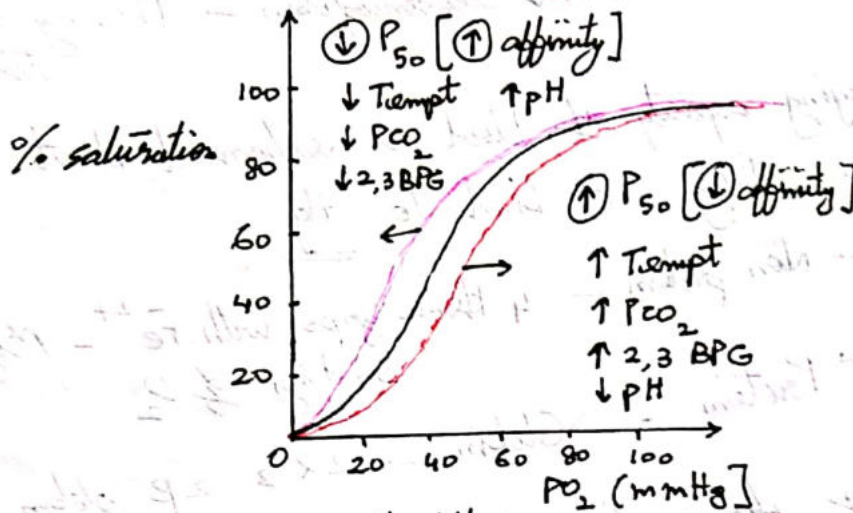


- Transport of O_2 - $\left\{ \begin{array}{l} \text{As dissolved } O_2 - \text{contribution almost negligible} \\ \text{As Oxyhemoglobin} - \text{Primary mode of transport} \end{array} \right.$
- O_2 carrying capacity of blood is enhanced about 65 times by its ability to bind to Hg.
- Hg - $\left\{ \begin{array}{l} \text{Non protein} - 4 \text{ heme groups with } Fe^{2+} - \text{Major site of binding of } O_2 \\ \text{Protein} - \text{Globin} - 2\alpha \text{ \& } 2\beta \text{ globin chains} \end{array} \right.$
- Binding & ~~de~~ dissociation of O_2 with Hg occur in millise
- 280 million Hg molecules per RBC
- CO, intrates (NO) and cyanides can oxidise the iron molecule in the heme group and change it from the reduced ferrous state Fe^{2+} to the ferric state (Fe^{3+}) thus reducing the ability of O_2 to bind to Hg.

Oxyhemoglobin Dissociation Curve :-

- It illustrates the relationship b/w PO_2 in blood & the number of O_2 molecules bound to Hg
- 'S' shape of the curve - dependence of Hg saturation on PO_2 especially at $PO_2 < 60 \text{ mmHg}$
- Clinical significance of flat portion - drop in PO_2 over a wide range of partial pressure (100 to 60 mmHg) has a minimal effect on Hg saturation
- The point on the curve at which Hg is 50% saturated with O_2 is called the P_{50} & it is 27 mmHg in adults.

- Physiological factors that shift the oxyhemoglobin dissociation curve :-



Lft shift - P_{50} - 10 mmHg

Rt shift - P_{50} - 40 mmHg

Normal - P_{50} - 27 mmHg

- Curve is shifted to right when the affinity of Hg for O_2 which enhances O_2 dissociation - P_{50} $\uparrow$ ie decreased Hg binding to O_2 at a given PO_2
- Curve shift to lft - opposite

- Shifts have little effect when they occur at O_2 partial pressures within the normal range (80 to 100 mmHg).

① H^+ conc and CO_2 :-

- ↑ in CO_2 production $\Rightarrow$ more generation of H^+ ions $\Rightarrow$ ↓ pH. This shifts the curve to the right.
- The shift to right is due to ↓ in pH & a direct effect of CO_2 on Hg. This occurs at the level of tissues.
- At the level of lungs - opposite occurs.
- The effect of CO_2 on the affinity of Hg for O_2 is known as the Bohr effect. It serves to enhance O_2 uptake in the lungs & delivery of O_2 to the tissues.

② Temperature :-

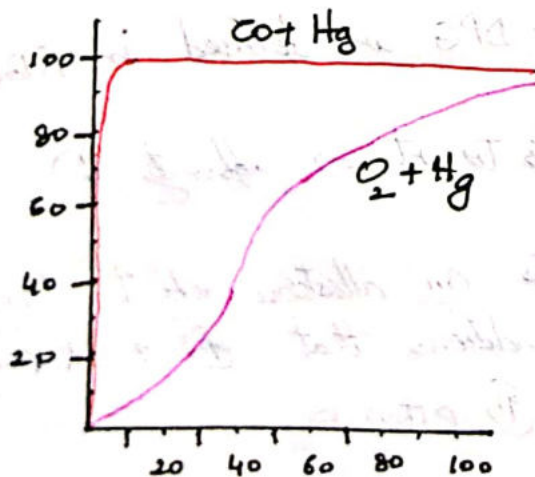
- ↑ in body temperature - shifts to right
- ↓ in body temp - shifts to left [extremities like fingers, toes etc]

③ 2,3 - diphosphoglycerate :-

- Large quantities of 2,3 - DPG are formed in RBC's during glycolysis.
 - ↑ 2,3 DPG $\Rightarrow$ shifts to right $\Rightarrow$ affinity ↓
- Binding of 2,3 DPG creates an allosteric effect that inhibits the binding of O_2 . Conditions that ↑ 2,3 DPG include hypoxia, ↓ Hg and ↑ pH.
- Applied :- ↓ levels of 2,3 - DPG in stored blood samples and may present problem to blood transfusion patients bcoz of ↓ affinity of Hg for O_2 .

④ Carbon Monoxide:-

- $\text{CO} + \text{Hb} \rightarrow \text{HbCO}$
[carboxyhemoglobin]
- The affinity of CO for Hb is about 200 times greater than it is for O_2
- In the presence of CO, the affinity of Hb for O_2 is enhanced. This causes shift to the left, which further prevents the unloading and delivery of O_2 to tissues.
- When $\text{PCO} = 1 \text{ mmHg} \Rightarrow$ All Hb are bound to CO
 $\hookrightarrow$ CO poisoning
- In healthy individuals, HbCO occupies about 1% - 2% of Hb binding sites
- HbCO - ~~5 to 7%~~ 5 to 7% - hazardous
- Cigarette smokers + Residents of high density urban traffic areas $\Rightarrow$ HbCO 10%



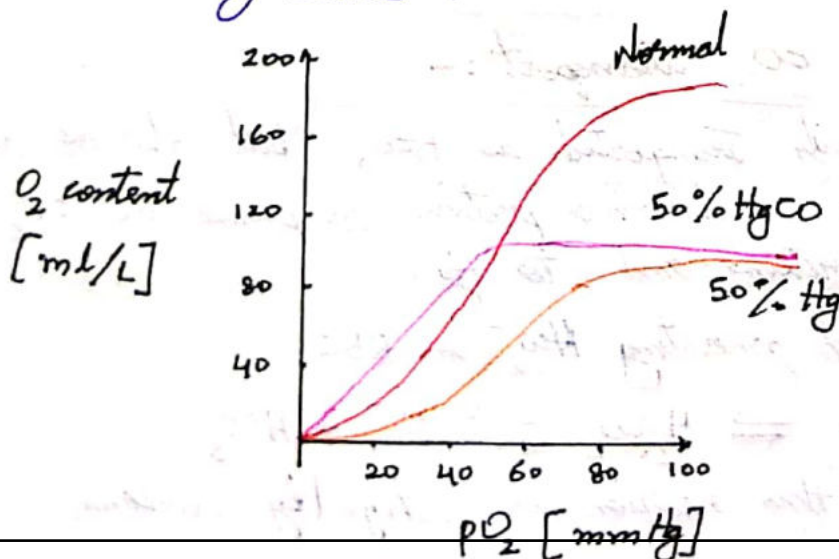
- Treatment of individuals with high levels of CO - consist of administering high conc of O_2 to displace CO from

Note:- NO has great affinity [200,000 times greater than O_2] for Hg & it binds irreversibly to Hg at the same site that O_2 does.

NO poisoning is not common but the clinician must be cautious when administering NO therapy for long periods.

- O_2 saturation, Content and Delivery:-

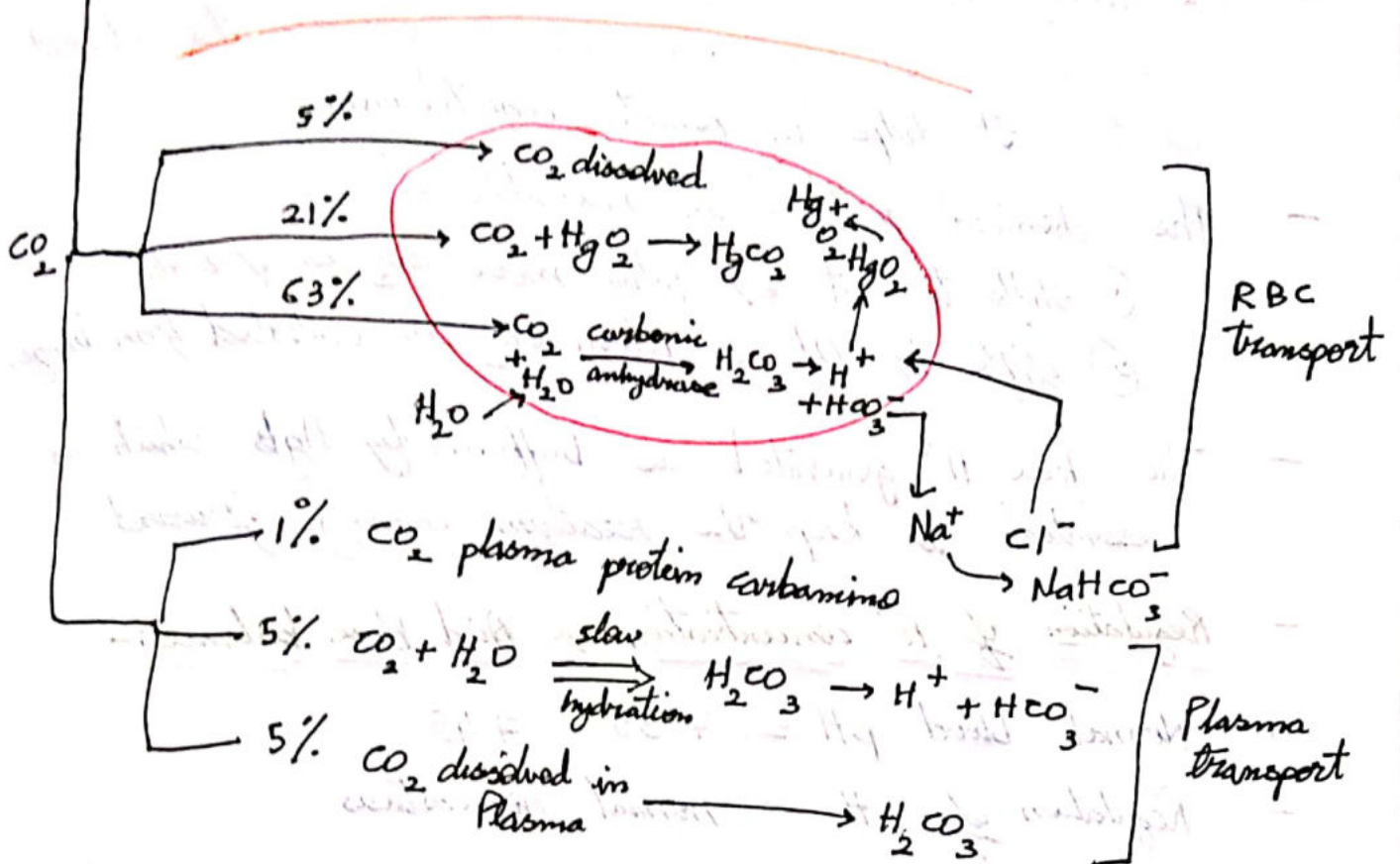
- Each Hg molecule can bind upto four O_2 atoms & each gram of Hg can bind upto 1.34 ml of O_2
- O_2 saturation (SO_2) refers to the amt of O_2 bound to Hg in relation to the maximal amt of O_2 (100% O_2 capacity) that can bind Hgb.
- Binding of O_2 to each heme group ① the affinity of Hg molecule to bind additional O_2
- O_2 delivery from the lungs to tissues depends on
 - ① cardiac output
 - ② the Hg content of blood
 - ③ Ability of the lung to oxygenate the blood.
- Under normal conditions Hgb leaves the tissues 75% saturated with O_2 and only about 25% is actually used by tissues.



- Erythropoiesis :- RBC production
- It is stimulated by erythropoietin which is synthesised in the kidneys by cortical interstitial cells.
- $\downarrow O_2$ delivery, low Hg concentration & low PaO_2 stimulate the secretion of erythropoietin.
- Chronic renal disease $\Rightarrow$ damage to cortical interstitial $\Rightarrow$ $\downarrow$ erythropoietin $\Rightarrow$ $\downarrow$ RBC production.

CARBON DIOXIDE TRANSPORT :-

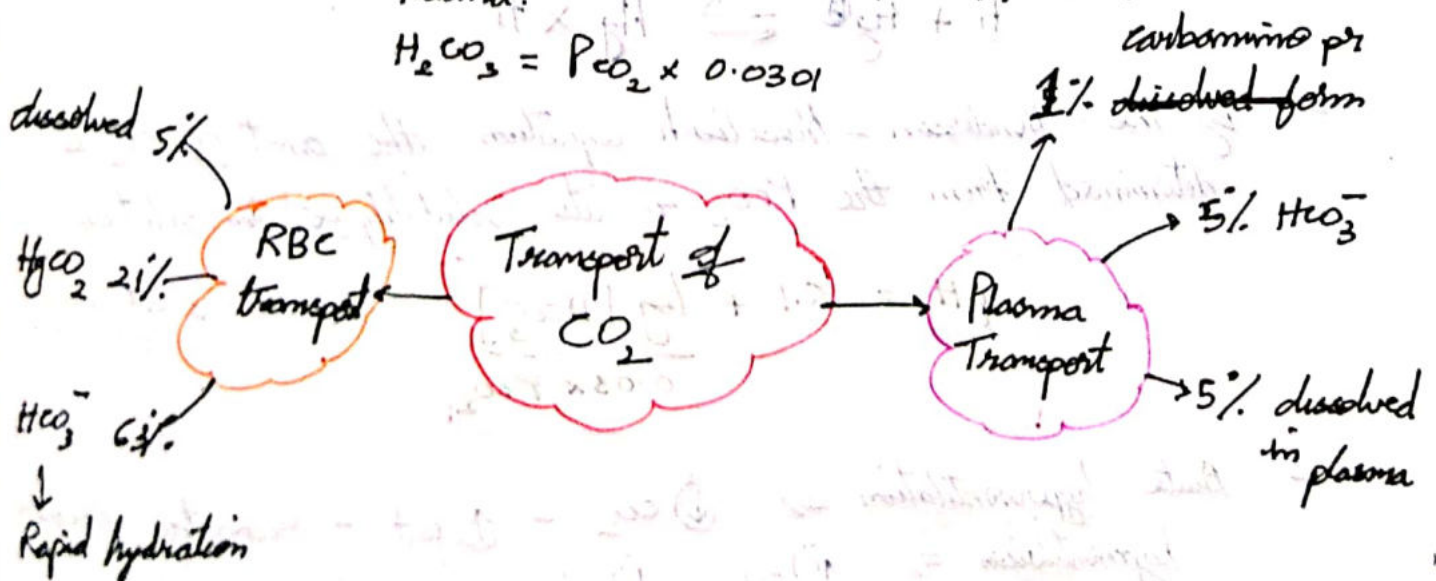
- CO_2 production :-
 - Rate of prod $\Rightarrow$ 200 ml/min - healthy condition
 - 80 molecules of CO_2 are expired by the lungs for every 100 molecules of O_2 that enter the capillary bed.
 - The body has enhanced storage capabilities for CO_2 in comparison with O_2 & hence PaO_2 is much more sensitive to changes in ventilation than in $PaCO_2$.
 - There is an inverse relationship B/W alveolar ventilation and $PaCO_2$.
 - Bicarbonate & CO_2 transport :-
 - CO_2 is primarily transported as HCO_3^- but also as dissolved CO_2 and as carbamino protein complexes. i.e. CO_2 binds to plasma proteins and to Hg.
 - Major mech for generating HCO_3^- in RBC
- $$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$
- Within RBC's this reaction is catalysed by carbonic Anhydrase.



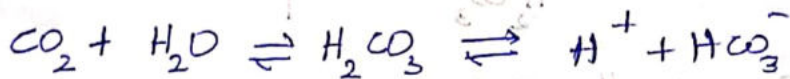
$$\frac{NaHCO_3}{H_2CO_3} = \frac{20}{1}$$

P_{CO_2} directly affects the H_2CO_3 levels in Plasma:

$$H_2CO_3 = P_{CO_2} \times 0.0301$$



- The HCO_3^- diffuses out of the Red blood cell in exchange for Cl^- in a process known as the chloride shift. It helps in osmotic equilibrium.
- The chemical reaction is reversible:-
 - ① shifts to rht $\Rightarrow$ when more CO_2 is present
 - ② shifts to lft $\Rightarrow$ when CO_2 is vented from lungs.
- The free H^+ generated is buffered by Hgb. which is essential to keep the reaction moving forward.
- Regulation of H^+ concentration & Acid Base balance:-
 - Normal blood pH = 7.35 - 7.45
 - Regulation of pH - normal homeostasis
 - $\text{CO}_2 \rightarrow \text{HCO}_3^- \Rightarrow$ Major Mech of buffering & regulating H^+ concentration



- By the Henderson - Hasselbalch equation the amt of CO_2 is determined from the PCO_2 & its solubility (α) in solution

$$\text{pH} = 6.1 + \frac{\log [\text{HCO}_3^-]}{0.03 \times \text{PCO}_2} \quad \alpha = 0.03 \text{ at } 37^\circ\text{C}$$

- Acute hyperventilation $\Rightarrow$ $\downarrow \text{CO}_2$ - $\uparrow \text{pH}$ - respiratory alkalosis
 hypoventilation $\Rightarrow$ $\uparrow \text{CO}_2$ - $\downarrow \text{pH}$ - respiratory acidosis.

- Carbon dioxide dissociation curve :-
- linear & directly related to PCO_2
- Deoxygenated Hg has greater affinity for CO_2
- CO_2 & O_2 bind to Hg at different sites
- **Haldane effect** :- The effect of changes in oxyhemoglobin saturation on the relationship of CO_2 content to PCO_2 is referred to as haldane effect and is reversed in the lungs when O_2 is transported from alveoli to RBC.