



Student Notes

PHYSIOLOGY

1st Edition

Unit 6

Respiratory System



Preface

Dear Medicos,

Agam Medical Organization has been dedicated to fostering a culture of academic excellence and knowledge sharing among medical students. Our organization has always recognized the importance of passing on the torch of learning to the next generation. Today, we are proud to present the culmination of years of dedication and hard work: the Agam Medical Organization's Physiology Study Material.

This comprehensive study material is not just a book; it's a testament to the spirit of collaboration and the unwavering commitment of our fellow students to their academic pursuits. As we navigate the challenging journey of medical education, we understand the significance of having reliable and concise resources at our disposal. This study material has been meticulously crafted with this understanding in mind.

The material within these pages is the result of countless hours of research, study group sessions, and the collective wisdom of our seniors. It has been designed to aid you in comprehending the intricacies of physiology and, more importantly, to empower you to excel in your undergraduate university exams.

Each chapter within this book delves into various aspects of physiology, offering not just theoretical knowledge but also practical insights. We have strived to simplify complex concepts, making them accessible to all readers, regardless of their level of familiarity with the subject.

Furthermore, we have incorporated summaries, and diagrams to facilitate effective revision. We firmly believe that learning should be a dynamic process, and this study material encourages active engagement with the subject matter.

As you embark on your journey through the pages of this book, remember that you are not alone. You have the collective wisdom and support of Agam Medical Organization and its members behind you. We are here to help you succeed.

We extend our heartfelt gratitude to all the contributors, without whom this project would not have been possible. Their dedication and passion for the subject shine through in every page.

We hope that this Physiology Study Material serves as a valuable companion on your academic path, guiding you toward a deeper understanding of the human body and fostering a love for the subject. May it be a beacon of knowledge that illuminates your path to success.

Best wishes,

Agam

Acknowledgment

In the journey of creating the Agam Medical Organization's Physiology Study Material, we have been fortunate to receive support, guidance, and inspiration from numerous sources. We would like to extend our heartfelt gratitude to:

Contributors:

We are deeply appreciative of all the individuals who contributed to this material, whether through research, content creation, or editorial work. Your collective efforts have resulted in a resource that will benefit countless students. A special thanks to **Jwala S**, for leading the team to bring the material in perfect form. We would like to express our deepest appreciation to:

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God:

We begin by expressing our gratitude to the Almighty for bestowing upon us the wisdom, strength, and determination to undertake this endeavour.

Pioneers in the Field of Physiology:

We stand on the shoulders of giants—those pioneering scientists and researchers who paved the way for our understanding of the human body's intricate workings. Their dedication to advancing the field of physiology has been our guiding light.

Doctors and Professors:

To the medical professionals and educators who have tirelessly imparted their knowledge and expertise to generations of students, we owe a debt of gratitude. Your dedication to teaching and healing has inspired us to strive for excellence.

Seniors:

A heartfelt thanks to our senior colleagues who generously shared their wisdom and experiences with us. Your mentorship and guidance have been invaluable in shaping this study material.

Supportive Families and Friends:

Behind every student is a network of family and friends who offer unwavering support. We thank our loved ones for their patience, encouragement, and understanding throughout this journey.

The entire Agam Medical Organization:

To our dedicated members and the organization itself, thank you for providing a platform where students can collaborate, learn, and grow together. Your commitment to knowledge-sharing is the driving force behind this initiative.

Fellow Students:

Last but not least, we extend our gratitude to our fellow students who will use this study material. It is for you that we embarked on this journey, and we hope that this resource empowers you to excel in your academic pursuits.

This study material is a testament to what can be achieved through collective effort and a shared passion for learning. As we move forward, let us remember the importance of giving back and supporting one another in our pursuit of knowledge.

With sincere thanks,

Agam

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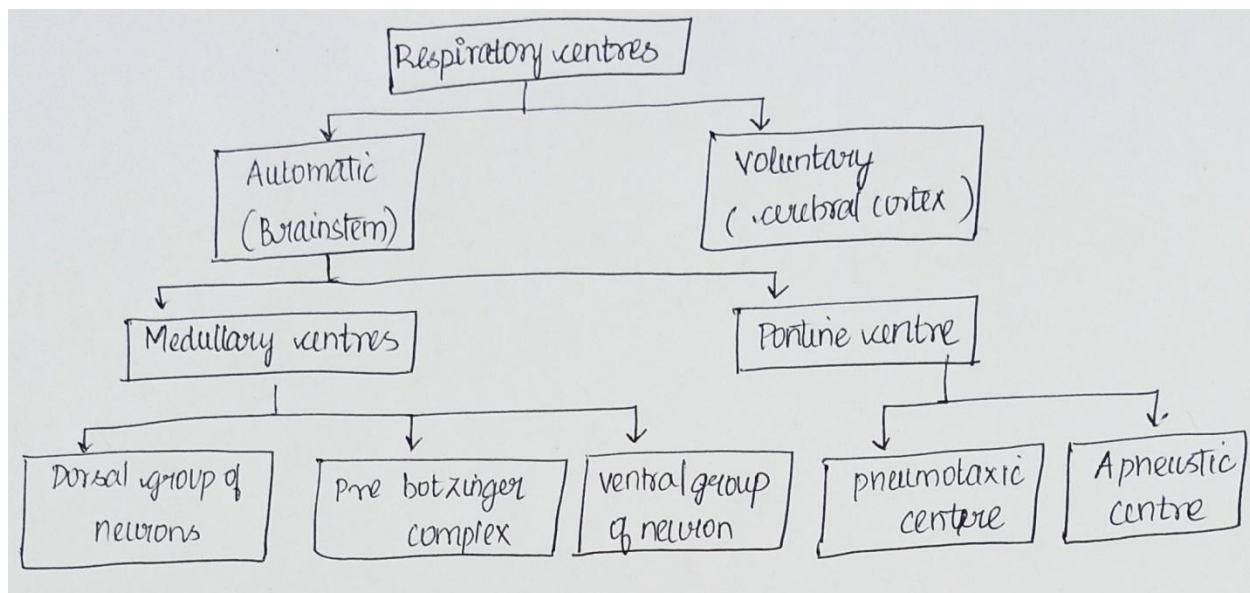
ESSAY

NEURAL REGULATION OF RESPIRATION

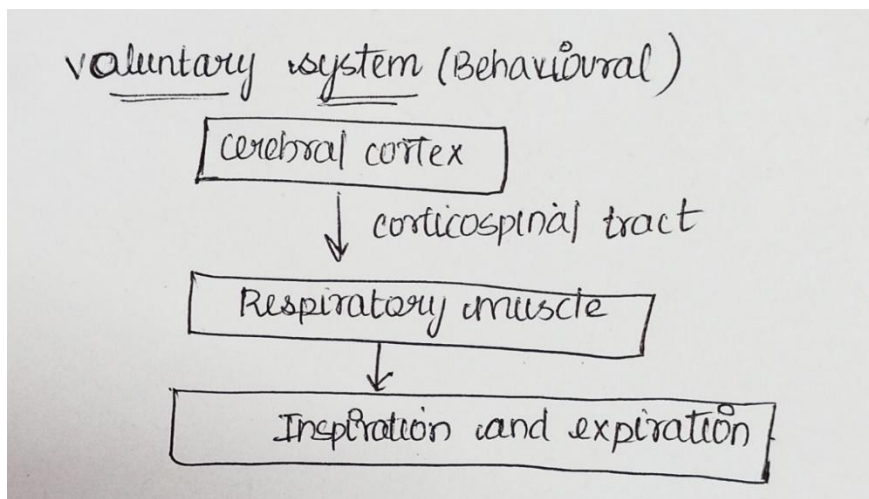
RESPIRATION

1. Exchange of gases between the organism and environment.
2. The normal respiratory rate in adult is 12 to 16 per min.
3. Respiration is regulated by two mechanisms. They are
 - a. Neural respiration
 - b. Chemical respiration

RESPIRATION CENTRES:



VOLUNTARY SYSTEM



FUNCTIONS

1. PONTINE CENTRE

PNEUMOTAXIC CENTRE

- Located in nucleus parabrachialis in upper pons.
- Primary function is to limit the inspiration.
- This is done by inhibiting apneustic centre.
- It increases the respiratory rate.

APNEUSTIC CENTRE

- It prolongs the inspiration. Which means increase in the depth of inspiration.

MEDULLA

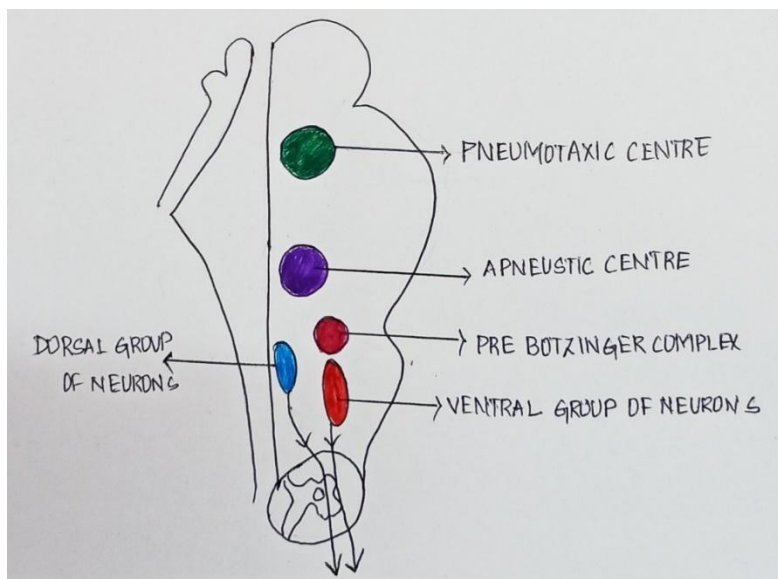
PREBOTZINGER COMPLEX: pacemaker [involuntary]

DORSAL RESPIRATORY GROUP [DRG]

- Generates ramp signal leads to smooth rise in tidal volume

VENTRAL RESPIRATORY GROUP [VRG]

- Expiration is a passive process at rest.
- This is needed during forceful expiration. [active process mainly during exercise]
- This is so called over dive phenomenon



INTEGRATION OF NEURAL AREAS

- Prebotzinger complex → signal from medulla to → spinal cord → activated phrenic nerve → diaphragmatic contraction → initiation of inspiration.
- Death is inevitable if this circuit is disrupted.

MAINTAINANCE OF INSPIRATION

- Apneustic centre → activates DRG → generates ramp signal

TERMINATION OF INSPIRATION

- Pneumotaxic centre → inhibits apneustic centre → -termination of inspiration
- Tidal volume reaches 500 ml → stretched lung → activates vagal afferents → inhibits apneustic centre
- Complete inhibition of apneustic centre occur if both the sources are present
- Partial inhibition occurs if only one source is present
- If apneustic centre is inhibited DRG is automatically inhibited

EXPIRATION

- Passive process at rest
- For forceful expiration needs VRG.
- MEDULLA: initiates the respiration
- PONS: regularizes respiration

LESIONS

1. Lesion below medulla

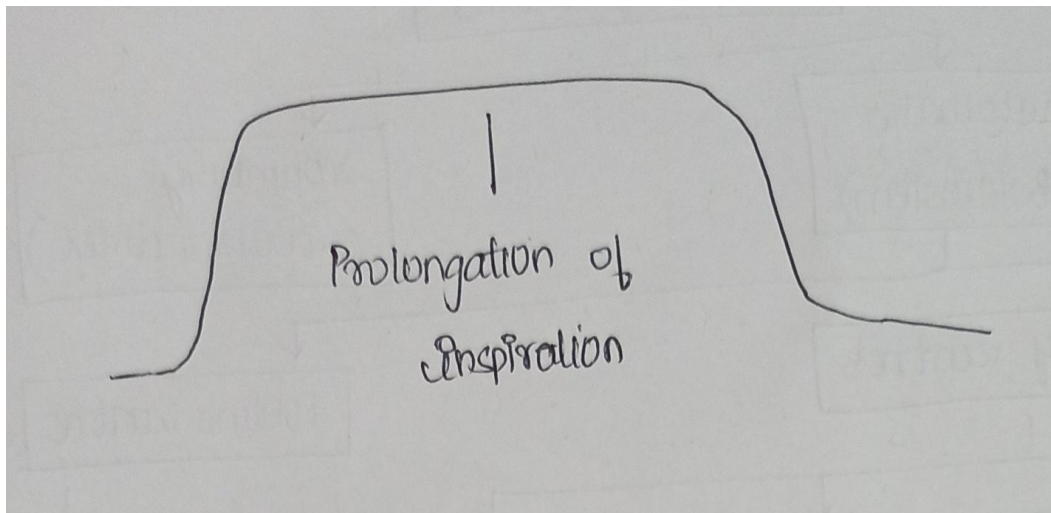
- Death is inevitable
- Circuit between prebotzinger complex and phrenic nerve is cut.
- Involuntary respiration is very essential during sleep. Absence of prebotzinger complex → respiration becomes voluntary → if they sleep, they die
- This is called as Ondine curse
- Treatment: mechanical ventilation during sleep.

2. Lesion at pontomedullary junction

- Initiation is normal
- Regulation of respiration does not that leads to irregular respiration.

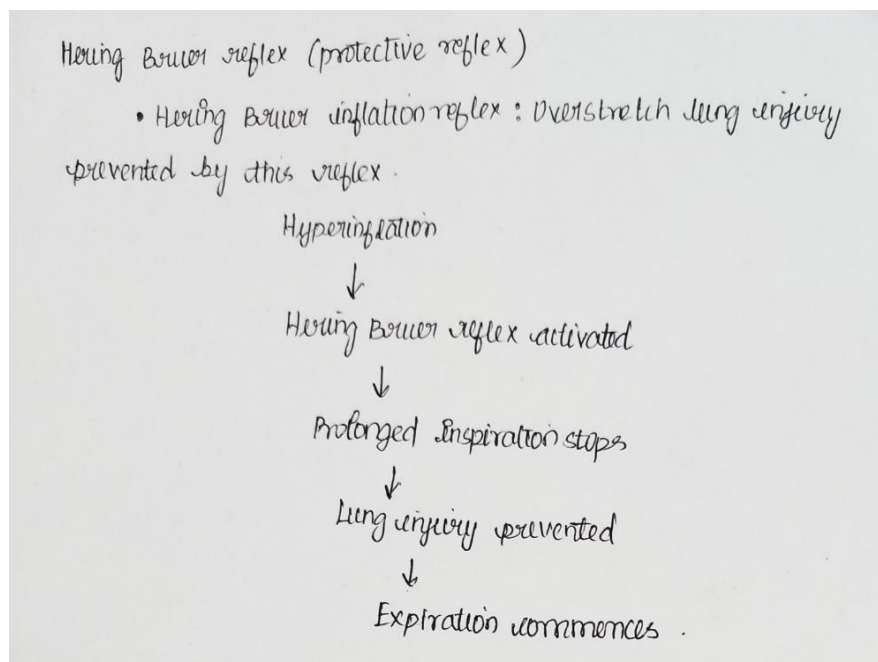
3. Lesion at mid pons with cut vagus nerve

- Both cause constant stimulation to apneustic centre leads to prolongation of respiration
- This is called apneustic spasm.



PULMONARY REFLEXES:

HERING BRUER REFLEX [PROTECTIVE REFLEX]



This reflex stops inspiration and decreases the duration of inspiration and increases expiratory duration.

stops and

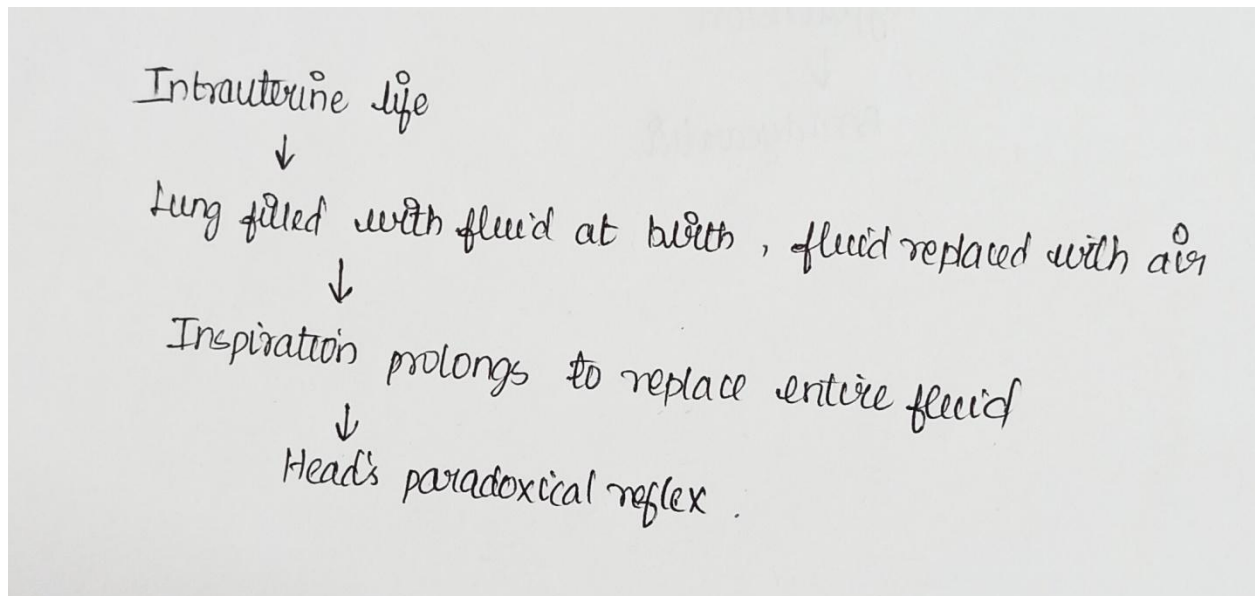
HERING BRUER DEFLATION REFLEX

- Prolonged expiration stops that leads to continued inspiration.
- Prolonged expiration can cause lung collapse
- Prevent lung collapse

HEADS PARADOXICAL REFLEX

- Prolonged inspiration → overstretch → increase further inspiration
- Opposite to Hering Bruer reflex

NEW BORN FIRST BREATH



J REFLEX:

- It is seen in juxta pulmonary capillary receptors
- It is activated by inflammation and oedema
- It contributes to rapid shallow breathing
- It causes weakness of skeletal muscles.

J reflex

- Pulmonary edema : c/o Breathlessness

- Pulmonary edema

↓
Fluid comes out pulmonary capillaries

↓
Activates J-receptors

↓
J reflex

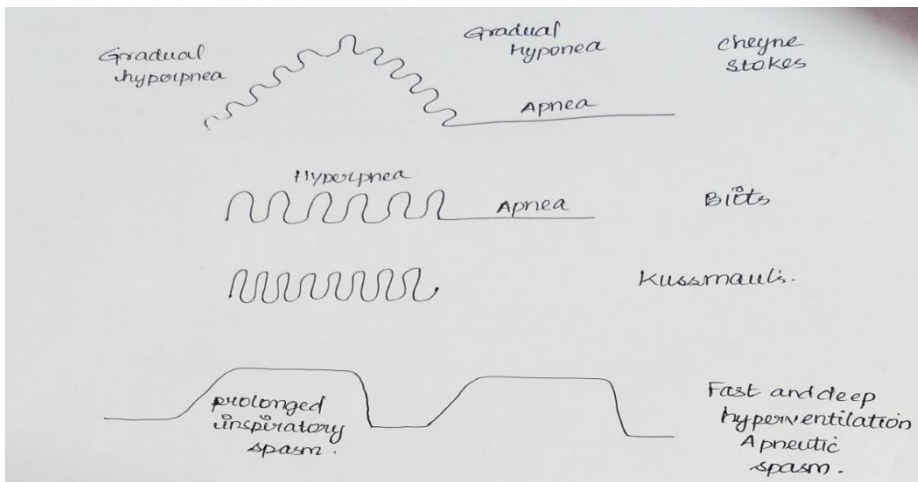
↓
Apnea

↓
Breathlessness

↓
Hypotension

↓
Bradycardia

PERIODIC BREATHING



CHEYNE STOKES RESPIRATION

- Gradual hyperpnea → mode of hyperventilation → -absence of respiratory centre
stimulus → gradual hypopnea → apnoea → stimulation of respiratory centre →
next cycle of respiration
- Seen in normal, congestive heart failure, uraemia.

BIOTS / ATAXIA BREATHING

- Hyperpnea → leads to apnoea
- Seen in: damage to medulla and meningitis

ACIDOTIC BREATHING / KUSSMAUL BREATHING

- Respiration is fast and deep
- Stimulated by acid
- Seen in diabetes

LESION AT MID PONS WITH CUT VAGUS NERVE

- Prolonged inspiration spasm

CHECMIAL CONTROL OF RESPIRATION

Overview:

- The hydrogen ion concentration and the respiratory gas composition of the arterial blood influence respiration.
- There are 2 sets of receptors that detect the chemical changes in the blood

Peripheral receptors:

- They are mainly located in the carotid and aortic bodies
- They response to changes in the PO₂, PCO₂ and Ph in arterial blood
- They are more sensitive to hypoxia
- They send signals to the dorsal respiratory group in the medulla to increase ventilation.

1)Carotid bodies:

- ☐ They are very small chemo sensitive receptors that are located at the bifurcation of the common carotid arteries
- ☐ There are 2 special features of carotid bodies
 - o Blood flow is 2L per 100g of tissue
 - o Higher metabolic rate
- ☐ They detect very minor changes in the blood PO₂, PCO₂ and pH due to the high blood flow
- ☐ They consist of type 1 and type 2 cells
- ☐ Type 1 cells are the chemo sensitive cells called the glomus cells. They release catecholamines, mainly dopamine that is released in hypoxia
- ☐ Type 2 cells are called sustentacular cells that act as glial cells for support

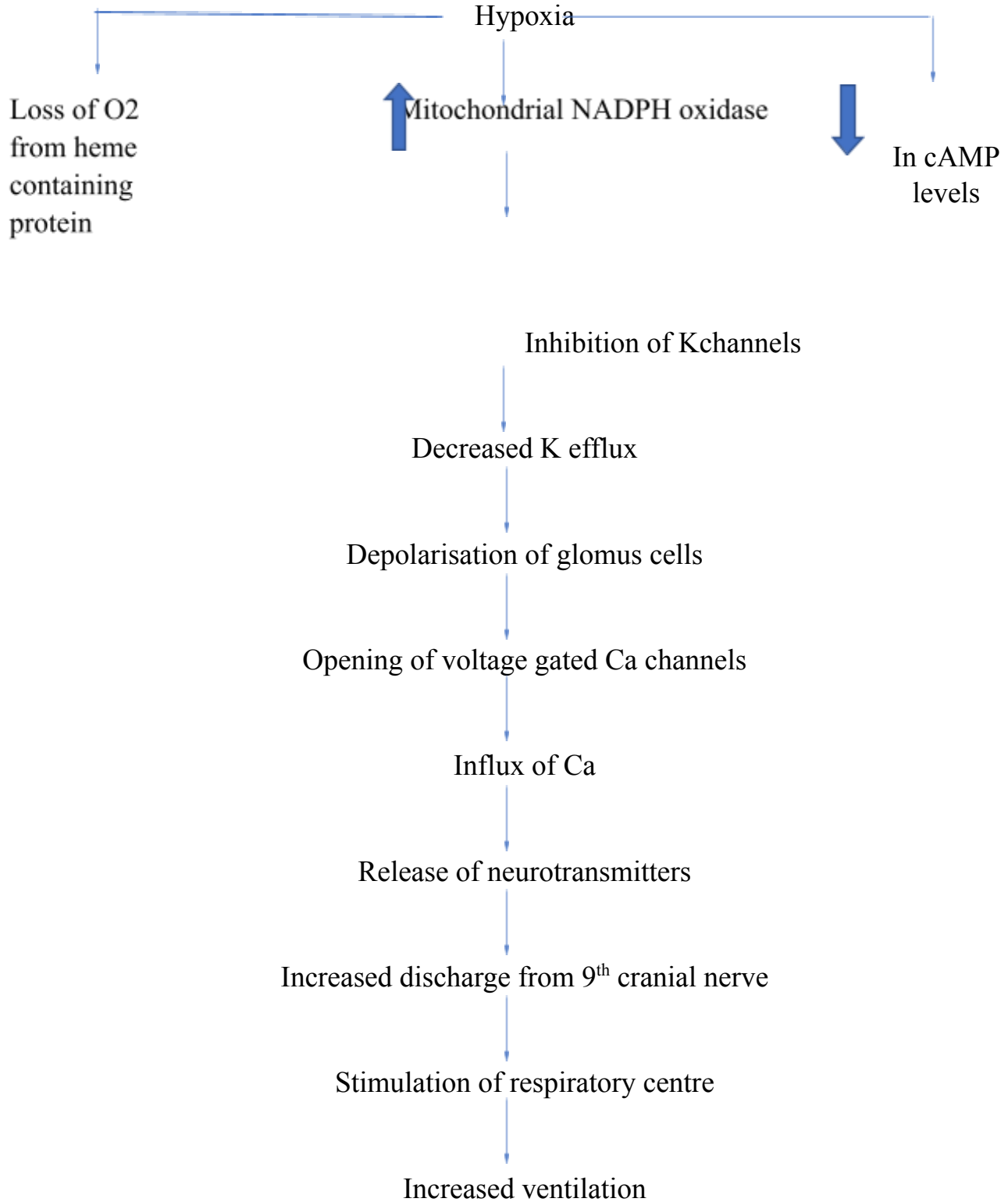
2)Aortic bodies:

- ☐ They are located along the ascending aorta and arch of aorta
- ☐ They are innervated by vagal efferent and contain glomus cells
- ☐ They are relatively less sensitive when compared to carotid bodies.

Sensitivity of chemoreceptors:

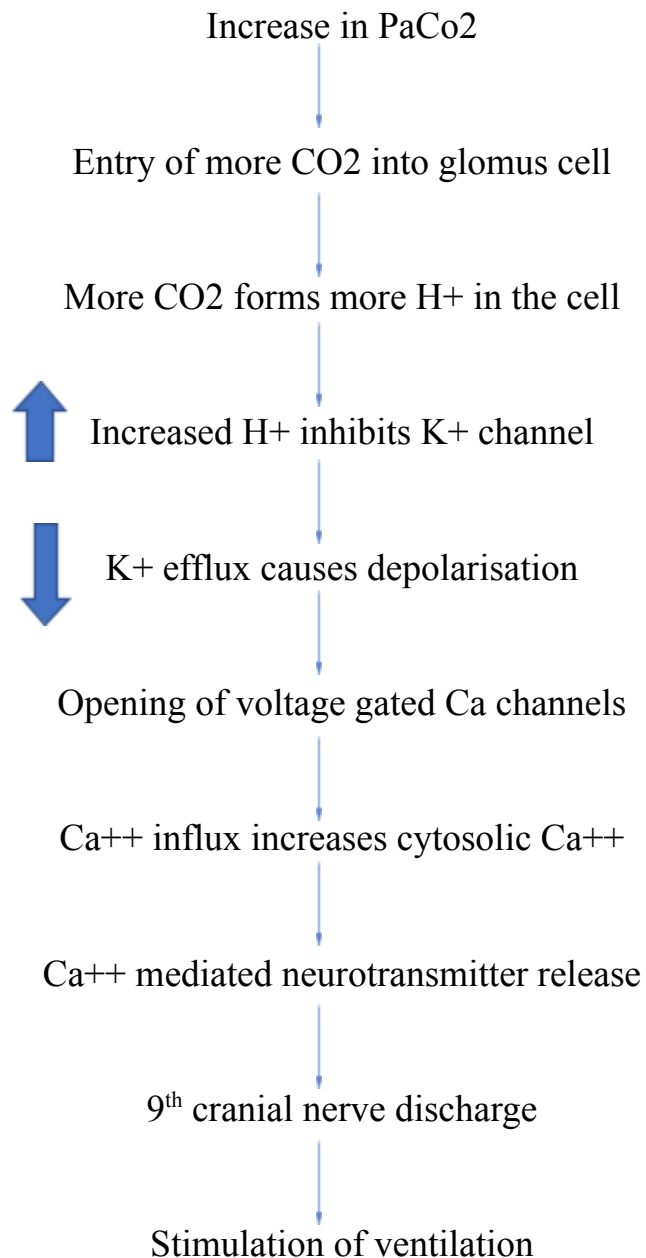
- Chemoreceptors respond more to hypoxia, hypercapnia and acidosis
- The sensor is the glomus cell, which responds to all 3 chemical changes.
- They final pathway is the inhibition of K⁺ channels that results in depolarisation induced opening of voltage gated Ca²⁺ channels

1) Mechanism of stimulation by hypoxia:



- Hypoxia is the major stimulus for activation of peripheral chemoreceptors
- The response is most effective at $PO_2 < 60\text{ mm Hg}$
- Unless hypoxia is strong enough to overcome the inhibitory effect of decreased H^+ and PCO_2 in arterial blood, there is no prominent effect.
- The response of peripheral chemoreceptors depends on the PaO_2 of the blood and not on the O_2 content.

1) Mechanism of stimulation of hypercapnia:

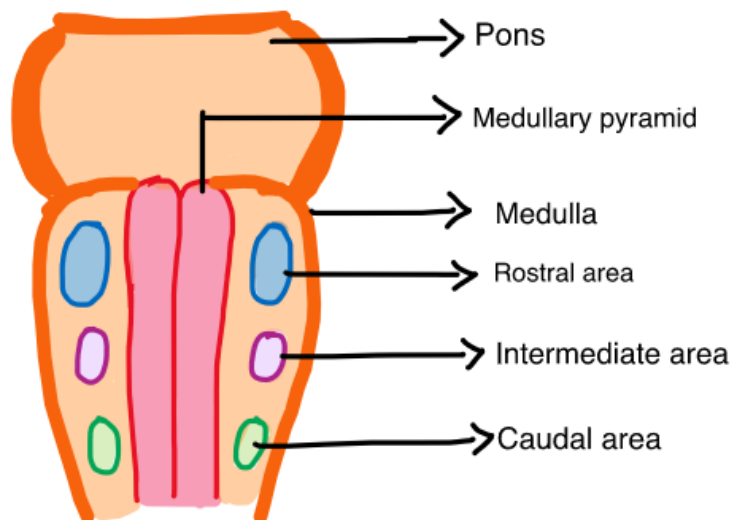


- The actual stimulus is the formation of H_2CO_3 in the glomus cells that causes closure of K^+ channels
- Hypercapnia affects ventilation mainly by central chemoreceptors
- Hyperventilation removes CO_2 from the blood and decreases alveolar PCO_2
- High hypercapnia can lead to CO_2 narcosis that leads to coma

2) Mechanism of stimulation by acidosis:

Acidosis stimulates the peripheral chemoreceptors and increases the sensitivity of the receptors to PaCO_2 .

Central chemoreceptors:



- Central chemoreceptors are bilaterally located as cell groups just below the surface of the venterolateral medulla caudal to the pontomedullary junction
- On each side, the receptors are divided into rostral, caudal and intermediate group
- They respond to the change in H^+ of the surrounding interstitial fluid

Mechanism of stimulation:

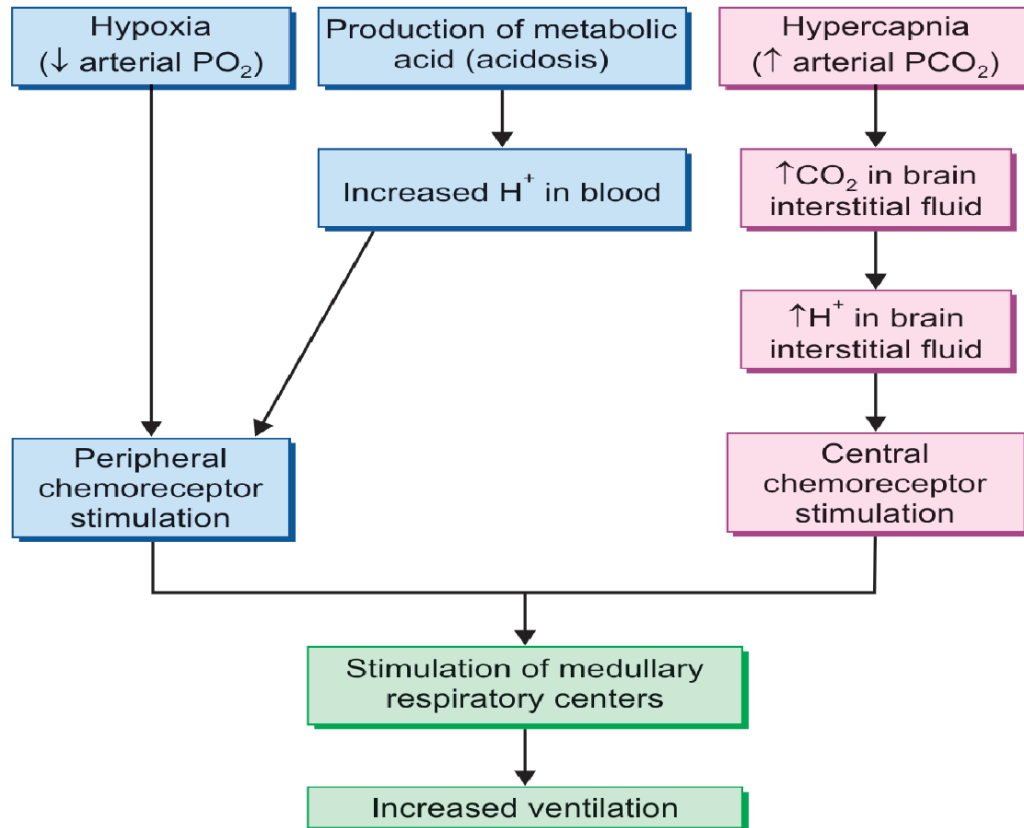
- Bicarbonate ions are the main buffer in CSF
- Molecular CO₂ diffuses readily into the CSF, therefore blood PCO₂ influences the pH of CSF.
- The ventilatory response to hypercapnia is more in the presence of hypoxia
- Increase in pH (respiratory alkalosis) allows hypoxic stimulation to be less effective
- The interaction of hypercapnia, hypoxia and acidosis is best studied in metabolic and respiratory acidosis.

Response in metabolic acidosis:

- Metabolic acidosis is due to the accumulation of non-volatile acids like lactic acid, ketone bodies etc.
- In the initial phase, hyperventilation is produced by the increase in H⁺, so there is excessive wash off CO₂ from the bloodstream leading to compensatory respiratory alkalosis
- Profound hyperventilation occurs in metabolic acidosis, eg: Kussmaul breathing

Response in respiratory acidosis:

- Respiratory acidosis occurs due to accumulation of carbon dioxide
- It mainly occurs in COPD like emphysema, asthma or due to failure of respiratory apparatus or failure of respiratory centres
- In the acute phase, there is an acute increase in minute ventilation proportional to the rise of PaCO₂
- If hypercapnia continues for a few days, acute severe hyperventilation subsides due to compensatory increase in bicarbonate that shifts the response curve to the right (central adaptation).
- Therefore, in chronic lung diseases, inspite of persistent hypercapnia, the central chemoreceptor drive for ventilation is less. In such patients, the hypoxic stimulus for ventilation will be lost which will result in severe hypercapnia and acidosis. The mainstay of management in such patients is adequate support for ventilation.



HYPOXIA

The term hypoxia is used to denote deficiency of oxygen supply at the tissue level.

Causes

Hypoxia can occur because of any one or more of the following defects:

- Decreased oxygen tension (pO_2) of the arterial blood,
- Decreased oxygen carrying capacity of the blood,
- Decreased rate of blood flow to the tissue or
- Decreased utilization of oxygen by the tissue cells.

Types

Depending upon the mechanism of occurrence, there are four types of hypoxia:

- Hypoxic hypoxia,
- Anaemic hypoxia,
- Stagnant hypoxia and
- Histotoxic hypoxia

HYPOXIC HYPOXIA

It occurs due to decrease in O_2 tension (decreased arterial pO_2). In this type of hypoxia, PO_2 decreases in the blood. O_2 saturation of Hb is reduced. However, the Hb content and O_2 -carrying capacity of blood is normal.

Causes:

- **Low PO_2 in inspired air:** It occurs at high altitude and in ill-ventilated rooms.
- **Hypoventilation:** It occurs in obstructive diseases such as asthma, respiratory muscle paralysis, damage to respiratory centers, and pneumothorax.
- **Decreased diffusion:** It occurs in conditions such as pulmonary edema, emphysema, and fibrosis of lungs.

ANEMIC HYPOXIA:

It occurs when there is a decrease in the O_2 -carrying capacity of blood.

Causes:

- Severe anemia as seen in bone marrow depression
- Formation of carboxy hemoglobin due to carbon monoxide poisoning
- Altered hemoglobin like methemoglobin in which iron is present in ferric form

STAGNANT HYPOXIA:

It occurs due to sluggish flow of blood through the tissues. The oxygen content of the blood is normal and hemoglobin is present in adequate amounts.

Causes:

- Circulatory shock due to haemorrhage causing decrease in tissue blood flow
- Cardiac failure causing decreased venous return and decreased cardiac output
- Localized vascular obstruction caused due to atherosclerosis and thrombosis

HISTOTOXIC HYPOXIA:

The tissues are unable to use oxygen in spite of normal PO_2 in the blood. It occurs due to destruction of cellular enzymes by poisonous substances causing damage of the cytochrome-oxidase enzyme system.

Causes:

- Cyanide poisoning
- Sulphide poisoning

Symptoms of Hypoxia:

- i. Impaired judgment,
- ii. Drowsiness and excitement,
- iii. Disorientation,
- iv. Loss of time sense, headache.

Other symptoms include anorexia, nausea, vomiting, and tachycardia

Hypoxia affects the brain. A sudden drop in PO_2 to 20 mm Hg causes unconsciousness in 10–15 seconds and death in about 4–5 minutes.

Types of hypoxia and their characteristic features:

	Hypoxic hypoxia	Anemic hypoxia	Stagnant hypoxia	Histotoxic hypoxia
PO_2 in blood	Decreases	Normal	Normal	Normal
O_2 carrying capacity	Normal	Decreases	Normal	Normal
O_2 content of blood	Decreases	Decreases	Normal	Normal
Blood flow rate	Normal	Normal	Decrease	Normal
Tissue utilization of O_2	Normal	Normal	Normal	Decreases
O_2 therapy	Very useful	Moderate	Less useful	Not useful
Av difference of O_2	Normal	Normal	Increased	Decreases
Cyanosis	Present	No	Present	No

Effects of hypoxia on body systems:

Normally, the effects are not severe when the ascent is slow with camping at different heights.

However, the effects of hypoxia on a subject vary depending on the severity of hypoxia. Sudden exposure to a low pressure occurs when an aircraft loses cabin pressure. Slow and prolonged exposure as is seen in mountaineers taking several days to climb a mountain, and life-long exposure is seen in permanent residents at high altitudes.

1. Severe hypoxia (altitude more than 20,000 feet)

When a subject is suddenly exposed to severe hypoxia, the effects are mainly on the CNS, cerebral ischaemia and cerebral oedema develops. The subject becomes unconscious and feels as if he is knocked down within 10-15 sec. This is equivalent to sudden arrest of circulation, e.g.: -

- Sudden entry into the mines where there is methane. CO₂ and other gases in excess.
- Sudden cutting of O₂ supply to a pilot flying at a high altitude.
- Severe hypoxia may cause instant death due to cerebral ischaemia and cerebral oedema within 4-5 min.

2. Moderate hypoxia (gradual onset of hypoxia < 15,000 feet)

When the mountaineers ascending a high altitude are exposed slowly to a moderate hypoxia. The effects are seen on several systems.

a) Nervous system: Brain is highly susceptible to hypoxia. All types of hypoxia affect the brain function. The symptoms resemble alcoholic intoxication.

- The subject may be depressed and at times elated with a sense of well-being.
- There is a general loss of self-control and the subject becomes talkative.
- The subject may become quarrelsome, ill-tempered, and rude.
- Loss of co-ordination and easy fatiguability present.
- Power of judgement is impaired. Loss of memory and euphoria are seen.

b) Respiratory system: All types of hypoxia stimulate respiratory centres through peripheral chemoreceptors. As a result, the rate and depth of respiration increases. This may cause alkalaemia due to loss of CO₂. Some people develop pulmonary oedema and dyspnoea due to pulmonary vasoconstriction. Periodic breathing may develop in some people.

c) CVS: Initially the subject develops tachycardia and an increase in the myocardial contractility. Cardiac output and BP increase. There will be an increase in the cerebral and coronary blood flow and a decrease in cutaneous and splanchnic blood flow. After some time, there is reduction in cardiac output and BP, but tachycardia persists.

d) Digestive system: The subject develops loss of appetite (anorexia), nausea, vomiting and diarrhoea.

e) Kidney: Erythropoietin production increases due to hypoxia. It starts producing alkaline urine.

f) Blood: RBC, WBC and platelet count increases. This is due to: (i) Shift of storage pool to circulating pool, (ii) Slight increase in the production. O₂ saturation of blood declines proportional to the hypoxia.

TREATMENT OF HYPOXIA:

In mild hypoxia, O₂ therapy is not indicated. Only in severe hypoxia with dyspnoea, 100% O₂ therapy is indicated. This increases O₂ in dissolved state from 0.3 mL to 2.0 mL per 100 mL of blood.

Pure oxygen can be administered by using: -

1. An oxygen tent 2. A mask 3. An intranasal tube.

Oxygen therapy is highly useful in only some types of hypoxia and not all hypoxia

O₂ Therapy in Hypoxic Hypoxia: -

Oxygen therapy is highly beneficial in hypoxic hypoxia caused by low Po₂ in the atmosphere, hypoventilation, and impaired diffusion in the lung. It increases alveolar Po₂ by several times and increases arterial O₂ content both in dissolved and combined states. However, it is harmful to subjects with depressed respiratory centres due to a rise in Pco₂ to higher levels. Pure O₂ is not beneficial due to A-V shunts.

O₂ Therapy in Anaemic Hypoxia: -

Oxygen therapy in this case is moderately beneficial 100% O₂ therapy increases O₂ content in a dissolved form from 0.3 mL to 2.0 mL per 100 mL of blood and thus helps in providing extra supply of O₂ to tissue. Although this is small, yet this small amount of extra O₂ may be the difference between life and death. In CO poisoning when 100% or hyperbaric O₂ is given, it facilitates not only dissociation of CO₂ from Hb but also increases the transport of O₂ in dissolved state. blood transfusion will be more beneficial to these patients.

O₂ Therapy in Stagnant Hypoxia: -

O₂ therapy is less useful in this hypoxia. When the therapy is given, it increases the transport of O₂ in a dissolved state. This little extra O₂ in the dissolved state sometimes is useful.

O₂ Therapy in Histotoxic Hypoxia: -

Tissues are unable to utilize O_2 Hence O_2 therapy may not be beneficial. However, if the metabolic poisoning is not severe, hyperbaric O_2 therapy may benefit the individual

Hyperbaric O_2 Therapy in Clinical Practice: -

At one atmosphere of PO_2 about 2.0 mL of O_2 is present in 100 mL of blood in dissolved state. This is proportional to the increase in O_2 pressure. At two atmospheres, dissolved O_2 in blood doubles (4 mL/100 mL).

Hyperbaric O_2 therapy is useful in the following clinical conditions:

1. CO poisoning
2. Dysbarism
3. Gas gangrene
4. Anaemic crisis
5. Air embolism
6. Leprosy.

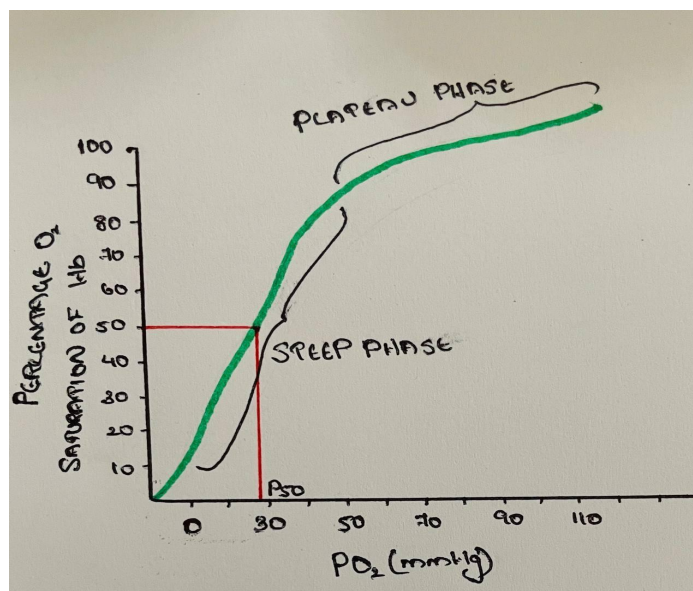
Gas gangrene is caused by Clostridium, an anaerobic organism which stops multiplying in the presence of O_2 and the same is the case in leprosy. However, the toxic effects of hyperbaric O_2 therapy are proportionate to the pressure at which it is administered

OXYGEN-HEMOGLOBIN DISSOCIATION CURVE

- It is the curve that demonstrate the relationship between partial pressure of oxygen and the percentage saturation of the haemoglobin with oxygen
- The sigmoid shape of the curve results from **haemoglobin affinity for oxygen** at various PO₂ levels
- Saturation of hemoglobin with oxygen depends upon the partial pressure of oxygen.
- When the partial pressure of oxygen is more, hemoglobin accepts oxygen and when the partial pressure of oxygen is less, hemoglobin releases oxygen.

● The curve is divided into two major phases: - **steep phase and plateau phase**

STEEP PHASE



- It is in between po₂ of **10mmHg and 60mmHg**.
- Oxygen saturation of Hb is about **90% at PO₂ 60 mm Hg**.

Significance of steep phase

- ☐ oxygen saturation of Hb is **very high**
- ☐ facilitates oxygen loading.
- ☐ causes **unloading of oxygen in the tissues**
- ☐ Large quantities of hemoglobin is released by shifting the curve to right by increased H⁺ or increased CO₂

PLATEAU PHASE

- It is in between **PO₂ around 60mmHg and flattens at PO₂ of 70mmHg**
- Above 60mmHg only small amount of increase in oxygen binding and then it remains **apparently constant**

Significance of plateau phase

There are two significances

1. Plateau in the curve **provides a safety factor** through which even a significant decrease in lung function can allow normal saturation of Hb.
2. Oxygen saturation and content remain constant in spite of wide fluctuations in alveolar PO₂

This is the reason why oxygen content cannot be raised to 100% by hyperventilation because Hb is already been saturated with oxygen at PO₂ of 100mmHg. **This only true for normal people at sea level.**

P50

P50 is the partial pressure of oxygen at which hemoglobin saturation with oxygen is 50%.

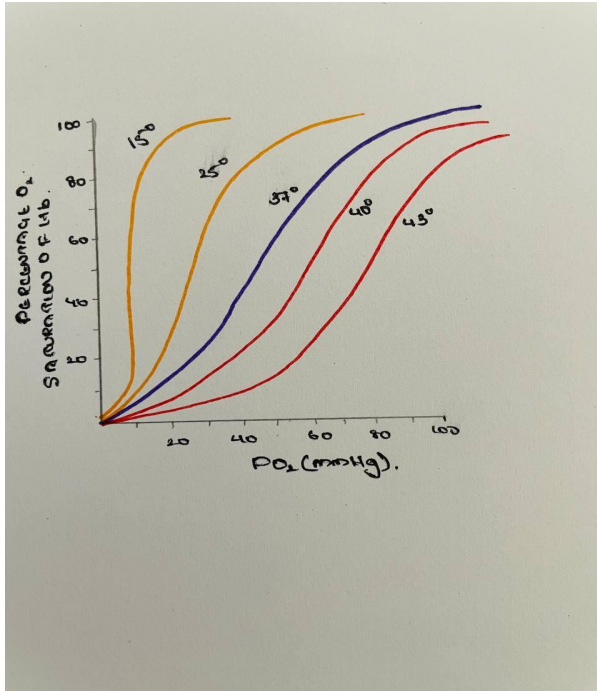
- It occurs at a PO₂ of **27mmHg**.
- It has great impact on steep phase
- **If P50 is high**, decrease in affinity of Hb for oxygen and right shift of curve occurs
- **If the P50 is low**, increase in affinity of Hb for oxygen and left shift of curve occurs.

Factors Affecting Hb-binding Affinity with Oxygen

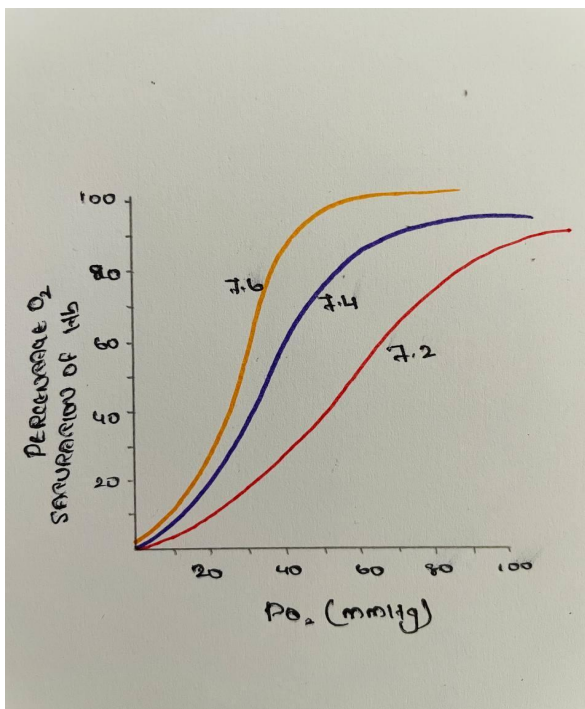
1. The important factors are **temperature, PCO₂, PH and 2,3-Diphosphoglycerate**.
2. Rise in PCO₂, fall in PH and rise in temperature all **shifts the curve to the right**. And vice versa.
3. Shift to right is physiologically **advantageous at tissue level**. As it facilitates unloading of oxygen

Temperature

- High temperature decreases the affinity of Hb for oxygen.
- This helps in release of oxygen in metabolically active tissue in which temperature is high.



pH:



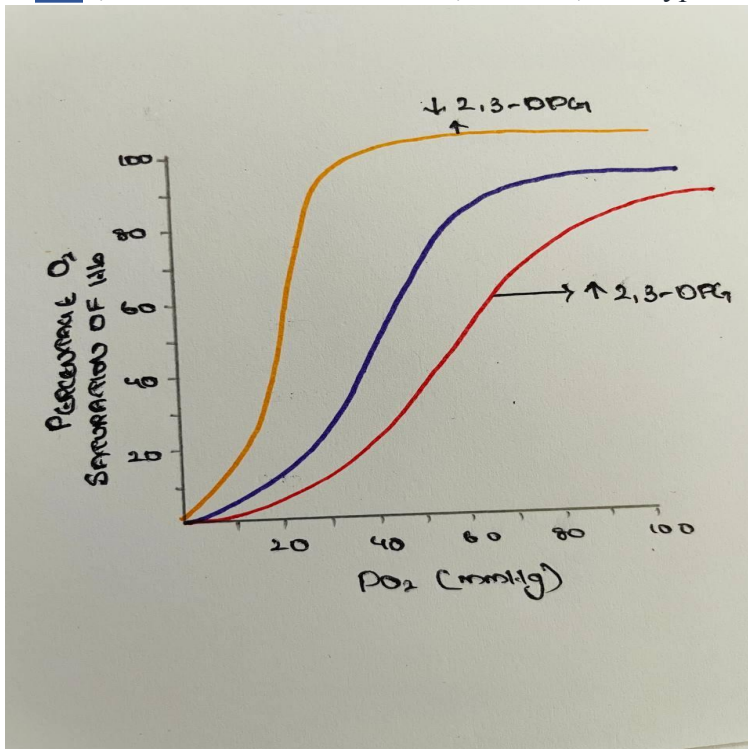
- Decrease in pH shifts the curve to right and vice versa
- When blood passes through capillaries, CO_2 enters red cell that decreases intracellular pH and shifts the Oxy-Hb dissociation curve to right.
- when blood passes through tissue capillaries, the acidic environment facilitates release of oxygen from Hb into the tissues

Carbon Dioxide

- During cellular metabolism, CO₂ is released into circulation that increases generation of H⁺ and decreases pH.
- This shifts the curve to the right.
- This helps in release of oxygen from Hb.

2,3-diphosphoglycerate [2,3-DPG]

- 0 It is a byproduct formed as a result of anaerobic respiration (glycolysis) in the red blood cells.
- 0 Thus, binding of 2,3 DPG with Hb shifts the Oxy-Hb dissociation curve to right and facilitates release of oxygen.
- 0 At tissue level, it helps on the unloading of oxygen from red blood cell.
- 0 2,3-DPG increases in anemia, exercise, and hypoxic condition.



Factors that shift Oxy-Hb Dissociation Curve

Factors that shift the curve to right

1. Increased temperature
 2. Increased PCO₂
 3. Increased 2,3-DPG
 4. Decreased PH
 5. Hypoxia
- Shift of curve to right increase P₅₀ which facilitates oxygen release.

Factors that shift the curve to the left:

1. Decrease temperature
2. Decrease PCO₂
3. Decreased 2,3-DPG
4. Increase PH
5. Fetal Hb
6. Carbon monoxide.

Shift of curve to left decrease P₅₀ which facilitates oxygen uptake.

BOHR EFFECT

Bohr effect is the effect by which presence of carbon dioxide decreases the affinity of hemoglobin for oxygen.

- In the tissues, due to continuous metabolic activities, the partial pressure of carbon dioxide is very high and the partial pressure of oxygen is low
- Due to this pressure gradient, carbon dioxide enters the blood and oxygen is released from the blood to the tissues.
- Presence of carbon dioxide decreases the affinity of hemoglobin for oxygen.
- It enhances further release of oxygen to the tissues and oxygen dissociation curve is shifted to right

Factors influencing Bohr effect

- All the factors, which shift the oxygen-dissociation curve to right (mentioned above) enhance the Bohr effect.

MECHANISM OF BREATHING

Breathing: -

The process of respiration, during which air is inhaled into the lungs through the mouth or nose due to muscle contraction and then exhaled due to muscle relaxation. It comprises of both inspiration and expiration with pressure changes during it.

Inspiration: -

Drawing in of oxygen rich air inside the lung by contraction of diaphragm & EICM to make intrapleural pressure more negative

Muscles of inspiration =>

Primarily diaphragm & External intercostal muscles are involved in the process of inspiration.

Other than the above-mentioned muscles scalenes, sternocleidomastoid and muscles of upper respiratory tract facilitate the inspiration.

1) Diaphragm:

This is the main muscle of inspiration. Contraction of the diaphragm expands the thoracic cavity in 2 ways

- ☐ Because of the contraction of diaphragm, the dome shape is flattened and the thoracic cavity expands in a rostro-caudal direction
- ☐ Contraction of the diaphragm also pushes the rib cage outwards that enlarges the thoracic cavity in the antero-posterior plane.

Clinical significance

- ☐ In cases of severe obesity, tight clothing around the thoracic and abdominal walls, there is decreased expansion of the thoracic cage
- ☐ Diaphragm is innervated by the phrenic nerve, so lesions can cause diaphragm palsy

2) External intercostals:

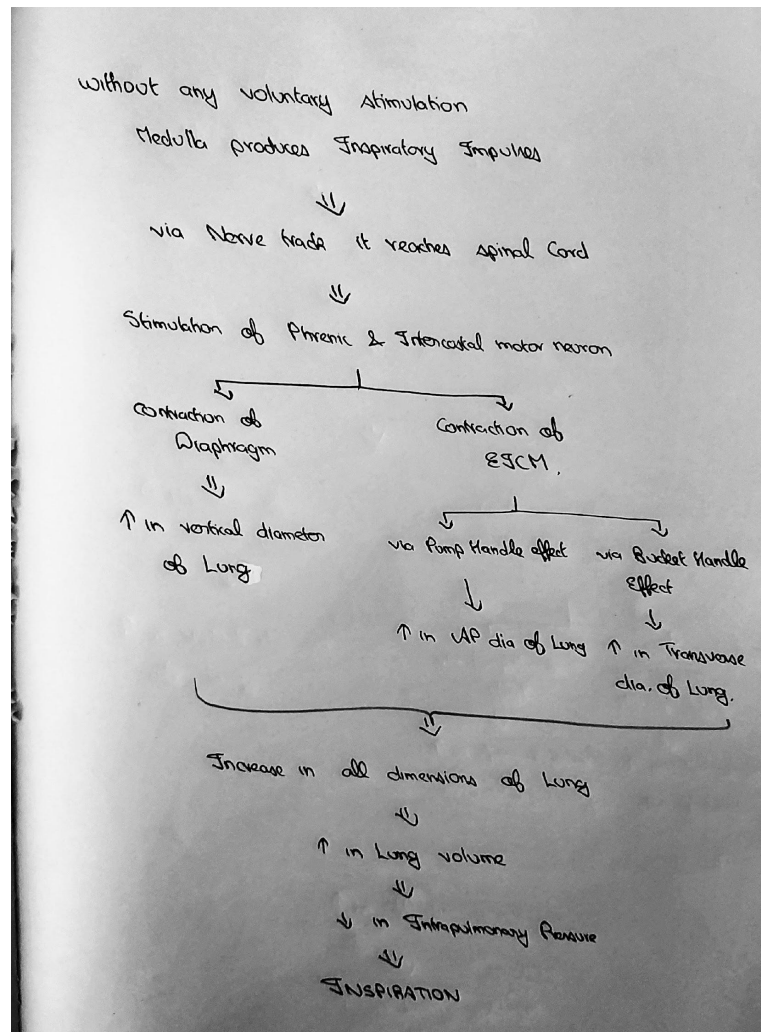
- ☐ Contraction of external intercostals increases the transverse and antero-posterior diameter.
- ☐ The 2nd to 10th ribs rotate upwards and outwards by a bucket handle movement
- ☐ The upper 4 ribs rotate the sternum in upward and outward direction by a pump handle effect.

3) Accessory muscles of inspiration:

- ☐ Scalenes: elevate the upper part of the rib cage
- ☐ Sternocleidomastoid: lift the sternum outwards and elevate the rib cage by pump handle effect.

- Neck and back muscles: they elevate the pectoral girdle and extend the back that increases the transverse and vertical area of the thorax

Mechanism of inspiration: -



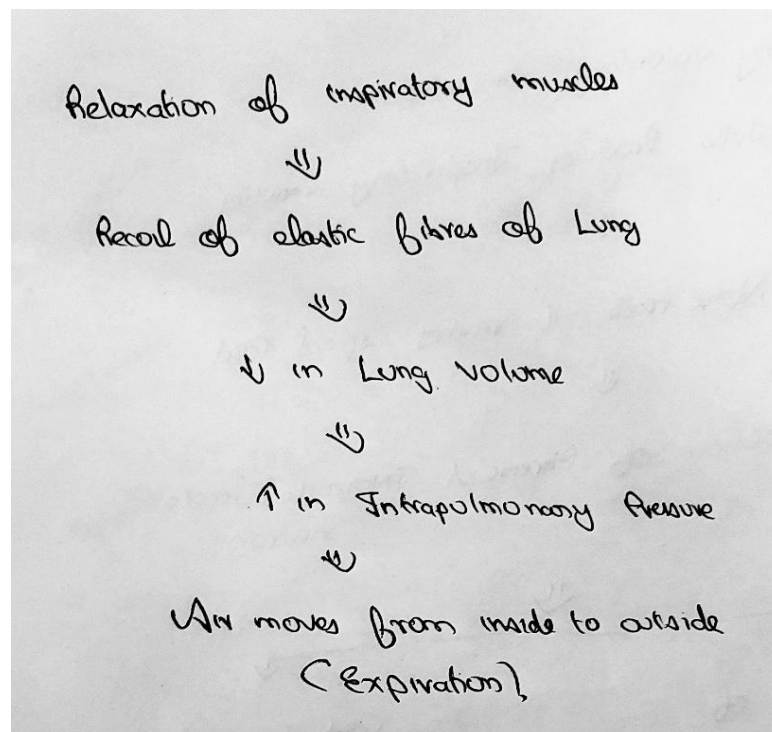
- From the above flowchart we can see that inspiration is an involuntary process.
- As the volume of lungs is increased it creates a negative intrapulmonary pressure due to which the air from external atmosphere into the lungs.
- The accessory muscles will assist in forced inspiration.

Expiration: - It is a simpler process when compared to inspiration as it is a passive process in which CO₂ rich air is released from the lungs

Muscles of expiration: -

- There is no primary muscle of expiration. It mainly involves the elastic recoil of the lungs. But in case of forced expiration, accessory muscles like abdominal muscle, intercostal muscles, neck and back muscles are involved.
- Abdominal muscles increase the intra- abdominal pressure and pushes the diaphragm upwards into the chest cavity. This decreases the rostro-caudal diameter of thorax.
- Internal intercostals pull the rib cage downwards and decrease thoracic volume both in anteroposterior and transverse diameter. These muscles are helpful in conditions that involve forced expiration like coughing, vomiting and strenuous defecation.

Mechanism of expiration: -



- From the above flowchart we can see that in normal expiration that no muscles are involved.
- But in forced expiration the accessory muscles will help to overcome the resistance to airflow unlike in forced inspiration where increase in lung volume is done by accessory muscles of inspiration
- Quiet expiration is purely passive but in case of patients suffering from lung disease airway resistance is high. Here they require participation of accessory expiratory muscles

Pressure changes during breathing :-

Alveolar pressure:

- The pressure within the pulmonary parenchyma is known as intrapulmonary pressure which mainly focuses on facilitating respiration
- Normal intrapulmonary pressure: - 0 mmHg
- During inspiration intrapulmonary Pressure decreases to -1 mmHg again during breathing expiration it increases to +1 mmHg
- Significance of intrapulmonary pressure: - During inspiration it decreases which Helps air to suck into the lungs and during expiration it increases which removes air from the lungs

Intrapleural pressure:

- Intrapleural pressure refers to the pressure within the pleural cavity. Normally, the pressure within the pleural cavity is slightly less than the atmospheric pressure, which is known as negative pressure
- Normal intrapleural pressure: -2.5 mmHg
- During inspiration it decreases to -6 mmHg and while expiration it increases to -4 mmHg
- The intrapleural pressure is negative because of the opposite direction of recoil in lungs and chest wall
- The chest wall recoils outwards and lungs recoil inward that causes this pressure to be negative.
- Pleural pressure is negative during quiet breathing and more negative during deep inspiration.
- The measurement of intrapleural pressure is by recording the intra-esophageal pressure as intrapleural pressure reflects the intra-esophageal pressure.
- In upright posture, intrapleural pressure is about -2.5 cm H₂O at the base of lung and -10 cm H₂O at the apex of the lung. This is because of the effect of gravity
- In supine posture, when the person lies straight, there is no gravitational force so there is no gradient generated.
- Significance of intrapleural pressure: -
 - It helps in preventing the collapse of lung
 - It helps to increase the venous return
 - Loss of normal intrapleural pressure results in lung collapse and barrel shaped chest.

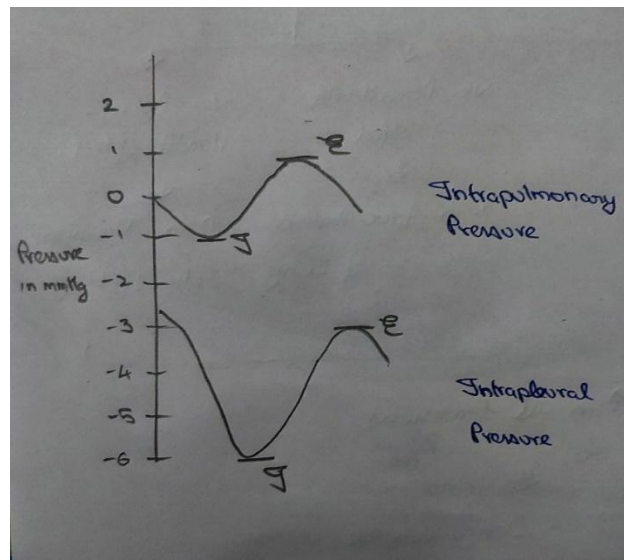
Transpulmonary pressure:

- It is the pressure difference across the lung wall.
- This is measured by subtracting the pleural pressure from alveolar pressure
- This is the pressure that keeps the lungs inflated and prevents the lungs from collapsing.

Trans-airway pressure:

- This is the pressure difference across the airway which is the difference between the pressure inside and outside the airway.
- This pressure is important in keeping the airways open during forced expiration.

Graph representing the pressure changes during respiration



SHORT NOTES

NON-RESPIRATORY FUNCTIONS OF LUNGS

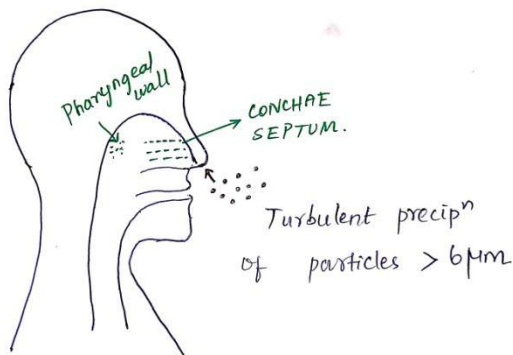
1) FILTRATION

- a) Particles $> 6 \mu\text{m}$
- b) Particles $1 - 5 \mu\text{m}$
- c) Particles $< 1 \mu\text{m}$

Particles $> 6 \mu\text{m}$: These particles are filtered by

- 1) Hair in nostrils
- 2) turbulent precipitation

TURBULENT PRECIPITATION:



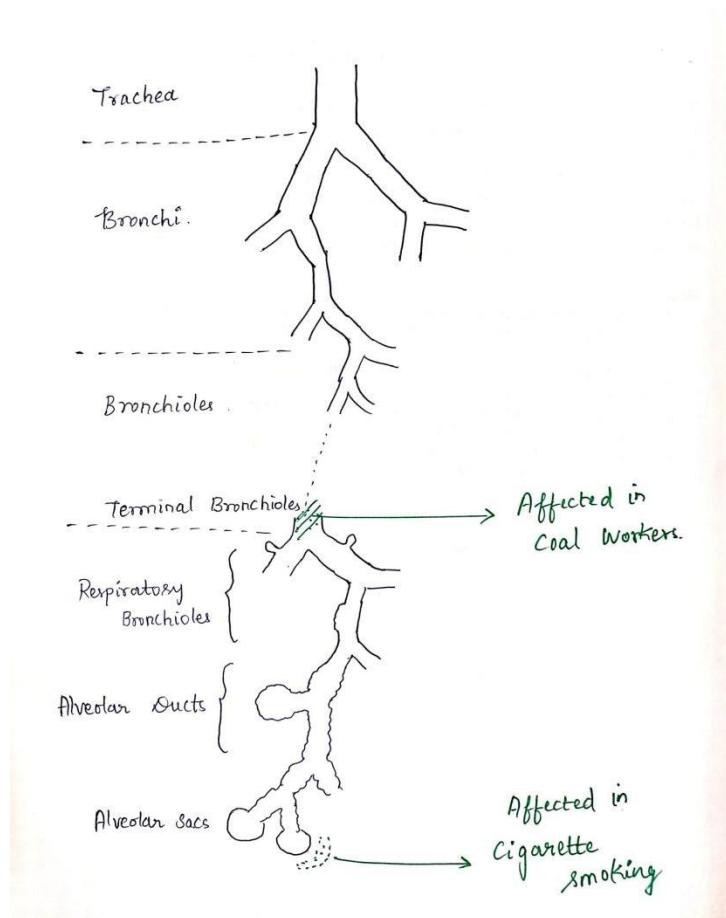
- Air passing through nasal passage hits many surfaces such as conchae, septum, pharyngeal wall
- Now air can change the direction but particles in air can't.
- So they are entrapped in the mucosa, then get expelled or transported to the pharynx by ciliary movement.

Particle size $1 - 5 \mu\text{m}$: These settle in the terminal bronchiole as a result of Gravitational precipitation.

- ☐ Clinical aspect: Coal particles are of the size 1 to 5 microns, that's why coal workers disease affects the Terminal bronchioles

Particle size $< 1 \mu\text{m}$: These particles can enter the alveoli, consequently they can diffuse into alveolar fluid or get expired

- ☐ Clinical aspect: Cigarette smoke contains particles of size 0.3 microns. Mostly these particles can enter alveolar fluid or get expired and don't get precipitated.



2) IMMUNE FUNCTION

Alveoli are lined by PAM (Pulmonary Alveolar Macrophages). These can phagocytose particles entrapped in alveoli

- A) if the particle is digestible, then its digested and taken into lung lymphatics
- B) if a particle is Not digestible then, a giant cell capsule is formed, slowly digested

Clinical aspect: TB bacillus, silica particles are non-digestible, thus granuloma are formed by PAM

3) METABOLIC FUNCTIONS OF PULMONARY ENDOTHELIUM

- A) ACE (Angiotensin Converting Enzyme): Present in pulmonary endothelium. Converts Angiotensin 1 to Angiotensin 2
- B) Metabolize serotonin inside pulmonary endothelium

C) Pulmonary endothelium secretes prostaglandins, NO, clotting factors, cytokines

4) **PHONATION AND ARTICULATION**

- Phonation is by Larynx (Vocal cords/ folds, muscles)
- Articulation is by structures of mouth, nose, PNS, Pharynx, chest

5) **ACID BASE BALANCE**: By eliminating CO₂ from the body

PULMONARY CIRCULATION AND ITS SPECIAL FEATURES

Pulmonary circulation consists of

A) Pulmonary arteries

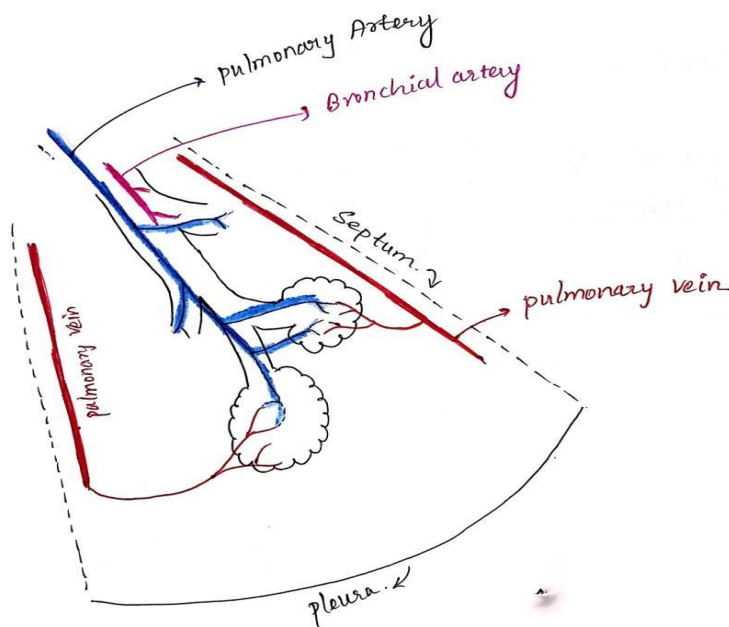
B) Pulmonary arterioles

C) Pulmonary capillaries

D) Pulmonary veins

PULMONARY CIRCULATION	SYSTEMIC CIRCULATION
1) less extensive so low peripheral resistance	More extensive, high peripheral resistance
2) RV can pump at low Pressure of 25 mm Hg owing to low resistance	LV (Left Ventricle) pumps at high pressure of 120 mm Hg
3) <u>Pulmonary arteries</u> Thin walled Highly distensible Large lumen	<u>Aorta</u> Thick walled Elastic comparatively narrow lumen
4) Pulmonary arteries have Rich sympathetic innervation but lack resting vasomotor tone	Aorta has Rich sympathetic innervation with high resting vasomotor tone

5) <u>Pulmonary arterioles</u> Responds to Hypoxia by Vasoconstriction	Systemic arterioles are the main reason for high peripheral resistance They respond to hypoxia by Vasodilation
6) <u>Pulmonary capillaries</u> Blood flow is pulsatile	Systemic capillaries Blood flow is continuous
7) In pulmonary capillaries, gas exchange takes place across alveocapillary membrane, no interstitial fluid is present	In systemic capillaries, exchange of O ₂ , nutrients takes place across the capillary endothelium between blood and interstitial fluid
8) Pulmonary veins Has a pressure of about 8 mm Hg Carry Oxygenated blood	Systemic veins Pressure of 5mm Hg Carry deoxygenated blood
9) Lymphatics Abundant	Relatively fewer lymphatics in systemic circulation



Intra pulmonary Blood Circulation

LUNG VOLUMES AND CAPACITIES

Pulmonary ventilation is studied by recording volume of movement of air in and out of lungs by spirometry

- To easily describe the events of pulmonary ventilation
- Air in the lungs is divided into

4 VOLUMES

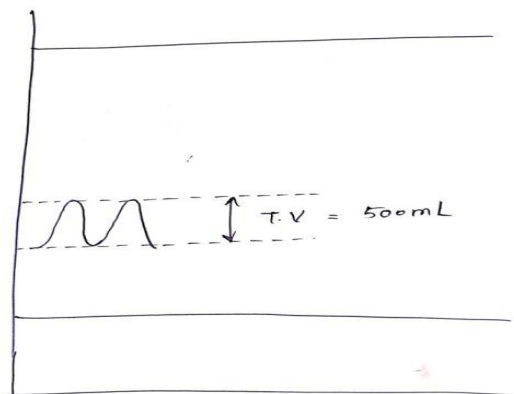
- A) Tidal volume (TV)
- B) Inspiratory Reserve Volume (IRV)
- C) Expiratory Reserve Volume (ERV)
- D) Residual volume (RV)

5 CAPACITIES

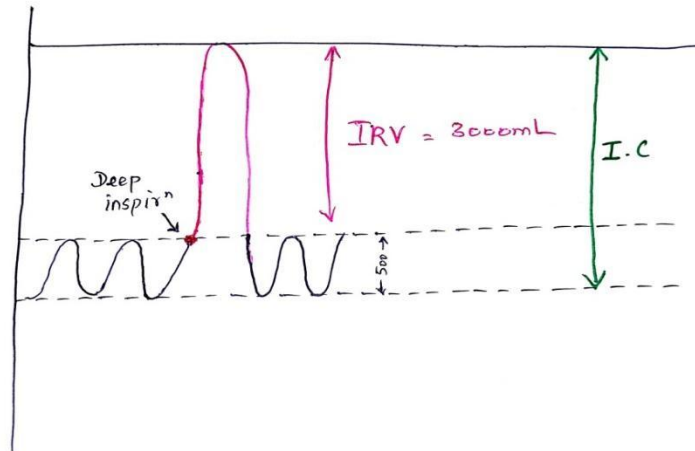
- A) Inspiratory Capacity (IC)
- B) Expiratory Capacity (EC)
- C) Functional Residual Capacity (FRC)
- D) Vital Capacity (VC)
- E) Total Lung Capacity

1) Tidal volume (TV)

Volume of air moving in and out of lungs with each breath, normal value: 500ml



2) IRV (inspiratory reserve volume)

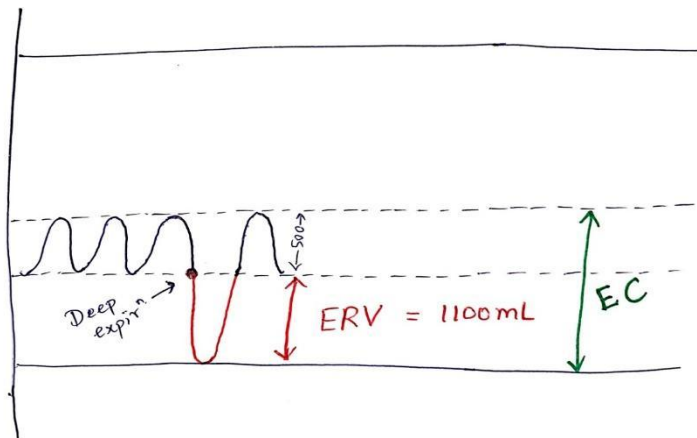


- Extra volume of air inspired in excess of inspiratory TV, normal value: 3000 ml
- For example, swimmer about to swim will inspire IRV

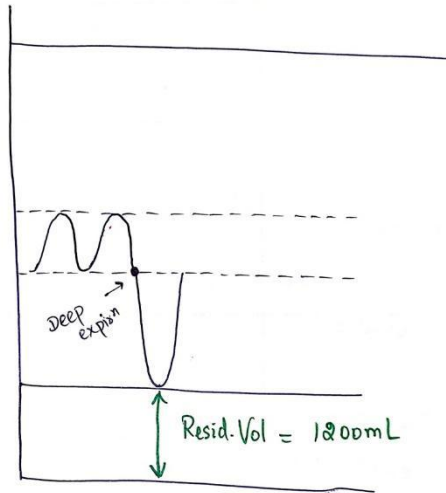
3) IC (inspiratory capacity):

- $IC = TV + IRV$
- Maximum volume of air that can be inspired from the resting expiratory level.

4) ERV (expiratory reserve volume): Extra volume of air expired forcefully in excess of Expiratory TV, normal value: 1100 ml.

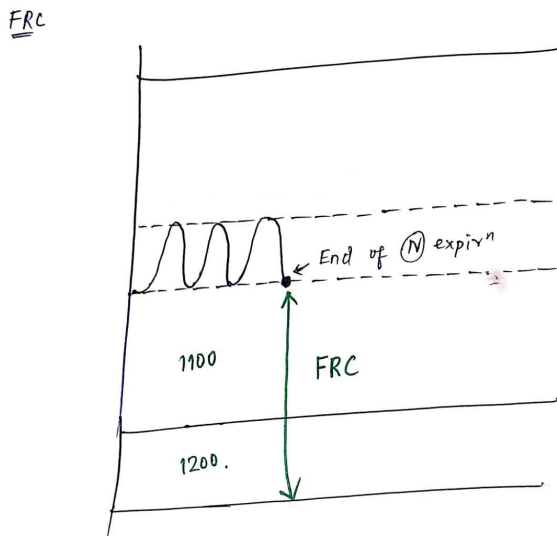


5)RV (residual volume): Volume of air remaining in lungs sheet most forceful expiration, normal value: 1100-1200 ml



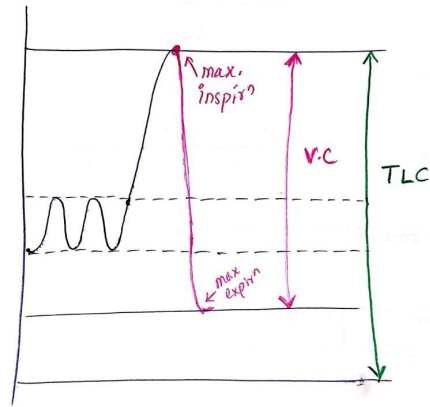
6)FRC (functional residual capacity):

- It is the volume of air that remains in the lung at the end of tidal expiration, normal value: 2200-2500 ml
- $FRC = ERV + RV$



7) VC (vital capacity):

- $VC = IRV + TV + ERV = IC + ERV$



- Volume of air that can be forcefully expired after maximum inspiration, normal value: 3000-4000 ml.

8) TLC (total lung capacity):

- Maximum volume of air present in lungs after maximal inspiration
- Normal value: 4200-6000 ml

Values to be memorized

Volumes and Capacities	Normal Values mL
Tidal volume	500
IRV	3000
ERV	1100
Residual Volume	1200
IC	3500
FRC	2300
Vital Capacity	4600
TLC	5800

VENTILATION-PERFUSION RATIO

DEFINITION: Ratio of Alveolar ventilation to blood flow in the lung

$$= \frac{\text{Alveolar Ventilation (V}_a\text{)}}{\text{Blood flow in the lung (Q)}}$$

Normal value = 0.8

Regional difference:

- APEX- increased ventilation
Decreased perfusion (blood flow)
Ratio is increased – 3.6
- BASE- increased perfusion
Decreased ventilation
Ratio is decreased- 0.6

There is twofold difference of ventilation and 5 fold difference in blood flow

PHYSIOLOGICAL IMPORTANCE – regional difference of the ratio

CLINICAL IMPORTANCE-

Altered ventilation perfusion ratio causes specific disease to specific part of the lung (eg. tuberculosis)

Wasted perfusion: shunt

Shunt is the admixture of oxygenated and unoxygenated blood

Shunt can be anatomical or physiological

ANATOMICAL SHUNT- atrial septal defect, ventricular septal defect

PHYSIOLOGICAL SHUNT- in bronchial circulation

PULMONARY SURFACTANT

- Pulmonary surfactant is a mixture of lipoprotein rich in phospholipid.
- Chief component- DIPALMITOYLPHOSPHATIDYLCHOLINE (DPPC)

COMPOSITION:

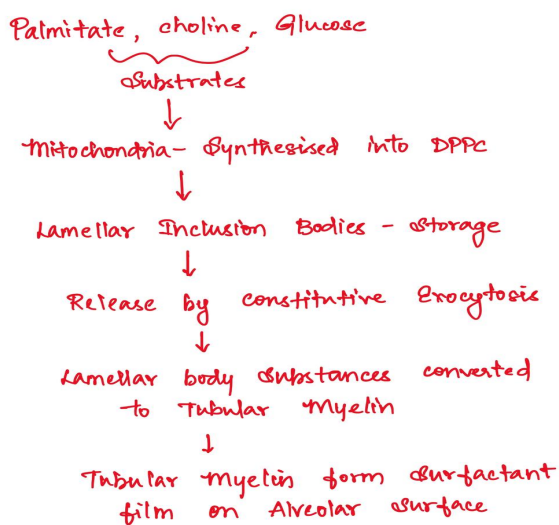
- LIPIDS- 90%
 - Dipalmitoyl phosphatidylcholine 62%
 - Phosphatidylglycerol 5%
 - Other phospholipids 10%
 - Neutral lipids 13%
- PROTEINS- 8%
 - Albumin
 - Immunoglobulin A
 - Apoproteins (SP- A, B, C, D)

SOURCE:

- Type 2 pneumocytes
- Contain more mitochondria, lamellar inclusion bodies

SYNTHESIS AND SECRETION:

Palmitate, choline, glucose are substrates



SYNTHESIS IN FETAL LIFE

Starts about 34 weeks and 90% at term

Premature newborn has low surfactant and it causes lung collapse

REGULATION OF SURFACTANT SYNTHESIS

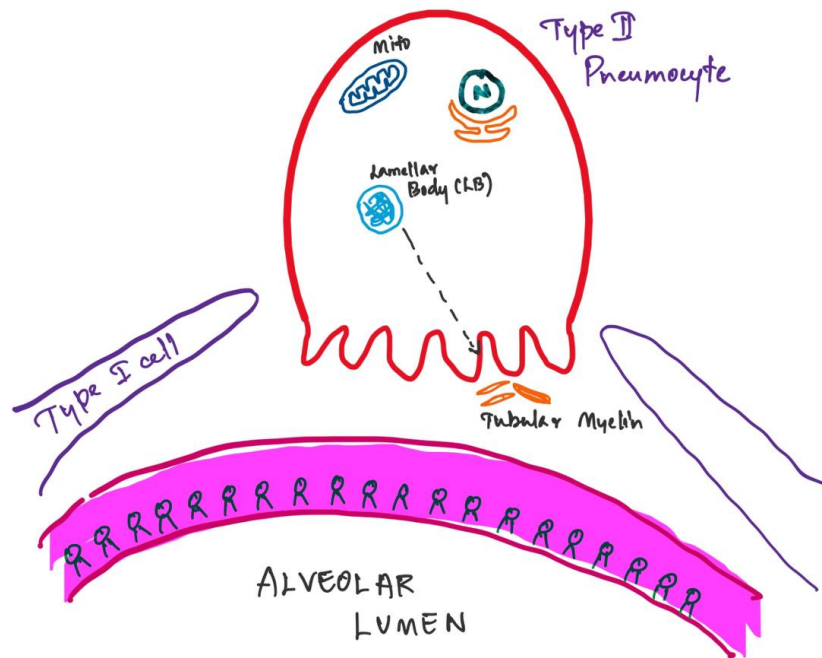
- Hormonal: Glucocorticoids, thyroxine, insulin (all promote synthesis)
- Quantity and quality of proteins: surfactant proteins A, B, C, D
SP A controls reuptake of surfactant by type 2 cells
- Stretching of lungs: yawning and sighing, slow pranayama
- Pharmacological agents: beta agonists, calcium
- Exercise

FUNCTIONS:

- Prevent lung collapse by decreasing the surface tension
- Promotes alveolar stability
- Prevent edema in the lung
- Decreases the work of breathing
- Immunoglobulin A and apoproteins provide innate immunity by acting as opsonin.

CLINICAL IMPORTANCE:

- Infant respiratory distress syndrome
- Atelectasis following surgery



IRDS:

- Lack of surfactant synthesis
- Preterm Infants
- Diab. in Preg.
- d/t High Surface Tension
 - ↓ Pulm. Edema
 - ↓ Atelectasis
- Rx: Phospholipid by Inhalation
- Inhalation - synthetic surfactant
- Glucocorticoid Therapy

FOLLOWING SURGERY:

- Patient Recovering Anesthesia to Take Deep Breathing
- This is done to enhance proper spreading of surfactant

ALVEOLAR CAPILLARY MEMBRANE

- Also called respiratory membrane
- Form Blood gas interface

COMPOSITION:

Alveolar epithelium, interstitial fluid layer, capillary endothelium

LAYERS: 10

- Surfactant
- Alveolar epithelial cell
- Basement membrane of alveolar epithelium
- Interstitium
- Basement membrane of capillary endothelium
- Capillary endothelial cells
- Plasma
- RBC membrane
- Intraerythrocyte fluid
- Hemoglobin

Thickness: – 0.2 to 0.5 μ

FACTORS:

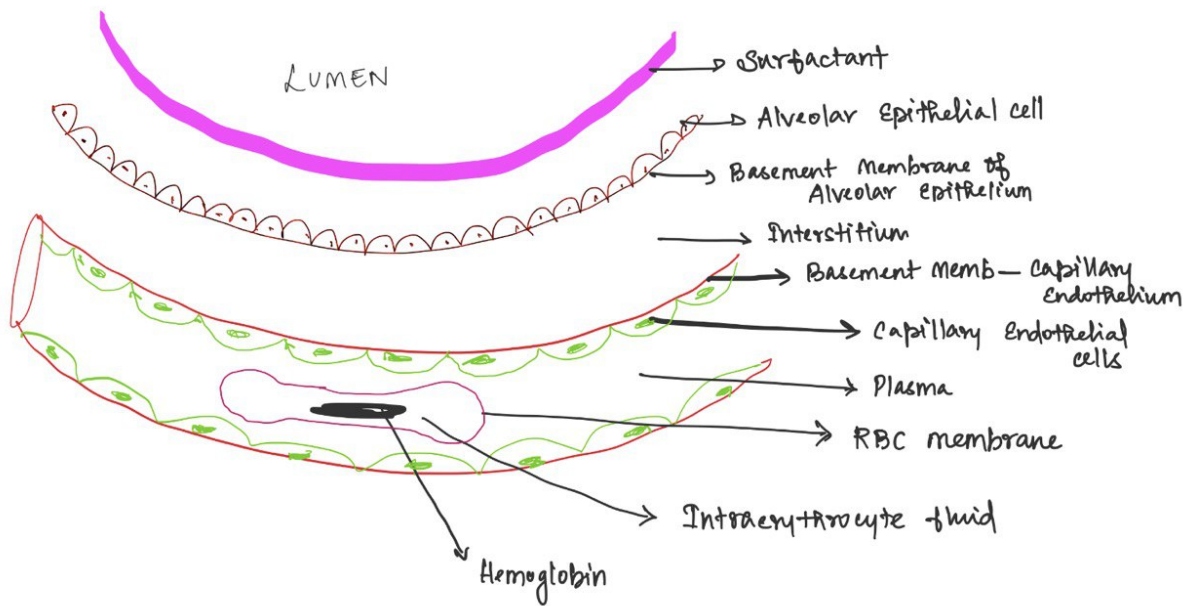
- Difference in partial pressure of gases on both sides
- Diffusing capacity of membrane for the gases
- Surface area of membrane
- Solubility of gas
- Thickness of membrane
- Molecular weight of the gas

CLINICAL SIGNIFICANCE:

ALVEOLAR CAPILLARY OBSTRUCTION SYNDROME

- Due to increased thickness of membrane
- Increased distance between alveolar and capillary membrane (edema due to heart failure)

In hypoxemia only oxygen diffusion is affected (pO_2 decreased) and no changes in pCO_2 because CO_2 solubility is 20 times more than O_2



Transport of O₂ & CO₂ & add a note on Hamburger phenomenon and Haldane phenomenon

Transport of O₂:

- ☐ Transport in 2 forms: dissolved form & combined form as **HbO₂**
- ☐ Each **gram** (Hb) can carry **1.34 ml of O₂**
- ☐ 100 ml blood **delivers about 5ml of O₂ to tissue**
- ☐ **5 litres** of blood flows to organ & tissue in one minute, so total O₂ delivered to tissue in **1min** is **250 ml**

	Dissolved form	Combined form	Total
Arterial	0.30ml/100 ml	18.7ml/100 ml	19ml
Venous	0.12	13.88	14.0ml
Difference (A-V)	0.18	4.82	5.0ml

Delivery of O₂ to tissue:

- ☐ Arterial blood --- ☐ interstitial tissue --- ☐ Intracellular
- ☐ Due to **pressure gradient**, O₂ diffuse from **arterial blood** to **tissue**
- ☐ In tissue, delivery of O₂ affected by:  PO₂,  PCO₂,  Temperature,  H⁺ ions 
2,3 -DPG

Transport of CO₂:

- ☐ Each 100 ml of blood picks up of 4ml of CO₂
- ☐ CO₂ is transported in arterial & venous blood in various form:
 - A) dissolved form – 10%
 - B) Carbamino compounds – 20%
 - C) Bicarbonate – 70%
- ☐ The total CO₂ content of either arterial or venous blood gives an idea about **HCO₃⁻ content**
- ☐ **HCO₃⁻** Content is referred to alkali reserve

- ☐ **100 ml** of blood transports 4ml of CO₂ from tissue to lung
- ☐ **5 litres** carry **200ml/min** to lungs

	Arterial blood	Venous blood	Difference
Dissolved form	2.6ml	3.0ml	0.4ml
Carbamino compounds	2.6ml	3.4ml	0.8ml
HCO₃	42.8ml	45.6ml	2.8ml
Total	48.0ml	52.0ml	4.0ml

Delivery of CO₂ to lung:

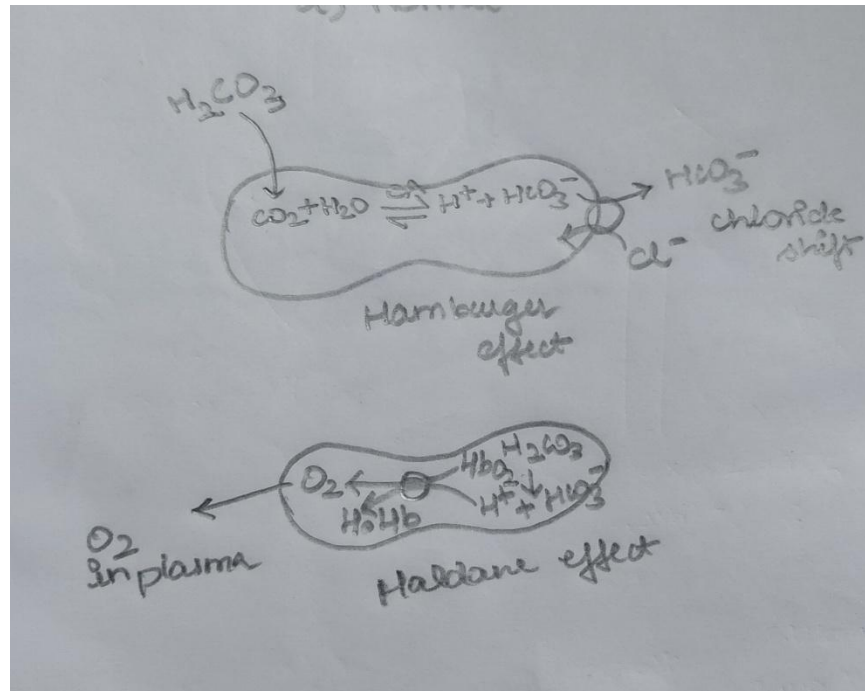
- ☐ Venous blood delivers **CO₂** to **lung** -- ☐ expired air
- ☐ Two influence factors: (Dissociation of CO₂)
 - o Pressure gradient (PCO₂)
 - o PO₂ (Haldane effect)
 - o Temperature

Hamburger effect / chloride shift:

- ☐ **H₂CO₃** ready diffuse into H⁺ & HCO₃⁻
- ☐ At that time, HCO₃⁻ Increase in **RBC**
- ☐ **HCO₃⁻** diffuse out of the cell & simultaneously **Cl⁻** goes into the cell from **plasma** (Neutrality maintain)
- ☐ **Also known as:** chloride shift, anion exchanged 1, chloride – bicarbonate exchanger

Haldane effect:

- ☐ **Blood** passes through pulmonary capillary, **O₂** diffuse into blood to form **HbO₂**
- ☐ **Oxygenation** of Hb leads to **dissociation** of CO₂ curve to right
- ☐ **Loading** of O₂ leads to **unloading of CO₂**
- ☐ **Deoxygenated** Hb binds to H⁺ Vigorously than that of oxygenated Hb, **binding** of O₂ with **Hb**, **decrease** CO₂ affinity



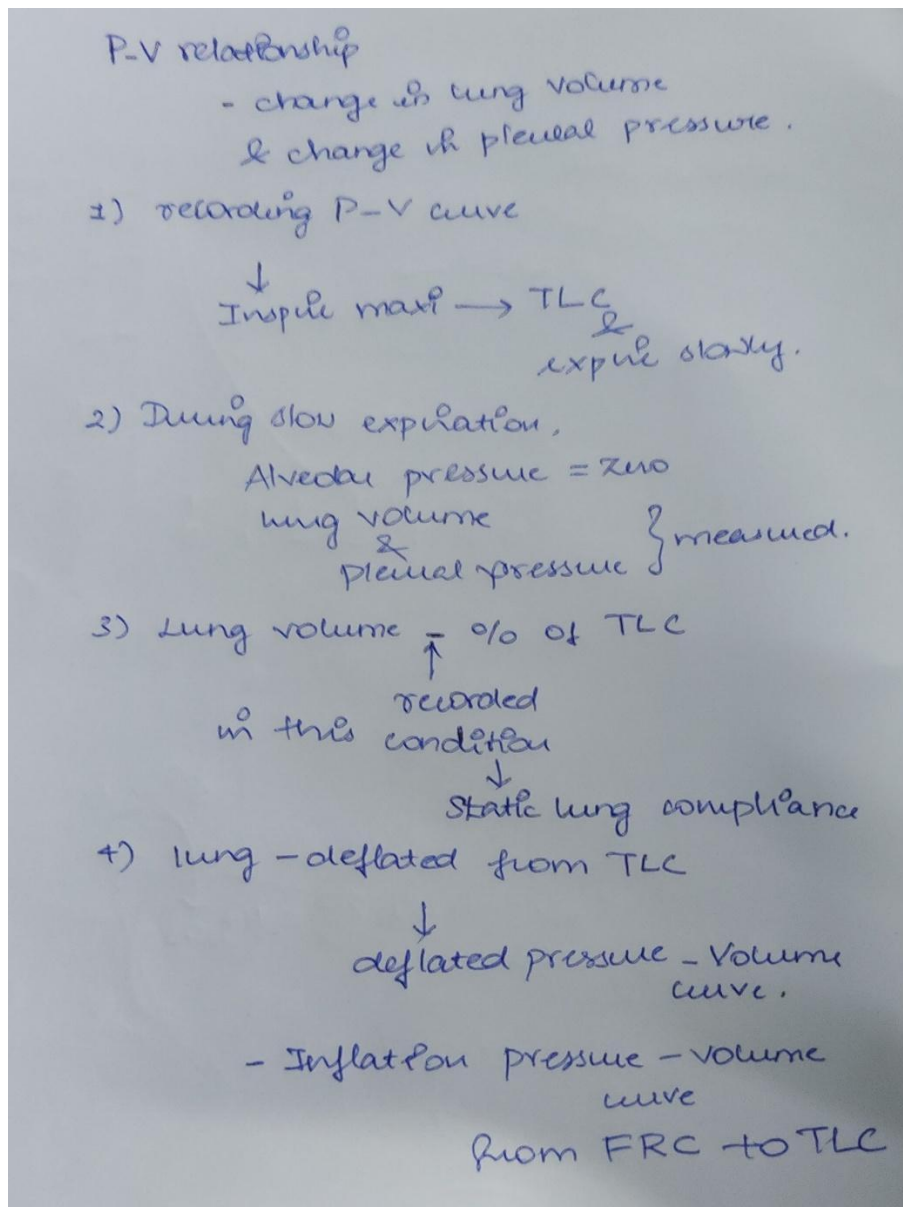
LUNG COMPLIANCE

- ☐ **Compliance** – ability to recoil or ability to stretch
- ☐ Assessed by pressure / volume relationship
- ☐ Compliance is **measure of its distensibility**
- ☐ **Volume change per unit pressure change**
- ☐ **Compliance = $\Delta V / \Delta P$**

Measurement:

- ☐ **Static compliance**
- ☐ **Dynamic compliance**

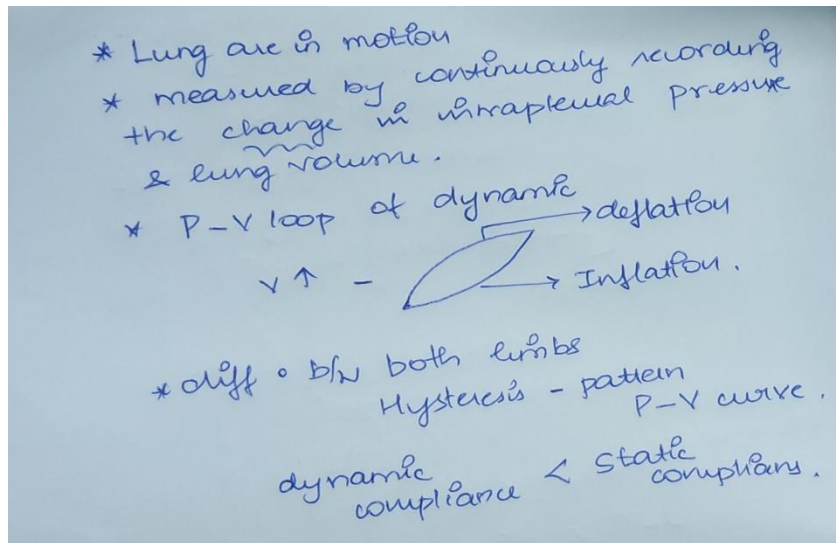
Static compliance :



Stages of compliance:

- ☐ Stage 1: stage of stable lung volume
- ☐ Stage 2: stage of opening of airways
- ☐ Stage 3: stage of linear increase in lung volume
- ☐ Stage 4: stage of cessation of inflation

Dynamic compliance:



Clinical significance:

- ☐ **Low compliance – less distensibility:** more work required for lung to inflate to achieve TV
~ Occurs in restrictive lung disorders & lung fibrosis
- ☐ **High compliance – more distensibility:** occurs in obstructive lung disease & emphysema

TIMED VITAL CAPACITY

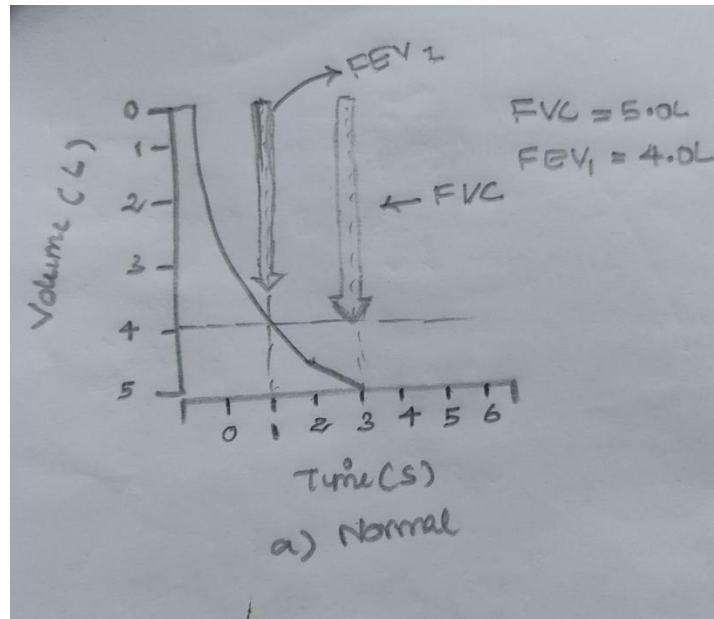
TVC or FVC

- ☐ If VC is recorded on a spiograph at known speed, volume of air **expelled** can be timed
- ☐ Thus, FVC – maximum volume of air which can be **breathed out** as **forcefully & rapidly** followed by **maximum inspiration**
- ☐ TVC – special stress on **rapid, forcible & complete exhalation**

Components of TVC:

- ☐ **Forced expiratory volume in 1 sec (FEV1)** – Volume of FVC expired in 1st sec of exhalation, Normal: 80% of FVC

- **Forced expiratory volume in 2 sec (FEV₂)** – Volume of FVC expired in first 2 sets of exhalation, Normal: 95% of FVC
- **Forced expiratory volume in 3 sec (FEV₃)** – Volume of FVC expired in first 3 sec of exhalation, Normal 98 to 100% of FVC



Clinical significance:

- To distinguish between **restrictive & obstructive lung** disorders
- In **restrictive Disorder** (emphysema, kyphoscoliosis) – arthritis of vertebral column leads to **chest expansion** is restricted
- Therefore, VC decrease while FEV normal

DEAD SPACE

DEFINITION :

> It is the amount of air in the **respiratory passage** which does not take part in exchange of gases

Types:

1. Anatomical dead space
2. Physiological dead space or total dead space

1. Anatomical dead space:

- ☐ It is the volume of air present in the 'conducting zone' of the respiratory passage i.e., from nose and mouth up to terminal bronchioles.
- ☐ Dead space is due to the structural arrangement (anatomy) of the airways
- ☐ Often it is referred to as anatomical dead space where exchange of gases does not take place.
- ☐ Normal value: **150 mL** (approx. equal to the body weight pounds).
- ☐ The volume of wasted air is known as dead space volume

2. Physiological dead space or total dead space:

- ☐ The volume of air in these alveoli is referred to as alveolar dead space
- ☐ Physiological dead space = anatomical dead space + alveolar dead space
- ☐ Normal healthy individuals: anatomical dead space is almost equal with the physiological dead space
- ☐ Various lung disease: alveolar dead space is high in which the physiological dead space is more than anatomical dead space

Measurement of dead space

Dead space is estimated by three methods:

1. Radford formula
2. Single-breath CO_2 technique
3. Single-breath N_2 technique

1.Radford formula:

- ☐ Radford formula predicts the anatomical dead space of the individual
- ☐ >The anatomical dead space of an individual in milliliters is equal to his weight in pounds
- ☐ E.g : person with body weight of 150 lbs (70kg) , the dead space is 150ml
- ☐ This prediction is fairly reliable for healthy individuals, but not in patients with respiratory problems

2.Single-breath co2 technique:

- ☐ The volume of dead space (V_D) is usually measured by the single-breath uses Bohr's equation in the form of a gas such as CO₂.
- ☐ CO₂ used because it is almost absent in the inspired air, and its alveolar concentration is same as in systemic arterial blood
- ☐ Equation:

$$V_D = (F_{AX} - F_{EX}) \frac{V_E}{F_{AX}}$$

- V_D is the volume of dead space,
- V_E is the volume of expired air,
- F_{AX} and F_{EX} represent the concentration of gas in the expired air respectively. As alveolar concentration of gas is same as arterial blood
- F_{ax} (concentration of substance in arterial blood) replaces F_{AX} .

By using CO₂ as the gas for this estimation,

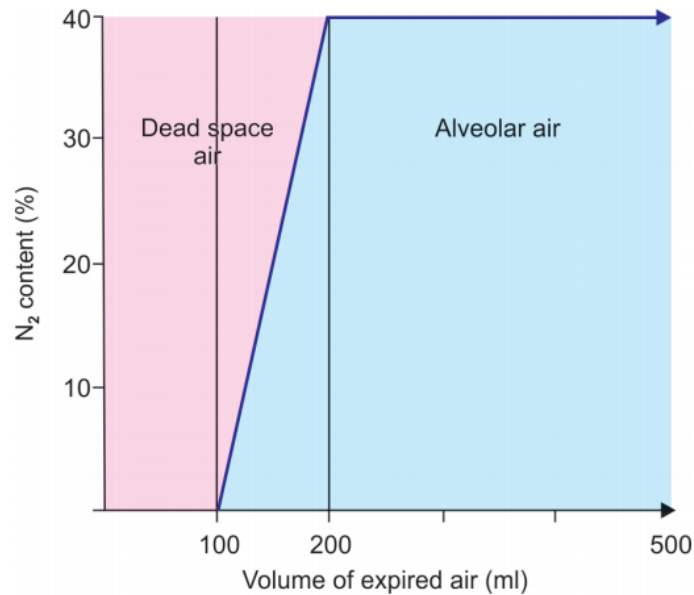
$$V_D = (P_aCO_2 - P_ECO_2) \frac{V_E}{P_aCO_2}$$

P_aCO_2 and P_ECO_2 represent the PCO_2 in the arterial blood and mixed expired air respectively.

3.Single Breath Nitrogen Technique

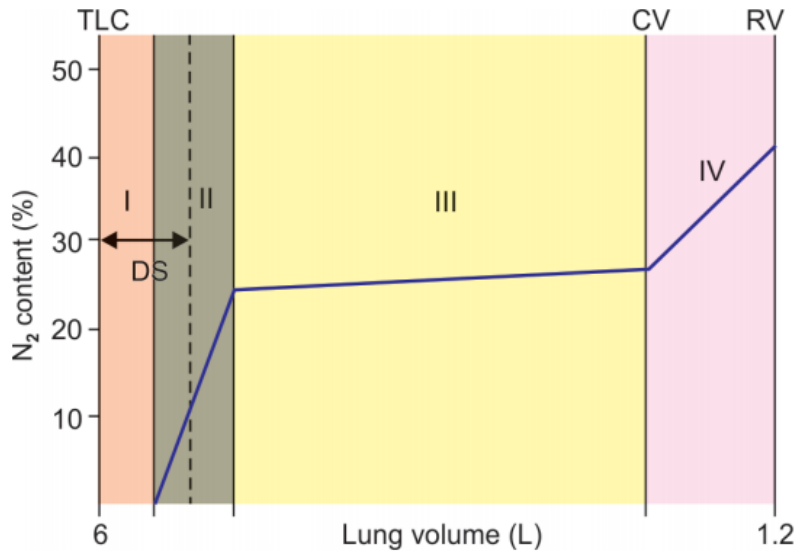
- ☒ The subject sitting comfortably breathes room air calmly for few breaths.
- ☐ Then, he is instructed to take a deep breath from a normal mid-inspiration during which he is switched over to a pure oxygen source (takes deep breath with pure oxygen).

- The subject is then asked to expire slowly and steadily to the maximum, so that the volume expired is his vital capacity.



- As he expires, a simultaneous record is made of the volume flow rate and the percentage concentration of N₂ in the expired air is obtained from the single-breath N₂ test in two ways:
 - i. By constructing the equivalent dead space-alveolar air boundary
 - ii. By planimetry measurement

1. The initial gas exhaled is the **phase I**, which fills the dead space and therefore does not contain N₂.
2. The **phase II** is the mixture of dead space and alveolar gas, and
3. **phase III** is the alveolar gas
4. In **phase IV**, content of expired air increases, which ends at residual volume.



Clinical importance:

- ☐ Alveolar ventilation represents the amount of air reaching the alveoli. This is the air that **takes part in gas exchange**.
- ☐ Even in the absence of lung diseases, **if anatomic dead space volume is increased** due to any cause, **alveolar ventilation decreases**.
- ☐ For example, a patient **on mechanical ventilator**, alveolar ventilation decreases due to increased dead space volume (**by tubing etc.**). In such patients, if minute ventilation remains constant, alveolar gas exchange suffers.

Physiological Significance

- ☐ **In rapid and shallow breathing**, though minute ventilation does not change much, **alveolar ventilation is grossly impaired** because most of the air inhaled is utilized to occupy the anatomic dead space (the air available to enter into alveoli is less).
- ☐ Therefore, patients with rapid and shallow breathing **develop hypoxia and hypercapnia**.
- ☐ In contrast, a subject with **deep and slow breathing** will have adequate alveolar ventilation though the minute ventilation does not change much. Such subjects have alveolar ventilation even greater than subjects with normal breathing.
- ☐ Thus, **to improve alveolar ventilation**, it is important to increase the depth of breathing than to increase the frequency.
- ☐ In fact, during moderate to severe exercise, a **trained athlete** achieves the target alveolar ventilation by mainly increasing the depth rather than the frequency of breathing

HERING-BREUER REFLEX

Lung inflation decreases tidal volume and increases respiratory frequency. There are **two Hering Breuer reflexes**:

- ☐ Hering-Breuer inflation reflex and
- ☐ Hering Breuer deflation reflex.

1. In **Hering-Breuer inflation reflex**:

- ☐ Steady increase in lung volume (lung inflation) results in increase in duration of expiration.
- ☐ Marked inflation of lungs with sustained pressure may even abruptly terminate inspiration in progress in addition to the prolongation of expiration.

2. In **Hering-Breuer deflation reflex**:

- ☐ Marked deflation of lung results in decrease in duration of expiration.
- ☐ As described above, the receptors are slowly adapting stretch receptors in lung parenchyma and airways and afferent and efferent pathways are vagus nerve

Significance of Hering-Breuer Reflex

- ☐ This is a **protective reflex that protects lung from over inflation**
- ☐ It is more useful in infants than in adults.
- ☐ It controls tidal volume during eupnea (normal breathing) in infants.
- ☐ In adults, this reflex does not operate unless tidal volume is much greater than the normal inspiration.

Slowly adapting receptors:

- ☐ The slowly adapting receptors are located within the smooth muscle of the conducting airways.
- ☐ They are sensory terminals of myelinated afferent nerve fibers.
- ☐ As they respond to airway stretch, they are also known as pulmonary stretch receptors

Rapidly adapting receptors:

- ☐ The rapidly adapting receptors are sensory terminals of myelinated afferent fibers that are found in the larger conducting airways
- ☐ They respond to a sudden maintained inflation with rapid increase in firing rate.
- ☐ They are very sensitive to various chemokines like bradykinin, histamine, serotonin and prostaglandins
- ☐ They are also called as irritant receptors as they respond to irritation of the airways by various noxious substances like smoke, dust, ammonia. They are also stimulated by acute congestion and inflammation.

STAGES OF COMPENSATION IN HYPOXIA

- ☐ At a high altitude, there is decrease in PO₂ that decreases O₂ supply to the tissues.
- ☐ To deliver the normal amount of O₂, there are certain compensatory mechanisms
- ☐ The most immediate mechanism is hyperventilation that is not prominent until the PO₂ decreases to 60 mmHg
- ☐ Normally, the drop of PO₂ occurs in an altitude of approximately 4500m.
- ☐ The **hyperventilation induced by hypoxia** at high altitude appears in **two stages**.

In First Stage

- ☐ In the first stage that appears immediately on exposure to hypoxia ventilation increases instantly though the increase in ventilation is small compared to the increase in ventilation in the second stage.
- ☐ The hyperventilation in first stage is mainly due to hypoxic stimulation of the carotid bodies.
- ☐ The magnitude of increase in ventilation is less because the hypoxic stimulation of peripheral chemoreceptor is opposed by the decrease in arterial PCO₂ that occurs due to excess removal of carbon dioxide induced by hyperventilation.
- ☐ This also increases arterial pH.
- ☐ Decreased arterial PCO₂ and alkalosis together blunt the hypoxic response.

In Second Stage

- ☐ In second stage, ventilation increases slowly in 8 to 10 hours and then remains sustained.
- ☐ The sustained increase in ventilation is due to the ventilatory acclimatization at high altitude.
- ☐ Ventilatory acclimatization is a physiological response that occurs during prolonged exposure to hypoxia. After about 2 weeks, hyperventilation induced by hypoxia reaches a stable plateau.
- ☐ There are two mechanisms for ventilatory acclimatization

1. Chemoreceptor mechanism:

- ☐ The pH of CSF is alkaline in the acute phase
- ☐ Ventilation stimulated by hypoxia brings pH close to normal by the movement of HCO₃ outside the CSF
- ☐ In prolonged exposure to hypoxia, sensitivity of carotid bodies to arterial PO₂ alters.

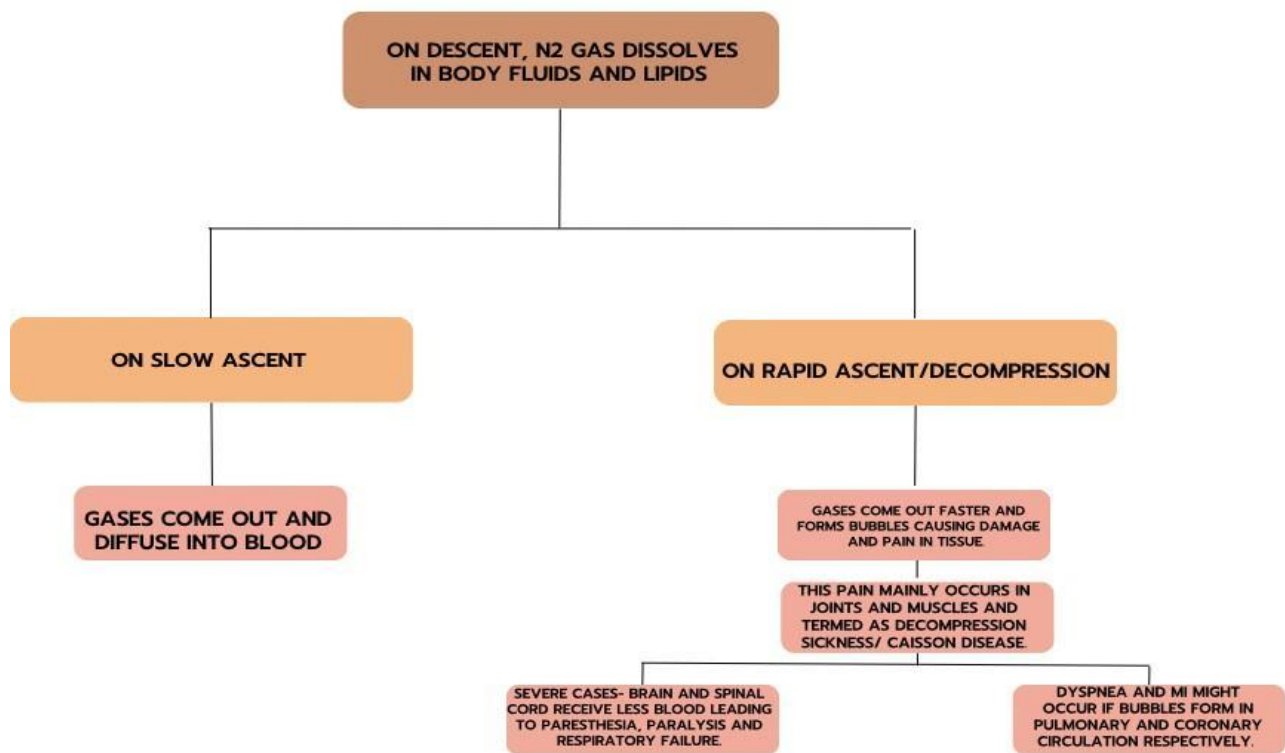
2. Renal mechanism

- ☐ The alkaline blood pH that occurs due to hypoxia induced hyperventilation opposes the hypoxic response that decreases ventilation.
- ☐ Kidney compensates pH by excreting more bicarbonates
- ☐ This decreases the blood pH towards normal in about 3 days
- ☐ This allows hypoxic drive to further increase minute ventilation and then attain a steady state.

CAISSON'S DISEASE

Definition: A chronic form of decompression sickness in which recurrent or persistent gas emboli in the bones lead to multifocal ischemic necrosis is called caisson disease.

- It commonly occurs in deep sea divers or people working in watertight chambers underwater (caisson) who return/ascend to surface rapidly. It also occurs when ascending up in sky.
- At sea level, press is 1atm, and increases by 1atm for 10 meters increase in depth of water.



- **Prevention** is usually by gradual ascent to sea level and reduction should not be less than 50% and use saturation diving technique by mixing helium oxygen mixtures while deep diving.
- **Treatment** is by recompressing immediately in a pressurised cabin. slow decompression after this should be done. Hyperbaric oxygen can also be used.

Note: Important factor that severity of sickness depends on is percentage decrease in pressure.
Nitrogen narcosis

CPR

Definition: The supportive and specific treatment given immediately to patients, in whom for some reasons the cardiac and ventilatory activities have stopped, is called cardiopulmonary resuscitation.

Indications:

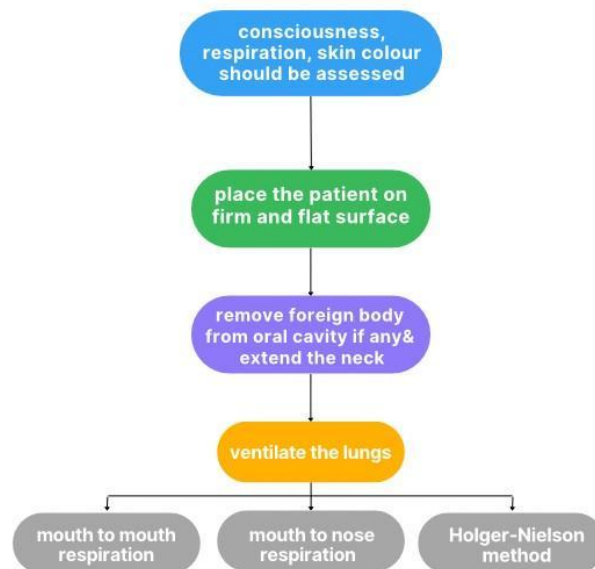
1. Acute and healed MI
2. Arrhythmias
3. Accidents
4. Cardiomyopathy
5. Drowning
6. Electric shock
7. Embolism

Objectives: A) To initiate and maintain circulation
B) To provide adequate pulmonary ventilation

Steps: 3 stages

1. Initial evaluation and basic life support

Initial evaluation and basic life support



Mouth to mouth respiration: clear airway and extend the airway, close patient's nostrils and take a deep breath, exhale forcefully into his mouth and Look for chest expansion and abdominal distension, maintain the rate at 10-15 per minute.

2. Advanced life support

A) primary therapy

*Defibrillation- It is control fibrillations and converts it into flutter or normal rhythm so **effective** ventricular pumping occurs

*Airway management and O2 therapy- 100% O2 administration and endotracheal tube intubation should be done

B) Adjunctive therapy includes self-induced cough, atropine sulphates, pacemakers, sodium bicarbonate.

3. Post Resuscitation care

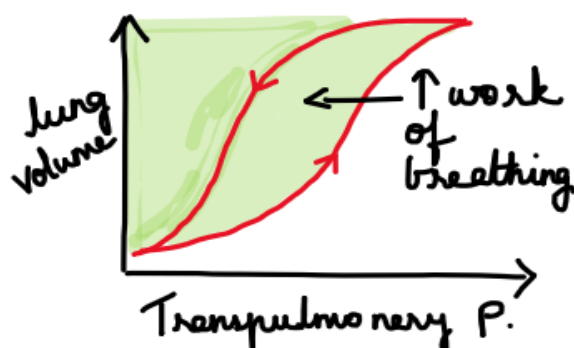
- Treatment of underlying cause for cardio respiratory arrest

- Managing the effects of arrest like hypoxia encephalopathy, cerebral edema.

OBSTRUCTIVE AND RESTRICTIVE LUNG DISEASE

Restrictive lung disease	Obstructive lung disease
Reduction in lung volumes, so volume of inhaled air decreases	Reduction in airflow into lung
Decrease in FEV1 and FEV1/FVC ratio	Normal FEV1/FVC ratio
Work of breathing is increased due to increased effort exerted by patient to inhale as lung compliance is reduced	work of breathing is increased due to more energy usage to overcome increased airway resistance
Patients take rapid and shallow breaths	Patients take slow deep breaths
Increased respiratory rate	Decreased respiratory rate
Eg: COPD, Asthma, Bronchiectasis	Eg: Marked obesity, Scoliosis

RESTRICTIVE LUNG DISEASE



OBSTRUCTIVE LUNG DISEASE

