BREATHING AND EXCHANGE OF GASES

* Oxygen is utilized by the organisms to indirectly break down nutrient molecules like glucose and to derive energy for performing various activities.

* Carbon dioxide which is harmful is also released during the above catabolic reactions.

* It is, therefore, evident that O_2 has to be continuously provided to the cells and CO_2 produced by the cells have to be released out.

* This process of exchange of $O_2$from the atmosphere with CO_2 produced by the cells is called breathing, commonly known as respiration.

* Place your hands on your chest; you can feel the chest moving up and down.

* You know that it is due to breathing. How do we breathe? The respiratory organs and the mechanism of breathing are described in the following sections of this chapter.

RESPIRATORY SYSTEM

* Respiration is the process of biological oxidation of nutrients to produce energy. Depending upon the use of oxygen respiration is of two types

1) Anaerobic respiration is not required

2) Aerobic respiration is required

1) Anaerobic Respiration

An efficient process

Relatively simple process

Mainly glucose is used as a fuel

It is incompletely degraded to lactic acid in some bacteria and specialize condition in muscle fibers and in RBC itself and ethyl alcohol in yeast

It is exhibited by lower organism, endoparasite, yeast cell, some bacteria and in abnormal muscle contraction

2) Aerobic Respiration

It is active efficient process. O_2 is required or used and CO_2 is produced. During aerobic respiration cells produce bio energy by complete chemical combustion or oxidation of glucose and other fuel substances into CO_2 and water using molecular oxygen obtained from environment. It involves

1. External respiration - Gaseous exchange of O_2 and CO_2 between blood and air (or water)

2. Transport of gases to the tissues.

3. Internal respiration - Gaseous exchange between blood and tissues.

4. Cellular respiration - Oxidation of nutrients in the cells and liberation of energy.

Important Respiratory Organs

(i) Lungs - Vertebrates - It is characteristic of pulmonary respiration

(ii) Gills - Aquatic animals. Ex- Fishes, tadpole larva of amphibia, mollusca, Arthropoda, Annelida.

(iii) Skin - Amphibia, earthworm, tadpole larva, Booklung, Arthropoda such as spider

(iv) Accessory respiratory organs - Fishes (May be tree or tubular)

(v) Tracheae and spiracle - Class - Insecta of arthropoda. E.g. Mosquito, cockroach

(vi) Water Lung - Holothuria of Echinodermeta, Planorbis, Pila

(vii) Buccal cavity - Amphibians. E.g. frog

(viii) Alimentary canal - In fishes air bubble reach in intestine and exchanges of gases takes place.

(ix) Allantois - In embryonic condition, excretory waste are stored.

(x) Rectum and cloaca - In fishes rectum and cloaca are also respiratory.

(xi) Parapodia - Annelida such as Nereis.

(xii) General body surface - Members of porifera, coelenterata, Protozoa and some animals of platyhelmithes

(xiii) Book lungs - Spider and Scorpion, many lamellae are present for exchange of gases.

RESPIRATORY ORGANS OF HUMAN

Respiratory system divides into two parts

1. Upper respiratory tract
2. Lower respiratory tract

Upper respiratory tract includes Nose and Pharynx while lower respiratory tract has Larynx, Trachea, Bronchi, Lungs and Diaphragm

Nose

* Nose is the outer most part of respiratory tract, it surrounds nasal cavity.
* It filters the air and also conditions the air according to body temperature.
* It opens to outside with two openings called nostrils or **external nares** (separated by mesethmoid bone). It is a cavity
* Which is inferior to the cranium and superior to the mouth.
* It is internally (posteriorly) opens in pharynx through two **internal nares**. Nasal cavity divides into two chambers called nasal fossae with the help of bony partition called nasal septum.
* Nasal septum is formed by the union of nasal, vomer and ethmoid bone.
* Each nasal fossa divides into three parts

  1. Vestibule 2. Respiratory part 3. Olfactory part
* A vertical nasal septum divides the anterior part of the nasal cavity into right and left vestibules surrounded by cartilage and lined with coarse hairs to filter dust particles.
* Four paranasal sinuses called frontal, sphenoidal, maxillary and ethmoidal along with nasolacrimal ducts open into nasal chamber.
* Ethmoid bone forms the roof and palatine and maxilla and hard palate form its floor.
* Respiratory part is the largest part and performs conduction of air.
* Its posterior cavity has projections of **superior, middle** and **inferior conchae** or **turbinal bone** and is lined with the mucous membrane.

* The space between conchae is called Meati and lined by Pseudostratified cilliated columnar epithelium along with mucus gland which performs conduction of air.
* Superior part of the nasal cavity has olfactory are lined with **Schneiderian membrane**. Below it, there is lining of pseudostratified cells which also secrete mucous.

  It helps in olfaction.

Pharynx

It is 13 cm long, starting with soft palate area representing the crossing point of air route and food route. *Uvula*, the free posterior and muscular part of soft palate divides it as anterior oropharynx and posterior nasopharynx.

Nasopharynx is the posterior part of the pharynx behind nasal cavity.

There are four openings in its walls, two internal nares and two openings of Eustachian tubes.

Lower part of the pharynx is called **laryngopharynx** extending down the hyoid bone, and opens into the oesophagus (*gullet*) and larynx (*glottis*) anteriorly; lined with stratified squamous epithelium.

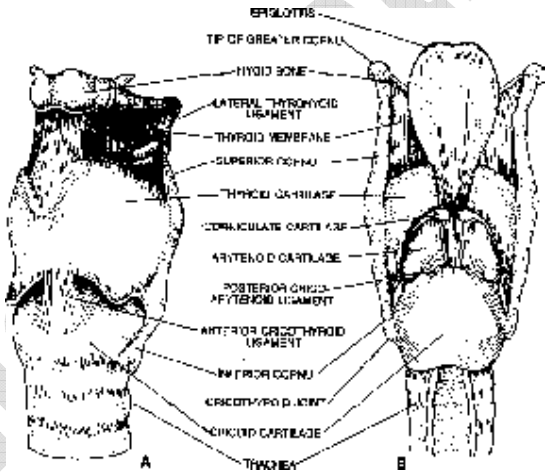

Fig. Cartilages and main ligaments of larynx: A–Front view; B–Back view

Larynx (voice box)

* The upper part of trachea makes cartilaginous box called larynx.
* Larynx is made up of nine cartilages three of them are unpaired while three of them are paired cartilages.
* The unpaired cartilages are 1.Thyroid 2.Cricoid 3.Epiglottis.

  Thyroid cartilage: It is hyaline type largest cartilage of larynx.

  In males it is larger and protrudes in the neck area where it is called **Adam's apple**.
* Thyroid constitutes most of the body of larynx and covers it like a shield.

* **Cricoid cartilage**: It is a signet ring shaped cartilage and constitute the inner part of the larynx.
* **Epiglottis:** It is yellow elastic cartilage and covers the glottis like a flap.
* The paired cartilages are 1.Arytenoid 2.Cuneiform 3.Corniculate.
* **Arytenoid :** It is pyramid shaped and forms the lateral wall of larynx.
* Between thyroid and arytenoid elastic ligaments are present.
* These ligaments are called vocal folds.
* One of them is anterior while the other is posterior.
* The anterior fold is called **false vocal fold** and maintains the air pressure while the posterior vocal fold is called **true vocal cord** which vibrate to produce sound.
* **Corniculate**: These are two conical nodules of elastic fibro-cartilage which lie at the apices of arytenoid cartilages.
* **Cuneiform**: There are two small elongated club shaped nodules of elastic fibro-cartilage which lie above and anterior to corniculate cartilages.
* These connect epiglottis to arytenoid cartilage.
* When air is forced through the larynx, it causes vibration of the true vocal cords and sound is produced. The pitch of a sound is determined by the tension on the vocal cords - the greater the tension, the higher the pitch.
* Sound production at the larynx is called phonation which is one component of speech production, but clear speech also requires articulation, the modification of those sounds by other structures.
* Speech occurs during expiration when the sounds produced by the vocal cords are manipulated by the tongue, cheeks and lips.
* In male vocal cords are longer and thicker under the influence of androgens.
* This changes the male sound as deep or low pitch at puberty. In children and female vocal cords are usually short (as no significant thickening occurs in the female at puberty) and the voice is sharp or high pitch.
* True vocal cords are 2 in number and made up of Yellow fibrous connective tissue (fibro elastic band).
* In female vocal cord = 1.7cm. In male vocal cord = 2.3cm. (Male has deep voice)

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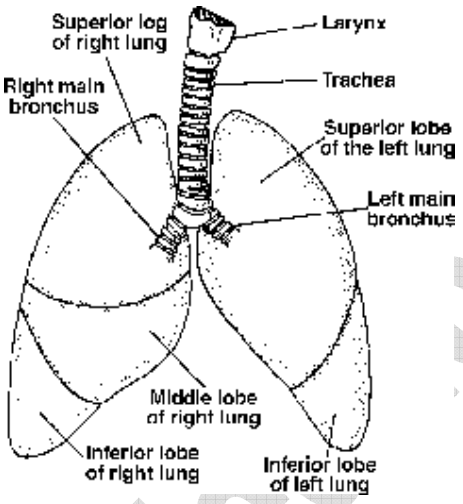
Trachea (wind pipe):

* It of about 12 cm length and 2.5 cm in diameter and joins the pharynx to bronchi point of bronchi.
* It is supported by dorsally incomplete (C-shaped) rings of hyaline cartilage and lined by pseudostratified ciliated columnar epithelium.
* All the cilia of trachea and bronchi beat towards pharynx and push the mucus along with it.
* This ciliary movement helps in the cleansing of lungs.
* **Bronchi:** In thorax trachea divides into right and left primary bronchus with cartilaginous ring.
* These bronchi enter into lungs of their side

LUNGS



* These are paired, cone shaped, spongy organs in the thoracic cavity enclosed within pleural cavity.
* The outer pleura attached to the wall of the thoracic cavity is called **parietal pleura** and the inner layer is called the **visceral pleura**.
* Space between right and left pleural cavities is mediastinum.
* The right and left lungs are divided into three and two lobes respectively.
* Left lung contains a concavity called the **cardiac notch** in which lies the heart.

* The right lung is thicker and broader but shorter than the left lung because the diaphragm is higher on the right side to accommodate the liver lying below it. Inside lungs bronchi keeps on dividing during this division the cartilage rings become smaller and irregular.
* Within lungs it branches into bronchioles—**primary, secondary** and **tertiary** (or terminal) bronchioles leading to alveoli.

Human trachea, bronchi and lungs

Bronchioles are without cartilaginous rings. They are lined by cuboidal or columnar epithelium along with surfactant producing Clara cells.

* Terminal bronchioles are the smallest while respiratory bronchioles are the first structure through which ventilation is possible.
* Though respiratory structures before respiratory bronchioles do not participate in gaseous exchange but they do remain filled with air.

  This air is called **Dead space Air** and the space is called **Dead Space**.
* Terminal (or respiratory) bronchioles divide to form many alveolar ducts or atria with many alveoli around.
* Exchange of respiratory gases takes place here by simple diffusion across the alveoli and capillary walls.
* Lungs contain 300-400 million alveoli with surface area of 100 m^2.

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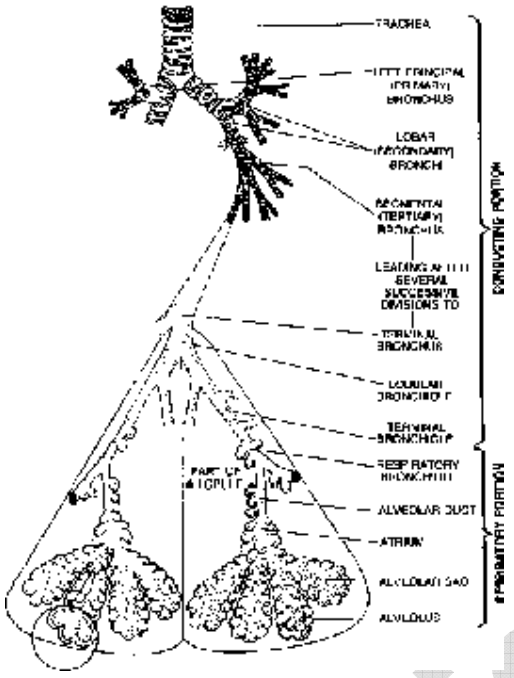

Fig. Bronchiolar branching and their connection with alveoli

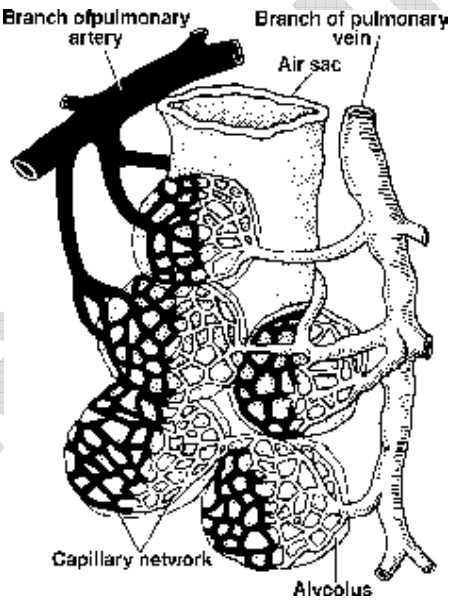

Fig. Blood circulation in respect to alveoli in lungs

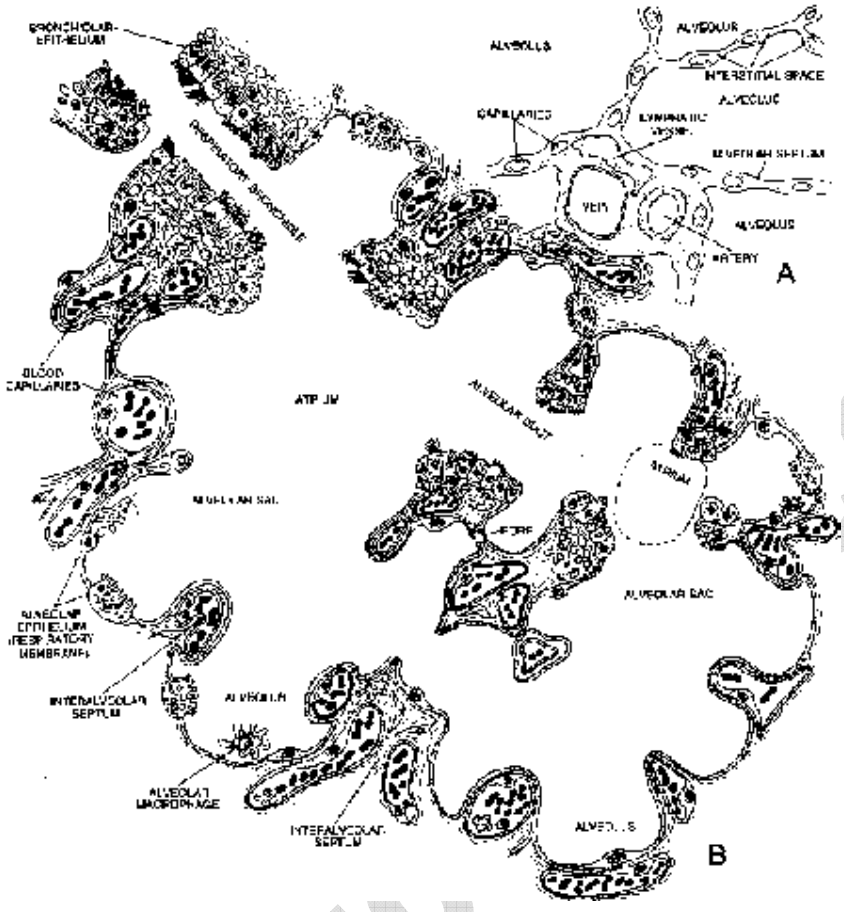

Fig. Microscopic structure of alveoli (A) and ultra structure of respiratory portion of lungs (B)

Respiratory membrane

Alveoli are functional units of lungs. They are lined by three types of cells

1. Type I Alveolar cells
2. Type II Alveolar cells
3. Dust cells

Types of alveolar cells

Type I alveolar cells: These are part of the alveolar epithelium.

* They are thin cells specialized for gas exchange, which rest on a basement membrane.
* Type I cells are present in alveoli and respiratory bronchioles, but they are not present in terminal bronchioles.

* The basement membrane of the alveolar epithelium is thin and closely associated with the thin basement membrane of capillaries.

Type II alveolar cells: These are part of the alveolar epithelium and are joined to type I alveolar cells by extensive junctional complexes.

* Unlike squamous type I cells, type II cells are rounded cells containing an abundance of multilamellar bodies.

* Type II cells create **surfactant** by synthesizing and secreting multilamellar bodies that are rich in phospholipid.

* The surfactant reduces the surface tension at the gas-liquid interface in alveoli.

* Gas interface is denoted by inhaled air whereas liquid interface by intracapillary fluid.

* The alveoli lining lies in between the two and the surfactant help to keep the alveoli expanded so that efficient gas exchange occurs.

Dust Cells: These are also known as **alveolar macrophages**.

* They are found on inner surface of lung alveoli.

* They eat up pathogens or any foreign particles there.

* Activity of the alveolar macrophage is relatively high, because they are located at one of the major bound aries between the body and the outside world.

* Dust cells are another name for monocyte derivatives in the lungs that reside on respiratory surfaces and clean off particles such as dust or microorganisms.

* Aveolar macrophages are frequently seen to contain granules of exogenous material such as particulate carbon that they have picked up from respiratory surfaces.

* Such black granules may be especially common in smoker's lungs or long-term city dwellers.

The gaseous exchange across the respiratory membrane proceeds very rapidly, because:

(a) The distance is small and

(b) Both oxygen and carbondioxide is lipid - soluble

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MECHANISM OF BREATHING

Breathing or Ventilation is the exchange of gases through lung surface.

* Breathing is of two types,
  1. Positive pressure breathing
  2. Negative pressure breathing
* In positive pressure breathing an external pressure pushes the air inside lung, normally it occurs in those animals where diaphragm is absent such as Frog.
* While in negative pressure breathing an internal negative pressure is created which sucks the air inside lungs, normally it occurs in animals which respire through diaphragm.

BREATHING (VENTILATION) IN MAMMALS:

* It takes place by change in volume of air tight thoracic cavity, (in frog it occurs by change in volume of buccal cavity).
* Lower boundary of thoracic cavity is formed by diaphragm which divides body cavity into upper thoracic and lower abdominal cavity.
* Diaphragm is an elastic, dome-shaped, plate like structure with its convex side towards thoracic cavity while thoracic cage is formed by 12 pair of ribs obliquely attached between vertebral column and movable sternum.
* Last two pairs of ribs are **floating ribs** which have no role in breathing.
* Two sets of muscles, **external intercostal muscles** and **internal intercostal muscles** are present between every two ribs.
* The dorsal end of external intercostal muscles is attached to anterior rib while its ventral end joins with posterior rib; hence their attachment is in opposite manner.
* Volume of thoracic cavity is changed by (i) shifting of ribs or sternum and (ii) flattening of diaphragm.

In humans breathing involves two processes

1. Inspiration
2. Expiration

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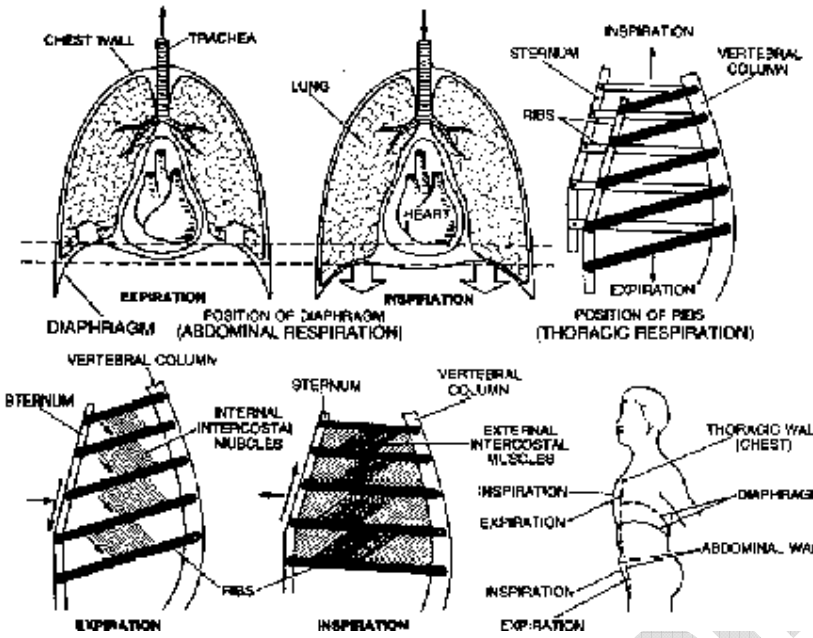

Fig. Movement of diaphragm and ribs and of thoracic and abdominal walls in breathing in rabbit

Inspiration:

* It takes place by contraction of phrenic (radial) muscles which pulls diaphragm downwards increasing the volume of thoracic cavity.
* Contraction of external intercostal muscles pulls the ventral end of ribs making it straight.
* This pushes the sternum ventrally and hence volume of thoracic cavity increases towards this side.
* This increase in volume decreases the pressure in thoracic cavity and air enters into lungs.
* The elevation of thoracic cavity is supported by external intercostal muscles therefore these muscles are defined as
* Inspiratory muscles.

Expiration:

* During expiration diaphragm simply relaxes which decreases the surface area of lungs and air comes out.
* Diaphragm returns to original shape and place due to relaxation of phrenic muscles.
* While contraction of internal intercostal muscles pull back the ribs obliquely which shift sternum back to original position but this is related to state of activity.
* In humans expiration is a passive process and no muscles are defined as expiratory muscles during normal quiet expiration.
* But during forceful expiration internal intercostals and abdominal rectus muscles participate and called expiratory muscles.

CONTROL OF BREATHING:

* Normal rate of breathing is 12 to 15 times per minute in man but it may range upto to 20.
  In humans ventilation rate per minute is 6000 ml, it is equal to respiratory rate in terms of tidal volume per minute.
* In humans control of respiration is of two types involuntary and voluntary.
* Voluntary control is regulated by cerebrum and centers of pons and medulla while involuntary control is regulated by pons and medulla only. In humans normal quiet respiration is generally involuntary and depends upon the concentration of CO2 in arterial blood
* Involuntary control operates from respiratory centres in **medulla oblongata** and **pons varolii**
* Breathing can be controlled by central nervous system.

1. **Respiratory center**: Located in the medulla oblongata and pons varolii.

* These centers regulate the rate and depth of breathing by controlling contraction of diaphragm and other respiratory muscles.
* Medulla oblongata contains inspiratory centre in dorsal portion and expiratory centre in the ventral portion.
* The expiratory centre is connected with vagus nerves that innervate the lungs.
* Pons varolii contains pneumotaxic or pontine center and apneustic area.
* Pneumotaxic area which helps to control both the rate and pattern of breathing is present in the dorsal portion.
* While the apneustic centre, which operates in association with the depth of inspiration, is present in the lower part of pons varolii.

2. **Chemical control**: A chemo sensitive area is situated near respiratory centre, medulla.

* It is highly sensitive to changes in CO_2 concentration (or change in blood pH, as blood CO_2 concentration influences its p^H by forming HCO_3^- within RBC using the enzyme carbonic anhydrase).
* Carbonic anhydrase is the '**fastest' enzyme** in the enzyme world.

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* Increase pCO_2, increased H^+ concentration and pO_2 input from the central and peripheral chemoreceptors causes the inspiratory area to become highly active and rate and depth of breathing increases.

* **Severe hypoxia** depresses the activity of central chemoreceptors and respiratory centre.

* The respiration rate decreases or breathing ceases altogether, pO_2 falls lower and lower **(Asphyxia)**

3. **Chemoreceptor cells**: Located in carotid arteries.

* These cells send signals to the respiratory centre in the brain and monitor the concentration of CO_2 and H^+ ions

4. **Hering-Breuer reflex**: In the walls of bronchi and bronchioles **stretch receptors** are located and are stimu

lated by overstretching of the lungs.

* This reflex serves as a protective mechanism for preventing excessive lung inflation but simultaneously it may increase breathing rate by reducing inspiratory time, like the pneumotaxic centre

* Respiratory centre is influenced by the chemical stimuli like levels of CO_2, O_2 and pH of the blood.
* At normal resting state inspiration is the active process while expiration is passive.
* Strong emotions, fright, excitement and other mental factors also influence the frequency.
* A rise in body temperature e.g. during fever or exercise blood pressure increases the breathing rate.
* The initiation of breathing in just born baby is made by rise in PCO_2 or fall in PO_2 in its blood, as circulation and breathing become independent of the mother after birth.
* Low PO_2 at high altitudes increases the rate of breathing but this cannot compensate the deficiency and results in mountain sickness.

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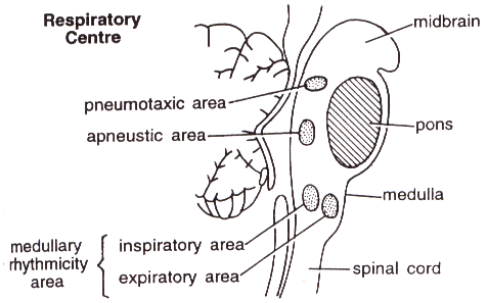

Fig. Respiratory centre and its working in man

Regulation of respiration at High Altitudes

* At high altitude composition of air remains almost same as at sea level, but density (barometric pressure) of air gradually decreases due to which arterial PO_2 is also decreased (Hypoxemia). While ascending up a mountain one inspires thin air and gets less oxygen

* Hypoxemia stimulates the peripheral chemoreceptors and increases the ventilation rate (hyperventilation). As respiration increases increase loss of CO_2less CO_2 in blood increases pH in blood alkalosis.

* The respiratory alkalosis can be treated by administering acetazolamide.

* Acetazolamide blocks the enzyme carbonic anhydrase conversion of CO_2 to HCO_3^-increase CO_2retention in blood reverses the alkalosis

* Hypoxemia also stimulates renal production of erythropoietin, which increases the production of red blood cells.

* As a result, there is increased hemoglobin concentration and increased O_2 carrying capacity of blood.

* The resulting decreased affinity of the hemoglobin for O_2 facilitates unloading of O_2 in the tissues

* Pulmonary vasoconstriction is another result of the hypoxemia.

* Consequently, there is an increase in pulmonary artery pressure, increased work of the right side of heart against the higher resistance present in lung because of pulmonary vasoconstriction.

* Number RBCs per unit volume of blood is likely to be higher in a person living at high altitudes.

* This is in response to the air being less dense at high altitude.

* More numbers of RBC's are needed to trap O_2 from rarefied air having low pO_2 (partial pressure of oxygen)

Parameter	**Response**
Alveolar pO_2	Decreases
Arterial pO_2	Decreases (Hypoxemia)
Ventilation rate	Increases (Hyperventilation)
Arterial pH	Increases (Respiratory alkalosis)
Haemoglobin concentration	Increases
2, 3-DPG concentration	Increases
Hemoglobin O_2 curve	Shift to right; Decreases affinity
Pulmonary vascular resistance Increases	

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EXCHANGE OF GASES

* It takes place in the alveoli by **simple diffusion** due to difference of pressure of CO_2 and O_2 in the alveoli and the perialveolar blood capillaries.
* Partial pressure of oxygen (PO_2) in inspired air is 158 mmHg, but in alveolar air is 100 mmHg (2 1%) the PO_2, in venous blood is 40 mm Hg (16%).
* Partial pressure of CO_2 (PCO_2) in alveolar air is about 36 mm Hg while in venous blood it is about 46 to 50 mmHg and in atmospheric air it is 0.03%.
* The exchange of gases between the alveoli and blood in the lungs, and between the blood and the tissues is the result of difference in partial pressure of the respiratory gases, that is, oxygen and carbon dioxide, nitrogen etc.
* Partial pressure of oxygen (pO_2) in alveolar air is 100mm Hg and it is only 40mm Hg in the arterial

  capillaries of the lungs.
* Therefore, oxygen from the alveolar air rapidly diffuses due to its higher pO_2 into the blood capillaries. The pO_2 in the venous blood capillaries of lung is about 95 mm Hg.
* Similarly the pCO_2 in the blood reaching the alveolar capillaries is 46mm Hg whereas pCO_2 in alveolar air is 40mm Hg.
* Therefore CO_2 rapidly leaves the blood capillaries and reaches the alveoli.
* The gaseous exchange between the blood and tissues is also due to the differential partial pressures.
* The pO_2 and pCO_2 of the arterial blood reaching the tissues is 95mmHg and 40mm Hg respectively, while pO_2 and pCO_2 of tissues is 20mm Hg and 52mm Hg respectively.
* Therefore, oxygen quickly leaves the blood and enters the cells whereas CO_2 produced in the tissues leaves the cells and enters the blood.

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Surfactant: It is a surface active agent, lines the alveoli. It is a mixture of several phospholipids, proteins and ions, secreted by type II alveolar epithelial cells.

* It reduces surface tension between the alveolar fluid and air and prevents small alveoli from collapsing and increases respiratory compliance (compliance means the quality of yielding to pressure without disruption, or an ability to do so, as an expression of distensibility of an air or fluid-filled organ

Gas	Atmospheric air	Inspired air	Alveolar air	Expired air
N_2	597.0 (78.62%)	563.4 (74.09%)	569.0 (74.9)	566.0 (74.5%)
O_2	159.0 (20.84%)	149.3 (19.67%)	104.0 (13.6%)	120.0 (15.7%)
CO_2	0.3 (0.04%)	0.3(0.04%)	40.0 (5.3%)	27.0 (3.6%)
H_2O	3.7 (0.5%)	47.0 (6.2%)	47.0 (6.2%)	47.0 (6.2%)
760.0 (100%)		760.0 (100%)	760.0 (100%)	760.0 (100%)

TRANSPORT OF GASES

Blood is the medium to carry O_2 from lungs to tissue and CO_2 from tissue to lungs.

TRANSPORT OF O_2

* Being less soluble in water, only 0.3 ml of O_2 per 100 ml. of blood is transported as dissolved in plasma, this is only a negligible amount.
* Mainly transported in bound form through the respiratory pigment, hemoglobin (Hb).

Hemoglobin (Hb) :-

* A conjugated protein consists of 4 globin chains (protein part) each with 1 heme group (a Fe-porphyrin) as non-protein part.
* It is a large molecule of quaternary structure and the molecular weight 66800 – 68000 D.
* Globin chains are of four α, β, γ and δ — types.
* Depending upon the number of different types of chains there are many types of Hb:
  (1) Embryonic or foetal Hb (HbF) — contains $2\alpha + 2\gamma$ globin chains $2\alpha + 2\gamma$.
  (2) Adult Hb (HbA) i.e. after birth is of two types:
  (i) HbA-l has $2\alpha + 2\beta$ chains $(\alpha_2\beta_2)$. (ii) HbA-2 $2\alpha + 2\delta$ has chains $(\alpha_2\delta_2)$

* In our body 98% Hb is of Hb A-1 type and 2% of Hb A-2 type.
* In Hb molecule Fe remains in Fe^{++} state and it is the site for O_2 combine

  1 Fe atom combines with 1 molec. of O_2

  1 molec. Hb combines with 4 molec. of O_2

  66800 gm (gm mol. wt.) of Hb combines with 4×22.4 liter O_2

  1 gm of Hb will combine with 1.34 ml O_2

  15 gmHb (l00 ml blood) will carry 15×1.34 ml $O_2 = 20$ ml. O_2.
* To carry about 20 ml O_2 in 100 ml blood (20% of its volume) is called as **total respiratory capacity** of blood.
* Combining with O_2 it forms oxyhaemoglobin (HbO_2) — an unstable compound which dissociates at lowers pressure of O_2 in the tissue undergoing metabolism.

  $Hb + O_2 \rightleftarrows HbO_2$ (Oxyhaemoglobin)
* This is no oxidation reduction reaction as Fe remains in Fe^{++} state on both sides.
* However, in higher nitrogen oxide level in the medium, Hb is oxidized and forms **methemoglobin** (or **ferrihemoglobin**). This causes a pollution disease, **methemoglobinemia** in child, where nitrate level is higher in underground (or drinking) water.
* The rate of association and dissociation depends upon P_{O_2}, the graph plotted as **Hb-O_2 dissociation curve** is typically a segmoid curve.
* At 60 mm Hg P_{O_2} there is more than 80% saturation of Hb and the rate of reaction below it is faster, this is called as **critical pressure** of O_2
* 50% saturation takes place only at 30 mm Hg of P_{O_2} (P50 value of O_2 is 30 mm Hg)
* Maximum saturation of Hb even at 100 mm Hg P_{O_2} is 97.8%.

Factors affecting Hb-O_2 dissociation curve

(i) **Effect of P_{CO_2}:** If the P_{CO_2} level is higher at the site of metabolism (tissue) the Hb releases O_2 at faster rate hence the curve shifts to right hand side, this is called **Bohr Effect**.

(ii) **Effect of pH:** The curve shifts to right hand side with the lowering pH i.e. increasing acidity, this also called as Bohr Effect.

(iii) **Effect of Temperature:** Same as of P_{CO_2}.

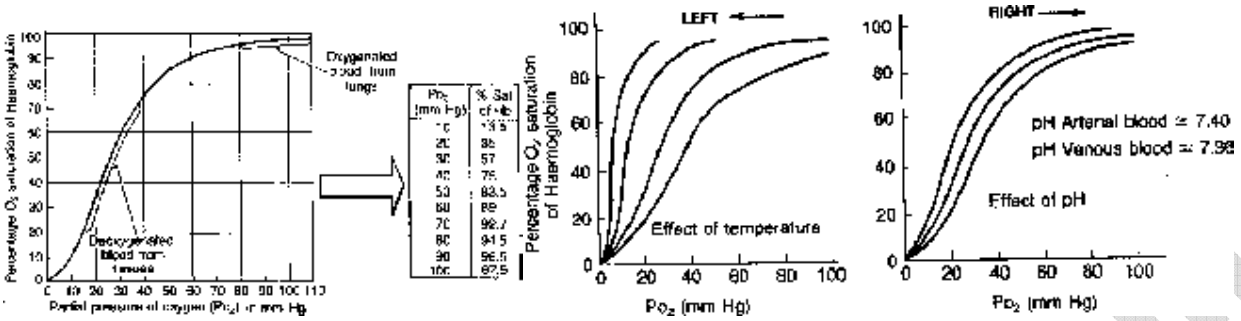

Fig. Effect of temperature and pH upon Hemoglobin - O_2 dissociation curve

II Transport of Carbon Dioxide

CO_2 is transported from tissues to lungs in three forms - (i) as dissolved CO_2, (ii) as carbamino compounds and (iii) as bicarbonate ion.

i. As Dissolved CO_2

Solubility of CO_2 is 20-25 times greater than that of oxygen. About 5-7% of the CO_2 is dissolved in plasma (like the CO_2 in soda). After reaching lungs, it diffuses into alveolar air.

$H_2O + CO_2 \rightleftarrows H_2CO_3$

ii. As Carbaminocompounds

About 10-20% of CO_2 is transported as carbamino compounds.

* In plasma, a small amount of CO_2 com bines with amino groups of plasma proteins to form carbamino compound.

* In RBC, CO_2 combines with the amino groups of amino acids of hemoglobin to form carbaminohaemoglobin.

$Pr + CO_2 \rightleftarrows PrCO_2$ (Carbamino protein)

$Hb + CO_2 \rightleftarrows HbCO_2$ (Carbamino hemoglobin)

* At lungs, where Pco_2 is low, the reaction is reversed and CO_2 diffuses into alveoli.

iii. As Bicarbonate ion

* About 65-85% of CO_2 is transported as bicarbonate ions.

* CO_2 that diffuses from tissues into systemic capillaries reacts with water to form **carbonic acid** (H_2CO_3).

* This reaction occurs about 5000 times faster in RBC than in plasma due to the enzyme **carbonic anhydrase**.

* Carbonic acid dissociates into hydrogen ions (H^+) and bicarbonate ions $\left(HCO_3^-\right)$

$$H_2O + CO_2 \rightleftarrows H_2CO_3 \rightleftarrows H^+ + HCO_3^-$$

Chloride shift or Hamburger's shift:

* Due to carbonic anhydrase activity, concentration of HCO_3^- increases in RBC.

* Plasma membrane of RBC is permeable to anions but nearly impermeable to cations.

  HCO_3^- diffuses into blood plasma.

* To maintain electrical balance, Cl^- ions diffuse from plasma into RBC.

* This exchange of chloride and bicarbonate ions between erythrocytes and plasma is termed the **chloride shift** or **Hamburger's phenomenon**.

* Hydrogen ions combine readily with deoxyhaemoglobin (which acts as a buffer) to form HHb.

* At lungs, as hemoglobin loads oxygen, its affinity for H^+ declines, H^+ dissociates from the hemoglobin and binds with bicarbonate forming that dissociates into CO_2 and H_2O.

* Dissociation of into CO_2 and H_2O is catalyzed by carbonic anhydrase. CO_2 diffuses into alveoli

Fig. Transportation of CO_2 by blood

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Haldane Effect:

* It expressed in various following ways:

  In presence of O_2 the Hb does not combine with CO_2; or releases CO_2 immediately to combine with O_2; or Hb has 20-30 times higher affinity for O_2 than CO_2; or HbO_2 is acidic in nature and CO_2 can not combine with it.

* The binding of O_2 with Hb tends to displace CO_2 from blood. This is very important to promote the transport of CO_2.

  In tissue capillaries the Haldane effect causes increased pick up of CO_2 after O_2 splits from Hb and in the lungs it causes increased release of CO_2 as the Hb combines with O_2 here

Why foetal hemoglobin dissociation curve is shifted to left related to adult oxygen hemoglobin dissociation curve?

Foetal hemoglobin takes oxygen from mothers hemoglobin across the placenta due to double bohr effect. Its concentration at term (nine months foetus) is 15-20gm/dl in which 10-45% if it is adult hemoglobin (HbA) and the remainder is foetal hemoglobin (HbF). Foetal Hb is a tetramer having and is exhaled.

As concentration of HCO_3^- declines in RBC, HCO_3^- diffuses from plasma into RBC in exchange for Cl^- **(reverse chloride shift)**.

α_2 and β_2 as polypeptide chains.

* There is no β chain as it is replaced by γ chain, so HbF is insensitive to a shift due to 2-3 DPG. (Di phosphoglyceric acid)

* The foetal hemoglobin has a sigmoid dissociation curve which is shifted to left relative to adult Hb dissociation curve because they lower P_{50} 918 to 20mmHg) than adult Hb (26.6 mmHg).

* This means foetal hemoglobin has a higher oxygen affinity as it binds, 2, 3 - DPG less avidly by - γ polypeptide chains than that in HbA ad this assists it to load oxygen in the placenta while maternal

hemoglobin is unloading oxygen thereby enabling the foetal body cells to utilize O_2.

* So the less binding of 2,3 - DPG with hemoglobin molecule the more affinity to oxygen which make a left shift of the foetal Hb-O_2 dissociation curve.

Why oxygen dissociation curve for myoglobin of muscle is hyperbolic?

* Myoglobin lacking quaternary structure, consists of a single polypeptide chain of 153 aminoacyl residues with compact shape.

* Myoglobin is a muscle (skeletal) protein with oxygen carrying characteristics.

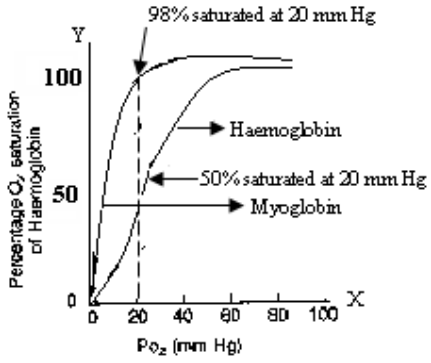
* The shape of oxygen dissociation curve for myoglobin, which is hyperbolic, clearly shows that it has great affinity for oxygen and binding of oxygen to the single polypeptide chain is non cooperative.

* The shape of its dissociation is hyperbolic because its curve is to the left of the hemoglobin curve.

  It takes up O_2 from the hemoglobin in the blood and releases it only at low pO_2 values, since pO_2 in the lung capillary bed is 100mm Hg, myoglobin could effectively load oxygen in the lungs.

* Since myoglobin cannot deliver a large fraction of its bound oxygen even at 20mmHg, it cannot serve as an effective vehicle for delivery of oxygen from lungs to peripheral tissues.

* However, the oxygen deprivation that accompanies serve physical exercise can lower the pO_2 of muscle tissue to as little as 5mm Hg.



RESPIRATORY VOLUMES AND CAPACITIES

(Aerodynamics of Human lungs)

* **Tidal Volume (TV):** Volume of air inspired or expired during a normal respiration.
  It is approx. 500ml., i.e., a healthy man can inspire or expire approximately 6000 to 8000mL of air per minute.
* **Inspiratory Reserve Volume (IRV):** Additional volume of air, a person can inspire by a forcible inspiration.
* This averages 2500 ml to 3000ml
* **Expiratory Reserve Volume (ERV):** Additional volume of air, a person can expire by a forcible expiration.
* This averages 1000mL to 1100 ml
* **Residual Volume:** Volume of air remaining in the lungs even after a forcible expiration.
* This averages 1100 ml to 1200 ml.
* By adding up a few respiratory volumes described above, one can derive various pulmonary capacities, which can be used in clinical diagnosis.
* **Inspiratory Capacity (IC):** Total volume of air a person can inspire after a normal expiration.
* This includes tidal volume and inspiratory reserve volume (TV+IRV) IC=500 ml +2500 ml =3000 ml
* **Expiratory Capacity (EC):** Total volume of air a person can expire after a normal inspiration.
* This includes tidal volume and expiratory reserve volume (TV+ERV) EC=500 ml +1000 ml = 1500 ml
* **Functional Residual Capacity (FRC):** Volume of air that will remain in the lungs after a normal expiration.
* This includes ERV+RV FRC=1000 ml +1100 ml =2100 ml
* **Vital Capacity (VC):** The maximum volume of air person can breathe in after a forced expiration.
* This includes ERV, TV and IRV or the maximum volume of air a person can breathe out after a forced inspiration.
  VC=1000 ml +500 ml +2500 ml = 4000 ml
* **Total Lung Capacity:** Total volume of air accommodated in the lungs at the end of a forced inspiration.

* This includes RV, ERV, TV and IRV or vital capacity + residual volume i.e., 4000 ml +1100mL=5100 ml

Dead Air Volume:

The volume of air (=150 ml) that passes out unexchanged (or unused) and which remains in trachea, bronchi and bronchioles, (these parts are called **Dead Air Space**).

Only 350 ml of the atmospheric air (T.V.) is actually exchanged during breathing i.e., 1/7th of total air in the lungs.

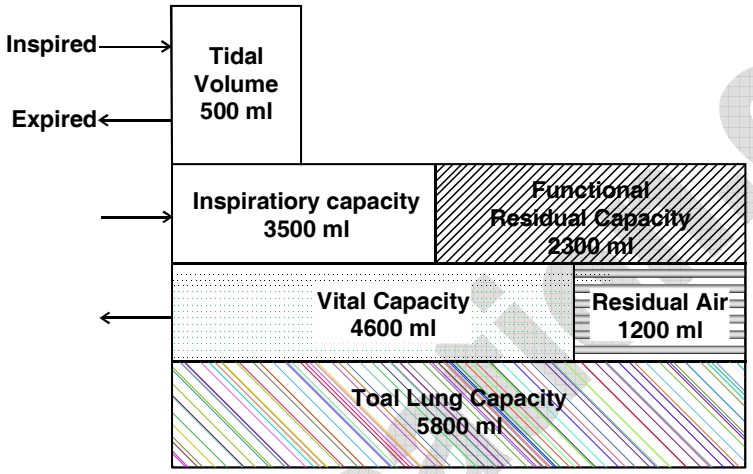


Fig. Pulmonary capacities in man

Respiratory Pigments

	Name of the respiratory pigment	Metal Present	Colour	Features
1.	Hemoglobin	Iron	Red	Plasma of some annelids (e.g. earthworm and Neries)
2.	Hemoglobin	Copper	Blue	Plasma of crustaceans (e.g. prawn), some Snails (pilla), Cephalopods (e.g. Sepia)
3.	Hemoglobin	Iron	Red	Blood cells of some annelids (e.g. polychaete Magelona)
4.	Chlorocruorin	Iron	Green	Plasma of some annelids (e.g. polychaete sabella)
5.	Pinnaglobin	Maganese	Brown	Plasma of some molluscs (e.g. Pinna)
6.	Echinochrome	Iron	Red	Coelomic fluid of sea urchin (echinoderm)
7.	Vanadium	Vanadium		---Blood of many tunicates (urochordates). Ciona contains vanadium pigment in the plasma special green blood cells called vanadocytes of Ascidia.

RESPIRATORY QUOTIENT

The ratio of CO_2 formed and O_2 utilized during complete combustion of a fuel substance is called respiratory quotient. RQ is measured by Ganong's respirometer

$$RQ = \frac{Volume\ of\ CO_2\ formed}{Volume\ of\ O_2\ utilized}$$

Substrate	RQ Value
1.**Carbohydrate**	**One**
When it is used as source	Infinity
2. **Proteins**	**0.8** (slightly less than 1)
3. **Fat**	**0.7**
4. **Mixed diet**	**0.85**
5. **Organic acid**	**More than 1**
6. **Succulent xerophytes**	**Zero Respiratory disorders**

1. **Asphyxia**: It is a condition caused by increase in CO_2 concentration in tissue.

* In asphyxia produced by occlusion of the airway, acute hypercapnia and hypoxia develop together.

* There is pronounced stimulation of respiration, with violent respiratory efforts.

2. **Hypoxia** - A clinical term for lack of proper oxygen supply to the tissues.

There are 4 types of hypoxia

(a) **Hypoxic hypoxia** - The arterial pO_2 is low, can occur at high attitudes.

(b) **Anemic hypoxia** - The amount of oxygen carrying hemoglobin is reduced either by anemia on because the hemoglobin binding sites are already full.

(c) **Stagnant hypoxia** - caused by either intense local vasoconstriction or a poor cardiac output.

* The blood emerges from the vascular bed almost completely desaturated although arterial blood may have a normal pO_2.

(d) **Histotoxic hypoxia** - rare but is most often due to cyanide poisoning.

Cyanide poisons the cytochrome system so the cells cannot utilize the oxygen.

3. **Mountain Sickness**

* When a person living on ascends and stays on mountain above 8000 ft. from sea level, he develops certain symptoms in 8-24 hours.

* These symptoms include breathlessness, headache, dizziness, irritability nausea, vomiting, mental fatigue and a bluish tinge on the skin, nails and lips.

* This is known as **Mountain Sickness**.

* The barometric pressure falls progressively with the rise in altitude.

* Simultaneously, Po_2 falls proportionately in the atmospheric air.

* This lowers the alveolar Po_2 and consequently reduces the diffusion of oxygen from the alveolar air to the blood.

* So, oxygenation of blood is decreased progressively with the rise in altitude.

* The fall in oxygenation of blood produces the symptoms of mountain sickness.

4. **Emphysema:** Emphysema is a long-term, progressive disease of the lungs that primarily causes shortness of breath due to over-inflation of the alveoli (air sacs in the lung). In people with emphysema, the lung tissue involved in exchange of gases (oxygen and carbon dioxide) is impaired or destroyed.

* Emphysema is included in a group of diseases called chronic obstructive pulmonary disease or COPD (pulmonary refers to the lungs).

* Emphysema is called an obstructive lung disease because airflow on exhalation is slowed or stopped because over-inflated alveoli do not exchange gases when a person breaths due to little or no movement of gases out of the alveoli.

Classification

* Emphysema can be classified into primary and secondary.

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* However, it is more commonly classified by location into panacinary and centroacinary (or panacinar and centriacinar, or centrilobular and panlobular).

• *Panacinar* (or *panlobular*) emphysema:

* The entire respiratory acinus, from respiratory bronchiole to alveoli, is expanded.

* Occurs more commonly in the lower lobes, especially basal segments, and anterior margins of the lungs.

• *Centriacinar* (or *centrilobular*) emphysema:

* The respiratory bronchiole (proximal and central part of the acinus) is expanded.

* The distal acinus or alveoli are unchanged.

* Occurs more commonly in the upper lobes. **Causes**

* The majority of all emphysema cases are caused by **smoking tobacco**.

* Emphysema cases that are caused by other etiologies are referred to as secondary emphysema.

* In some cases it may be due to **alpha 1- antitrypsin** deficiency.

Other causes of emphysema can be anything that causes the body to be unable to inhibit **proteolytic enzymes** in the lung. This could be exposure to air pollution, second hand smoke or other chemicals and toxins.

5. Deep Sea Sickness

* The deep sea divers generally face this problem when he goes down deep into sea and is lifted rapidly to the surface. The phenomenon is as follows:
As the diver goes deep the water pressure rises which tends to collapse his lungs. Therefore, to prevent it he breaths compressed air at high pressure. But, this high pressure breathing increases the partial pressure of gases in the alveoli. The rise of N_2 (79% in air) pressure affects the body most as it diffuses and dissolves into blood and body fat. Due to this the diver loses strength, work capacity and feel drowsy.

6. Decompression Sickness (or **Bend's disease** or **Caisson's disease** or **Dysbarism)**

* It is more severe than the former if the diver is lifted rapidly to the surface. Due to rapid fall in pressure nitrogen from the tissue evolves as gas bubbles which block the pulmonary vessels causing loss of breath. By blocking the vessels in brain and spinal cord it causes dizziness, mental derangement, paralysis etc. It may block general circulation causing local pains and itching.
* It is, therefore, advised that the divers should be lifted very slowly so that N_2 is evolved slowly and removed from the body effectively without forming bubbles.
* To avoid this problem deep divers use helium-oxygen mixture at high pressure.

7. Carbon-monoxide poisoning

* Hb has 300 times higher affinity for CO than O_2 and combines to form carboxy hemoglobin (HbCO) a relatively more stable compound

  Hb + CO HbCO
* 0.1% CO is sufficient to occupy all Hb in the blood to impair the O_2 transport completely. This is why CO is a deadly poison as person dies of anoxia.
* This generally happens when a person sleeps in closed room with a lamp burning inside. Also in the midst of thick vehicular traffic CO is released in the fume of half burnt fuel.
* Ventilation decreases during sleep and sometimes it is so profound that it causes sleep apnoea even for longer (1 to 2 mts) time.

8. **Pneumonia:** Due to bacterial infection of lungs the surface area of diffusion decreases.

9. **Berylliosis:** Due to thickening of alveolar and capillary membranes, the exchange of gases is hindered

10. **Pneumothorax:** Collapse of lungs due to pressure of thoracic cavity this generally happens due to sneaking of air bubble in this cavity. Also in the midst of thick vehicular traffic CO is released in the fume of half burnt fuel.

11. **Silicosis:** Due to deposition of silica in alveoli, the thickening of alveolar and capillaries membrane occurs. This generally is found in workers of mica mines and brick-kiln factories.

12. **Asbestosis:** Due to asbestos dust or cement dust deposition in the lungs, common among the workers of cement or asbestos factories.

13. **Brancheal Asthma**

* It is difficult breathing, mucous is more secreted in alveoli
* Muscular spasm of smooth muscles of alveoli, bronchiole, and bronchi takes place and cough start to force out mucus outside.

14. Artificial breathing

* In many conditions like drowning, electrocution, CO poisoning etc. the breathing may stop. Then artificial method is applied to ventilate the lung.

15. Mouth-to-mouth method

* Patient is made to lie on the back, neck is raised by applying hand below it to open the air way; nostril is closed and then operator blows air into patients mouth from its mouth to fill the lungs of patient.
* Next the air is allowed to pass out.
* This is repeated 10 -15 times per minute.

16. Atelectasis : Means collapse of alveoli.

* When a bronchus or bronchiole is obstructed, the gas in the alveoli beyond the obstruction is absorbed and the lung segment collapses. Collapse of alveoli is called atelectasis.
* The atelectatic area may range in size from a small patch to a whole lung.
* Some blood is diverted from the collapsed area to better ventilated portions of the lung and this reduces the magnitude of the decline in arterial pO_2.
* When a large part of the lung is collapsed, there is an appreciable decrease in lung volume.
* The intrapleural pressure therefore becomes more negative and pulls the mediastinum, which in humans is a fairly flexible structure to the affected side.
* Another cause of atelectasis is absence or inactivation of surfactant, the surface - tension - depressing agent normally found in the thin fluid lining the alveoli.
* This abnormality is a major cause of failure of the lungs to expand normally at birth.
* Collapse of the lung may also be due to the presence in the pleural space of air (Pneumothorax), tissue fluids (hydrothorax, chylothorax), or blood (hemothorax).

17. Sleep apnoea syndrome (SAS): Persons with snoring habit suffer with sleep apnoea syndrome because their upper respiratory tract closes on inhalation leading to apnoea and sleep breaks.

18. Severe Acute Respiratory syndrome (SARS): Caused by corona virus.

Symptoms : The hallmark symptoms are fever greater than 100.4 degrees F (38.0 degrees C) and cough, difficulty breathing, or other respiratory symptoms.

* Symptoms in the order of how commonly they appeared have included

Fever, Chills and shaking, Muscle aches, Cough, Headache etc.,

Less common symptoms include (also in order):

Dizziness, Productive cough (sputum), Sore throat, Runny nose, Nausea and vomiting, Diarrhea

19. Chronic Obstructive Pulmonary Disease (COPD): Includes emphysema, chronic bronchitis and Asthma

20. Acapnia: It is the conduction of lower concentration of CO_2 in the blood, as a result temporary cessation of breathing occurs.

21. Epistaxis: It is nose bleeding

22. Occupational Respiratory Disorders: In certain industries, especially those involving grinding or stone-breaking, so much dust is produced that the defense mechanism of the body cannot fully cope with the situation.

* Long exposure can give rise to inflammation leading to fibrosis (proliferation of fibrous tissues) and thus causing serious lung damage.
* Workers in such industries should wear protective masks.

23. Asthma: Asthma is a difficulty in breathing causing wheezing due to inflammation of bronchi and brnochioles

Special Respiratory Movements

1. Cough - It is reflex action.

* Stimulation takes place from trachea and lung.
* Centre in medulla oblongata
* It is forcible expiration preceded by prolong inspiration
* In cough air exploded through the mouth.

2. Sneeze

* Reflex action stimulated by olfactory epithelium of nasal chamber
* Air exploded out through mouth and nose both.

3. Yawning

* It is prolonged inspiration due to increase of CO_2 concentration in lung.

4. Hiccough

* It is noisy inspiration due to muscular spasm of diaphragm at irregular intervals.
* Noise is due to sudden sucking of air through vocal cords.

5. Apnea - Absence of breathing
6. Eupnea - Normal breathing
7. Hypopnea - Decrease breathing rate
8. Hyperpnea - Increase breathing rate
9. Dyspnea - Painful breathing

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10. Anoxia - No O_2 in inspired air

11. Hypoxia - Less O_2 in inspired air

12. Asphyxia - O_2 starvation by cells

13. Bronchitis - Inflamation of bronchial tract.

14. Cyanosis - Blueness of skin due to deoxygenated Hb in blood vessel.

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