RESPIRATORY PHYSIOLOGY

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DEFINITION & DIVISIONS OF RESPIRATION

- The term respiration refers to the processes involved in the supply of the tissue cells with O2 as well as the elimination of the produced CO2

- During rest *the O2 consumption in a normal young adult individual averages 250 ml/minute, while the CO2 production averages 200 ml/minute*

- In man the process of respiration is divided into *3 stages*

(1) External respiration (pulmonary respiration)

1- Pulmonary ventilation

- This is the process of aeration (= renewal of air) of the lungs It occurs through the *breathing* movements which include inspiration *and expiration.*

- Such movements occur in cycles called the *breath or respiratory cycles,* each of which consists of *one inspiration and one expiration followed by a short expiratory pause.*

- These cycles result in continuous inflow of air from the atmosphere into the lung's alveoli and outflow of air in the opposite direction

❑Their frequency during rest is normally high in newly born infants (40 per minute or more), but it gradually declines during childhood, and in young adult individuals, *the breathing rate is 12 - 16 per minute.*

B- Pulmonary gas exchange

❑This is the process of O2 diffusion from the alveolar air into the pulmonary capillaries, and the diffusion of C02 in the opposite direction.

(2) Transport of gases (O_2 and CO_2)

- This is carried out by the blood, which transports O_2 from the lungs to the tissues and CO_2 in the opposite direction.

(3) Internal respiration (or tissue respiration)

- This includes the process of gas exchange between the tissue cells and their fluid medium as well as the processes involved in the utilization of O_2 and production of CO_2 by the cells.

THE RESPIRATORY SYSTEM (OR APPARATUS)

- The respiratory system consists of the following structures :

l. The respiratory tract (= the airways or passages) and the lungs.
2. The thoracic cage and respiratory muscles.
3. The nerve centres that control the respiratory muscles, as well as the tracts and nerves that mediate such control

THE AIR PASSAGES (OR AIRWAYS)

- These are divided into *upper and lower parts.*

- The upper passages include the nasal cavities and the 3 *parts* of the pharynx (the nasal , *oral* and laryrngeal parts), while the lower passages include the larynx and the trachea as well as the bronchi and the bronchioles.

The trachea and bronchial tree

- In adults, the trachea is l0-12 cm long and 1.6-2 cm wide.

- The larynx is present at its *upper* end, while at its lower end it bifurcates into 2 large bronchi, one for each lung.

- Each bronchus divides in the corresponding lung into progressively narrower and thinner bronchi, which in turn divide into still smaller tubes called the *bronchioles.*

- This system simulates a branching tree, so it is frequently called the bronchial tree. The bronchial diameter is generally more than 1.5 mm, while that of the bronchioles is less than 1.5 mm

- There are 20-25 (average 23) generations of branching in the bronchial tree. In the first 16 generations, gas exchange does not occur and they only conduct air into and out of the lungs.

- The 16th generation consists of small *terminal bronchioles*, the diameter of which is about 1 mm.

- The terminal bronchioles branch into smaller *respiratory bronchioles*, which have a diameter of about 0.5 mm and occupy the 17th, 18th and 19th generations of the bronchial tree

- Each respiratory bronchiole divides into several *alveolar ducts*. each of which leads to several *atria*.

- The atria conduct *air* to the *alveolar sacs and alveoli* and *all* these parts *occupy* the last 4 generations of the bronchial tree

- The multiple dividing of the bronchial tree greatly increases the cross-sectional area of the small airways *(from 2.5 cm^2 in the trachea to about 11800 cm^2 in the alveoli),* and also results in marked reduction of the air-flow velocity in these airways.

- Functionally, the bronchial tree is divided into 3 zones

1. Conduction zone : This extends from the trachea down to the terminal bronchioles (the 16th generation of the bronchial tree). lt receives blood supply from the *bronchial arteries* (which are branches from the aorta)

- Since no gas exchange occurs in this zone, it is called the *anatomic dead space*

2. Transition zone : This consists of the *respiratory bronchioles* (the l7th, 18th and 19th generations of the bronchial tree)

- lt conducts air and *also allows some gas -exchange* because these bronchioles contain some alveoli in their walls.

3. Respiratory zone *:* This includes the alveolar ducts, atria and alveolar sacs, and it receives blood supply from the *pulmonary arteries.*

- It is the *main site of gas exchange,* which occurs in the alveoli. The latter are *located mainly in the alveolar sacs,* and few are also present in the alveolar ducts and respiratory bronchioles

- The trachea and large bronchi are kept open by *incomplete cartilagenous rings* in their walls.

- There are also cartilagenous plates in the walls of the smaller bronchi, but they become progressively less in the later generations of bronchi, and are almost absent in the bronchioles.

- The walls of the tracheobronchial tree also contain smooth muscle fibres (which are few in the trachea and large bronchi but abundant in the bronchioles, specially the *terminal bronchioles).*

- These muscle fibres *relax by sympathetic stimulation* (resulting in bronchodilatation) and *contract by parasympathetic stimulation* (resulting in bronchoconstriction)

- The inner walls of the tracheobronchial tree are lined by mucous membranes consisting of ciliated columnar epithelial cells (about 200 cilia on each cell).

- In the trachea and large bronchi, these membranes contain *goblet cells* as well as submucosal *mucous & serous glands*, the secretion of which is stimulated by parasympathetic stimulation (but these glands are almost absent in the bronchiolar walls).

- Cilia are present till the beginning of the respiratory bronchioles and they *beat upwards* at a rate of l000- 1200 times/minute (which drives mucus and foreign particles towards the pharynx at a velocity of l0- 16 mm/minute to be eliminated).

- This mechanism is called *ciliary escalator,* and if it is defective e.g. congenitally (= *Kartagener's syndrome*), it leads to chronic sinusitis and recurrent lung infection

THE LUNGS

- The lungs contain the bronchial trees, and their main bulk is made up by the *respiratory zones of these trees* in addition to *a very rich blood supply from both the pulmonary arteries and the bronchial arteries*

- They are formed of *lobes* (3 in the right lung and 2 in the left lung), each of which consists of a large number of *lobules*

- The lung lobule receives one terminal bronchiole, which subsequently divides into several respiratory bronchioles.

- Each respiratory bronchiole then divides into several alveolar ducts, each of which leads to many atria.

- The *alveolar sacs* open at these atria, and their walls are composed entirely of the *alveoli.*

- Each respiratory bronchiole and its related alveolar ducts, atria air sacs and alveoli, constitute *a respiratory unit*

- Normally, there is a thin layer of fluid between the lungs and chest wall in the pleural cavity which *facilitates free sliding* of the lungs on the chest wall

- It also keeps them in close contact with each other (in the same way that 2 moist pieces of glass slide on each other but resist separation)

The lung alveoli

- These are the site of gas exchange in the lungs. There are about *300 million alveoli in both lungs* that have a total surface area of *70-80 square meters,* and the diameter of each alveolus is 0.2-0.3 mm.

- The alveolar walls are formed of *a single layer of flat epithelial cells* that are surrounded by an *extensive network of pulmonary capillaries.*

- Gas exchange occurs across this *alveolo-capillary membrane*, the thickness of which is only about *0. 6 micron which allows easy diffusion of gases.*

- The alveolar epithelial cells are 2 types :

(a) *Type I cells* : These are flat cells that constitute the main lining cells.

(b) *Type II cells (= granular pneumocytes):* These are much less in number and they secrete an important substance called *surfactant*

- The subepithelial tissue contains lymphocytes, plasma cells and mast cells while large phagocytic cells called *dust cells or pulmonary alveolar macrophages (PAM)* are present in the alveolar cavities.

- The pulmonary interstitial tissue contains *elastin and collagen fibres*, which are elastic fibres that allow both distension and recoil of the lungs.

- The alveoli are also lined by *a very thin film of fluid*, and the surface tension that develops in this film resists excessive alveolar distension and increases the recoil forces in the lungs

The pleural sac (pleura)

- Each lung is surrounded by a closed thin serous sac called the pleural sac.

- This sac has 2 layers

(a) An inner layer called the visceral pleura, which covers the surface of the lung.

(b) An outer layer called the parietal pleura, which lines the inner surface of the thoracic cage and the mediastinum, as well as the upper surface of the diaphragm.

- There is a potential space between the 2 layers (= the pleural cavity) the pressure in which is normally negative

- It contains only a thin film of serous fluid, which acts as a lubricant that facilitates the lung movements within the thoracic cavity.

FUNCTIONS OF THE RESPIRATORY SYSTEM

(A) respiratory function

- This is the uptake of *O2* from the surrounding atmosphere and the elimination of CO2 to it. Such function is performed by the *respiratory and transition zones of the respiratory passages*

(B) Non-respiratory functions

(I) The breathing movements (i.e. inspiration and expiration) affect the rate of venous return and lymph flow.

(2) The venous blood is filtered in the pulmonary capillaries, so that no blood clots or other emboli would reach the arterial blood.

(3) By controlling the rate of CO2 excretion, the respiratory system plays a basic role in the *regulation of the acid-base balance*.

(4) The *volatile waste products other than CO2 (e.g. acetone) are excreted via the respiratory system* (more than 250 different volatile substances have been identified in the human breath).

(5) The lungs perform several *metabolic and endocrinefunctions*

(6) The *conducting zone of the respiratory passages* performs the following *non-respiratory functions* :

a- *Perception of smell sensation* by the olfactory mucosa in the nose.
b- *Phonation or vocalization* (by supplying air to the larynx). ·
c- *Regulation of the body temperature* (by *helping heat loss* through water evaporation from the respiratory mucous membranes).
d- Adjusting the air flow resistance (by *controlling the bronchial tone).*
e- Providing *many protective (defense) mechanisms*

THE RESPIRATORY PROTECTIVE MECHANISMS

❑The following *"lung defense mechanisms"* operate together to protect the *delicate alveoli* from both *infection* as well as damage.

(A) Role of the alveoli : Foreign particles that reach the alveoli (e.g. dust and the microganisms less than 2 microns in diameter) are attacked and phagocytosed by the pulmonary alveolar macrophages,

(B) Role of the respiratory passages :

1- Air conditioning : This means humidification of the inspired air and adjusting its temperature to equal that of the body. This process protects the pulmonary epithelium and alveoli from damage that can be produced by too dry and too cold or hot air

2- The bronchial secretion contains *immunoglobulins* which are antibodies that resist infections & maintain the integrity of the resp. mucosa.

3- Trapping and elimination of large foreign particles: Particles more than,l0 microns in diameter are trapped by hair at the nostrils then eliminated by the *sneeze reflex*

- Some of these particles also impact on the *tonsils and adenoids,* which are immunologically-active collections of lymphoid tissue.
- On the other hand, particles 2- 10 microns in diameter stick to the mucus that lines the trachea and bronchi then eliminated by the *cough reflex*

- The nasal and bronchial secretions are directed *towards the pharynx* by the *ciliary movement*, where they are either eliminated outwards in the form of *sputum*, or swallowed (and in the stomach most bacteria are killed by tie HCl secreted *by* the gastric mucosa).

The cough reflex

- This is a protective reflex that is initiated by irritation of the larynx, trachea or bronchi.

- The stimulus excites certain mucosal rapidly-adapting irritant receptors that discharge signals via afferent vagal nerve fibres to the respiratory centres in the brain stem, leading to coughing.

- Coughing starts by a short inspiration (about 2.5 litres of air), then the glottis is closed by the epiglottis and approximation of the vocal cords.

- This is followed by a forcible expiration, which increases the pressure of the trapped air in the lungs to about 100 mmHg.

- The glottis is then suddenly opened, so the air in the lungs is expelled at a high velocity (75-100 miles per hour) which drives the irritant substance out.

- In addition to producing coughing, laryngeal irritation also causes reflex contraction of the laryngeal muscles *(= laryngeal spasm reflex)* which also prevents entrance of foreign or irritant bodies into the trachea.

The sneeze reflex

- This is a protective reflex initiated by irritation of the nasal mucosa.

- The stimulus excites certain *nasal irritant receptors* that discharge signals via *afferent trigeminal nerve fibres* to the respiratory centres in the brain stem leading to sneezing.

- Sneezing starts by a short inspiration followed by a forced expiration while the glottis is kept open.

- The uvula is depressed and the rapidly moving expired It expels the irritant substance in the nasal passages outwards.

Functions of the nose

1- Warming and humidification of the inspired air.
2- Trapping of foreign particles larger than 10 microns in diameter.
3- Initiation of the sneezing reflex.
4-Perception of the sensation of smell

Functions of the larynx

- In addition of being a part of the air passage, the larynx is also concerned with *vocalization or phonation* (sound production).

- This is produced as a result of vibrations of the vocal cords while air is passing out of the lungs by a voluntary expiratory effort, and the pitch of the sound is determined by the frequency of vibration of these cords.

- Such frequency in turn depends on the tightness of the vocal cords as well as their shape and mass of edges.

- All these changes in the vocal cords are produced by activity of the laryngeal muscles, which are voluntary muscles supplied by the vagi nerves.

Metabolic and endocrine functions of the lungs

1- The type II alveolar epithelial cells secrete the *surfactant* for local use.

2- The lungs *synthesize certain substances and release them into the blood* e.g. some prostaglandins, histamine and kallikrein.

3- The lungs partially *remove certain substances* from the blood e.g. serotonin, bradykinin, acetylcholine, norepinephrine and some prostaglandins.

4- The lungs contain *a fibrinolytic system* that lyses blood clots in the pulmonary vessels.

Metabolic and endocrine functions of the lungs

5- *Heparin* is secreted by the mast cells (which are abundant in the lungs).

6- Angiotensin I is converted to angiotensin II mainly in the lungs by activity of the ACE *(Angiotensin-converting enzyme).* This enzyme is located in small pits called *caveolae* on the vascular surface of the pulmonary capillary endothelial cells , and it also *inactivates bradykinin* .

7- VIP (Vasoactive intestinal *polypeptide)* is secreted in the lungs, probably by the *nonadrenergic-noncholinergic nerves* that cause relaxation of the bronchial smooth muscle

The bronchial tone

- The tone of airway smooth muscle is the functional expression of a dynamic equilibrium between various excitatory and inhibitory mechanisms.

- The bronchial tone is produced by activity of the bronchial musculature and its main function is to maintain an equal distribution of ventilation in the lungs.

- It normally shows a circadian rhythm with maximal constriction (i.e. parasymp. activity) at 6 AM and maximal dilatation (i.e. symp. activity) at 6 PM (so asthmatic attacks are more severe at late night and early morning).

- The bronchial muscles receive both symp. and parasymp. nerve fibres as well as nonadrenergic-noncholinergic nerves . The latter produces bronchodilatation and VIP is probably the responsible mediator.

- These muscles contain *muscarinic cholinergic as well as beta 1 & 2 adrenergic receptors (the beta 2 type predominates in humans).*

- Parasympathetic stimulation produces bronchoconstriction and increases the bronchial secretion (by acting on the muscarinic receptors)

- Sympathetic stimulation produces bronchodilatation and decreases the bronchial secretion (by acting on the beta receptors), so the *beta-stimulator drugs are used for relieving acute asthmatic attacks*

- Some nerves in the lungs also contain substance P, which produces bronchoconstriction and increases the secretion of the mucus

❑The following table shows *the various agents that affect the bronchial tone:*

CAUSES OF BRONCHOCONSTRICTION	CAUSES OF BRONCHODILATATION
Cholinergic drugs e.g. **acetylcholine**	Muscarinic receptors blockers e.g. **atropine**
Beta-adrenergic receptors blockers e.g. **propranolol**	Beta-adrenergic receptor stimulators e.g. **isoproterenol and salbutamol**
Histamine and leukotrienes	Vasoactive intestinal polypeptide (VIP)
Tachykinins (specially substance P)	Certain prostaglandins
Cool air and muscular exercise	
Certain irritants and chemicals e.g. SO_2	

ASTHMA

- This is a disease characterized by extremely-difficult breathing due to *airway obstruction.* Its usual cause is *allergic hypersensitivity* to a foreign substance (= antigen or allergen) in air (commonly plant pollens).

- The lungs of the patient contain large amounts of immunoglobulins (Ig) i.e. antibodies against that antigen (specially IgE) that are attached to the mast cells.

- On inhaling the antigen, an antigen-antibody reaction is initiated and causes the mast cells to release substances that cause spasm of the bronchial muscle, localized inflammatory edema in the bronchial walls and secretion of thick mucus

- All these effects lead to bronchial obstruction and increase the airway resistance

- Of these substances are *histamine and slow-reacting substance of anaphylaxis* (the latter is a mixture of *leukotrienes).* In some cases, there is also *deficiency of VIP or excess release of substance P*

- Breathing is difficult *mainly during expiration* because the already constricted bronchioles are also compressed in the deflating lungs.

- The attacks are more severe in the late night and early morning and are *treated by beta adrenergic receptors stimulators and muscarinic receptors blockers* as well as by *anti-histaminic drugs and glucocorticoids* (the latter depress the allergic response)

EMPHYSEMA

- This is a degenerative lung disease characterized by loss of the lung's elasticity and breakdown of the alveolar walls (so the alveoli are replaced by large air sacs).

- Its commonest cause is heavy cigarette smoking. The smoke increases the number of the PAMs (= pulmonary alveolar macrophages), which release a chemical substance that attracts the leukocytes to the lungs, and these secrete

(a) The elastase enzyme, which attacks the elastic tissue in the lungs
(b) O2 radicals, which block the action of a protein in the plasma called alpha 1 antitrypsin that normally inactivates the elastase enzyme.

In about 2 % of cases there is congenital deficiency of antitrypsin 1, and smoking in such cases leads to a severe kind of emphysema early in life

EFFECTS OF SMOKING

1- Predisposition to lung infection and emphysema as well as lung cancer.

2- Irritation and damage of the respiratory mucosal epithelium.

3- Inhibition of the ciliary movement

4- Decreased secretion of the surfactant.

5- Less release of antibodies from the plasma cells.

6- Inefficient gas exchange in the lungs.

7- Delivery of harmful substances into the body specially carbon monoxide.