# RESPIRATORY FUNCTIONS OF LUNGS

# Respiratory Function

*Respiration can be studied under four heads :*

1. Pulmonary Ventilation
2. Gaseous exchange
3. Transport of gasses in the blood
4. Regulatory mechanisms

# NON RESPIRATORY FUNCTIONS OF LUNG

In addition to their functions in gas exchange, the lungs have other functions as well.

- **1.Defence mechanism**
- **2. Functions of Pulmonary Circulation**
- **3. Metabolic and Endocrine Functions of the Lungs**

# DEFENCE MECHANISM

Like the skin ,the lung is exposed to the external environment, the membranes are delicate and need to be kept moist.

Everyday the lungs are exposed to >7000 lit. Of air and its fine tissues req. Protection from the daily bombardment of particles incl. Dust ,pollen,pollutants,viruses,bacteria

The respiratory tract is protected by different mechanisms at its various levels.....

- Physical mechms. Incl. COUGH are imp. In the upper airways.
- The lower airways are served

- By the mucociliary clearance mechanism
- The gas exchange units are protected by surfactant& cellular defenders including the patrolling alveolar macrophages

# PHYSICAL DEFENCES

- The nose is the 1st imp. contributor to the physical defences of the upper airway
  - It comprises a stack of fine aerodynamic filters of respiratory epithelium covering the turbinate bones that remove most large particles from the inspired air.
  - The filtering effect is greatly enhanced by fine hairs in the antr. nares &by mucociliary action which apart from a small area anterior to the infr. turbinates is directed postrly such that trapped particles are swallowed or expectorated.

- During cough & expectoration ,the larynx acts as a sphincter ,which is an essential protective mechanism for the lower airways during swallowing & vomiting.
- Larger particles that penetrate the nose and are deposited by impaction or sedimentation in the main airways are trapped by the lining fluids of trachea & bronchi and cleared by the mucociliary clearance mechanism.(mucociliary escalator)

Mucociliary clearance (2).mp4

- Those smaller particles ,down to a few nm in size ,deposited in the acinar part of the lung are dealt with by the alveolar macrophages

# cough

- Cough is generated in 4 distinct phases
- 1.Inspiration
- 2.Compression of intrathoracic gas against a closed glottis
- 3.Explosive expulsion as the glottis opens
- 4.relaxation of the airways

How Do We Cough The Mechanism of Coughing Cough Reflex Animation Learn Human Body.mp4

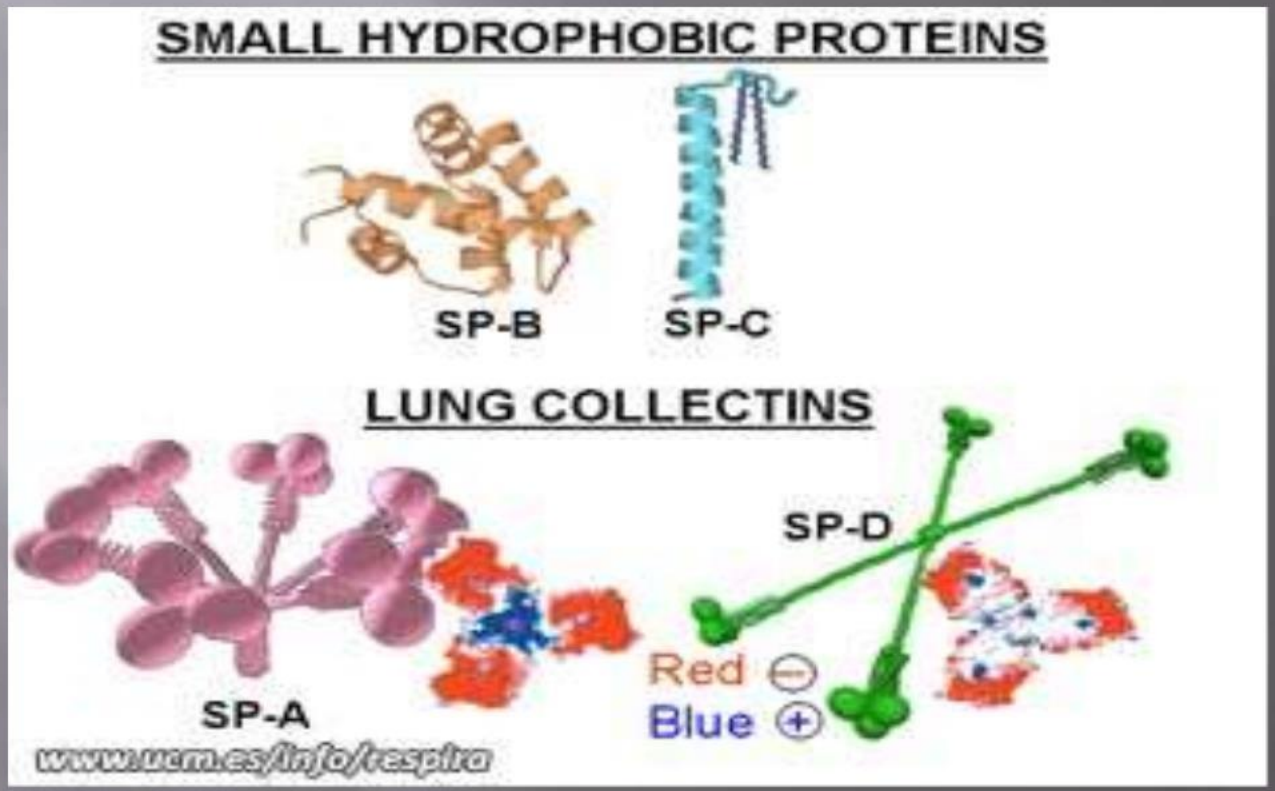
# Mucociliary Escalator

- Its entirely responsible for tracheobronchial cleanliness
  - The mucus forms a raft on the top of the cilia ,which sweep in a cephalic direction
  - Each epithelium lining the bronchi possess about 200 cilia on its surface
  - The cilia beat 12-14 times/sec

# Surfactant

- Complex surface active material lining the alveolar surface that reduce the surface tension
- And prevents the lung from collapsing at resting transpulmonary pressures
- Surfactant also provides a simple but elegant mechanism for alveolar clearance,since at end expiration surfacetension decreases and the surface film moves from the alveolus towards the bronchioles .,thus carrying small particles towards the mucociliary transport system

- Surfactant is synthesised by alveolar type2 pneumocytes
  - Comprises atleast 4 different specific proteins
  - Sp –A,B,C,D
  - These proteins have important roles in host defence
    - Many studies show that surfactant exerts a variety of influences on alveolar macrophages,incl., chemotaxis & enhancement of phagocytosis & kiling of microbes


SMALL HYDROPHOBIC PROTEINS
SP-B
SP-C
LUNG COLLECTINS
SP-D
Red ⊖
Blue ⊕
SP-A
www.ucm.es/info/respira

- Normal surfactant also enhances local pulmonary non specific immune defence mechanism by suppressing the development of specific T lymphocyte mediated immune responses to inhaled antigens and T cell proliferation
- Its also likely that surfactant exerts influences on neutrophil functions incl., neutrophil adherence

# Protective proteins in lung lining fluids

| ANTI bacteraial | ANTI Proteinases |
|---|---|
| Surfactant proteins | Alpha1 proteinase inhibitor |
| Igs esplly IgA | Alpha1 antichymotrypsin |
| defensins | alpha2macroglobulin |
| Lactoferrins,lysozyme | Secretory mucoproteinase inhibitor |
| Complement esplly c3 | ELAFFIN,<br>Tissue inhibitors of metalloproteinases |

# ALVEOLAR MACROPHAGE

- These are derived from blood borne monocytes that originate in the bonemarrow
  - Possess marked phagocytic ability,being able to ingest and destory pathogenic bacteria & particles
  - Able to generate mediators in the initiation of inflammation and to present Ags in the initiation of immune responses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# Functions of macrophage

- Primary host defence-----phagocytosis & killing of microorganisms by oxgen radicals and Nitirc oxide dependent mechanisms and enzymes
- Inflammatory response.....
- Initiation....generation of neutrophil chemokines eg..IL8
- generation of monocyte chemokines eg..MIP-1 alpha
- Generation of agents that activate endothelial cellseg..IL1,TNFalpha
- Generation of acute phase response..IL1,TNFalpha,IL6

- Amplification.....secretion of agents that stimulate bonemarrrow generation of leucocytes...IL1,TNFalpha
- Resolution.....Scavenging of necrotic ,apoptotic cells &debris
- Repair & Fibrosis.....remodelling..elastase&collagenase
- Scar formation...IL1,PDGF,FGF
- Immune response....Ag presentation, Lymphocyte activation

- Anti tumor effects.....lysis of tumor cells by TNFalpha and NO-dependent mechanisms
- Phagocytosis & bacterial killing.....
  - Macrophages can recognize and ingest (via CR3 or FcR receptors) opsonised or non opsonised particles
  - Within the phagolysosome ingested particles are subjected to the combined destructive forces of both reactive oxygen intermediates generated via the metabolic burst and the degradative enzymes that have the capacity to digest proteins,lipids,CHO

Local intracellular generatioon of NO is an imp., defence mechanism against microorganisms

Activated macrophages also form nitrate & nitrite which contribute to antifungal& antiparasitic,tumorocidal activities of macrophages

- Tissue remodelling &repair
- Alveolar macrophages can screte proteins incl.,vitronectin,fibronectin,laminin that are important in tissue repair
- They also secrete growth factor cytokines....PDGF,TGFbeta ,IL1.....all of which influence the behavior of fibroblasts in terms of both proliferation and secretion of collagen and other matrix proteins

# Pulmonary marginated pool of neutrophils

- Unlike RBCs ,upto 1\2 of neutrophils remain in the vascular compartment at any given time are not circulating but form the marginated pool which is in dynamic equillibrium with the circulating pool of vascular neutrophils
- The marginated pool can be released into the circulating pool by exercise or epinephrine
- The vascular bed of the lung &spleen make the most important contributionsto the marginated pool and therefore serve as a souce of rapidly releasable neutrophils in time of stress or injury

- The presence of a large no. Of neutrophils loitering in the pulmonary microvascular bed may be of local advantage in host defence
- Their mobilisation and effectiveness is likely to be augmented in local lung responses to inhaled microbes or toxins and in the generation of local inflammatory response to lung invasion by streptococci
- there may be a downside to the presence of this marginated pool of neutrophils in pulmona microvessels.,they may put the lung particularly risk of developing injury in multiorgan failure

# Maintenance of water balance

- Respiratory tract plays a role in water loss mechanism.
  - During expiration ,water evaporates through the expired air and some amount of body water is lost by this process
- In COPD pts. Expiration is prolonged.....so more water is lost .....l/t dehydration.

# Regulation of body temperature

- During expiration,along with water,heat is also lost from the body.
- Thus respiratory tract plays a role in heat loss mechanism

# Regulation of acid base balance

- Lungs play a role in maintenance of acid base balance of body by regulating the $CO_2$ content in blood
- $CO_2$ is produced during various metabolic reactions in tissues of the body
- When it enters the blood,$CO_2$ combines with water to form carbonic acid
- Since carbonic acid is unstable,it splits into hydrogen and bicarbonate ions
- $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$

- Entire reaction is reversed in lungs when $CO_2$ is removed from blood into the alveoli of lungs
- $H^+ + HCO_3^- \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$
- As $CO_2$ is a volatile gas,it is practically blown out by ventilation.

- When metabolic activities are accelerated ,more amount of $CO_2$ is produced in the tissues
- Concentration of $H^+$ is also increased
- This leads to reduction in pH.
- Increased $H^+$ ion conc., causes increased pulmonary ventilation(hyperventilation)
- By acting through various mechanisms like chemoreceptors in aortic & carotid bodies and in medulla of the brain
- Due to hyperventilation,excess of $CO_2$ is removed from body fluids and the pH., is brought back to normal

# Hemostatic functions

- Lungs contain a fibrinolytic system that lyses clots in the pulmonary vessels

- i.e why breathing exercises (alternate nose breathing) are advised to

DVT,Thromboembolic cases

# Blood volume &pressure regulation

- By renin angiotensin metabolism
- AT2 causes release of aldosterone from adrenal cortex..,which in turn causes Na+ retention,

- AT2 causes vasoconstriction = l/t increased BP

# Biologically active substances met. By the lungs

- Lungs release a variety of substances that enter the systemic arterial blood
- They remove other substances from the systemic venous blood that reach via the pulmonary artery
- Prostaglandins are removed from the circulation,but PG s are also synthesised in the lungs and released into the blood when lung tissue is stretched

- Substances which are synthesised and used in the lungs.....surfactant
- Substances which are synthesised or stored and Released into the blood
  - histamine,
  - kallikrein
- Substances which are partially removed from the lungs PGs, bradykinin, adenine nucleotides,serotonin,norepinephrine, acetylcholine

- Substances which are activated in the lungs
- Angiotensin 1 → angiotensin2

# Angiotensin metabolism

- Large amounts of the angiotensin converting enzyme responsible for this activation are located on the surface of the endothelial cells of the pulmonary capillaries.
- The converting enzyme also inactivates bradykinin
- Circulation time through the pulmonary capillaries is <1sec
- Yet 70% of the angiotensin1 reaching the lungs is converted to angiotensin2 in a single trip through the capillaries

- Four other peptidases have been identified on the surface of the pulmonary endothelial cells,but their physiological role is unsettled.

- Removal of serotonin and norepinephrine reduces the amounts of these vasoactive substancesreaching the systemic circulation
- so that the effect of these stress hormones is decreased

- Many other vasoactive substances pass through the lung without being metabolised
- Epinephrine
- Dopamine
- Oxytocin
- Vasopressin
- Angiotensin2

- Also various amines and polypeptides are secreted by neuroendocrine cells in the lungs

# Briefly.....

## Non respiratory functions:

- alter the pH of blood
- filter out small blood clots formed in veins
- filter out gas micro-bubbles occurring in the venous blood stream(exp. while scuba diving)
- influence the concentration of some biologic substances and drugs used in medicine in blood
- may serve as a layer of soft, shock-absorbent protection for the heart, which they enclose
- protect the body from harmful substances by coughing, sneezing, filtering or swallowing them

# THANK YOU