Non respiratory functions of the respiratory system

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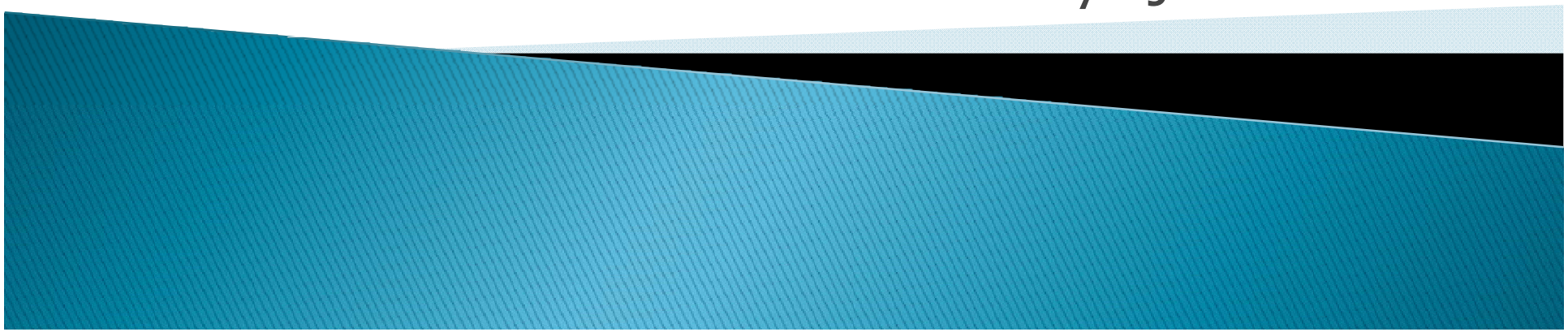
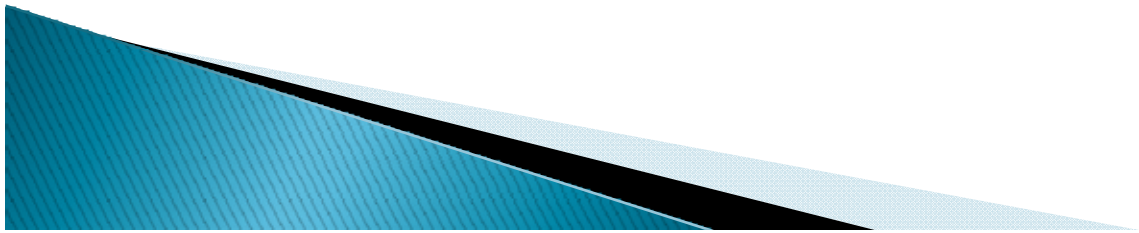


- Earlier concept of lung working only as a bellows
- Research on non respiratory functions of lung
- Lung is part of the body as a whole
- Functions are shared among different organ systems and do not respect artificial anatomical boundaries
- However, some functions are unique



Non-Respiratory Functions Of the Respiratory System

- Olfaction
- Speech
- Heat and water conservation
- Electrolyte transport
- Host defense
- Xenobiotic metabolism
- Surfactant
- Excretion of volatile substances
- Metabolic functions
- Reservoir function
- Filtration

Olfaction

- The olfactory receptors are located in the posterior nasal cavity → person can *sniff* to attempt to detect potentially hazardous gases or dangerous material in the inspired air

- This rapid, shallow inspiration brings gases into contact with the olfactory sensors without bringing them into the lung

Speech

- Speech and language are generated by coordinated activity of the cerebral cortex, the brain stem respiratory drive center, and structural components of the upper airway

- Speech is composed of two mechanical functions:

(1) *Phonation → by the* larynx

(2) *Articulation→ by the* structures of the mouth

- Phonation → purposeful expiration of air through the vocal cords located in the larynx

- Changes in the pitch of sound emitted by the larynx → by stretching or relaxing the vocal cords & by altering the shape and mass of vocal cord edges

- Resonance → added by several structures, including mouth, nose, paranasal sinuses, pharynx, and chest cavity

- Final articulation of sound into language → the lips, tongue, and soft palate

HEAT AND WATER CONSERVATION

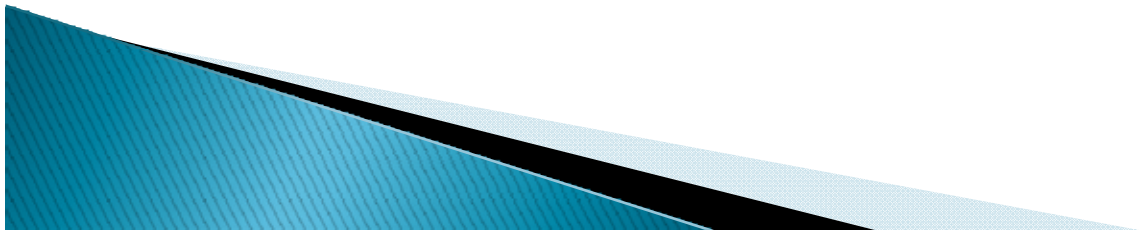
- Countercurrent exchange of heat and water during normal tidal respiration allows conditioning of inspired air while thermal energy and water are conserved during expiration

- Under normal circumstances, tidal respiration results in a net loss of 250 ml of water and 350 kcal of heat from the airways in a 24-hr period

- Net transfer of heat and water depends on temperature and vapor pressure gradients between the airway surface and passing air stream

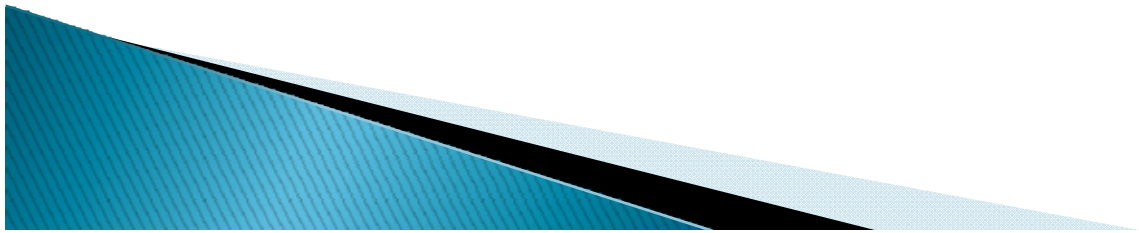
- Low environmental temperatures increase convective cooling of the airway surface; low humidity enhances evaporative cooling of the airways

- The additional heat and water required to condition inspired air raise caloric requirements in cold climates



- Higher flow velocities are associated with lower rates of heat and water transfer to the air stream during inspiration and reduced condensation during expiration

- The respiratory tract has a major role in temperature control in fur-bearing animals; however, it is not thought to affect core temperature regulation significantly in humans under normal circumstances



Electrolyte transport

- Airway epithelia also actively and passively transport electrolytes
- This process is regulated by a variety of hormones
- Anatomically :
  1. Tight junctions
  2. Polarity of the epithelial cells
- ASL depth →5 to 15 µm
- 500 to 1500 nl of ASL / cm^2

Regulation

•Hormones, neurotransmitters, and autocoids regulate the intracellular levels of cAMP

• The epithelia contain receptors for β-adrenergic agonists, prostaglandins, adenosine, and vasoactive intestinal peptide

•The level of [Ca2+] is controlled by bradykinin, substance P, leukotrienes, and nucleotides, such as ATP

Submucosal glands

- located in the submucosal tissue between cartilage plates in trachea and bronchi
- Normally absent from the bronchiolar region

- Functions:
  - the secretion of fluid and electrolytes, which contributes to the periciliary fluid layer and hydration of mucus
  - the secretion of macromolecules that contribute to host defenses in the airways.

Host defense

- ***Each day a surface as large as a tennis court is exposed to a volume of air and contaminants that would fill a swimming pool***

- Respiratory tract is continuously in contact with the external environment → 10,000 L of air is inspired each day

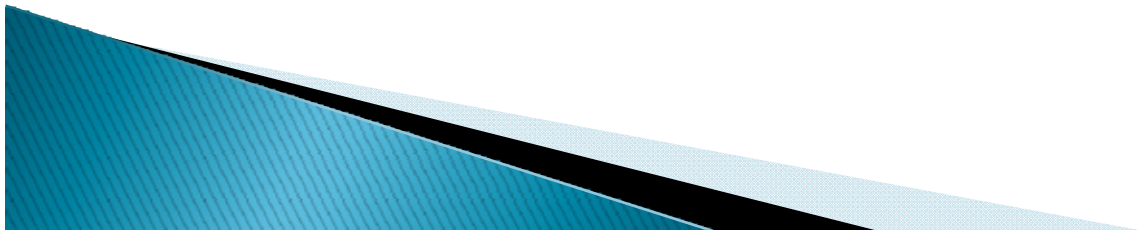
- Defense mechanisms are present throughout and normally keep the lower tract free of infection

Upper respiratory tract

- Nose acts a mechanical barrier
  - Particles are filtered by nasal hair
  - Sneezing/blowing
  - Secretions
- Mouth → sweeping action of tongue
- Oral and nasal secretions contain sIgA and lysozyme

Conducting airways

- Mainly cough and mucociliary clearance
- Branching structure
- Coating of sIgA & antimicrobial factors such as lysozyme, lactoferrin, cathelicidin, and defensins
- BALT – especially present at branching points



Mucociliary clearance

- Airway epithelial cells have multiple cilia on their surface
- These beat rhythmically at a frequency of 20 Hz
- The lining of cilia is uninterrupted from the bronchioles to the larynx

- Covered by a layer of aqueous mucus (5 – 10 μm) which is propelled up by the cilia

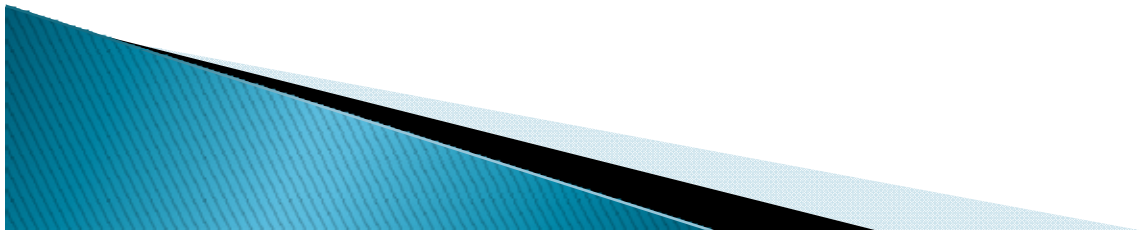
- Mucus with trapped particles → larynx → pharynx → swallowed/coughed out

Respiratory bronchioles

- Transition zone between distal conducting airways and acini
- Last surface to capture airborne particles and microbial or antigenic debris before entering the alveolar space
- Pulmonary brush cells with a tuft of microvilli are found here
  - chemosensing
  - trapping inhaled particles and pollutants
  - with regulating fluid and solute absorption

- Dendritic macrophage-like cells
  - constitute 1 percent of the cells in the surface of this segment
  - capture and process antigens

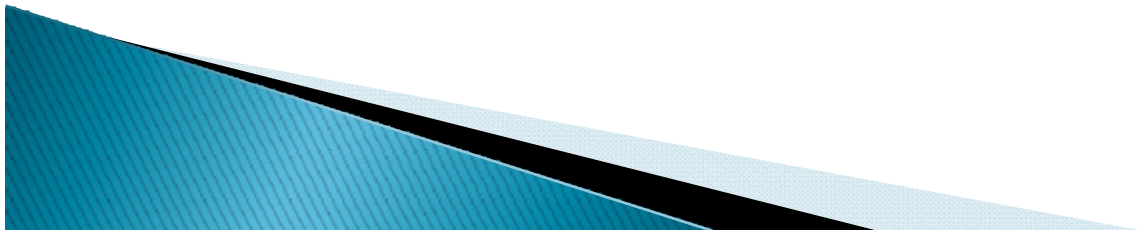
- Lymphatic channels collect the lymphatic fluid from the interalveolar interstitial spaces



Alveolar spaces

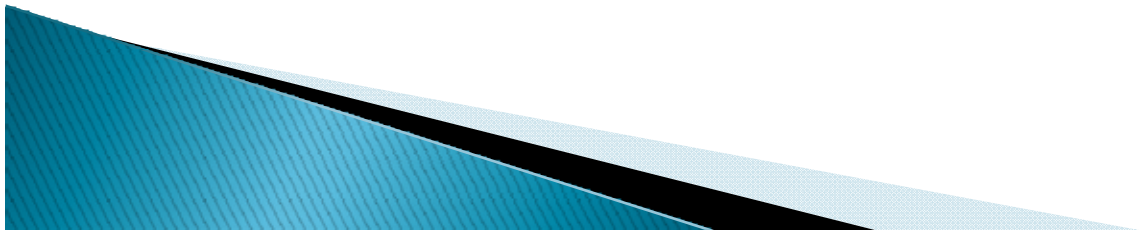
- Normally sterile

- Three levels of defence
  - 1st level →alveolar lining layer
    - Alveolar macrophages
    - SP-A, SP-D
    - Antimicrobial peptides – lysozyme, lactoferrin, defensins, cathelicidins



- 2nd level → interstium
  - Interstial macrophages (histiocytes)
  - Granulocytes
  - Mast cells
  - Dendritic cells – antigen presentation
  - Plasma cells – antibody production

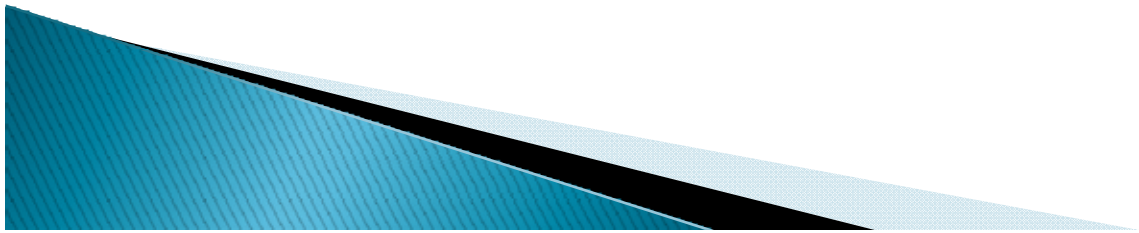
- 3rd level → lymph nodes
  - Prevent particulate material and microbes from entering the blood stream



Macrophages

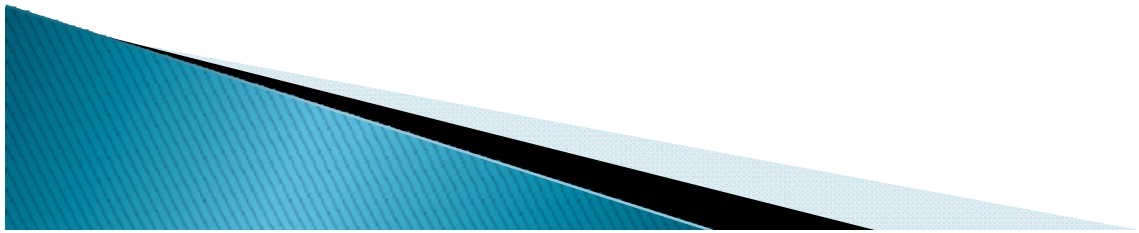
- Ingest inhaled particles or antigens and are then removed on the mucociliary escalator
- Serve as “professional” antigen presenting cells, traveling to regional lymph nodes where they sensitize T and B lymphocytes
- Release a variety of cytokines and biologically active arachidonate metabolites → influence function of T cells, B cells, endothelial cells & fibroblasts
- Ingest microorganisms & kill them → toxic oxygen metabolites and nitric oxide

- Categorized as alveolar macrophages, interstitial macrophages, DCs, Langerhans' cells, blood monocytes, or blood macrophages



Lymphocytes

- Distribution
  - Lymphocytes at the epithelial surface (LES), including those in the bronchoalveolar space
  - Lymphocytes associated with the epithelium in lymphoid aggregates (BALT)
  - Interstitial and intraepithelial lymphocytes
  - Intravascular pool



Bronchial associated lymphoid tissue (BALT)

- Lymphoid nodules occur in the mucosa of large and medium sized bronchi ; concentrated at branching sites

- Covered by flattened, non-ciliated epithelium infiltrated by lymphocytes
- Uncommon in adults; present in children and in chronic inflammation

- B-cells predominate
- May act in concert with other mucosal immune systems as a source of generation of activated immune cells

Xenobiotic metabolism

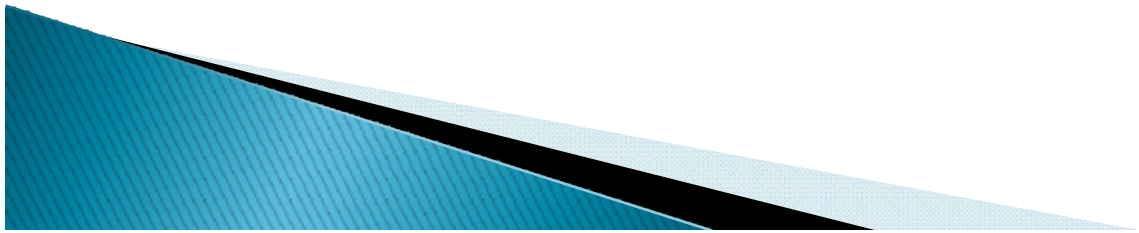
- Xenobiotic metabolism is largely a function of the liver; however, the presence of xenobiotic metabolizing enzymes in the human lung is well documented
- Significant first-pass removal has been demonstrated for propranolol, meperidine, fentanyl, and sufentanil

Surfactant

- Molecular forces create an area of high surface tension at the alveolar surface
- Can lead to alveolar collapse and respiratory failure
- Presence of surfactant reduces the surface tension and prevents lung collapse

- Synthesized by Type II alveolar epithelial cells

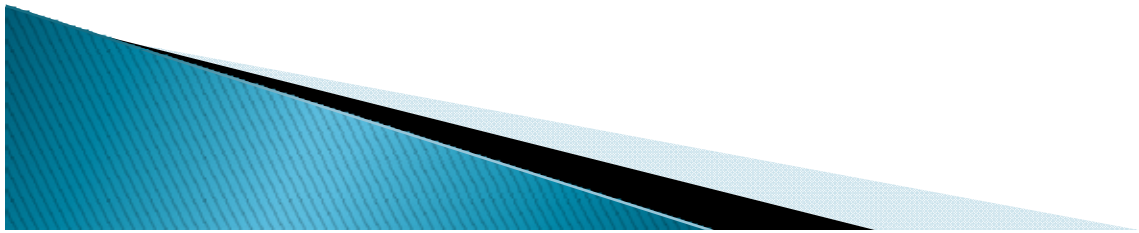
- Phospholipid-protein aggregates
  - Phospholipids → 80 – 90%
    - Phosphatidylcholine → 70 – 80%
    - Phosphatidylglycerol → 10%
    - Others → phosphatidylserine, sphingomyelin, neutral lipids, etc
  - Proteins → 5 – 15%
    - A, B, C & D
    - SP B & C → small, hydrophobic proteins ; critical role in surfactant function



- SP A & D → hydrophilic compounds
  - Weak surfactant activity ; regulation of surfactant structure and aggregation
  - Able to bind complex macromolecules
  - Opsonization
  - Macrophage activation
  - Anti oxidant function

- Forms a layer between the air–fluid interface, reducing the surface tension

- Recycled by Type II cells; 10 – 15% catabolised by alveolar macrophages

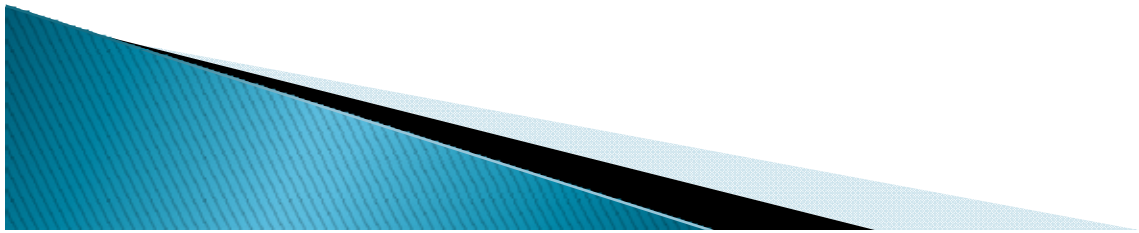


Metabolic functions

- Common to other organs of the body, the lung also metabolizes a variety of substances

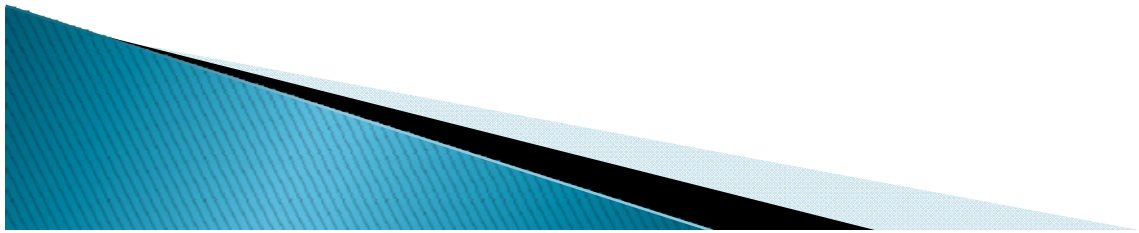
- Occurs in the vascular endothelium

- Vasodilators
  - Prostacyclin
  - NO
- Vasoconstrictors
  - Endothelin
  - Cyclooxygenase products
  - Superoxide ions



Nitric oxide

- Synthesized in the capillary endothelium
- Acts as a pulmonary vasodilator
- Transported by Hb in RBCs to systemic circulation → muscle relaxation



Endothelins (ET)

- ET 1, 2 &3; only ET 1 is produced by endothelium
- Receptors
  - ET A → vascular smooth muscle → vasoconstriction and growth promotion
  - ET B → endothelium → release of prostacyclin/NO → vasodilatation

- Other functions
  - constriction of extravascular smooth muscle
  - mitogenesis
  - release of prostacyclin, NO, ANP
  - bronchoconstriction

Serotonin

- Synthesized in the enterochromaffin cells of the gut from dietary tryptophan
- Mainly removed by the liver; excess by the endothelial cells of the pulmonary circulation
- Vasomotor activity
- Bronchoconstriction
- Platelet aggregation

Reservoir function

- The pulmonary circulation, because of its high compliance and the negative intrapleural pressure, contains 250 to 300 mL blood/m^2
- Adult male → 500 mL
- If left ventricular output is transiently greater than systemic venous return, left ventricular output can be maintained for a few strokes by drawing on blood stored in the pulmonary circulation.

Filtration

- The systemic circulation is protected by the pulmonary circulation from materials that enter the blood

- Particles may enter the circulation
  - natural processes
  - trauma
  - therapeutic measures

- Includes
  - small fibrin or blood clots, fat cells, bone marrow, detached cancer cells, gas bubbles, agglutinated erythrocytes (especially in sickle cell disease), masses of platelets or leukocytes, and debris from stored blood or intravenous solutions

- Destroyed by
  - lytic enzymes in the vascular endothelium
  - ingestion by macrophages
  - penetration to the lymphatic system