# Al-Rasheed University/ Collage of Pharmacy
# Toxicology Lec.(3)
# Toxicity of the respiratory system

**By**

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# TOXIC RESPONSES OF THE RESPIRATORY SYSTEM

- **LUNG STRUCTURE AND FUNCTION**

**1-Nasal Passages**

The nasal passages function as a filter for particles, which may be collected by diffusion or impaction on the nasal mucosa. Highly water soluble gases are absorbed efficiently in the nasal passages, which reach from the nostril to the pharynx .The nasal turbinates thus form a first defensive barrier against many toxic inhalants.

**2-Conducting Airways**

The proximal airways (trachea and bronchi) of humans have a pseudo-stratified epithelium containing ciliated cells and two types of non-ciliated cells: mucous and serous cells.

- Mucous cells (and glandular structures) produce respiratory tract mucus.
- Serous cells produce a fluid in which mucus may be dissolved.

## 3-Gas Exchange Region

- Human lungs are divided into five lobes: the superior and inferior left lobes and the superior, middle, and inferior right lobes.
- The lung can be further subdivided at the periphery of the bronchial tree into distinct anatomic broncho-pulmonary segments, then into lobules, and finally into acini.
- An **acinus** includes a terminal bronchiole and all its respiratory bronchioles, alveolar ducts, and alveolar sacs. An acinus may be made up of 2–8 ventilatory units.
- A **ventilatory unit** is defined as an anatomical region that includes all alveolar ducts and alveoli distal to each bronchiolar-alveolar duct junction

- Gas exchange occurs in the alveoli, which comprise approximately80–90% of the total parenchymal lung volume .Type I and type II alveolar cells represent approximately 25% of all the cells in the alveolar septum.
- Type I cells cover a large surface area (approximately 90% of the alveolar surface).
- Type II cells are cuboidal and show abundant perinuclear cytoplasm, They produce surfactant and, in the case of damage to the type I epithelium, may undergo mitotic division and replace damaged cells.
- human alveolus with a surface area of 200,000–300,000 μm2 contains an average of 32 type I cells and 51 type II cells.
- The mesenchymal interstitial cell population consists of fibroblasts and myofibroblasts that produce collagen and elastin as well as other cell matrix components and various effector molecules. Pericytes, monocytes, and lymphocytes also reside in the interstitium and so do macrophages before they enter the alveoli.

# GENERAL PRINCIPLES IN THE PATHOGENESIS OF LUNG DAMAGE CAUSED BY CHEMICALS

## 1-Toxic Inhalants, Gases, and Dosimetry

- The sites of deposition of gases in the respiratory tract define the pattern of toxicity of those gases. Water solubility is the critical factor in determining how deeply a given gas penetrates into the lung.
- Highly soluble gases such as $SO_2$ do not penetrate farther than the nose unless doses are very high.
- Relatively insoluble gases such as ozone and $NO_2$ penetrate deeply into the lung and reach the smallest airways and the alveoli.
- Very insoluble gases such as CO and $H_2S$ efficiently pass through the respiratory tract and are taken up by the pulmonary blood supply to be distributed throughout the body.

- **2-Particle Deposition**
- Particle size is usually the critical factor that determines the region of the respiratory tract in which a particle or an aerosol will be deposited. Particle surface area is of special importance when toxic materials are adsorbed on particles and thus are carried into the lung.
- Large particles (larger than 5 μm) are usually trapped in the upper respiratory tract, whereas smaller particles (0.2–5 μm) can be transported to the smaller airways and the alveoli.

- **Particle Clearance**
- The clearance of deposited particles is an important aspect of lung defense. Rapid removal lessens the time available to cause damage to the pulmonary tissues or permit local absorption.
- The only mechanisms by which deposited particles can truly be removed from the upper respiratory system are coughing and blowing of the nose.

- **Pulmonary Clearance:**
- There are several ways by which particulate material is removed from the lower respiratory tract once it has been deposited:
- 1. Particles may be directly trapped on the lining layer of the conducting airways by impaction and cleared upward in the tracheobronchial tree via the mucociliary escalator.
- 2. Particles may be phagocytized by macrophages and cleared via the mucociliary escalator.
- 3. Particles may be phagocytized by alveolar macrophages and removed via the lymphatic drainage.

- 4. Materials may dissolve from the surfaces of particles and be removed via the bloodstream or lymphatics.
- 5. Small particles may directly penetrate epithelial membranes minutes after particles are inhaled, they may be found in alveolar macrophages.

- Insoluble particles, especially long narrow fibers, may be sequestered in the lung for very long periods, often in macrophages located in the interstitium.