Al-Farahidi University
Pharmacy college
3rd stage

pathophysiology LEC.8

Pulmonary disorders

Assistant lecturer

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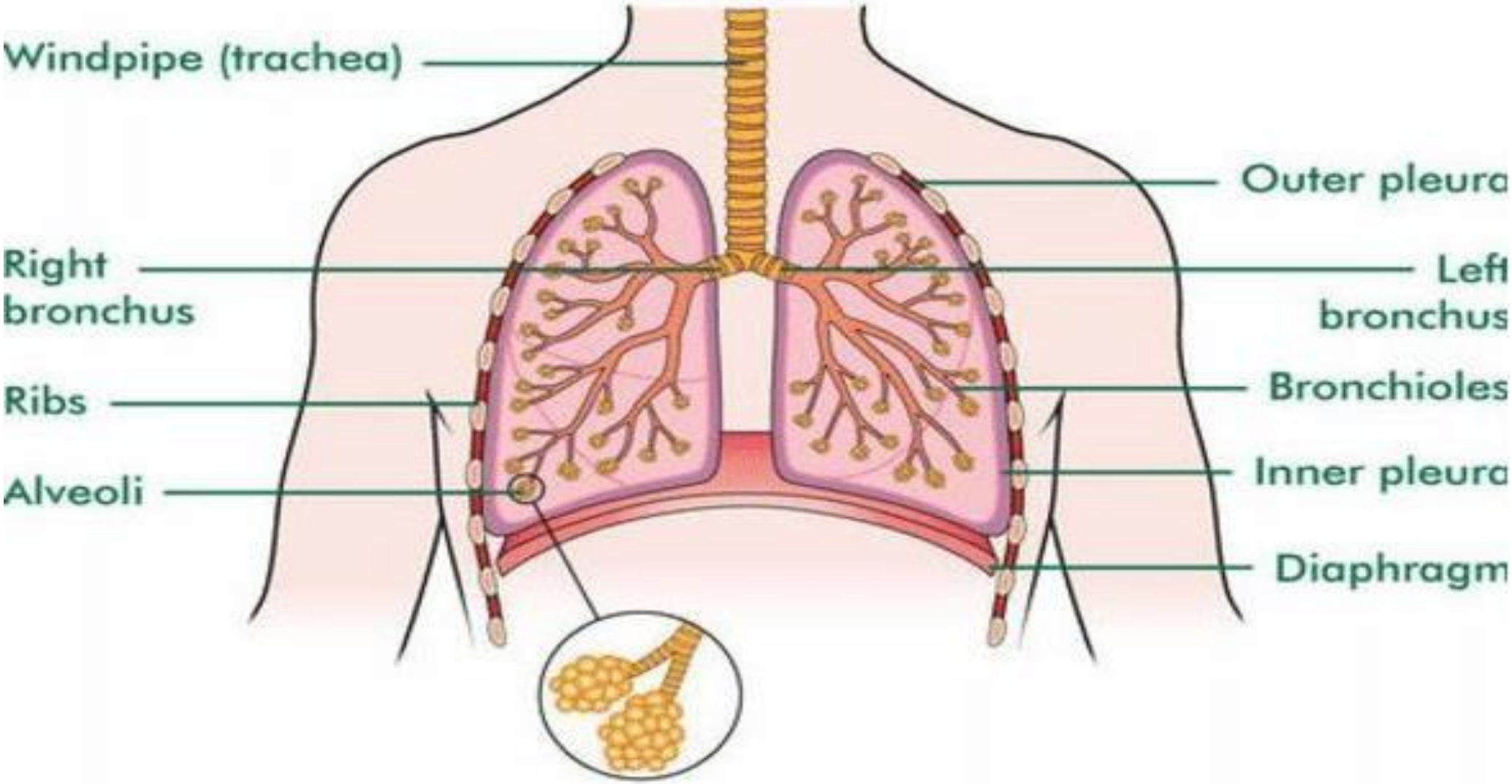
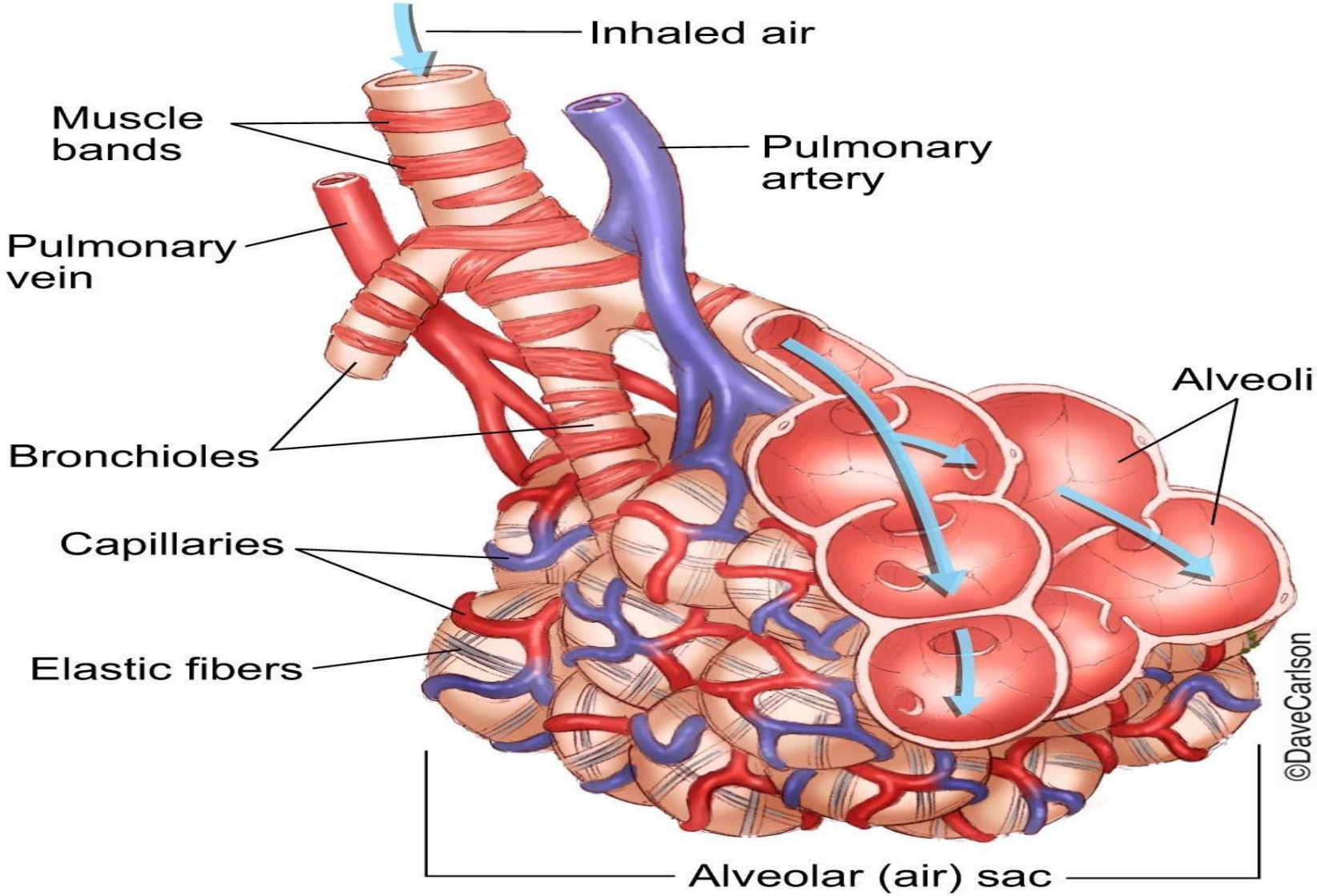
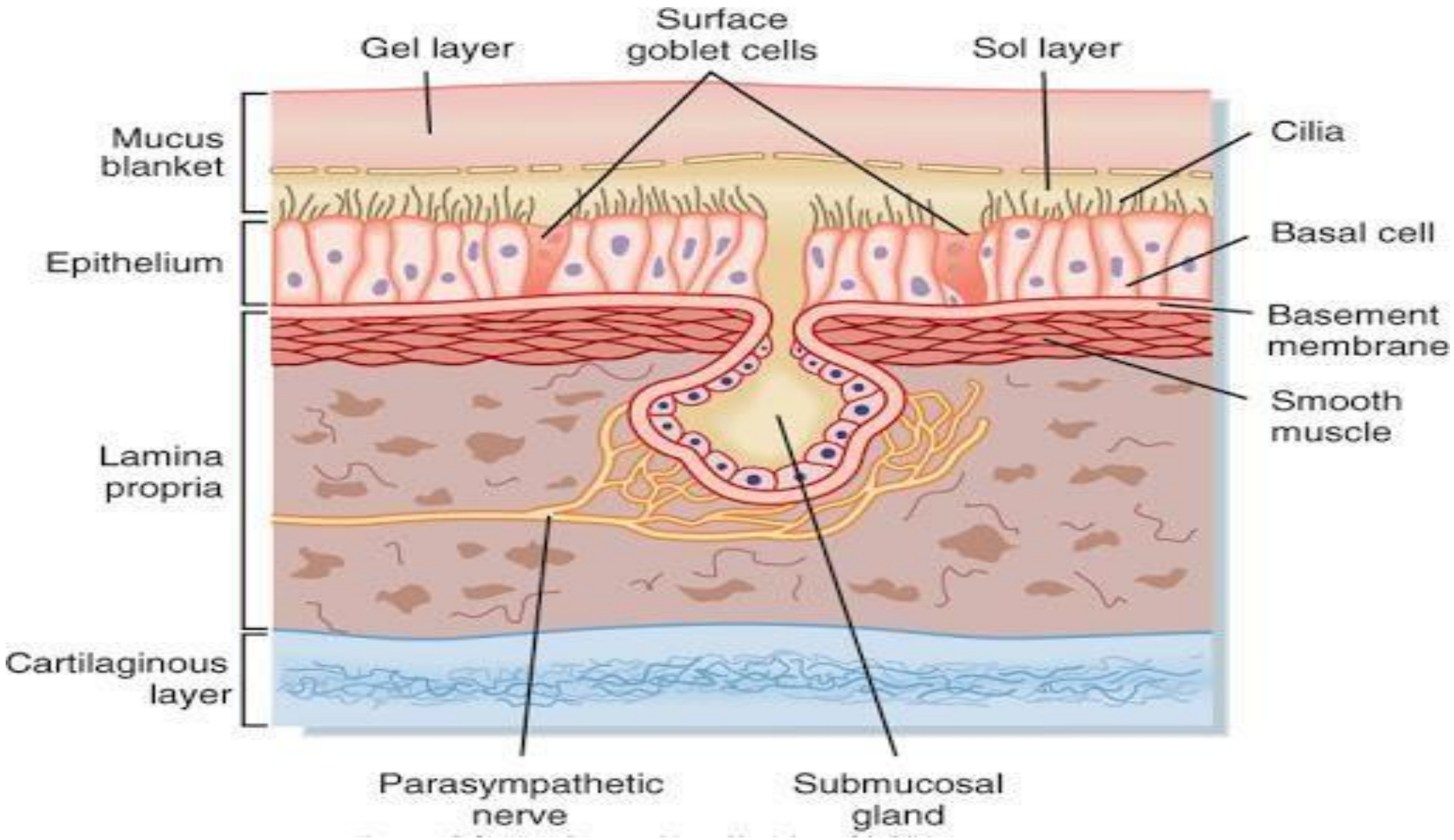
Lung structure



Alveoli structure



Histological structures of bronchi



Pulmonary disorders

Obstructive pulmonary diseases	Restrictive pulmonary diseases
Disorders of large and small airways	Normal airways but other diseases restrict the lungs
Deficit in exhalation(expiration)	Deficit in inhalation(inspiration)
Asthma, bronchitis, emphysema	Fibrosis, pulmonary edema, neuromuscular diseases
Can be diagnosed by spirometer Forced Expiratory Volume(FEV1)	Can be diagnosed by spirometer Total Lung Capacity(TLC)

Pulmonary diseases

1-Diseases of airways (COPD , ARDS)

2-Infectious Diseases of the lung tissue (eg. pneumonia, bronchitis)

3-Diseases of pulmonary vessels (pulm. Embolism, thrombosis, hemorrhage, and pulm. Hypertension).

- **Diseases of Airways (COPD , ARDS)**

A- Chronic Obstructive Pulmonary Diseases (COPD)

1- Emphysema

2-Chronic bronchitis

3-Asthma

3-Bronchiectasis

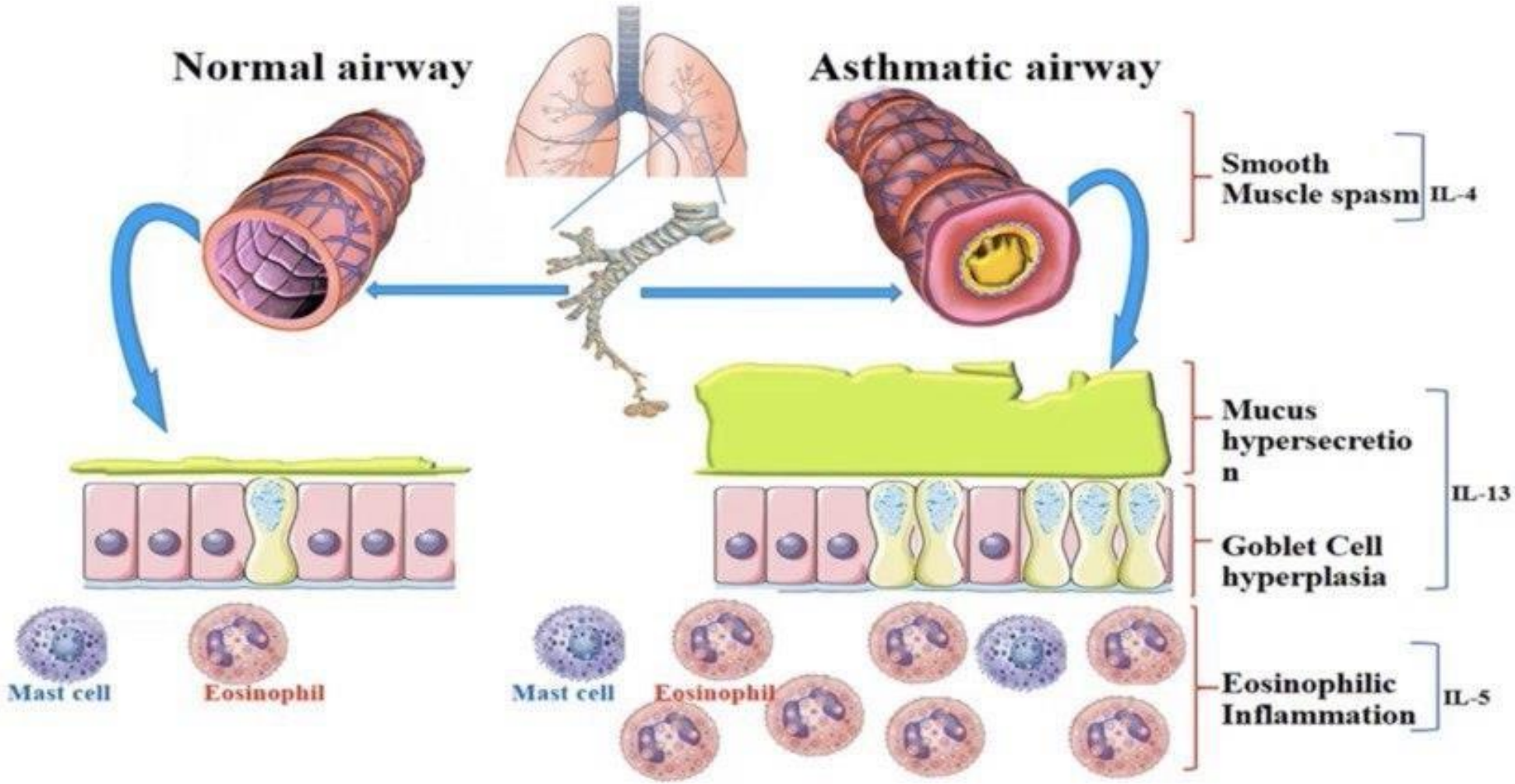
Bronchial asthma

- It is **chronic inflammatory** airway disease. It is characterized by

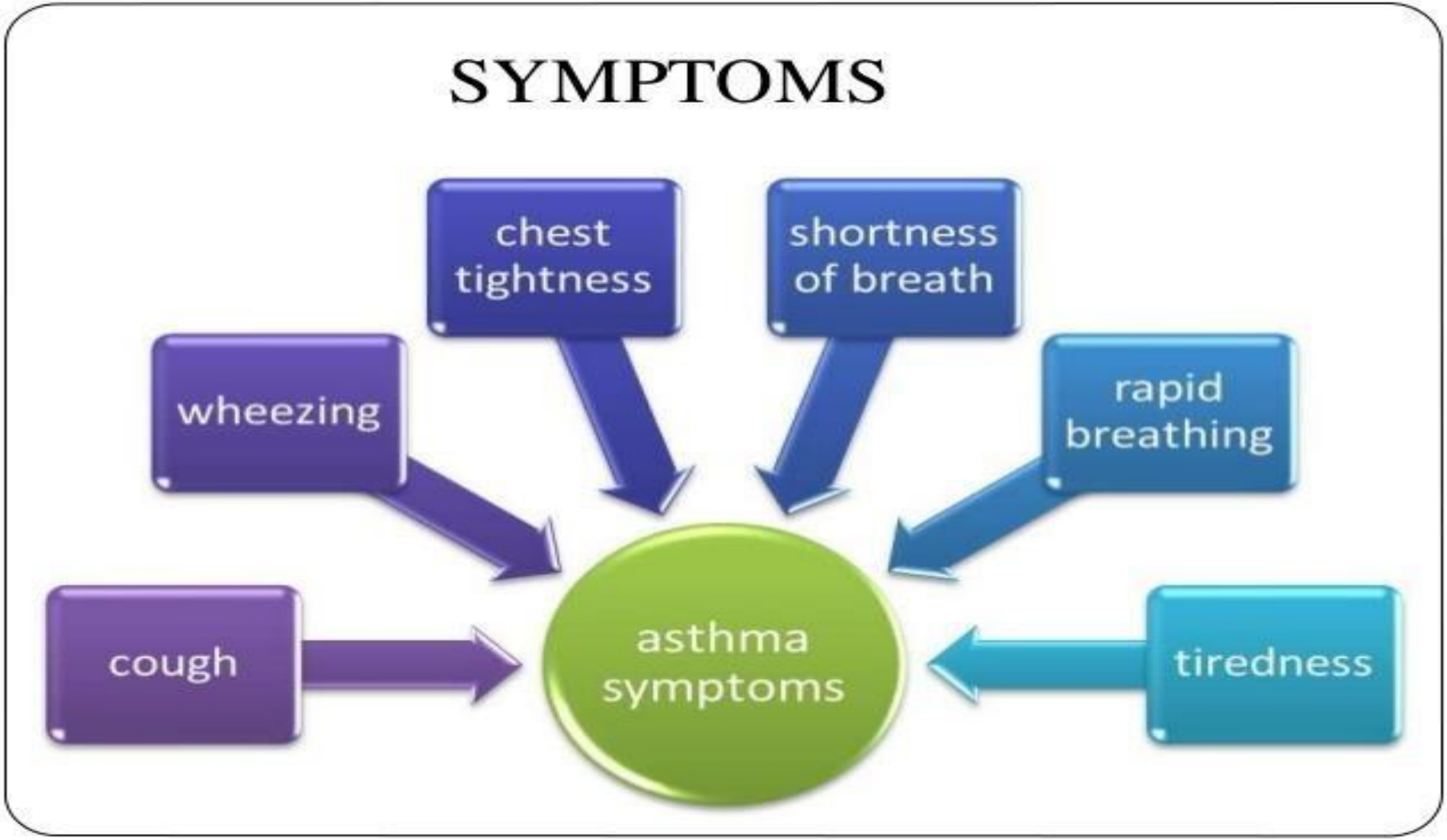
1- Airflow limitation which is usually **reversible** spontaneously or with treatment.

2-Airway hyper-responsiveness to a wide range of stimuli.

3-Bronchial inflammation with T-lymphocytes, mast cells, eosinophils with associated plasma exudation, odema, smooth muscle hypertrophy, matrix deposition, mucus plugging and epithelial damage.


Normal airway
Asthmatic airway
Smooth Muscle spasm
IL-4
Mucus hypersecretion
Goblet Cell hyperplasia
IL-13
Eosinophilic Inflammation
IL-5
Mast cell
Eosinophil
Mast cell
Eosinophil

SYMPTOMS

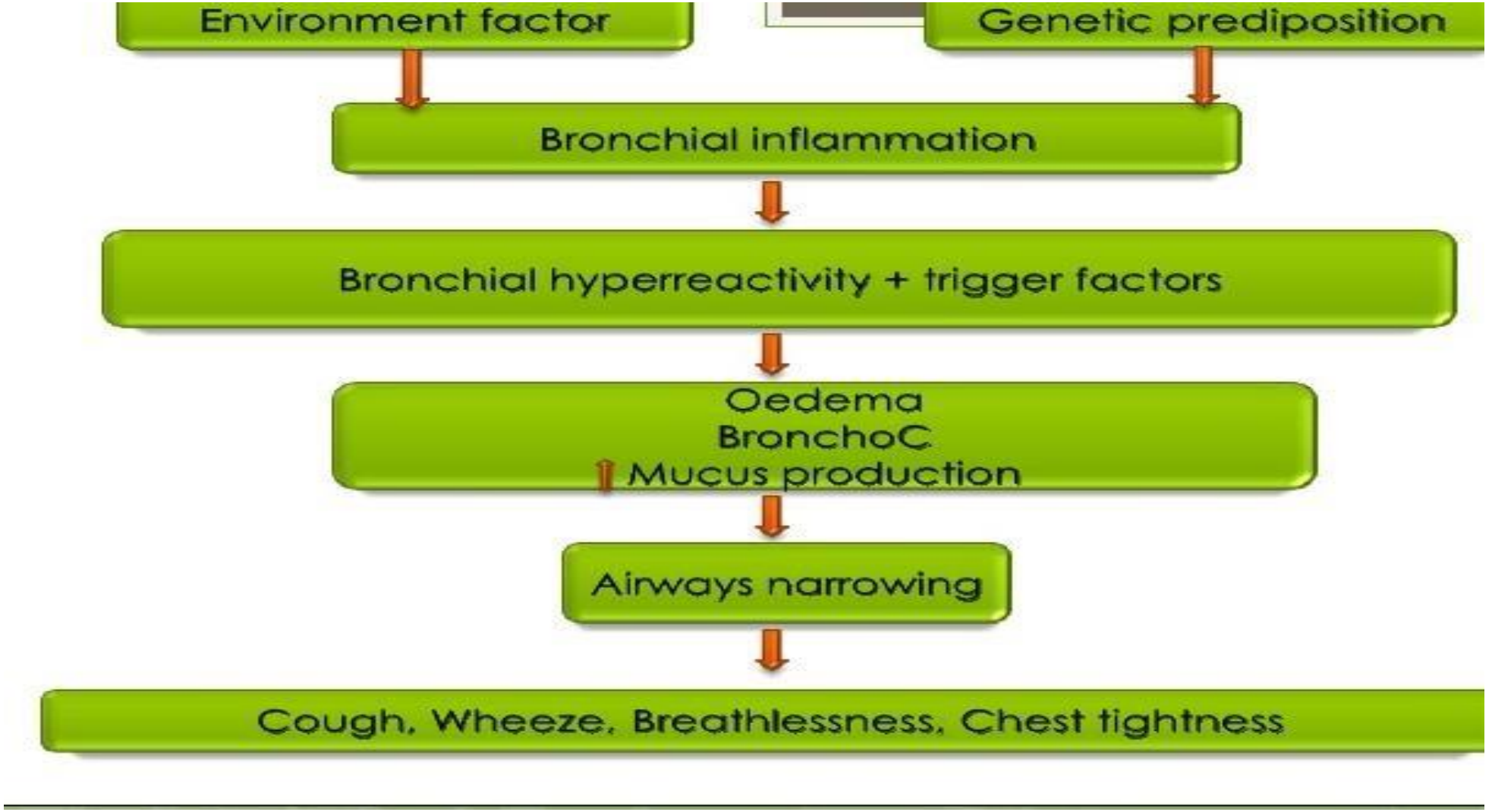

chest tightness
shortness of breath
wheezing
rapid breathing
cough
asthma symptoms
tiredness

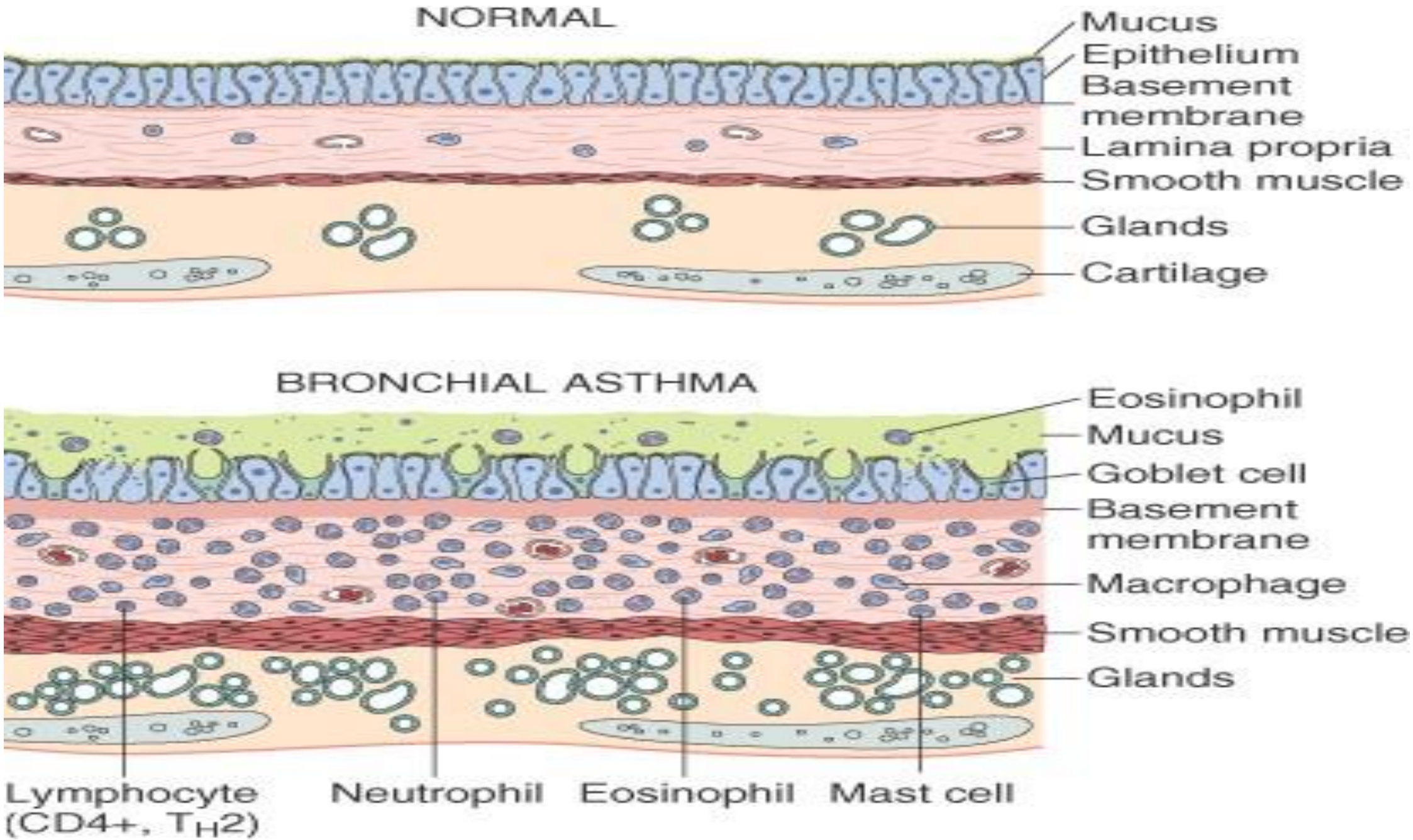
Types of asthma

- **Atopic or extrinsic**(type I hypersensitivity to environmental antigens such as pollen, dust----). It is IgE mediated. It begins in the childhood.
- **Non-atopic or intrinsic** (irritant mediated)non-immune. Triggers include environmental factors such as cold weather, exercise, aspirin, stress, upper respiratory tract infections. Starts at adulthood.

Asthma Triggers

Pathogenesis of asthma




NORMAL
Mucus
Epithelium
Basement membrane
Lamina propria
Smooth muscle
Glands
Cartilage
BRONCHIAL ASTHMA
Eosinophil
Mucus
Goblet cell
Basement membrane
Macrophage
Smooth muscle
Glands
Lymphocyte (CD4+, TH2)
Neutrophil
Eosinophil
Mast cell

Chronic obstructive pulmonary disease(COPD)

- COPD is **Irreversible** disease characterized by the presence of airway obstruction that cause breathing difficulties. It includes

1- Chronic bronchitis(long term inflammation of the airways).

2- Emphysema(damage to the air sacs in the lungs).

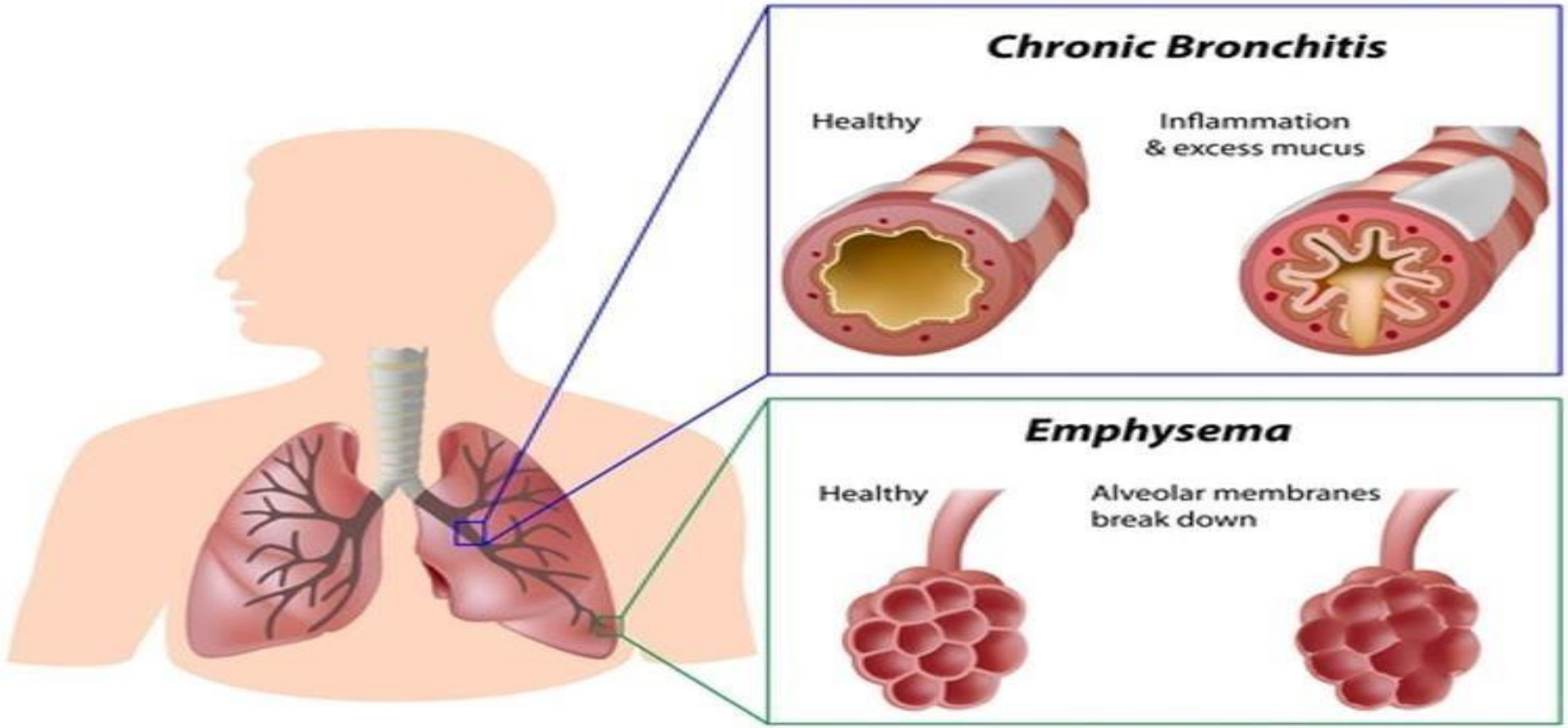
Etiology

1 Smoking

2 Upper airway infections

3 Alpha 1 Antitrypsin deficiency.

COPD


Chronic Bronchitis
Healthy
Inflammation
& excess mucus
Emphysema
Healthy
Alveolar membranes
break down

Emphysema

It is an abnormal **permanent** enlargement of the air space distal to the terminal bronchiole with **destruction** of their wall, there is **NO** fibrosis.

Types of emphysema

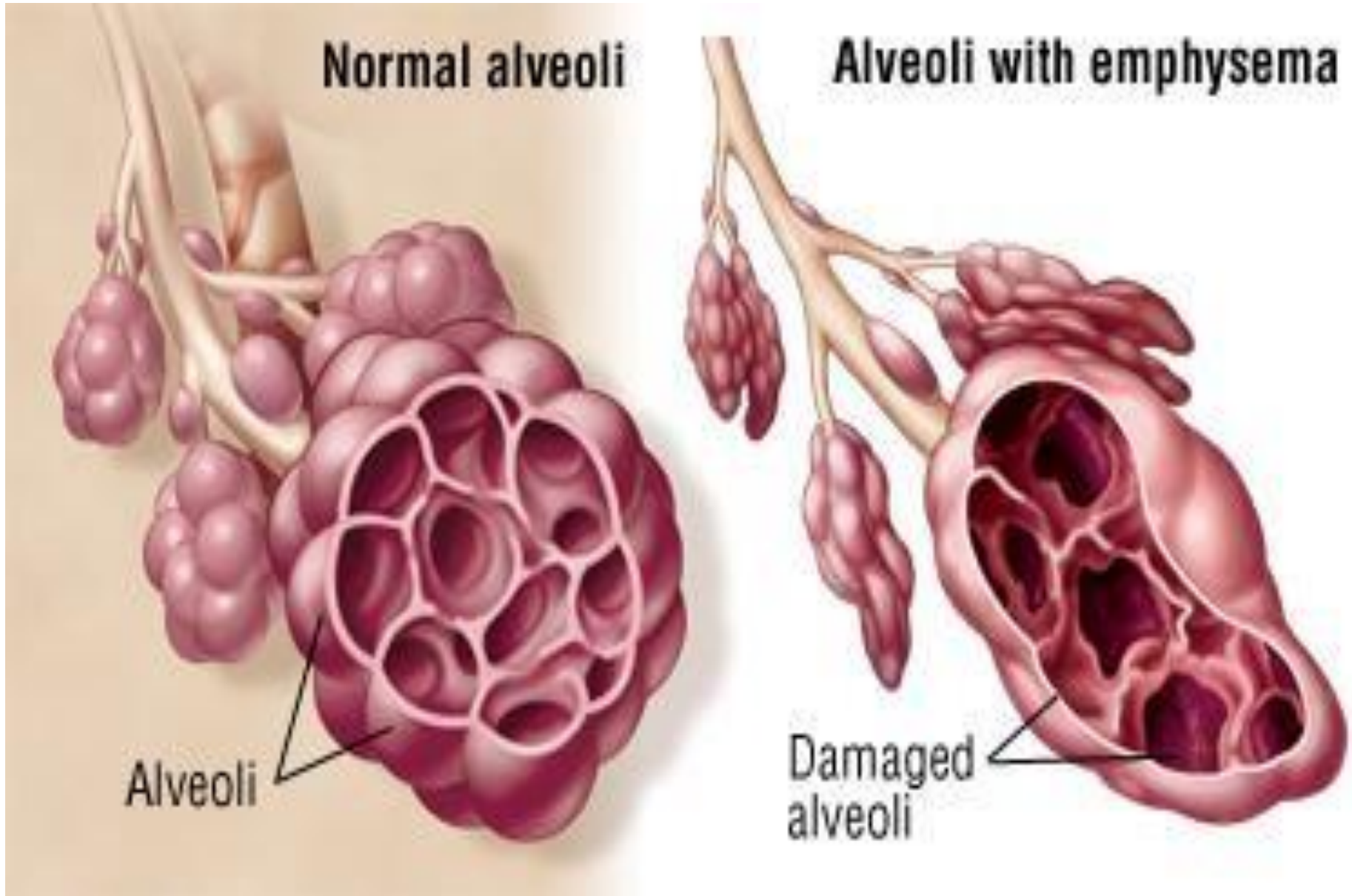
1-Centriacinar emphysema (centrilobular)

-It is the **most common** type.

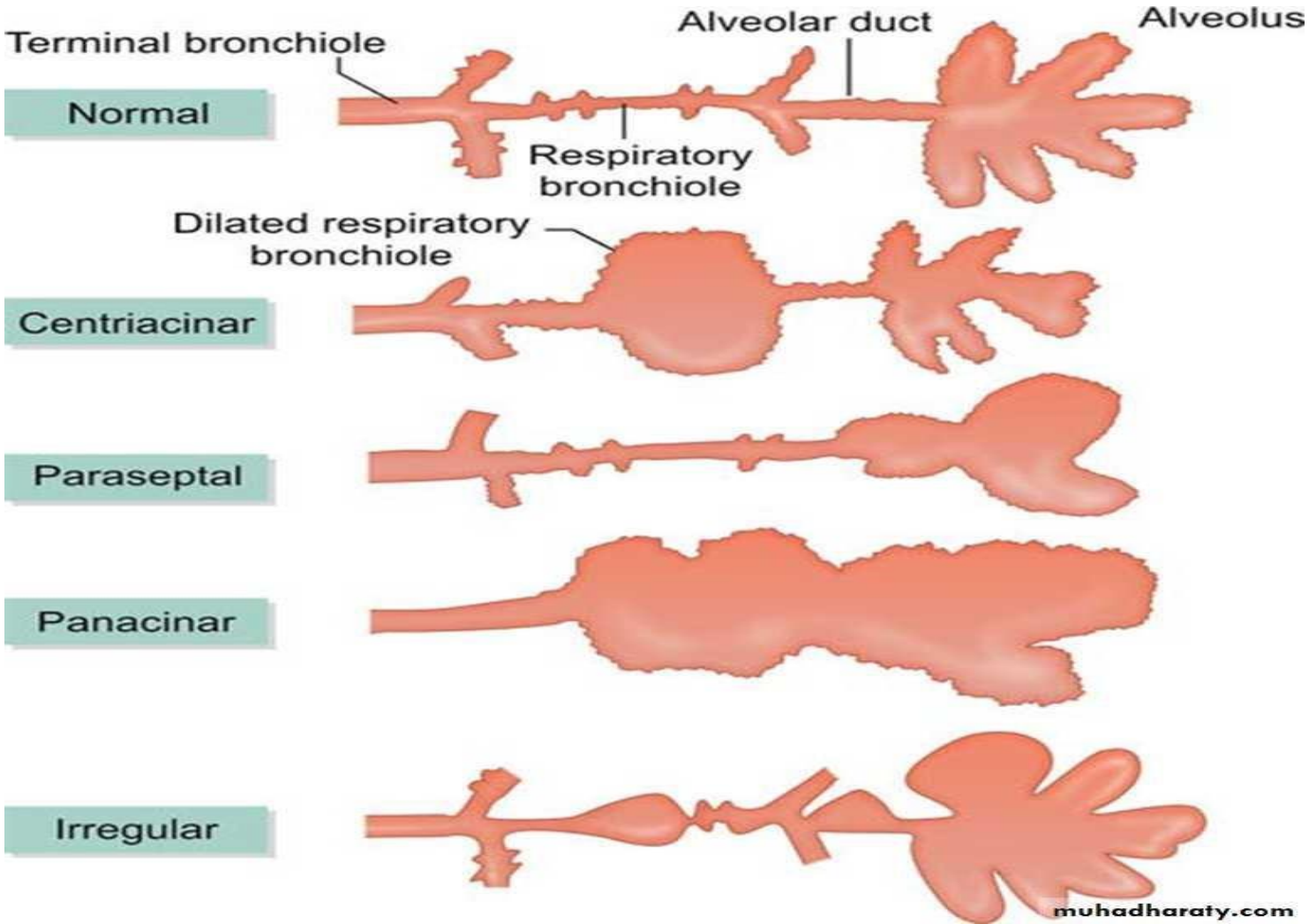
-Occur in heavy smokers.

-The dilatation includes the **respiratory bronchiole only,** while the distal alveoli are spared

-Affects the upper lobe mostly.


Normal alveoli
Alveoli with emphysema
Alveoli
Damaged
alveoli

Types of emphysema



2-Panacinar emphysema

- → The **Whole acinus** is uniformly dilated.
- → Affects the lower zones mostly.
- → Associated with anti elastase deficiency e.g. α-1 atni-trypsin deficiency.

3 Distal acinar (paraseptal) emphysema

-Only the **distal part of the acinus** is involved

-The common site is that adjacent to the **pleura** and lobular connective tissue septa.

-It causes the formation of multiple cysts (0.5cm- 2 cm) that may rupture and → spontaneous **pneumothorax** in young adult.

4 Irregular Emphysema

-The acini are **irregularly** involved.

-Associated with scaring following a healed inflammatory process.

Pathogenesis of emphysema

- The key role in the whole process is:
- **Proteases (elastase)--- Anti-protease** (α-1 ati-trypsin) imbalance.
- **Proteases**: are enzymes which digest the tissue.
- **Anti-proteases**: are the counteracting enzymes that **stop** the action of digestion.
- **Normal persons have a balance between the two enzymes.**

▪The main **cellular elastase** (protease) is secreted from the **NEUTROPHILS**, it is capable to digest human lung if not inhibited by the anti-elastase enzyme e.g. (α-1 anti-trypsin).

- The **free radicals** released from the neutrophils can inhibit the release of this α-1 atni-trypsin.

Other sites that release proteases:

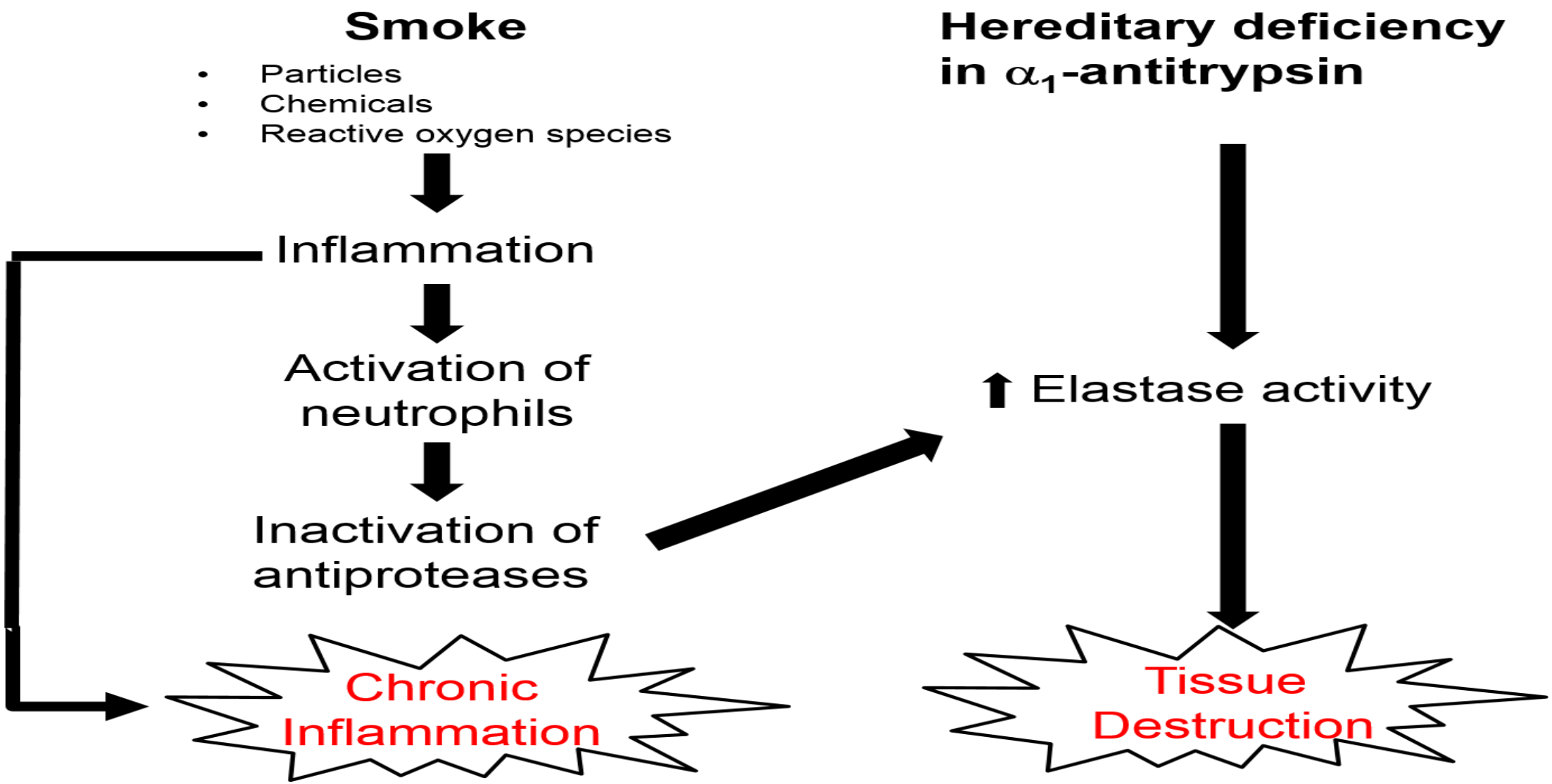
- Macrophages, Bacteria, Mast cell, Pancreas.

- ***So the Development of emphysema occurs:***

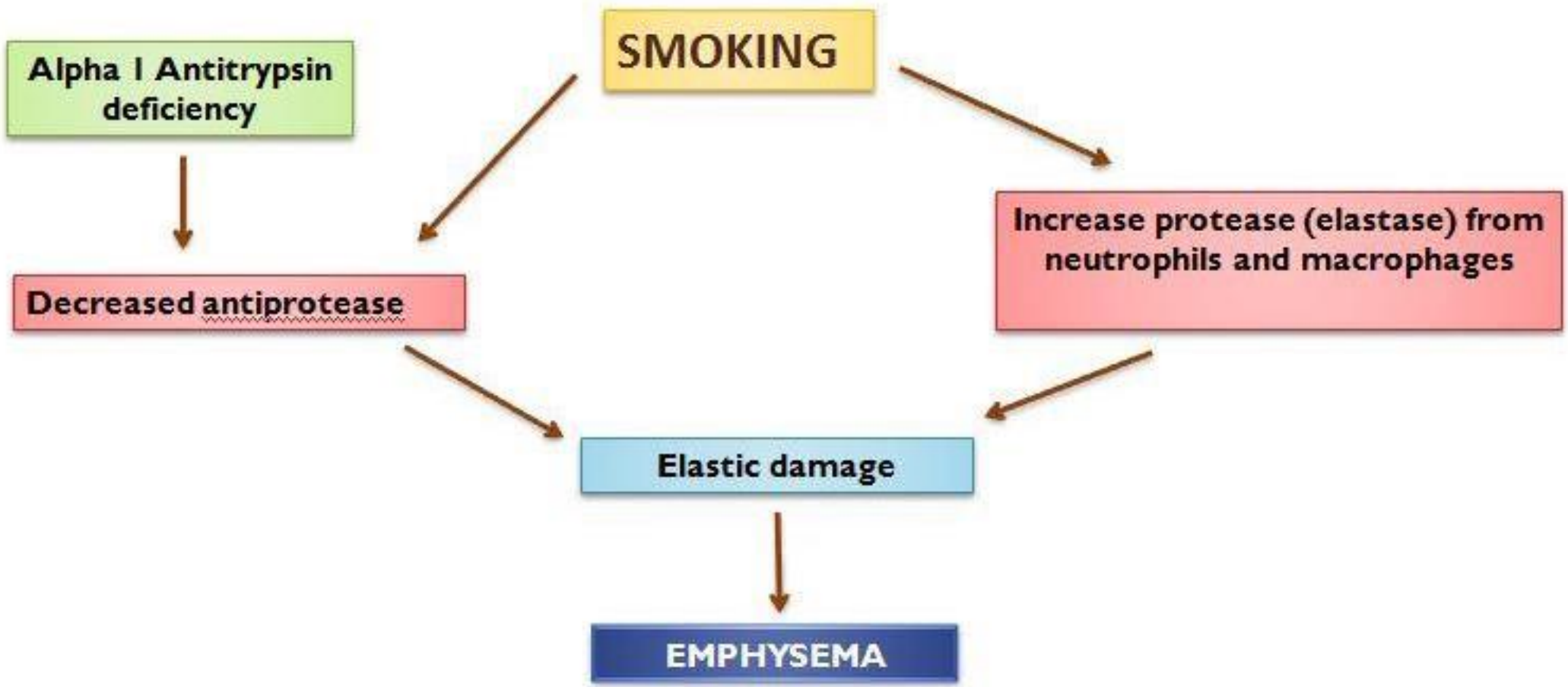
1-When there is increase in ***elastase activity*** as in smoking.

2-When there is decrease in ***anti-elastase activity*** as in :

- **-Hereditary** α-1 anti- trypsin deficiency.
- **-Acquired** as in smokers due to the effect of nicotine, O2 free radicals that inhibit the release of anti-elastase.


Smoke
Particles
Chemicals
Reactive oxygen species
Inflammation
Activation of neutrophils
Inactivation of antiproteases
Chronic Inflammation
Hereditary deficiency in α_1-antitrypsin
Elastase activity
Tissue Destruction

Pathogenesis of emphysema



Bronchitis

- **Acute bronchitis**: It is short illness that usually lasts for few days or weeks(1-3).
- Main causes are: Viral or bacterial infection.
- **Chronic bronchitis**: It is a serious ongoing illness that lasts longer than 3 months.
- Main causes are: Smoking, air pollution, and chemical fumes.

Chronic bronchitis

It is a clinical term characterized by productive cough (cough +sputum) for at least 3 months in at least 2 consecutive years.

Pathogenesis:

1**- Chronic irritation** by smoking leading to **hyper secretion of mucous** in the **large** airways (trachea & bronchus). Prolong irritation leads to hypertrophy of mucous gland a**nd marked increase** in mucin secreting goblet cells of small airways (small bronchi & bronchioles).

2. Inflammation with infiltration of CD8 T lymphocytes, macrophages and neutrophils.

3.Microbial infection: which is often present but has a secondary role in pathogenesis but responsible for maintaining the inflammation and augment the clinical signs and symptoms..

- Although other environmental irritant may provoke irritation, smoking still the single most common cause).

Symptoms of bronchitis

Wheezing

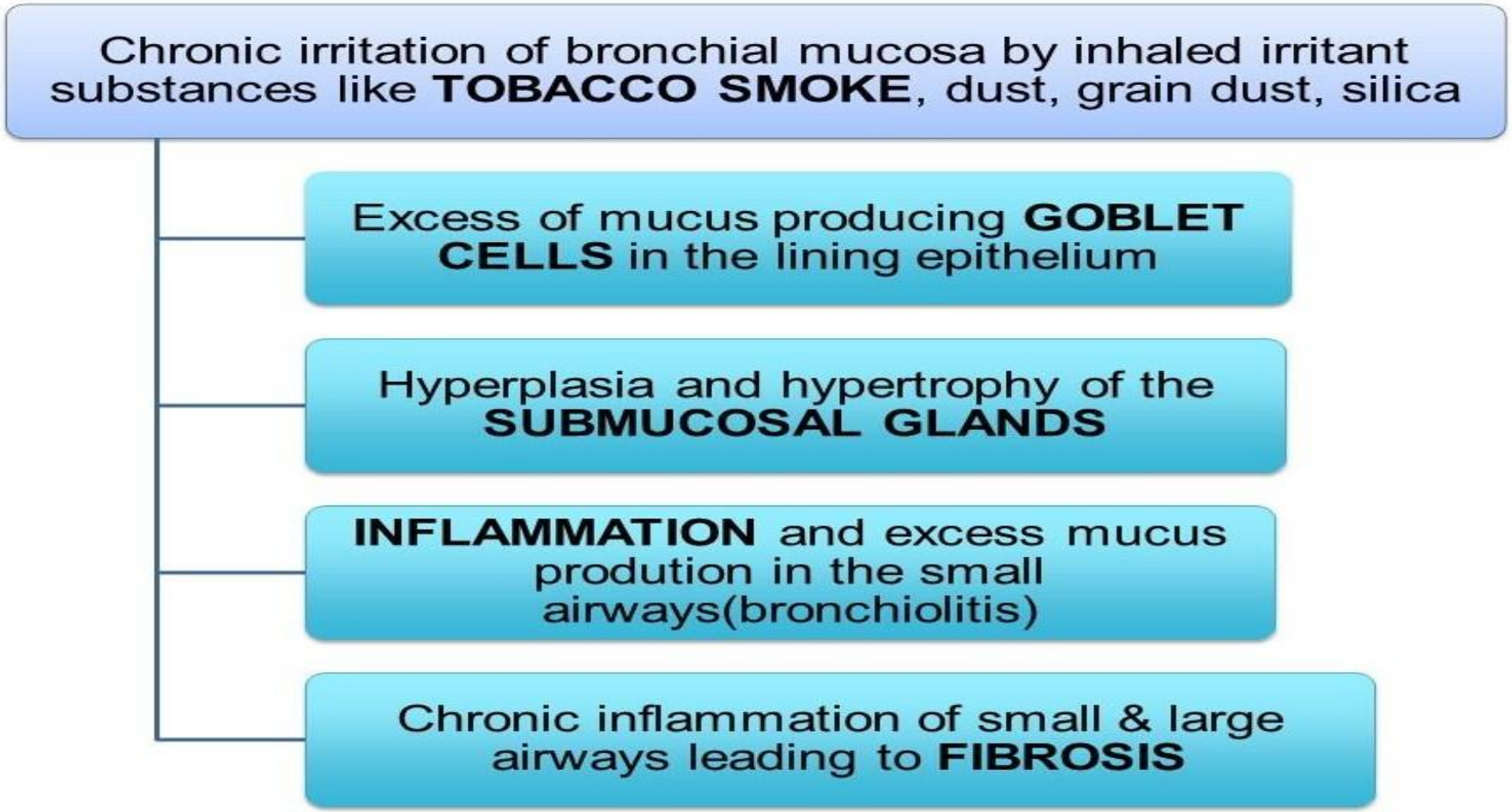
Cough with yellow or green mucous

Chest tightness,

Shortness of breath

Low fever

Pathogenesis of chronic bronchitis



Infectious Diseases of the Lung Tissue

- ***Pulmonary infection***: it includes upper and lower respiratory tract infection.

1.Upper respiratory tract infection URTI include(common cold, flu, sinusitis, laryngitis,…..

2. Lower respiratory tract infection LRTI:

a) include infection of airways from trachea and below

b) infection of lung parenchyma (pneumonia)

- Acute LRT infectious diseases include ***pneumonia***. ***lung abscess*** and ***fungal infections***.

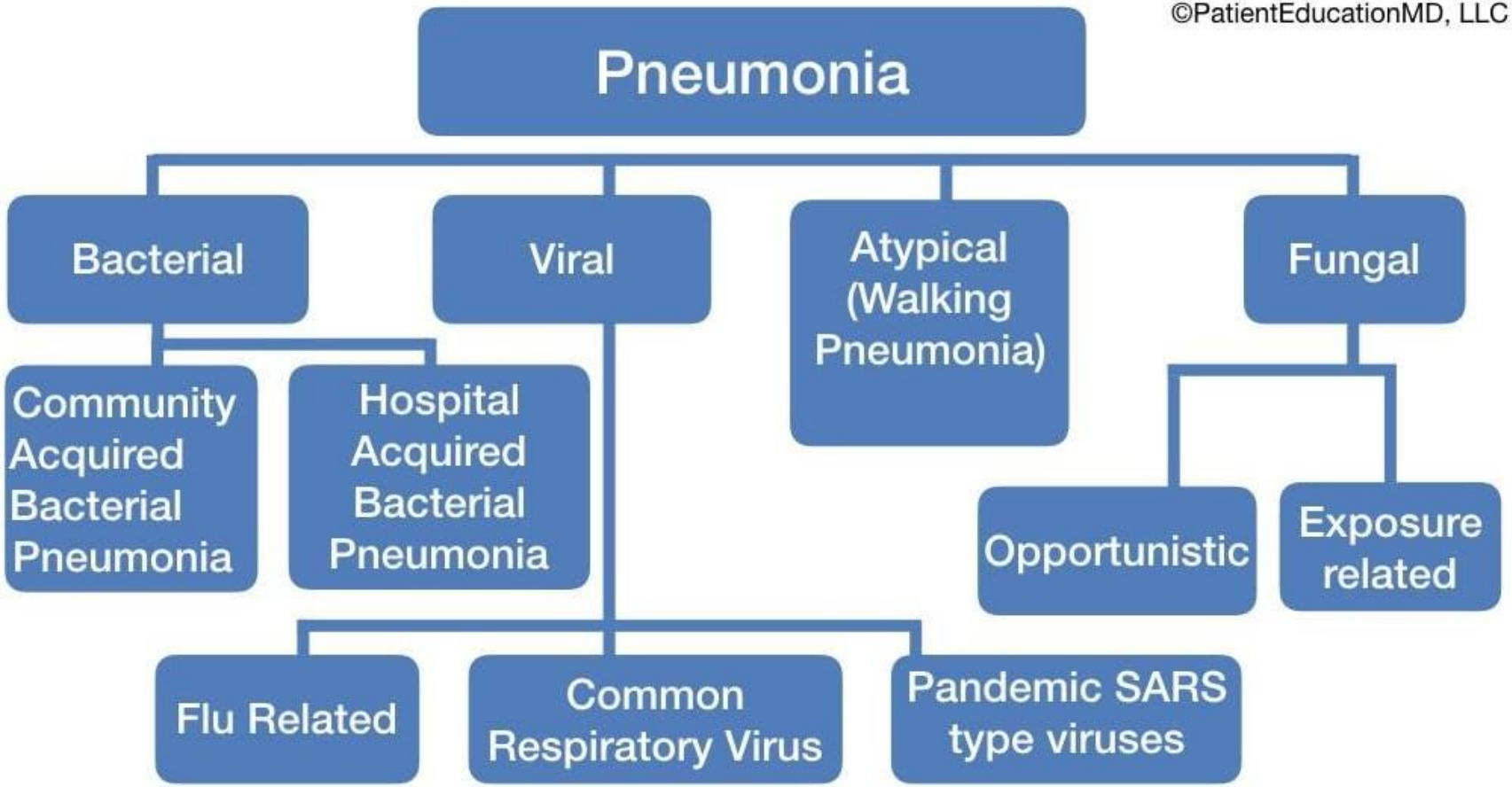
Pneumonia

- Pneumonia is one of the common causes of death.
- It is defined as acute inflammation of LRT (the lung parenchyma) distal to the terminal bronchioles.
- **Consolidation (meaning solidification)** is the term used for gross and radiologic appearance of the lungs in pneumonia.
- The microorganisms or the injurious materials gain entry into the lungs by one of the following four routes**:**
- ***Inhalation, aspiration, hematogenous spread* and *direct spread*.**

Classification of pneumonia

- Classification depends on the cause:

1. Bacterial pneumonia
2. Viral and atypical pneumonia
3. Fungal pneumonia
4. Pneumonias from other etiologies eg aspiration pneumonia



Clinical presentation of pneumonia

- **it is life threatening infection**
- □ Fever
- □ Malaise
- □ Pleuritic chest pain
- □ Productive mucopurulent cough and hemoptysis in half of cases.
- □ Clubbing of the fingers and toes appears in about 20% of patients.
- □ All these will **improve** within 48-72 hours of antibiotic administration.

Predisposing factors

a)Loss or **suppression of cough reflex** (coma, anesthesia), gastric aspiration.

b)Injury to the **mucociliary apparatus** e.g. cigarette, inhaled hot or corrosive gases, viral diseases or genetic diseases (immotile cilia syndrome).

c) Interference with **phagocytosis.**

d) Pulmonary congestion and **pulmonary edema**.

e)Accumulation of secretion e.g. cystic fibrosis& bronchial obstruction

Bacterial Pneumonia

- Two types of acute bacterial pneumonias are distinguished

A. lobar pneumonia (community acquired pneumonia)

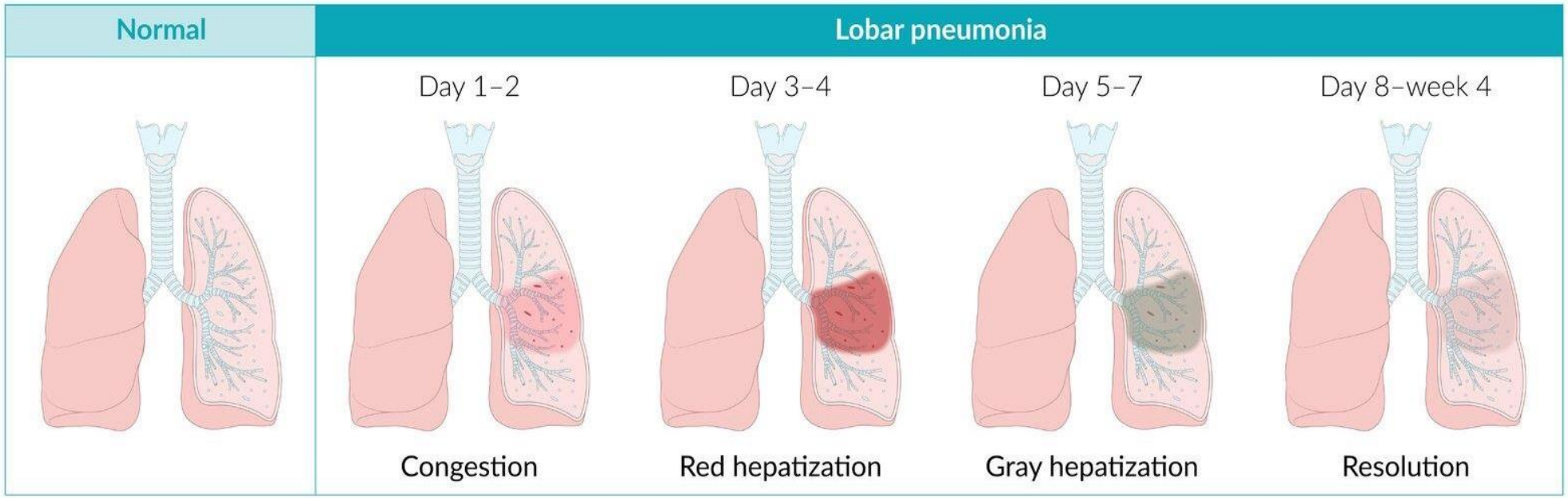
B. bronchopneumonia, (lobular pneumonia)

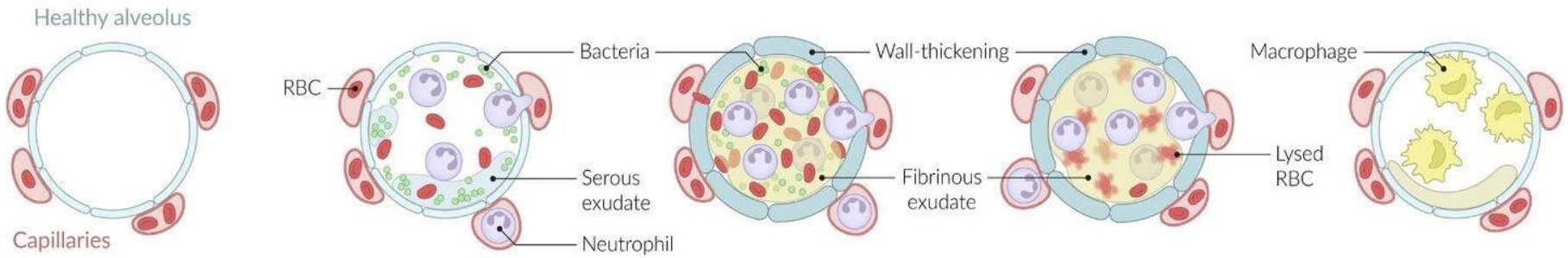
A- Lobar bacterial Pneumonia (community acquired pneumonia)

- Lobar pneumonia is an acute bacterial infection of a part of a lobe or the entire lobe. The consolidation involves portion of a lobe or the whole lobe.
- Different types of bacteria may cause this type of pneumonia(staph, strep, kelbeseilla, proteus, e.coli).

Morphology of lobar pneumonia

- There are four stages of evolvement of lobar pneumonia, they are:
- **A. Stage of congestion**
- **B. Stage of red hepatization**
- **C. Stage of grey hepatization**
- **D. Stage of resolution.**


Normal
Lobar pneumonia
Day 1–2
Day 3–4
Day 5–7
Day 8–week 4
Congestion
Red hepatization
Gray hepatization
Resolution


Healthy alveolus
Capillaries
RBC
Bacteria
Serous exudate
Neutrophil
Wall-thickening
Fibrinous exudate
Lysed RBC
Macrophage

Bronchopneumonia (Lobular Pneumonia)

- Bronchopneumonia or lobular pneumonia is infection of the **terminal bronchioles that extends into the surrounding alveoli.**

•Caused by staphylococcus, streptococcus, pneumococcus, hemophilus influenzae.

•The consolidation is ***patchy*** due to patchy distribution of inflammation that generally involves more than one lobe.

- Occur in ***infancy and old*** age groups caused by:

1- Low immune resistance (eg steroid therapy, diabetes, starvation,,,).

2- As complication of pulmonary diseases.

3- Can complicate long term heart failure.

Complications of pneumonia

- **90% of cases will end up with resolution**, otherwise complication includes:
- **Abscess** formation, especially if the m.o is Klebsiella and pneumococcal infection.
- Spread of infection to the pleural cavity→ **empyema** (pus inside the pleural cavity).
- **Organization** of the exudate → part of the lobe will turn solid.
- **Bacteremic** dissemination to: heart valves, brain, pericardium, kidney.

Atypical pneumonia

- Viral and mycoplasma pneumonia is characterized by patchy inflammatory changes, largely confined to interstitial tissue of the lungs, without any alveolar exudate.
- Other terms used for these respiratory tract infections are ***interstitial pneumonitis***, reflecting the interstitial location of the inflammation.
- It was called *atypical pneumonia*, due to the absence of alveolar exudate commonly present in other pneumonias.
- **Etiology:** Interstitial pneumonitis is caused by a wide variety of agents,

1. respiratory syncytial virus (RSV) the most common one

2. Mycoplasma pneumoniae

3.influenza and parainfluenza viruses, adenoviruses, rhinoviruses, coxsackieviruses and cytomegaloviruses (CMV). Occasionally,

4. psittacosis *(Chlamydia)* and Q fever *(Coxiella)* are associated with interstitial pneumonitis.

END