Pathology of diffuse obstructive airway diseases

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Objectives

- **Classify** the obstructive airway diseases
- Describe the **pathogenesis** of obstructive airway diseases
- Describe the **macroscopy** of obstructive airway diseases
- Describe the **microscopy o**f obstructive airway diseases

Obstructive airway diseases

Increase resistance to airflow due to partial /complete obstruction at any level from trachea to terminal bronchioles.

- Bronchial asthma
- Emphysema
- Chronic bronchitis
- Bronchiectasis

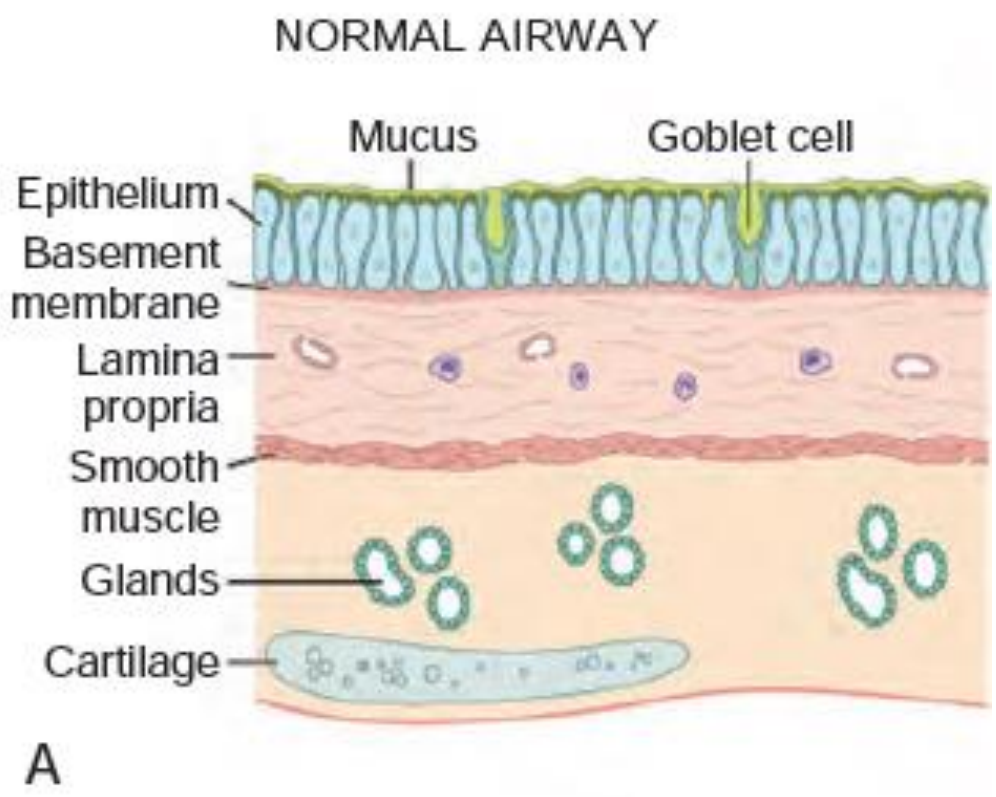
- **Bronchial asthma**
- Emphysema
- Chronic bronchitis
- Bronchiectasis

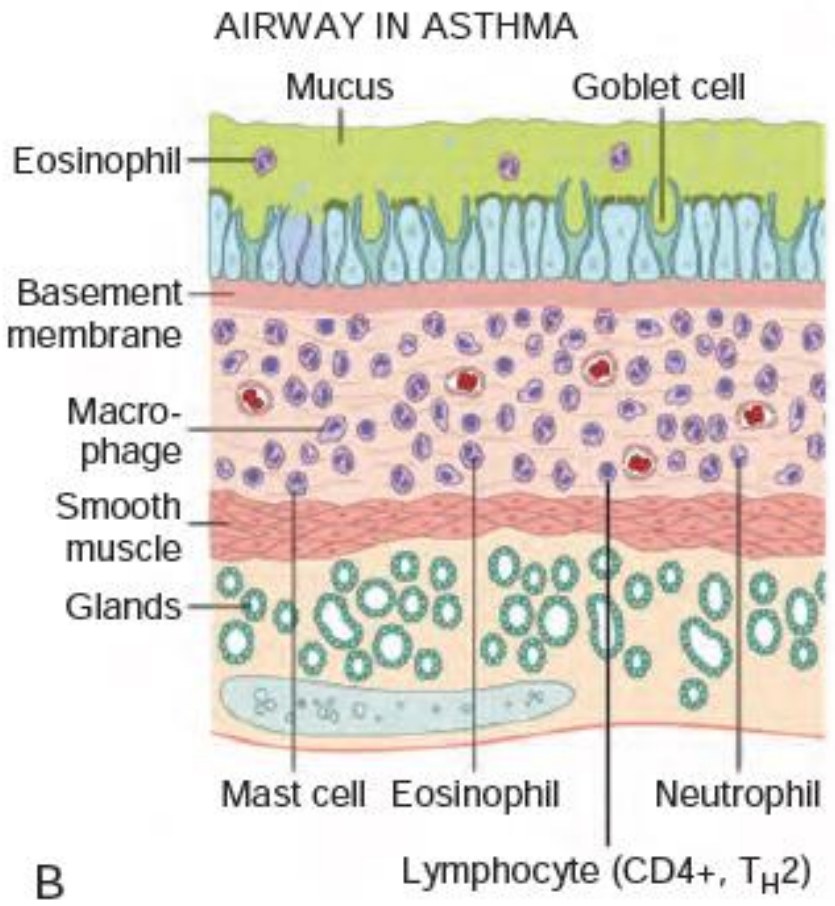
Bronchial asthma

A chronic relapsing inflammatory disorder of the airways.

Characterized by

- Intermittent and reversible airway **obstruction**
- Chronic **inflammation** of the bronchial wall
- Bronchial smooth muscle **hypertrophy** and hyperreactivity
- **Increased mucous** secretion.


NORMAL AIRWAY
Mucus
Goblet cell
Epithelium
Basement membrane
Lamina propria
Smooth muscle
Glands
Cartilage
A


AIRWAY IN ASTHMA
Mucus
Goblet cell
Eosinophil
Basement membrane
Macro-phage
Smooth muscle
Glands
Mast cell
Eosinophil
Neutrophil
Lymphocyte (CD4+, T_H2)
B

What are the clinical features??

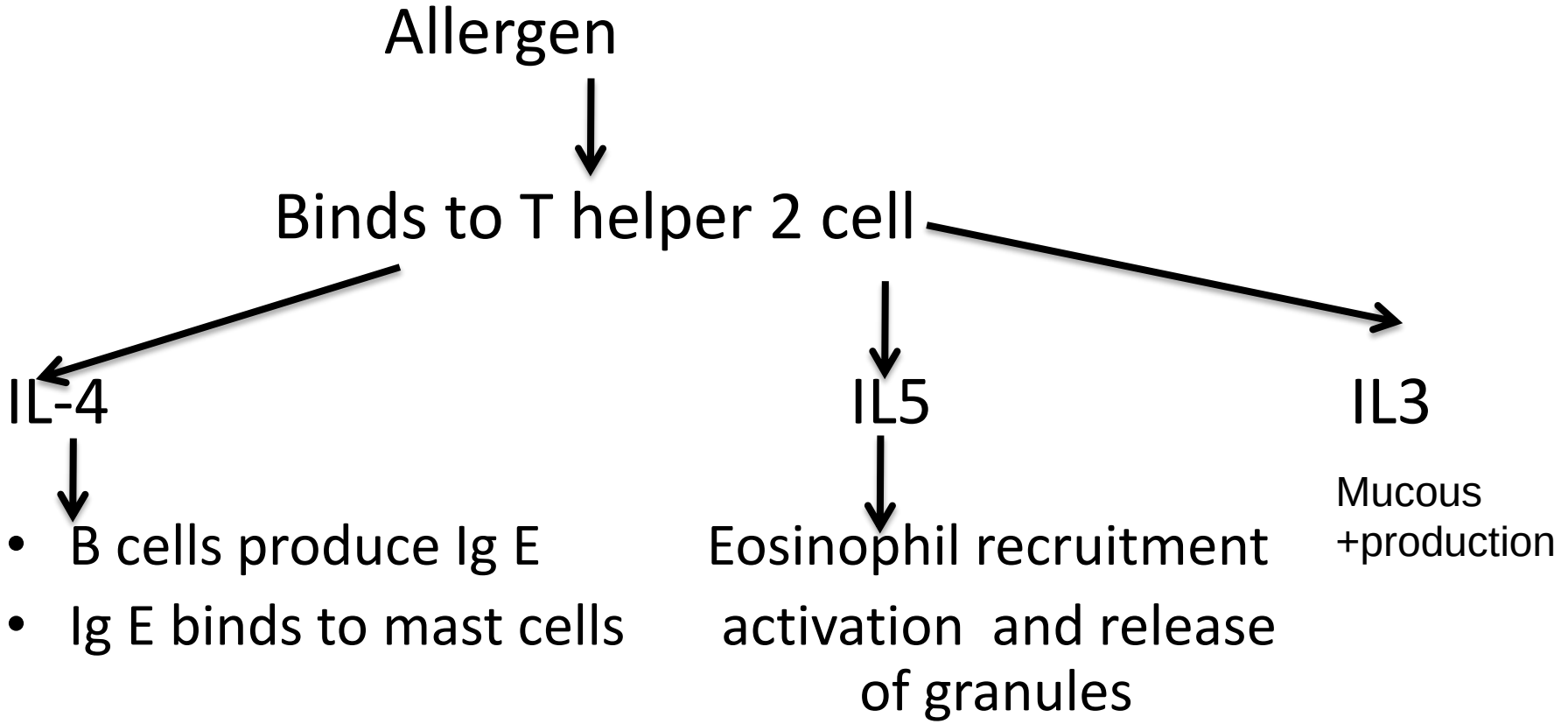
- can categorize as - Atopic asthma
  Non atopic asthma

Atopic asthma

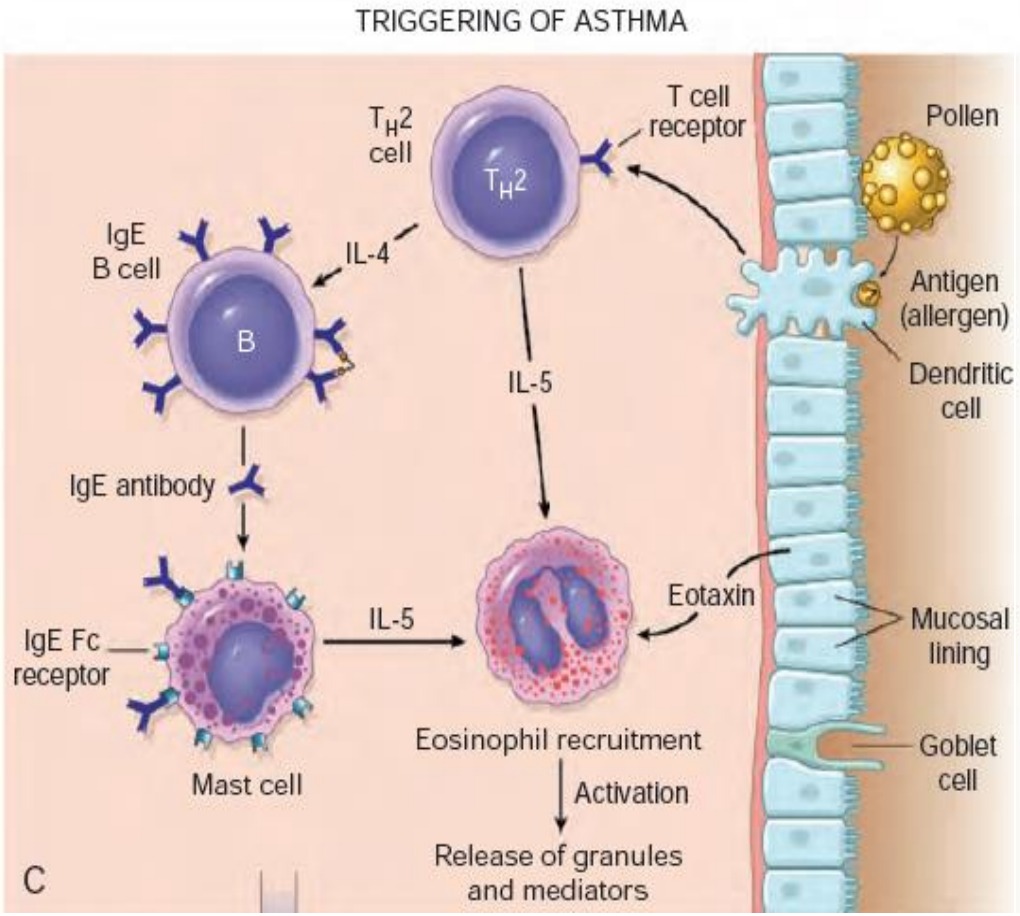
- Type 1 Ig E mediated hypersensitivity reaction (atopy)
- Positive family history common.
- May preceededby Rhinitis, eczema, urticaria
- Triggered by environmental antigens(Duct, pollen, food, animal hair etc)

- Excessive T Helper 2 cell reaction against environmental antigens plays a key role in atopic asthma.

Initial sensitization



Atopic asthma



Acute phase (minutes)

Ag binds to pre-sensitized IgE bound mast cells

↓

Mast cell - degranulation

Mediators released

↓

- Bronchoconstriction
- Increased mucous production
- vasodilation

Late phase (hours)

Cytokines released by mast cells ,T cells and epithelial cells

- Influx of other leucocytes
  eosinophils , neutrophils,
  basophils , lymphocytes

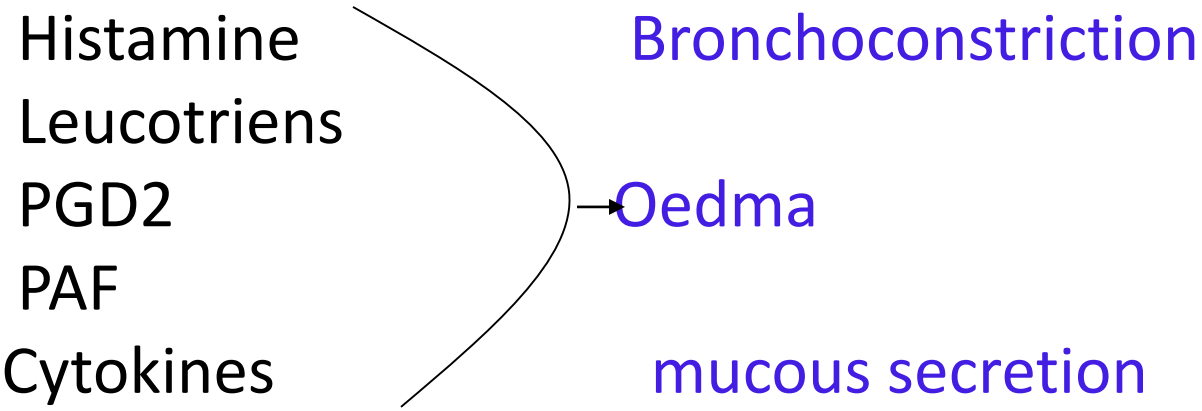
Release other mediators

amplifying the inflammatory response

Repeated bouts lead to airway remodelling

- Hypertrophy of bronchial SM and mucous glands
- Increased vascularity, deposition of subepithelial collagen

- Mediators


Histamine
Leucotriens
PGD2
PAF
Cytokines
Bronchoconstriction
Oedma
mucous secretion

Non-Atopic Asthma.

- No evidence of allergen sensitization.
- A positive BA family less common.
- Respiratory infections are common triggers
- Inhaled air pollutants, may also contribute
- Attacks may be triggered by events, such as exposure to cold and even exercise.

- The ultimate humoral and cellular mediators of AW obstruction (eg Eosinophils) are common to both atopic and non atopic variants.

- Treated similar way!

Read

1. Drug induces asthma

– asprin (ricurrent rhinitis, nasal pllyps, urticariya and bronchospasm)

2. Occupational asthma

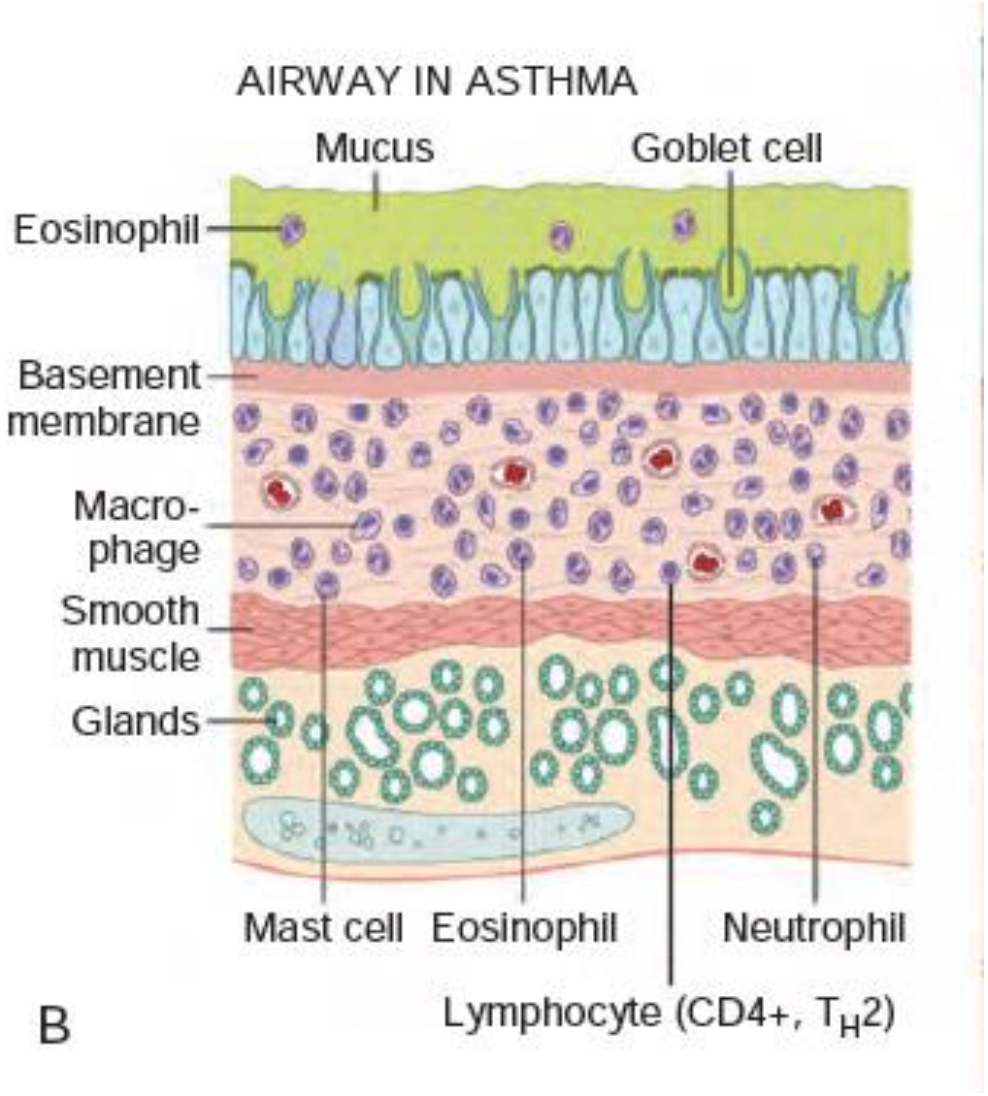
– By fumes (epoxy resins, plastics), organic and chemical dusts (wood, cotton, platinum), gases (toluene), and other chemicals.
– Usually develop after repeated exposure to the inciting antigen(s).

Bronchial asthma cont.

Macroscopy: Lungs

- Over distended
- Small areas of atelectasis
- Thick mucous plugs occluding bronchi & bronchioles

Microscopy…….cont



- Thickened airway walls
- Oedema
- Mucus in the lumen
- BM thickened
- Increased vascularity
- Inflammation – mainly eosinophils
- Enlarged S.M., glands and increased goblet cells
- Hypertrophy and hyperplasia of bronchial wall muscle

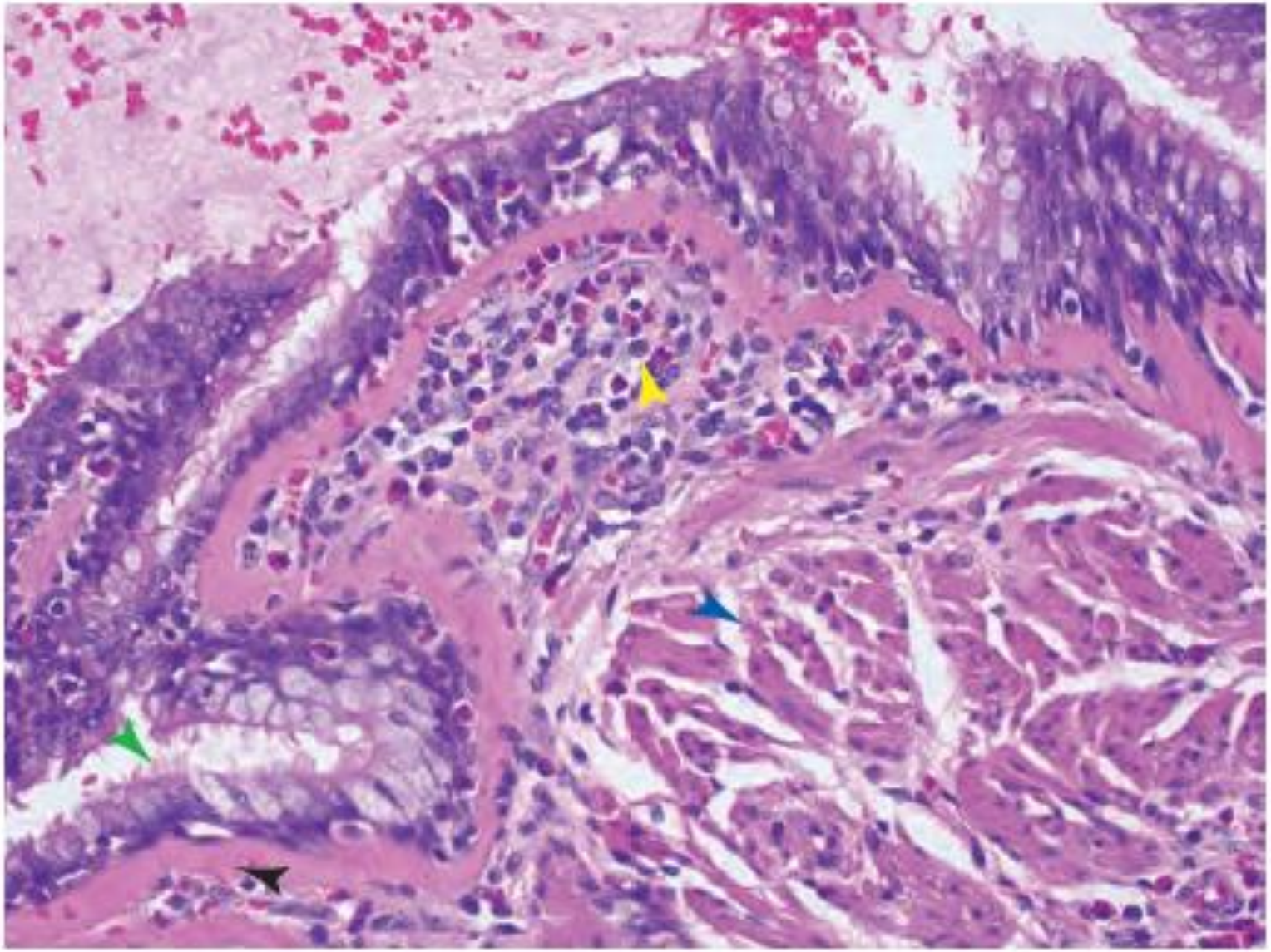
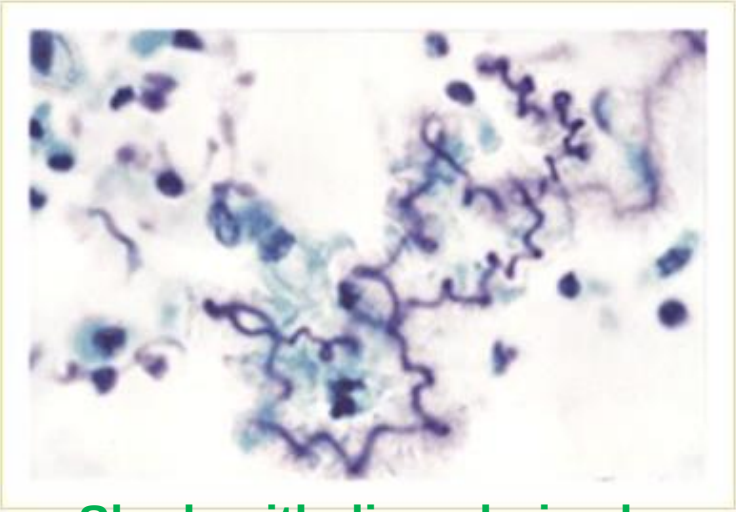


Figure 15-11 Bronchus from an asthmatic patient showing goblet cell hyperplasia *(green arrowhead)*, subbasement membrane fibrosis *(black arrowhead)*, eosinophilic inflammation *(yellow arrowhead)*, and muscle hypertrophy *(blue arrowhead)*.

Microscopy cont.

Curschmann spirals

- Coiled, basophilic plugs of mucus formed in the lower airways and found in sputum and tracheal washings



Shed epithelium derived

Charcot-Leyden crystals.

- Eosinophilic needle-shaped crystalline structures.

Eosinophil membrane derived

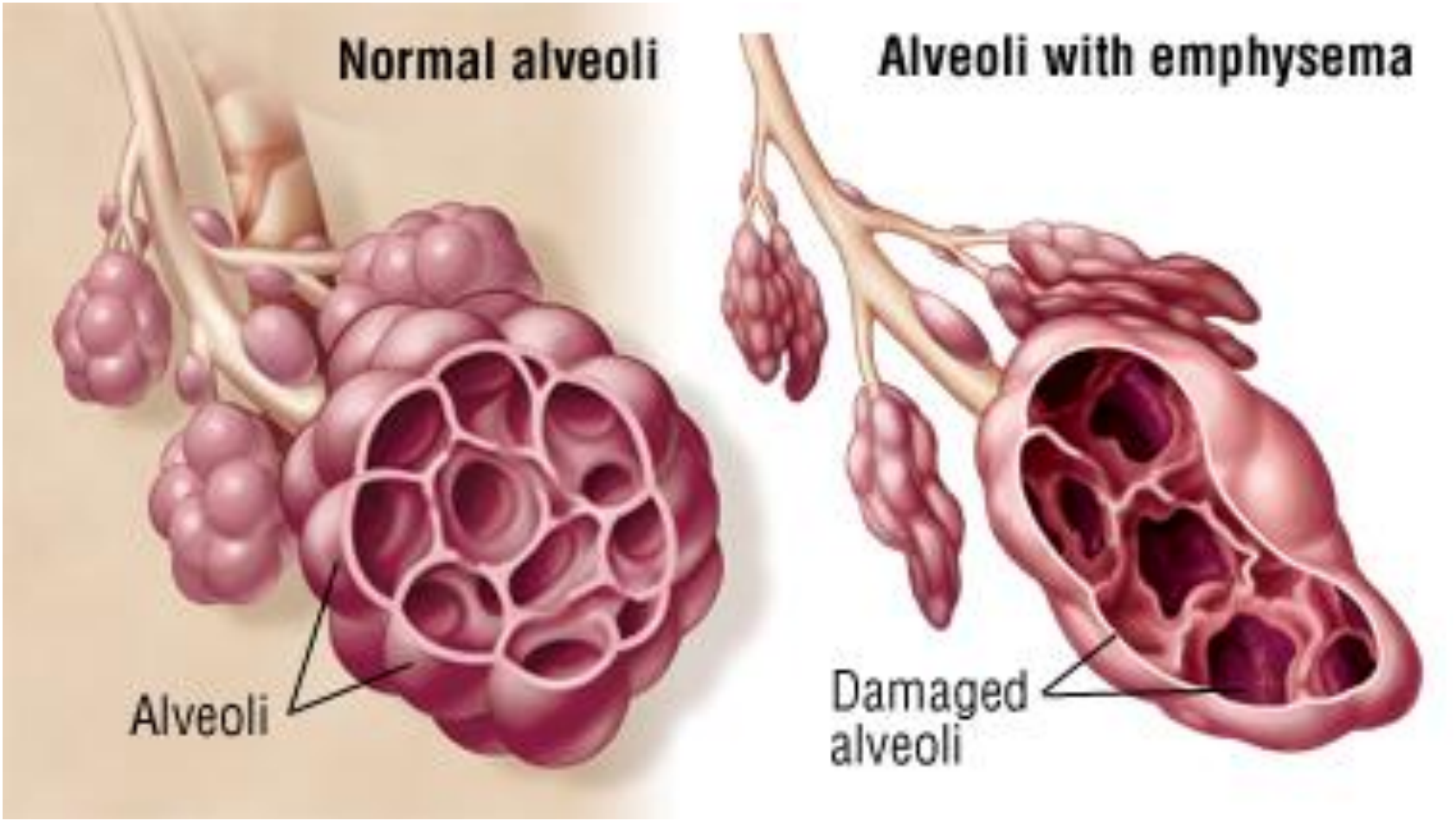
Obstructive airway diseases

- Bronchial asthma
- Emphysema
- Chronic bronchitis
- Bronchiectasis

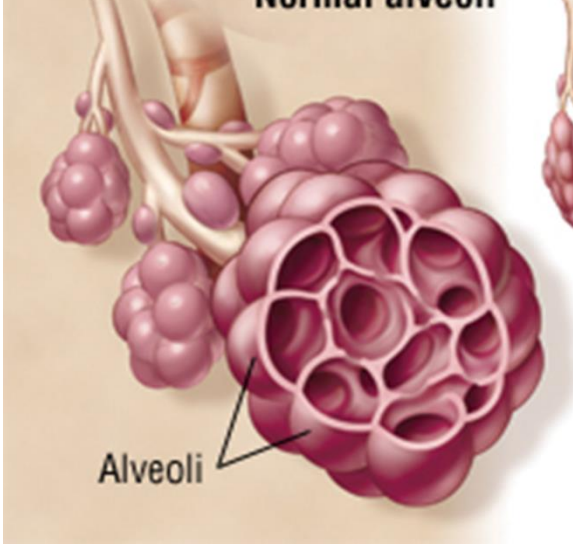
Emphysema

- A condition of the lung characterized by abnormal **permanent enlargement** of the air spaces **distal to the terminal bronchioles** with **destruction** of their wall

Emphysema


Normal alveoli
Alveoli with emphysema
Alveoli
Damaged alveoli

Classification



Emphysema is classified according to its anatomic distribution within the lobule

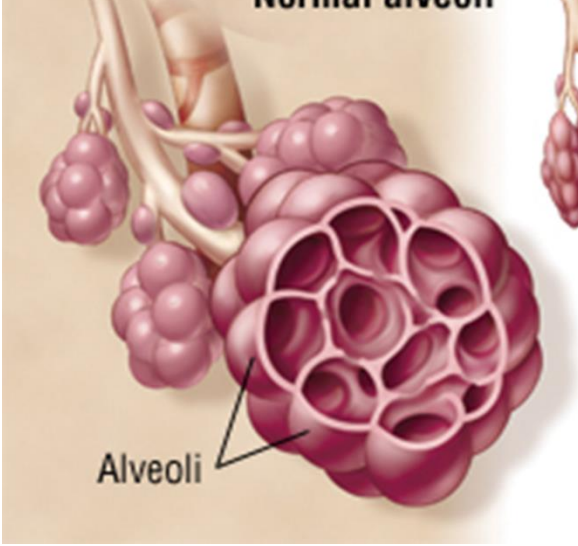
1)Centrilobular / Centriacinar

2)Panacinar

3)Distal acinar (Paraseptal)

4)Irregular emphysema

Classification



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1)Centrilobular / Centriacinar

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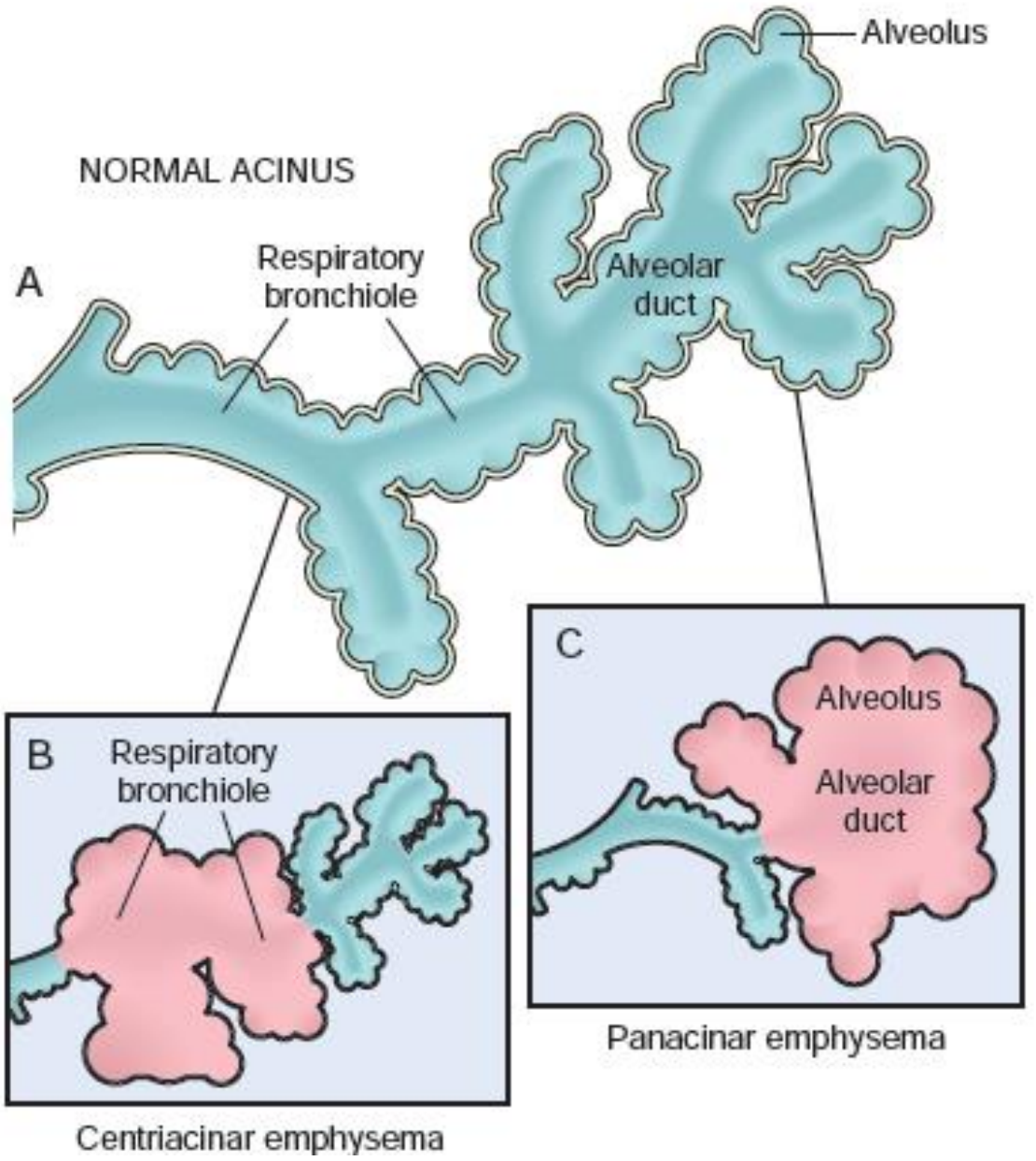
4)Irregular emphysema

Cause clinically significant airflow obstruction.

A Structure of the normal acinus.

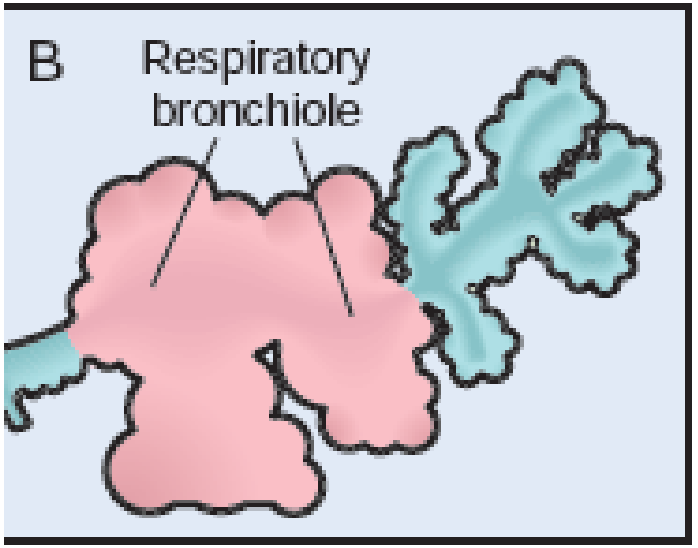
B Centriacinar emphysema with dilation initially affecting respiratory bronchioles.

C Panacinar emphysema with initial distention of the alveolus and alveolar duct.



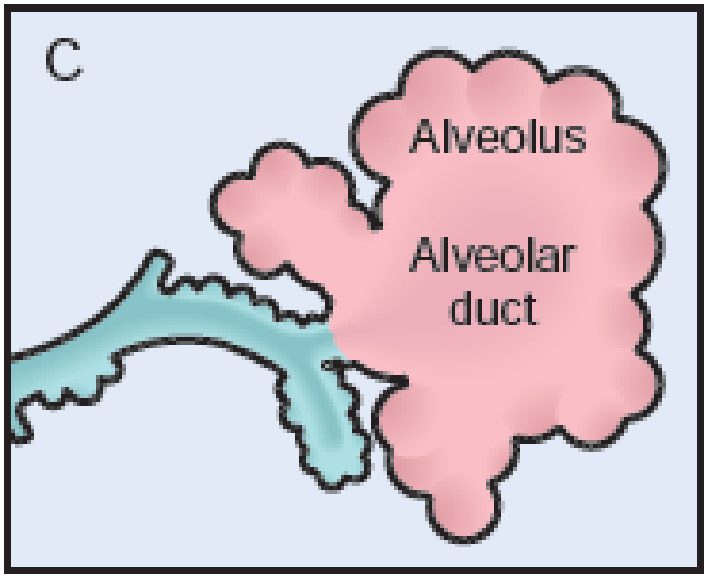
1) Centriacinar

- Central or proximal parts are affected (respiratory bronchiole)
- Distal alveoli spared
- Common
- Usually in upper lobes
- Heavy smokers

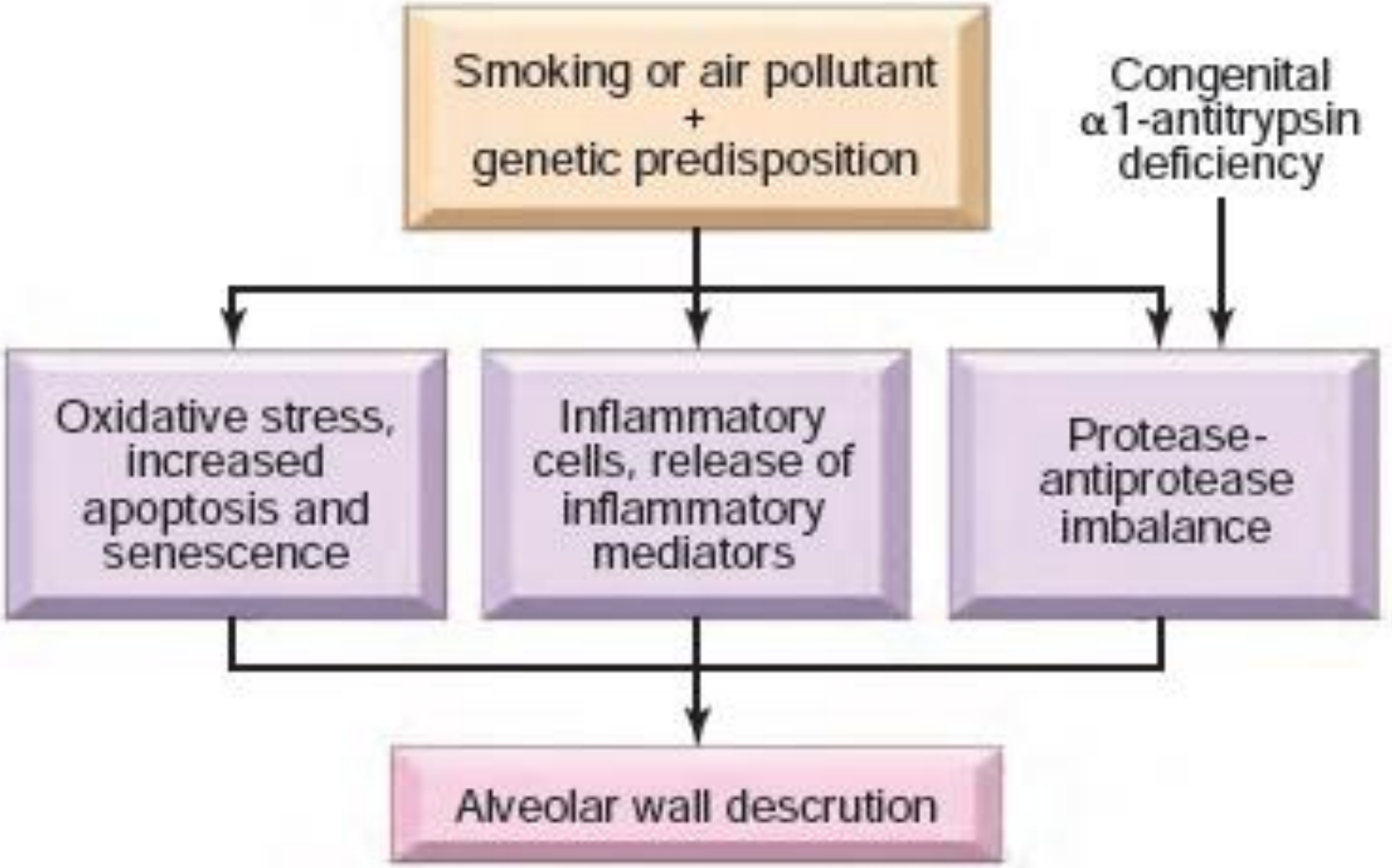


2)Panacinar

- Acini uniformly enlarged.
- from the level of the respiratory bronchiole to the terminal alveoli
- Severe at lower zones
- Associated with alpha 1 antitrypsin deficiency



Pathogenesis of emphysema



- Smoking and inhaled pollutants cause ongoing accumulations of inflammatory cells, releasing elastases and oxidants, which destroy the alveolar walls.

Factors that influence the development of emphysema

- **Inflammatory mediators and leukocytes-**
  - released by resident epithelial cells and macrophages
    - Attract cells from the circulation (chemotactic factors),
    - Amplify the inflammatory process (proinflammatory cytokines)
    - induce structural changes (growth factors).

- **Oxidative stress.**

  Substances in tobacco smoke, alveolar damage, and inflammatory cells all produce oxidants,

  Result more tissue damage and inflammation**.**

- **Infection.**

  does not play a role in the initiation of tissue destruction,

  may exacerbate the associated inflammation and chronic bronchitis

- Several proteases are released from the inflammatory cells and epithelial Cells that break down connective tissue components.

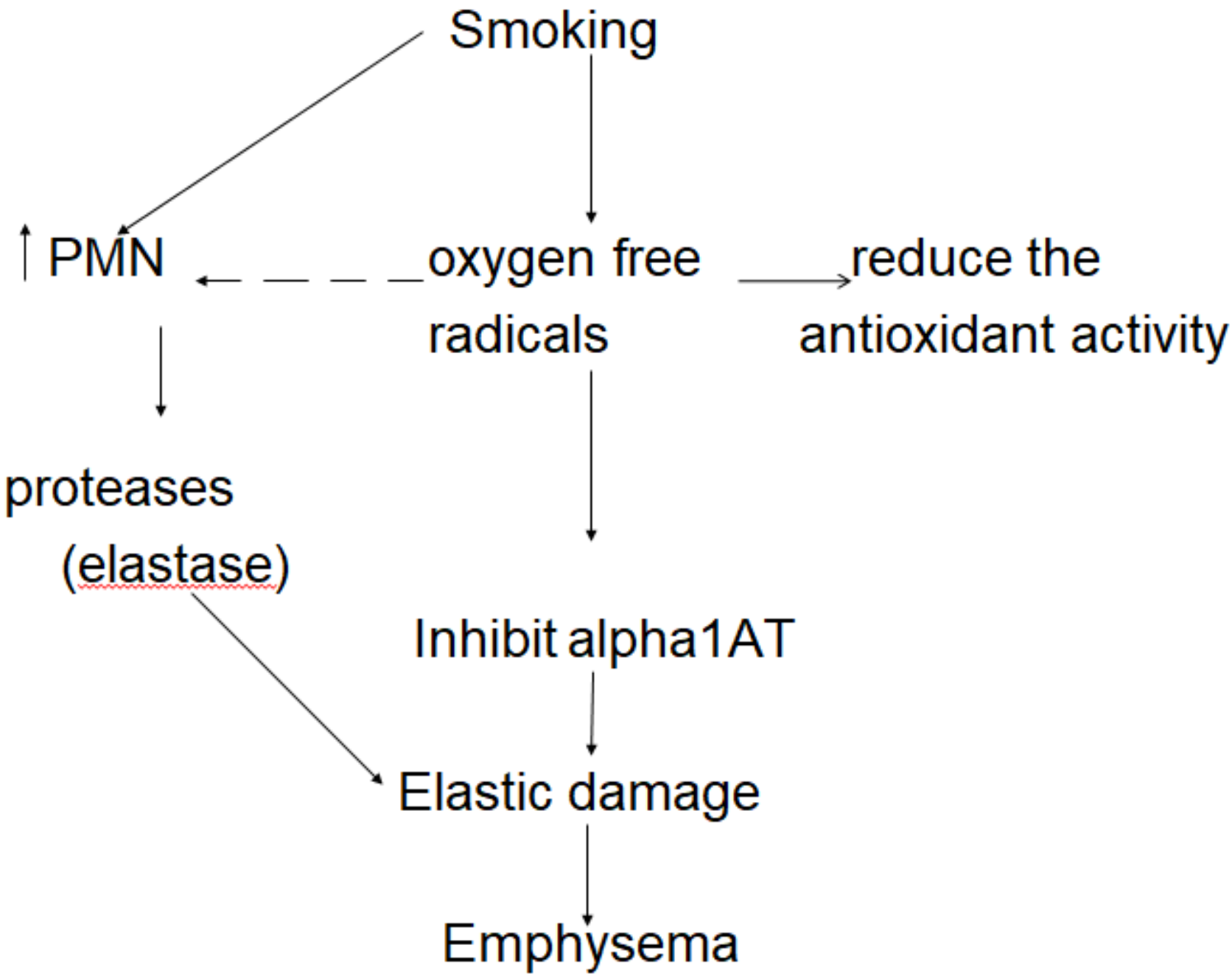
- α1-antitrypsin is a major inhibitor of proteases.

  (normally present in serum, tissue fluids, and macrophages)

- In patients who develop emphysema, there is an increase of proteases and a relative deficiency of protective antiproteases.

- In some instances has a genetic basis.

  (Congenital α1-antitrypsin deficiency develop panacinar emphysema , earlier age, more severe if the person smokes)


Smoking
PMN
oxygen free radicals
reduce the antioxidant activity
proteases (elastase)
Inhibit alpha1AT
Elastic damage
Emphysema

Pathogenesis- emphysema- summary

Imbalance between

proteases & antiproteases

Oxidants & antioxidants

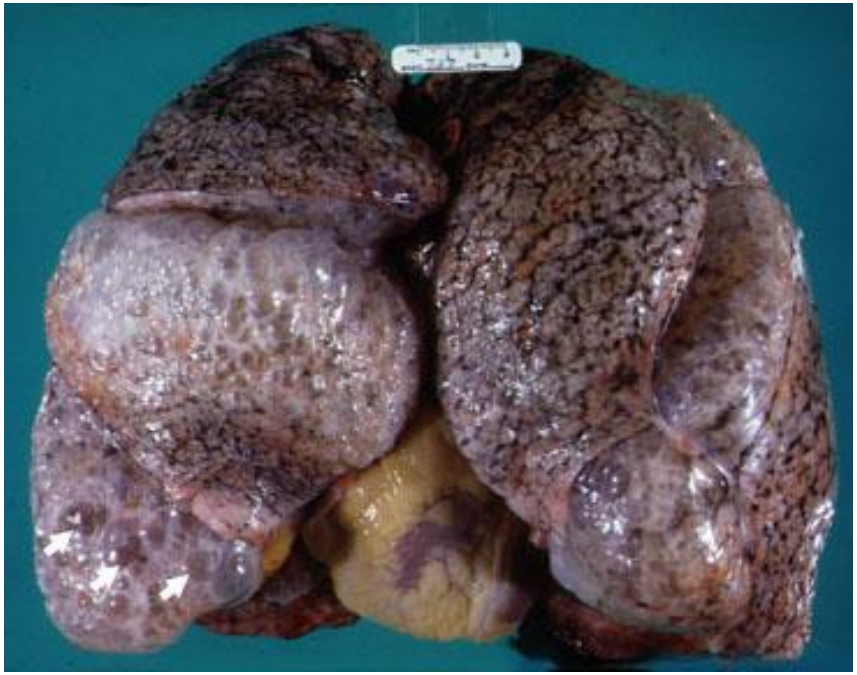
Macroscopy- Emphysema

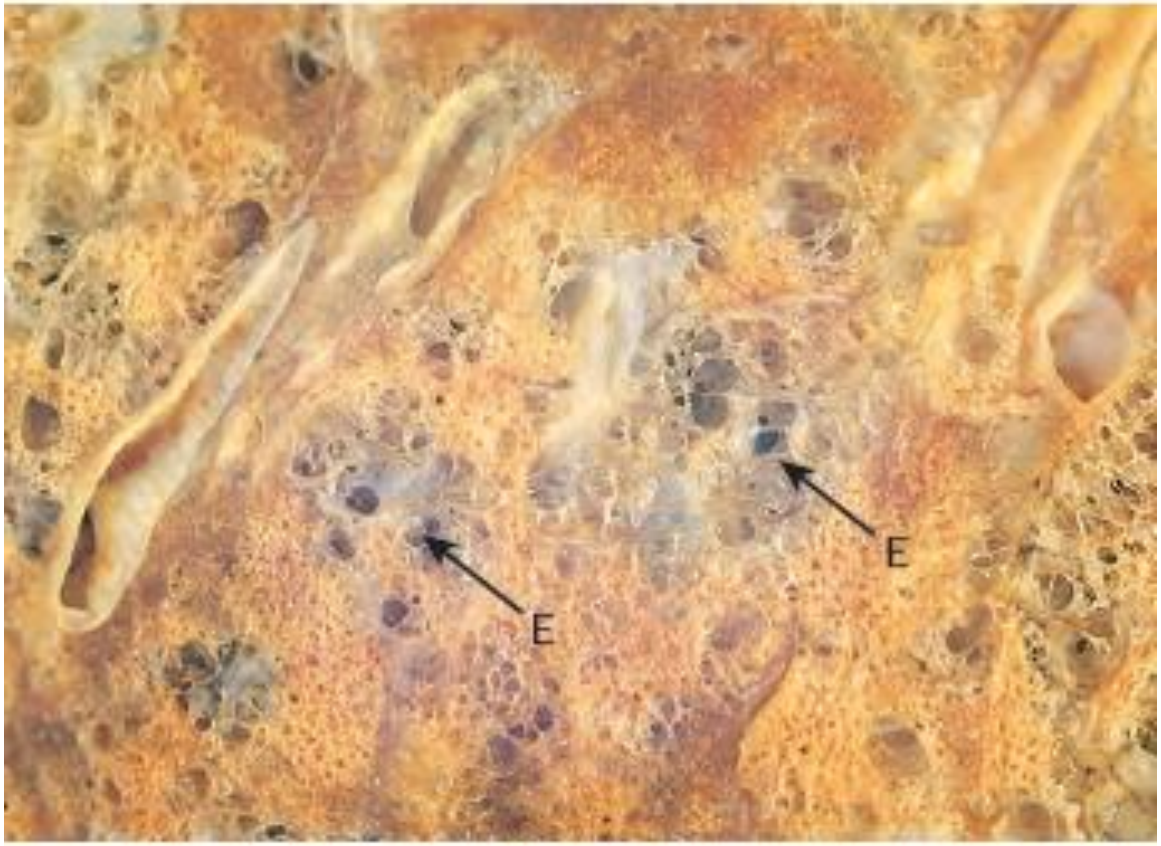
Normal lung

Emphysematous lung

Voluminous and covering the heart

Pale, Apical blebs and bullae

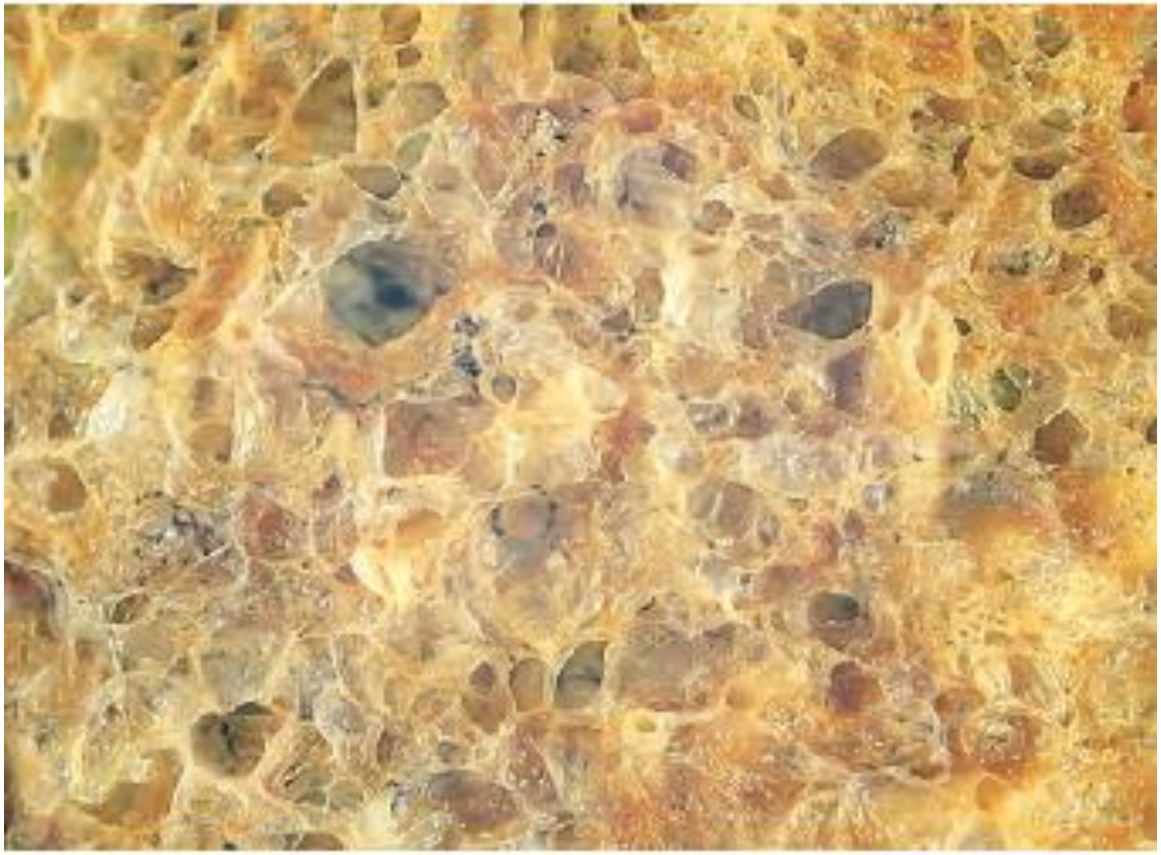




Centriacinar emphysema.

Central areas show marked emphysematous damage (E),

Formalin inflated fixed lung will show enlarged alveoli, surrounded by relatively spared alveolar spaces.



Panacinar emphysema involving the entire pulmonary lobule.

Microscopy

- Large alveoli separated by thin septae.
- Complete destruction of alveolar walls without fibrosis
- Enlarged air spaces

Large alveoli fuse

↓

Large spaces

↓

Blebs and bullae

Microscopy cont.

-Goblet cell hyperplasia with mucus plugging

-Inflammatory cell infiltrate of the walls with PMN , macrophages , B cells and T cells

-Thickening of bronchiolar wall due to smooth muscle hypertrophy and peribronchial fibrosis

Reading assignment

- Other instances where emphysema term is applied

-Compensatory hyperinflation

-Obstructive overinflation

-Bullous emphysema

-Interstitial emphysema

- **Compensatory emphysema**

  dilation of residual alveoli in response to loss of lung substance elsewhere

  occurs after surgical removal of a diseased lung or lobe.

- **Obstructive overinflation**

  expansion of the lung due to air trapping.

  cause is subtotal obstruction of an airway by a tumor or foreign object.

  Can be life-threatening if expansion of the affected portion produces compression of the remaining normal lung.

- **Bullous emphysema**

  any form of emphysema that produces large subpleural blebs or bullae

  Such blebs represent localized accentuations of one of the four forms of emphysema;

  most often the blebs are subpleural, and on occasion they may rupture, leading to pneumothorax.

- **Mediastinal (interstitial) emphysema**

  by entry of air into the interstitium of the lung, from where it may track to the mediastinum and sometimes the subcutaneous tissue. It may occur spontaneously if a sudden increase in intraalveolar pressure (as with vomiting or violent coughing) produces alveolar rupture, which allows air to dissect into the interstitium. Sometimes it develops in children with whooping cough. It may also occur in patients on respirators who have partial bronchiolar obstruction or in individuals with a perforating injury (e.g., a fractured rib). When the interstitial air gets into the subcutaneous tissue, the patient may literally blow up like a balloon, with marked swelling of the head and neck and crackling crepitation over the chest (subcutaneous emphysema). In most instances the air is resorbed spontaneously after the site of entry seals.

Obstructive airway diseases

- Bronchial asthma
- Emphysema
- Chronic bronchitis
- Bronchiectasis

Chronic bronchitis

- Clinical definition

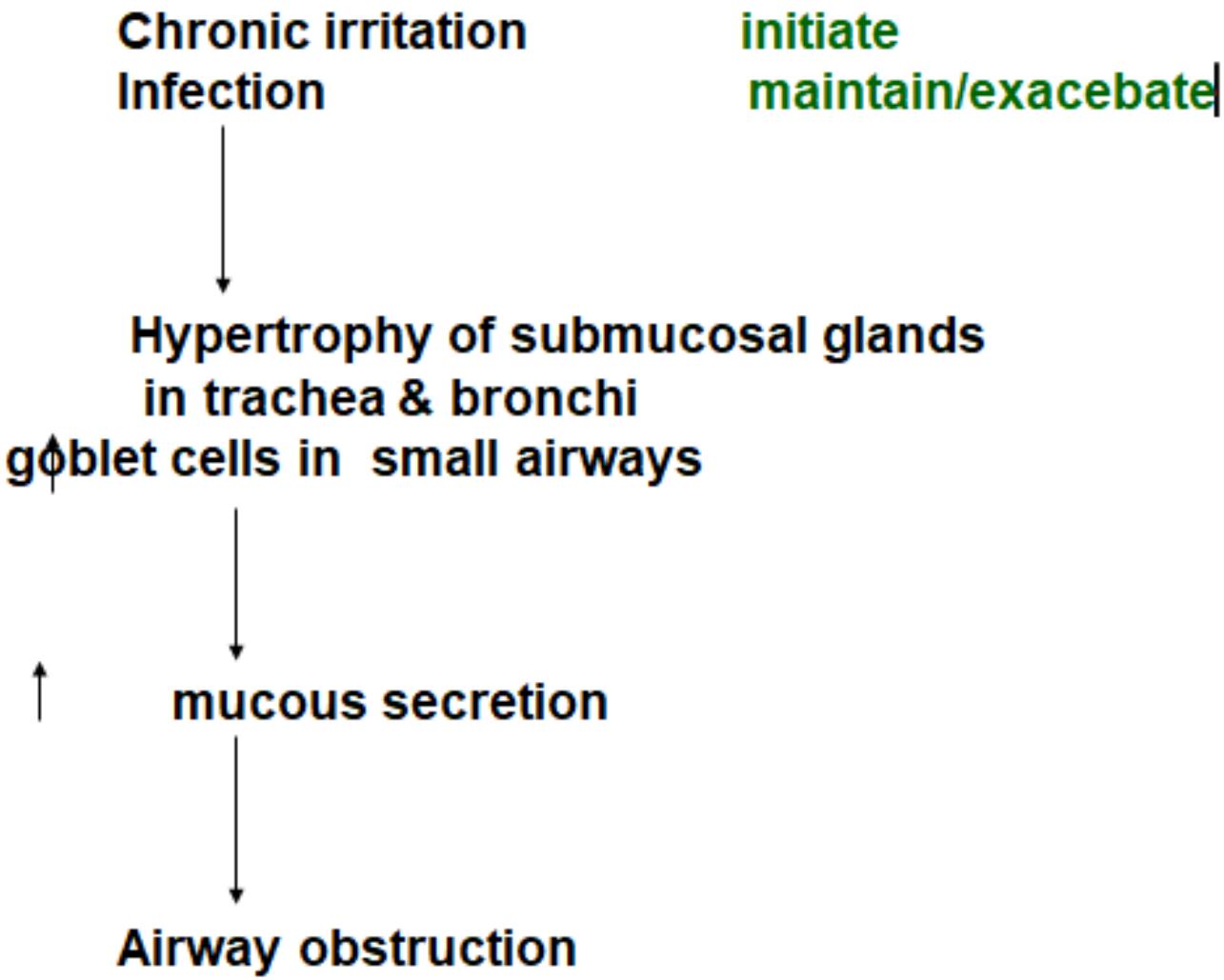
  A patient having persistent cough with sputum production for at least 3 months in at least 2 consecutive years

- Smokers(90%)

  4-10 times commoner in smokers
- People in urbanized areas

Initiating irritant – Smoke, dust from grain, silica and cotton

Pathogenesis



Macroscopy

- Hyperaemia & swelling of mucous membranes.

- Mucous or mucopurulent secretions layering the epithelium.

Microscopy

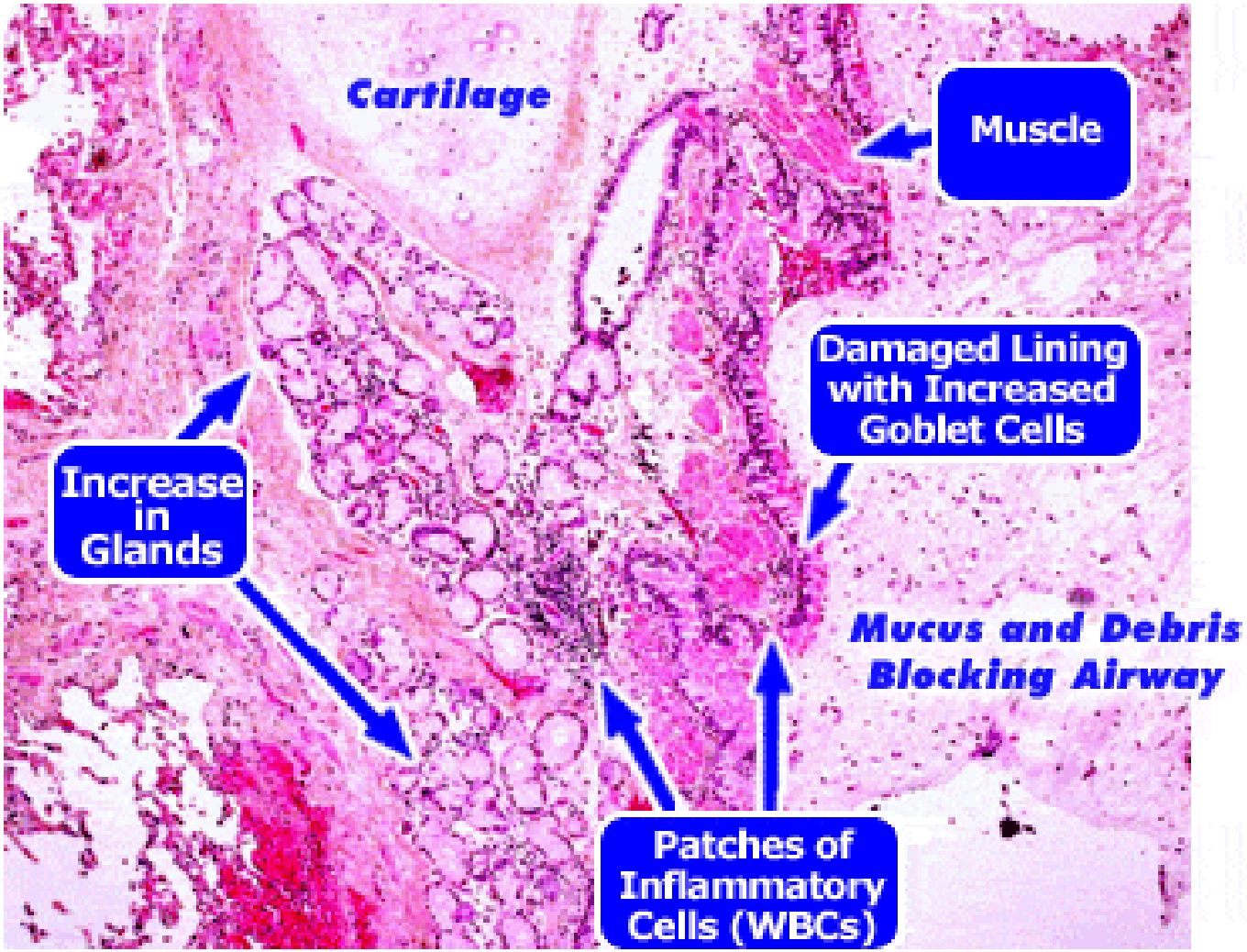
- Hypertrophy of the mucosal glands in trachea & bronchi (Larger airways)
- Enlargement of mucus secreting glands
- Increases goblet cells in small airways
- Areas of squamous metaplasia

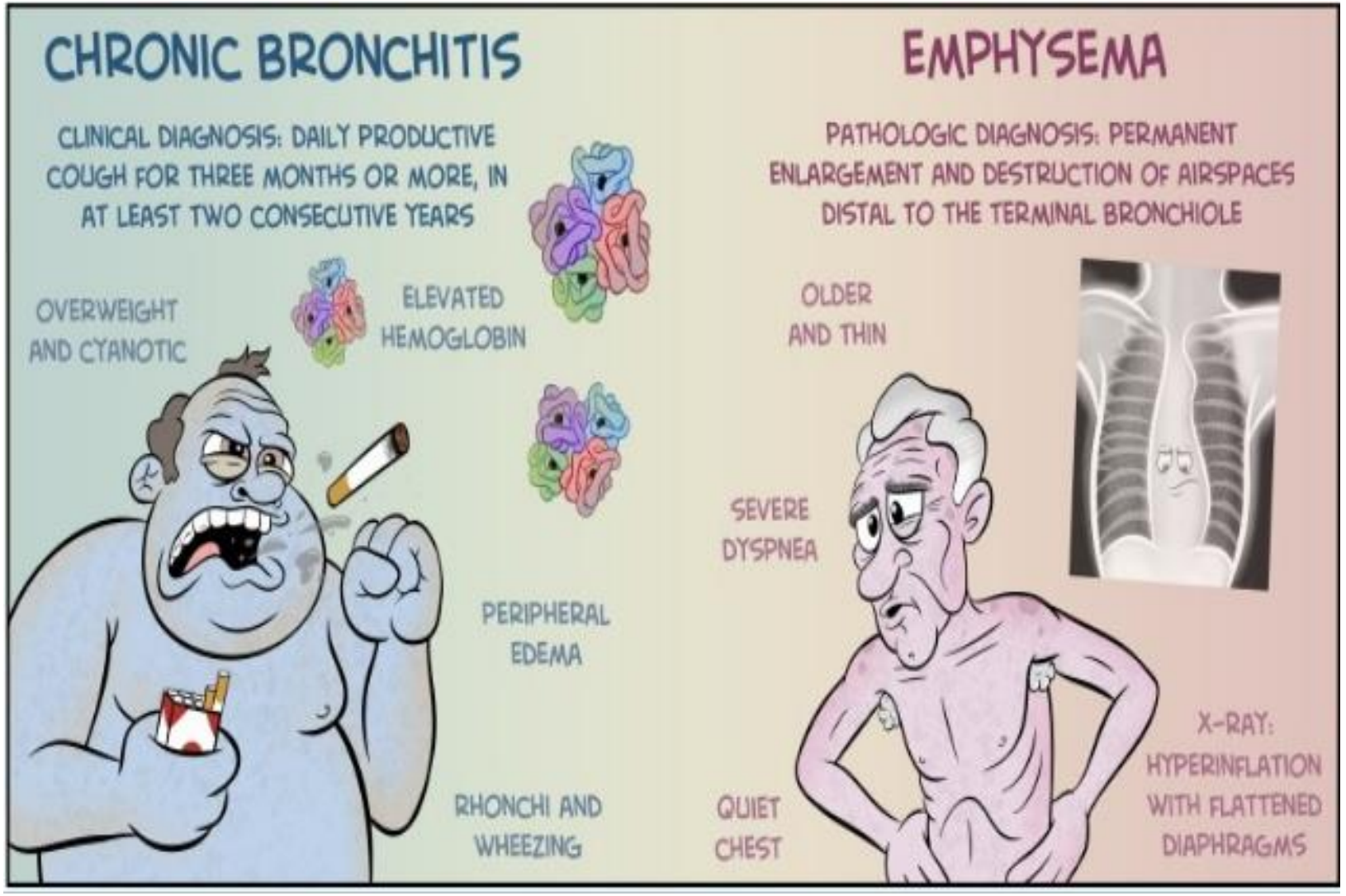
- Chronic inflammation
- Fibrosis of muscular wall
- Mucus plugging

narrowing of small airways

- Marked fibrosis in severe cases – bronchiolitis obliterans

Chronic bronchitis




CHRONIC BRONCHITIS
CLINICAL DIAGNOSIS: DAILY PRODUCTIVE COUGH FOR THREE MONTHS OR MORE, IN AT LEAST TWO CONSECUTIVE YEARS
OVERWEIGHT AND CYANOTIC
ELEVATED HEMOGLOBIN
PERIPHERAL EDEMA
RHONCHI AND WHEEZING
EMPHYSEMA
PATHOLOGIC DIAGNOSIS: PERMANENT ENLARGEMENT AND DESTRUCTION OF AIRSPACES DISTAL TO THE TERMINAL BRONCHIOLE
OLDER AND THIN
SEVERE DYSPNEA
QUIET CHEST
X-RAY: HYPERINFLATION WITH FLATTENED DIAPHRAGMS

- Emphysema and chronic bronchitis often clinically grouped together- *chronic obstructive pulmonary disease* (COPD)
- Since the majority of patients have features of both
- Because they share a trigger—cigarette Smoke

- Assignment-
  - What are the complications of emphysema, chronic bronchitis , COPD?

Obstructive airway diseases

- Bronchial asthma
- Emphysema
- Chronic bronchitis
- Bronchiectasis

Bronchiectasis

- Chronic necrotizing infection of bronchi and bronchioles leading to abnormal permanent dilatation of airways.
- This is resulted by destruction of the muscle and the supportive connective tissue.

- Pathogenesis

  Obstruction

  Infection(Chronic and persistent)

- Obstruction (*F.B./Tumour* /mucous plug)

↓

Inflammation &

2ry infection → Weakening & dilatation

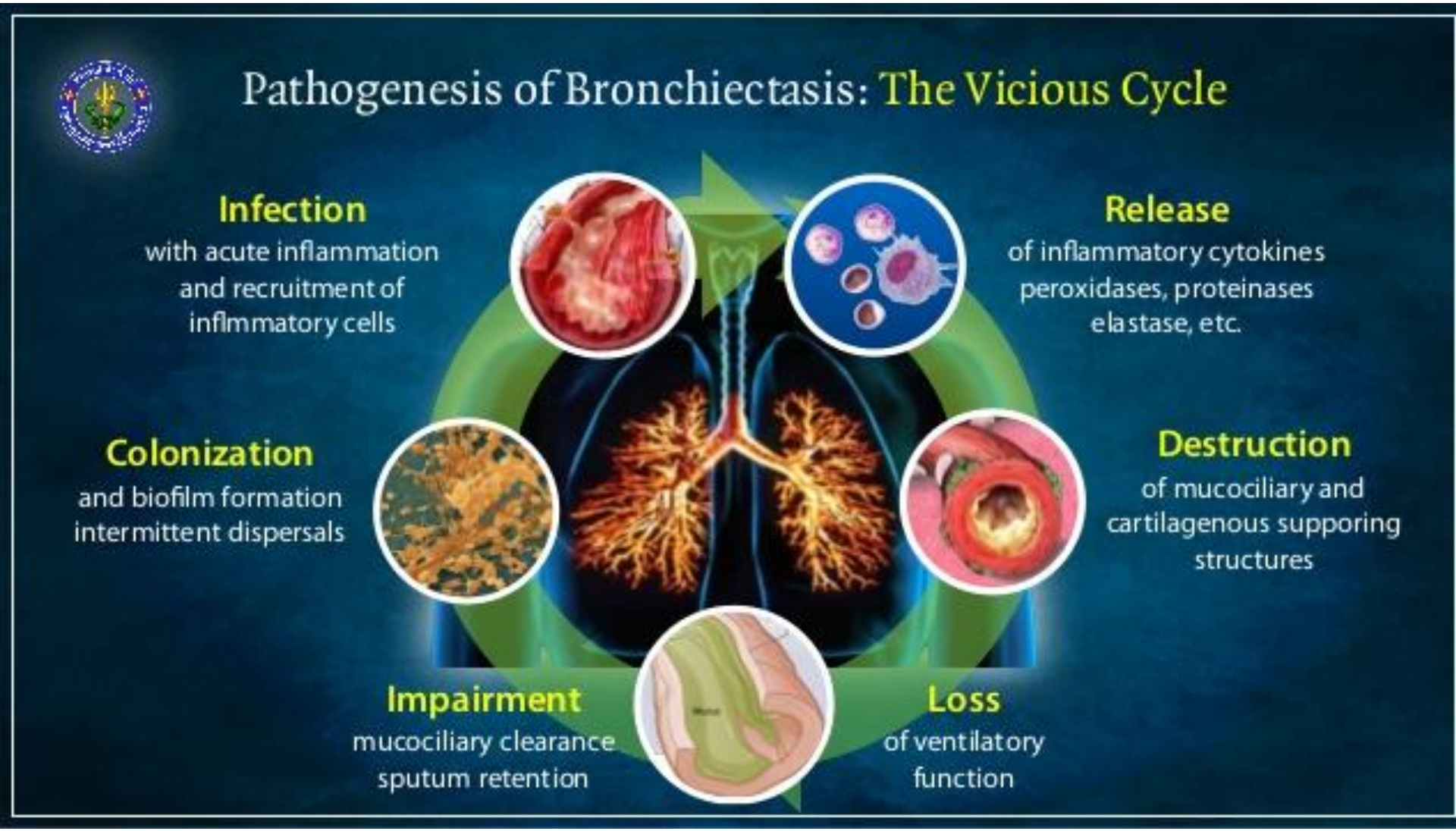
↓

Fibrosis

↓

Permanent dilatation

Pathogenesis of bronchiectasis



Causes

1)Bronchial obstruction

Tumour, F.B. → Localized

Mucous plugs → Diffuse

2)Post infectious

Necrotizing pneumonia (TB , Staph,Pseudomonas)

3)Congenital / Heriditary

Cystic fibrosis(thick mucous plugs)

Immunodeficiency syndrome

Primary cilliary dyskinesia

Kartageners syndrome - Bronchiectasis

(Cilliary defect) Situs inversus

Sinusitis

4)Immunodefficiency state

Causes cont.

5) Rheumatoid arthritis

   SLE

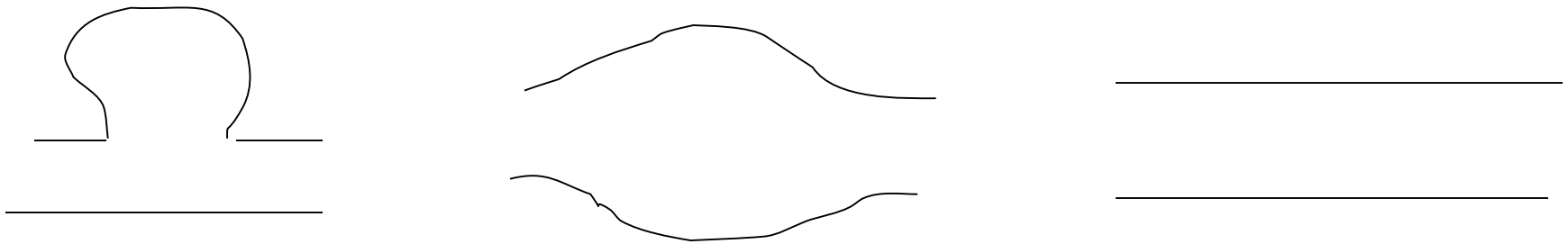
   Inflammatory bowel disease

6) Allergic bronchopulmonary aspergillosis

Morphology

Macroscopy

- Usually - B/L
  Affects lower lobes
- Single segment affected when there is a FB / Tumour
- Airways dilated - saccular
  (4xnormal) fusiform
  cylindrical
- Bronchioles dilated upto a point closer to the pleura
- Filled with mucopurulent material



Bronchieactasis macroscopy

Note the markedly dilated bronchi close to the pleura

Microscopy

- Desquamated lining epithelium
- Ulceration
- Squamous cell metaplasia
- Wall - acute & chronic inflammatory cell infiltrate
- Fibrosis of bronchi and bronchioles
- Peribronchiolar fibrosis leading to subtotal / total obstruction of lumen
- +/- lung abscess formation

- **Complications**
    1) Corpulmonale
    2) Brain abscess
    3) Amyloidosis

Summary

- Obstructive airway disease result from obstruction of different parts of the airways
- Different pathogenic mechnisms are seen Asthma , emphysema , chronic bronchitis and bronchiectassis.
- All these cases will show an obstructive type of lung function test results

Summary

Clinical Term	Anatomic Site	Major Pathologic Changes	Etiology
Chronic bronchitis	Bronchus	Mucous gland hyperplasia, hypersecretion	Tobacco smoke, air pollutants
Bronchiectasis	Bronchus	Airway dilation and scarring	Persistent or severe infections
Asthma	Bronchus	Smooth muscle hyperplasia, excess mucus, inflammation	Immunologic or undefined causes
Emphysema	Acinus	Airspace enlargement; wall destruction	Tobacco smoke