MID

Lecture 2&3

بسم الله الرحمن الرحيم

Pathology Mind Maps

Obstructive Lung Diseases

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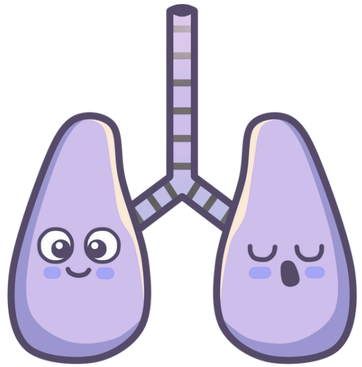


This file contains the lecture material presented through mind maps to make the information clearer, more organized, and easier to follow. It is designed to simplify studying and make revision more effective.

We truly hope you find it beneficial.
If it helps you in any way, please remember us in your prayers.

Best of luck in your studies💜!

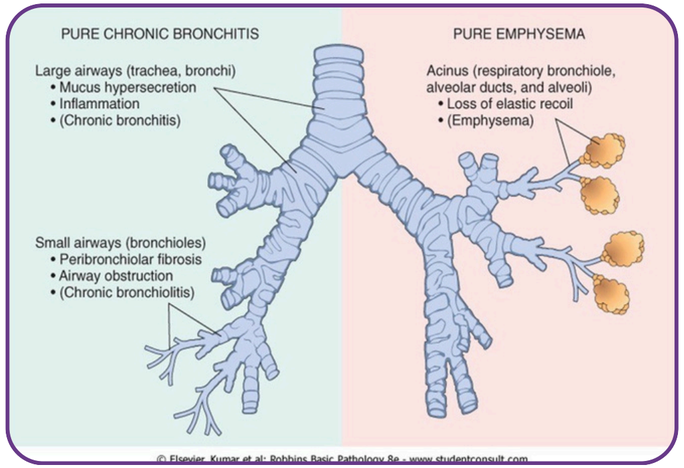
Chronic Obstructive Pulmonary Disease (COPD)

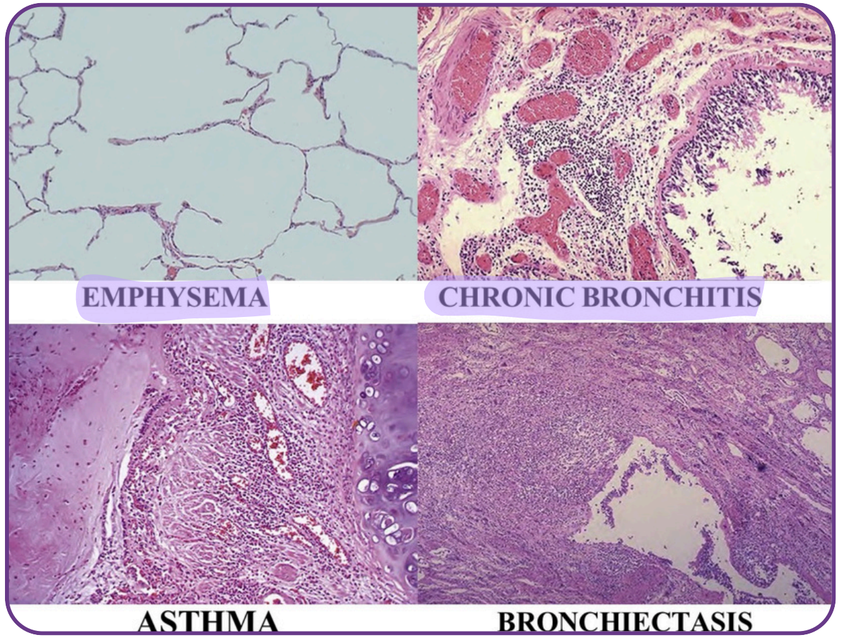
Defined by the WHO as “a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities caused by exposure to noxious particles or gases.”

4th leading cause of death in the world

There is a strong association between ***heavy cigarette smoking*** and COPD.
35% to 50% of heavy smokers develop COPD.
80% of COPD is attributed to smoking

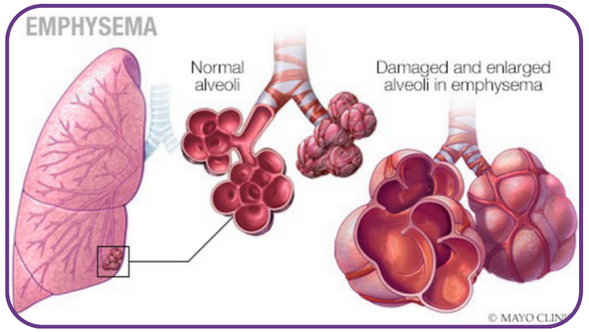
It’s hard to get the air OUT
It’s hard to EXHALE
Lungs are hyperinflated





EMPHYSEMA

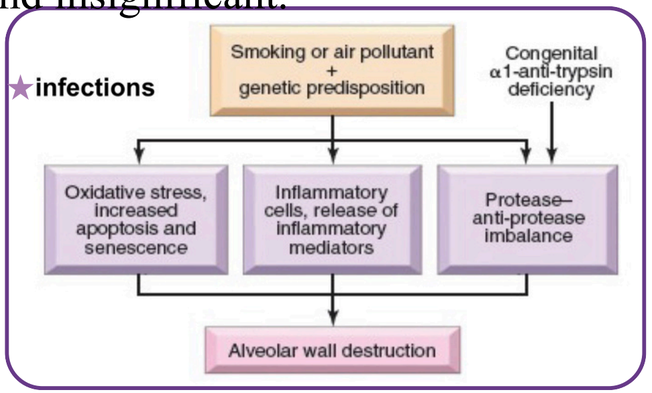
Definition : Permanent (irreversible) enlargement of the airspaces distal to the terminal bronchioles with destruction of their walls.
Subtle but functionally important small airway fibrosis > significant contributor to airflow obstruction.



Types : Classified according to its anatomic distribution:

- **Centriacinar :** is the most common type because it is strongly associated with smoking and chronic bronchitis
- **Panacinar :** α1-antitrypsin deficiency.
- **Distal acinar (Paraseptal) :** adjacent to fibrosis, scarring or atelectasis ,adj to pleura, along the lobular connective tissue septa, & at the margins of the lobules.
- **Irregular :** almost invariably associated with scarring , clinically asymptomatic and insignificant.

Pathogenisis : -Smoking / Air Pollutant + Genetic Predisposition.
-Oxidative stress.
-Inflammatory cells / Mediators release.
-Protease-antiprotease imbalance (α1-antitrypsin deficiency).
-Alveolar wall destruction.



★Infections cannot directly cause emphysema but can exacerbate the condition or trigger acute attacks in patients with existing disease.

Morphology:

Macroscopic: **Advanced emphysema** > voluminous lungs

Centriacinar emphysema[1]: Central areas show marked emphysematous damage surrounded by relatively spared alveolar spaces.

Panacinar emphysema[2]: involving the entire pulmonary lobule.

Microscopic[3]: Abnormally large alveoli are separated by thin septa with only focal centriacinar fibrosis.

Presentation:

-Symptoms appear after 1/3 parenchyma damaged

-Dyspnea (Early, progresses steadily)

-Barrel-chested

-Weight loss

-Prolonged expiration

-Sitting forward (hunched position)

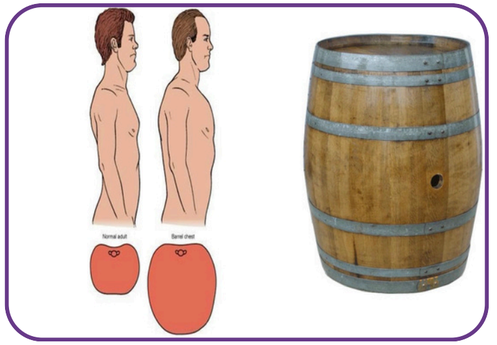
-Pursed-lip breathing

-Hyperventilation

-Adequate oxygenation at rest

-Severe dyspnea → "Pink puffers"

-Cough & wheezing (if asthma or chronic bronchitis coexist)



Outcome: Decreased capillary bed area

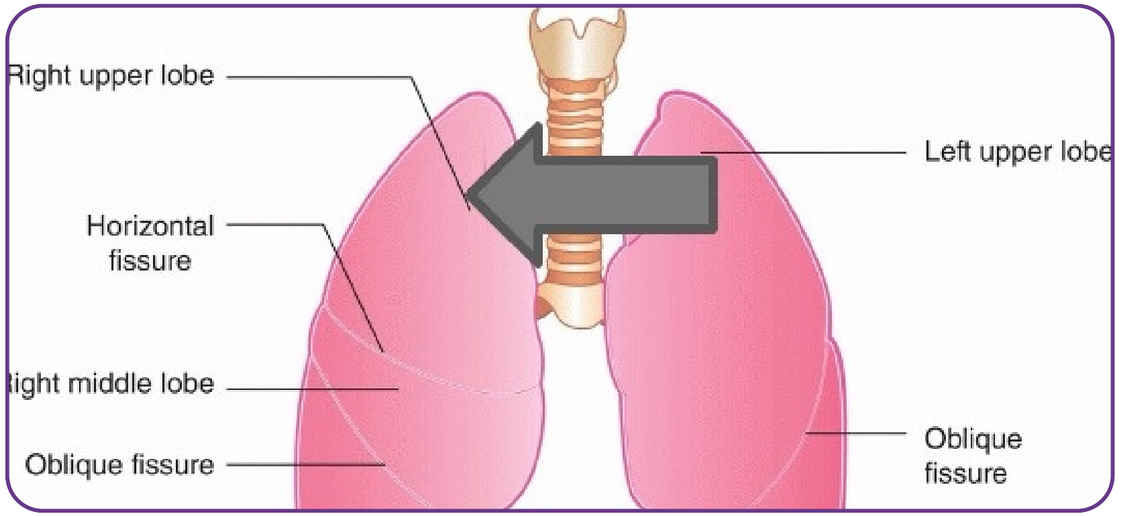
Due to: Destruction of alveolar walls

Enlarged airspaces (bullae & blebs) > Compression of respiratory bronchioles & lung vasculature

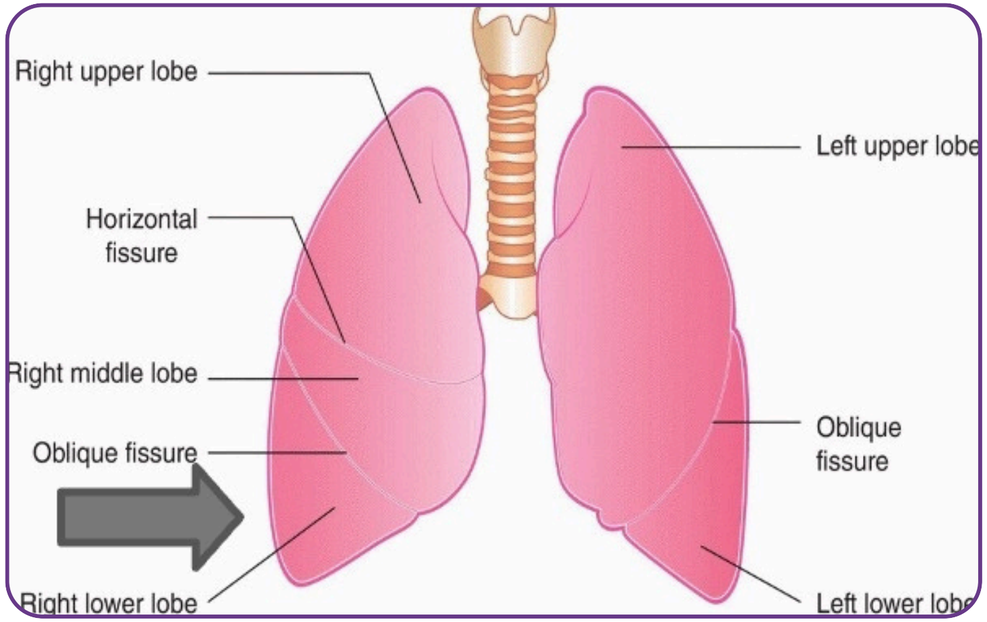
Inflammatory changes in small airways.

Effect: Hypoxia.

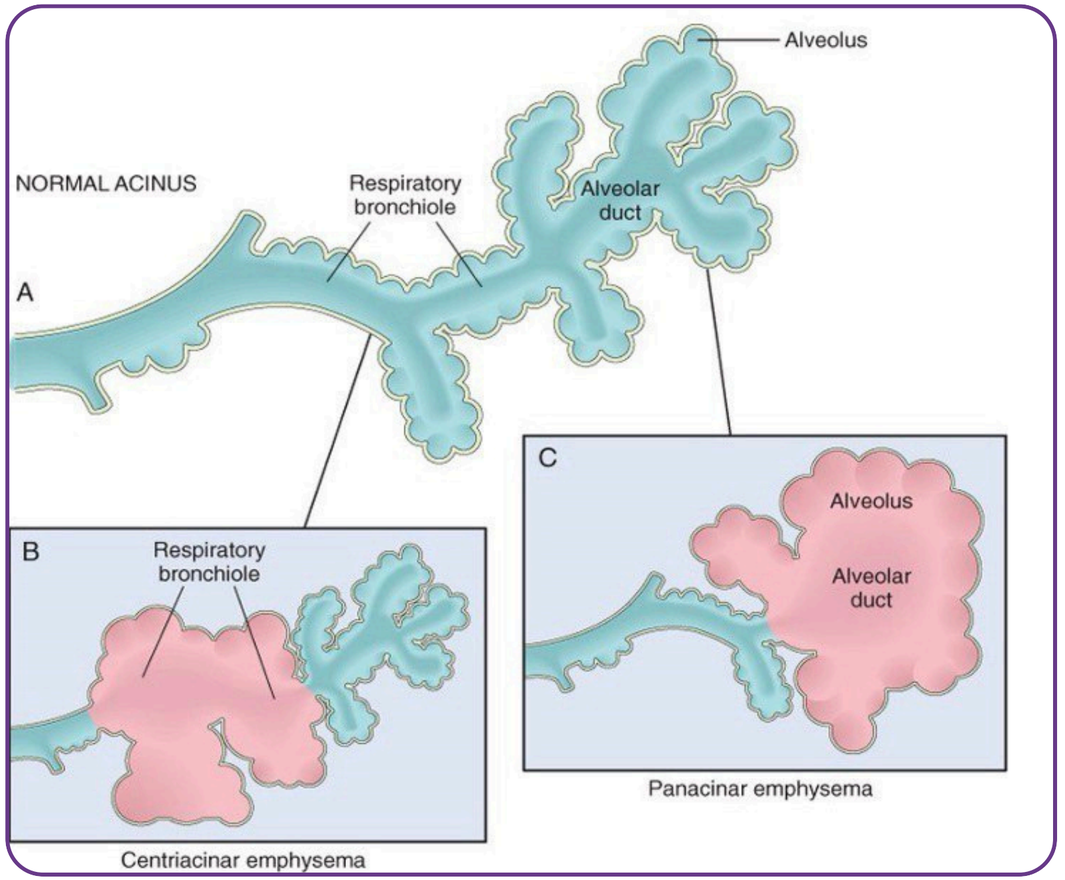
Consequences of hypoxia: Pulmonary vascular spasm ,Gradual development of secondary pulmonary hypertension , in 20-30% > Right-sided heart failure (cor pulmonale).

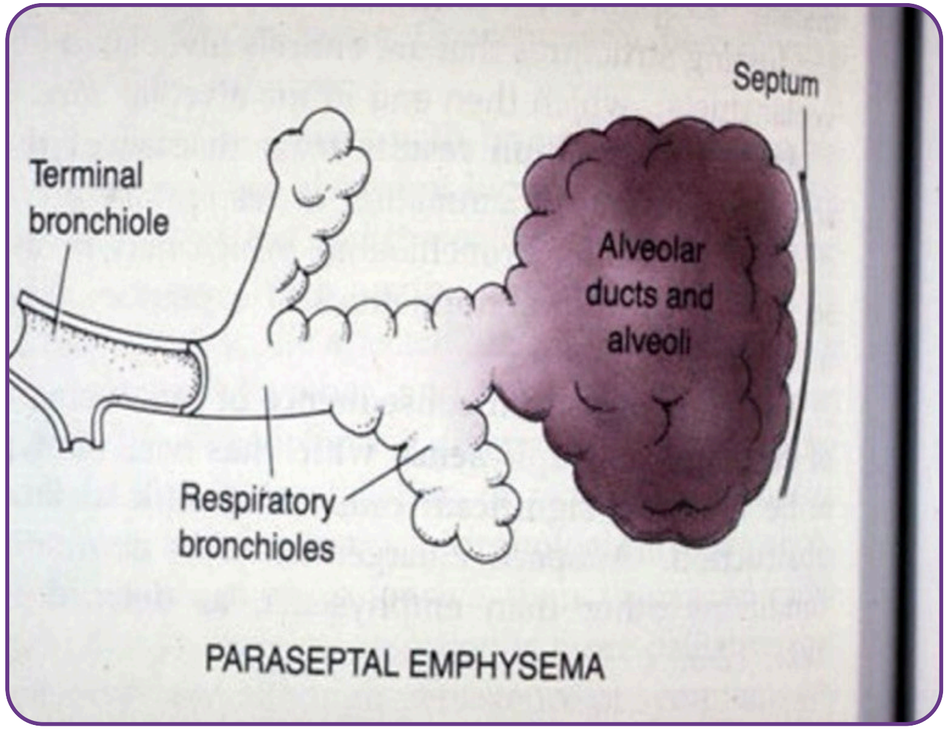


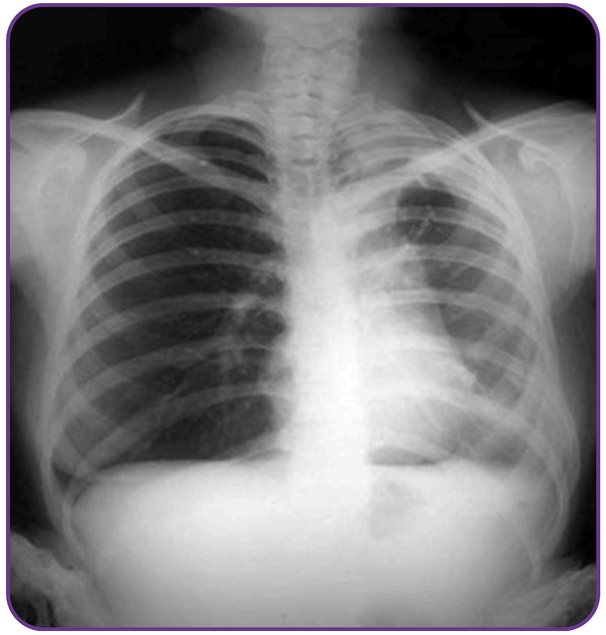
Centriacinar emphysema is much more common and more severe in the upper half of the lung, especially the apical segments



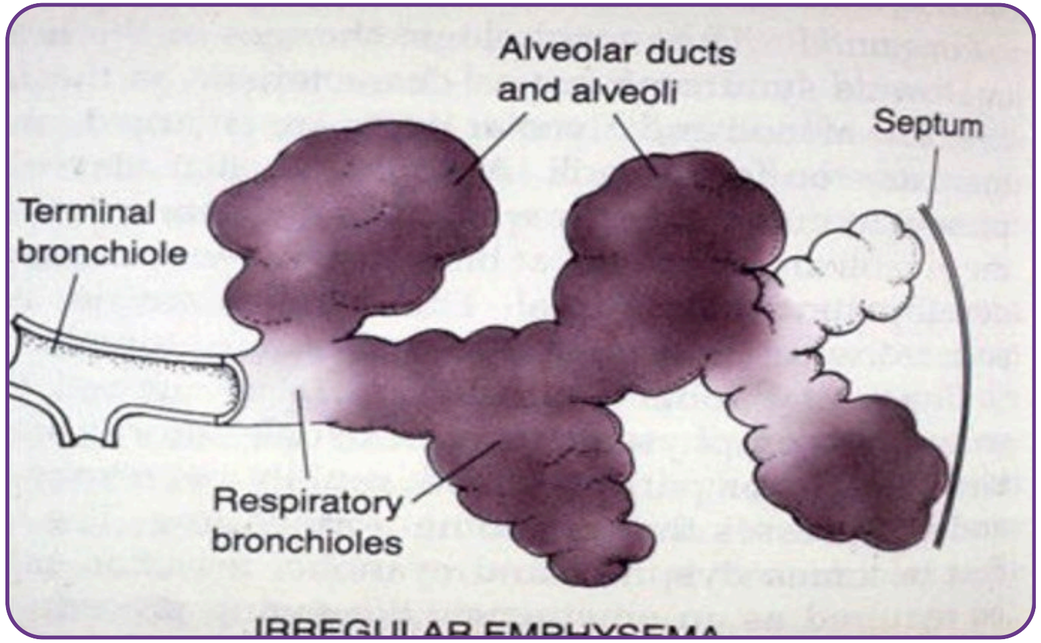
Panacinar emphysema more commonly and severely affects the lower part of the lung, especially the lung base and anterior margin

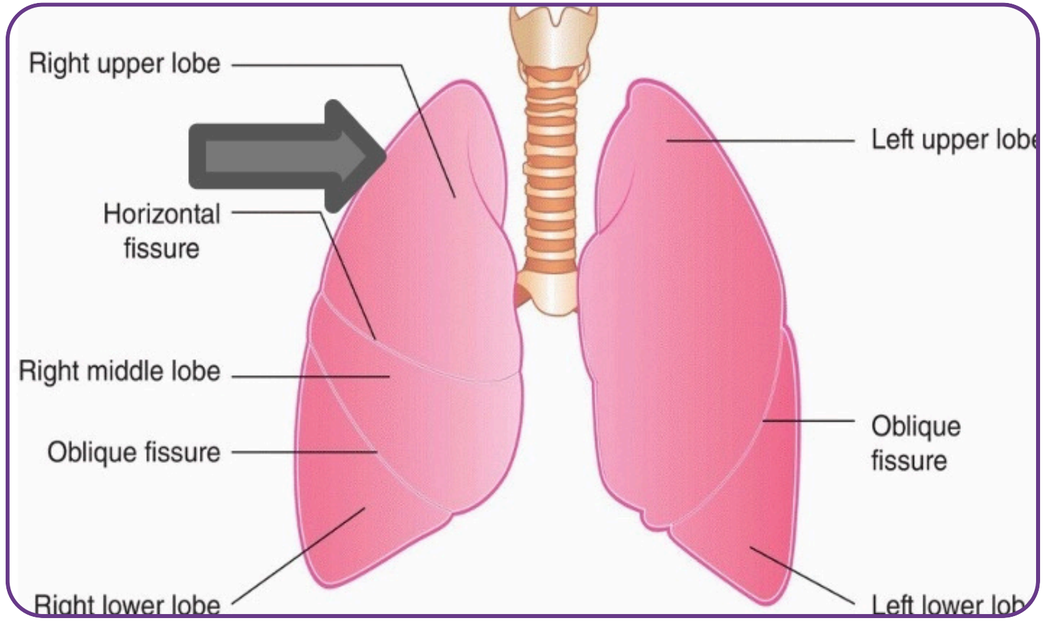






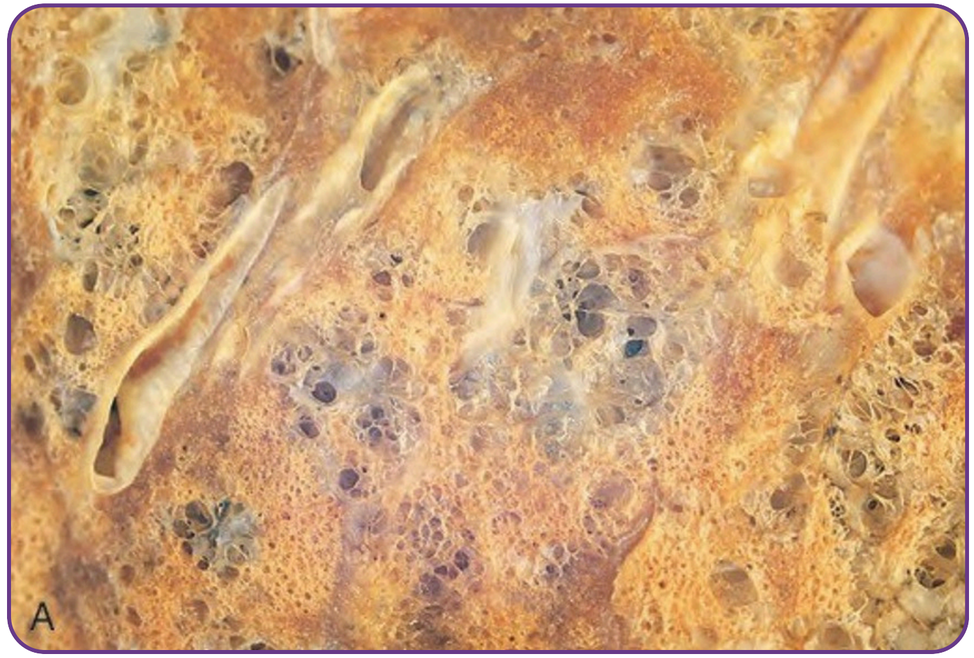
The right side is affected by pneumothorax.
The black color indicates a loss of lung markings (pneumothorax is covering the whole right lung).
Heart and mediastinum are shifted to the left due to air accumulation in the right pleural cavity.





Distal emphysema is more common and more severely affects the upper part of the lung, especially the apical segments

1



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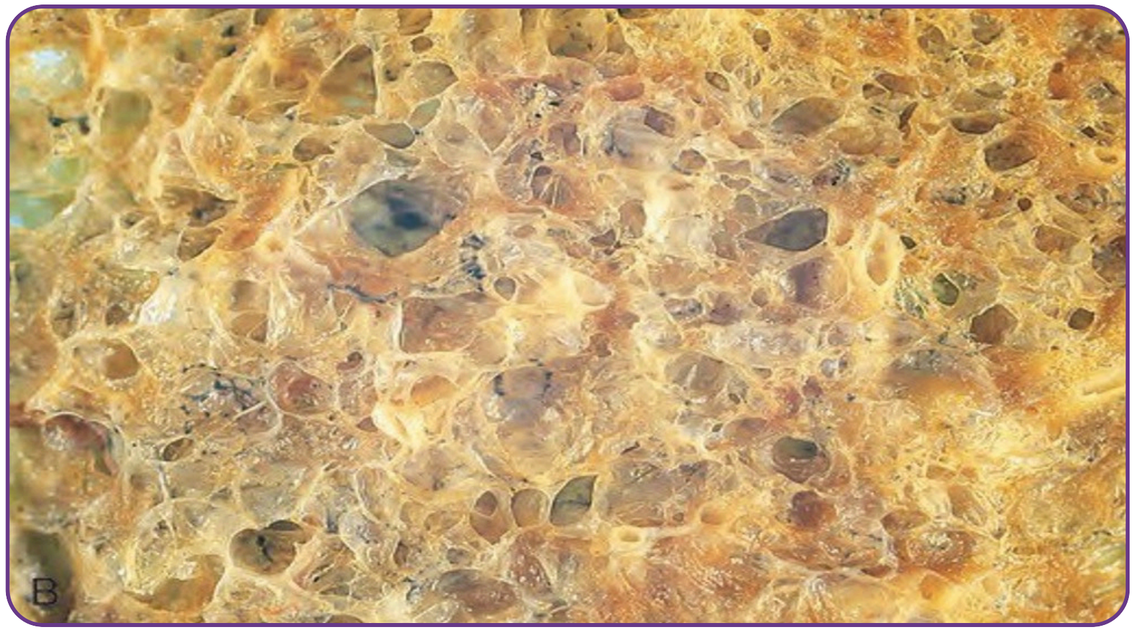

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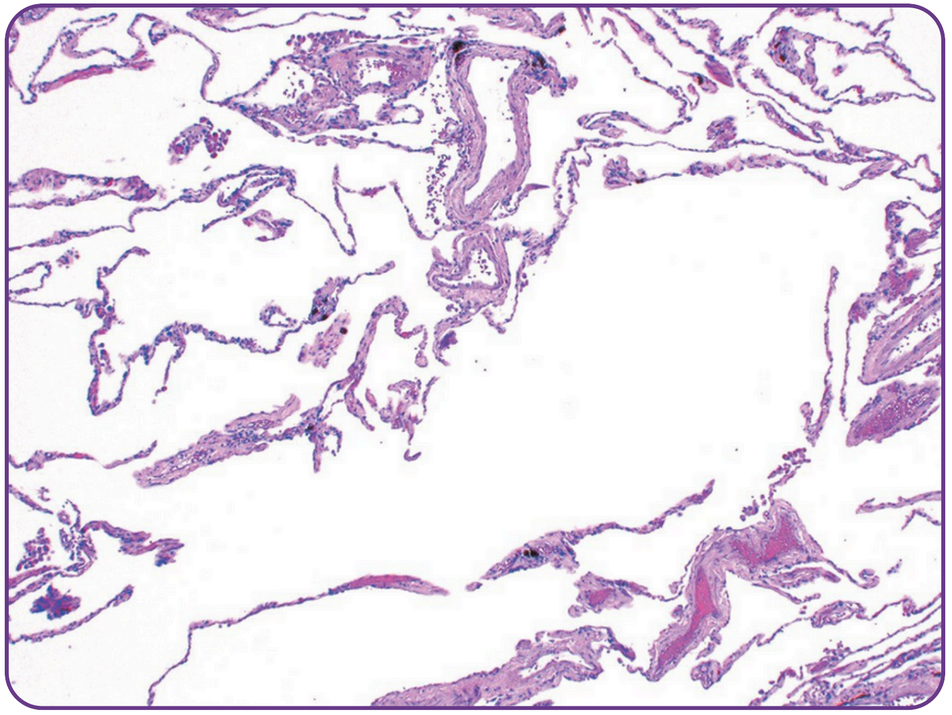


Chronic bronchitis

Definition : Persistent productive cough for ***at least 3 consecutive months in at least 2 consecutive years*** in the absence of any other identifiable cause

Pathogenisis : -90% Cigarette smokers -Air Pollutant
-Dust from grain, cotton, and silica

Pathophysiology:

Hypersecretion of Mucus: Earliest feature, starts in **large airways**
Acquired **CFTR dysfunctio**n > caused by smoking > abnormal dehydrated mucus > worsens chronic bronchitis

Inflammation: Caused by inhalants, **No eosinophils**
Long-standing inflammation & fibrosis in small airways (<2–3 mm) > chronic airway obstruction

Infection : Does **not initiate** chronic bronchitis, Contributes to acute exacerbations

Airflow Obstruction: Early stages: **no obstruction**
Later stages caused by:
1.Small airway disease
-Chronic bronchiolitis results in mild airflow obstruction
-Due to: mucus plugging, inflammation, wall fibrosis
2.Coexistent emphysema the cause of significant obstruction

Table 15-4 Emphysema and Chronic Bronchitis

	Predominant Bronchitis	Predominant Emphysema
Age (yr)	40-45	50-75
Dyspnea	Mild; late	Severe; early
Cough	Early; copious sputum	Late; scanty sputum
Infections	Common	Occasional
Respiratory insufficiency	Repeated	Terminal
Cor pulmonale	Common	Rare; terminal
Airway resistance	Increased	Normal or slightly increased
Elastic recoil	Normal	Low
Chest radiograph	Prominent vessels; large heart	Hyperinflation; small heart
Appearance	Blue bloater	Pink puffer

Long-term Consequences: -Decline in lung function > cor pulmonale
-Atypical metaplasia & dysplasia of the respiratory epithelium > risk of cancer
-May coexist with hyper-responsive airways > intermittent bronchospasm & wheezing (asthmatic bronchitis)

Morphology:

Macroscopic: -Mucosal lining is hyperemic and swollen
-Layers of mucinous or mucopurulent secretions

Microscopic: -Mild chronic inflammation of the airways (predominantly lymphocytes)
-Hyperplasia of the mucus-secreting glands of the trachea and bronchi
-Squamous metaplasia and dysplasia of the bronchial epithelium
-Changes of emphysema often co-exist

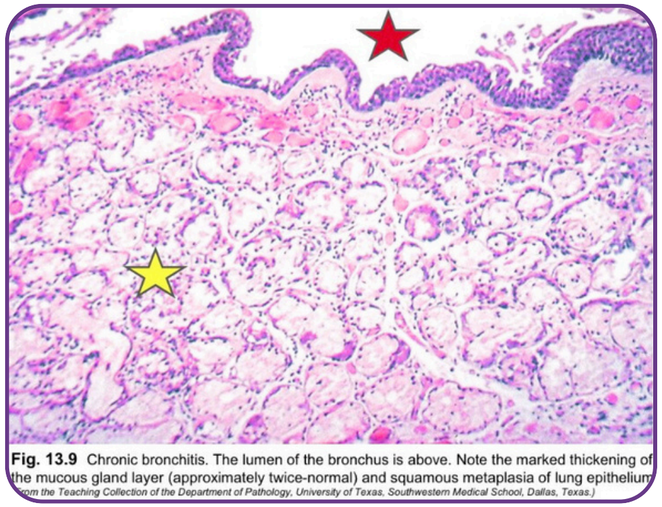


Fig. 13.9 Chronic bronchitis. The lumen of the bronchus is above. Note the marked thickening of the mucous gland layer (approximately twice-normal) and squamous metaplasia of lung epithelium. *(From the Teaching Collection of the Department of Pathology, University of Texas, Southwestern Medical School, Dallas, Texas.)*

Clinical features :

- Persistent cough with sparse sputum
- Initially no respiratory impairment, later dyspnea on exertion
- Frequent exacerbations in chronic bronchitis & COPD patients
- Rapid disease progression ,poorer outcomes compared to emphysema alone

Outcomes :

Progressive disease > pulmonary hypertension, cardiac failure, recurrent infections, respiratory failure
Death ***may occur*** from superimposed acute infections
Less dyspnea
Absence of increased respiratory drive > lungs retain CO_2 > hypoxia & cyanosis
Obesity tendency → "blue bloaters" > CO_2 retention, hypoxia, cyanosis

Asthma

Definition : -Chronic inflammatory disorder of the airways .
-Causes recurrent episodes of wheezing, Dyspnea, chest tightness and cough particularly at night and/or early in the morning.

Hallmarks: a.**Intermittent and reversible** airway obstruction (bronchospasm)
b.Chronic bronchial inflammation **with eosinophils**.
c.Bronchial smooth muscle cell **hypertrophy and hyperreactivity**.
d.increased **mucus secretion.**

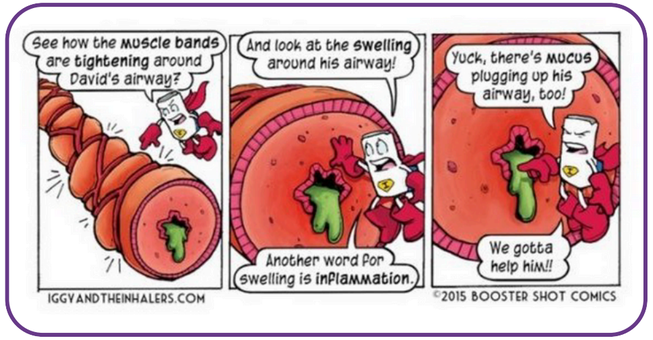
Major Factors: -Genetic predisposition to type I hypersensitivity (atopy)
-Acute and chronic airway inflammation
-Bronchial hyperresponsiveness to a variety of stimuli

Triggers: -respiratory infections (especially viral)
-airborne irritants (smoke, fumes)
-cold air
-Stress
-exercise

Pathogenesis:

Initial Sensitization[1]: IgE production via TH2/IL-4, IL-5

early (immediate) phase reaction[2]:



-Mechanism:
1.re-exposure to antigen.
2.triggered by Ag-induced cross-linking of IgE bound to Fc receptors on mast cells.
3.mast cells release preformed mediators that directly and via neuronal reflexes.
-Dominated effects:1.bronchoconstriction 2.increased mucus production 3.vasodilation 4.recruitment of leukocytes

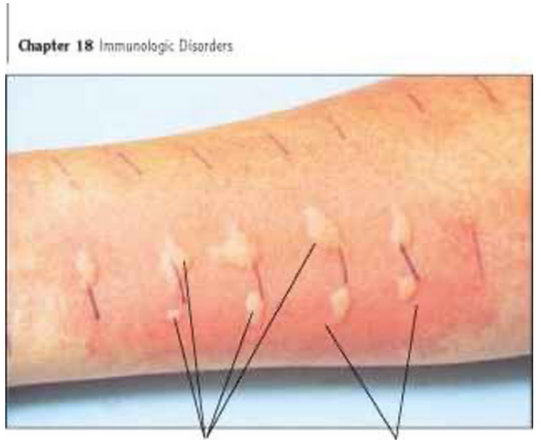
Late-phase reaction (inflammatory)[3]:

-Inflammatory mediators >stimulate epithelial cells to produce chemokines (eotaxin) >recruit TH2 cells, eosinophils, and other leukocytes >amplifying the inflammatory reaction.
-Leukocytes recruited to the site of reaction (neutrophils, eosinophils, and basophils; lymphocytes and monocytes) > release mediators > initiate the late phase of asthma.
-eosinophils release major basic protein and eosinophil cationic protein that cause damage to the epithelium

Airway Remodeling (Structural changes from repeated inflammation)[4]:

1.hypertrophy of bronchial smooth muscle
2.hypertrophy of Mucus glands
3. increased vascularity
4. deposition of subepithelial collagen

Types:



Atopic Asthma:

-The most common

-type I **IgE–mediated hypersensitivity** reaction

-beginning in ***childhood***

-Positive family history of ***atopy and/or asthma***

- attacks are preceded by **allergic rhinitis, urticaria, or eczema**

- Attacks are triggered by allergens in ***dust, pollen, animal dander, or food, or by infections***.

-Exposure to the antigen > ***excessive activation of type 2 helper cells*** > Cytokines production > IL-4 and IL-13 stimulate IgE production > IL-5 activates eosinophils > IL-13 also stimulates mucus production

IgE coats submucosal mast cells> release of Mast cell– derived mediators > produce two waves of reaction:

1.**early** (immediate) phase 2.**late** phase

-**Skin test with the antigen:**immediate wheal-and-flare reaction

-**serum radioallergosorbent tests (RASTs)**: a blood test using radioimmunoassay to detect specific IgE antibodies, to determine the substances a subject is allergic to

Non-Atopic Asthma:

-No evidence of allergen sensitization

-Negative skin test

-A positive family history of asthma is **less common.**

-Triggered by:a.viral respiratory infections (rhinovirus, parainfluenza virus)

b.inhaled air pollutants (sulfur dioxide, ozone, nitrogen dioxide).

Drug-induced Asthma:

- Eg: Aspirin induced asthma > present with recurrent rhinitis ,nasal polyps , urticaria, and bronchospasm
-The precise pathogenesis is unknown > involve some abnormality in prostaglandin metabolism from inhibition of cyclooxygenase by aspirin

Occupational Asthma:

-triggered by fumes (epoxy resins, plastics), organic and chemical dusts (wood, cotton, platinum), gases (toluene), and other chemicals.
-Asthma attacks usually develop after repeated exposure to the antigen.

Morphology:

-occlusion of bronchi and bronchioles by **thick mucous plugs**
- mucous plugs contain whorls of shed epithelium called **Curschmann spirals** [1].
-fibrosis, eosinophilic inflammation, and smooth muscle hyperplasia [2].
-**Charcot-Leyden crystals**[3]: crystalloids made up of the eosinophil protein galectin-10
-**airway remodeling**[4], including:*(Thickening of airway wall , Sub-basement membrane fibrosis , Increased submucosal vascularity ,An increase in size of the submucosal glands and goblet cell metaplasia of the airway epithelium , Hypertrophy and/or hyperplasia of the bronchial muscle)*
-In fatal cases> distension of lungs

Managment:

-Anti-inflammatory drugs **(glucocorticoids)** - Bronchodilators **(beta-adrenergic drugs)** - Leukotriene inhibitors

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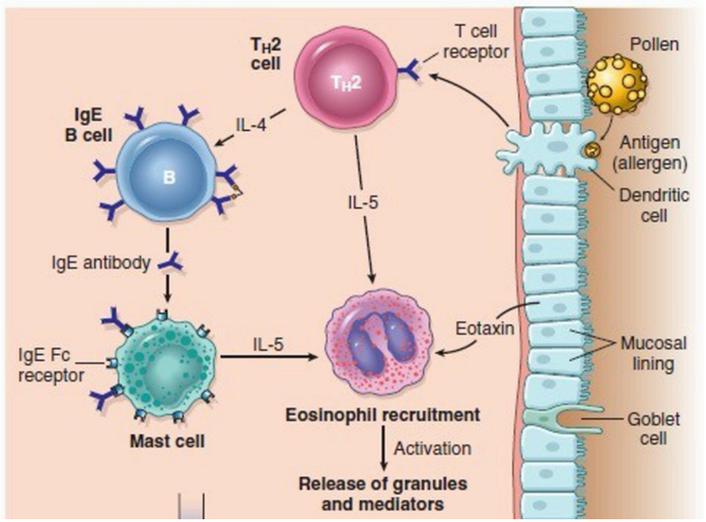

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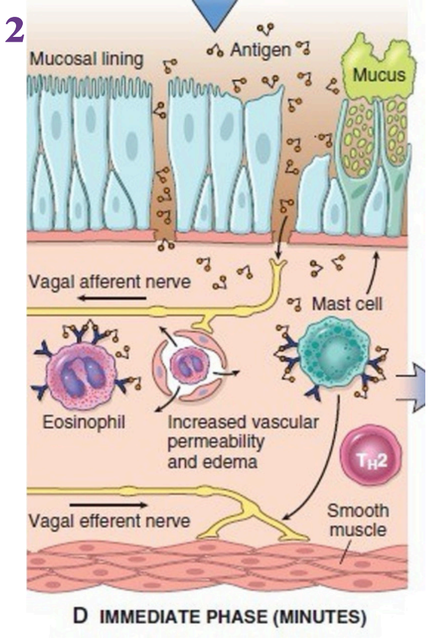

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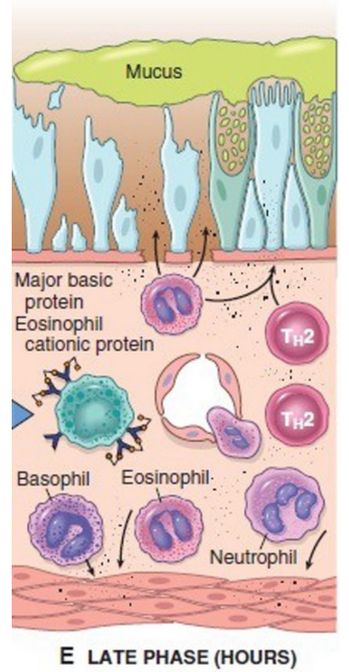

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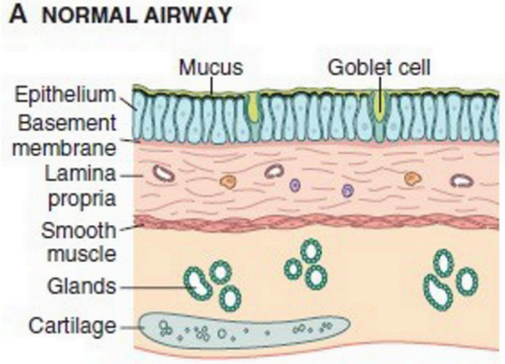
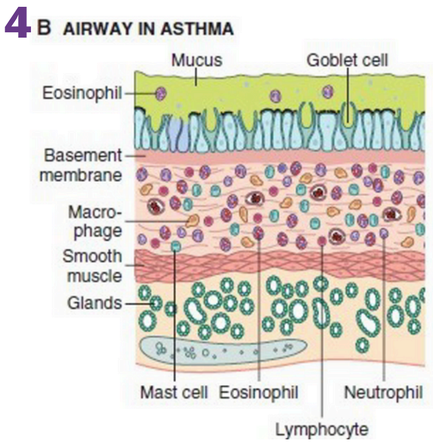
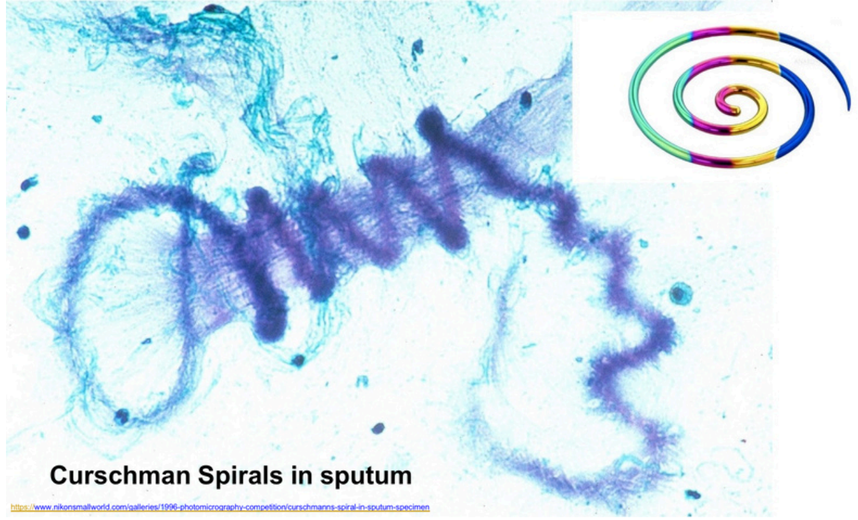




increased number of mucus-secreting goblet cells
hypertrophy of submucosal glands
accumulation of mucus in the bronchial lumen
thickened basement membrane
intense chronic inflammation
hypertrophy and hyperplasia of smooth muscle cells

CLINICAL FEATURES

1



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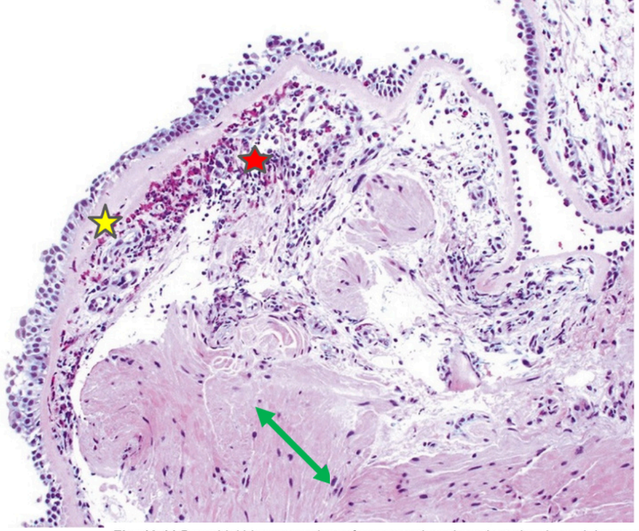
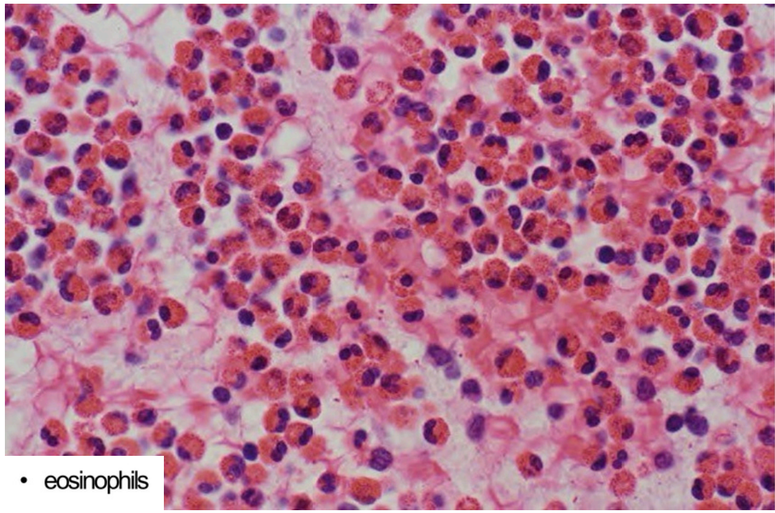


Fig. 13.11 Bronchial biopsy specimen from an asthmatic patient showing sub basement membrane fibrosis, eosinophilic inflammation, and smooth muscle hyperplasia



- eosinophils

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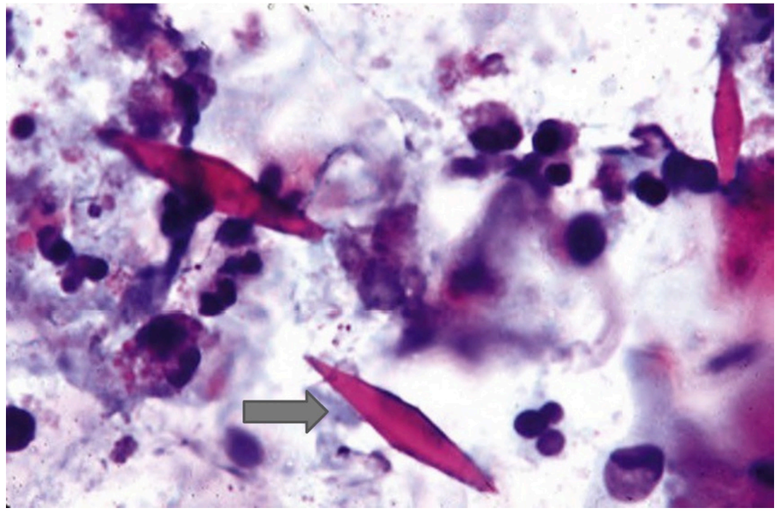

- **Charcot-Leyden crystals:** crystalloids made up of the eosinophil protein galectin-10

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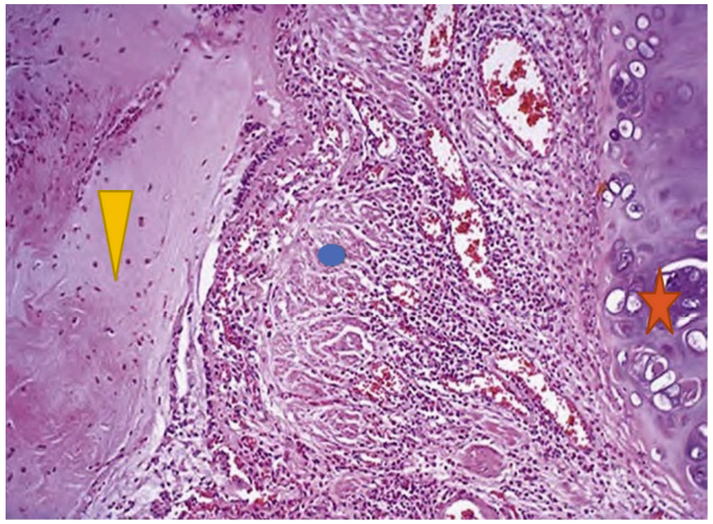
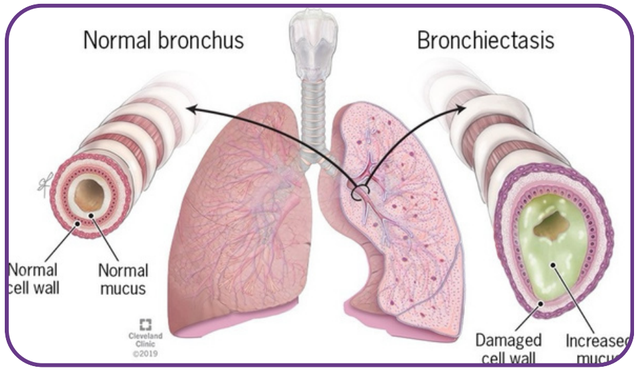


Status asthmaticus:

A severe, life-threatening asthma attack that does not respond to standard treatments (inhaled bronchodilators), leading to progressive airway obstruction, hypoxia, and possible respiratory failure.

Bronchiectasis

Definition : -**Permanent** dilation of **bronchi and bronchioles** caused by destruction of smooth muscle and the elastic tissue
-Results from chronic **necrotizing infections**
-It is not a primary disorder, as it always occurs **secondary** to persistent infection or obstruction



Clinically: cough and expectoration of copious amounts of purulent sputum

Diagnosis: appropriate **history and radiographic** demonstration of **bronchial dilation.**

Pathogenesis:

Obstruction: obstruction > impairs clearance of secretions > superimposed infection > inflammatory damage to the bronchial wall + the accumulating exudate > airways distention > **irreversible dilation.**

Chronic infection: persistent necrotizing infection in the bronchi or bronchioles > poor clearance of secretions, obstruction, inflammation with peribronchial fibrosis and traction on the bronchi > **irreversible dilation**

Predisposing Conditions:

Bronchial obstruction: -By tumors, foreign bodies, and impaction of mucus OR as a complication of atopic asthma and chronic bronchitis
-bronchiectasis is localized

Cystic fibrosis: -Widespread severe bronchiectasis
-Due to obstruction caused by abnormally viscid mucus and secondary infections

Immunodeficiency states: -Due to recurrent bacterial infections
-Localized or diffuse

Primary ciliary dyskinesia(immotile cilia syndrome):
-rare autosomal recessive disorder > abnormalities of cilia > persistent infections.
-bronchiectasis + sterility in males

Necrotizing, suppurative, pneumonia: particularly with virulent organisms such as **Staphylococcus aureus** or **Klebsiella spp.**

Morphology:

Macroscopic: **-Lower lobes bilaterally**
-Most severe involvement in **distal bronchi and bronchioles.**
-The airways may be dilated to as much as four times their usual diameter [1]

Microscopic[2]: **In full-blown active cases:**

-intense acute and chronic inflammatory exudate within the walls of the bronchi and bronchioles > desquamation of lining epithelium and extensive ulceration

-mixed flora are cultured from the sputum

When healing occurs:

-the lining epithelium may regenerate completely

-abnormal dilation and scarring

-fibrosis of bronchial and bronchiolar walls

-peribronchiolar fibrosis

-abscess formation in some cases

Clinical Features: -severe, persistent cough with mucopurulent sputum.*(Other symptoms: dyspnea, rhinosinusitis, and hemoptysis)*

-episodic

-precipitated by URTI.

-Severe widespread bronchiectasis : *significant obstructive ventilatory defects, hypoxemia, hypercapnia, pulmonary hypertension, and cor pulmonale*

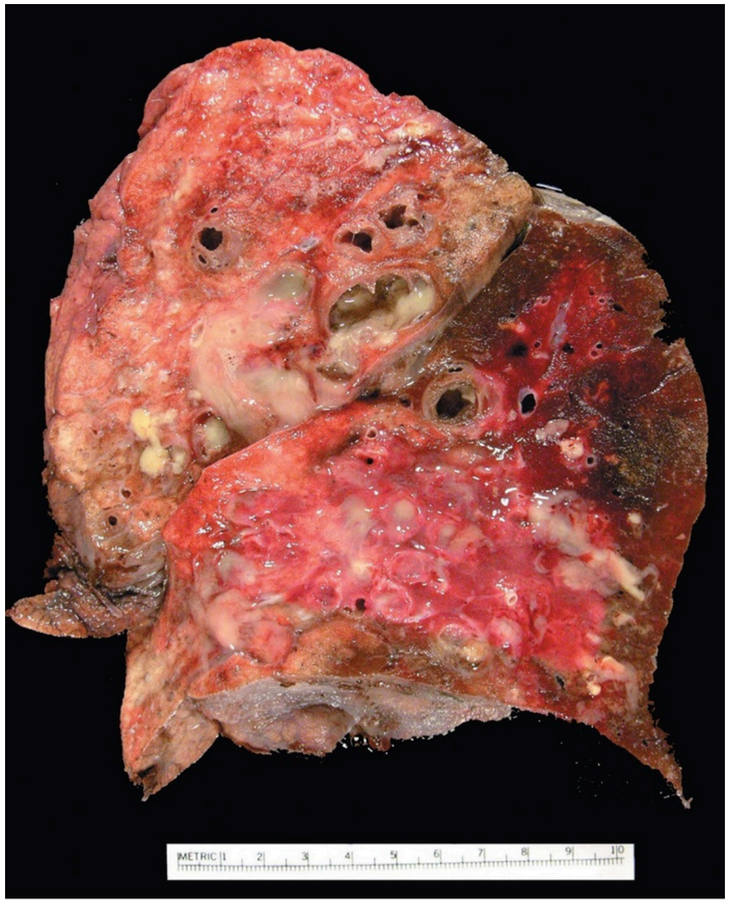
In Summary :

Table 13.1 Disorders Associated With Airflow Obstruction: The Spectrum of Chronic Obstructive Pulmonary Disease

Clinical Entity	Anatomic Site	Major Pathologic Changes	Etiology	Signs/Symptoms
Chronic bronchitis	Bronchus	Mucous gland hypertrophy and hyperplasia, hypersecretion	Tobacco smoke, air pollutants	Cough, sputum production
Bronchiectasis	Bronchus	Airway dilation and scarring	Persistent or severe infections	Cough, purulent sputum, fever
Asthma	Bronchus	Smooth muscle hypertrophy and hyperplasia, excessive mucus, inflammation	Immunologic or undefined causes	Episodic wheezing, cough, dyspnea
Emphysema	Acinus	Air space enlargement, wall destruction	Tobacco smoke	Dyspnea
Small airway disease, bronchiolitis*	Bronchiole	Inflammatory scarring, partial obliteration of bronchioles	Tobacco smoke, air pollutants	Cough, dyspnea

*Can be present in all forms of obstructive lung disease or by itself.

1



markedly dilated bronchi filled with purulent mucus

2

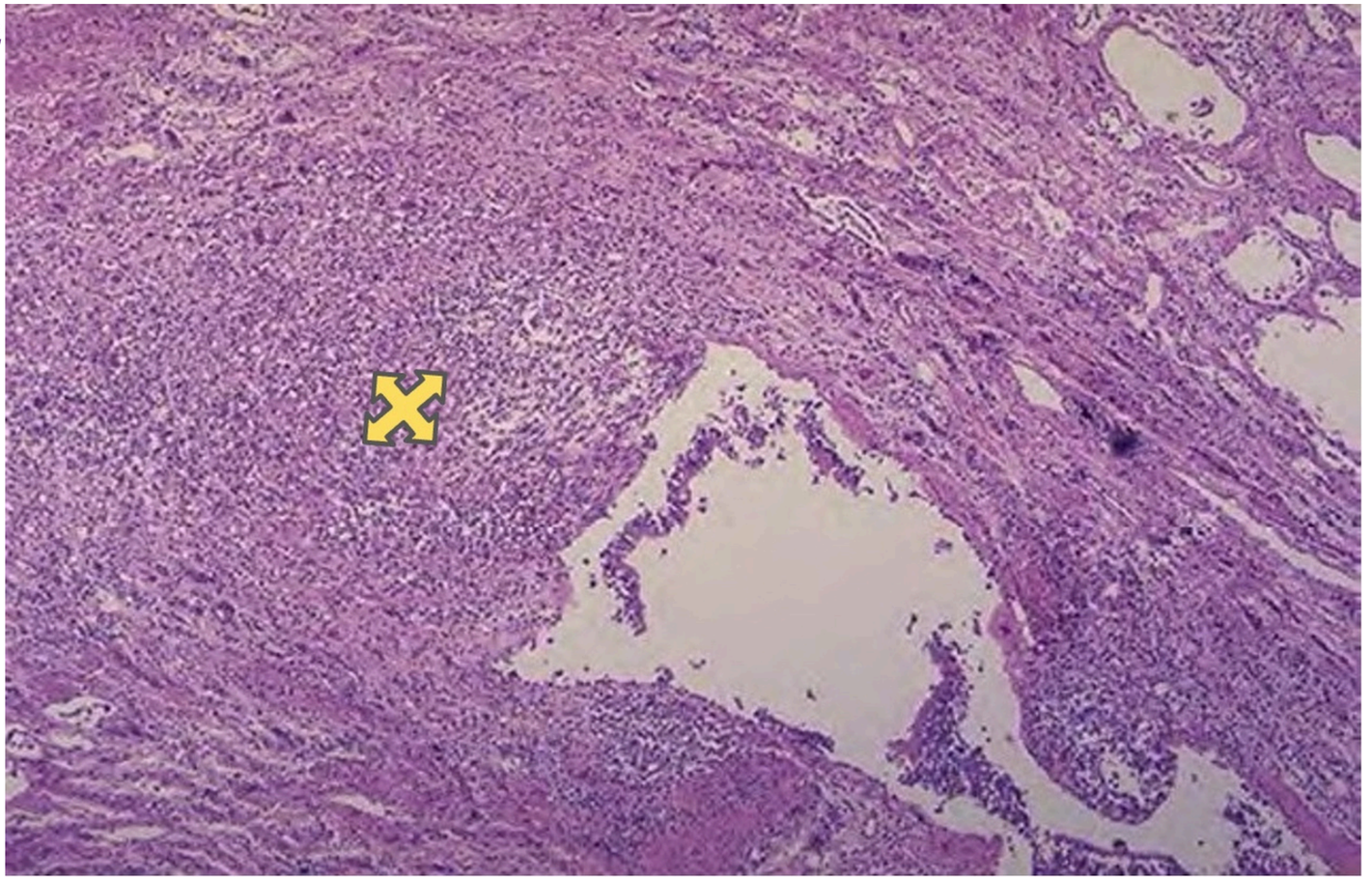


Figure 5-34 **Bronchiectasis, microscopic** dilated bronchus in which the mucosa and bronchial wall are not seen clearly because of the necrotizing inflammation with tissue destruction.

Robbin's and Cotran Atlas of pathology, 3rd edition

{رَبَّنَا أَتْمِمْ لَنَا نُورَنَا وَاغْفِرْ لَنَا ۖ إِنَّكَ عَلَىٰ كُلِّ شَيْءٍ قَدِيرٌ}

A 20-year-old, previously healthy gentleman is jogging one morning when he falls to the ground. He suddenly becomes markedly short of breath. in ER no breath sounds audible over the Rt side of the chest. **A CXR shows shift of the mediastinum from right to left. A chest tube is inserted on the right side, and air rushes out**. Which of the following underlying diseases is most likely to have produced this complication?

A) Centriacinar emphysema

B) Chronic bronchitis

C) Distal acinar emphysema

D) Panlobular emphysema

الحمد لله أقصى مبالغ الحمد، والشكر لله من قبل ومن بعد

Ans:
C) Distal acinar emphysema

﴿ الَّذِينَ يَتَّبِعُونَ الرَّسُولَ النَّبِيَّ الْأُمِّيَّ الَّذِي يَجِدُونَهُ مَكْتُوبًا عِندَهُمْ فِي التَّوْرَاةِ وَالْإِنجِيلِ يَأْمُرُهُم بِالْمَعْرُوفِ وَيَنْهَاهُمْ عَنِ الْمُنكَرِ وَيُحِلُّ لَهُمُ الطَّيِّبَاتِ وَيُحَرِّمُ عَلَيْهِمُ الْخَبَائِثَ وَيَضَعُ عَنْهُمْ إِصْرَهُمْ وَالْأَغْلَالَ الَّتِي كَانَتْ عَلَيْهِمْ ۚ فَالَّذِينَ آمَنُوا بِهِ وَعَزَّرُوهُ وَنَصَرُوهُ وَاتَّبَعُوا النُّورَ الَّذِي أُنزِلَ مَعَهُ ۙ أُولَٰئِكَ هُمُ الْمُفْلِحُونَ ﴾

[الأعراف: 157]

كلمة أخيرة لزملائنا وزميلاتنا

مثل قالت الدكتورة انه التدخين راح ينذكر معنا بكل محاضرات أمراض الجهاز التنفسي تقريبًا، لأنه سبب رئيسي لكثير من هذه الأمراض

كلمة بسيطة بنحكيلكم إياها من باب النصيحة: ديروا بالكم على صحتكم، وحاولوا تبعدوا عن التدخين، حرصًا على دينكم، صحتكم وصحة اللي حواليكم

ونسأل الله أن يديم علينا الصحة والعافية

وارجعوا احضروا الفيديو يلي بالأول 🙏