بسم الله الرحمن الرحيم

DOPAMINE SCIENTIFIC TEAM

PATHOLOGY

MID | Lecture # 2

Emphysema & bronchitis

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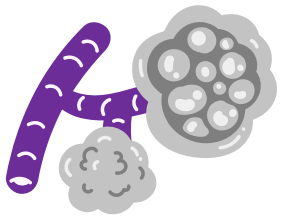
﴿وَلَقَدْ نَعْلَمُ أَنَّكَ يَضِيقُ صَدْرُكَ بِمَا يَقُولُونَ ﴿٩٧﴾ فَسَبِّحْ بِحَمْدِ رَبِّكَ وَكُن مِّنَ السَّاجِدِينَ﴾

سبحان الله وبحمده، سبحان الله العظيم



وَلِلَّهِ الْأَسْمَاءُ الْحُسْنَى فَادْعُوهُ بِهَا

المعنى: القادر على كل شيء أراده، فلا يُعجزه شيء في الأرض ولا في السماء، و (المقتدر) مبالغة في الوصف بالقدرة، و(القدير) كامل القدرة.

الورود: ورد اسم القادر (١٢) مرة، أما اسم القدير فورد (٤٥) مرة، واسم المقتدر (٤) مرات.

الشاهد: ﴿قُلْ هُوَ الْقَادِرُ عَلَىٰ أَن يَبْعَثَ عَلَيْكُمْ عَذَابًا مِّن فَوْقِكُمْ أَوْ مِن تَحْتِ أَرْجُلِكُمْ﴾ [الأنعام:٦٥]، ﴿وَهُوَ عَلَىٰ كُلِّ شَيْءٍ قَدِيرٌ﴾ [الروم:٥٠]، ﴿فِي مَقْعَدِ صِدْقٍ عِندَ مَلِيكٍ مُّقْتَدِرٍ﴾ [الرحمن:٥٥].

اضغط هنا لشرحٍ أكثر تفصيلًا

OBSTRUCTIVE LUNG DISEASES

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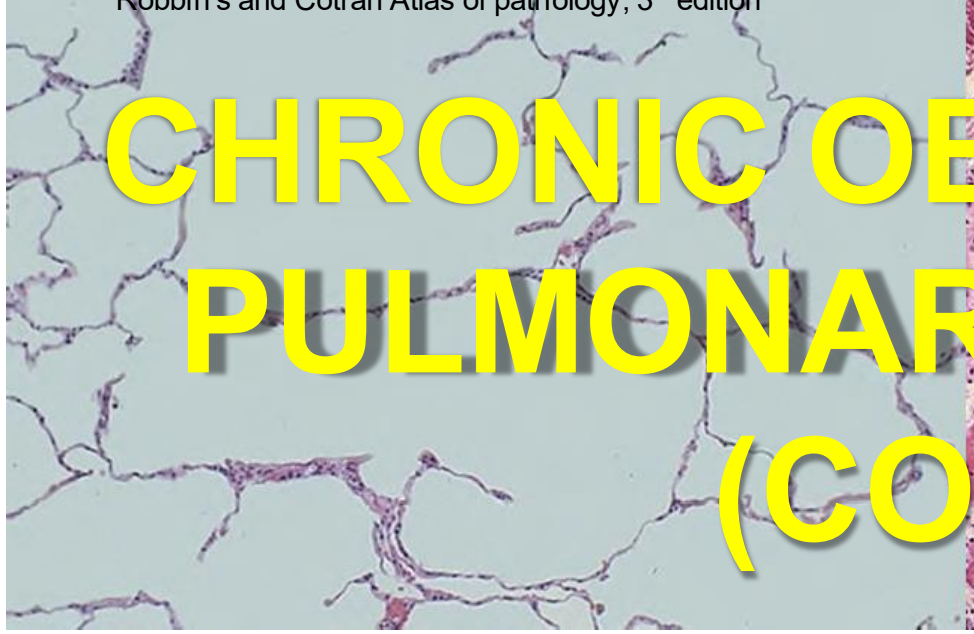
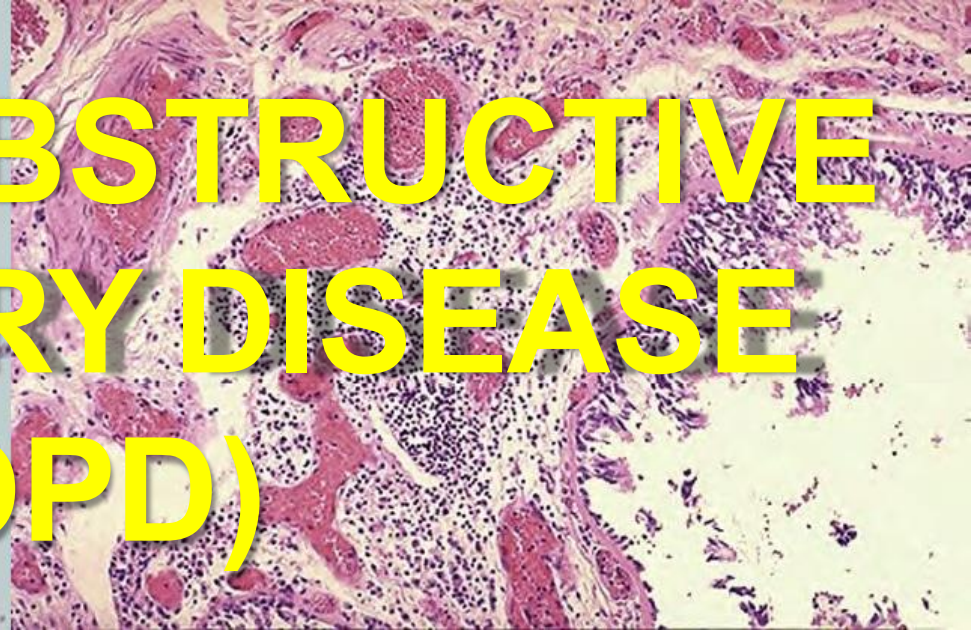
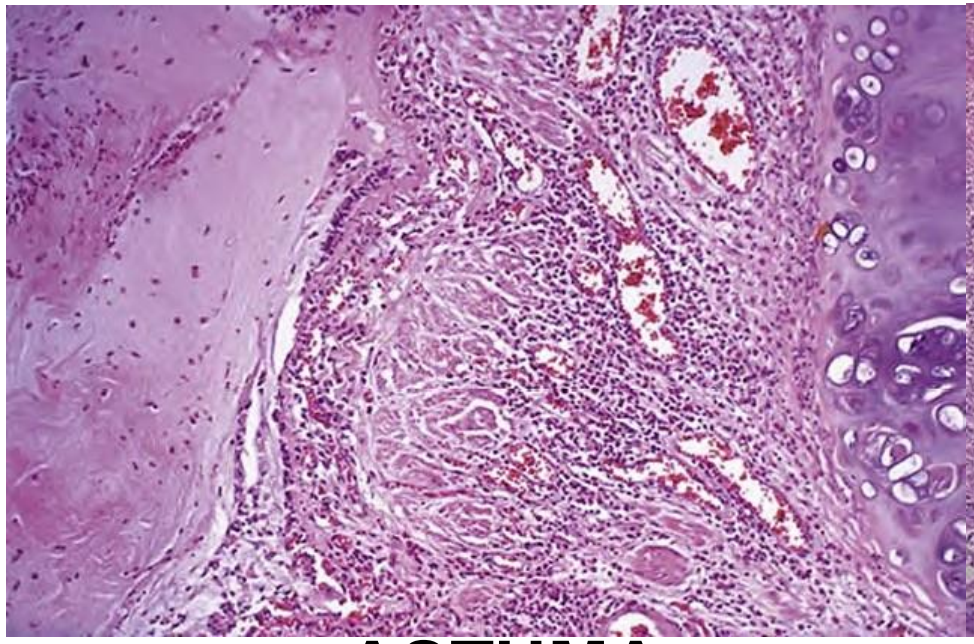
CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)



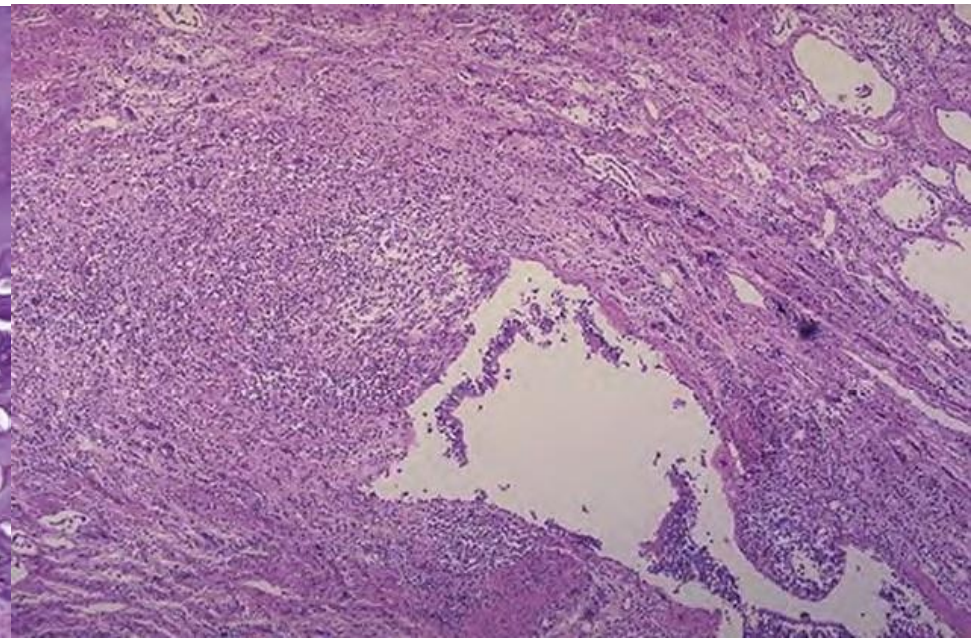
EMPHYSEMA



CHRONIC BRONCHITIS



ASTHMA



BRONCHIECTASIS

There are four major types of diffused obstructive pulmonary diseases :

- emphysema
- chronic bronchitis
- asthma
- bronchiectasis

Despite each one has its own clinical, morphologic and anatomic features , the overlap is consider common , so we can see a patient with two of the above diseases

Same thing applied to emphysema and chronic bronchitis but they are special , they tend to affect the same patient, and they share one of the common etiology of both which is tobacco smoking ..

Normally they are under the rubric of COPD

In diffused obstructive pulmonary diseases in general

It's hard to get the air OUT

It's hard to EXHALE the problem is in the exhaling , the Air will trapped in the lungs

Lungs are hyperinflated so the total lung volume and capacity will be either normal or slightly increased

It's like an old rubber band we can expansion because it has compliance but its ability to recoil is decreased because it lost its elastic fibers like in obstructive pulmonary diseases

In restrictive pulmonary diseases they are like new brand rubber band it's difficult to stretch but it easy to recoil .. Go back to restrictive lungs it's hard to inhale and easy to exhale .. Compliance ↓ elasticity ↑ total lung volume and capacity are decreased

- Total lung capacity: (TLC) is the volume of air in the lungs upon the maximum effort of inspiration.
- lung compliance is a measure of the lung's ability to stretch or expand

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

COPD:

- **defined by the WHO as** "a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation (obstructive)that is due to airway and/or alveolar abnormalities caused by exposure to noxious particles or gases." mainly in cigarette smoking
- 4th leading cause of death in the world
- There is a strong association between heavy cigarette smoking and COPD.

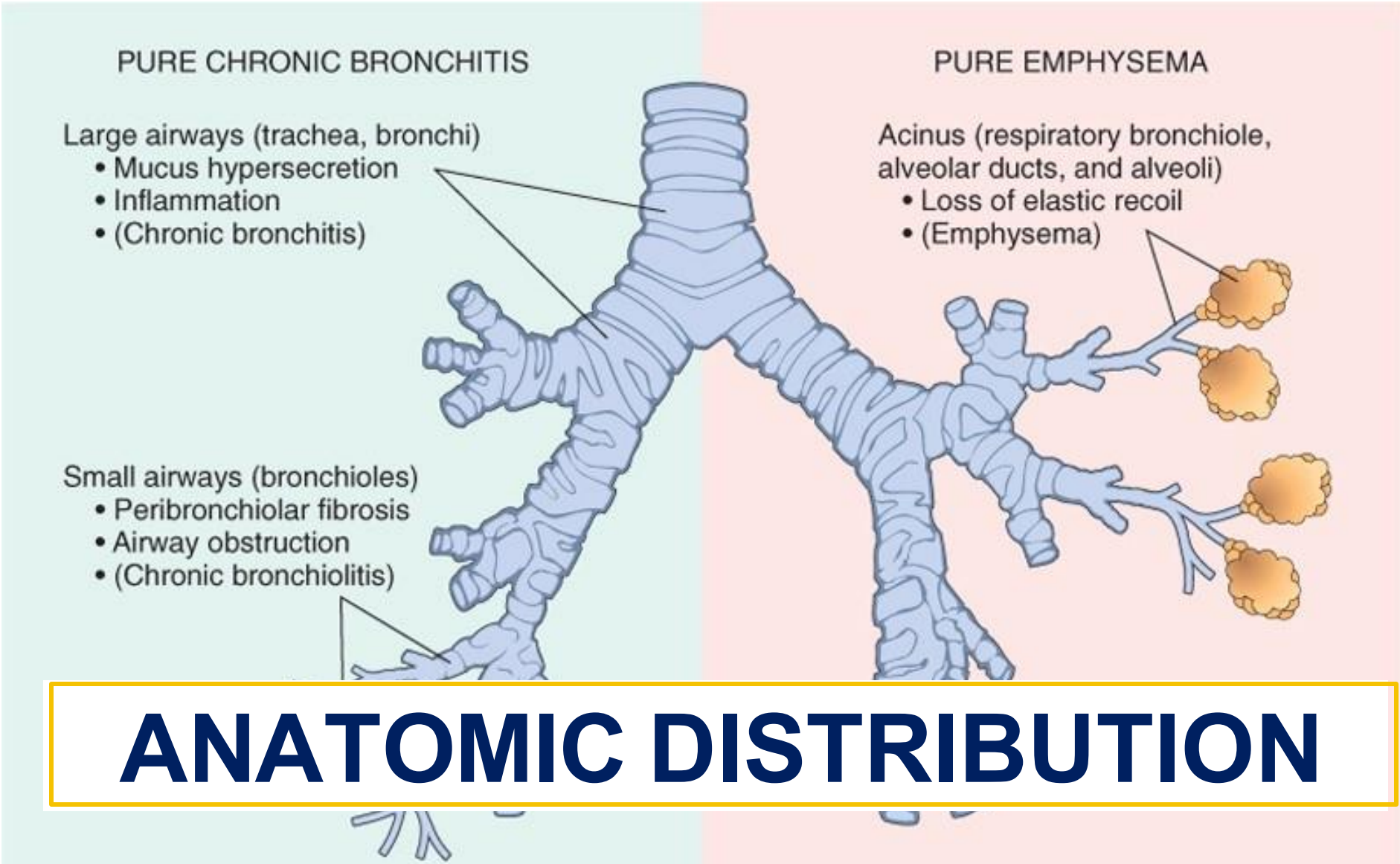
Not all smokers suffer from COPD

- 35% to 50% of heavy smokers develop COPD.
- 80% of COPD is attributed to smoking.

COPD is like a spectrum , at one end we have emphysema and the other end is chronic bronchitis, the patient will come with symptoms between them, the overlapping is common here

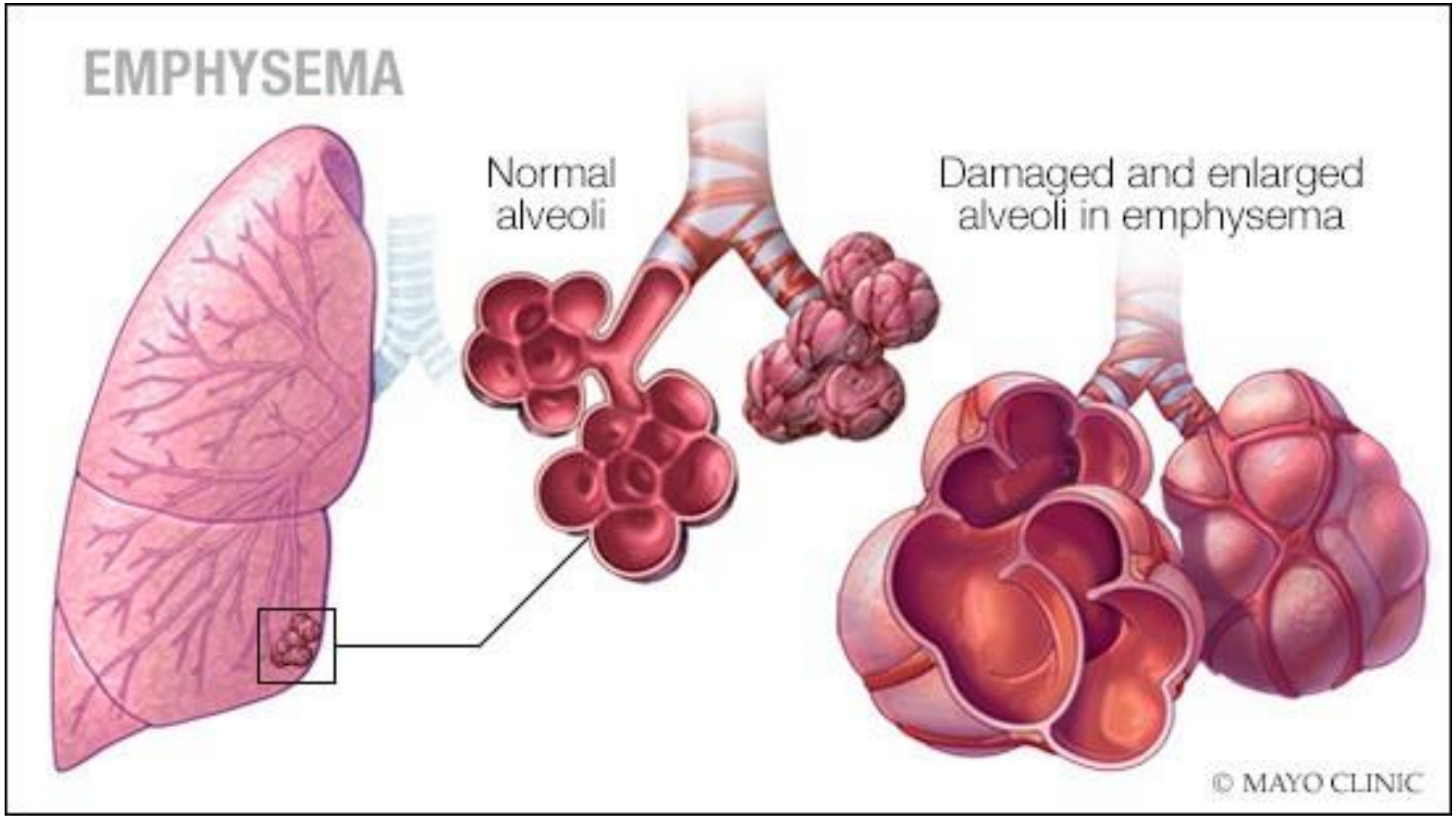
To understand the features for each one we will study pure emphysema and pure chronic bronchitis but we have to insure that they are overlapping

To diagnose a patient with chronic bronchitis the symptoms are: persistent productive cough every day for at least 3 months in at least 2 years
But in emphysema it's complicated and want radiology , morphology and clinical features



ANATOMIC DISTRIBUTION

DEFINITION


EMPHYSEMA
Normal alveoli
Damaged and enlarged alveoli in emphysema
© MAYO CLINIC

1. EMPHYSEMA

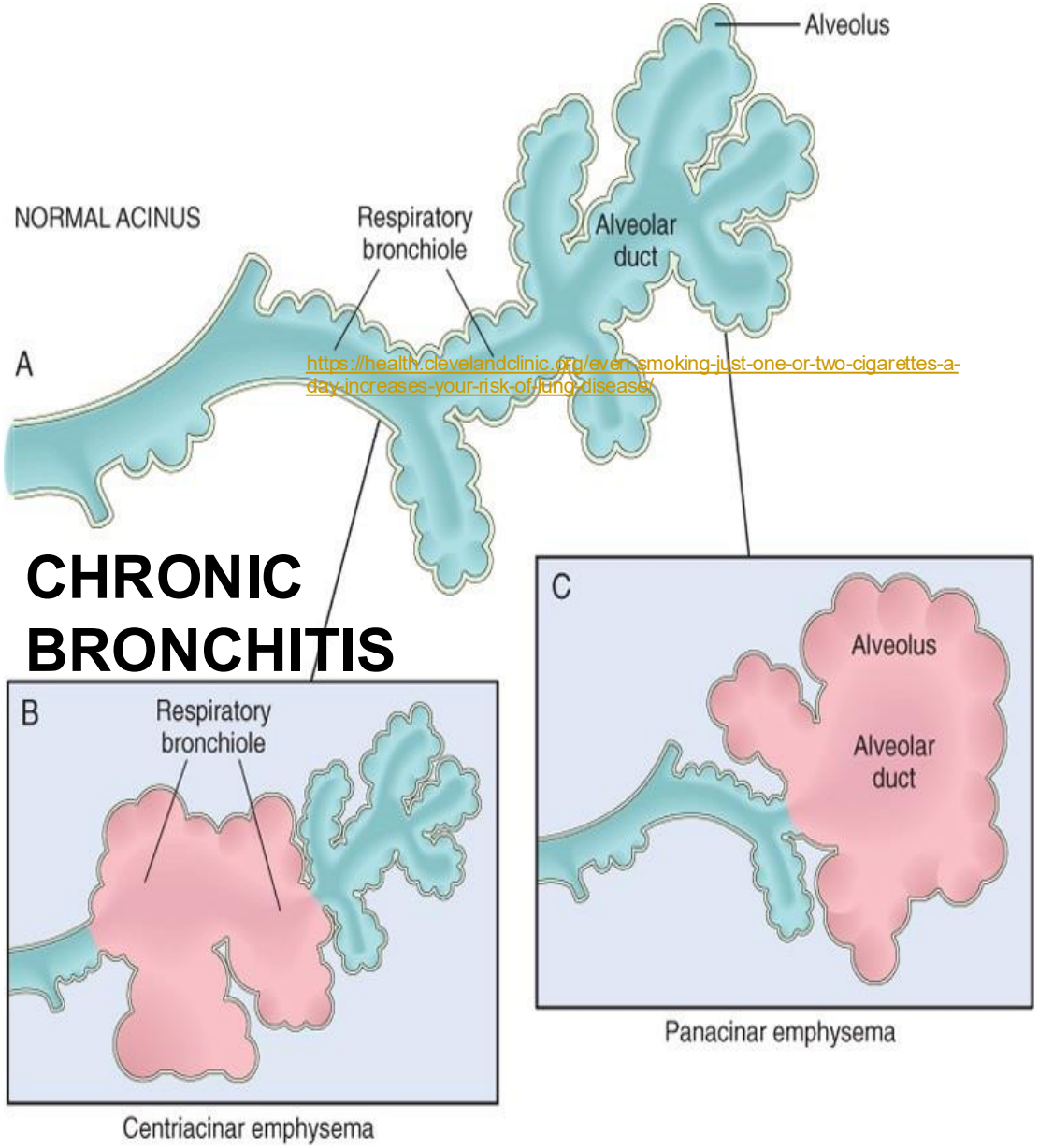
- **Permanent** (irreversible) enlargement of the airspaces **distal** to the terminal bronchioles acinus with destruction of their walls.
- Subtle but functionally important small airway fibrosis → significant contributor to airflow obstruction.
- Classified according to its anatomic distribution:

(1) Centriacinar (centrilobular) the most common and significant one**,**

(2) panacinar (panlobular) , (3) distal acinar(paraseptal),and (4) irregular

Every one has its own underlying etiology, relationship and anatomic distribution within the acinus

TYPES OF EMPHYSEMA

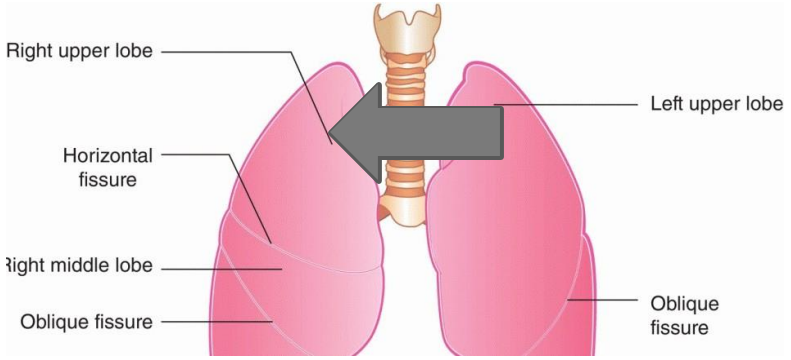


Emphysema affect acinus either respiratory bronchioles, (which is a branch of the terminal the bronchioles) >alveolar duct > alveolar sac.

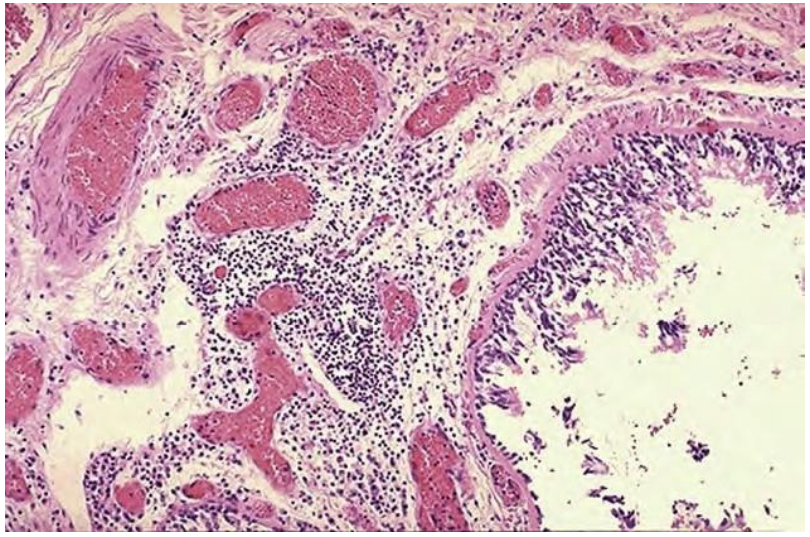
Centriacinar Emphysema (B) : it affects the central part (proximal part) which is the respiratory bronchioles, while alveolar duct and sac are spared (not affected), specially on early disease (the most clinically symptomatic) this type has a great association with smoking so it also will be associated with chronic bronchitis because they share the same etiology .

The most part of lung will be affected is the upper part especially the apical segment

Strongly associated with tobacco smoking, that's why it is the most common (since tobacco smoking is common)

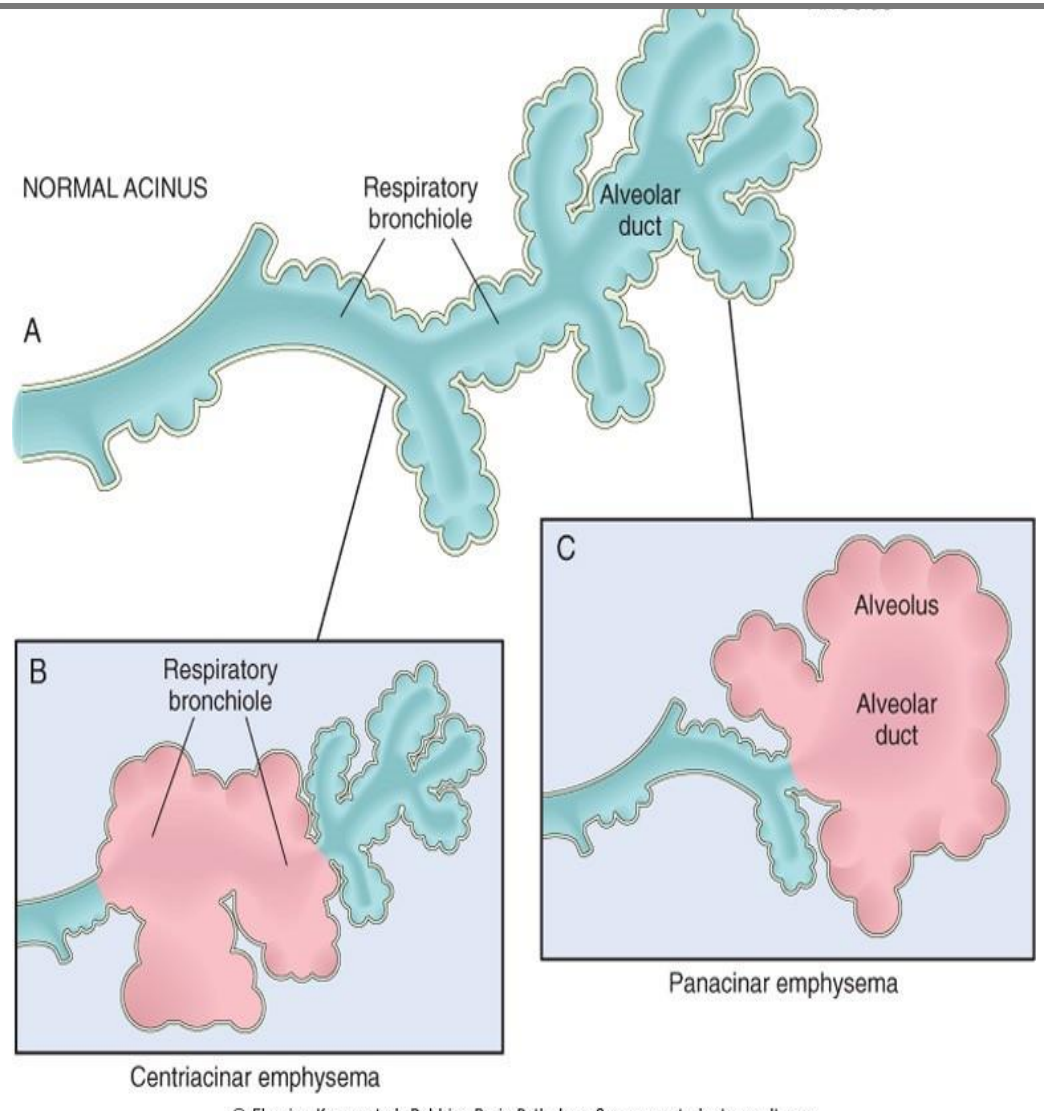


In terms of lung involvement Centriacinar emphysema is much more common and more severe in the upper half of the lung specially the apical segments



Because 90% of chronic bronchitis is associated with tobacco smoking, centriacinar emphysema is the most common type to be associated with chronic bronchitis

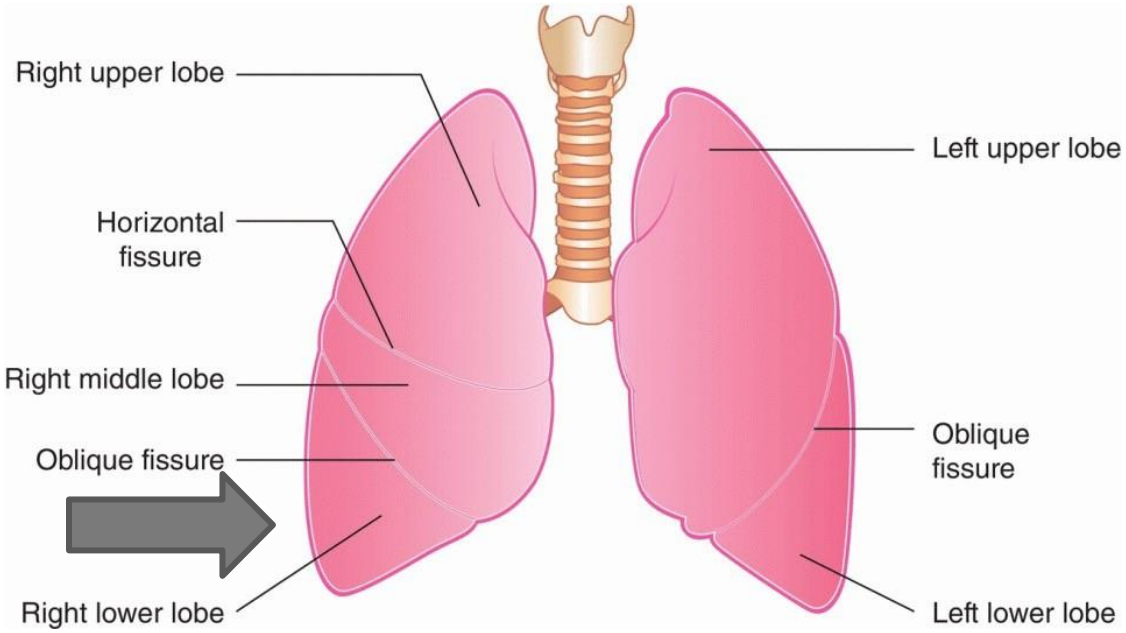
α_1-antitrypsin deficiency

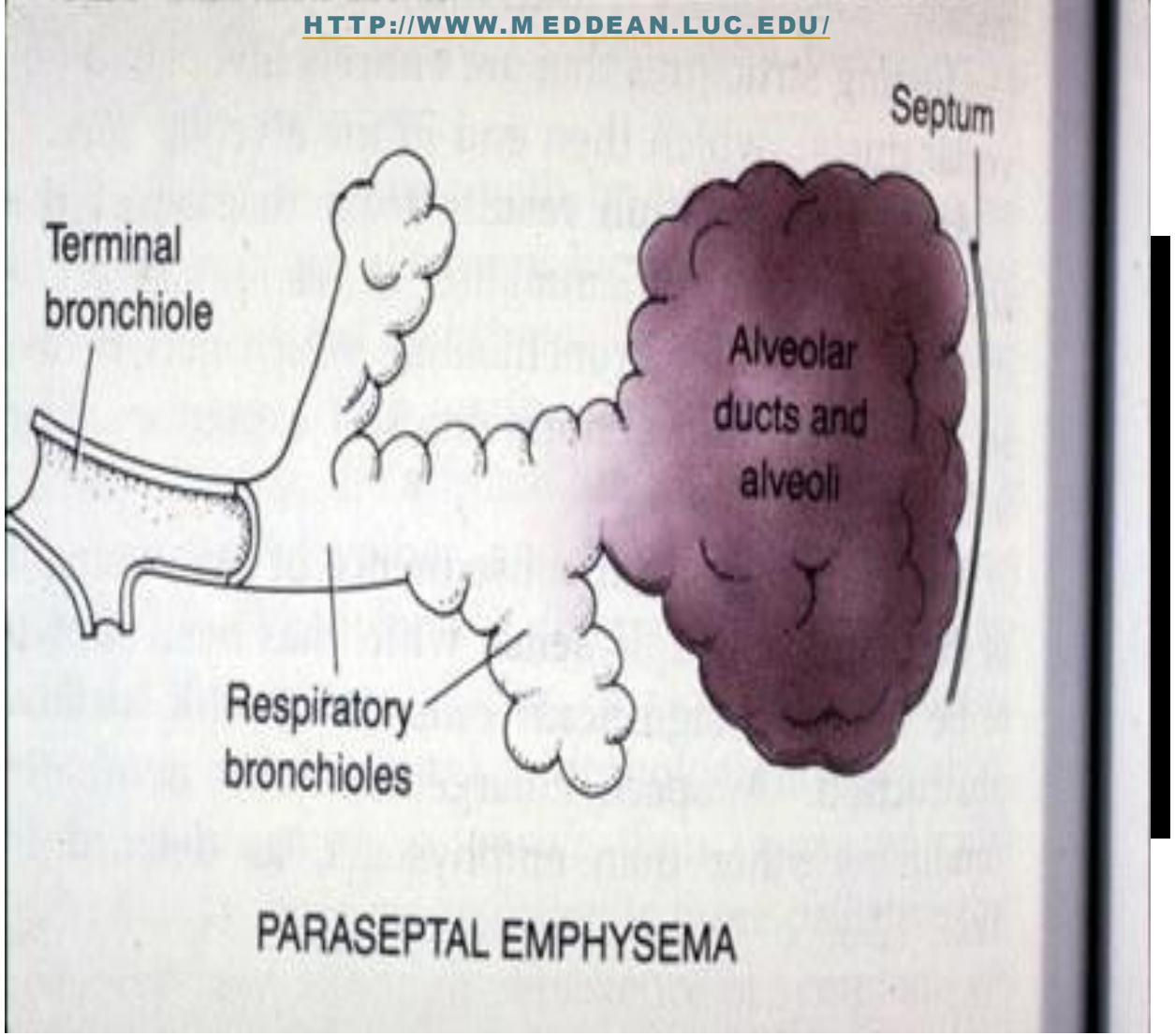


Panacinar emphysema (C) : (pan means all) all acinus will be involved in this disease , it will involve respiratory bronchioles, alveolar sac and duct

This type is associated with α1-antitrypsin deficiency which is a genetic disease that is associated with liver and lung diseases

The lower half of the lung is the most commonly involved part in this disease especially the lower base and anterior margin of the lung .





Distal : it involves the distal part of the acinus (permanent enlargement of the alveolar duct and sac) while respiratory bronchioles are preserved

Paraseptal : adjacent to the septae,

- Most importantly: Adjacent to pelural cavity
- Etiology : unknown

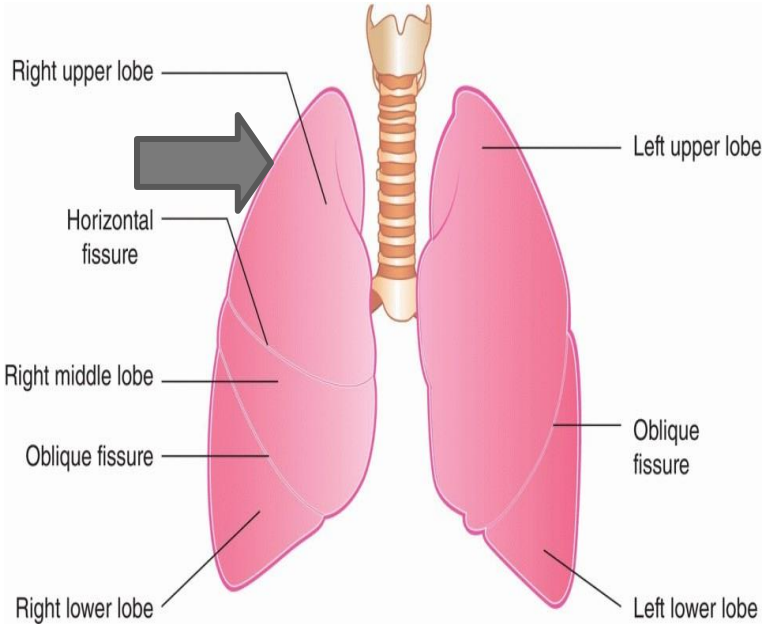
Adj to fibrosis, scarring or atelectasis

Adj to pleura, along the lobular connective tissue septa, & at the margins of the lobules

Paraseptal DISTAL ACINAR EMPHYSEMA

https://thoracickey.com/2-embryology-anatomy-and-physiology-of-the-lung/

As we said it is adjacent to the pleural cavity, it might cause cystic structures (0.5 mm- 2 cm) They could be large and we call them bullae or blebs , These spaces contain air, and are prone to spontaneous rupture ,once they rupture, they leak air into the pleural cavity, causing Spontaneous pneumothorax.
It is The most common type of emphysema associated with spontaneous pneumothorax in young adults

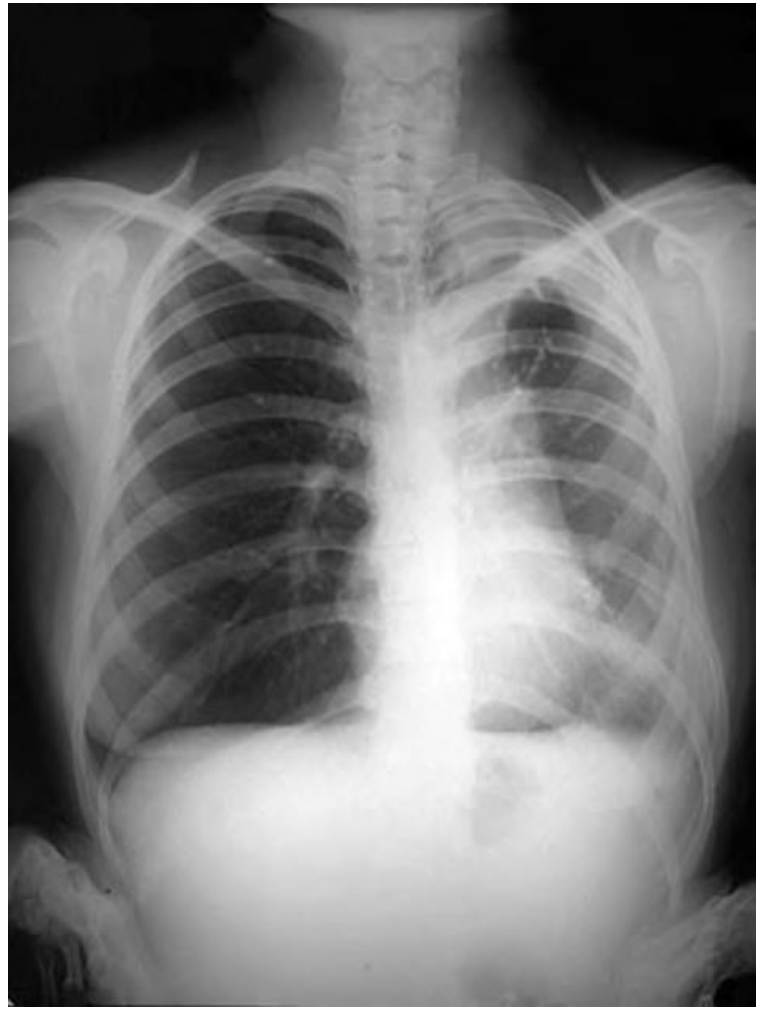


The upper half of the lung is more common and severely affected, especially the apical segment.

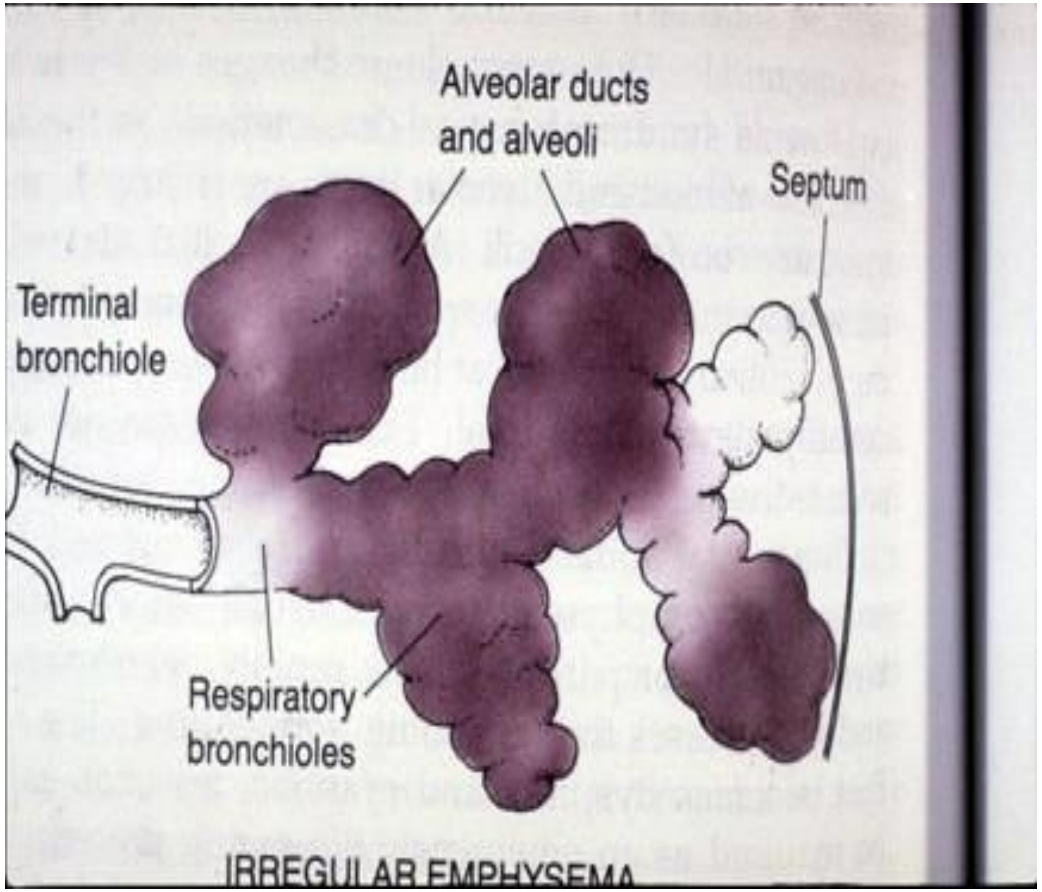
How to know that the patient has pneumothorax
The two lungs should be identical if they aren't identical so one isn't abnormal
The signs we could see : one lung may be more white or more black

In this x-ray The right lung is abnormal because its color is too black due to excess air while in normal lung it's usual to see hazy white color as a marking in normal lungs
The right side is affected by pneumothorax that collapse the adjacent lung
Heart , trachea and mediastinum are shifted to the left due to accumulation of air within the pleural cavity of the right side.

Treatment involves entering a tube to get the air out and allowing normal inflation of the lung



Irregular emphysema



Any part of acinus can be involved
– it is almost invariably associated with scarring
Although it's common, but it's clinically asymptomatic and insignificant, usually diagnosed at the autopsy level
Remember : the Most common clinically diagnosed or symptomatic emphysema is the centriacinar emphysema

Almost invariably associated with scarring

clinically asymptomatic and insignificant

https://baytowncrimestoppers.com/baytowns-most-wanted/unsolved-crimes/

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

A 20-year-old 1. Young healthy, previously healthy gentleman is jogging one morning when he falls to the ground. He 2. 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 there is collapse. A chest tube is inserted on the right side, and air rushes out the etiology is pneumothorax. 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

PATHOGENESIS OF EMPHYSEMA

infections

Explanation in the upcoming slides ;)

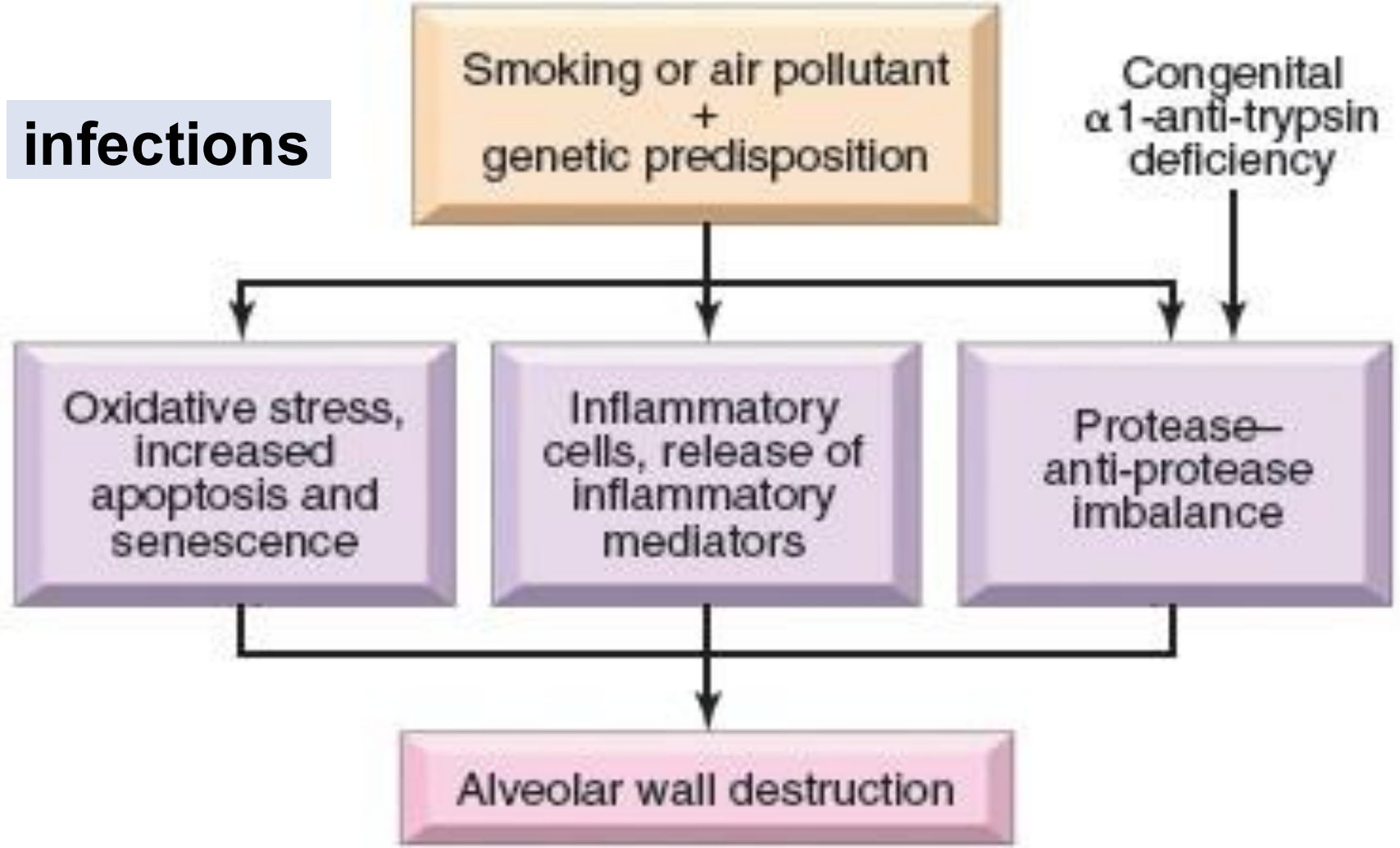


Fig. 13.6 Pathogenesis of emphysema. See text for details.

,ROBBINS BASIC PATHOLOGY, 10TH EDITION

- In order to develop a clinically significant emphysema, at least 1/3 of the functioning lung parenchyma (functioning tissue that does the gas exchange) must be lost.
This can be caused by two etiologies: smoking and a1 anti-trypsin deficiency.

How? By causing significant destruction in alveolar wall that leads to a clinically significant disease.

- In other words, someone who developed a clinically significant emphysema has to be either a smoker (centriacinar emphysema) or hasa1 anti-trypsindeficiency (panacinar emphysema) or both.

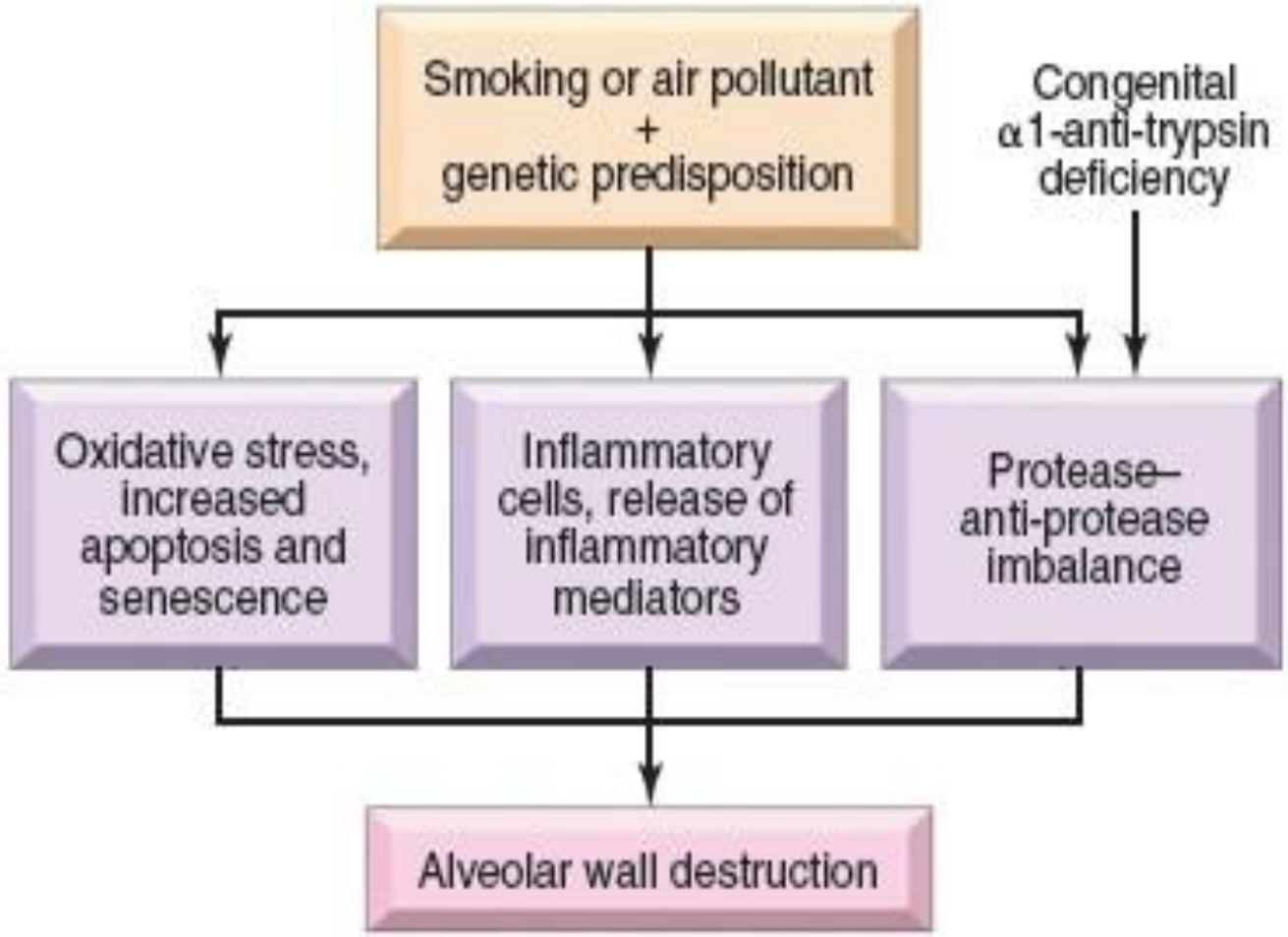


Fig. 13.6 Pathogenesis of emphysema. See text for details.

- This is the chain of events: TWO mechanisms:

1) Exposure of the tobacco smoke will lead to injury in the epithelial lining of the respiratory passages and activates the alveolar macrophages that stimulate an inflammatory reaction by releasing inflammatory mediators such as IL-1, IL-8, TNF..

This attracts neutrophils in the circulation to come and release their inflammatory mediators as well as their destructive forces such as elastases, ROS, proteases.. this results in destruction at the site of inflammation that causes alveolar wall destruction

2) Death of epithelial cells caused by this damage and the inflammatory reaction and the substances in the tobacco smoke lead to oxidative stress and release of ROS and nitrogen species that will add more to the damage whether it's epithelial damage or endothelial dysfunction and to the process of inflammation.

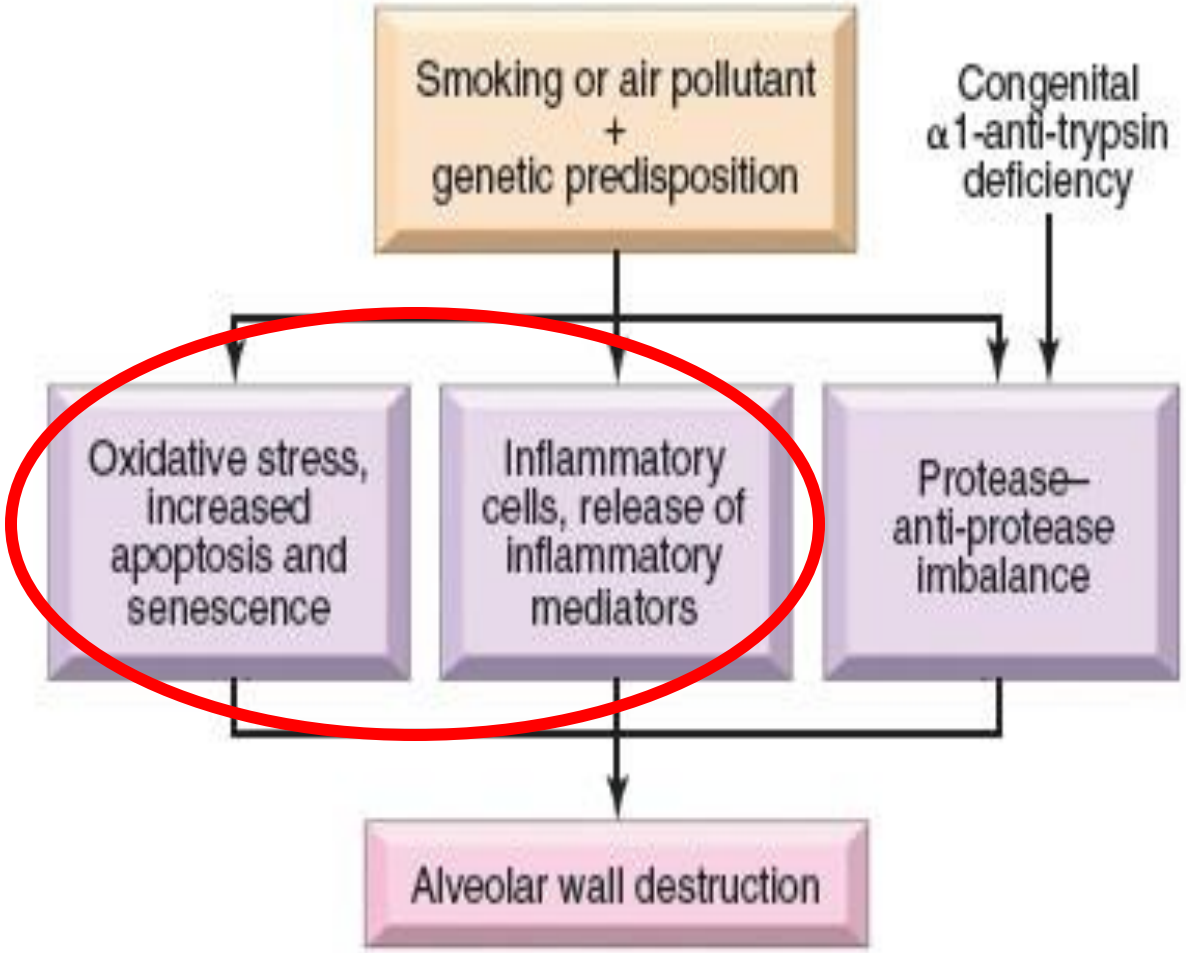


Fig. 13.6 Pathogenesis of emphysema. See text for details.

- Not all smokers end up with emphysema. **The process is modified by protease and anti-protease imbalance.**
- Normally this inflammatory process is stopped/reduced by the protective forces in our bodies which are the anti-protases which regulate the damaging effect of neutrophils with anti-oxidants.
- People with emphysema suffer deficiencies in anti-proteases, so there's no adequate amounts of it to stop the inflammatory process and this leads to the significant damage we talked about before.
- People with a1 anti-trypsin deficiency (one of the anti-protases – works against elastase) undergo inflammation and damage as well as destruction of the elastic fibers caused by any trigger

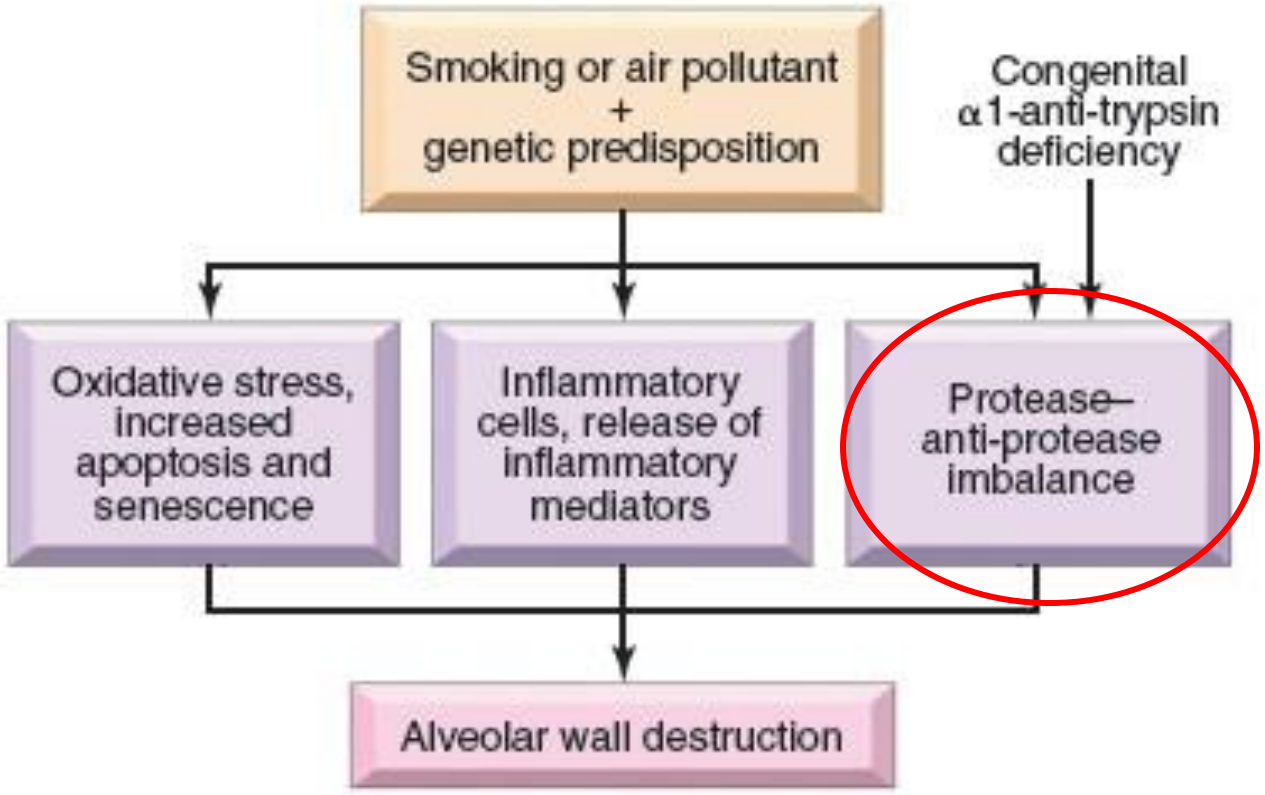


Fig. 13.6 Pathogenesis of emphysema. See text for details.

- Can infection cause emphysema? NO :)
- Infection causes acute attacks but it's not the main cause of emphysema. (to cause a clinically significant disease again it has to be one of the etiologies: smoking or a1 anti-trypsin deficiency)

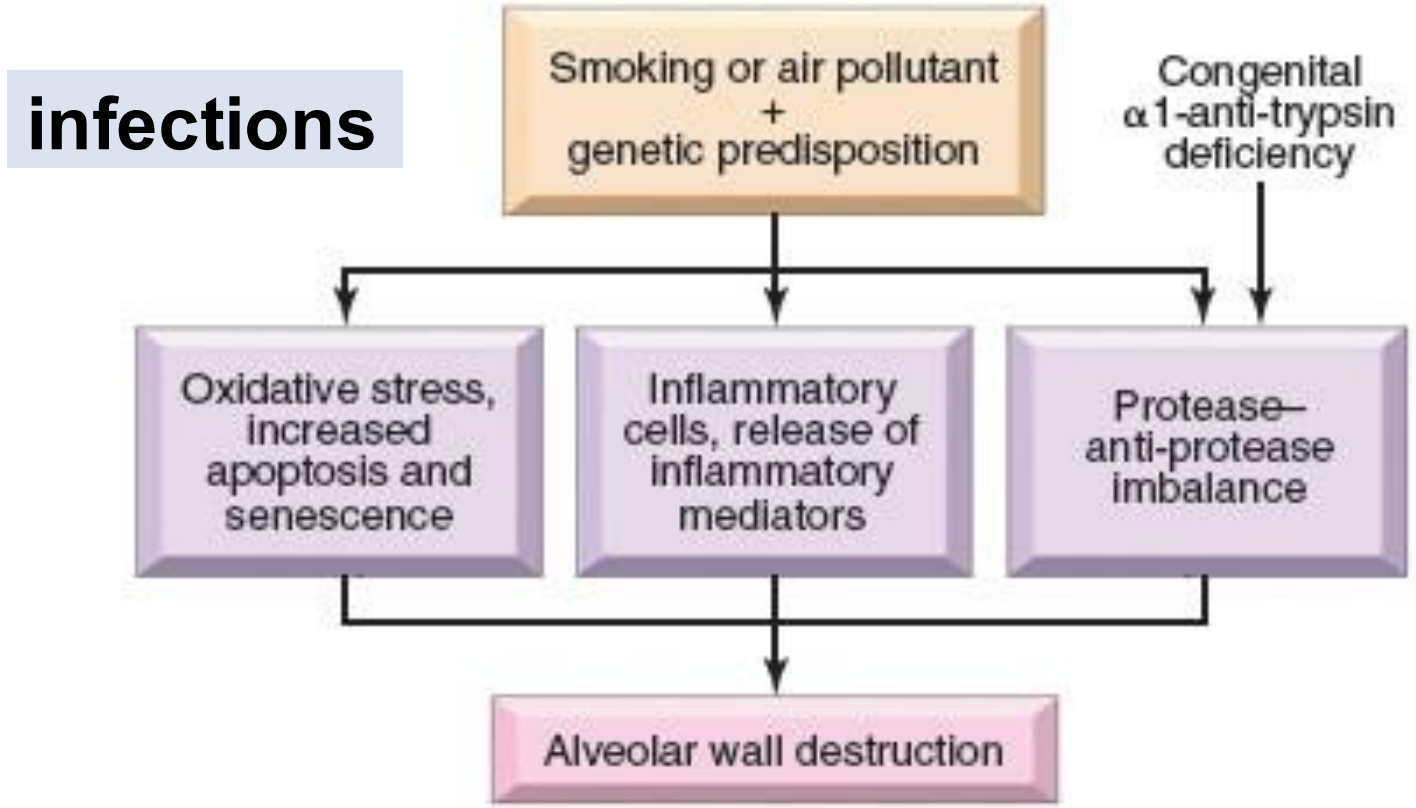


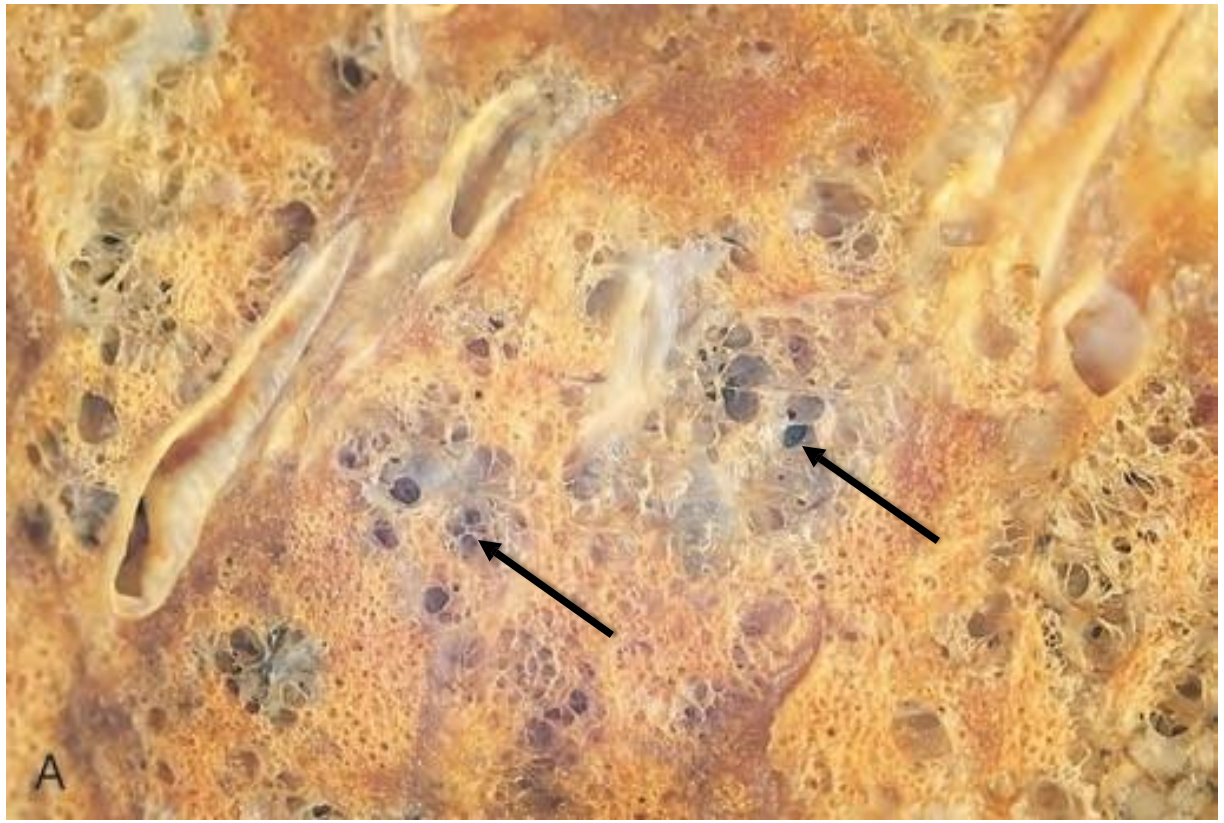
Fig. 13.6 Pathogenesis of emphysema. See text for details.

MORPHOLOGY

Distinction between types of emphysemas is NOT required

Macroscopic: **Advanced emphysema→ voluminous lungs**

Volume of the lung is larger in people with emphysema.
A section of a lung with emphysema shows cystic (dilated) structures: permanent enlargement of the air spaces caused by destruction of the walls
Centriacinar, distal & irregular emphysemas are characterized by a patchy distribution of cystic structures (not uniform)



Centriacinar emphysema
Central areas show marked emphysematous damage (arrows) surrounded by relatively spared alveolar spaces.

If all parenchyma is replaced by cystic structures, this is a landmark of panacinar emphysema.

Panacinar emphysema involving the entire pulmonary lobule.

- **Microscopic examination of the lung:**
- abnormally large alveoli are separated by thin septa with only focal centriacinar fibrosis and later on breaks in the alveolar wall.

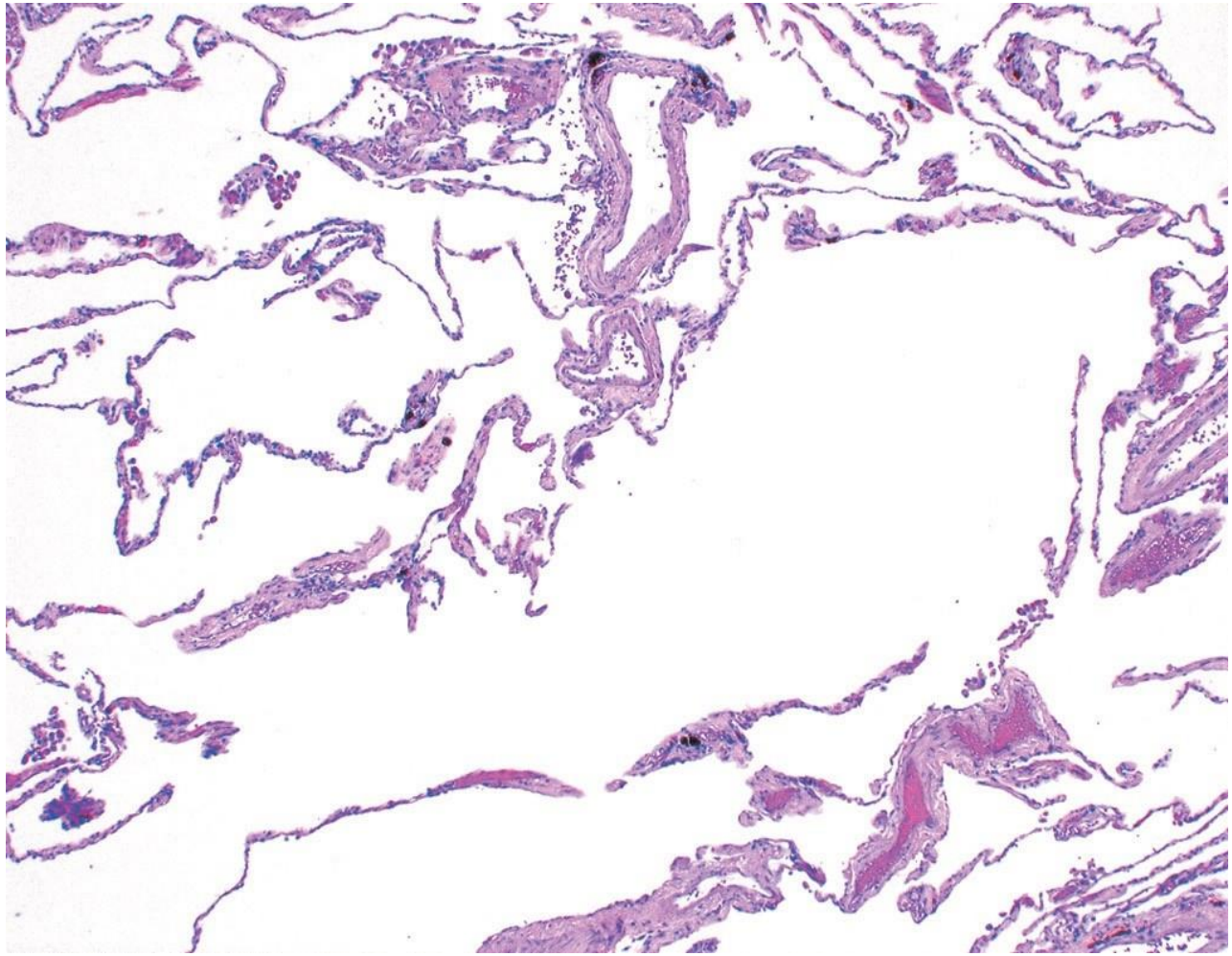


Figure 13.5 ROBBINS BASIC PATHOLOGY, 10TH EDITION

EMPHYSEMA, PRESENTATION:

- **Symptoms do not appear until at least 1/3 of the functioning pulmonary parenchyma is damaged**
- **Dyspnea** (shortness of breath): initial and most important symptom **appears first, beginning insidiously but progressing steadily**
- **Weight loss; common** caused by chest wall muscles involvement because of obstructed air flow.
- **barrel-chested (air is trapped inside)**

Increased lung compliance causes air trapping and lung hyperinflation and an increase in the intrathoracic pressure and eventually an increase of the anterior posterior diameter is chest wall

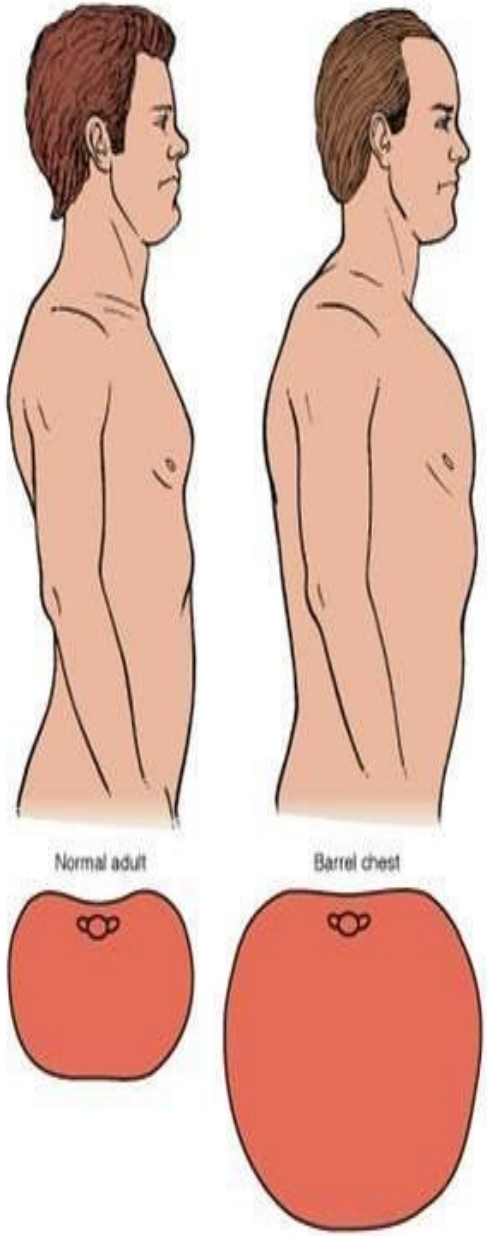


Figure 25-31 Profile and anteroposterior diameter of normal adult chest and barrel chest.

https://ratedmedicine.wordpress.com/barrel-chest/

- prolonged expiration to get rid of the air trapped inside
- sitting forward in a hunched-over

Position (to use every muscle in the chest wall to get rid of the air)

- breathes through pursed lips
- Dyspnea that starts early in the disease process causes Hyperventilation initially results in adequate oxygenation of Hemoglobin especially at rest and prominent dyspnea

→ "pink puffers." pink due to the pink completion of the mucous membrane (oxygenation) and puffers due to the pursed lips breathing

- Cough and wheezing if Coexistent asthma & chronic bronchitis (cough with sputum).

https://www.visualizepicture.com/c/emphysema-mnemonic_fWuJVQIShnPF2GEM1xUt3lRVdSQhKF4s22ZDS23ni8Q/

OUTCOME:

- Decreased capillary bed area available for the gas exchange due to:
  - ✓ Destruction of alveolar walls
  - ✓ enlarged airspaces (bullae and blebs) in advanced disease causing Compression of the respiratory bronchioles and lung vasculature.
  - ✓ Ongoing inflammatory changes in small airways that leads to fibrosis & affects the function

- Decreased capillary bed area→ hypoxia chronic & irreversible!

- Hypoxia-induced pulmonary vascular spasm →gradual development of secondary pulmonary hypertension (right side is pumping against resistance & circulation) → in 20-30% right-sided congestive heart failure (cor pulmonale).

II. CHRONIC BRONCHITIS

(other end of the COPD spectrum)

Defined clinically as Persistent productive cough for ATLEAST 3 consecutive months in AT LEAST 2 consecutive years in the absence of any other identifiable cause.

- 90% **cigarette smokers**; air pollutants also contribute.

- chronic bronchitis is one end of the spectrum of COPD, with emphysema being the other.

PATHOGENESIS

The primary factor in the genesis is exposure to irritating inhaled substances such as tobacco smoke (90%of pt) and dust from grain, cotton, and silica.

Exposure of these toxins leads to mucous hypersecretion

- **hypersecretion of mucus**: reversible
  - The earliest feature of chronic bronchitis
  - beginning in the large airways. (trachea & bronchi)

- **Acquired cystic fibrosis transmembrane conductance regulator (CFTR) dysfunction.**

  Mucous become sticky & thick and hard to get out so it accumulates in the small airways (bronchioles) and may block it which causes inflammation with presence of lymphocytes.

  ✓ smoking leads to acquired CFTR dysfunction→ secretion of abnormal dehydrated mucus→ increases the severity of chronic bronchitis.

- **Inflammation.**
  - Due to the Inhalants
  - No eosinophils

- Long-standing inflammation and fibrosis involving small airways (small bronchi and bronchioles, less than 2 to 3 mm in diameter) →chronic airway & airflow obstruction

• Chronic bronchitis is reversible at the beginning of it, it gets severe and irreversible with time (different from one patient to the other)

- **Infection.**
  - ✓ Infection **does not initiate** chronic bronchitis but is probably significant in maintaining it
  - ✓ Produces **acute exacerbations**.

- In early stages airflow is not obstructed.

- airflow obstruction in chronic bronchitis results from:

1. Small airway disease

chronic bronchiolitis: results in mild airflow obstruction. Induced by mucus plugging of the bronchiolar lumen, inflammation, and bronchiolar wall fibrosis

Chronic bronchitis with emphysema (commonly centriacinar) leads to significant airflow obstruction and not chronic bronchitis on its own. This is shown by a pulmonary function test.

2. Coexistent emphysema: The cause of significant airflow obstruction.

- **When chronic bronchitis persists for years** & causes obstruction**:**
  - decline in lung function, leading to cor pulmonale
  - cause atypical metaplasia and dysplasia (adaptive mechanism to avoid death of the epithelium by the irritation by tobacco smoke) of the respiratory epithelium, providing a rich soil for cancerous transformation.

- May coexist with hyper-responsive airways with intermittent bronchospasm and wheezing→ **asthmatic bronchitis**

MORPHOLOGY

Macroscopic:

- **Mucosal lining is hyperemic** (red in color due to excess blood) **and swollen** with edema

- **Layers of mucinous or mucopurulent secretions**

This figure shows a histology of one of the main bronchi. Red star represents the lumen. At the start (from left to right) the lining is a pseudostratified ciliated columnar epithelium. Squamous metaplasia occurred due to the exposure to the tobacco smoke.
Lymphocyte presence (colored dots) to mark chronic inflammation.

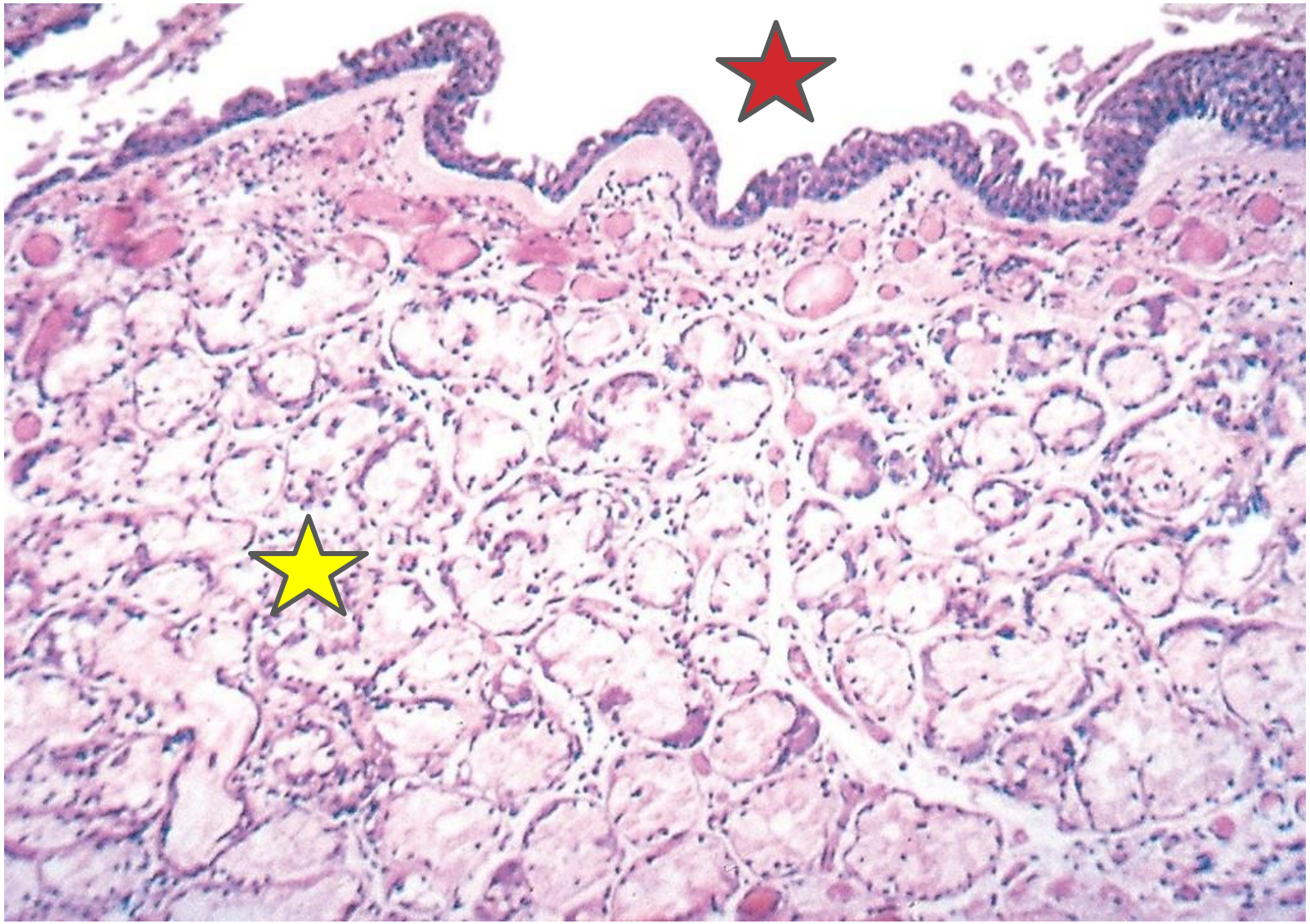


Fig. 13.9 Chronic bronchitis. The lumen of the bronchus is above. Note the marked thickening of the mucous gland layer (approximately twice-normal) and squamous metaplasia of lung epithelium.
(From the Teaching Collection of the Department of Pathology, University of Texas, Southwestern Medical School,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

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**

CLINICAL FEATURES:

- **persistent cough with production of sparse sputum**

- For many years no respiratory functional impairment is present, but eventually dyspnea on exertion develops.
- Patient becomes more prone to attacks

- chronic bronchitis and COPD patients show frequent exacerbations, rapid disease progression, and poorer outcomes than emphysema alone

OUTCOME:

- Progressive disease is marked by the development of pulmonary hypertension, the patient is at risk for cardiac failure due to the sticky mucous and obstruction, recurrent infections; and ultimately respiratory failure
- Death may also result from further impairment of respiratory function due to superimposed acute infections.

- Cough with sputum at first without airflow obstruction
- **Less dyspnea** compared to emphysema (caused by mild airflow obstruction if it's only chronic bronchitis)
- No stimulation of hyperventilation
- absence of increased respiratory

drive → the **lungs retain carbon dioxide→ hypoxic and cyanotic.**

- For unclear reasons, patients with chronic bronchitis tend to

be **obese**

hence the designation **"blue bloaters"**

→carbon dioxide retention, hypoxia, and cyanosis

Later on, they might develop right sided heart failure and fluid

overload

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

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Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			