

# Respiratory System

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# Diffuse Pulmonary Diseases:

## 1. Obstructive Diseases:

يعني اشئ بعمل محدود و ما بجاي الرئة تتمدد بشكل كامل

- Characterized by an increase in resistance to airflow caused by partial or complete obstruction at any level.

زي ما حكينا بالفسيولوجي ، مشكلة المريض هون بال *expiración* يعني هو بيقدر يدخل الهواء لكن صعب انه يطلعه برا بسبب هاد ال

## 2. Restrictive Diseases:

- Characterized by a **reduced expansion of lung** parenchyma and decreased total lung capacity.

اما هون بتكون المشكلة بال *inspiration* ، يعني بتقل قدرة الرئة على انها تتمدد بالتالي يكون عند المريض مشكلة بال *inhalation itself* من البداية مش قادر يدخل هوا لل *lungs* لانه الرئة بتكون *stiff* بسبب ال *fibrosis* غالبا

# Obstructive lung diseases

قبل ما نبش بدنا نعرف انه احيانا ال emphysema وال chronic bronchitis مع بعض بنسميهم Chronic obstructive pulmonary disease (COPD) وغالبا يكونوا الهم علاقة بالمدخنين smokers ، بس احنا رح ندرس كل مرض بحال



## 1. Emphysema

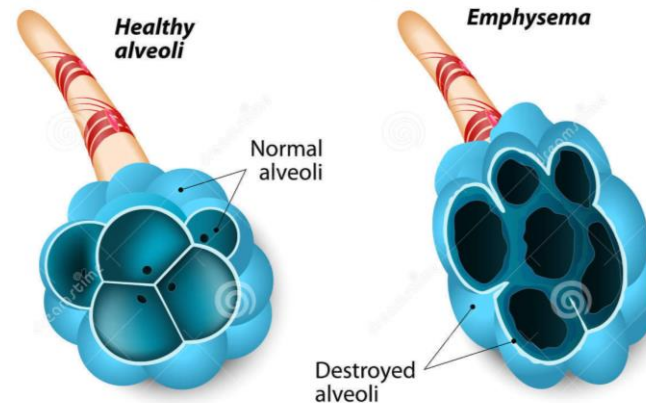
-Defined based on morphologic and radiologic features.

يعني بصير عنا تمدد دائم بال air spaces الموجودين بعد ال terminal bronchiole يعني بال acinus ، دائم لأنه عنا destruction in the wall but without significant fibrosis ، مهم نعرف انه ما بصير fibrosis ركزت عليها الدكتورة

### Definition:

-Abnormal **permanent enlargement** of the air spaces **distal** to the terminal bronchioles (in the **acinus**), associated with the **destruction of the wall** of acini but **without obvious fibrosis**.

حكيها عنها المظهرة الأوك .



صمم

# Types of emphysema:

بنقسما ل ٤ انواع حسب الجزء اللي  
تضرر من ال acini ، هل respiratory  
bronchiole or alveolar duct or alveoli

## 1. Centriacinar (centrilobular) Emphysema:

مهم نعرفت وينت بهيس كل واحد

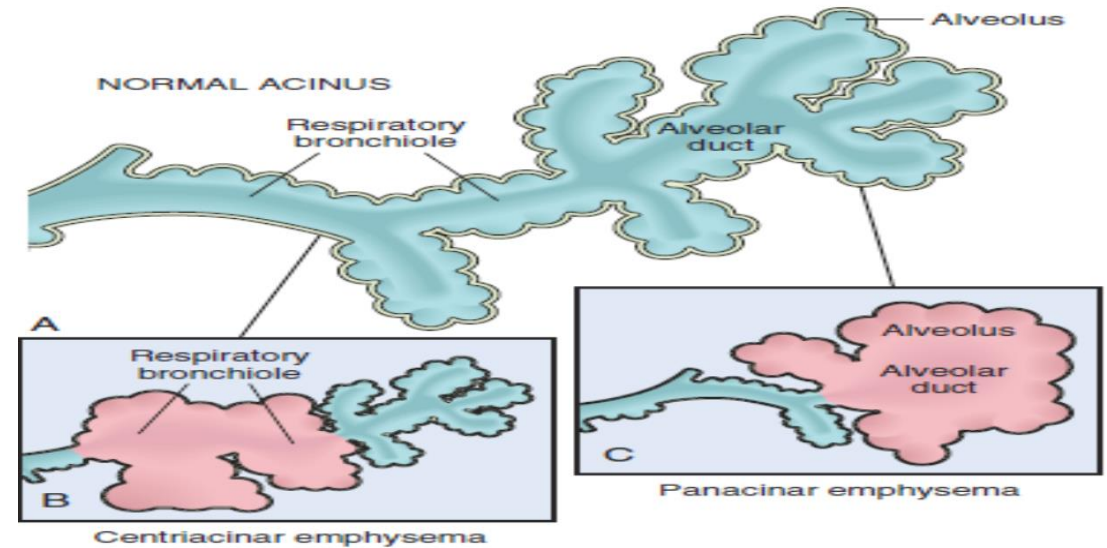
- The central or the **proximal part** of the acini, formed by the respiratory bronchioles, are **affected**, while the distal alveoli are spared.
- The lesions are more common & severe in the **upper lobes**
- Most commonly due to cigarette smoking, often in association with chronic bronchitis.



## 2. Panacinar (Panlobular) Emphysema : من اسمه كل ال acinus affected

- The **acini** are **uniformly enlarged** from the level of the **respiratory bronchioles** to the terminal blind alveoli.
- It tends to occur in the **lower lung zones**.
- Occurs in **alpha-1 anti-trypsin deficiency**.

ممکن يكون سببه التدخين ، و ممکن سبب ثاني  
شائع اكثر و هو ال congenital deficiency in  
alpha 1 antitrypsin ، (حکينا عنه بالبيوكيم)



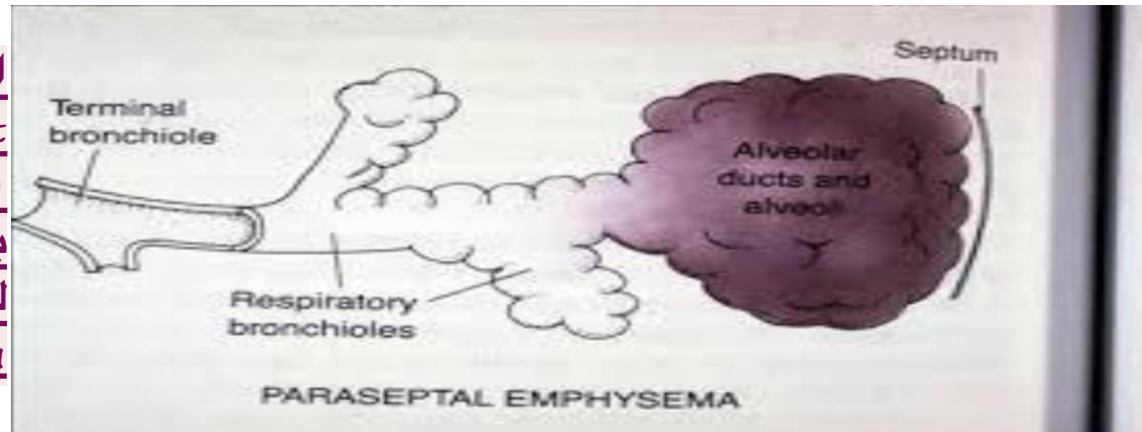
### 3. Distal acinar (Paraseptal) emphysema:

من اسمه

المشكلة بال (alveoli/alveolar duct) distal

- The proximal portion of the acinus is normal, but the **distal part** is primarily **involved**.
- More severe in the **upper half** of the lungs.
- The emphysema is more striking **adjacent to the pleura** and **along** the lobular connective tissue **septa**.
- It occurs adjacent to areas of fibrosis or atelectasis.

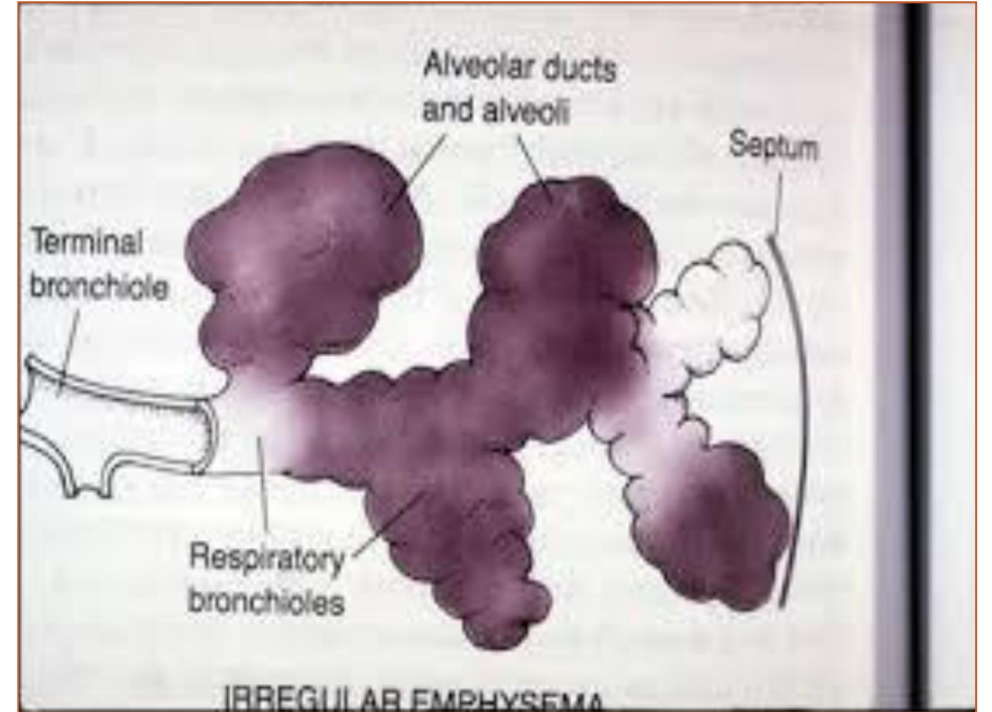
اسمه الثاني paraseptal لأنه ال alveoli and alveolar duct يلي بتكون جنب ال septum (paraseptal) هم اكثر اشني بكونوا متضررين ، واللي بكونوا قريبين لسطح ال lungs يعني قريبين لل pleura



## 4. Irregular Emphysema:

- The acinus is irregularly involved; it is associated with scarring in healed inflammatory diseases.
- Although clinically **Asymptomatic**, it is the **most common form of emphysema**.

يعني هو ال most common و اكثر واحد بكونه Asymptomatic



مهم تفرق بين الانواع الأربعة و كل نوع وبن بصير

# Pathogenesis:

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Two Pathways are involved :

1- PROTEASE -ANTIPROTEASE imbalance.

2- OXIDANT – ANTIOXIDANT imbalance

- Such imbalances almost always coexist.

- Complex interactions between inflammatory mediators and inappropriate activation of repair mechanisms may result in tissue destruction without fibrosis. \*

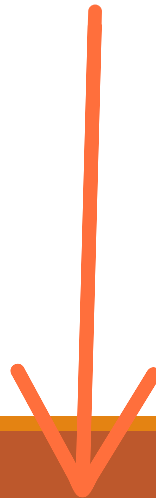


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-  **$\alpha$  1- antitrypsin** is a major inhibitor of protease, particularly elastase, which is secreted by neutrophils during inflammation.

- Exposure to toxic agents such as tobacco induces ongoing inflammation with infiltration of neutrophils, macrophages & lymphocytes in lung tissue

→ Elastases, cytokines & oxidants are released by these cells, causing epithelial injury, and unless inhibited by antitrypsin, anti-elastase, and antioxidants, the cycle of inflammation & proteolysis of ECM continues.



عشان نفهم الموضوع

المدخنين و يلي بكونوا heavy smoker ، بتعرضوا لل toxic agent in the tobacco ، و هاد ال toxic agent ببلش يحفز ال inflammation inside the lungs ، بتصير تيجي ال neutrophils , macrophages and lymphocyte و بتبلش تعطي acinar epithelial damage و بصير mediators, cytokines and oxidant cells ، هون بكون دور الجسم انه يشغل ال defence mechanism like

في عنا شغلتين بسببوا نقص او خلل بال antiprotease  
اما يكون genetics او يكون الشخص smoker ( ال toxic agent يلي بتكون  
جوا السيجارة بتعمل oxidative injury , و هاد بعمل inactivation لل  
antiprotease يعني الانزيم موجود بس في اشني ثبّطه و صار زي كأنه مش  
موجود)

## Decrease in these protective mechanisms produce damage.

Decrease in antiprotease activity may be :

i- Genetic:  $\alpha$  1- antitrypsin deficiency

ii- Acquired: Smoking

More than 80% of patients with congenital  $\alpha$  1- antitrypsin deficiency develop symptomatic panacinar emphysema.

A secondary consequence of oxidative injury caused by smoking is the inactivation of a native anti-protease, resulting in functional  $\alpha$  1- antitrypsin deficiency even in normal individuals.

Tobacco smoke contains abundant ROS (free radicals), which deplete anti-oxidant mechanisms

Activated neutrophils add to the pool of ROS in the alveoli

## How does obstruction occur?

- Small airways are normally held open by the elastic recoil of the lung parenchyma, and the loss of elastic tissue in the walls of alveoli that surround respiratory bronchioles reduces radial traction and thus causes the respiratory bronchioles to collapse during expiration → functional airflow obstruction despite the absence of mechanical obstruction.

Functional not mechanical  
يعني ما في اشي جوا القصيبات  
ال terminal bronchiole مسكرهم ،  
هم سكروا لأنه ال elastic tissue  
يلي بتضل فاتحيتهم مش موجودة

## Clinical Features : تذكروا احنا بنحكي عن ال emphysema

- Dyspnea (progressive).
- Weight loss (**thin**).
- Without concomitant chronic bronchitis usually presents with a **barrel chest**, dyspnea, and **prolonged expiration, sitting forward in a hunched-over position**. *very characteristic for emphysema*
- Hyperventilation.
- **The blood gases stay normal very until late in the disease due to hyperventilation, and there is adequate oxygenation of the blood.**
- Patients are called **Pink-puffers**.

emphysema عنده Pink panter



لأنه الهوا بيفل جوا ومشي حاد رين  
نظلمه ليزا بغير ال chest زي  
البرميل

بضل يتنفسوا بسرعة ، بالتالي بقدرنا يحافظوا على ال blood gases in the beginning of disease at least  
، فيكونوا good oxygenation عشان هيك لونهم بضل pink  
عشان هيك بنسميهم pink-puffers

بس نحكي emphysema  
بننذكر pink panther .  
ضعيف و ال chest برميل  
و لونه pink



احنا بنشخص ال emphysema بناء على ال morphology and radiology

## Morphology of Emphysema:

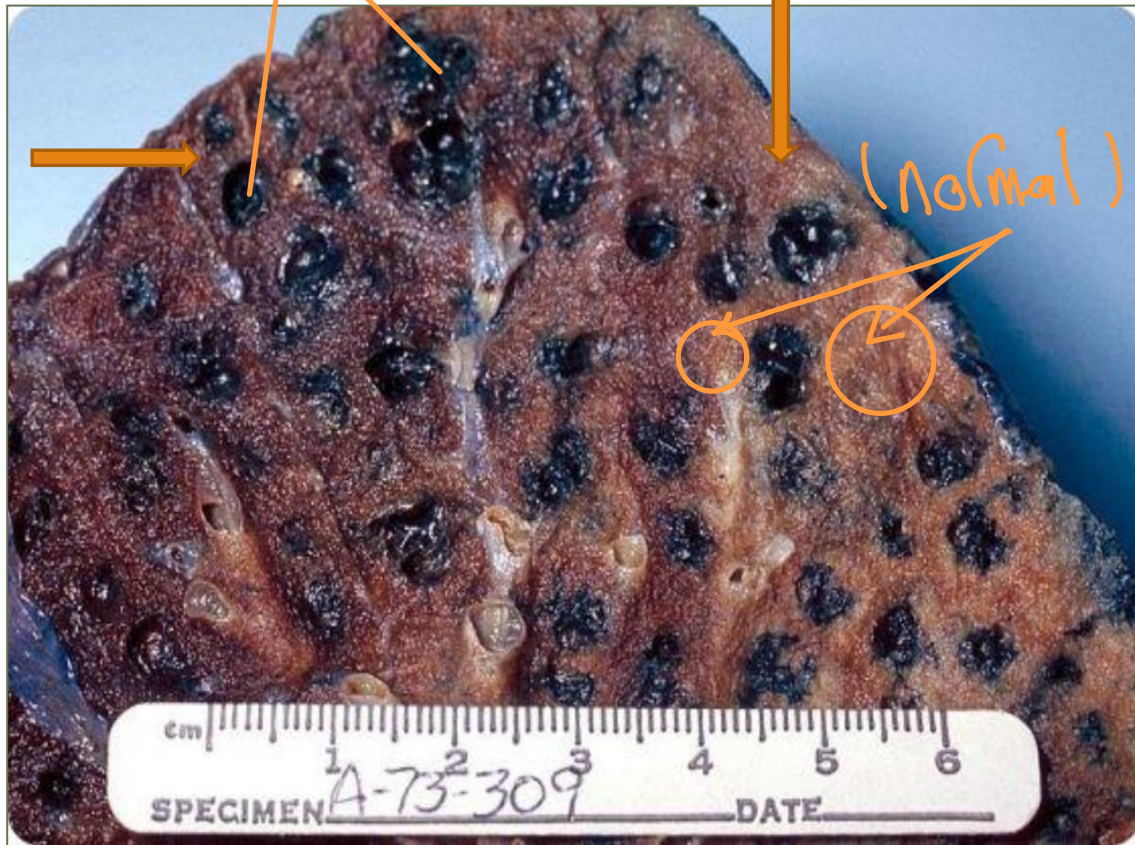
### Grossly:

- The diagnosis & classification of E . depend on the macroscopical appearance of the lung.
- In pan-acinar E. the lungs are pale voluminous hyperinflated and obscure the heart.
- In centriacinar E. the features are less impressive, the lung look deeper pink than in pan-acinar E., and less voluminous.

بال Panacinar لأنه معظم ال acini متضررة بتكون الرئة كبيرة و ممكن حتى تغطي على القلب ، لكن بال centriacinar بتكون التغيرات اخف لأنه بضل في مناطق normal

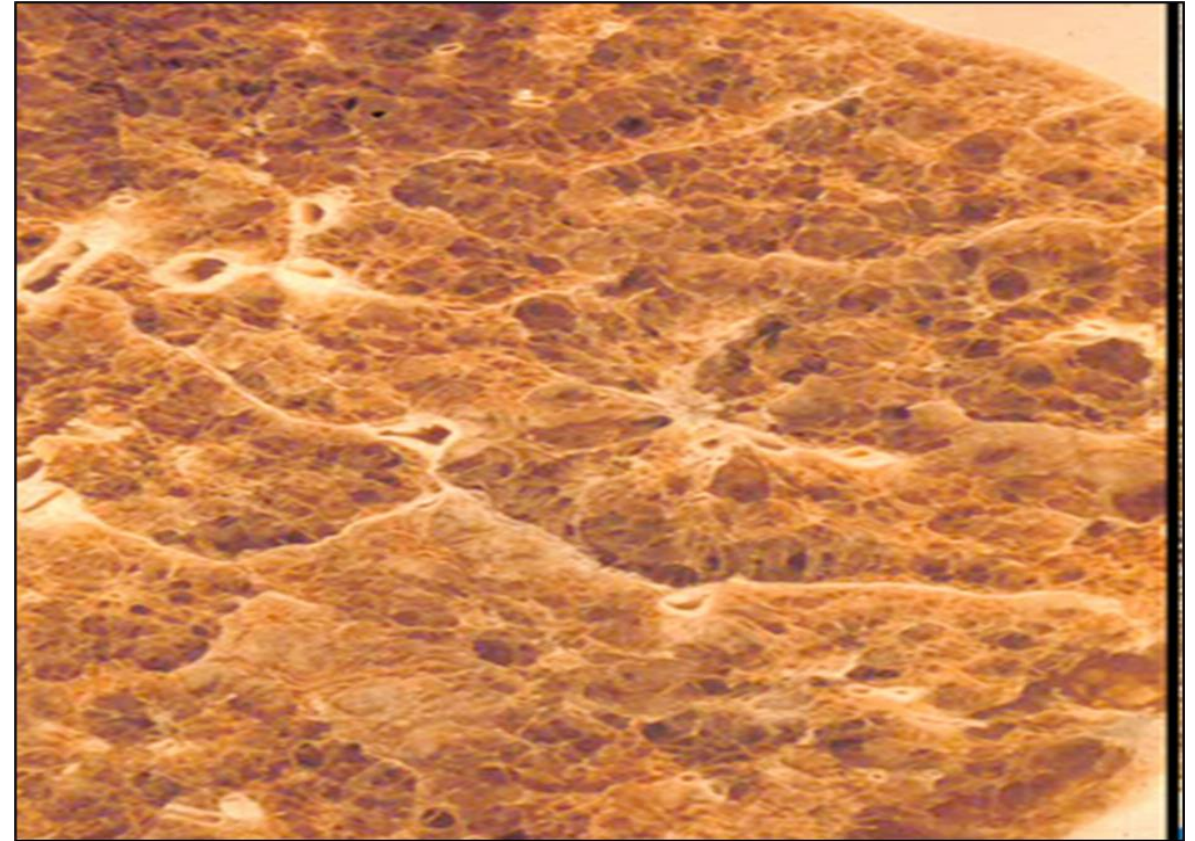
**Centriacinar emphysema** : centrilobular dilatation surrounded by normal lung tissue, with black color due to carbon particles (smokers).

dilated (abnormal) اللون اسود بسبب  
carbon from ال  
smoking



**Panacinar emphysema**: the expansion is diffuse throughout each affected acinus

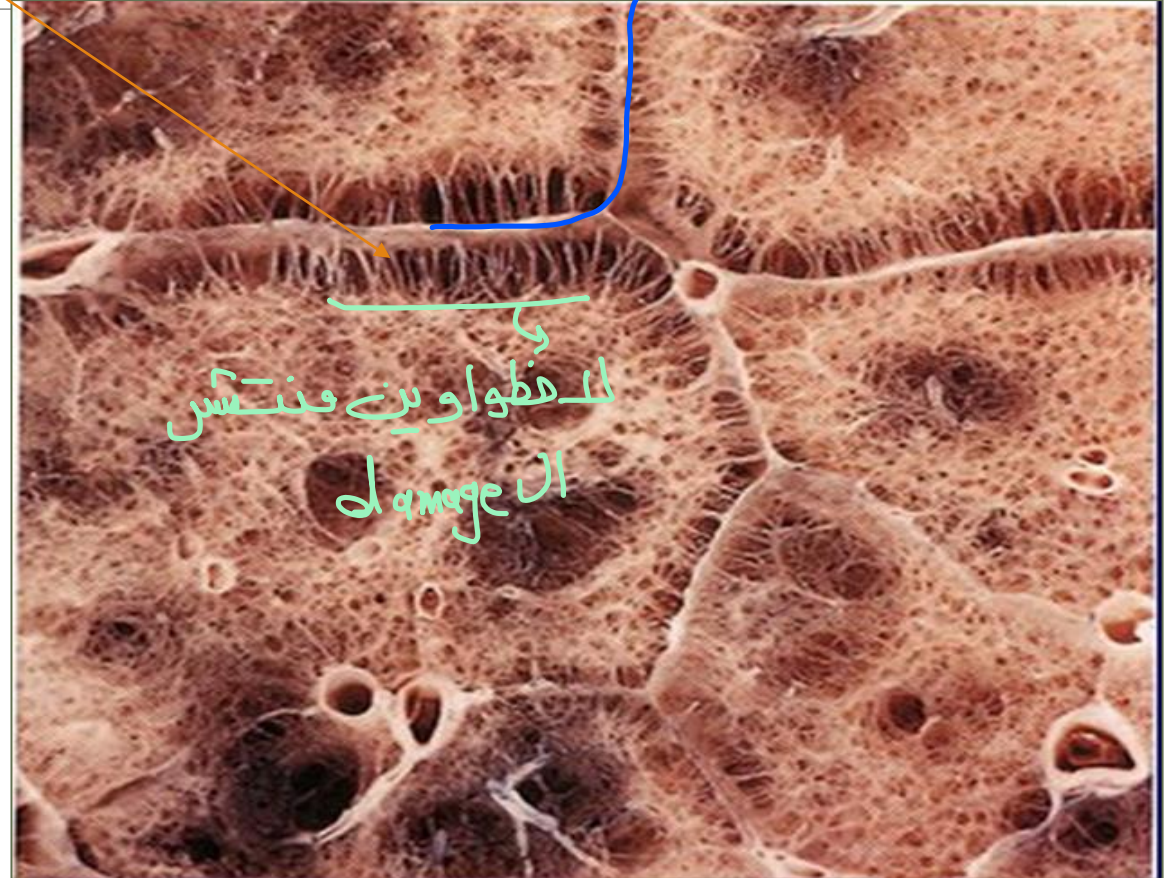
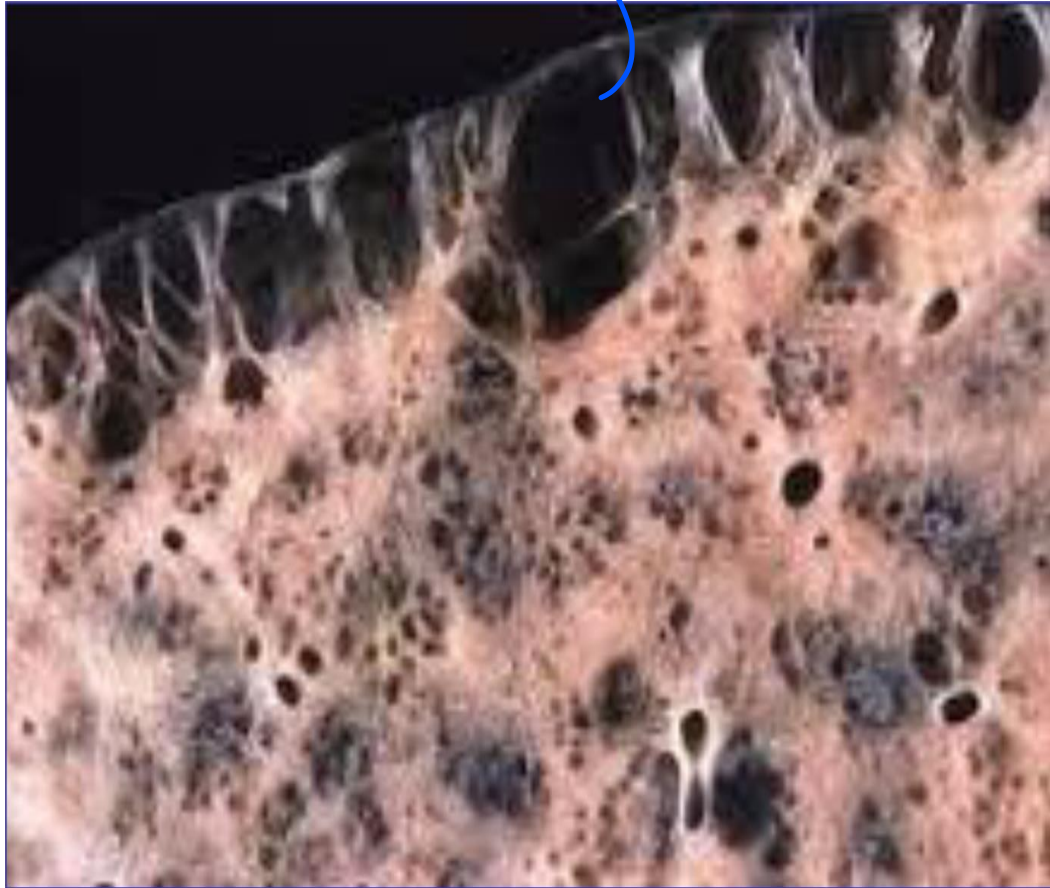
enlarge و dilated كل ال lung tissue



# Paraseptal & centriacinar emphysema

Enlargement air spaces adjacent to pelura  
بنلاحظ انهم

septal





ممكن تفجير وتسبب pneumothorax

Peripheral cystic bullae

## Bullous emphysema:

- Any form of emphysema that produces large subpleural blebs or bullae i.e. air spaces larger than 1cm., when rupture leads to **pneumothorax**

احياناً لما يصير destruction in the air spaces بصيروا يفتحوا على بعض و يشكلوا large air space بنسبيه bullous عادة حجمها اكبر من واحد سم ، مشكلة هاي الفقاعة انه ممكن يصير الها rupture و يطلع الهوا لل plural space و يسبب pneumothorax



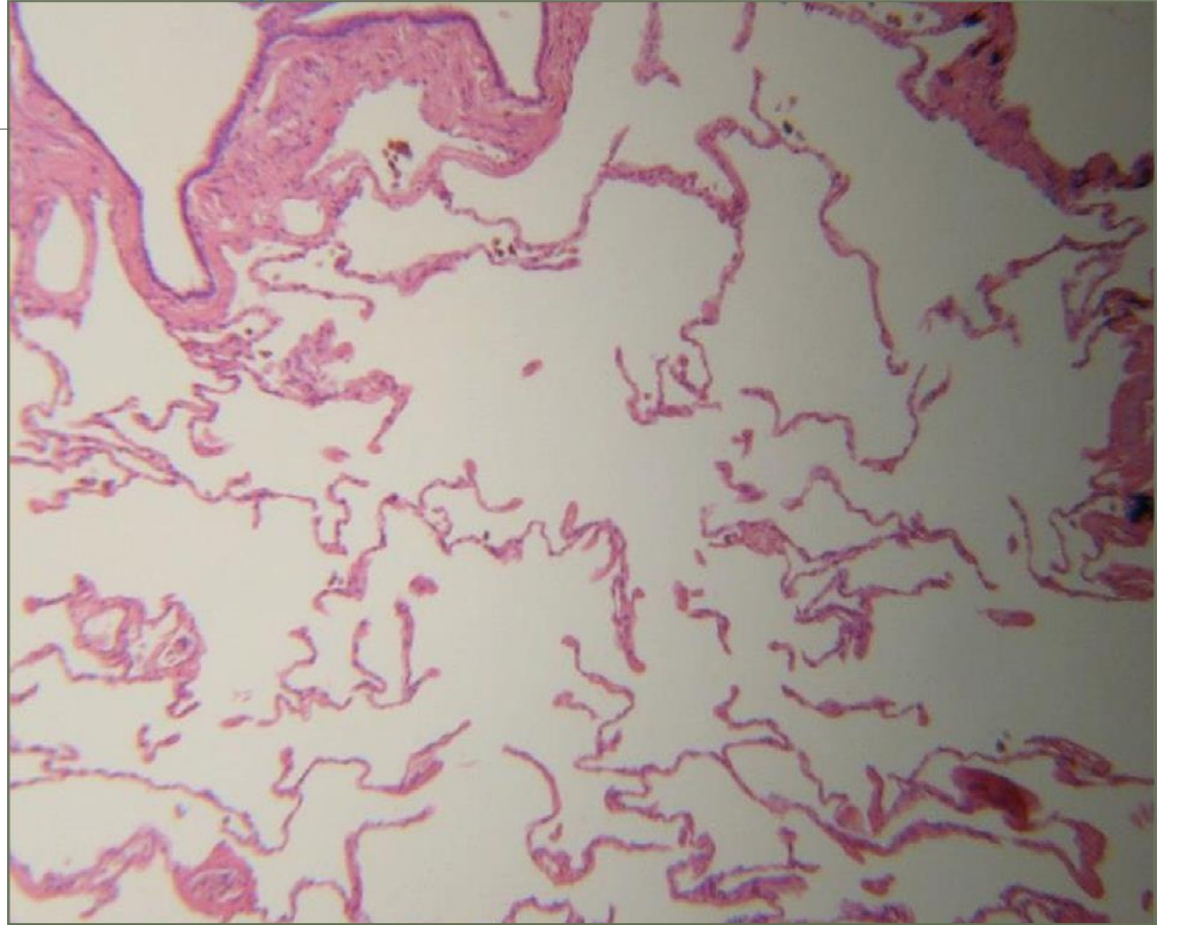
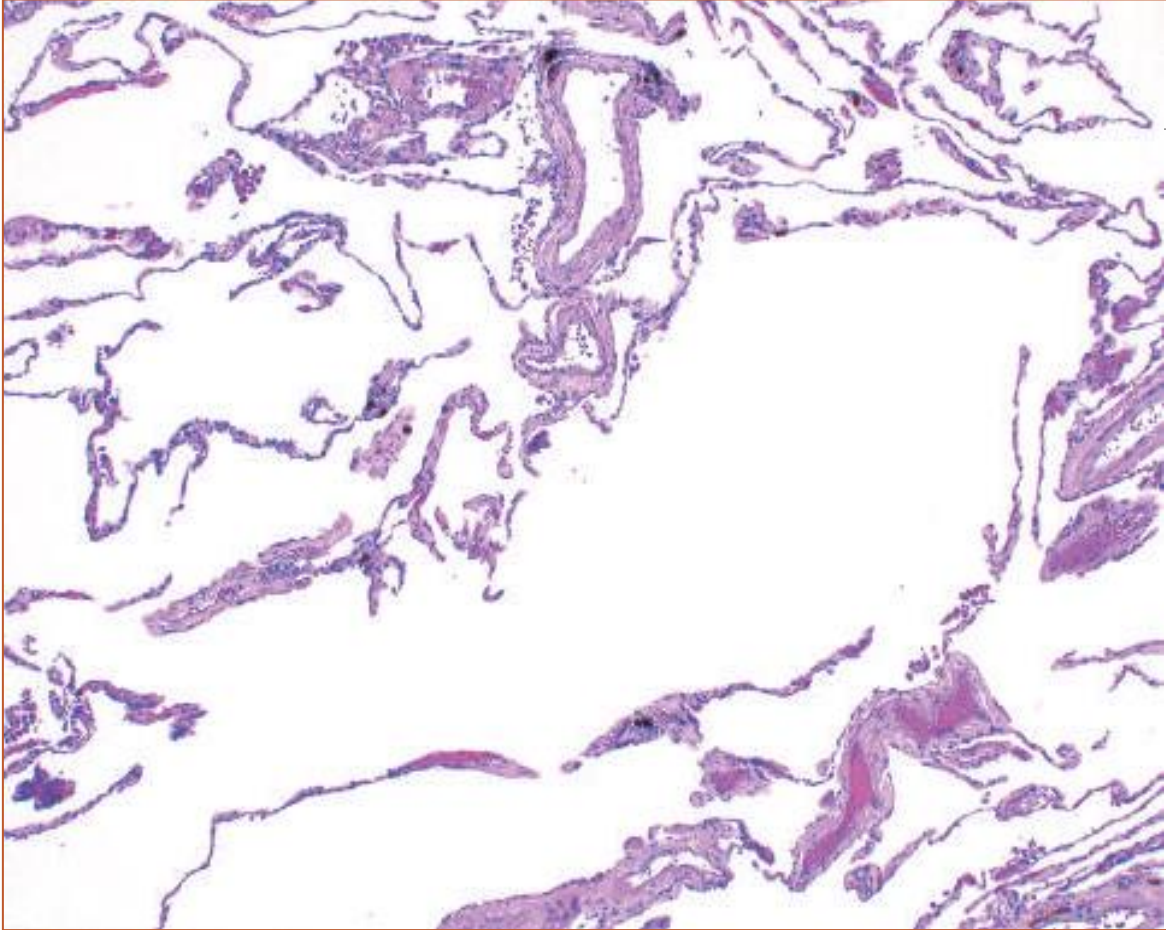
رجعت أكدت الدكتور على موضوع انه  
ما بنشوف significant fibrosis

## Histologically :

- ❑ Thinning & destruction of alveolar walls; with advanced disease, the adjacent alveoli create large air spaces.
- ❑ Terminal & respiratory bronchioles may be deformed
- ❑ Alveolar capillaries are diminished.
- ❑ Bronchiolar inflammation and submucosal fibrosis are consistently present in advanced disease

↳ mild not significant  
بكو

↙ abnormal ↘



هيك خلصنا موضوع ال emphysema

## 2. Chronic Bronchitis :

عكس ال emphysema  
حكينا انه ال emphysema بنعرفها حسب ال radiology and morphology ،  
مثش والله اذا اجى المريض ب dyspnia or barrel chest بنحكي خلص  
المريض عنده emphysema ، بينما بال chronic bronchitis بنشخص  
المريض حسب ال presentation يعني بيجي المريض عنده كحة مستمرة مع  
بلغم لمدة ٣ اشهر خلال السننتين الأخيرات وعادة يكون cigarette smokers  
شروط تكون productive cough و الفترات المذكورة ، مش لو كان عنده  
productive cough من شهر ، وبس هاي السنة ، هذا ما بحكي عنه chronic  
bronchitis

## 2. Chronic Bronchitis :

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Chronic bronchitis is defined based on clinical features.

### Definition :

- A clinical condition characterized by a persistent productive cough for at least **three consecutive months** in at **least two consecutive years** (WHO)
- It is common among **cigarette smokers** and **urban dwellers**.

رعت على هاد الدكتور

## Chronic bronchitis can occur in several forms :

### 1- Simple chronic bronchitis :

-Patients have a productive cough with mucoid sputum, <sup>بس هیلے</sup> but airflow is not obstructed.

### 2- Asthmatic bronchitis :

- Patients may demonstrate hyper-responsive airways with intermittent bronchospasm and wheezing. → <sup>زیا أعراض ال Asthma</sup>

### 3- Chronic obstructive bronchitis : most severe

- Including heavy smokers who develop frank chronic outflow obstruction, usually with associated emphysema.

## Pathogenesis :

من اسمها chronic bronchitis معناتها  
التغيرات رح تبلش من ال bronchi لكن مع  
الزمن بصير تغيرات كمان بال bronchioles

المريض بكون بشكي من productive cough  
يعني كحة مع بلغم و mucus production

من اسم المرض

- Hypersecretion of mucus, beginning in the large airways as major bronchi.
- In advanced disease, even small bronchioles are involved.
- The environmental irritants induce hypertrophy of mucus glands in the bronchi & goblet cell metaplasia, which leads to a marked increase in mucus-secreting goblet cells in the bronchi & bronchioles.
- In addition to inflammation with infiltration of lymphocytes, macrophages & neutrophils.
- **Eosinophils are NOT seen in chronic bronchitis.**
- Microbial infection is often present but has a secondary role chiefly by maintaining the inflammation.

مهم جداً نعرف انها ما الها دور في ال chronic  
asthma، و هاد يلي بميزها عن ال bronchitis

( Not primary )

طيب شو يلي بصير عند المريض لحتى يزيد ال mucus production؟

المواد الموجودة بال smoking ، أو إذا كان بيتعرض ل irritant from environment بتصير تحفز منتجات ال mucus in the airway ، طيب شو هاي المنتجات؟  
شغلتين الأولى submucosal mucus gland و الثانية goblet cells ، فهدول المرضي بصير عندهم hypertrophy in the mucus gland and goblet cells  
metaplasia ، وبالتالي راح يزيد ال mucus production

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Whereas the defining mucus hypersecretion is primarily a reflection of the involvement of large bronchi, the airflow obstruction in chronic bronchitis results from: ← البداية

1- So called **small-airways disease** induced by **goblet-cell metaplasia** with mucus-plugging of the bronchiolar lumen, inflammation, and fibrosis.

2- **Co-existent emphysema.**

يعني لو مريض عنده chronic bronchitis و تأزمت حالته و وصل لمرحلة ال air flow obstruction معناته هذا المريض صار عنده إما انه ال bronchiol also affected و صار عندهم goblet metaplasia and hyperplasia بشكل كبير و ال mucus زاد انتاجه و صار يعمل obstruction and inflammation .... او انه صار عند المريض كمان COPD and this is called. emphysema



## Clinical features and course :

- Cough with the production of excessive mucoid or mucopurulent sputum
- Some patients may develop COPD with outflow obstruction; this is accompanied by hypercapnia, hypoxemia & in severe cases, cyanosis.
- For unknown reasons, they tend to be obese.

called **blue bloater**

عكس ال emphysema ، بيصير عندهم زيادة في ثاني أكسيد الكربون و نقص الاكسجين وبالتالي بيصير لونهم أزرق cyanosis، و كمان بكونوا obese

بس نحكي COPD او chronic bronchitis نتذكر هاد الديناصور ناصح و ازرق و مركب اسطوانة اكسجين



# Morphology:

## Grossly:

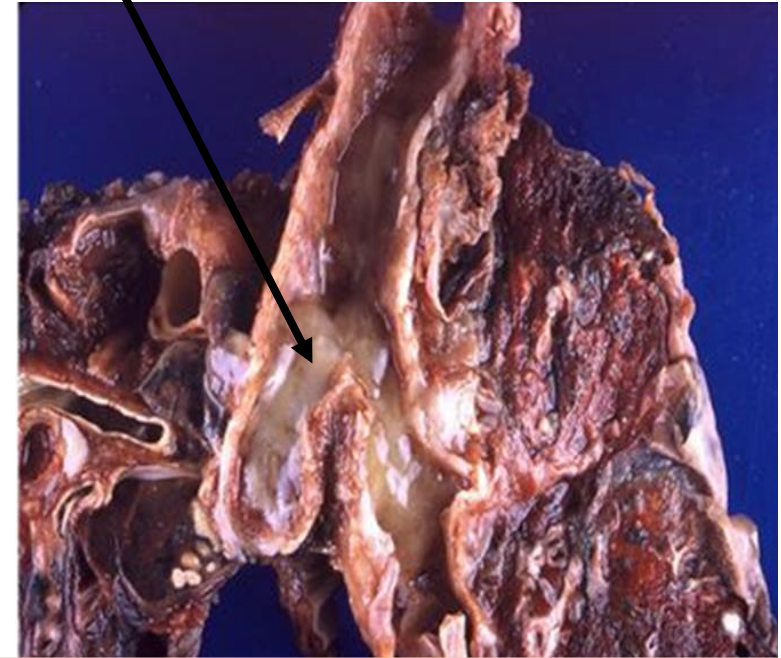
- ❖ The mucosal lining of larger airways is usually hyperemic & swollen by edema and covered by a layer of mucopurulent secretion.
- ❖ The smaller bronchi & bronchioles may also be filled with similar secretions.

## Histologically:

- ❖ The larger bronchi: goblet cell metaplasia of bronchial epithelium and
- ❖ hyperplasia of submucosal mucus-secreting glands.

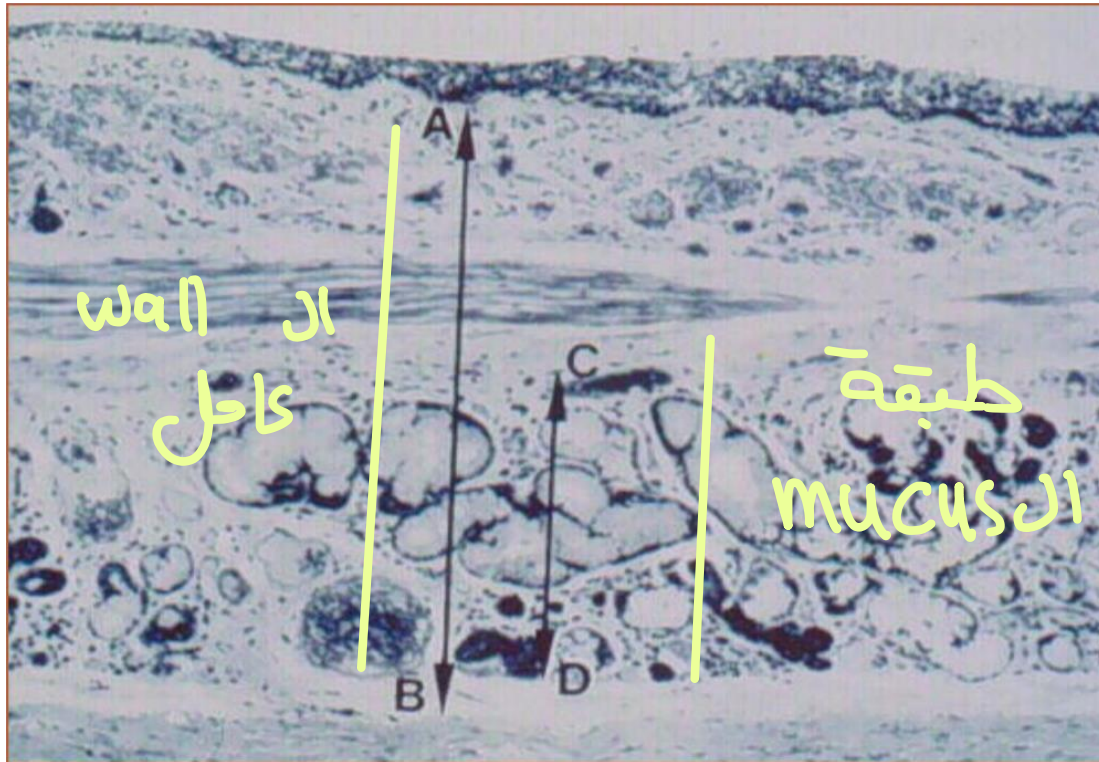
The magnitude of the increase in size is assessed by the ratio of the thickness of the submucosal gland layer to that of the bronchial wall from the epithelial layer down to the cartilage

This ratio is called the Reid index, which normally is (0.4)



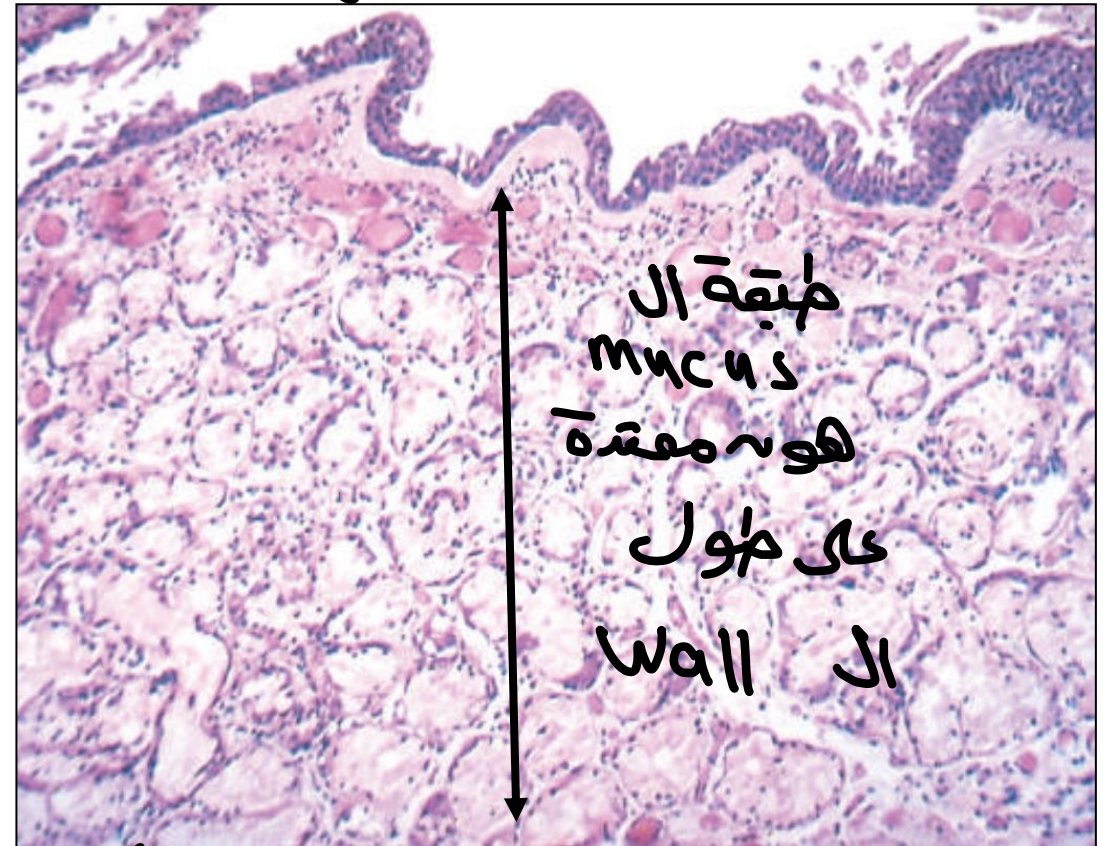
عشان ما يصير conflict بموضوع ال hypertrophy ( ممكن انا احكي انه normal و انت تحكي لا )  
عشان هيك عملولنا reid index يعني  
بنقيس سماكة طبقة ال submucosal gland بالنسبة لل  
Thickness of whole wall

Measuring Reid index, normal 0.4; in chronic bronchitis, it is increased by 1/1.



الوضع الطبيعي

hypertrophy



( chronic bronchitis )

- Variable inflammatory cells, largely mononuclear cells but sometimes with neutrophils, are present in the bronchial mucosa.

- **Chronic bronchiolitis** is inflammation of small bronchioles, showing goblet cell metaplasia, mucus plugging inflammation & fibrosis.

- In severe cases narrowing and obstruction with complete obliteration of the lumen due to fibrosis called **bronchiolitis Obliterans**.

- Squamous metaplasia ± DYSPLASIA

Goblet cell metaplasia (right ) of the bronchiolar epithelium (left) with inflammatory cells infiltrate in surrounding tissue .



← hyperplasia

→ (abnormal)  
hyperplasia & metaplasia goblet

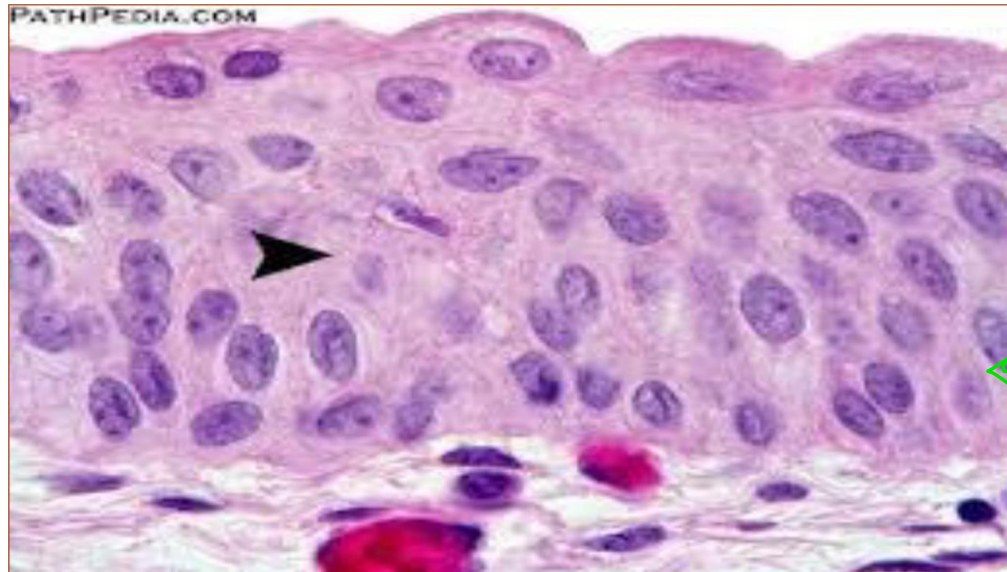
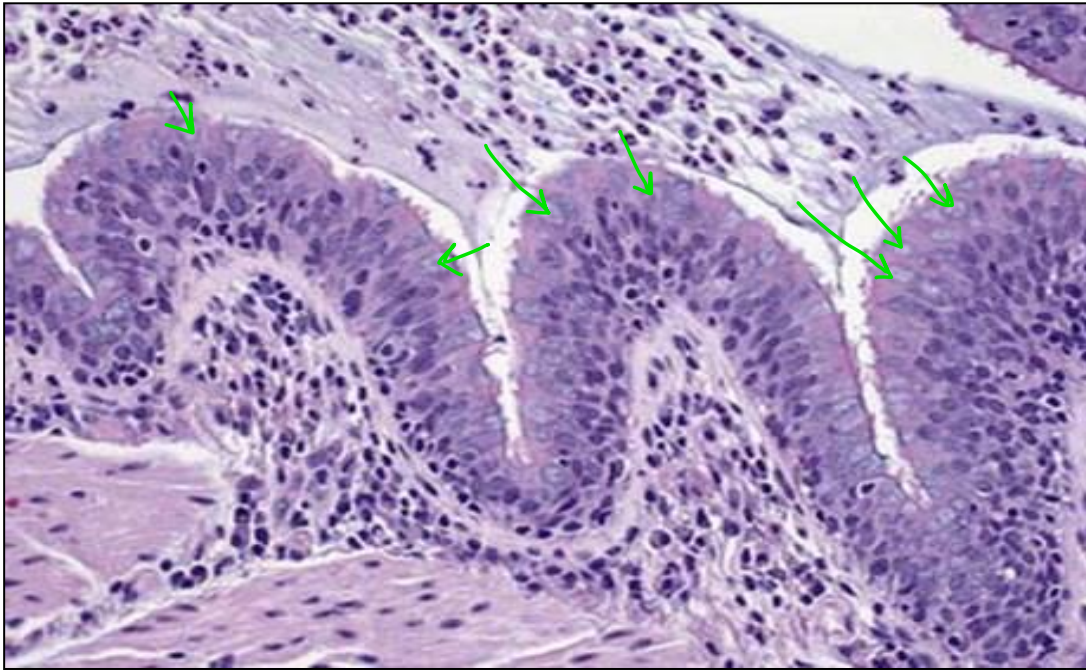
لاحظوا قديش زايدة ال goblet cells و في inflammation in the wall بس ما عنا eosinophills مهم تنتبهوا للنقطة هاي

### Chronic bronchitis:

- Goblet cell hyperplasia and chronic inflammation in the submucosa, and acute inflammation mixed with intraluminal mucus.

### Bronchial mucosa showing squamous metaplasia

هون صار نوع ثاني من metaplasia بصير يتحول ال respiratory columnar epithelium إلى squamous epithelium لأنه يكون اكثر مقاومة لل irritation فبدل ما نشوف ciliated columnar cells بنصير نشوف squamoid cells





يَعْطِيكُمْ الْعَافِيَةَ

Thank You

Done by Sadeel Alfaqeer