

وَقُلْ رَبِّ زِدْنِي عِلْمًا



RESPIRATORY SYSTEM

HAYAT BATCH



SUBJECT : Pathology

LEC NO. : 2

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Respiratory System

RS

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Diffuse Pulmonary Diseases:

يعني بنقدر نحكي انه مشكلة ال obstructive انه المريض
بيقدر ياخذ هوا بس صعب انه يطلعه بسبب ال obstruction
خصوصا في حالات ال partial obstruction

1. Obstructive Diseases:

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

2. Restrictive Diseases:

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

ال Restrictive Disease يكون عامل restrictive على ال lung
expansion فبتقل قدرة ال lung على انها تتمدد فبكون عند المريض
مشكلة بال inhalation لانه ال lung بتكون stiff بسبب وجود
ال fibrosis اللي راح نحكي عنه بعدين

راح نحكي عن ال obstructive disease وهي
بتشمل 4 entities في المحاضرة هاي راح نحكي عن
٢ والمحاضرة الجاي ال ٢ اللي ضلو

شغله لازم تفهموها in general احيانا
ال emphysema وال chronic bronchitis مع
بعض بسموهم chronic obstructive pulmonary
disease (COPD) لانه كثير مرضى ممكن يجو
عندهم 2 من هدول ال Obstructive lung disease
اللي هم ال emphysema وال chronic brochitis
مع بعض

بس هلا احنا راح نحكي عنهم كل واحد لحال
وغالبا الحالتين بكونو related to smoking وصعب
جدا تجدهم عند ناس مش smoker
وعشان هيك بيجو مع بعض كتطورات لبعض

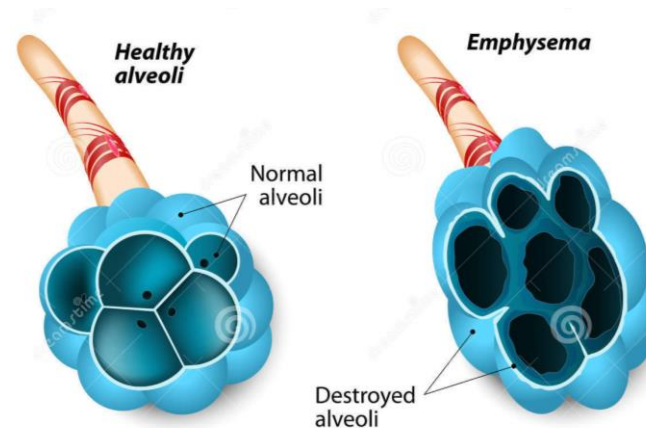
Obstructive lung diseases

1. Emphysema

-Defined based on **morphologic** and **radiologic** features.

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**.



Types of emphysema:

حسب مين الجزء اللي affected من ال acinus

1. Centriacinar (centrilobular) Emphysema:

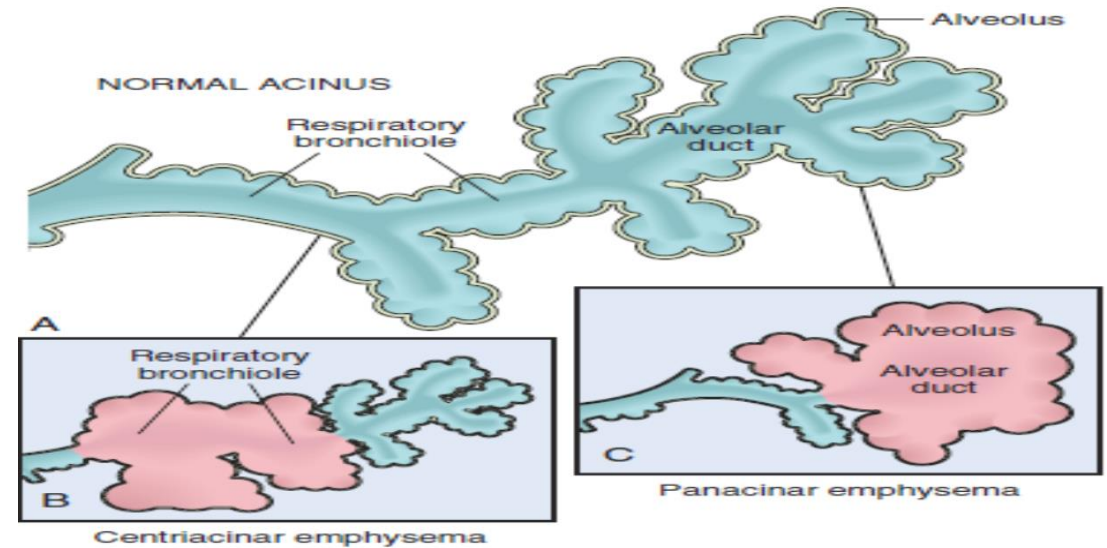
- The central or the **proximal part** of the acini, formed by the respiratory bronchioles, are **affected**, while the distal alveoli are spared.
- The lesions are more common & severe in the **upper lobes**
- Most commonly due to **cigarette smoking**, often in association with chronic bronchitis.

معناها كل اشئ يعني Pan
يعني كل ال acini affected

2. Panacinar (Panlobular) Emphysema :

- 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**.

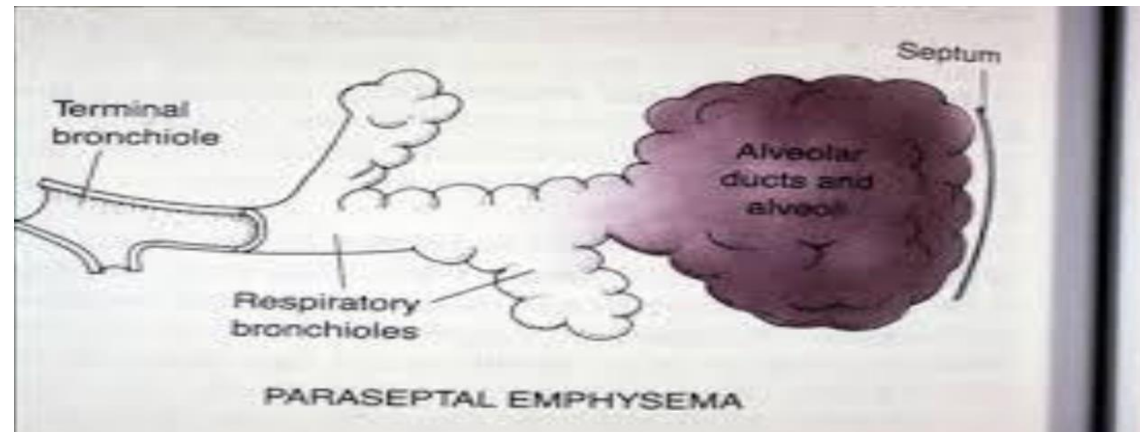
هاد هو السبب الرئيسي مش التدخين ولكن مازال
التدخين ممكن يزيد



سموها paraseptal لان ال alveoli وال alveolar duct اللي يكونو جنب ال interlobular septa وال plura هم يكونو اكثر اشي affected

3. Distal acinar (Paraseptal) emphysema:

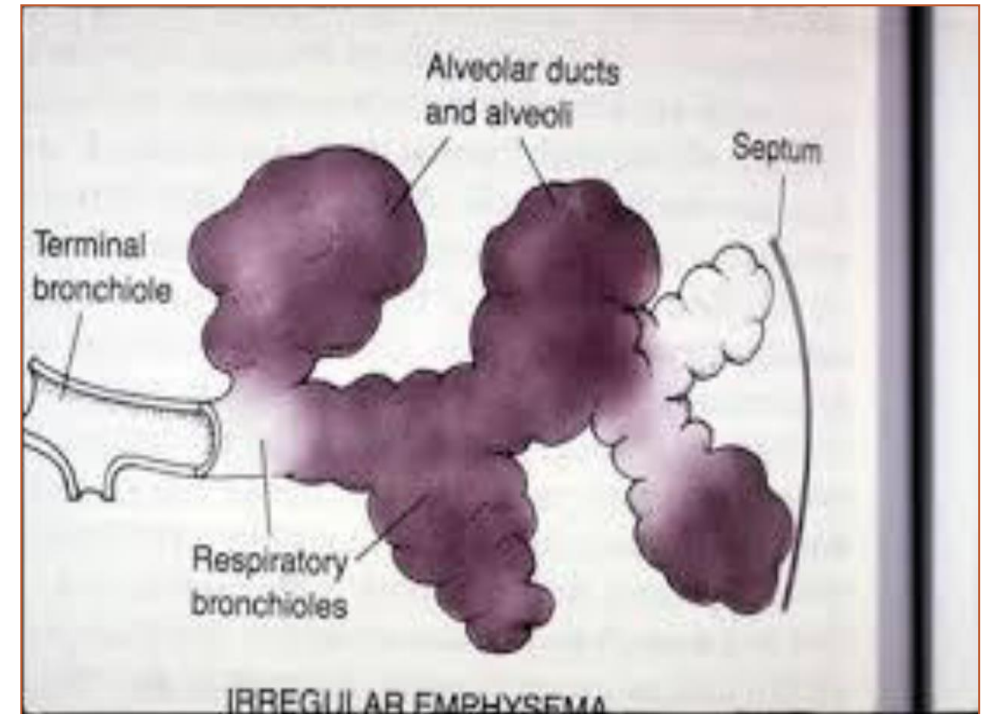
- The proximal portion of the acinus is normal, but the **distal part** is primarily **involved**.
- More severe in the **upper half** of the lungs.
- The emphysema is more striking **adjacent to the pleura** and **along** the lobular connective tissue **septa**.
- It occurs adjacent to areas of fibrosis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



من اسمه irregular يعني ما في pattern معين
ممکن تشوف acinus ال proximal part فيها affected و ممکن تشوف وحدة ثانية ال
alveolar duct هي اللي affected و ممکن وحدة ثالثة يكون كل ال acinus affected

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.**



Pathogenesis:

Two Pathways are involved :

1- PROTEASE -ANTIPROTEASE imbalance.

2- OXIDANT – ANTIOXIDANT imbalance

- Such imbalances almost always coexist.

وهاد الاشئ لاحتظه لما صارو يشوفو انو الناس اللي عندهم
congenital alpha 1 antitrypsen defeciency بصير
panacinur emphysema عندهم بشكل كبير
ومن هون وجدو انه هاد ال defect بال protease اله
علاقه

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

- **α 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.**

Decrease in these protective mechanisms produce damage.

Decrease in antiprotease activity may be :

i- Genetic: α 1- antitrypsin deficiency

ii- Acquired: Smoking

- More than 80% of patients with congenital α 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 α 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.**

ال termin bronchiole وال respiratory bronchiole عشان يضلهم فاتحين بكون ماسكهم ال elastic tissue اللي موجود حولين ال alveoli طيب هلا اذا صار destruction لل alveoli وبالتالي صار destruction لل elastic tissue معناها الاشياء اللي ماسك ال terminal وال respiratory bronchiole و بخليهم فاتحين راح فبصير المريض لما يجي ياخذ النفس و بده يعمل expiration بسكرو ال terminal وال respiratory bronchiole لانه ال alveoli اللي حوليهم مكسرين فهون بصير عند المريض مشكلة بال expiration

فهو فعليا اللي بصير بال emphysema
functional obstruction يكون وليس
mechanical يعني ما في اشى جوات ال airway
مسكره لا هم سكره لانو الاشى اللي كان فاتحهم مش
موجود

Clinical Features :

- Dyspnea (progressive).
- Weight loss (**thin**). ما بنعرف ليش.
- Without concomitant chronic bronchitis usually presents with a **barrel chest**, dyspnea, and **prolonged expiration, sitting forward in a hunched-over position**.
بكون الهم جلسة معينة عشان يعرفو يتنفسو
- 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**.

بكون لونه pink لانه عنده good oxygenation في بداية المرض



Morphology of Emphysema:

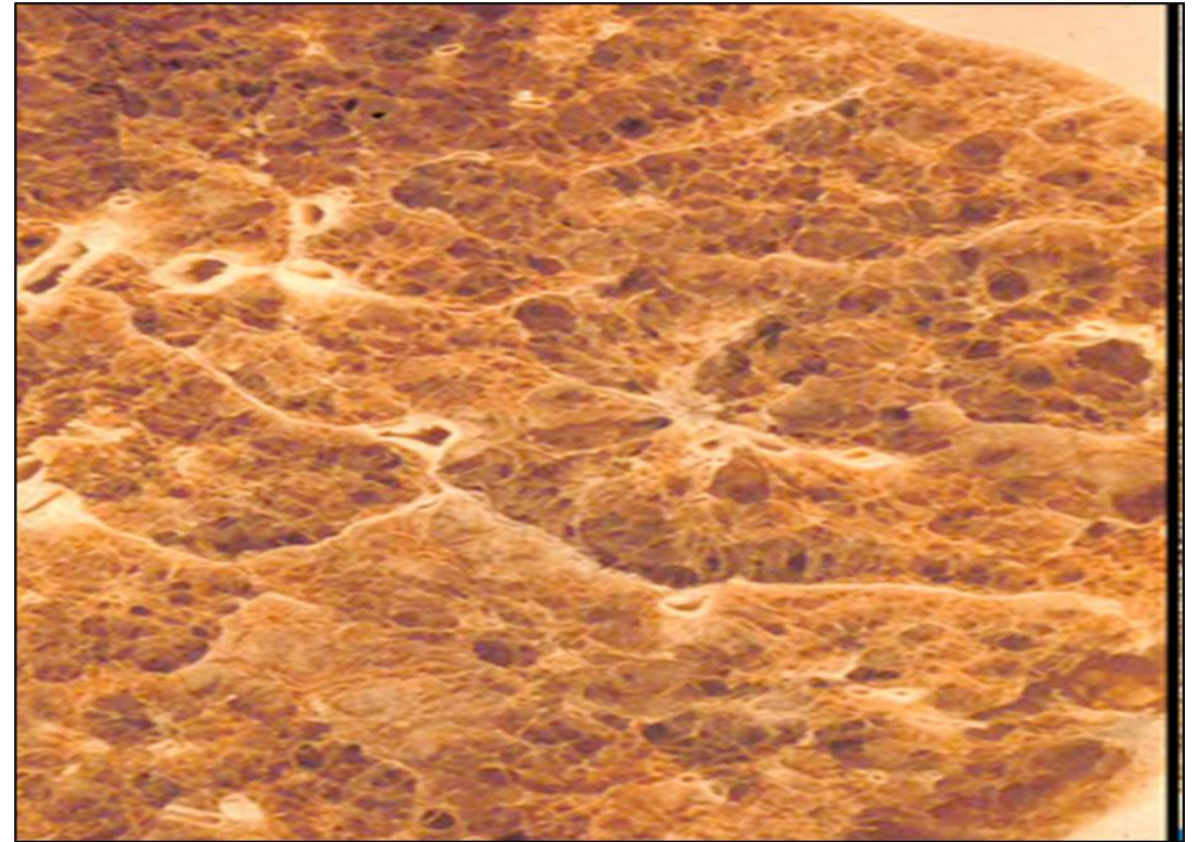
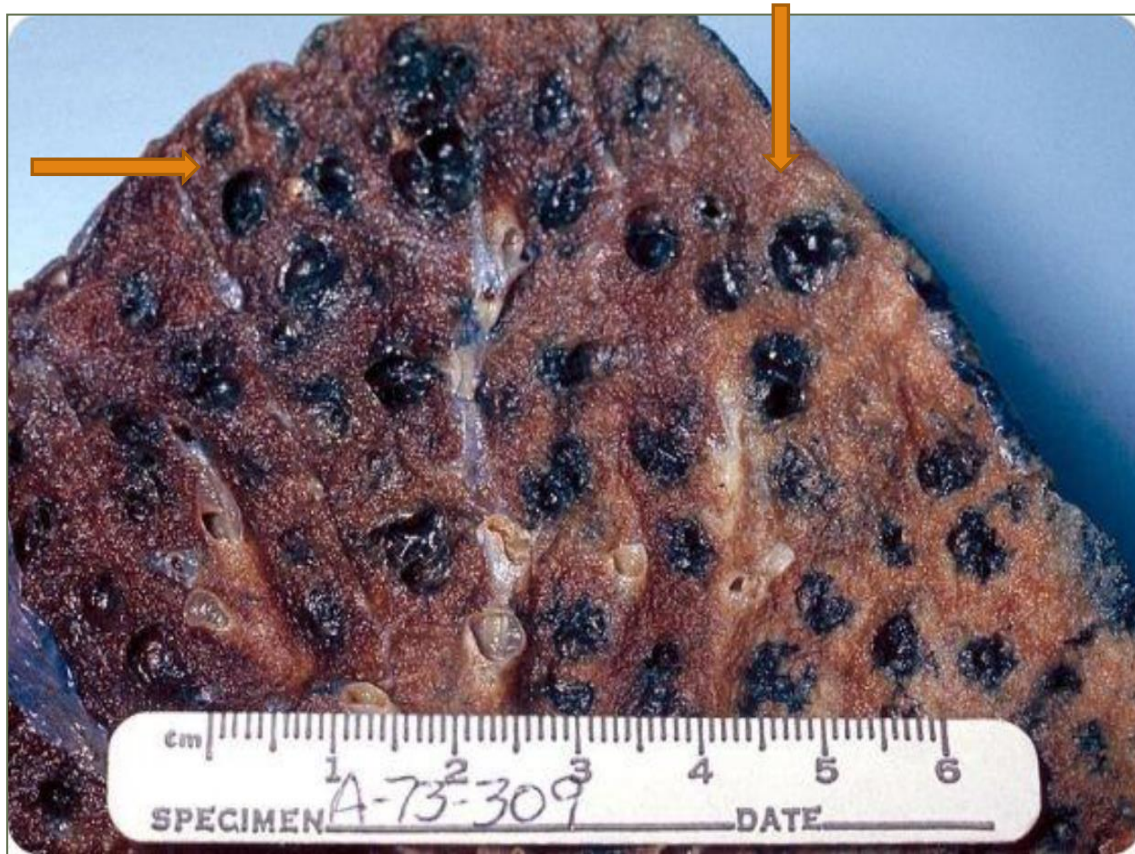
بيختلف منظرها حسب اذا كانت panacinar ولا centriacinar

Grossly:

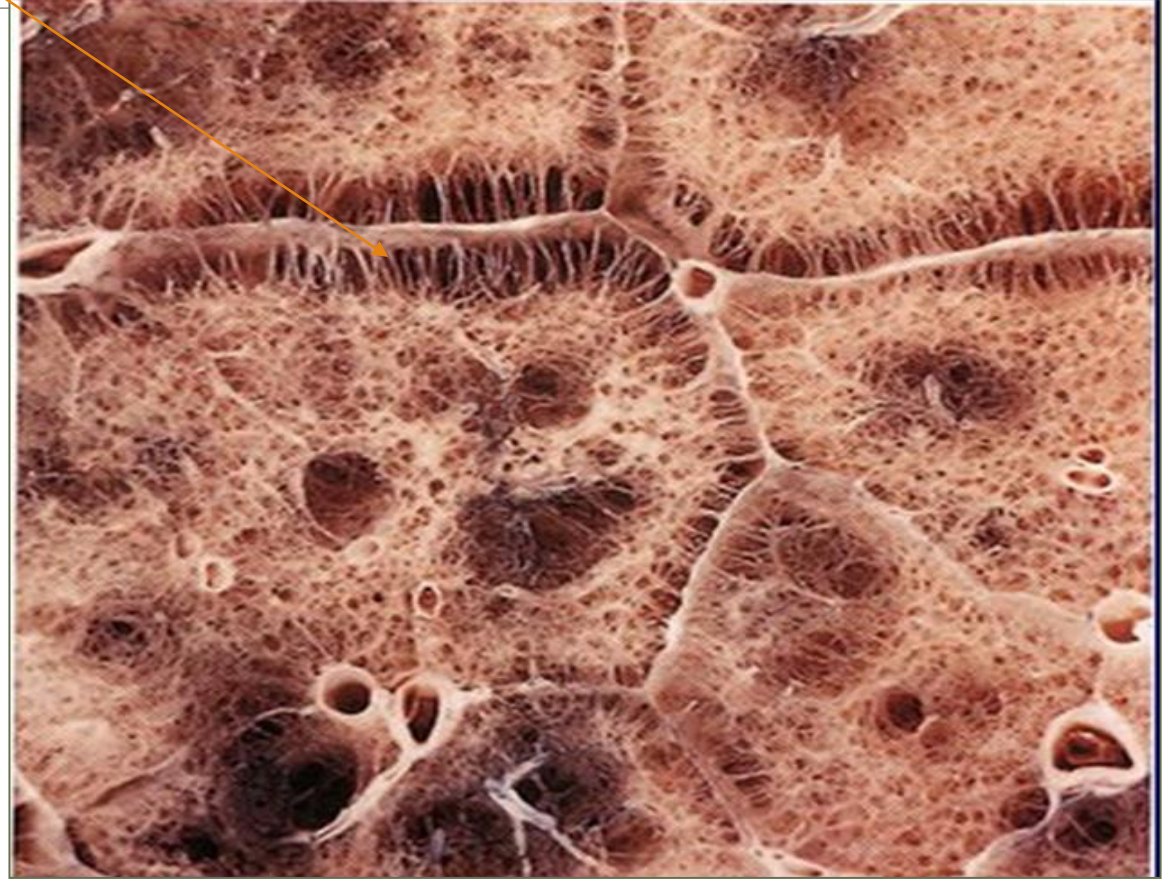
- The diagnosis & classification of E . depend on the macroscopical appearance of the lung.
- In pan-acinar E. the lungs are pale voluminous hyperinflated and obscure the heart.
- In centriacinar E. the features are less impressive, the lung look deeper pink than in pan-acinar E., and less voluminous.

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

Panacinar emphysema: the expansion is diffuse throughout each affected acinus



Paraseptal & centriacinar emphysema



destruction in the airspaces هلا احيانا لما يصير عندنا
بصير كل ال airspaces يفتحو على بعض فبيعملونا زي فقاعة
كبيرة air space كبير بنسميها Bullous
emphysema ممكن تصير بأي نوع من ال

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**



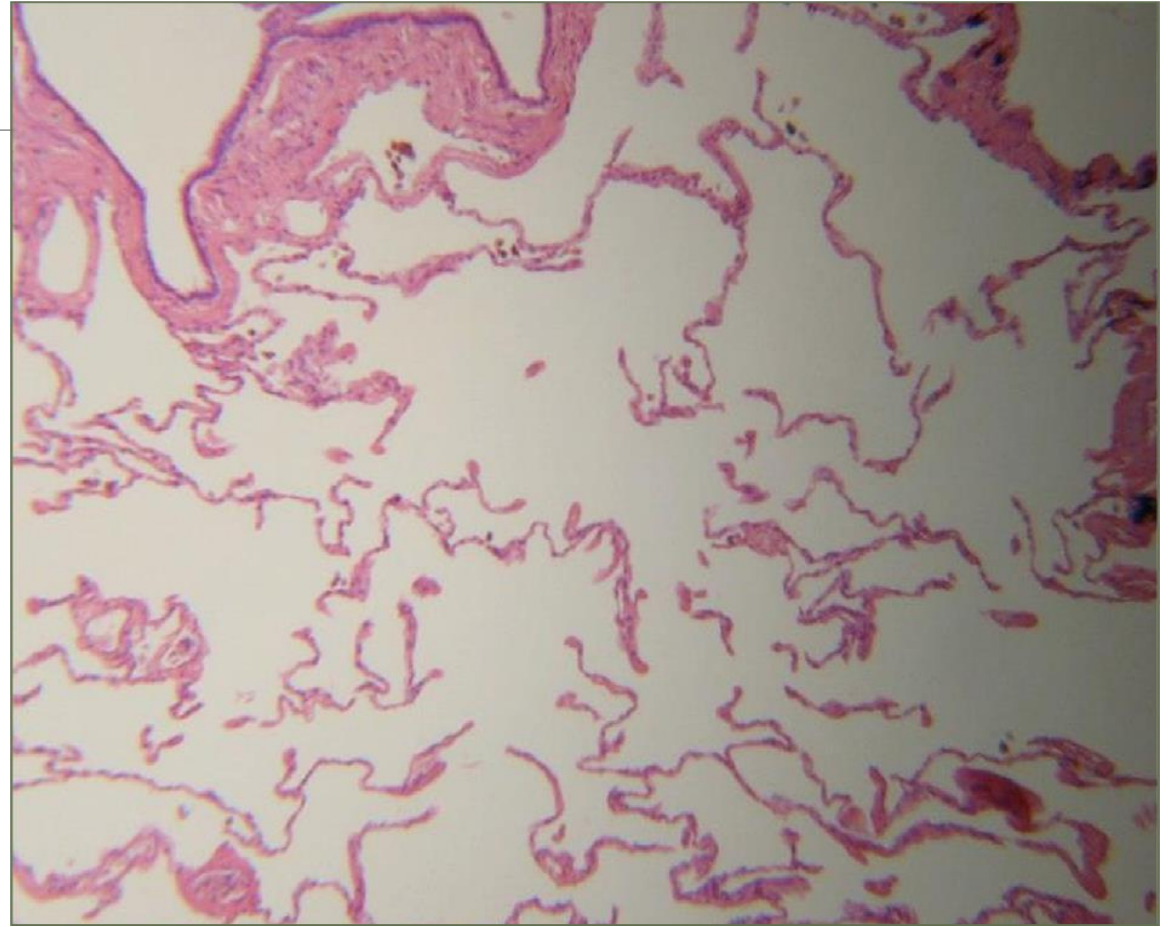
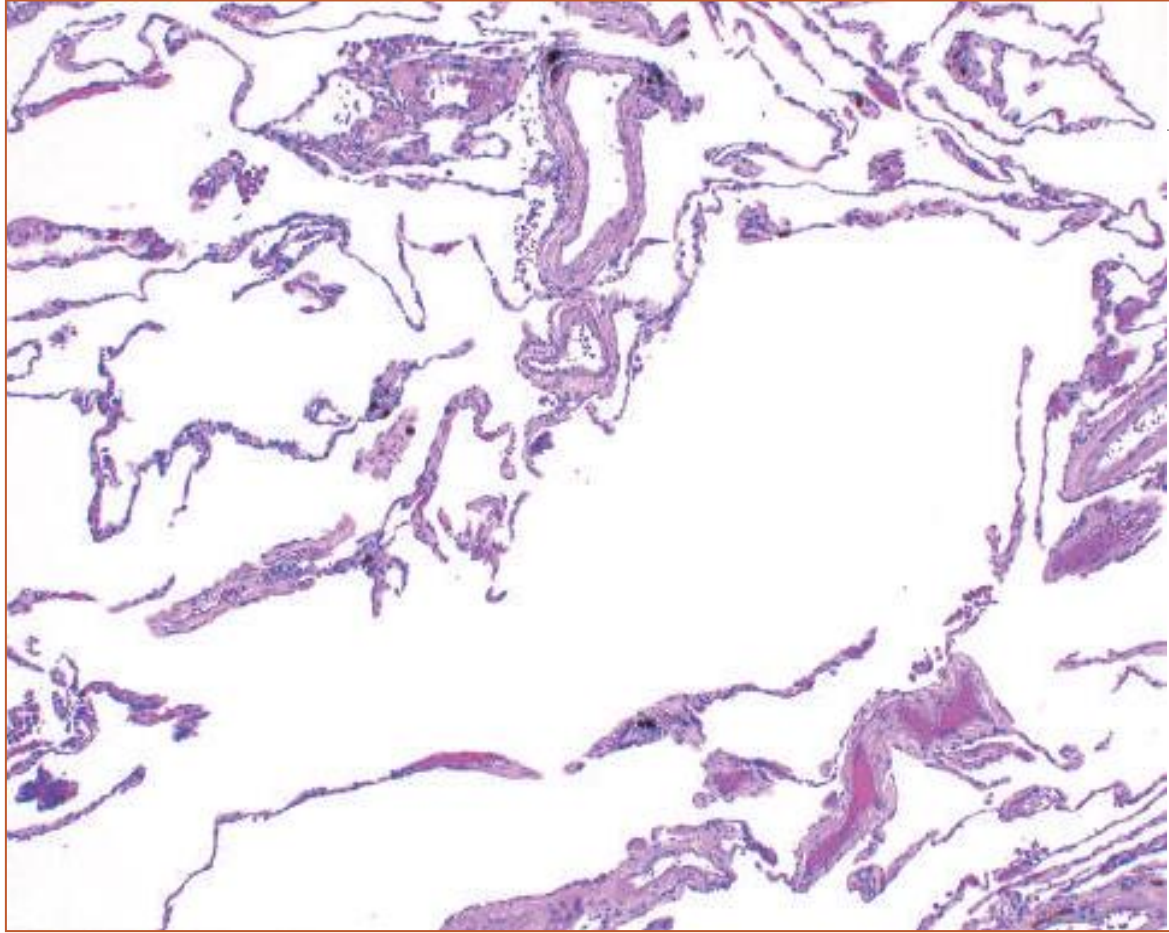
Histologically :

- ❑ 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

Fibrosis و inflammation ما بنشوف significant

حتى لو حكينا في شوية fibrosis ولكن ما بصير

emphysema ما بصير بال significant



2. Chronic Bronchitis :

Chronic bronchitis is defined based on **clinical features.**

شرط انهم يكونو مستمرين ٣ شهور ورا بعض لمدة سنتين ورا بعض هيك
منظمة الصحة بتعرف ال chronic bronchitis

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.**

يعني لو حكينا مريض اجى بيشكي من productive cough هاد ال cough كان مستمر معاه 4 او 5 شهور
ورا بعض خلال السنتين الى ٣ السابقات هاد معناها عنده

Chronic bronchitis

اما لو حكينا عنده productive cough لشهر واحد بس بعدين راح خلال سنة وحدة والسنة اللي قبلها ما
كان عنده هاد مش chronic bronchitis

Chronic bronchitis can occur in several forms :

1- Simple chronic bronchitis :

-Patients have a productive cough with mucoid sputum, but airflow is not obstructed.

2- Asthmatic bronchitis :

- Patients may demonstrate hyper-responsive airways with intermittent bronchospasm and wheezing.

3- Chronic obstructive bronchitis : اخطر مرحلة

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

Pathogenesis :

- ❑ 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.** هاي المعلومة مهمة عشان اميزها عن ال asthma (المحاضرة الجاي)
- ❑ Microbial infection is often present but has a secondary role chiefly by maintaining the inflammation.

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

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

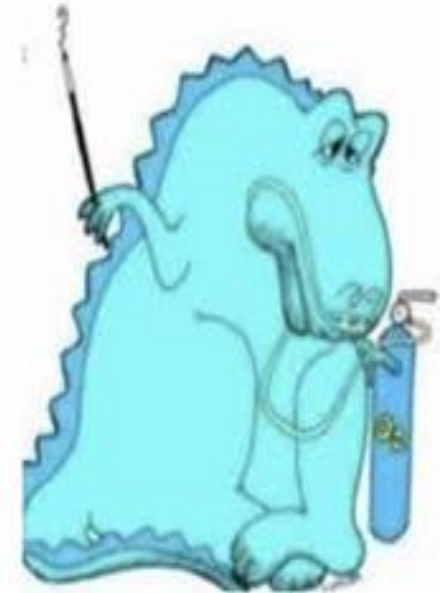
2- **Co-existent emphysema.**

يعني المراحل الاولى ك difination mucus hypersecretion بتكون ال air way large هي
اللي affected فقط بس لما يوصل لمرحلة obstruction يا يكون عنده small airway
involvement او بصير كمان صار عنده emphysema
يعني وصل لمرحلة COPD

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**



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:

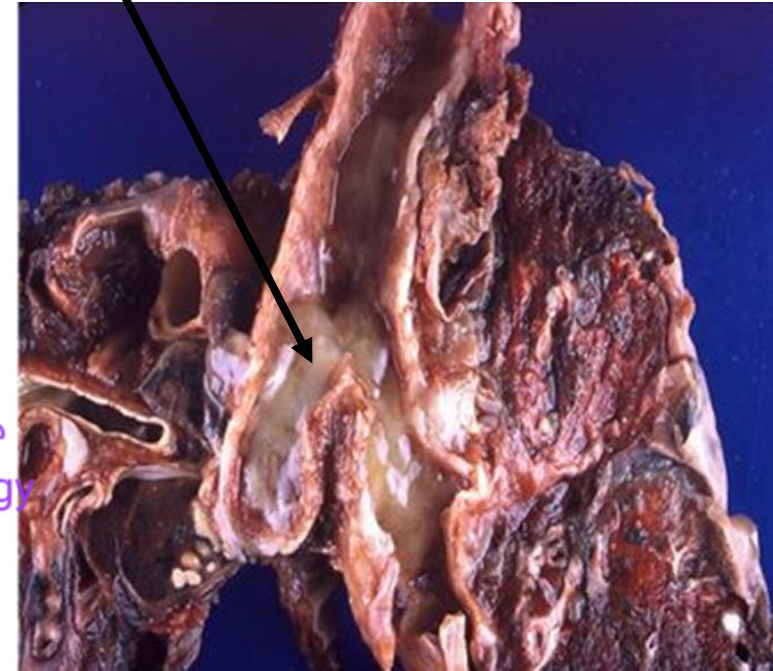
الوضع الطبيعي احنا بكون عنا بس شوي goblet cell

- ❖ The larger bronchi: goblet cell metaplasia of bronchial epithelium and hyperplasia of submucosal mucus-secreting glands. مهم جدا عشان تعرفو تميزو بال

morphology بين ال diseases

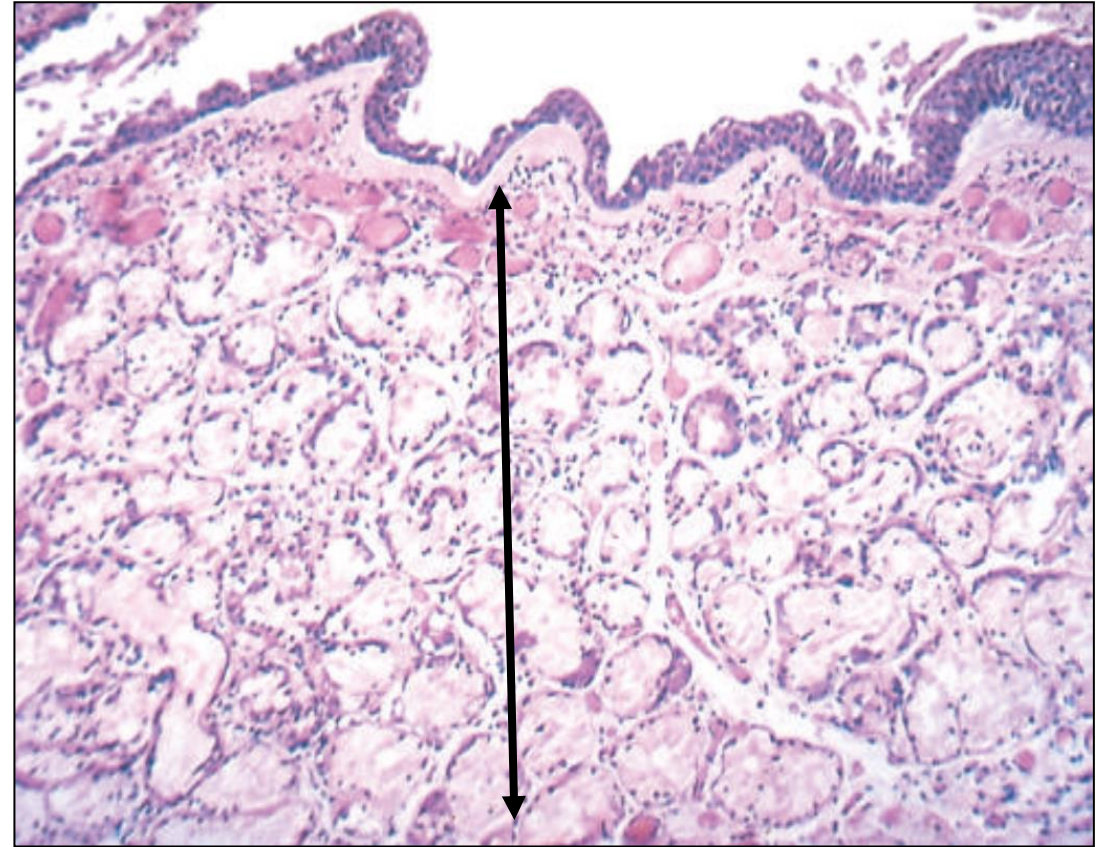
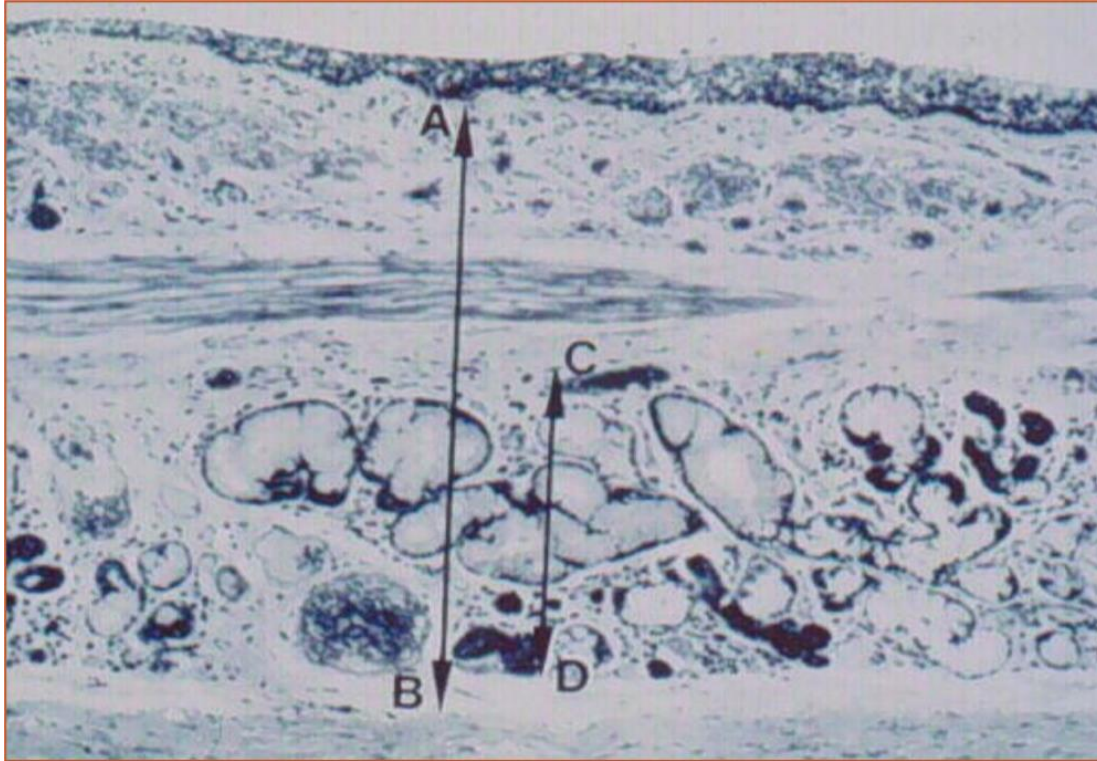
The magnitude of the increase in size is assessed by the ratio of the thickness of the submucosal gland layer to that of the bronchial wall from the epithelial layer down to the cartilage

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



ال Reid index يعني بنقيس سماكة طبقة ال sub mucosal gland ونحط هاد ال index عشان نكون موضوعيين وما تختلف القياسات من شخص الى اخر و بقيسوها عن طريق انه قديش نسبة سماكة ال mucosal gland لسماكة كل ال wall من ال epithilium لل cartilage

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



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

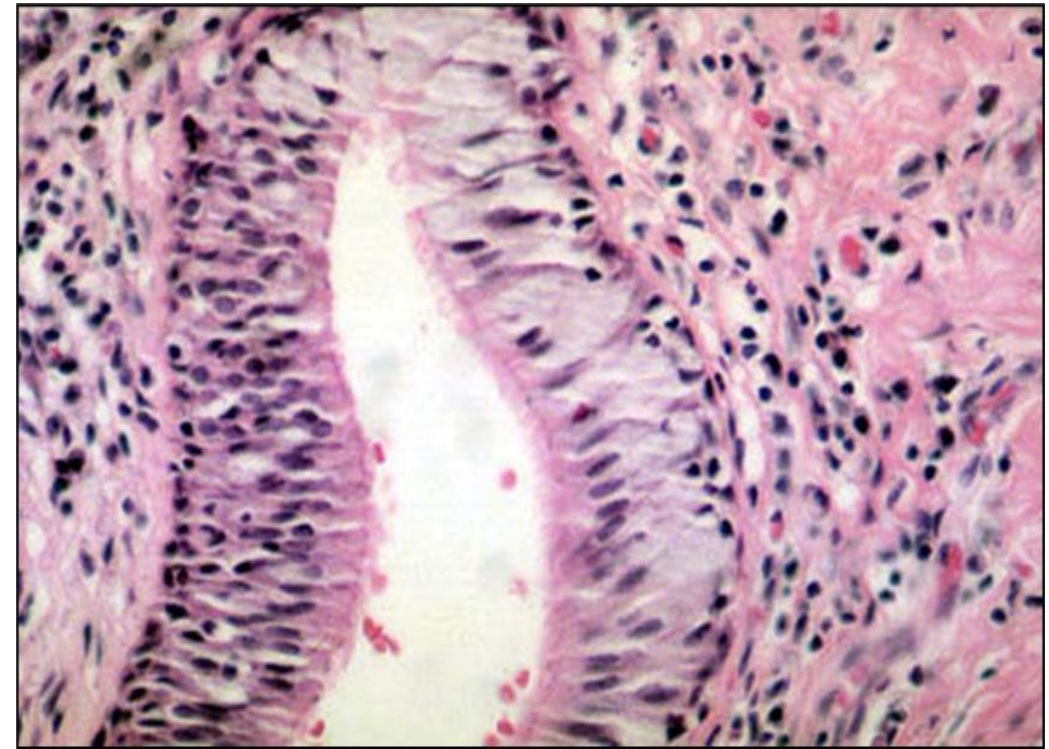
- **Chronic bronchiolitis** is inflammation of small bronchioles, showing **goblet cell metaplasia, mucus plugging inflammation & fibrosis.**

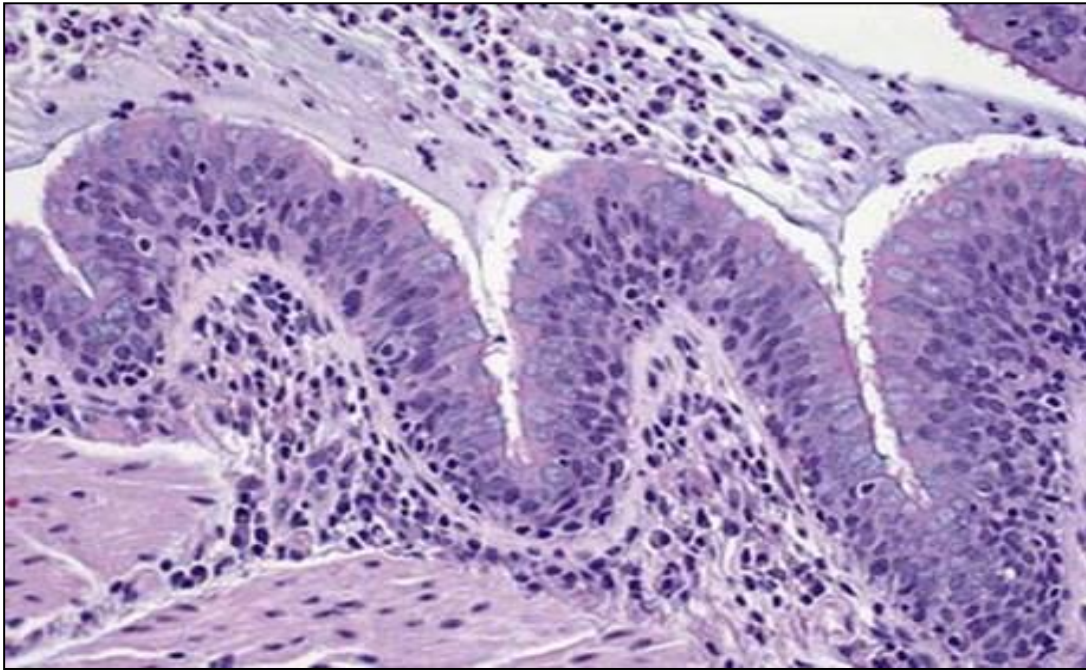
- In severe cases narrowing and obstruction with complete obliteration of the lumen due to fibrosis called **bronchiolitis Obliterans.** *obstruction او obliteration عندنا تسكير يعني بصير في*

- Squamous metaplasia ± DYSPLASIA

*واحيانا كمان بصير عندي نوع من ال metaplasia انو بصير يتحول
ال respiratory epithilium ل squamous metaplasia لانها
بتكون اكثر مقاومة لل irritation*

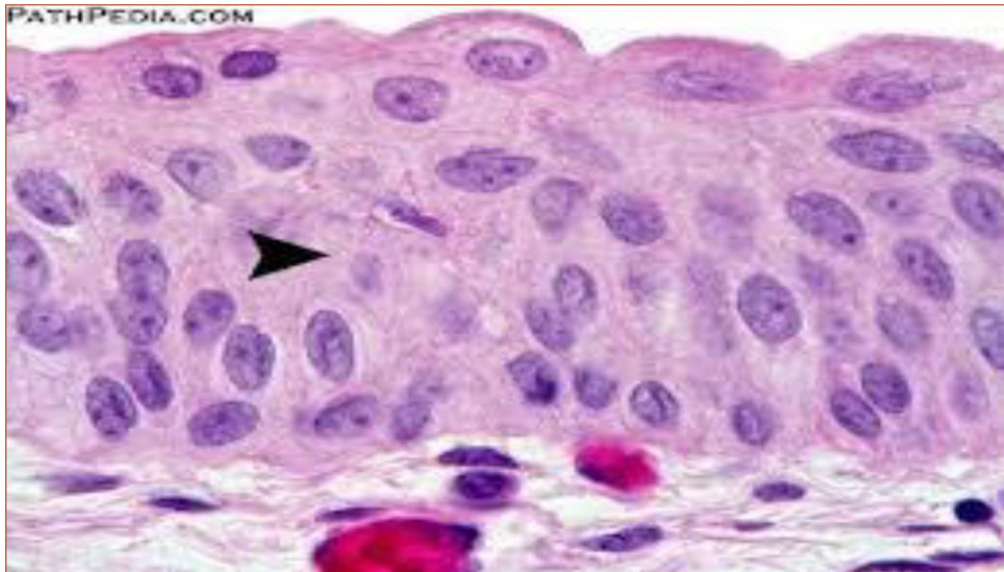
Goblet cell metaplasia (right) of the bronchiolar epithelium (left) with inflammatory cells infiltrate in surrounding tissue .





Chronic bronchitis:

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



Bronchial mucosa showing squamous metaplasia

الدكتورة عملت مراجعة سريعة بريكورد التيمز الدقيقة 34:15
عن ال chronic bronchitis وحكت انه على اشى تركزو
بشكل سريع للي حاب يسمعه



Thank You