PATHOLOGY TEAM
439

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Restrictive Pulmonary Diseases

Objectives

- Understand the structure and constituents of the lung interstitium as well as the restrictive changes which occur in diseases of the interstitium (ILD)
- Know the symptoms of ILD: progressive breathlessness and cough
- Know subtypes of ILD: acute and chronic
- Discuss the causes, morphology and outcome of acute ILD
- Appreciate the pathogenesis of chronic ILD regardless of their type.
- Become aware of the classification of interstitial lung diseases.
- Discuss examples of interstitial lung diseases including:

– idiopathic pulmonary fibrosis
– Pneumoconiosis
– Hypersensitivity
-pneumonitis
– Sarcoidosis

Index:
Important
NOTES
Extra Information

Rikabi's content

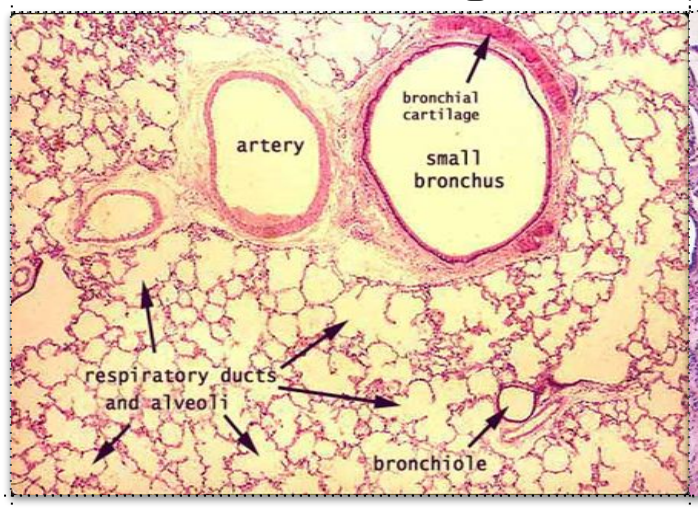
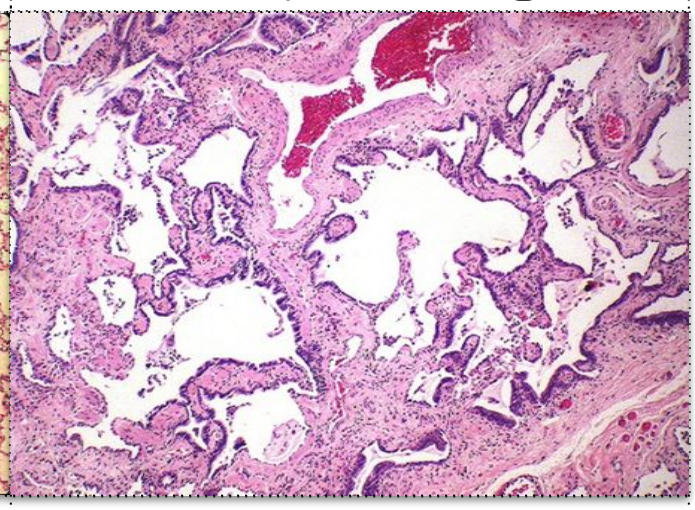
Restrictive Lung Disease

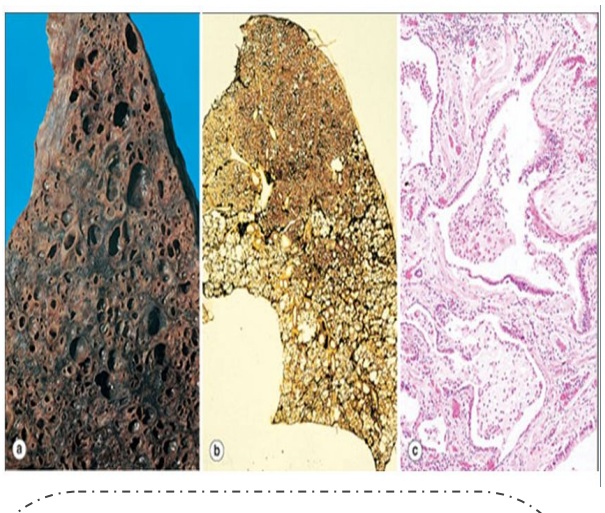
Definition	A decrease in lung compliance and reduction in the volume because of fibrosis and scars (causes depression in the area) which result in requiring more effort to breath (exhaustion) . -decrease in forced expiratory volume and decrease in forced vital capacity ;so the ratio of FEV1/FVC doesn't change
Symptomes	* Persistent dry cough (6 months or more) and dyspnea * In advanced cases: pulmonary hypertension (due to vasoconstriction after fibrosis), cyanosis, decrease in PO2, increase in PCO2.
Complications	Pulmonary pressure at rest =25mmhg Pulmonary Pressure during the exhaustion = 30 mmhg With time leads to increase in pressure on the right side of the heart affecting the right ventricles causing failure (تتوسع).
Treatment	Anti-fibrotic drugs (which is only used for IPF) **-if untreated;** respiratory failure later causing death.

	Intrinsic lung diseases	**Extrinsic disorders**
Definition	Diseases of the lung parenchyma/primary ILD	extraparenchymal diseases
Caused by /related to	**pneumonitis:** inflammation or scarring of the lung tissue (ILD) or result in filling of the air spaces with exudate and debris in the alveolar interstitial space and the interstitium.	causes outside the lung such as the chest wall, pleura, and respiratory muscles because they are the components of the respiratory pump, and they need to function normally for effective ventilation.
Lead to	**1- Stiff Lung**: the alveolar interstitial space and the interstitium becomes thickened and fibrotic 2- Honeycomb lung and decreased oxygen- diffusing capacity, because they affect the alveolar wall (interstitium) doesn't affect airway (bronchi) so it interferes with blood-gas exchange. You can see the picture + more explanation in the next slide	Lung can't expand,lose of compliance, reduced lung volumes
	Have 2 Type : 1-Acute: A-Adult respiratory distress syndrome (ARDS) B-Neonatal respiratory distress syndrome (NRDS) 2- chronic: Idiopathic (UIP) , Pneumoconiosis , immune disorders Drug,Radiation reactions	**The abnormalities of the chest wall include :** 1- Deformity in the thoracic cage 2-bony abnormalities (kyphosis حدبة في الظهر) or kypho-scoliosis (اعوجاج في الظهر يؤدي إلى تشوه thoracic cage) , The disease restrict the lung movement You can see the picture + more explanation in the next slide 3-Massive pleural effusion 4-morbid obesity 5-Neuromuscular disease of respiratory muscles (affect the intercostal muscles ; causing difficulty in breathing). ex: guillain virre (viral disease) , it affects the muscles, nerves, and diaphragm .

What is honeycomb lung?

Formation of cystic spaces separated by fibers septi, So the lung can't expand normally, and it's end-stage of **Intrinsic lung diseases**
(or diseases of the lung parenchyma/primary ILD)

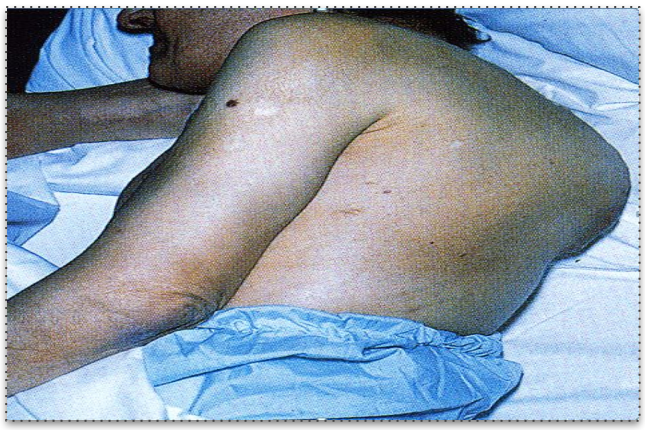
	Normal lung	Honeycomb lung
Lets compare the normal lung to honeycomb lung and see the differences		
The alveolar wall	Alveolar wall < 1cm	Alveolar wall>1cm (about 1.5 cm)
The fiber	Normal elastic fibers	fibrosis (thickening of the alveolar wall) which interfere with the blood gas exchange intraping the alveoli causing dilated parts (honeycombing) or non dilated parts which can be seen microscopically, grossly, by radiation and by CT scan
	contain simple squamous cell	contain inflammatory cells



Honeycomb lung. Macroscopically (a) honeycomb lung appears as large (b) the extent of abnormality and interstitial fibrosis can be better appreciated. (c) shows coalescence "التحام" of air spaces (both alveoli and bronchioles), to form cysts lined with cuboidal epithelium.

In the previous slide we talked about the causes of the extrinsic disorders, one of them was (kyphoscoliosis).

So what is kyphoscoliosis?



Extrinsic disorders or extraparenchymal diseases
Severe kyphoscoliosis of unknown etiology.
Flexion (kyphosis) and lateral deviation (scoliosis) of the spine have the combined effect of reducing chest volume. This compromises respiratory function and may cause restrictive lung disease.
To make it easier: If there is abnormality in vertebra will reduce the chest volume and the lung can't expand normally (and of course that will cause restrictive lung disease).

Quick quiz

Can you know the answers of theses questions?

* What is Restrictive lung diseases?
* What are the symptoms & complications?
* What are the two types of the Restrictive lung diseases?
* What are the two types of Intrinsic lung diseases?
* What are the types of each type of the Intrinsic lung diseases?
* What are the causes of the Extrinsic lung diseases?
* What is honeycomb lung?

إذا قدرتوا تجاوبون عليهم فأنتم ماشين صح وفاهمين كل حاجة لحد الآن، بس عشان تترتب الأجزاء الجاية من المحاضرة عندكم أبيكم تفهمون معي كيف راح تتقسم المحاضرة:

حنا حاليًا عرفنا الريستريكتف لنق ديزيزز وعرفنا أنواعها بشكل عام

بقية المحاضرة ما راح نتكلم عن الإكسترنتسك أبدًا وما راح نتعمق فيه، فقط راح نتكلم عن الإنترنسك بالنوعين التابعة له

(Acute & Chronic)

الأكيوت راح نتكلم عن النوعين كلها بتفاصيلها لكن الكرونيك فقط راح نتكلم عن الثلاثة أنواع الأولى

The Acute restrictive Lung diseases will discuss in slides (5-8).

The chronic restrictive Lung diseases will discuss in slides (10-21).

Type of Intrinsic diseases

Acute

Restrictive Lung Diseases

1

Adult Respiratory Distress Syndrome (ARDS)

Discussed in slide 6 & 7

2

Neonatal Respiratory Distress Syndrome (NRDS)

Discussed in slide 8

1 Adult Respiratory Distress Syndrome (DAD)

The pathogenesis

Damaging stimulus to lung
either direct (injury)or indirect

Will cause

Damage to alveolar capillary endothelium

Damage to alveolar lining cells mainly type 1 pneumocytes

Lead to

Hyaline membrane is pink because of fibrin+necrotic cells

Interstitial edema

1-High protein exudation into alveoli and form hyaline membranes

If it is severe will decrease O2 then lead to

Death in acute phase happen with 70% of the patients

If the patient enters the IC and get ventilation & +ve pressure to support the breathing may survive by

Regeneration of type II alveolar lining cells

Less Inflammation of interstitium

After that, the fluid with the fibroblast could be not absorbed totally and lead to

Organization leading to interstitial fibrosis

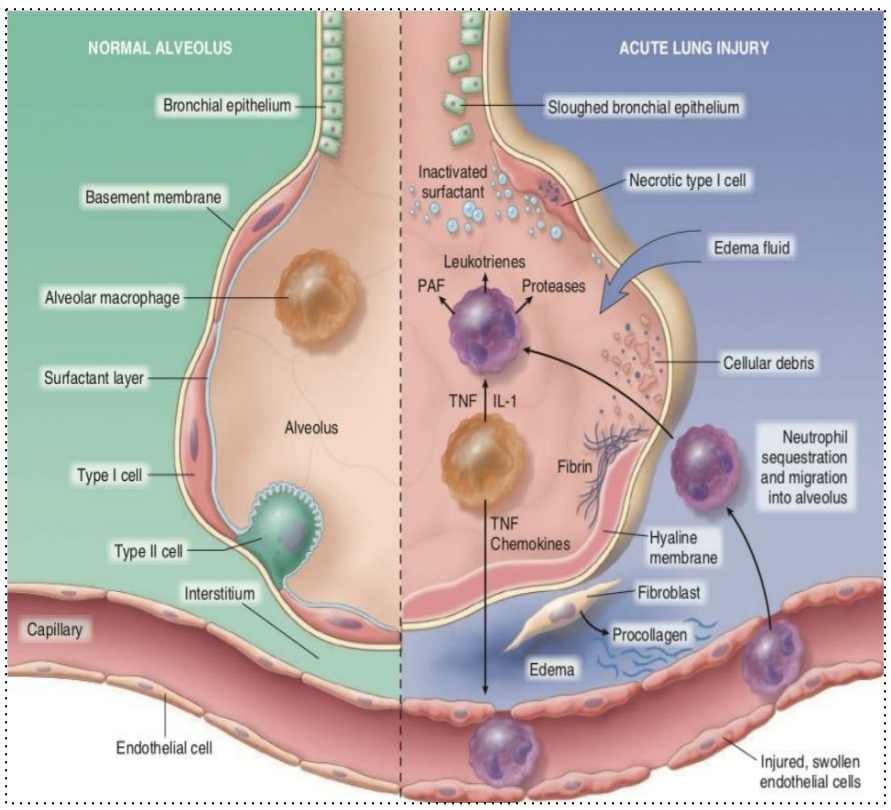
In this stage the patient has two possibilities:

Marked interstitial fibrosis (honeycomb Lung)

Death due to chronic severe respiratory impairment happen with 20% of the patients

Mild focal fibrosis: recovery with minimal residual respiratory dysfunction happen with 10% of the patients

Are you asking what is Acute phase? Let me tell you!
The Acute Phase means:
1- Alveolar & Interstitial Edema.
2- Injure to the lining epithelium.



Causes:

Direct injury to lung

* **Pneumonia (viral or atypical pneumonia lead to** Interstitial edema+inflammatory infiltrate so the wall very thick)

* Aspiration of gastric contents, Pulmonary trauma

* Fat embolism, Near drowning ,

* Toxic inhalation injury (irritants such as chlorine, O2 toxicity)

* Post lung transplant, Severe acute respiratory syndrome (SARS): The virus is a coronavirus that destroys the type II pneumocytes and causes diffuse alveolar damage

Indirect injury to lung

* **Sepsis**

* Severe trauma (e.g. bone fracture, head injury, burns, radiation), Septic shock, Cardiopulmonary bypass

* Acute pancreatitis, Transfusion, Uremia

* Overdose with street drugs such as heroin, Therapeutic drugs such as bleomycin, Hematologic conditions e.g multiple transfusion, coagulation disorders, complication in pregnancy or in cesarean section.

Clinical Features:

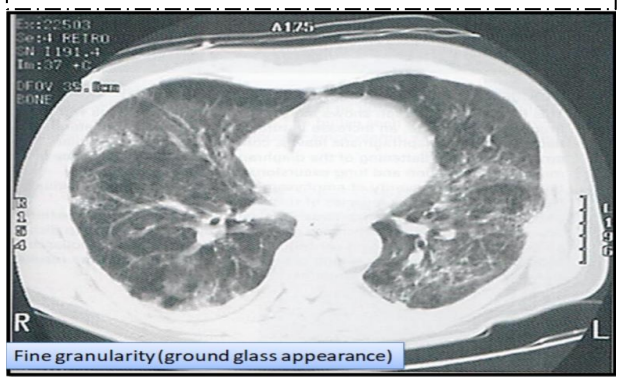
Respiratory distress " can't breath normally"

Hypoxia, Cyanosis

How can we identify it?

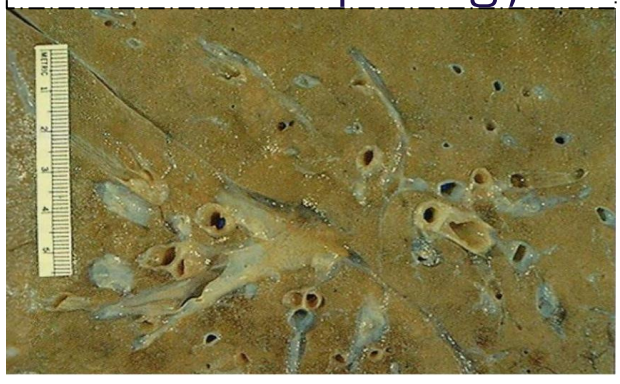
Diffuse alveolar damage due to edema

CT Image



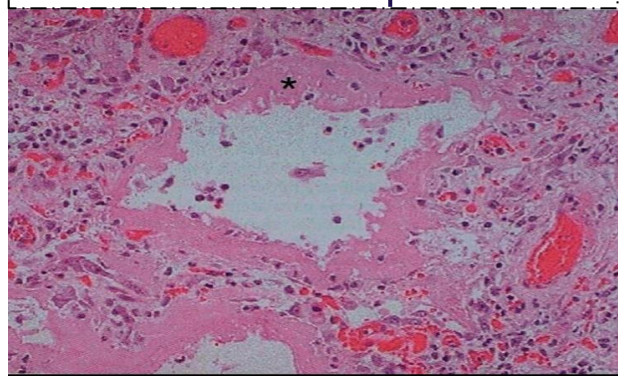
White lung syndrome
Fibrin + **Debris** form a **hyaline membrane** around the alveoli.

Gross "Morphology"



It looks shine and spongy tissue due to excessive fluid present in the lung.

Microscopic



The Alveolar spaces filled with fluid & lined by hyaline membrane (red membrane)

What is Hyaline membrane?
Necrotic lining epithelium

What are The stages of healing?

Not Important

01

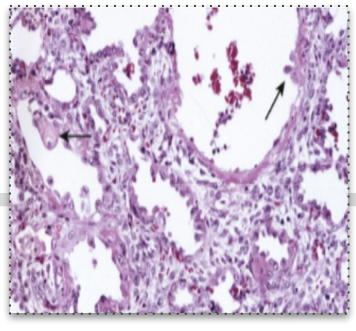
Reabsorption of hyaline membrane and the thickening of alveolar wall by

02

Inflammatory cells , fibroblasts And collagen

03

Numerous reactive type II pneumocytes are seen associated with regeneration and repair.



2 Neonatal Respiratory Distress Syndrome

or Hyaline membrane disease

It is the most common cause of respiratory failure in newborns and the most common cause of death in premature infants.

The etiology:

Absence or Deficiency of pulmonary surfactants in newborn, most often as a result of immaturity.

The pathogenesis:

The risk factors:

- Prematurity <36 weeks
- Multiple pregnancy
- Maternal diabetes (Diabetic mother)
- Cesarean section
- Amniotic fluid aspiration

↓

Immature and damage Type II pneumocytes

↓

Low level of surfactant

↓

Alveolar collapse

↓

Hypoxia

↓

Pulmonary vasoconstriction + Alveolar lining cell damage

↓

Endothelial damage

↓

Fibrin hyaline membranes

↓

Death

Quick quiz

Can you know the answers of theses questions?

* What are the two types of Acute Restrictive Lung Diseases?

Regarding to the first type (ARDS):

* What is the pathogenesis? You don't know?

let's make it easier for you

1-Injury of the lung will lead to damage of alveolar lining cells leading to formation of hyaline membrane (debris and fibrin)
2-damaging of endothelial cells cause proteins exudate
leading influx of inflammatory cells and cytokines into the intersium
Macrophage will attract the fibroblast to lay down (deposition) into collagen,later on with supporting fibrosis of the intersum will develop

* What are the causes?
* Do you know the morphologic/microscopic characteristics?
* What are the stages of healing?

Regarding to the second type (NRDS):

* What is the pathogenesis?
* What are the cause?

Type of Intrinsic diseases

Chronic

Restrictive Lung Diseases

Idiopathic fibrosing In slide 12 & 13	Occupational: Pneumoconiosis from slide 15 to 18	Immune diseases In slide 20 & 21	Drug
Smoking related		Radiation Reactions	

Occupational: Pneumoconiosis

Anthracosis and coal worker's pneumoconiosis, Silicosis, Berylliosis, Asbestosis

pneumoconiosis: Lung diseases after exposure to certain substances in occupational environment.

Idiopathic fibrosing

Another names:- Usual interstitial pneumonia (idiopathic pulmonary fibrosis).

Immune diseases

Sarcoidosis, Goodpasture syndrome, Hypersensitivity pneumonitis (extrinsic allergic alveolitis), Systemic lupus erythematosus, Systemic sclerosis (scleroderma), Wegener granulomatosis. RA

Major Categories of Chronic Interstitial Lung Disease

Radiation Reactions

Occur after radiation with diffuse alveolar damage, severe atypia of hyperplastic type II cells and fibroblasts

Drug

Chemotherapy:methotrexate bleomycin toxicity

Amiodarone: antiarrhythmic drug (cause pulmonary fibrosis and pneumonitis).

Smoking related

Eosinophilic granuloma, Desquamative interstitial pneumonia, Respiratory bronchiolitis-associated interstitial lung disease

The Pathogenesis of Chronic Interstitial Lung Disease

1- Lung injury leading to (2)
2- Influx of inflammatory cells into the alveoli and alveolar walls.
3- inflammatory cells Release The chemical mediators and promote of fibrosis leading to (4)
4- Distortion of the normal structure of alveoli.

Lung injury

Inhaled agents | Dusts | Blood-borne toxin | Unknown antigens

Activated macrophages: Influx of inflammatory cells into the alveoli and alveolar walls

Release of chemical mediators and promotion of fibrosis

Oxidants proteases

Recruitment of neutrophils

Fibrogenic and chemotactic cytokines

Injury to type I pneumocytes

Hypertrophy & hyperplasia of type II pneumocytes

Fibroblast

1 Idiopathic Pulmonary Fibrosis

Usual interstitial pneumonia

Etiology

Unknown the cause , could be :
1-Injury to lung that creates source of inflammation depends on activated T cells that stimulate fibroblast
2-short telomeres leading to senescence (death) of pneumocystis that stimulates fibroblast
3-MUCB5 gene mutation = tendency of developing fibrosis
4- down regulation of caveolin

Progressive dyspnea and dry cough
يعني بالبداية بيكون المريض عنده صعوبات بالتنفس وكحة بس في حالة معينة مثل لو طلع على الدرج أو مشى مسافة طويلة لكن بعدين بيتطور المرض وبيصير عنده صعوبة بالتنفس طول الوقت حتى بدون ما يتحرك

Age: 50 to 70 years

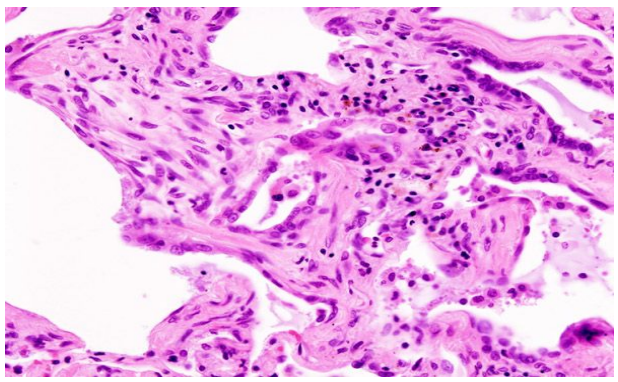
Progressive subpleural fibrosing disorders

The end result is: honeycomb (patchy and focal)

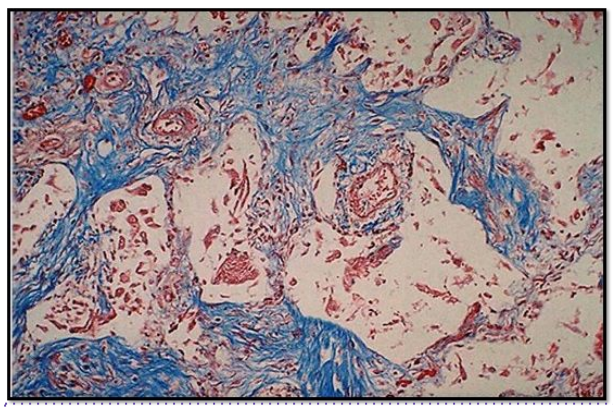
Prognosis: Poor

How can we identify it?

Microscopic

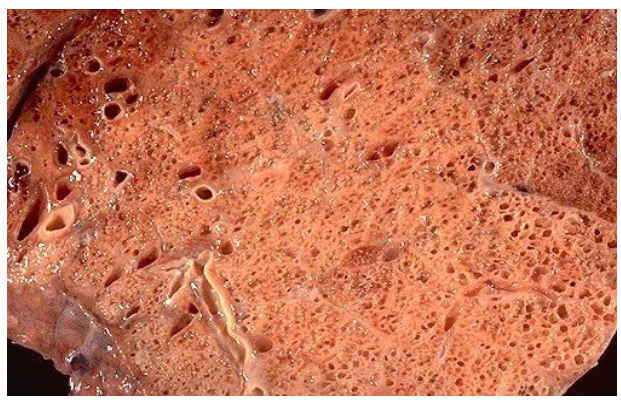


Fibroblastic focus with fibers running parallel to surface and bluish myxoid extracellular matrix.



Interstitial fibrosis.
by used special stain the collagen fibers appear blue and that means there is fibrosis on interstitium .

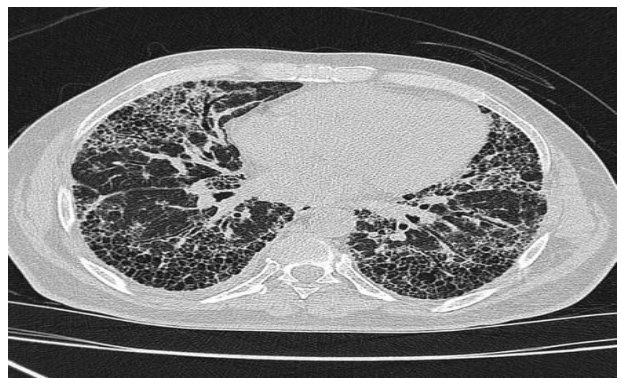
Gross “Morphology”



Fibrosis in subpleural region.

Proximal part of the lung is still spongy tissue but the peripheral part is fibrosis .

High resolution CT Image



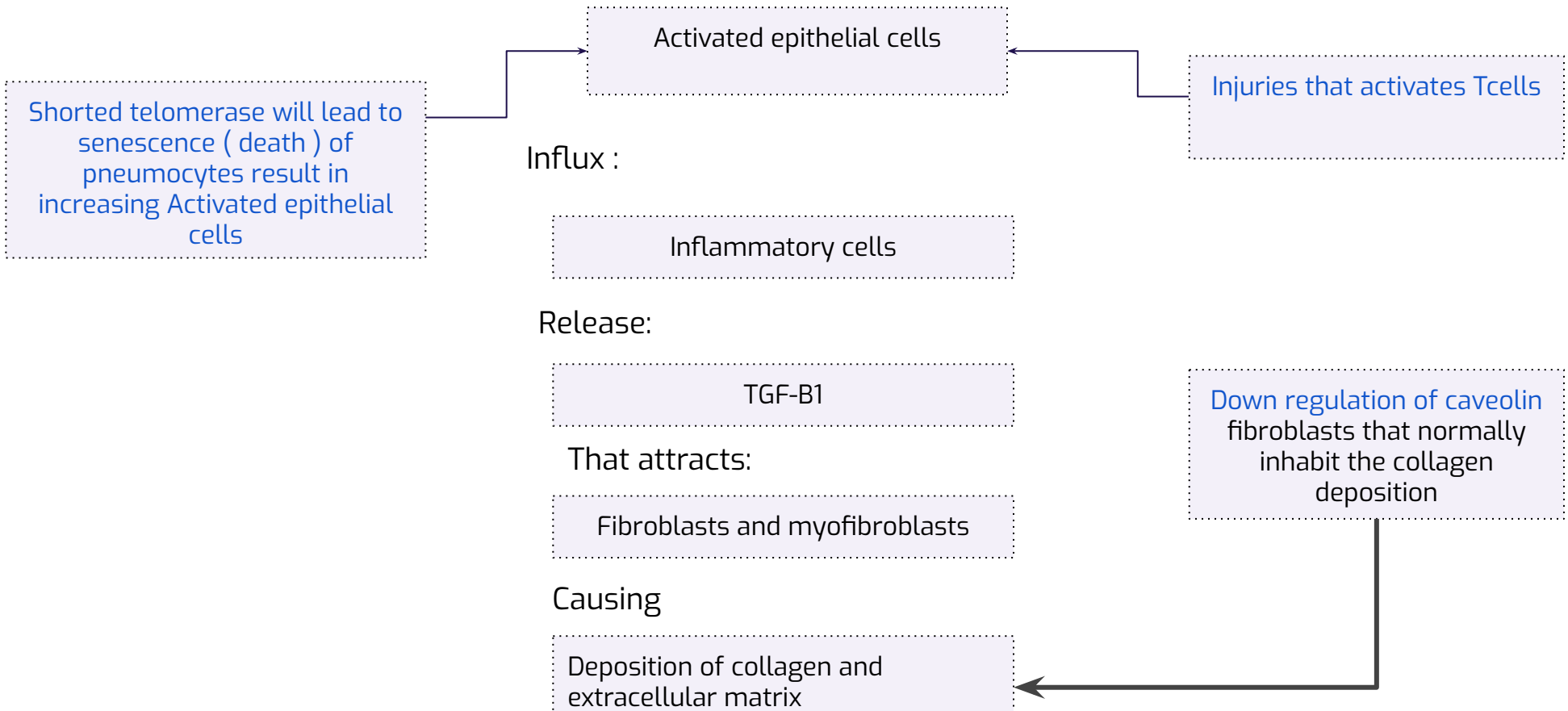
Patchy scarring and **peripheral cystic changes.**

It shows the peripheral part mainly affected by cystic spaces and patchy scarring

1 Idiopathic Pulmonary Fibrosis

Usual interstitial pneumonia

The pathogenesis



what is clubbing of nail?

Definition	- Periosteal reaction of distal phalanx with bulbous swelling of the connective tissue in the terminal phalanxes. -A symptom of diseases of the heart or lungs which cause chronically low blood levels of oxygen.
Pathogenesis	The megakaryocytes bypass the breakdown within the pulmonary circulation and enter the systemic circulation. They are then trapped within the capillary beds within the extremities, such as the digits, and release platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF) leading to hypertrophy of connective tissues .
Notes	**What are the diseases that show clubbing nail as sign or complication** - Bronchiectasis - Chronic pneumonia - Tumors most commonly in adenocarcinoma - IPF

Idiopathic Pulmonary Fibrosis

Usual interstitial pneumonia

Summary

Definition	A restrictive lung diseases characterized by reduced lung compliance. It is characterized by subpleural patchy interstitial fibrosis, fibroblastic foci and formation of cystic spaces (honeycomb lung).
Causes	- Unknown? Genetic - The resulting injury to alveolar epithelial cells set in motion event that lead to increase local production of fibrogenic cytokines such as TGF-β
Clinical features	- Gradually increasing *dyspnea on exertion* and dry cough - Most patients are 55 to 75 years - X ray: early: ground glass fine granularity, advanced: honeycomb lung
Complications	- Hypoxemia, cyanosis and clubbing - Gradual deterioration in pulmonary status despite medical treatment - The median survival is about 3 years

2 Occupational: Pneumoconiosis

Definition

Lung disorders caused by chronic **inhalation of mineral dusts** leading to lung damage, can be organic dust and inorganic

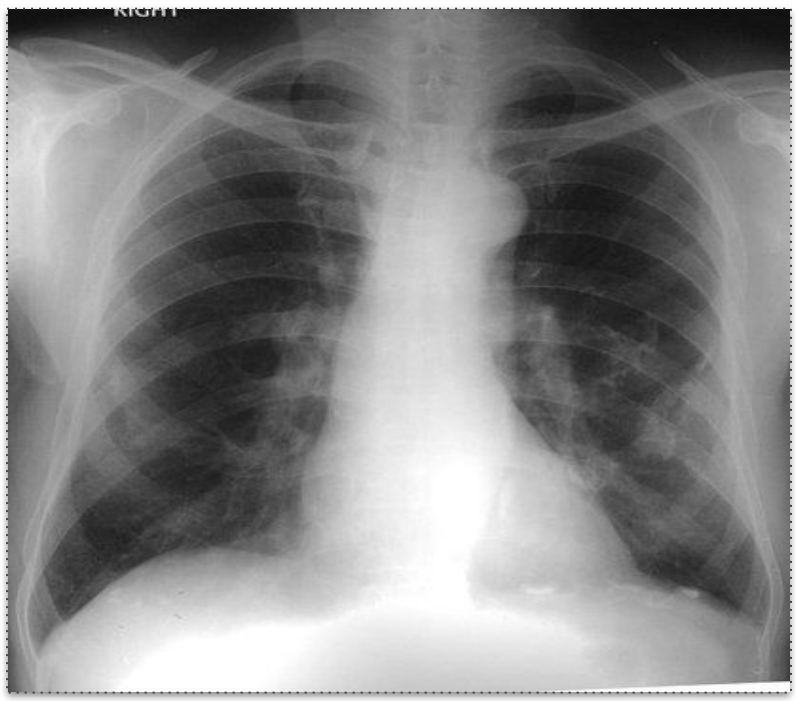
The development of pneumoconiosis depends on:

يعني هل بكل مرة نتنفس فيها مواد قوية راح تسبب لنا مرض؟ طبعًا لا فيه شروط معينة عشان تسبب مرض، من ضمن الشروط

1	2	3	4	5	6
Concentration of the dust in the ambient air.	Duration of the exposure.	Effectiveness of the clearance mechanisms.	**The size (1-5m) shape.** لو كانت أكبر من ٥ بتنمسك في الأنف وما راح تقدر تدخل ولو كانت أصغر من ١ راح تروح للأذن وما راح توصل للرئة	Their solubility and physiochemical activity.	The possible additional effects of other irritants, tobacco smoking.

Most common particles that cause the disease are carbon dust, silica, asbestos, beryllium.

How can we identify it?



Pneumoconiosis in radiograph

In the next slides we will discuss the three time of Pneumoconiosis with some details:

- Coal worker's pneumoconiosis.
- Silicosis.
- Asbestosis

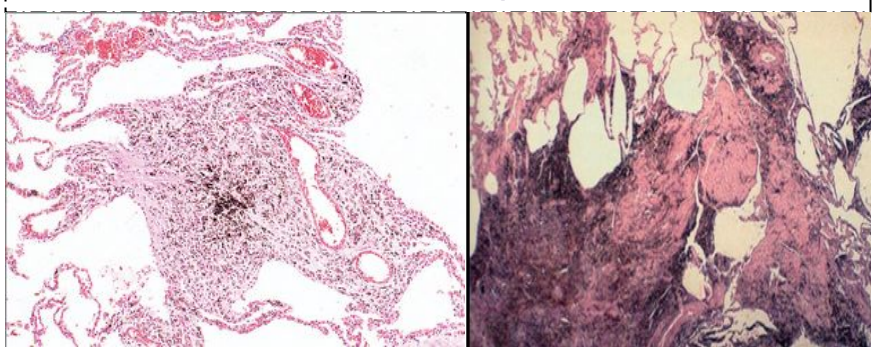
2

Occupational: Pneumoconiosis

Coal worker's pneumoconiosis.

How can we identify it?

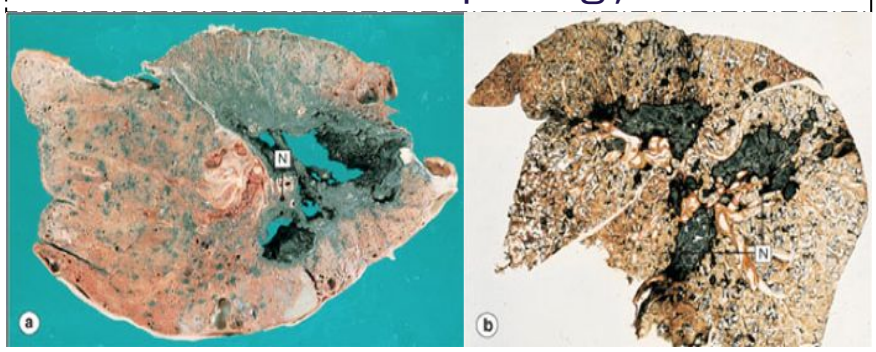
Microscopic



Simple Coal worker pneumoconiosis

Complicated Coal worker pneumoconiosis

Gross "Morphology"



To progressive massive fibrosis
(complicated coal worker's pneumoconiosis).
(a) Cut surface (b) thin section of whole lung.

CWP can be :

Anthracosis

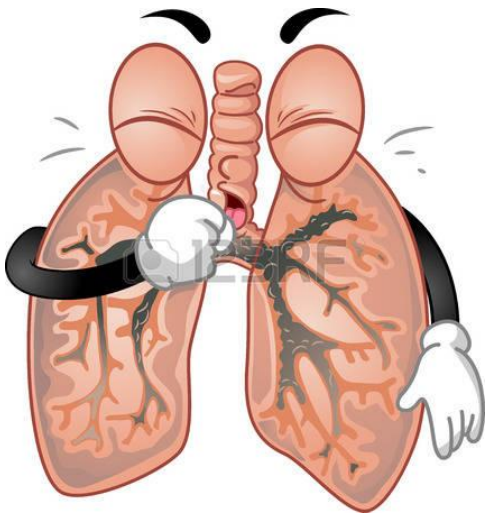
Alveolar macrophages with Carbon , don't lead to fibrosis
In smoker and citizens

Simple CWP

- Simple patchy with very little fibrosis.
- Asymptom

Complex CWP

-Sever (more white spread) Fibrosis with inflammatory cells
-The coal surrounded by T cells that stimulate Macrophages + TGF-B1 + fibrosis leading to restrictive disease
- Massive fibrosis, cause cor pulmonale & Respiratory dysfunctions



2

Occupational: Pneumoconiosis

Silicosis

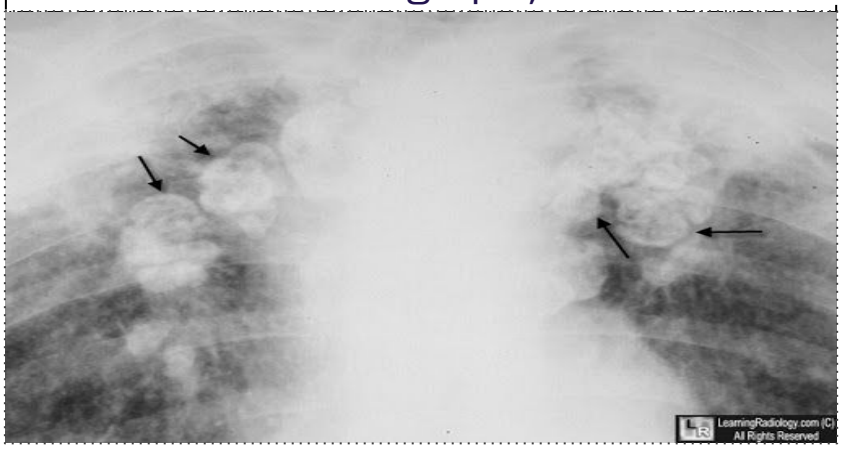
Definition

Fibro-nodular surrounded by chronic inflammatory cells + fibroblast , probably leading to develop TB ,lung disease caused by **long term** exposure to **inhalation of crystalline silica particles** (alpha-quartz or silicon dioxide).

Comes from Industrial exposure like mining of gold, tin, copper and coal, sandblasting, metal grinding, ceramic manufacturing , stones

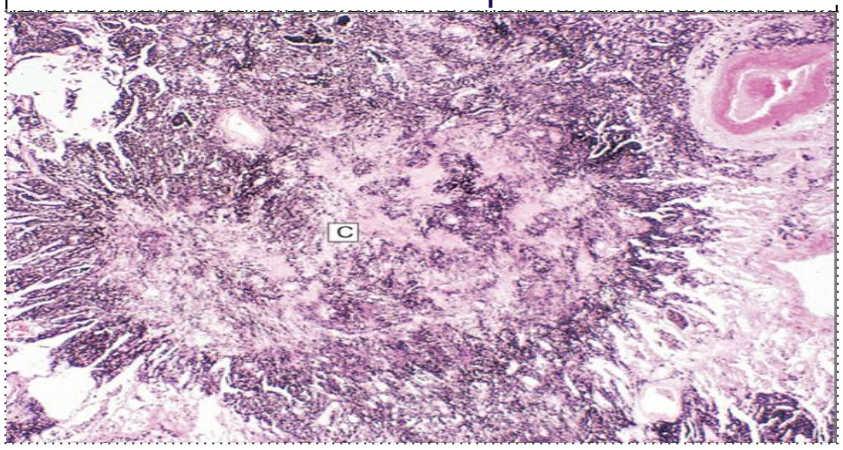
How can we identify it?

Radiography



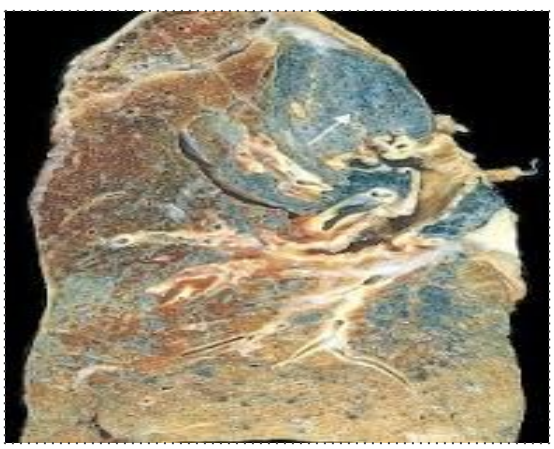
Eggshell calcification
Large area of fibrosis (Dence fibers) surrounded by zone of calcification

Microscopic



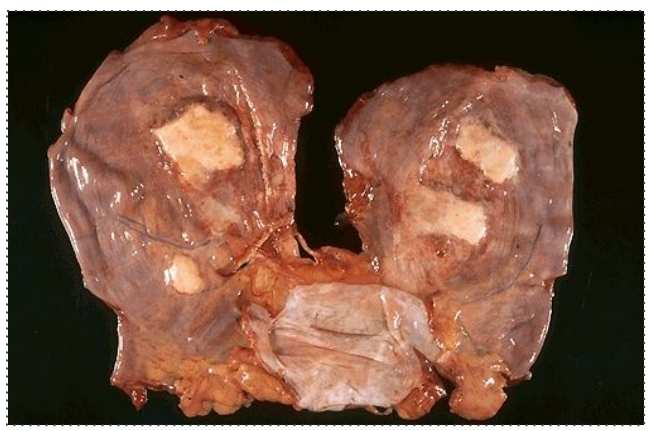
Silicosis of lung.
In silicosis, nodules of collagen (C) contain silica particles.

Gross "Morphology"



Stony-hard large fibrous scars
Scarring has contracted the upper lobe into a small dark mass (arrow). Note the dense pleural thickening.

Gross "Morphology"



Fibrous pleural plaques
Multi fibers plaques "Thick fibers tissues in the pleura"
Not always but in some cases

Predispose to lung cancer & tuberculosis

2

Occupational: Pneumoconiosis

Asbestosis

Definition

occupational exposure to asbestos is linked to parenchymal interstitial fibrosis.

Etiology

Asbestos exposure

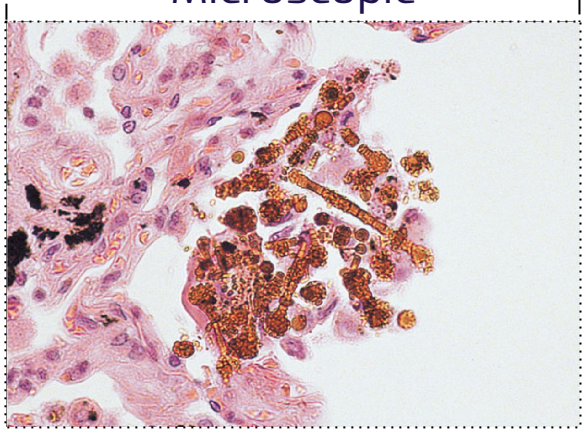
Characterized by the presence of **asbestos bodies** that cause damage to the lung , the result of it is hemorrhages ⟶ HB ⟶ Hemosiderin that coats the asbestos called (**Ferruginous** bodies)

Complications

Restrictive disease or respiratory fibrosis induced by asbestos	Pleural adhesions. Pleural effusion.	Localized fibrous plaques (Or rarely, diffuse fibrosis in the pleura) You can see the picture + Explanation in previous slide	Lung carcinoma (Bronchogenic carcinoma) With smoking: Causing laryngeal carcinoma Bronchial cancer	Malignant pleural and peritoneal mesothelioma

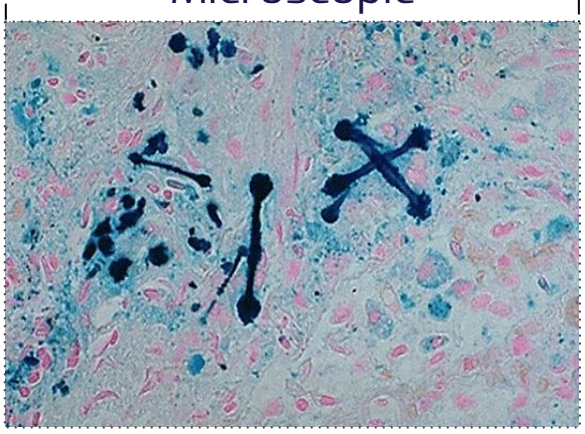
How can we identify it?

Microscopic



Asbestos bodies.
are long, thin asbestos fibers coated with hemosiderin (Iron) and protein to form brown filaments with a beaded or drumstick pattern.

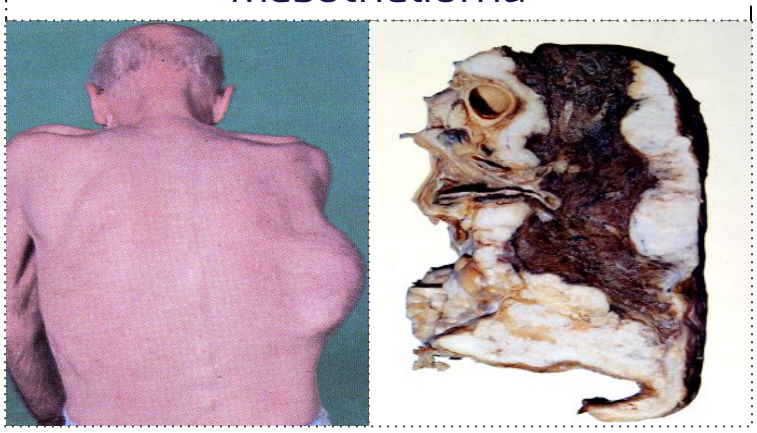
Microscopic



Ferruginous bodies.

Asbestos fibers coated with hemosiderin (Iron) and protein

Mesothelioma



This patient presented with an asbestos link pleural plaque.

Summary

Definition	A non neoplastic lung reaction to inhalation of mineral dusts (size: 1-5 μm) and fumes encountered in the workplace.
Coal related pneumoconiosis	- Simple Coal worker pneumoconiosis: Black macules 1 to 5 mm are scattered through the lung - Complicated coal worker's: produces cough, dyspnea, and lung function impairment. Complication: cor pulmonale
Silicosis	- Industrial exposure: mining of gold, tin, copper and coal, sandblasting, metal grinding, ceramic manufacturing - stony-hard large fibrous scars - eggshell calcification - Fibrous pleural plaques may develop - predispose to lung cancer and tuberculosis
Asbestosis	- Asbestos bodies are long, thin asbestos fibers coated with hemosiderin and protein (ferruginous bodies) - lead to lung scars containing asbestos bodies. - They can cause pleural effusion, pleural adhesions, parietal pleural fibrocalcific plaques' and mesothelioma. - Some types are carcinogenic and the risk of bronchogenic carcinoma is fivefold and for mesothelioma is 1000 fold and laryngeal carcinoma

3

Immune granulomatous diseases

Sarcoidosis

Definition

A multisystem disease of unknown etiology (idiopathic) chronic autoimmune disease characterized by noncaseating granulomatous inflammation in many tissues and organs

Manifestation

- Formation of granulomas and interstitial fibrosis
- **Bilateral hilar lymphadenopathy** (lymph node enlargement)
- **Lung involvement** occurs in 90% of cases
- **Eye involvement** (dry eyes) iritis, uveitis, **Joints**
- **Skin involvement** (erythema nodosum) painless subcutaneous nodules
- Viscera involvement (liver, skin, marrow)

Laboratory tests

- Hypercalcemia
- Hypercalciuria
- High ACE (angiotensin converting enzyme)
- Hypergammaglobulinemia

Prognosis

- Unpredictable, It can be progressive and chronic
- Majority of the patients respond well to treatment **(Steroid)**

Epidemiology

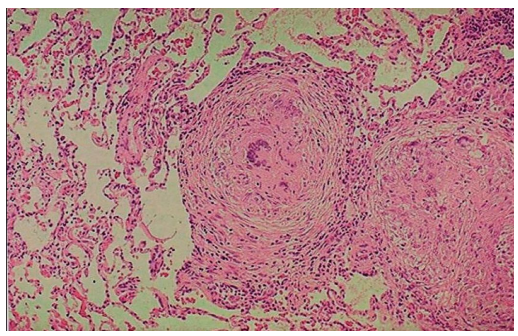
High incidence in Scandinavian countries and in United States among African Americans especially female.

Clinical features

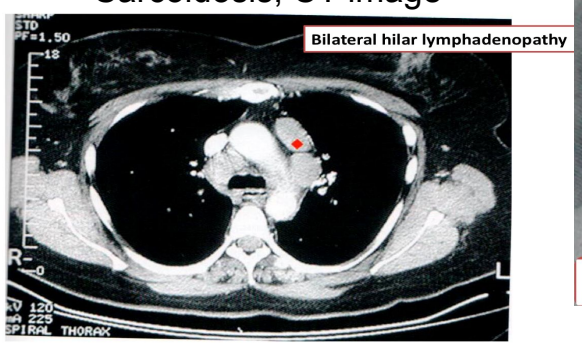
- Dyspnea
- Dry cough
- Fever
- Fatigue
- Weight loss

Could be asymptomatic

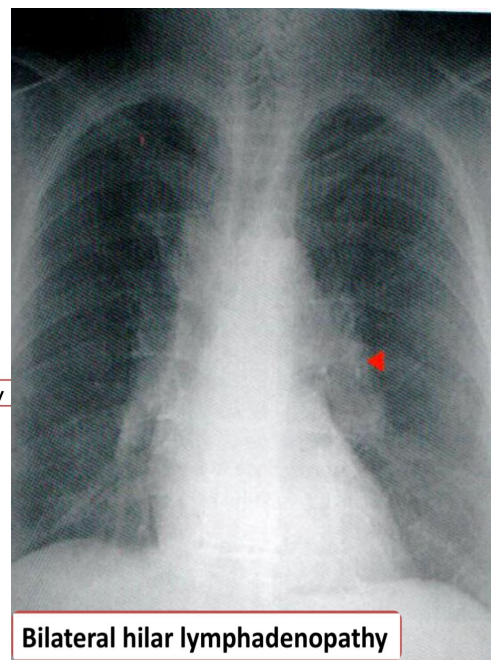
Sarcoidosis, microscopic noncaseating interstitial granulomas



Sarcoidosis, CT image



Sarcoidosis, radiograph



How can sarcoidosis causes restrictive lung disease?
Granulomas involve the lung and this can affect the interstitium (the tissue and alveolar space) > the presence of granulomas in the interstitium can make it hard for the lung to expand> less compliance> leads to restrictive lung disease.

Sarcoidosis is usually confused with **TB**
They both are systematic, cause granulomas and affect mainly the lung. But the main difference that **sarcoidosis** causes non-caseating granuloma and treated by steroids. While **TB** causes caseating granuloma and treated by antibiotics.

3

Immune granulomatous diseases

Hypersensitivity pneumonitis

(extrinsic allergic alveolitis, **Type 4**)

Results form

Inhalation of organic dust containing antigens

Clinical features

The patient is presented by symptoms of restrictive lung diseases: dry cough & dyspnea.

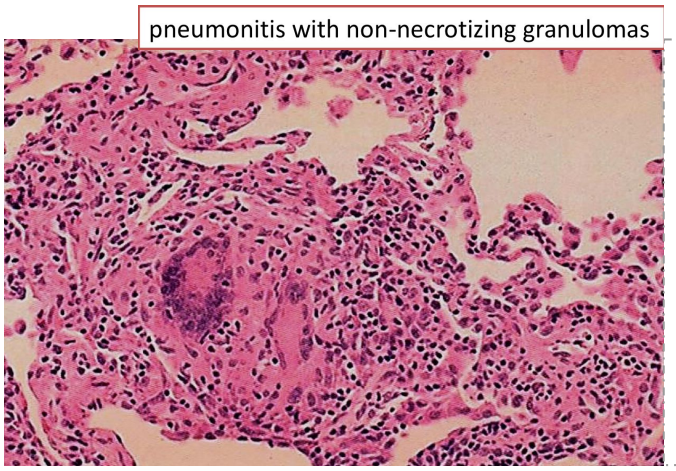
Disease	Source of antigen
Farmer's lung	- Thermophilic actinomycetes - Micropolyspora faeni (spores in mouldy hay) - microsporum→ extrinsic allergic alveolitis
Pigeon breeder's lung (psittacosis)	- Excreta (feces) - Feathers of birds
Air-conditioner lung	- Thermophilic bacteria
Bagassosis	- Sugarcane bagasse

Leads to

Interstitial pneumonitis, inflammation with lymphocytes, plasma cells, macrophages and **noncaseating granulomas** peribronchiolar.

If exposure is continuous, lead to progressive respiratory failure, dyspnea, and cyanosis and a **decrease in compliance**.

pneumonitis with non-necrotizing granulomas



Hypersensitivity pneumonitis, microscopic noncaseating interstitial granulomas and chronic inflammation along the bronchioles

Click here for Rikabi's lone lecture notes

Quiz

1- Happens due to inflammation or scarring of the lung resulting in pneumonitis			
a- intrinsic lung disease	b- extrinsic lung disease	c- pneumoconiosis	d- Asbestosis
2- 53-year-old man presents with increasing shortness of breath on exertion and dry cough that has developed over a period of a few years. Physical examination shows clubbing of the fingers. A chest X-ray discloses diffuse bilateral infiltrates, predominantly in the lower lobes, in a reticular pattern. Two years later, the patient suffers a massive stroke and expires. Histologic examination of the lung at autopsy is shown in the image. Patchy scarring with extensive areas of honeycomb cystic change predominantly affects the lower lobes. Which of the following is the most likely diagnosis?			
a- IPF (Usual interstitial pneumonia)	b- SARS	c- Goodpasture syndrome	d- Pneumonia
3- A 75-year-old man who had worked in a shipyard dies of a chronic lung disease. Autopsy reveals extensive pulmonary fibrosis, and iron stains of lung tissue show numerous ferruginous bodies?			
a- asbestosis	b-silicosis	c- CWP	d- DADt
4-25-year-old black woman presents with a 3-month history of cough and shortness of breath on exertion. A chest X-ray reveals enlargement of hilar and mediastinal lymph nodes. Laboratory studies show elevated serum levels of angiotensin converting enzyme and an increase in 24-hour urine calcium excretion?			
a- sarcoidosis	b-tuberculosis	c- Silicosis	d- Goodpasture syndrome
5-A 45 year old farmer presented with 3-weeks history of fever, cough and dyspnea. A lung biopsy showed non-necrotizing granulomas with inflammatory cells. Which of the following is the most likely diagnosis?			
a- Pneumoconiosis	b- Hypersensitivity pneumonitis	c- Sarcoidosis	d- Asbestosis
6- A 60 year African women with 2 months history of of cough and shortness of breath. A chest X-ray reveals enlargement of the hilar lymph node. Laboratory test show elevated level of calcium and elevated serum levels of angiotensin-converting enzyme. Which of the following is the appropriate diagnosis?			
a- Alveolitis	b- TB	C- Silicosis	d- Sarcoidosis

1- A
2- A
3- A
4- A
5: B
6: D

special thanks for
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