FINAL

Lecture 4&5

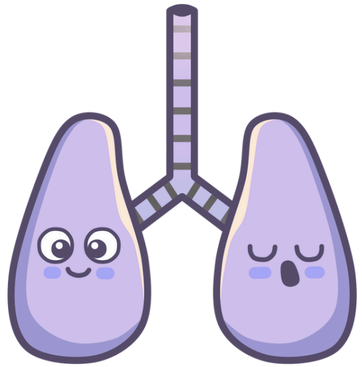
بسم الله الرحمن الرحيم

Pathology Mind Maps

Restrictive Lung Diseases

Done by : Roaa Maakoseh & Deema Nasrallah

Corrected by : Zeina Yassin



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

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

Best of luck in your studies💜!

Chronic interstitial lung diseases

General Characteristics

Hallmarks

• Stiff lungs • Reduced lung compliance (++)

Clinical & Pathophysiology

• **Dyspnea** (↑ effort to breathe)

• Damage of alveolar epithelium & interstitial vessels → abnormal V/Q ratio → **hypoxia**

• **Progression**: respiratory failure, pulmonary hypertension and cor pulmonale

• **Ground-glass** shadows on CXR: small nodules and irregular line

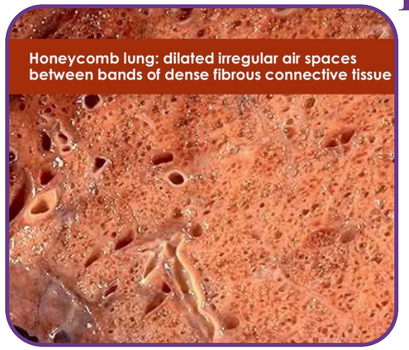
Lung Compliance

• Measure of lung's ability to stretch or expand

Table 15-5 Major Categories of Chronic Interstitial Lung Disease

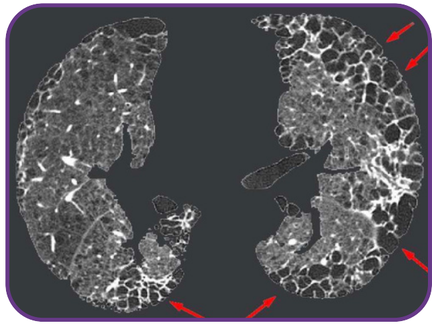
Fibrosing
Usual interstitial pneumonia (idiopathic pulmonary fibrosis)
Nonspecific interstitial pneumonia
Cryptogenic organizing pneumonia
Connective tissue disease-associated
Pneumoconiosis
Drug reactions
Radiation pneumonitis
Granulomatous
Sarcoidosis
Hypersensitivity pneumonitis
Eosinophilic
Smoking Related
Desquamative interstitial pneumonia
Respiratory bronchiolitis-associated interstitial lung disease
Other
Langerhans cell histiocytosis
Pulmonary alveolar proteinosis
Lymphoid interstitial pneumonia

End-Stage Disease



Honeycomb Lung

Dilated irregular air spaces between bands of dense fibrous connective tissue



• Diffuse scarring

• Gross destruction of lung

• Here the underlying etiology cannot be determined

Granulomatous Diseases

Sarcoidosis

Hypersensitivity pneumonitis

SARCOIDOSIS

رَبِّ اشْرَحْ لِي صَدْرِي وَيَسِّرْ لِي أَمْرِي وَاحْلُلْ عُقْدَةً مِّن لِّسَانِي يَفْقَهُوا قَوْلِي

Definition
- Multisystem disease
- Unknown etiology
- Noncaseating granulomas in many tissues & organs
- Diagnosis of exclusion

Epidemiologic Trends
- Adults **< 40 years**
- **African Americans** (2–3× Europeans)
- Higher prevalence in **nonsmokers**
- Recurs in **transplanted** lungs

Etiology & Pathogenesis
- Disordered immune regulation
- Genetically predisposed individuals
- Exposure to **undefined environmental agents** > Cell-mediated immune response > CD4+ helper T cells > ↑ TH1 cytokines: • IL-2 • IFN-γ • → T cell expansion • → macrophage activation

Clinical Presentation

Major
- Bilateral **hilar** lymphadenopathy
- Lung involvement
- Or **both** on CXR

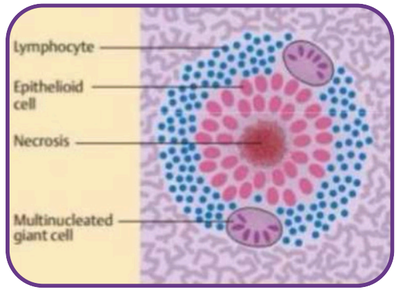
Occasional
- Eye involvement
- Skin involvement

Morphology

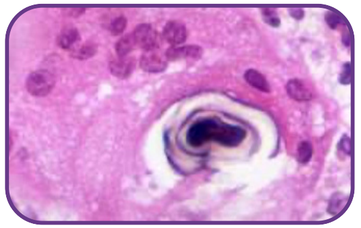
Cardinal Feature
• **Noncaseating epithelioid** granulomas:
- Epithelioid macrophages -Multinucleated giant cells -Rim of CD4+ T cell

Key Points
• **No caseation necrosis** (unlike TB)
• Over time granulomas replaced by hyalinized scars

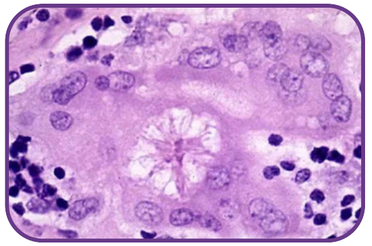
[1]Granuloma Composition



Schaumann bodies
• Laminated concretions
• Calcium & proteins

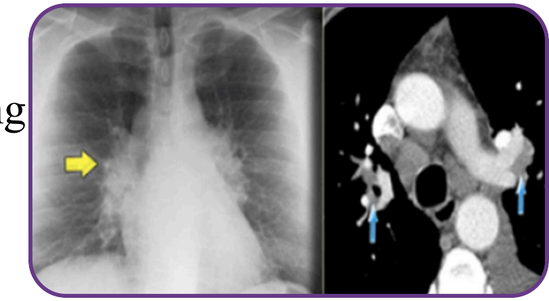


Asteroid bodies
• Stellate inclusions • Inside giant cells



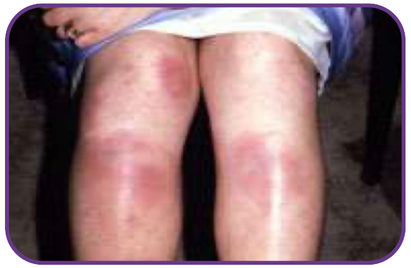
Organ Involvement

Lung
• Involved in **90%** • **Interstitium** NOT air spaces (Granulomas)
• Distribution: Peribronchial, Perivenular and Pleural
• **BAL**: Abundant CD4+ T cells, 5–15% → interstitial fibrosis → honeycomb lung



Lymph Nodes
• Enlarged Hilar & paratracheal (75–90%)
• Peripheral lymphadenopathy (⅓)
• **Nodes** (unlike TB): • Non-matted • Non-adherent • Do not ulcerate • Noncaseating

Skin • 25% of patients



Erythema nodosum

• Hallmark of acute sarcoidosis • **Panniculitis**
• Raised, red, tender bilateral **nodules** • **Anterior legs** • Granulomas uncommon

Subcutaneous nodules

• Discrete • Painless • Abundant noncaseating granulomas

Eye & Lacrimal Glands

• 20–50% • Iritis / iridocyclitis, unilateral or bilateral • Corneal **opacities** • **Glaucoma** • **Total loss of vision**
• Posterior uveal tract: Choroiditis, retinitis and optic nerve involvement.
• Sicca syndrome: Lacrimal inflammation > ↓lacrimation > Dry eyes

Salivary Glands

• **Parotid**: Unilateral or bilateral parotitis, painful enlargement <10% and **Xerostomia** (dry mouth)
• **Mikulicz syndrome**: Uveo-parotid involvement

Spleen, Liver, Bone Marrow

Spleen, Granulomas in ¾ • Enlarged in 10%.
Liver, Granulomas in portal triads • Hepatomegaly • Abnormal LFTs (⅓).
Bone marrow, Involved in 40%.

Calcium Metabolism

• Hypercalcemia and Hypercalciuria
- Not from bone destruction
- Active vitamin D production by macrophages in granulomas

Clinical Features

Many asymptomatic. Incidental CXR or autopsy

Symptomatic:

- Gradual respiratory symptoms: SOB, Dry cough and Substernal discomfort
- Constitutional: Fever, Fatigue, Weight loss, Anorexia and Night sweats
- Peripheral lymphadenopathy, Skin lesions, Eye involvement, Splenomegaly and Hepatomegaly

Diagnosis

- Noncaseating granulomas suggestive
- Must exclude other causes (TB)
- Requires:

1. Clinical findings 2. Radiologic findings 3. Histologic granulomas 4. Exclusion of other causes

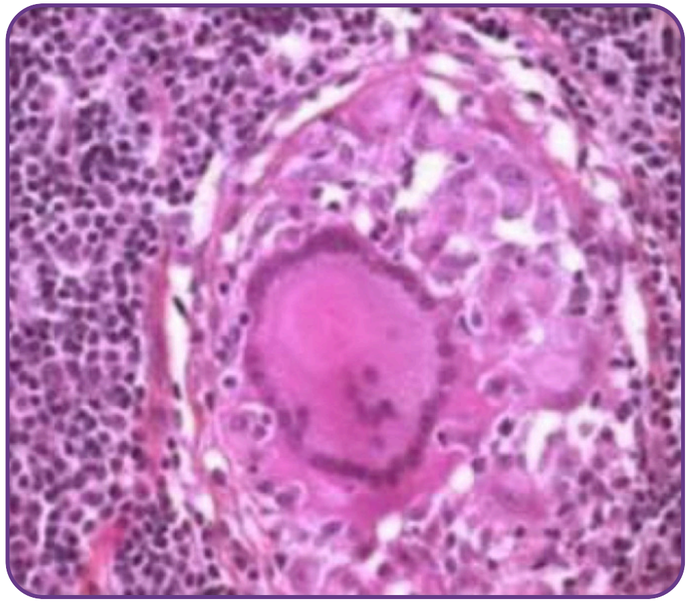
Outcome

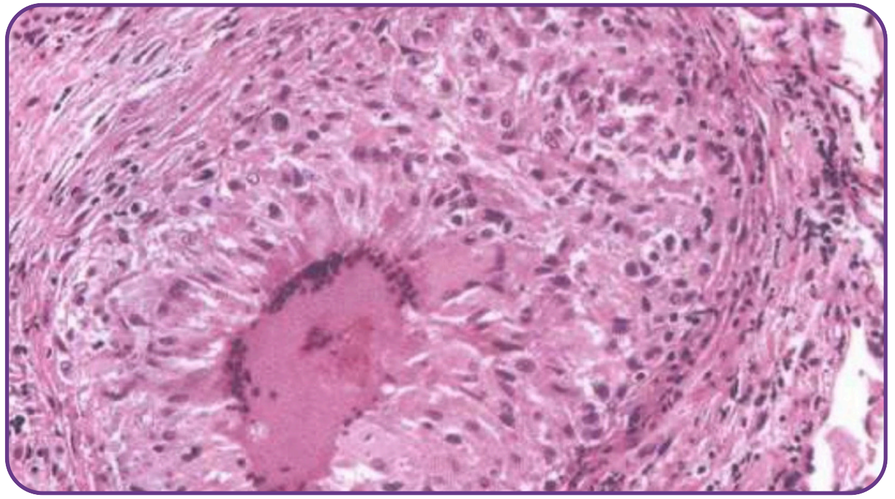
- **Unpredictable**

Progressive chronicity OR Remissions & relapses

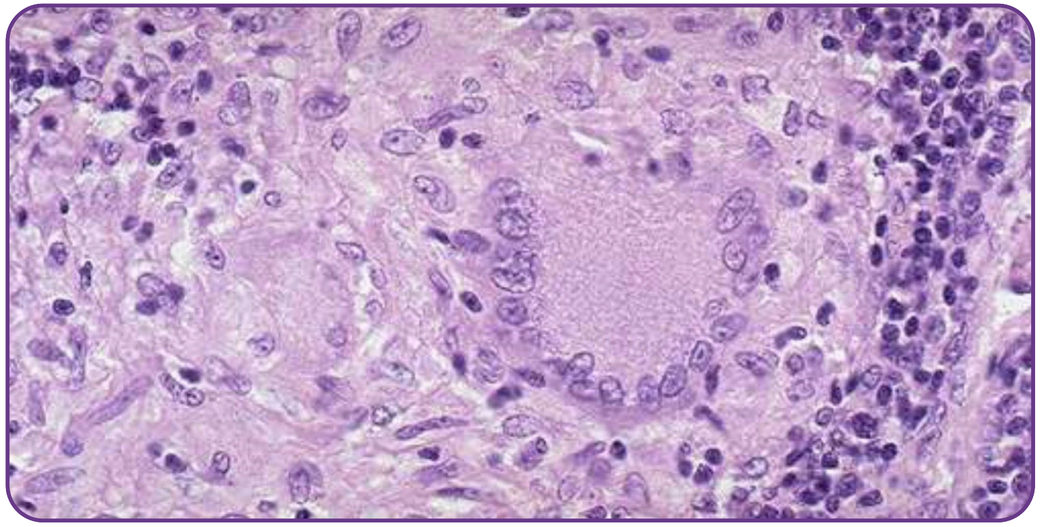
- Steroid-induced or spontaneous remission
- **Statistics**:
- 65–70% recover
- 20% permanent lung or visual damage
- 10–15% pulmonary fibrosis & cor pulmonale

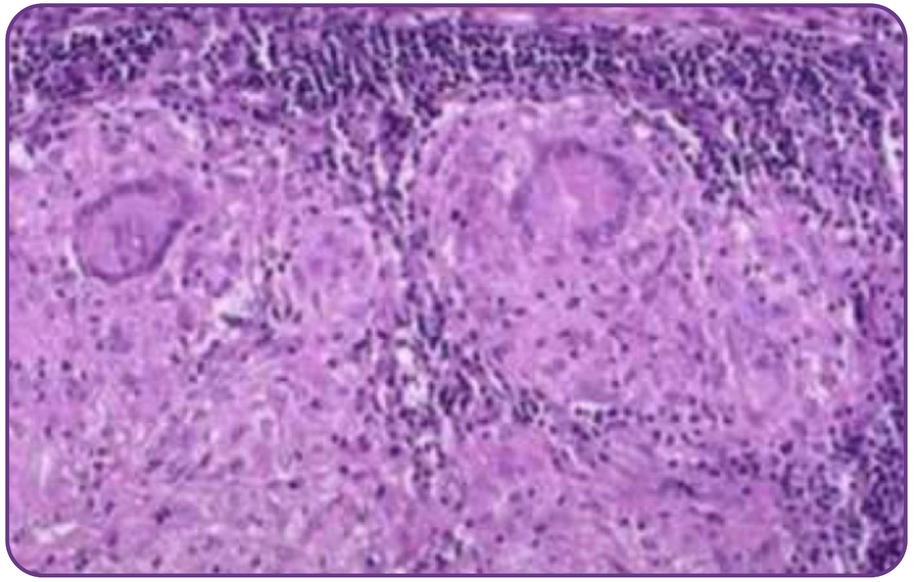
اللهم صلِّ وسلِّم وبارك على سيدنا محمد وعلى آله وصحبه أجمعين

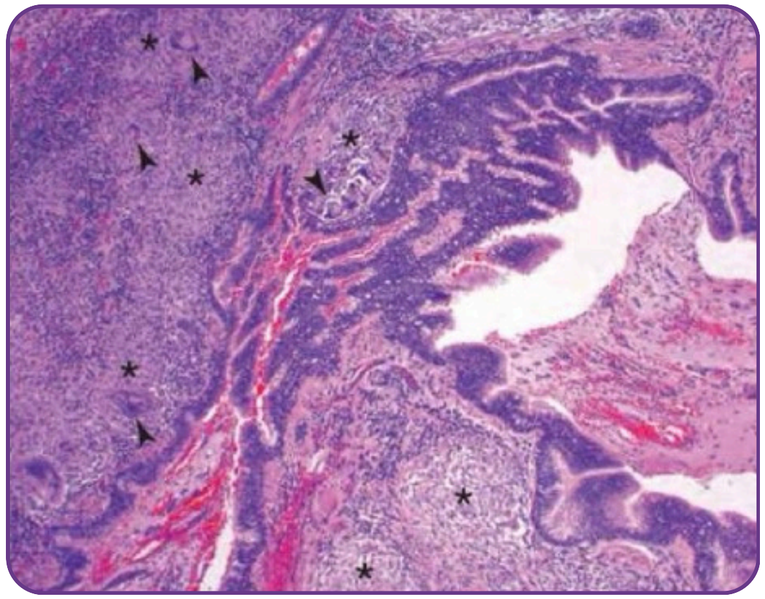




Granulomas[1]



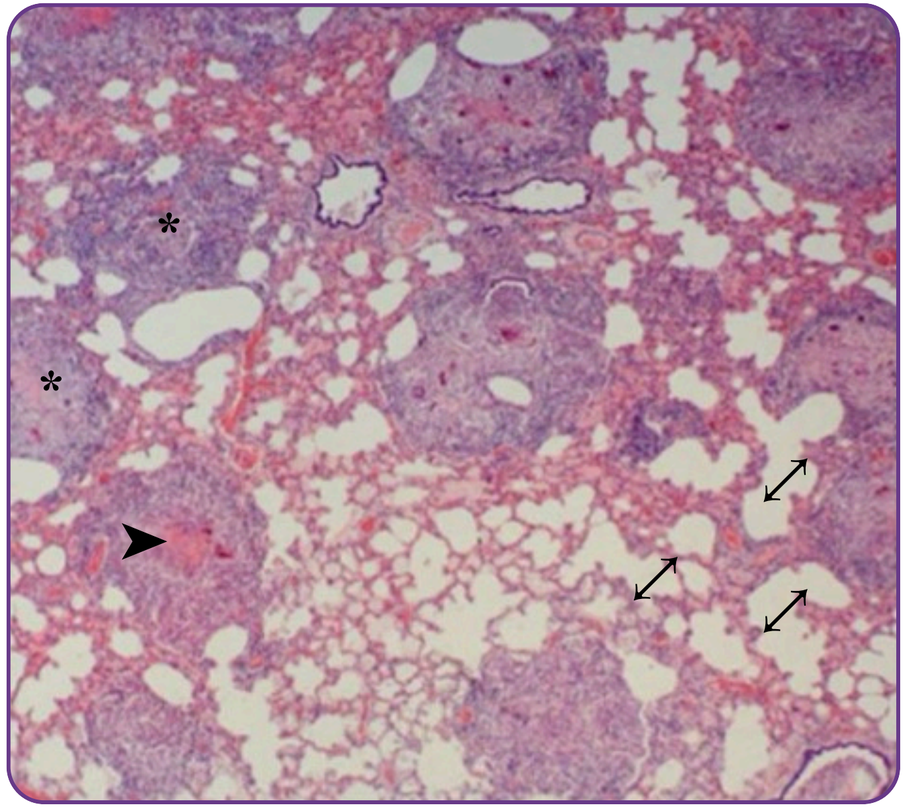


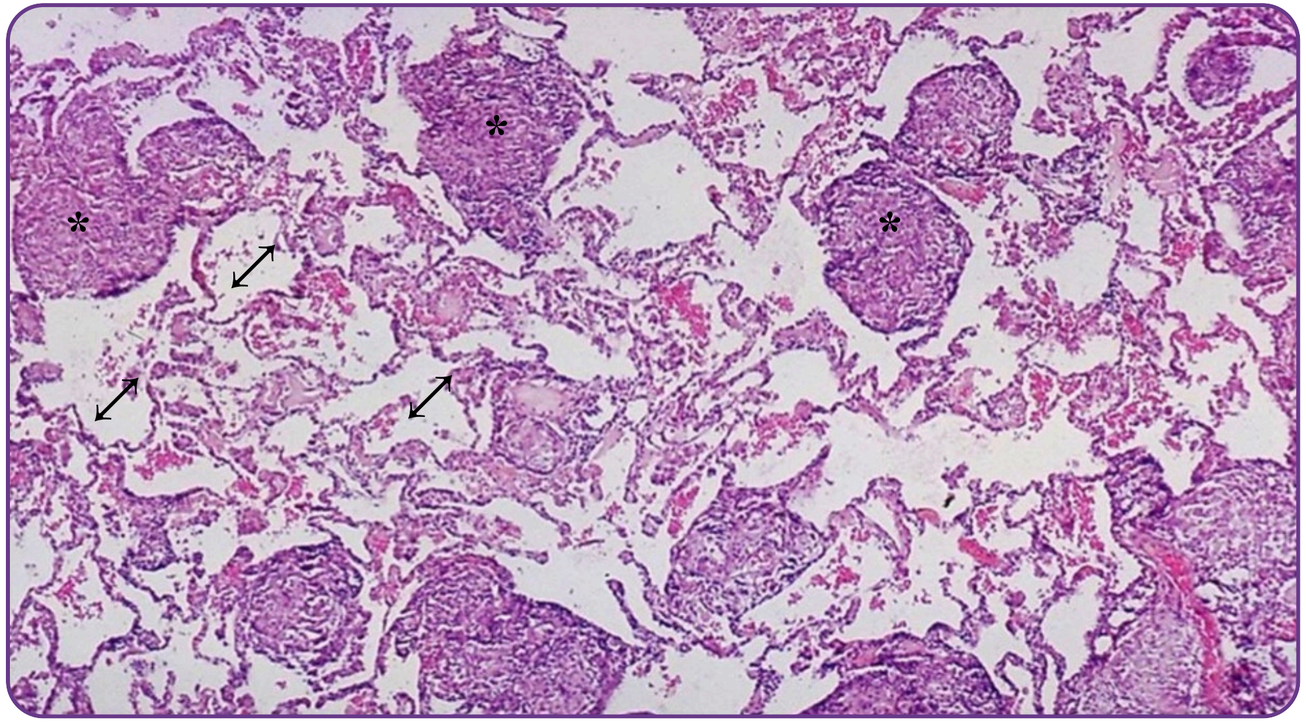


* Granulomas

➤ Multi-nucleated giant cells

⤢ Alveolar spaces





HYPERSENSITIVITY PNEUMONITIS

Definition

- Immunologically mediated
- Antibodies against offending antigens
- primarily **Affects alveoli (allergic alveolitis)**
- **Occupational exposure**
- Restrictive lung disease: ↓ diffusion capacity, ↓ lung compliance, ↓ total lung volume

Causes / Syndromes

- Organic dust inhalation:

  Bacteria spores, Fungi, Animal proteins and Bacterial products

Farmer's lung

dusts generated from humid, warm, newly harvested hay that permits the rapid proliferation of the spores of thermophilic actinomycetes

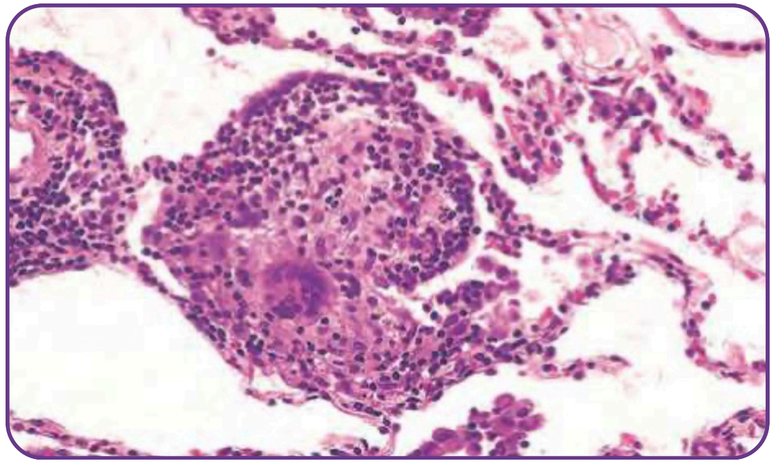
Pigeon breeder's lung

proteins from serum, excreta, or feathers of birds.

Humidifier or air-conditioner lung

thermophilic bacteria in heated water reservoirs

Morphology



Acute

Neutrophils

Chronic

- Patchy mononuclear infiltrates (peribronchiolar accentuation
- Lymphocytes predominate + plasma cells & epithelioid cells
- Interstitial (peribronchiolar) noncaseating loose granulomas (⅔)
- Advanced → diffuse interstitial fibrosis

Clinical Presentation

Acute

- Fever
- Cough
- Dyspnea
- Constitutional symptoms 4–8 hours post exposure

Chronic

- Insidious cough, Dyspnea, Malaise and Weight loss
- Stop exposure → complete resolution
- Continuous exposure → irreversible disease

Idiopathic Pulmonary Fibrosis

لا إله إلا الله وحده لا شريك له، له الملك وله الحمد وهو على كل شيء قدير

Definition

- Unknown etiology
- Patchy progressive bilateral interstitial fibrosis
- Radiologic and histologies pattern of fibrosi → usual interstitial pneumonia (UIP) pattern
- Also called cryptogenic fibrosing alveolitis
- Diagnosis of exclusion

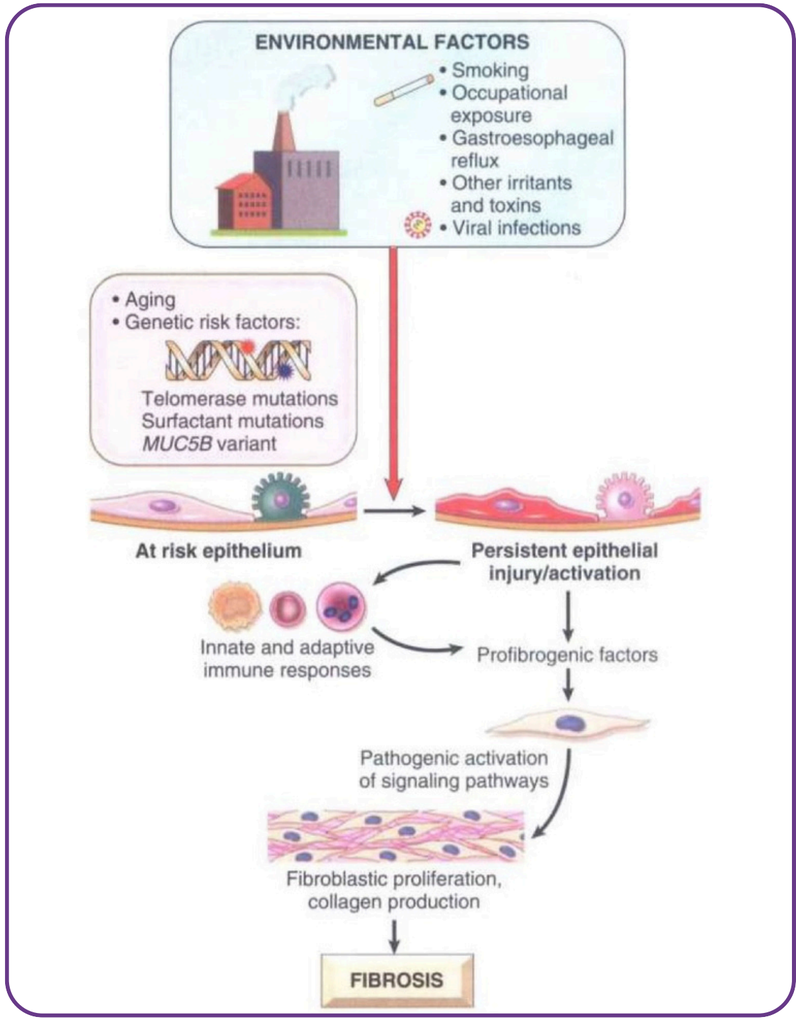
Epidemiologic Trends

- Males predominant
- Never occur before 50

Etiology & Pathogenesis

- Repeated injury to alveolar epithelium
- Defected repair leading to fibroblastic proliferation
- In genetically predisposed individuals
- The cause is obscure

This image demonstrates the pathogenesis is of IPF:



Morphology

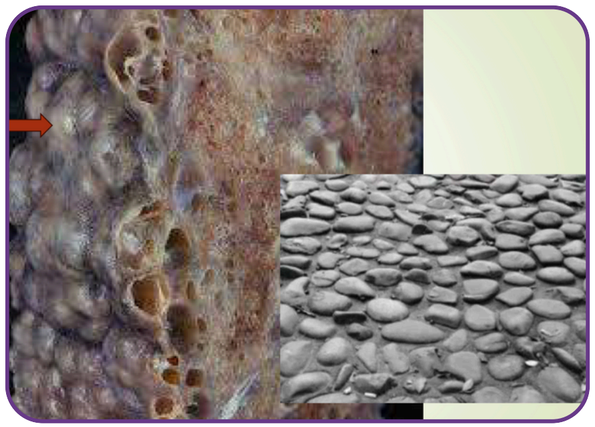
Macroscopic:

• Cobblestone appearance of pleural surface (retraction of scars along the interlobular septa
• Cut surface shows fibrotic firm, rubbery white areas
• Lower lobe, subpleural regions and along the interlobular septa are mostly affected

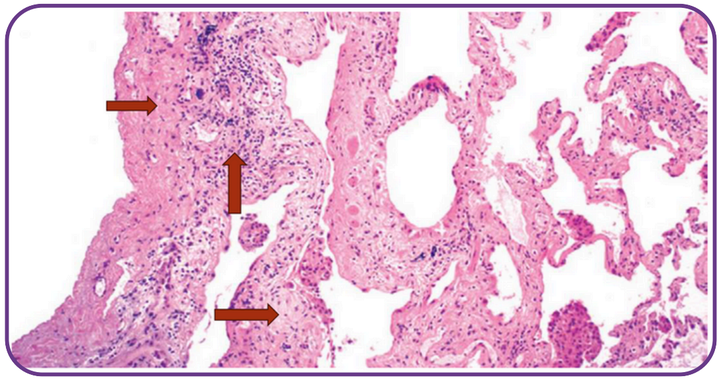
Microscopic:

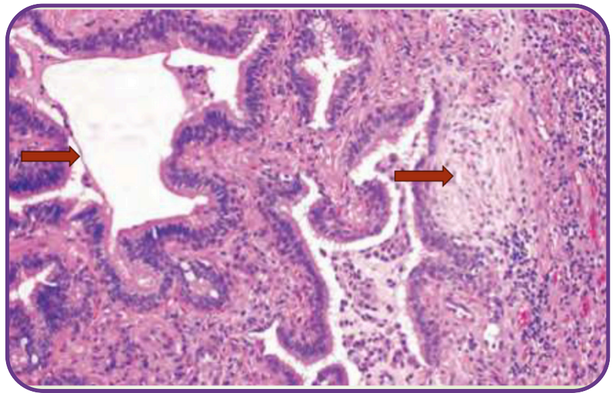
• **UIP pattern** of fibrosis
• **Hallmark**: patchy interstitial fibrosis (varies in intensity & worsens with time)
• **Earliest**: fibroblastic foci
• **Later**: collagenous and less cellular foci
• **Advanced**: honeycomb fibrosis
• **Typical finding**: co-existence of early and late lesions (temporal heterogeneit)
• Mild to moderate inflammation in fibrotic areas
• Secondary pulmonary arterial hypertensive changes (intimal fibrosis and medial thickening)

Macroscopic:



Microscopic:





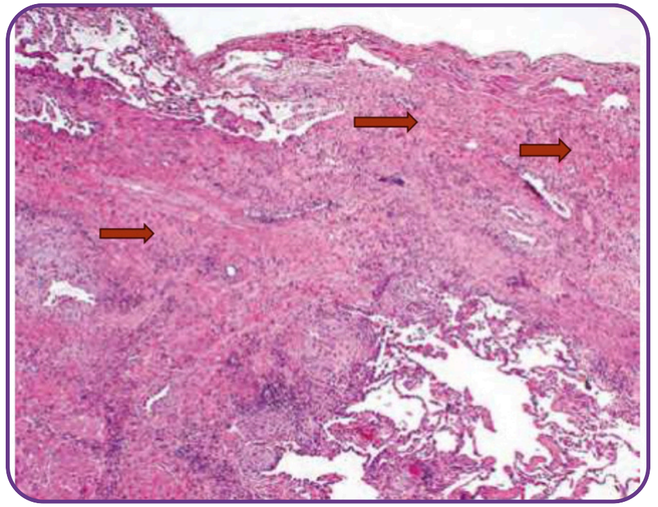
Clinical Features:

- Gradual onset of nonproductive cough and progressive dyspnea
- Cyanosis, cor pulmonale, peripheral edema may develop later
- P/E: dry or velcro-like crackles during inspiration
- CXR: subpleural and basilar fibrosis and honeycombing
- Clinical and radiologic findings are often diagnostic

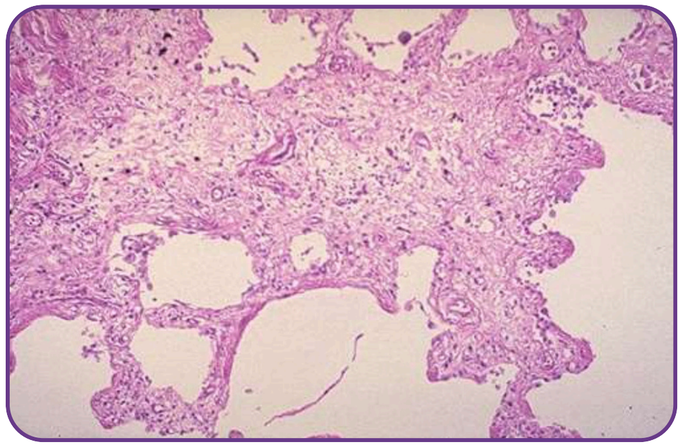
Prognosis:

- Progression despite medical therapy
- Mean survival is 3 years or less
- Lung transplantation is the only definitive therapy
- Anti-inflammatory & immunosuppressive therapy (little benefit)
- Main treatment: Antifibrotic therapy

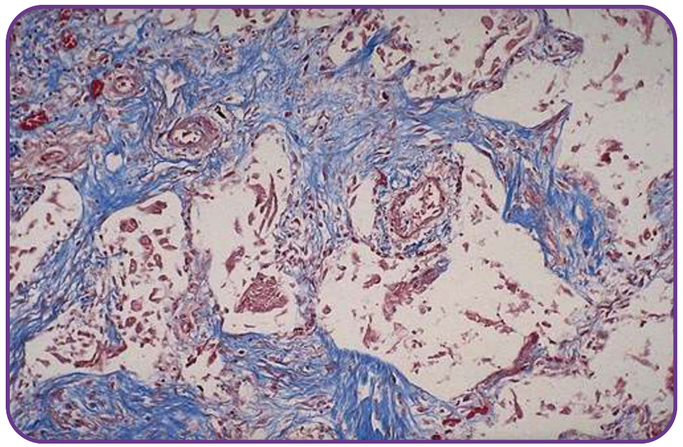
1.



2.



3.



These three images show the microscopic appearance of idiopathic pulmonary fibrosis

Massion trichrome special stain for fibrosis

Nonspecific Interstitial Pneumonia

أستغفر الله العظيم الذي لا إله إلا هو الحي القيوم وأتوب إليه

General Characteristics:

- Chronic bilateral interstitial lung disease
- Distinct clinical, radiologic, and histologic features
- Idiopathic
- Frequently associated with connective tissue disorders (rheumatoid arthritis)

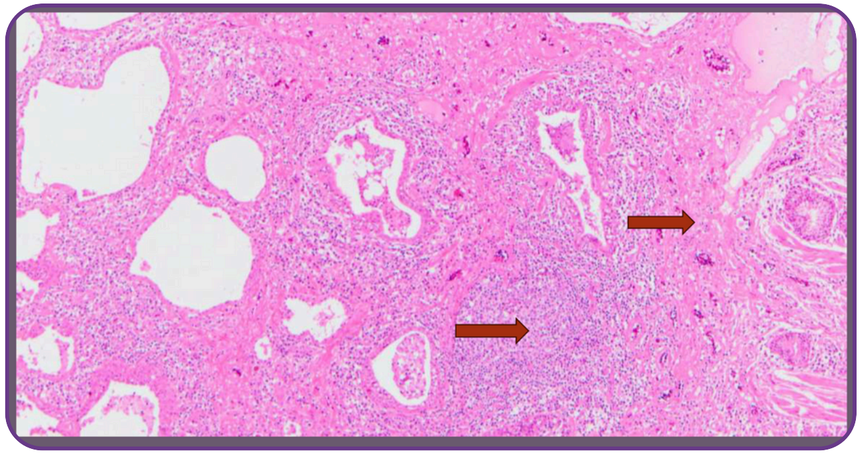
Clinical Features & Prognosis:

- Dyspnea and cough of several months
- Better prognosis than idiopathic pulmonary fibrosis

Morphology:

Cellular Pattern:

Mild to moderate chronic interstitial inflammation (lymphocytes and a few plasma cells) in a uniform or patchy distribution



Fibrosing Pattern:

Diffuse or patchy interstitial fibrosis but uniform in the areas involved

- Temporal heterogeneity characteristic of UIP is absent
- Fibroblastic foci is typically absent

Cryptogenic Organizing Pneumonia

سبحان الله وبحده

General Characteristics:

- Uncommon
- Unknown etiology

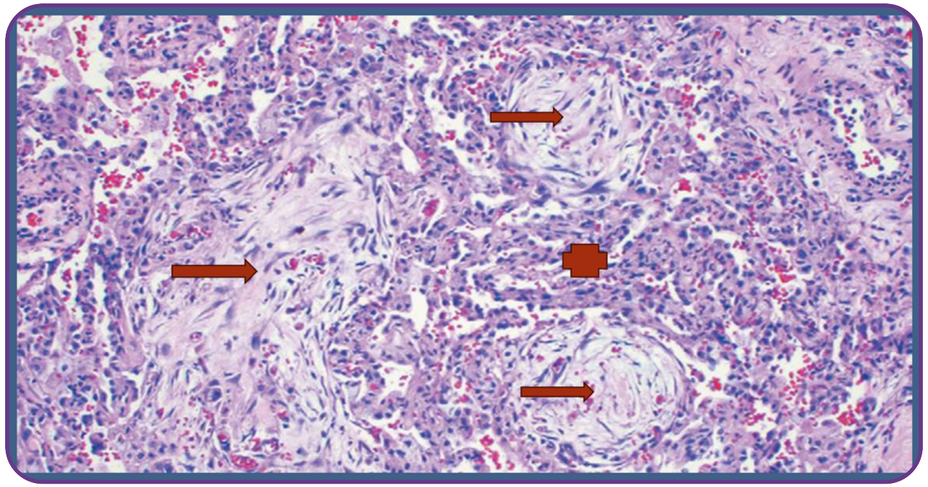
Clinical Features & Treatment :

- Dyspnea and cough
- Chest X-ray: Subpleural or peri bronchial patchy air space consolidation
- Some patients recover spontaneously
- Most patients require treatment with oral steroids

Morphology:

Microscopic:

- Polyploid plugs of loose organizing connective tissue within alveolar ducts, alveoli, and bronchioles (Masson Bodies)
- Connective tissue is all the same age
- Underlying lung architecture is normal
- No interstitial fibrosis or honeycomb lung



Masson Bodies:

Balls of fibroblasts that fill some alveolar spaces, compresse adjacent alveoli are relatively normal

Similar changes are seen in infections (e.g. pneumoni) or inflammatory injury (e.g. collagen vascular disease, transplantation injury), in this case it is not “cryptogenic”

Pneumoconiosis

Definition:

Lung reaction to inhalation of mineral dusts, organic and inorganic particulates, chemical fume and vapor

Etiologic Agents:

- Nearly always result from occupational exposure
- Coal dust, silica, and asbestos are most common mineral dust
- In asbestos, the increased risk of cancer extends to family members of asbestos workers

Table 12-4 Mineral Dust–Induced Lung Disease

Agent	Disease	Exposure
Coal dust	Simple coal worker's pneumoconiosis: macules and nodules Complicated coal worker's pneumoconiosis: PMF	Coal mining
Silica	Silicosis	Sandblasting, quarrying, mining, stone cutting, foundry work, ceramics
Asbestos	Asbestosis, pleural effusions, pleural plaques, or diffuse fibrosis; mesothelioma; carcinoma of the lung and larynx	Mining, milling, and fabrication of ores and materials; installation and removal of insulation

PMF, progressive massive fibrosis.

Pathogensis:

Reaction of the lung to mineral dust depends on:

Amount: Of dust retained in the airways and lung

Size and Shape: Particles that are 1 to 5 micrometers in diameter are the most dangerous

Solubility of Particles: Soluble particles produce acute lung injury

Proinflammatory Properties: Coal dust is inert, silica and asbestos provoke greater immune response

Key Cellular Element: The pulmonary alveolar macrophage is the key cellular element in the initiation and perpetuation of lung injury and fibrosis

Exacerbation: Tobacco smoking worsens the effects of **all** inhaled mineral dusts, more so with asbestos

اللهم اجعل أجر هذا العمل صدقة جارية عن روح **عمر عطيه عوده المرابي**

- اللَّهُمَّ اغْفِرْ له وَارْحَمْهُ، وَاعْفُ عنْه وَعَافِهِ، وَأَكْرِمْ نُزُلَهُ، وَوَسِّعْ مُدْخَلَهُ، وَ اغْسِلْهُ بمَاءٍ وَثَلْجٍ وَبَرَدٍ، وَنَقِهِ مِنَ الخَطَايَا كما يُنَقّى الثَّوْبُ الأبْيَضُ مِنَ الدَّنَسِ.
- اللَّهُمَّ أبدله داراً خيراً من داره، وأهلاً خيراً من أهله، وأدخله الجنّة، وأعذه من عذاب القبر ومن عذاب النّار.
- اللهمّ يمّن كتابه، ويسّر حسابه، وثقل بالحسنات ميزانه، وثبّت على الصراط أقدامه، وأسكنه في أعلى الجنات، بجوار حبيبك محمد صلّى الله عليه وسلم.
- اللهم اغفر لحينا وميتنا وشاهدنا وغائبنا وصغيرنا وكبيرنا وذكرِنا وأنثانا اللهم من أحييته منا فأحيِه على الإسلام ومن توفيته منا فتوفه على الإيمان اللهم لا تحرمنا أجره ولا تضلنا بعده.
- اللهم اغفر له وارفع درجته في المهديين، واخلفه في عقبه في الغابرين، واغفر لنا وله يا رب العالمين، وافسح له في قبره، ونوّر له فيه.
- اللَّهُمَّ أنزل على أهله الصّبر والسلوان وارضهم بقضائك.

اللهم لا تفجعنا بأنفسنا ولا أهلنا ولا أحبتنا، اللهم أعوذ بك من فواجع الأقدار ومن مصائب الدنيا وتقلب حوادثها، اللهم إنا نخاف الفقد فلا تحملنا ما لا طاقة لنا به.