INTERSTITIAL LUNG DISEASE

diffuse parenchymal lung diseases (DPLDs)

- **a heterogeneous group of conditions affecting the pulmonary interstitium and/or alveolar lumen.**
- **share similar symptoms, physical signs, pulmonary function abnormalities and radiological changes.**
- **HRCT : the critical first step in the investigation of DPLD**

Pathophysiology

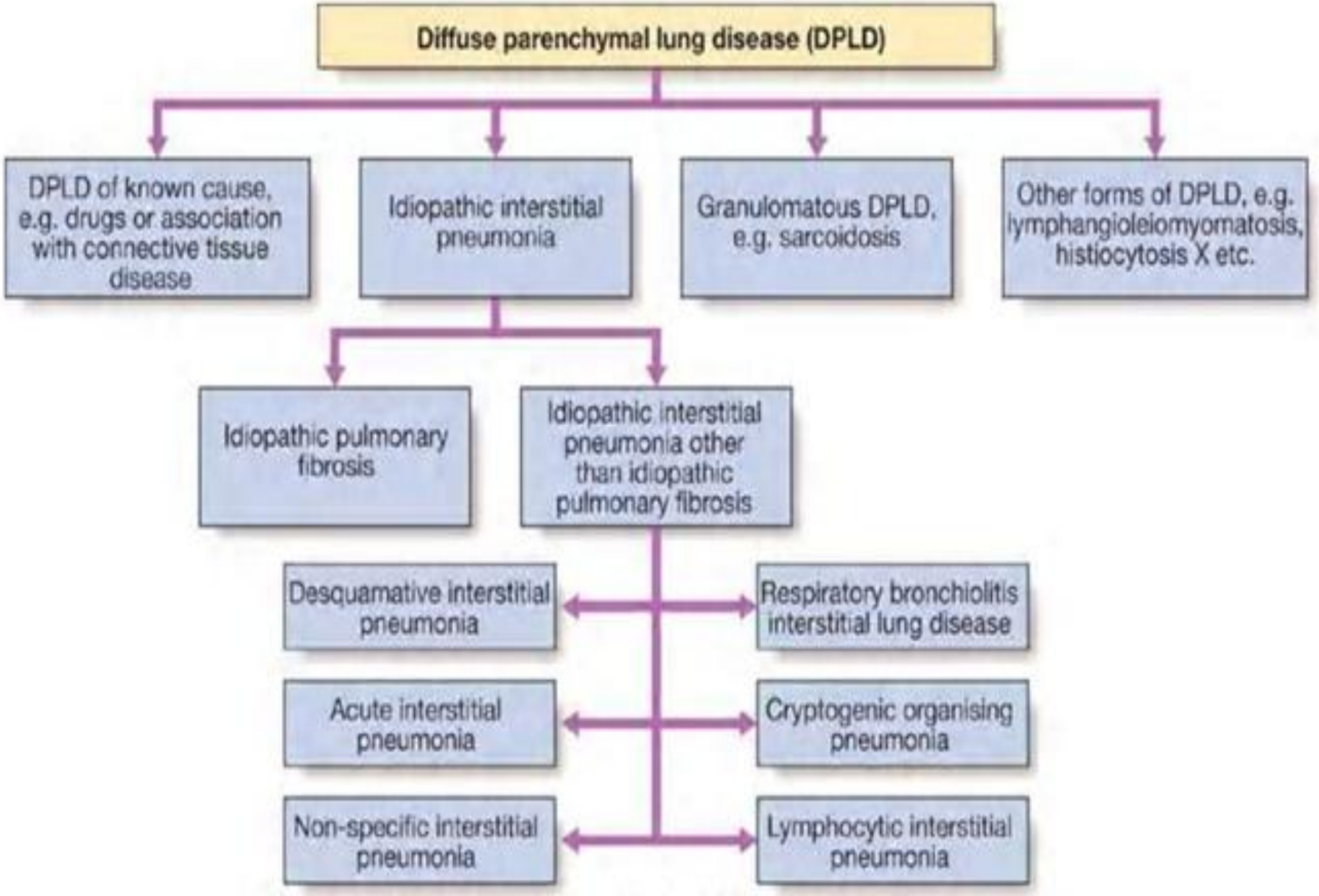
- **inflammatory process in the alveolar walls —> thickening and destruction of pulmonary vessels and fibrosis of interstitium leading to :**

  - **decreased lung compliance**
  - **decreased lung volumes**
  - **impaired diffusion**
  - **hypoxemia without hypercarbia (V/Q mismatch) due to vasoconstriction and fibrosis**
  - **pulmonary HTN and subsequent cor pulmonale secondary to hypoxemia and blood vessel destruction**

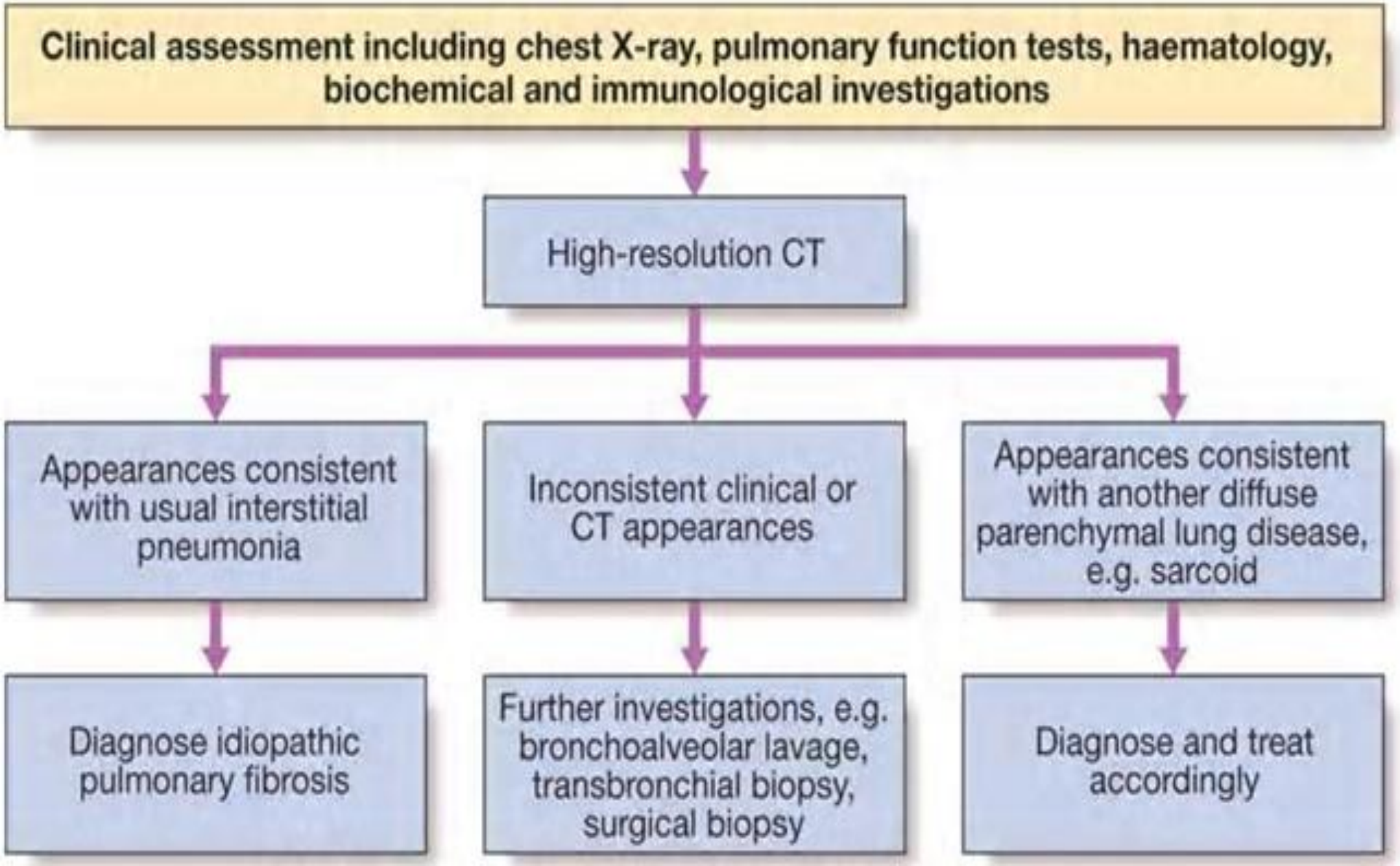
Causes of interstitial lung disease

- **65% due to unknown agents**

Classification of diffuse parenchymal lung disease



the investigation of patients with interstitial lung disease following initial clinical and chest X-ray examination.



Causes of Interstitial Lung Disease

Upper Lung Disease	Lower Lung Disease
F farmers lung A ankylosing spondylitis S sarcoidosis S silicosis TTB E eosinophillic granuloma N neurofibromatosis	B bronchiectasis bronchiolitis organizing pneumonia (BOOP) A asbestosis D drugs (nitrofurantoin, hydralazine, INH, amiodarone) R rheumatologic disease A aspiration S Scleroderma H Harmen Reich (Interstitial pulmonary fibrosis)

Clinical Presentation

- SOB, especially on exertion with decreasing SaO2
- dry crackles
- +/– dry cough
- clubbing
- features of cor pulmonale

Investigations in DPLD

Laboratory investigations :

- Full blood count: lymphopenia in sarcoid; eosinophilia in pulmonary eosinophilias and drug reactions; neutrophilia in hypersensitivity pneumonitis
- Ca^{2+}: may be elevated in sarcoid
- Lactate dehydrogenase (LDH): may provide non-specific indicator of disease activity in DPLD
- Serum ACE: non-specific indicator of disease activity in sarcoid
- ESR and CRP may be non-specifically raised
- Autoimmune screen, rheumatoid factor and anti-CCP antibodies may suggest connective tissue disease

Radiology

- Chest X-ray
- HRCT

Pulmonary function

- Spirometry, lung volumes, gas transfer, exercise tests

Bronchoscopy

- Bronchoalveolar lavage: infection, differential cell counts
- Bronchial biopsy may be useful in sarcoid

Lung biopsy (in selected cases)

- Transbronchial biopsy useful in sarcoid and differential of malignancy or infection
- Video-assisted thoracoscopy (VATS)

Others

- Liver biopsy may be useful in sarcoidosis
- Urinary calcium excretion may be useful in sarcoidosis

مقاربة التشخيص

- **تنظير القصبات :**

*** الغسالة القصبية السنخية : غير نوعية ، IPF :**

زيادة في العدلات و الحمضات و اللمفاويات .

سيطرة اللمفاويات ← تحسن البقيا

*** الخزعة عبر القصبات :**

محدودة الاستعمال ، استبعاد أي تشخيص آخر

*** الخزعة الرئوية المفتوحة : التشخيص دقيق ، قرار العلاج و الاستجابة و الانذار ، إجراؤها في كل الحالات ؟**

- **معايير التشخيص السريري ل IPF :**

حساسية : 62 % و نوعية 97 %

Investigations

- **CXR :**
  - **decreased lung volumes**
  - **reticulonodular pattern (nodular (< 3 mm)**
  - **Kerley B lines**
  - **hilar/mediastinal adenopathy**
  - **lytic bone lesions**
- **DDx: pulmonary fibrosis, pulmonary edema (CHF), PCP, TB (miliary), sarcoidosis, pneumoconiosis, lymphangitic carcinomatosis**
- **DDx of cystic lesions: end-stage emphysema, PCP, histiocytosis X, Lymphangiomyomatosis**

- **The CXR can be normal in up to 15% of patients with interstitial lung disease.**

Investigations

- **PFTs**
  - **restrictive pattern (decreased lung volumes and compliance)**
  - **normal FEV1/FVC (> 70-80%)**
  - **FEF25-75 may be decreased due to lower lung volumes**
  - **flow rates are actually normal or supernormal when corrected for absolute lung volume**
  - **Dco decreased due to less surface area for gas exchange**

- **ABGs**
  - **hypoxemia and normal or decreased PaCO2**

Idiopathic interstitial pneumonias

- **(IIPs) characterised by varying patterns of inflammation and fibrosis in the lung parenchyma**

- **idiopathic pulmonary fibrosis (IPF) accounts for over 85% of new cases.**

UNKNOWN ETIOLOGIC AGENTS

IDIOPATHIC PULMONARY FIBROSIS

19.81 Differential diagnoses of the interstitial pneumonias

Clinical diagnosis	Notes
Usual interstitial pneumonia (UIP)	Idiopathic pulmonary fibrosis
Non-specific interstitial pneumonia (NSIP)	See page 708
Respiratory bronchiolitis-interstitial lung disease	More common in men and smokers. Usually presents in those aged 40-60. Smoking cessation may lead to improvement. Natural history unclear
Acute interstitial pneumonia	Often preceded by viral upper respiratory tract infection. Severe exertional dyspnoea, widespread pneumonic consolidation and diffuse alveolar damage on biopsy. Prognosis is often poor
Desquamative interstitial pneumonia (DIP)	More common in men and smokers. Presents in those aged 40-60. Insidious onset of dyspnoea. Clubbing in 50%. Biopsy shows increased macrophages in the alveolar space, septal thickening and type II pneumocyte hyperplasia. Prognosis is generally good
Cryptogenic organising pneumonia ('bronchiolitis obliterans organising pneumonia'-BOOP)	Presents as clinical and radiological pneumonia. Systemic features and markedly raised ESR common. Finger clubbing is absent. Biopsy shows a florid proliferation of immature collagen (Masson bodies) and fibrous tissue. Response to corticosteroids is classically excellent
Lymphocytic interstitial pneumonia (LIP)	More common in women, slow onset over years. Investigate for associations with connective tissue disease or HIV. Unclear whether corticosteroids helpful

An illustration demonstrates the different types of Idiopathic interstitial pneumonias (IIPs) and their pathological distribution patterns:

(a) idiopathic pulmonary fi brosis,

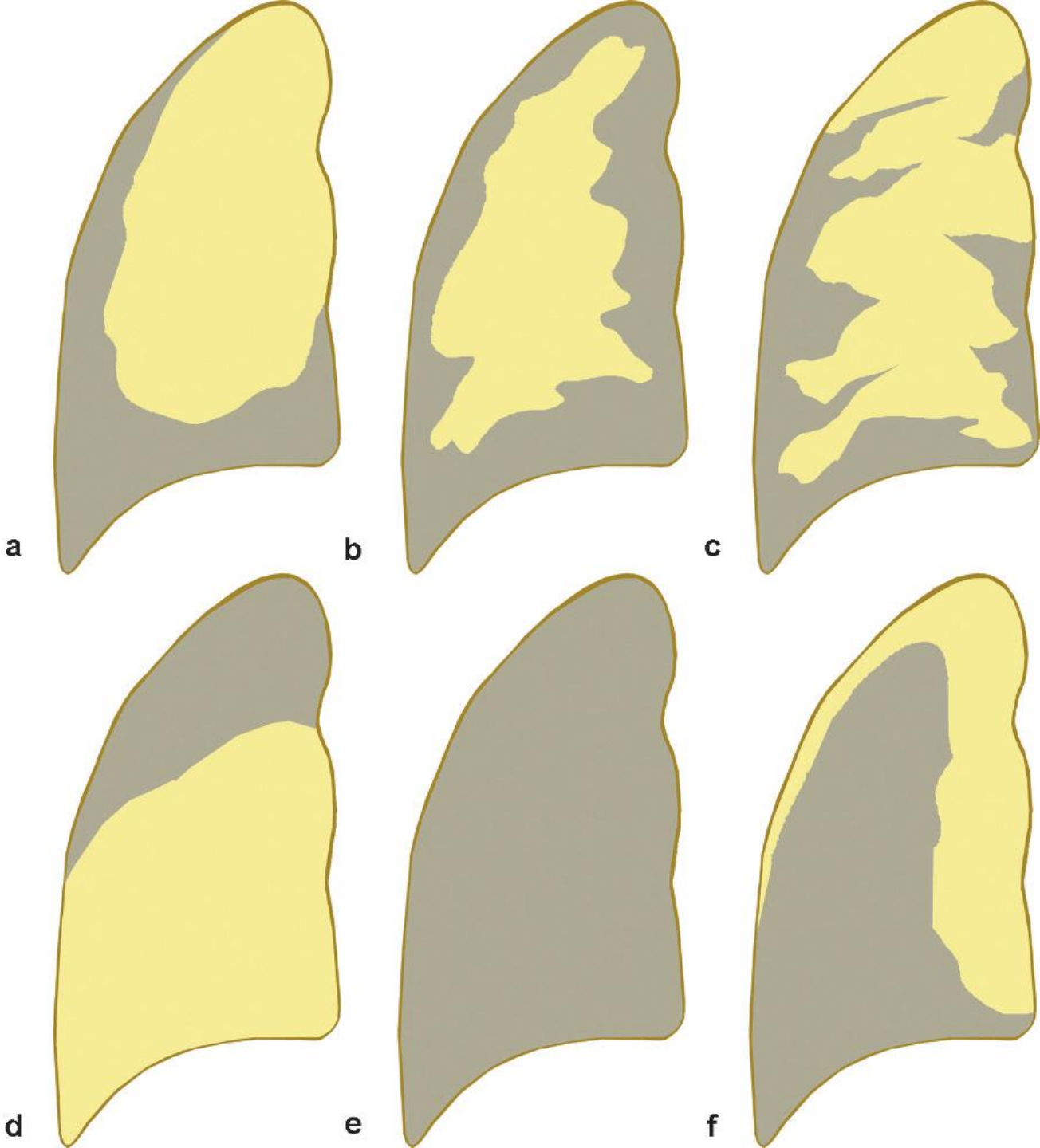
(b) nonspecifi c interstitial pneumonia (NSIP),

(c) cryptogenic organizing pneumonia (COP),

(d) Respiratory bronchiolitis-associated interstitial lung disease (RB-ILD),

(e) lymphoid interstitial pneumonia

(LIP),
(f) acute interstitial pneumonia (AIP)



IDIOPATHIC PULMONARY FIBROSIS

- a diagnosis of exclusion
- also known as cryptogenic fibrosing alveolitis or usual interstitial pneumonitis
- characterised by pathological (or HRCT) evidence of 'usual interstitial pneumonia' (UIP).
- uncommon before the age of 50 years.

aetiology

- Elusive

- factors :

- **viruses (e.g. Epstein-Barr virus)**
- **occupational dusts (metal or wood)**
- **drugs (antidepressants)**
- **chronic gastro-oesophageal reflux.**
- **Familial cases : rare**
- **genetic factors : likely to be important.**
- **strong association with cigarette smoking.**

التليف الرئوي مجهول السبب IPF

- المظاهر التشريحية المرضية : UIP

* توزع غير متجانس تحت جنبي من تليف نهائي و عش نحل متناوب مع مناطق التكاثر الخلوي لمولدات الليف &التهاب خلالي بؤري(لمفاويات+بلازميات+ناسجات)

* نقص المكونة الالتهابية : استجابة سيئة للعلاج

- UIP يمكن مشاهدته في : صلابة الجلد ،الداء الرثواني ، أسبستوز ، ذات الرئة بفرط التحسس

Clinical presentation

- **commonly presents between ages 40-75**

- **insidiously progressive breathlessness and a non-productive cough.**

- **additional clinical features**
  - **fatigue**
  - **anorexia**
  - **arthralgia**
  - **weight loss**
  - **cyanosis**
  - **clubbing**

- **bi-basal fine late inspiratory crackles**

natural history

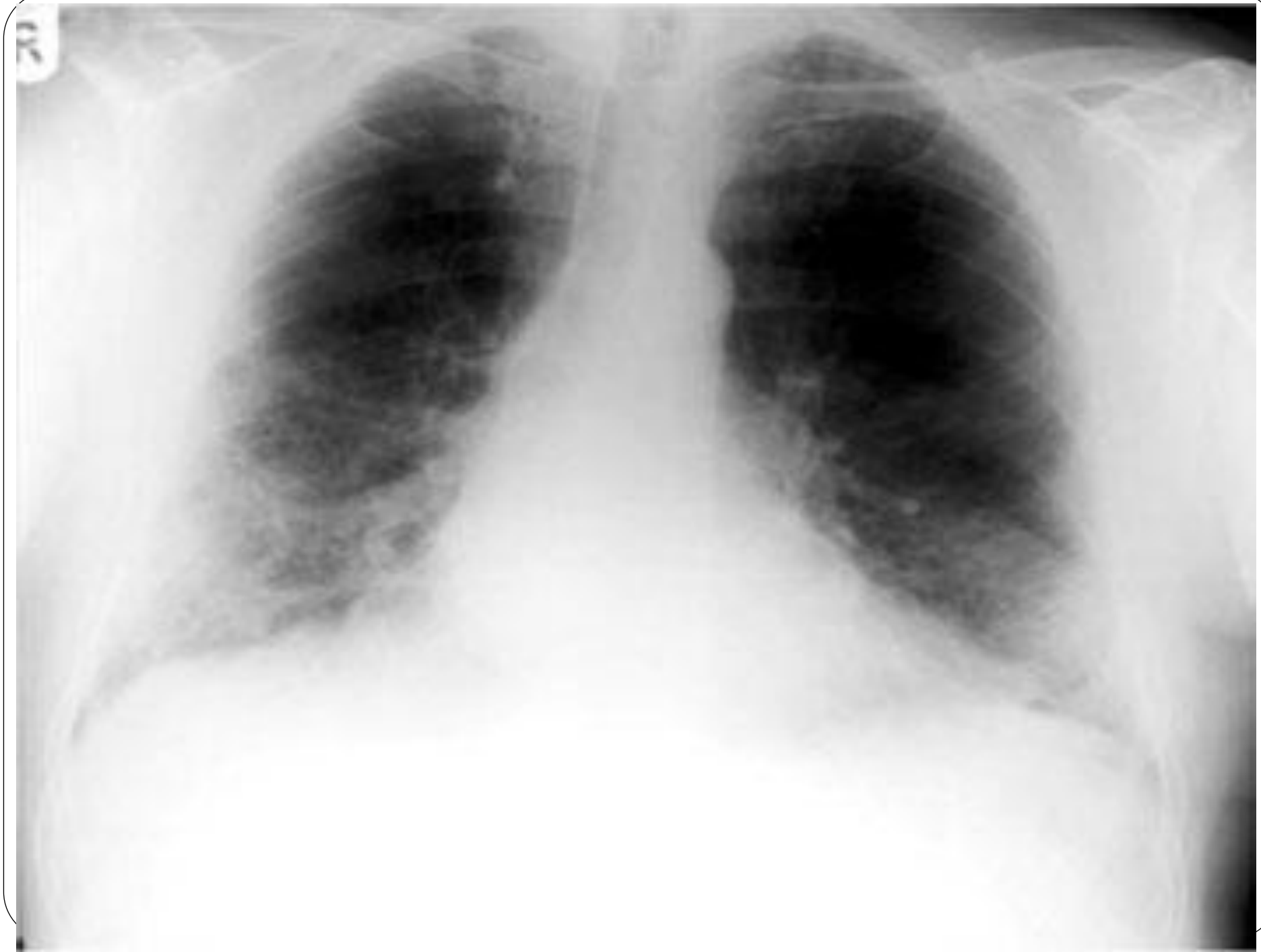
- **steady decline**
- **some patients are prone to exacerbations**
- **Exacerbations : acute deterioration in breathlessness, disturbed gas exchange, and new ground glass changes or consolidation on HRCT.**
- **advanced disease :central cyanosis , right heart failure.**

Investigations

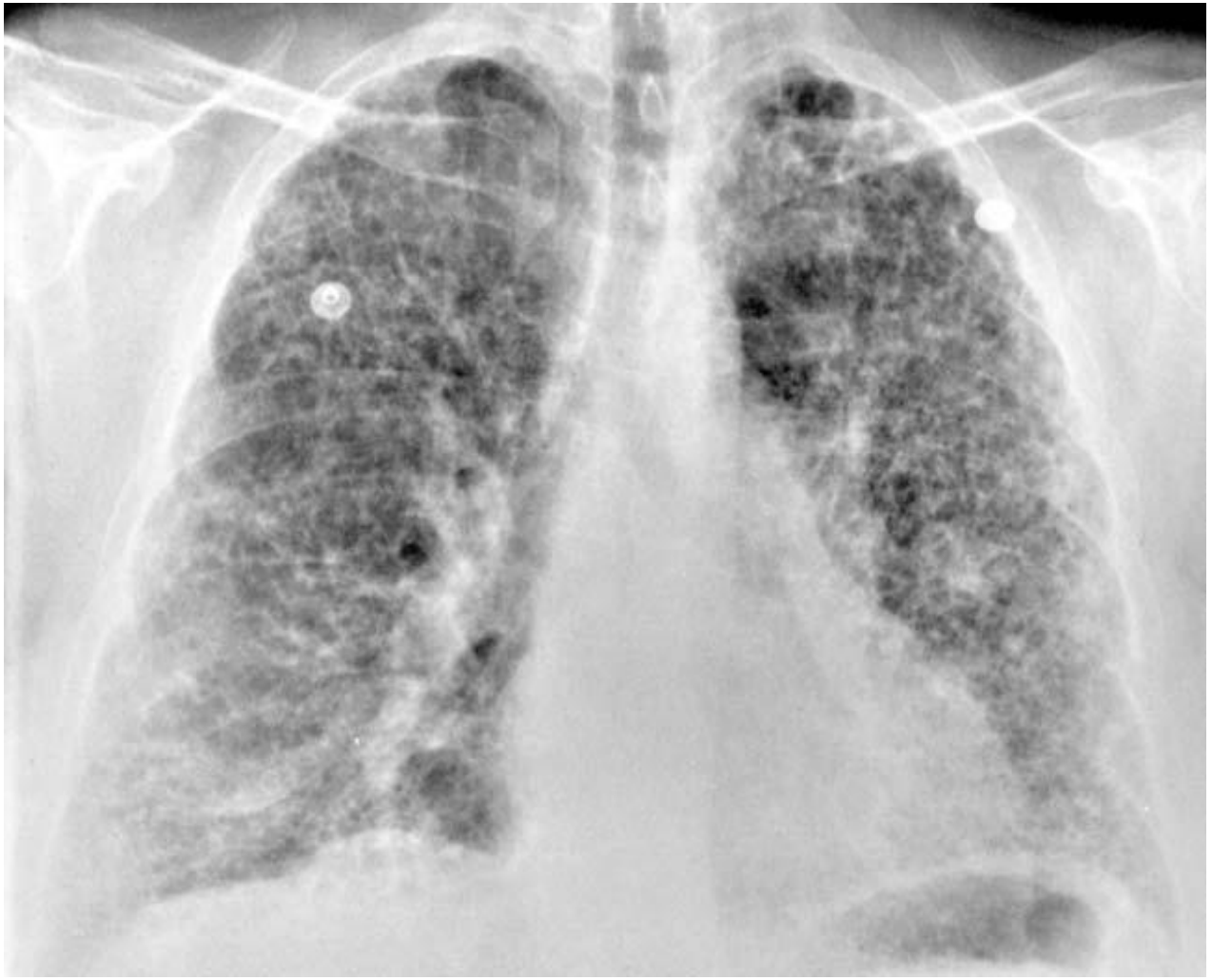
- **lab tests (nonspecific)**
  - **ESR increased**
  - **hypergammaglobulinema/hypocomplementemia < 10%**
  - **ANA and RF positive in 10%**

- **CXR**
  - **lower lung: reticulonodular or reticular pattern**
  - **generally bilateral and relatively diffuse**
  - **'honeycomb' appearance : in advanced disease but is non-specific**
  - **no pleural or hilar involvement**

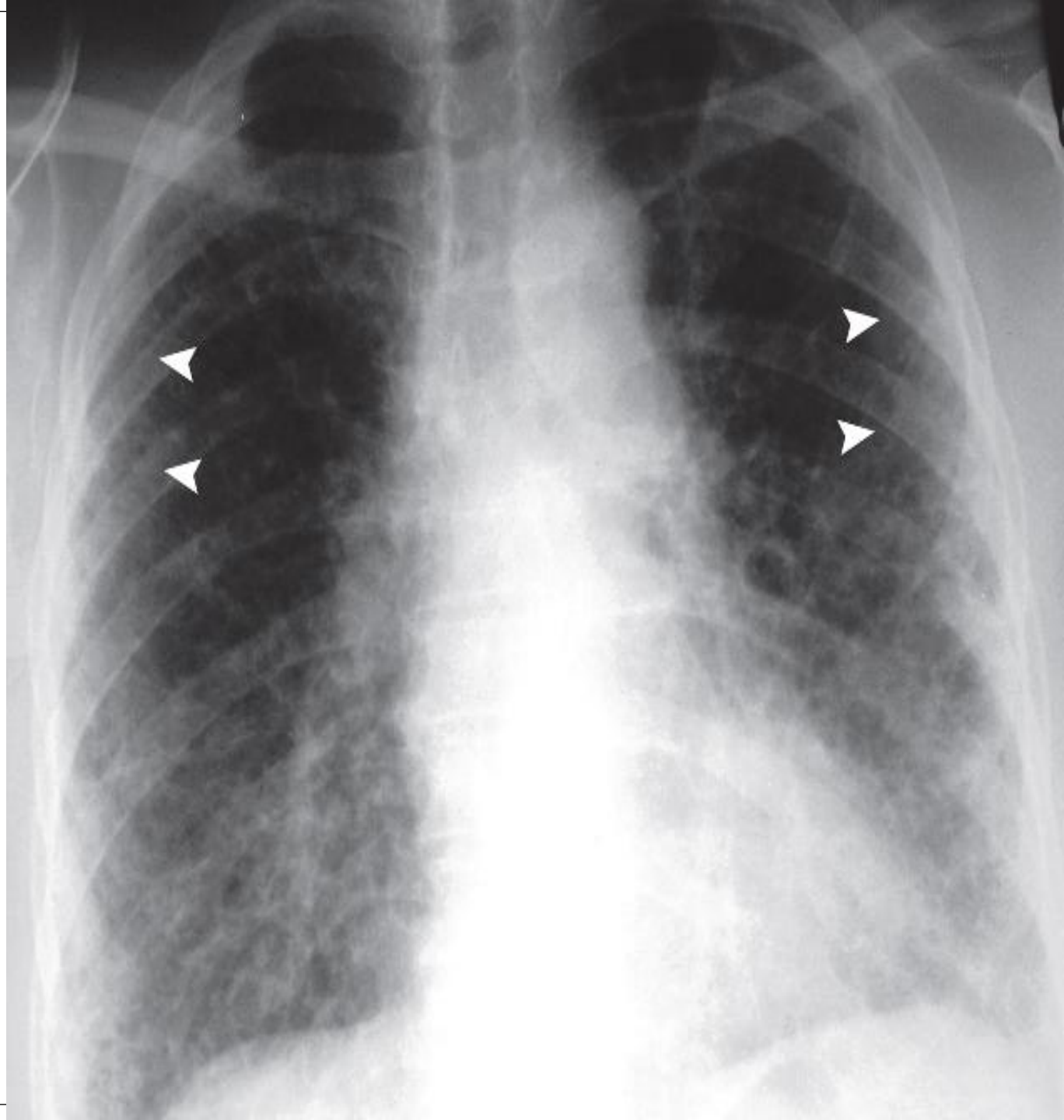
- **biopsy**
  - **not usually required in those with typical clinical features and HRCT appearances**
  - **to exclude granulomas (found in sarcoidosis and hypersensitivity pneumonitis)**



IPFصورة صدر



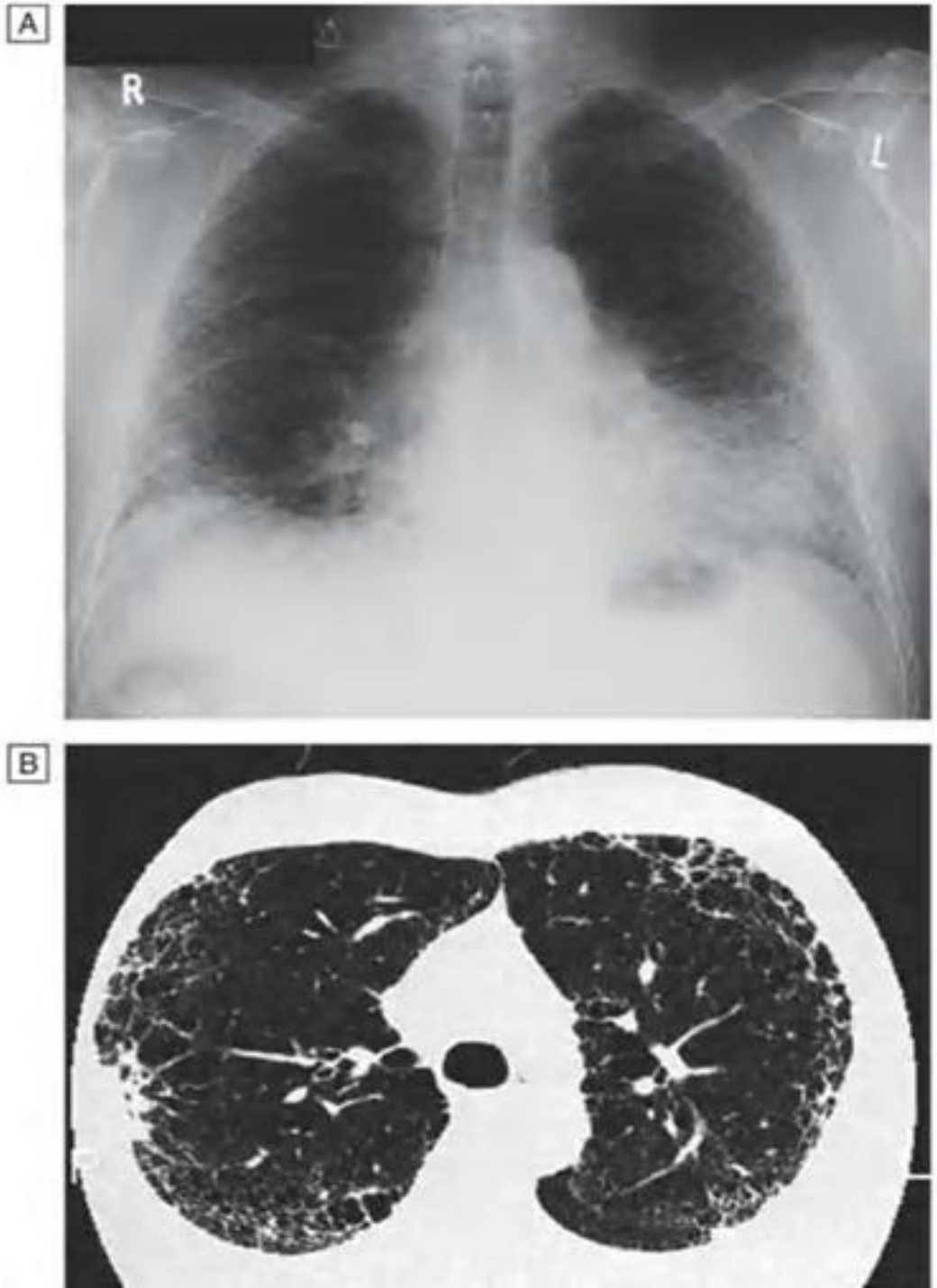
Idiopathic pulmonary fi brosis (IPF) shows bilateral reticular interstitial lung pattern located mainly at the base with gradient crawling toward the apices (*arrowheads*). *Notice the shaggy heart* appearance

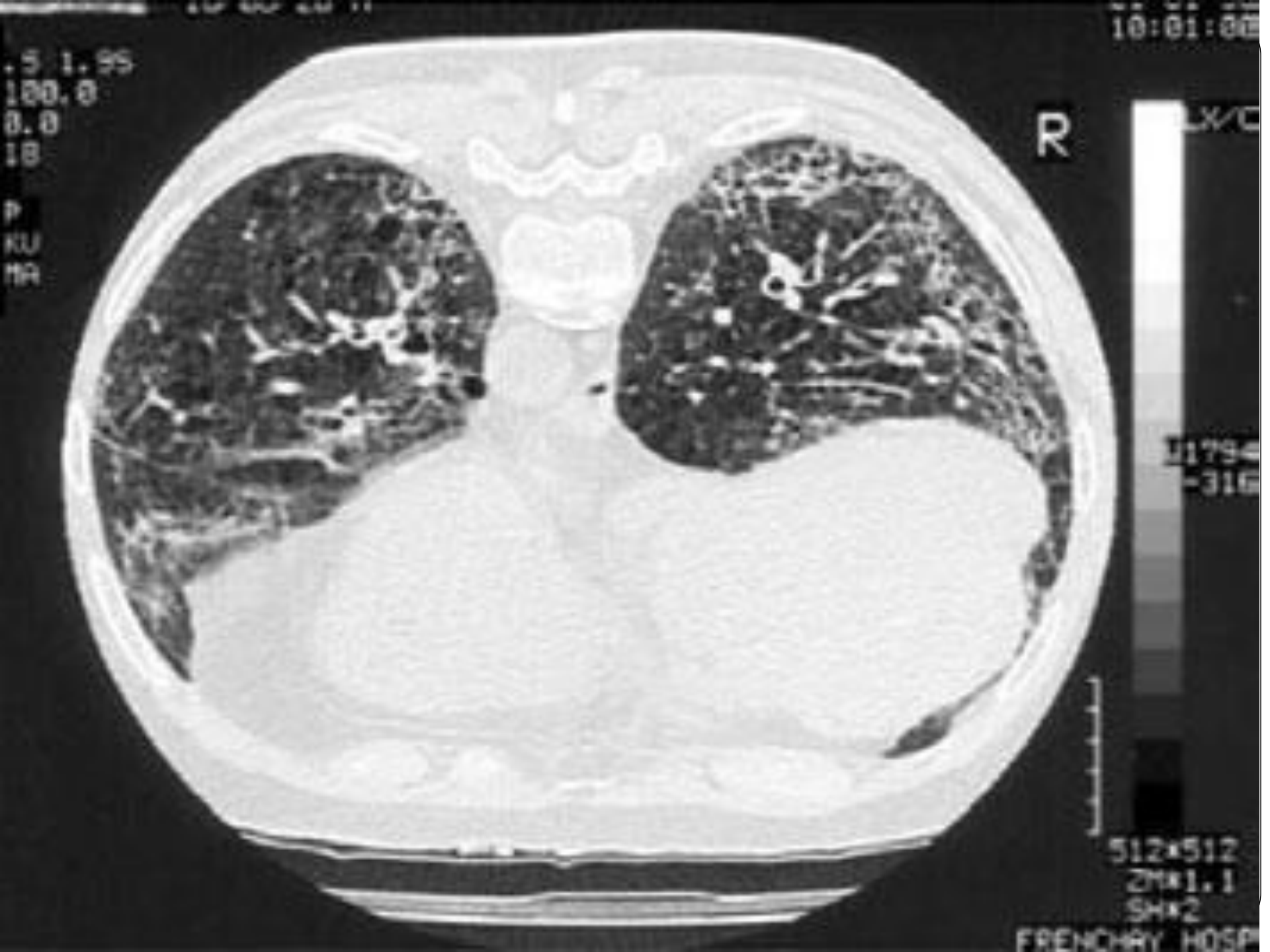


HRCT

- **patchy, predominantly peripheral, subpleural and basal reticular pattern**
- **subpleural cysts (honeycombing)**
- **and/or traction bronchiectasis**

Idiopathic pulmonary fibrosis. Chest X-ray showing bilateral, predominantly lower zone and peripheral coarse reticulonodular shadowing and small lungs. The CT scan shows honeycombing and scarring which is most marked peripherally.

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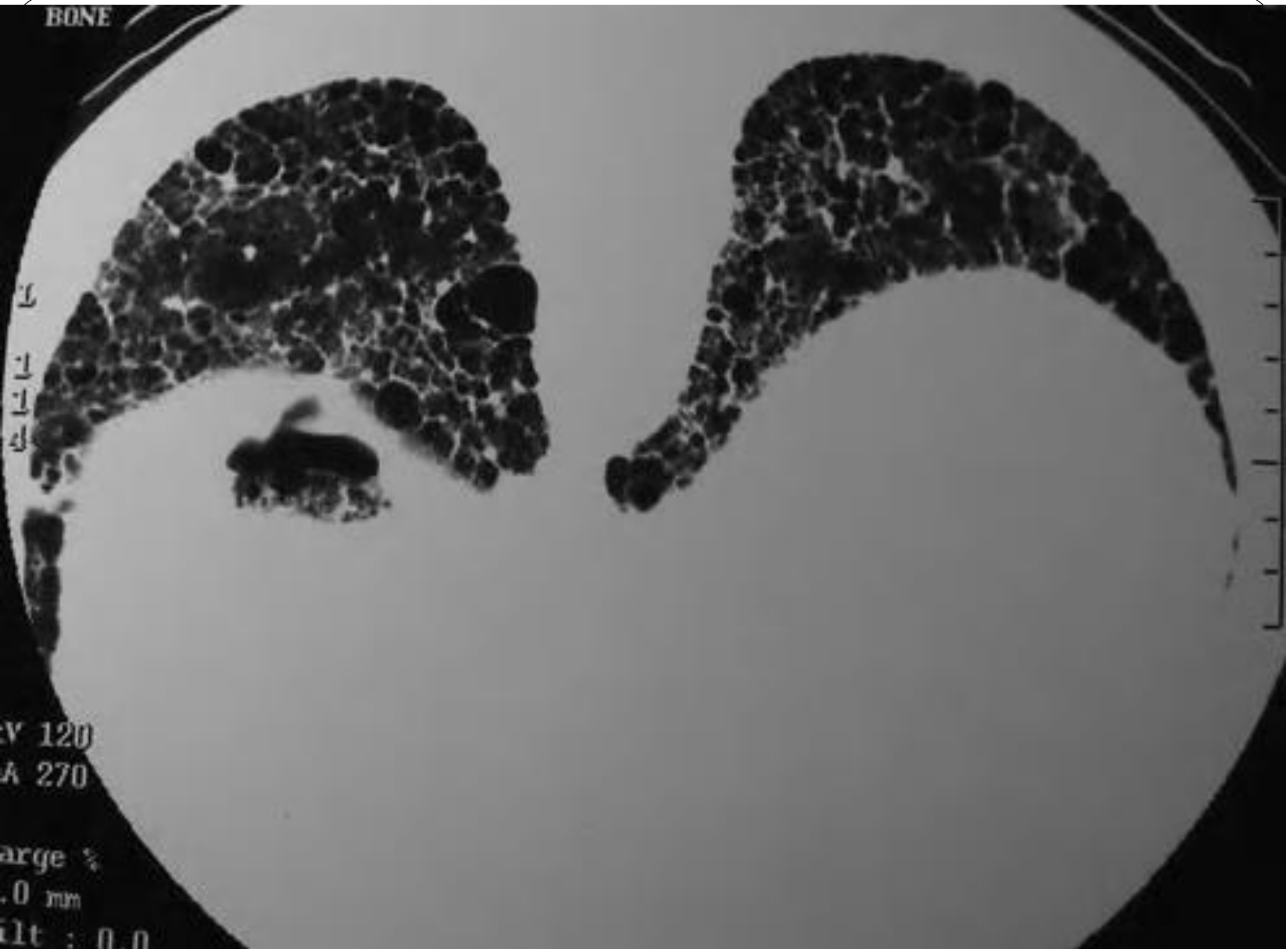
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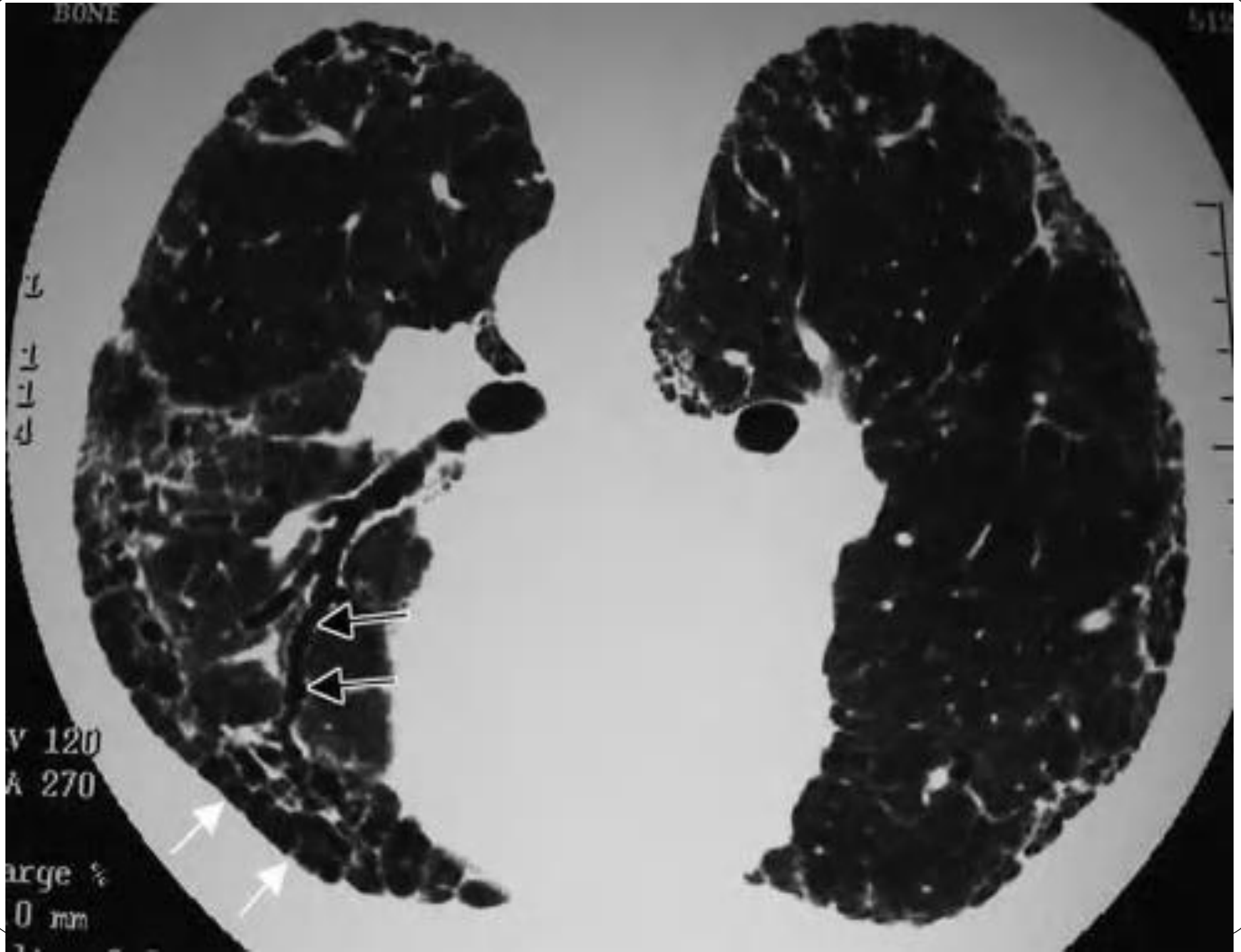
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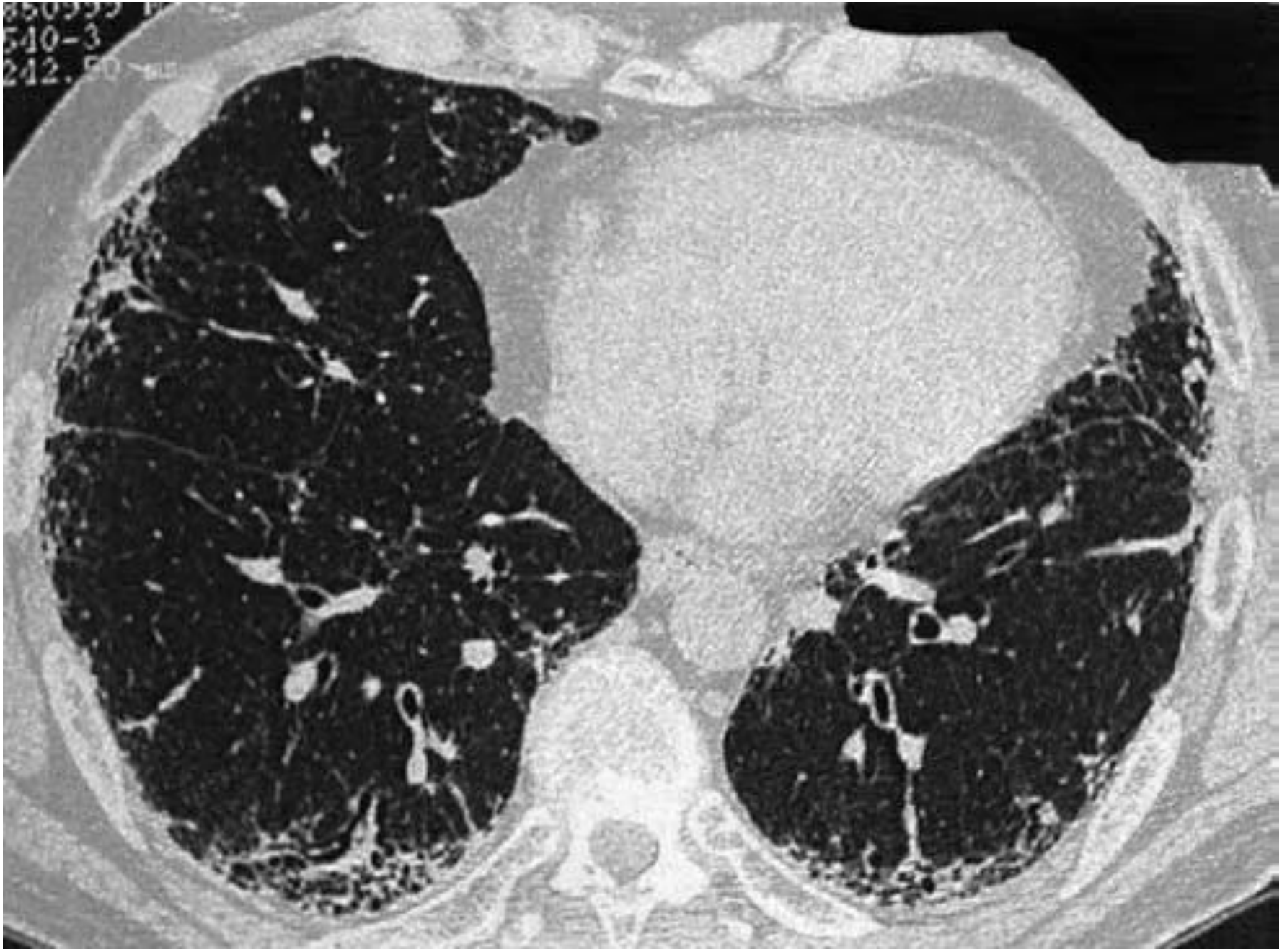
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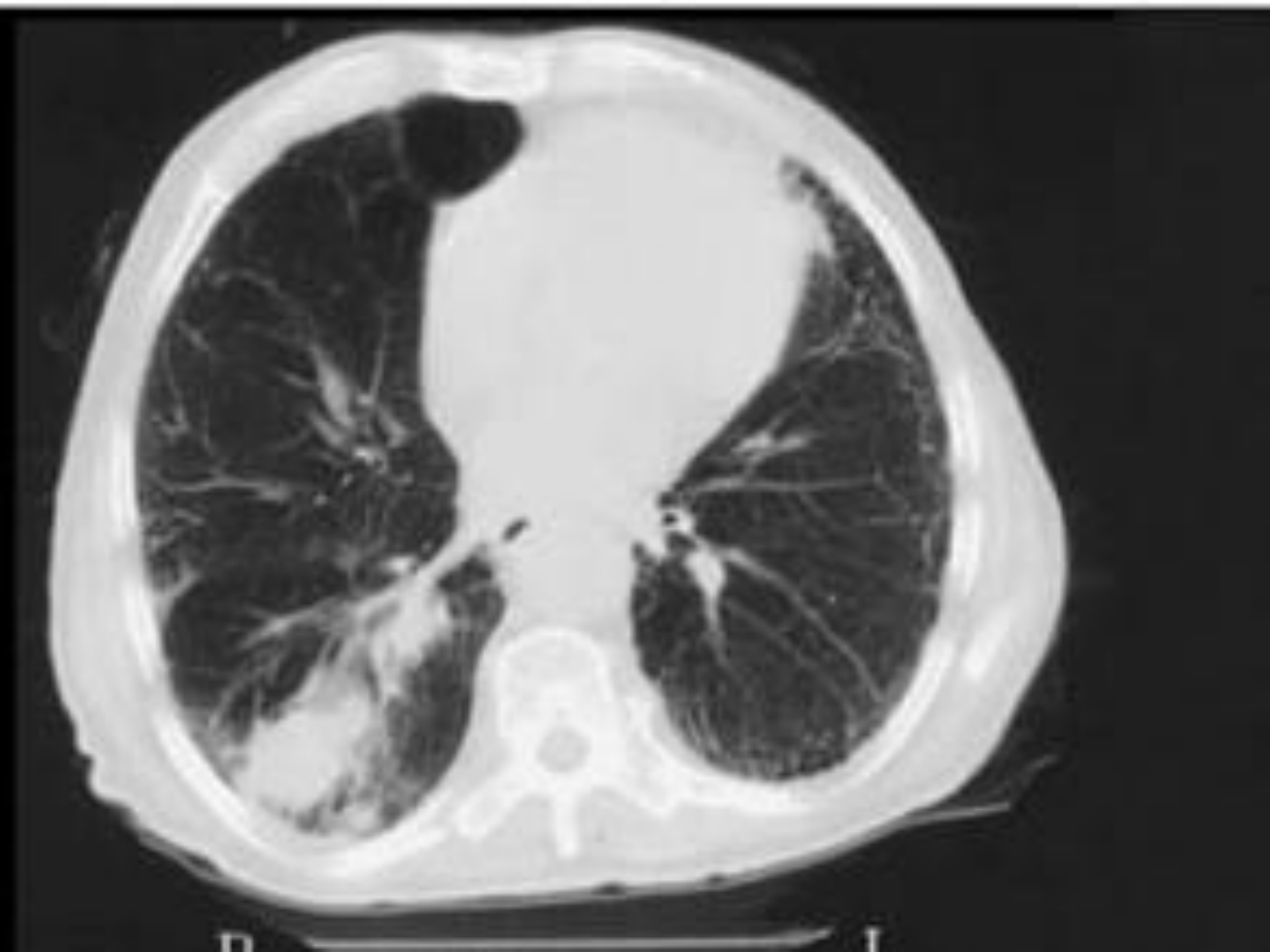
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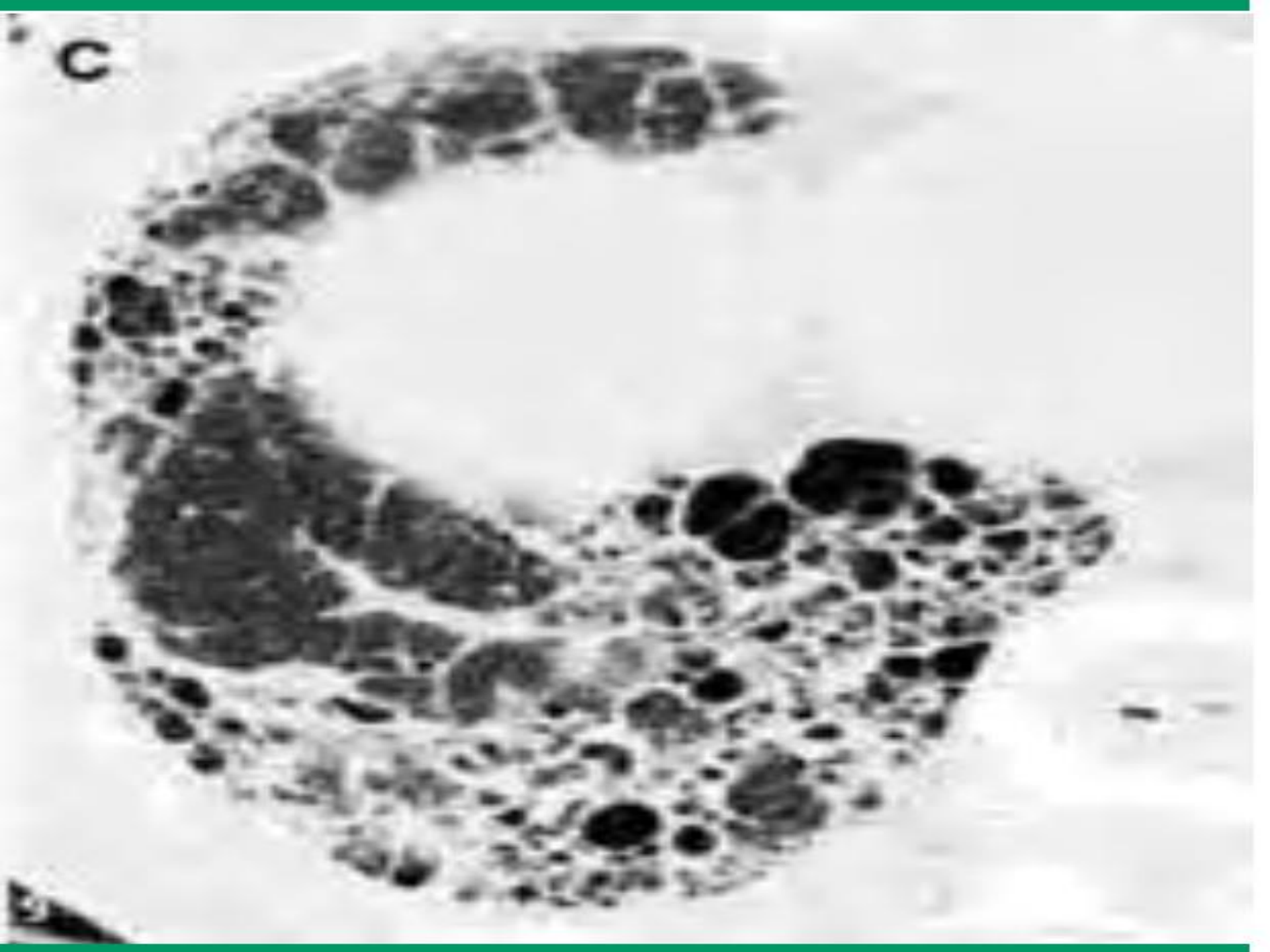
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treatment

- **steroids +/– immunosuppressants**
- **mean survival of 5 years after diagnosis**

treatment

- **Prednisolone therapy (0.5 mg/kg) combined with azathioprine (2-3 mg/kg)**

- is advocated for :

- **patients who are highly symptomatic or have rapidly progressive disease**
- **have a predominantly 'ground glass' appearance on CT**
- **a sustained fall of > 15% in their FVC or gas transfer over a 3-6-month period.**

*** objective evidence of improvement :prednisolone dose may be gradually reduced to a maintenance dose of 10-12.5 mg daily.**

*** response rates are notoriously poor**

*** Lung transplantation should be considered in young patients with advanced disease.**

Prognosis

- **median survival of 3 years is widely quoted**
- **desaturation on exercise heralding a poorer prognosis.**
- **The finding of high numbers of fibroblastic foci on biopsy suggests a more rapid deterioration.**
- **IPF is associated with an increased risk of carcinoma of the lung.**

CRYPTOGENIC ORGANIZING PNEUMONIA (BRONCHIOLITIS OBLITERANS WITH ORGANIZING PNEUMONIA- BOOP)

- **acute inflammation of bronchioles with granulation tissue and mononuclear cell infiltrate plugs**
- **idiopathic but may follow toxic fume inhalation/viral infection in children**
- **associated with connective tissue diseases, idiopathic pulmonary fibrosis, and hypersensitivity pneumonitis**

ذات الرئة المتعضية مجهولة السبب COP

- ذات الرئة المتعضية : تكاثر نسيج حبيبي في الأسناخ و الأقنية السنخية و ليس في الخلال
- يمكن مشاهدتها في : الانتان ، أدوية ، أمراض النسيج الضام زرع الأعضاء و UIP .
- BOOP
- سريرياً : زلة و سعال خلال أيام – أشهر & حمى
  * ذات رئة مكتسبة بالمجتمع
  * خراخر ناعمة بالقاعدتين شائعة و التبقرط نادر
- العمر : عمر وسطي : 50 سنة

ذات الرئة المتعضية مجهولة السبب COP

- الوظائف الرئوية : نمط حاصر خفيف ـ متوسط
- HRCT : تكثف بؤري في الجانبين تحت جنبي و حول قصبي ، عقيدات حول الأوعية ، كثافات خطية *
  الزجاج المغشى : أحياناً ، عش نحل نادر
- التشريح المرضي :
  *المظهر موحد للالتهاب خلالي خفيف مزمن & تليف ضمن لمعة القصيبات التنفسية و الأقنية السنخية و الأسناخ
  * لا يشاهد عش نحل

Clinical presentation

- **presents over weeks to months with systemic and respiratory symptoms, may have URTI 2-4 months prior to SOB**

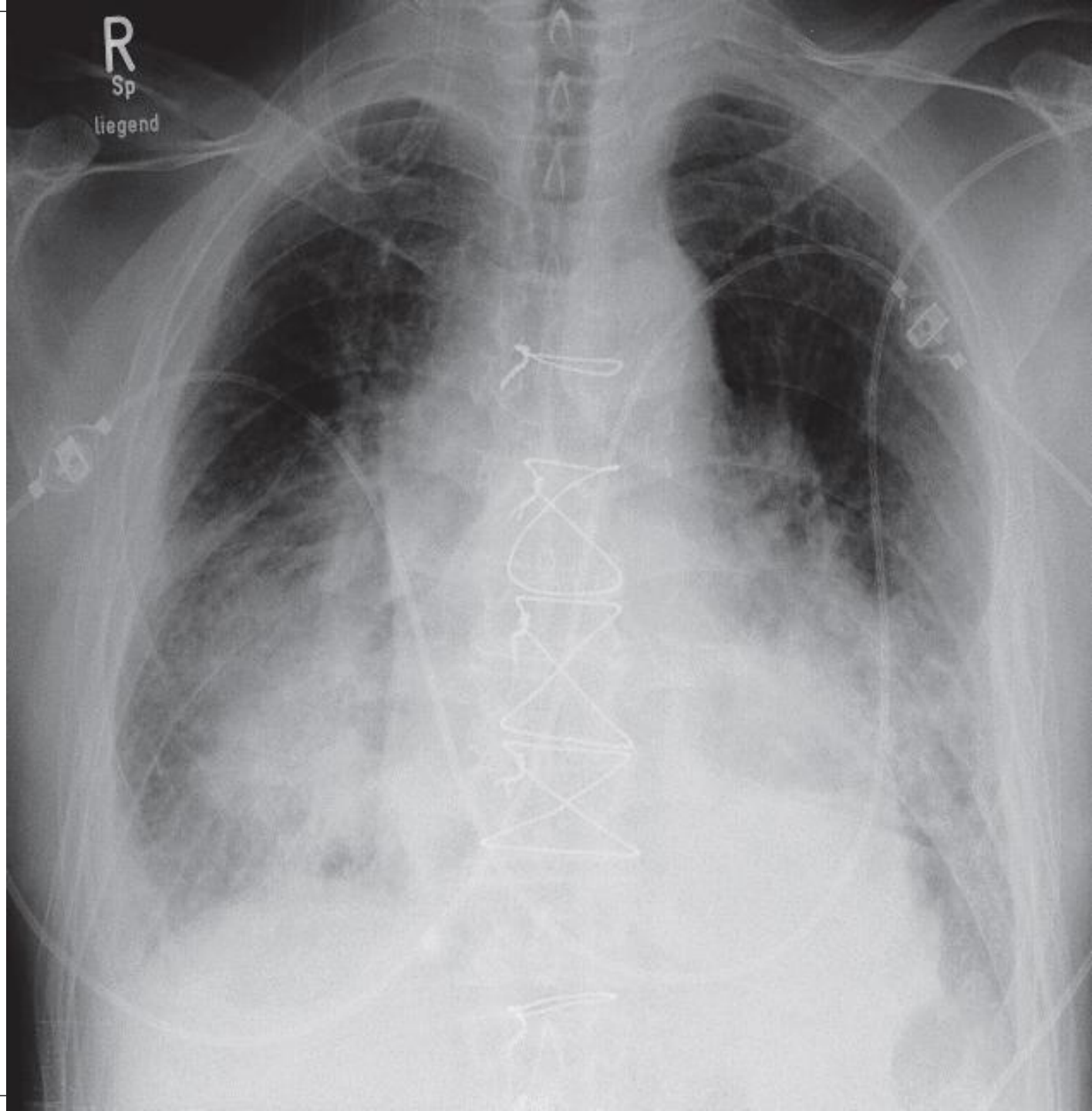
CXR

- **patchy peripheral infiltrates with alveolar pattern**

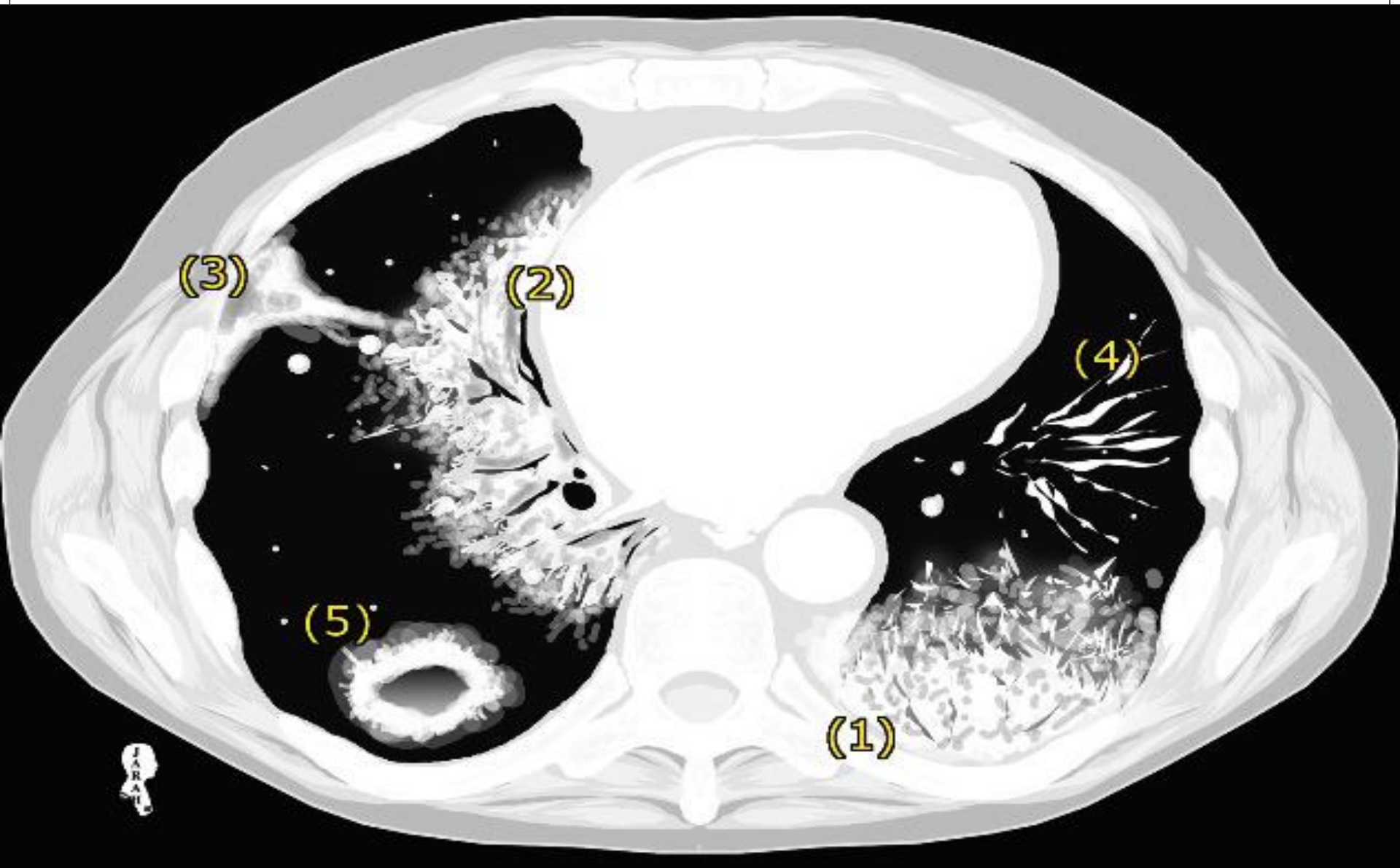
- **CT - "ground glass pattern"**

❑ **The CXR and CT often display a "ground glass" appearance.**

a patient with bone marrow transplant due to leukemia who developed COP shows bilateral patchy infi ltrations located at the lung bases with peripheral patchy infi ltration



HRCT demonstrates the different manifestations of COP: (1) peripheral classical patchy infi ltration of COP, (2) bronchogenic COP, (3) bronchocentric COP, (4) thickened interlobar septae, and (5) Atoll sign



treatment

- *corticosteroids (responds faster and more frequently (except in RA) than idiopathic pulmonary fibrosis)*

ذات الرئة المتعضية مجهولة السبب COP

- العلاج :
  * نسبة ضئيلة تشفى عفوياً
  * الستيرويدات : الجرعة المعتادة ـ 6 أشهر على الأقل
    الاستجابة : 80 %
  * سيكلوفوسفاميد : قليل الفائدة
- الانذار : البقيا بعد 5 سنوات 100 %
  تأخير العلاج ← الوفاة

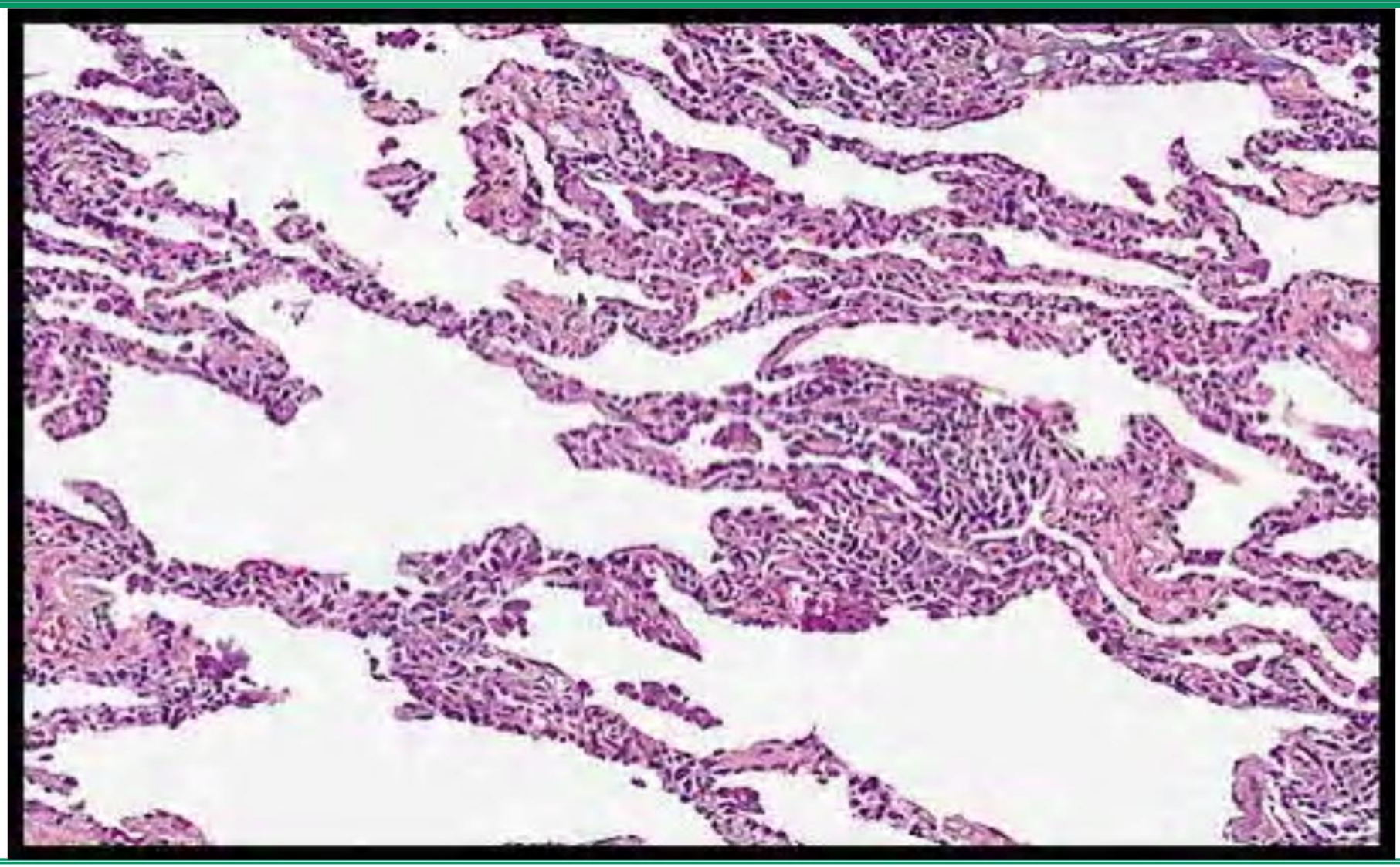
Non-specific interstitial pneumonia

- **The clinical picture : similar to that of IPF**
- **patients tend to be women and younger in age.**
- **associations occur with :**
  -connective tissue disease
  - certain drugs
  - chronic hypersensitivity pneumonitis.
- **HRCT findings are less specific**
- **NSIP is more likely to respond to immunosuppressive therapy than IPF**
- **prognosis is significantly better**
- **5-year mortality rate is typically less than 15%.**

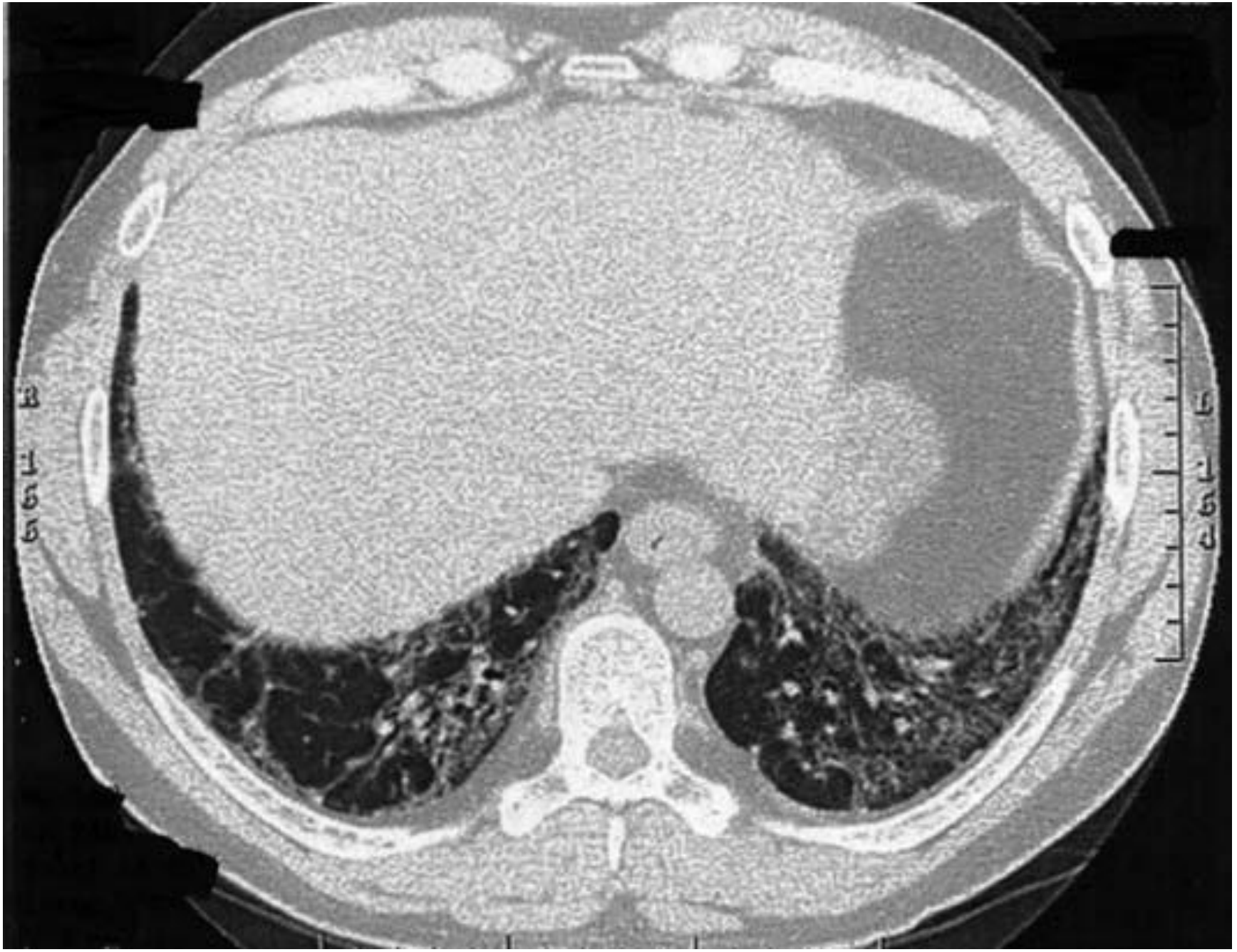
ذات الرئة الخلالية غير النوعية NSIP

- أسباب معروفة لها : أدوية ، أمراض النسيج الضام ، ذات الرئة بفرط التحسس
- لا تتميز بنمط سريري محدد (14% من IIP)
- سريرياً : زلة مزمنة & سعال و تبقرط نادر و حمى (ثلث المرضى) ، خراخر ناعمة بالقاعدتين
- العمر : 40 – 50 سنة
- الوظائف الرئوية : نمط حاصر
- HRCT : زجاج مغشى مسيطر تحت جنبي & نقص حجم بؤر تكثف & كثافات شبكية و عش نحل قليل

Nonspecific interstitial pneumonia, cellular pattern



The interstitium is infiltrated by a moderate chronic inflammatory infiltrate; fibrosis is absent. The infiltrate consists of lymphocytes and plasma cells.



ذات الرئة الخلالية الحادة AIP

- متلازمة هامان ريتش
- IIP حاد : تفاقم سريع خلال أيام ـ أسابيع ← قصور تنفسي
- التشريح المرضي : أذية سنخية منتشرة DAD
- سريرياً :
  - زلة & سعال خلال أيام – أسابيع ، أحياناً حمى
  - أعراض فيروسية
  - خراخر شهيقية منتشرة شائعة
- العمر الوسطي : 50 سنة
- وظائف الرئة : نمط حاصر & نقص أكسجة متفاقمة

ذات الرئة الخلالية الحادة AIP

- HRCT :
* الزجاج المغشي مع تكثف : مسيطر بالقاعدتين و كامل الساحتين
* المرحلة الباكرة : بؤرية
* عش نحل : نادر
- التشريح المرضي :
* مرحلة حادة من DAD :وذمة و تنخر ظهاري ، نتحة فيبرينية غشاء هيالينـي ، منتشرة .
* مرحلة متعضية :الأكثر شيوعاً ، تكاثر الخلايا الرئوية II مع زوال الغشاء الهيالينـي و النتحة & تكاثر الخلايا المولدة لليف
* التليف النهائي و عش نحل (مبطن بظهارة سنخية)

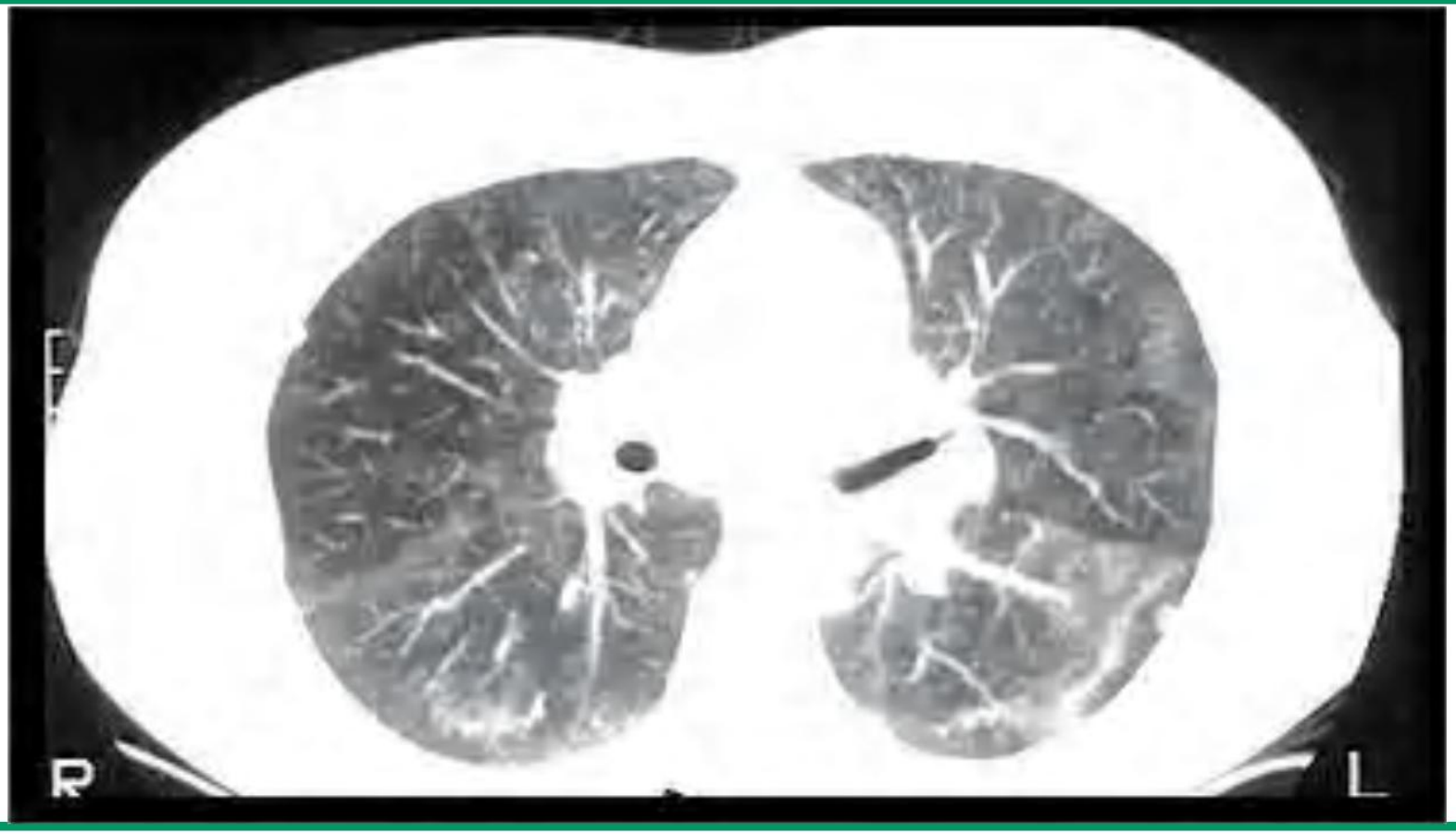
ذات الرئة الخلالية الحادة AIP

- العلاج :
  * الكورتيكوستيرويدات : دون فائدة واضحة
- الانذار : البقيا سيئة و أسوأ من ARDS
  الوفيات : 50 %

التهاب القصيبات التنفسية مع ذات رئة خلالية & ذات الرئة التوسفية RBILD & DIP

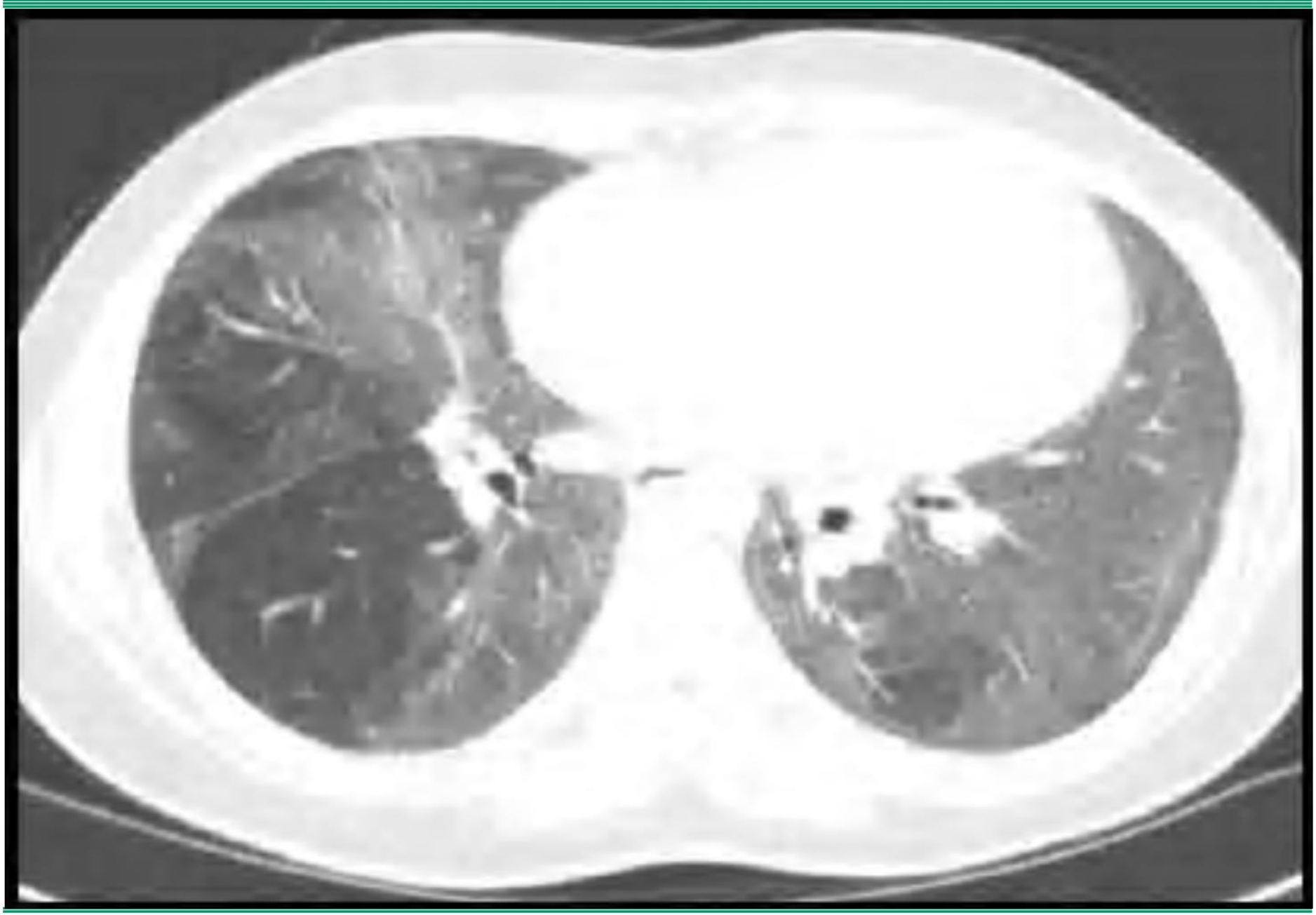
- تتحول RBILD إلى DIP (من IIP 8-16%)
- تظاهرات سريرية لتشريح مرضي واحد ؟
- سريرياً :
  زلة مزمنة & سعال ، خراخر شهيقية بالقاعدتين و أحياناً تبقرط
- العمر الوسطي : 30 – 40 سنة ، مدخنون ذكور أو تعرض سلبي
- الوظائف الرئوية : طبيعية أو ساد خفيف RBILD
  نمط حاصر DIP
- HRCT : RBILD : تسمك الجدار القصبي و عقيدات فصيصية مركزية و زجاج مغشى & حبس هواء
  DIP : زجاج مغشى معمم بتوزع محيطي ، عش نحل قليل

Respiratory bronchiolitis-associated interstitial lung disease



CT scan (5 mm thick section) in a 35-year-old woman with heavy smoking history and progressive dyspnea with exertion shows extensive ground-glass opacities. The plain chest film was normal. The diagnosis was confirmed by open

Desquamative interstitial pneumonia

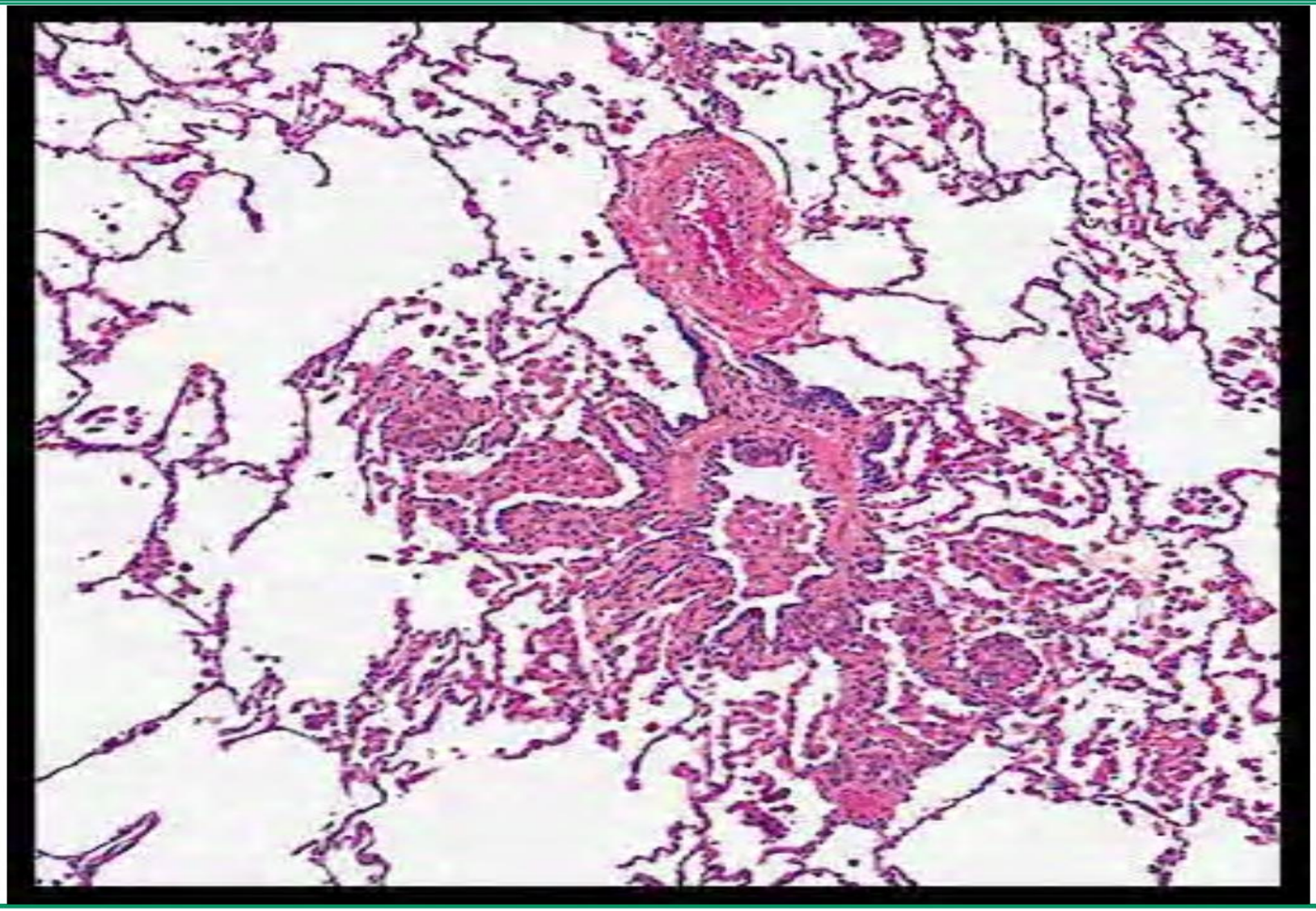


التهاب القصيبات التنفسية مع ذات رئة خلالية
& ذات الرئة التوسفية
RBILD & DIP

- التشريح المرضي :

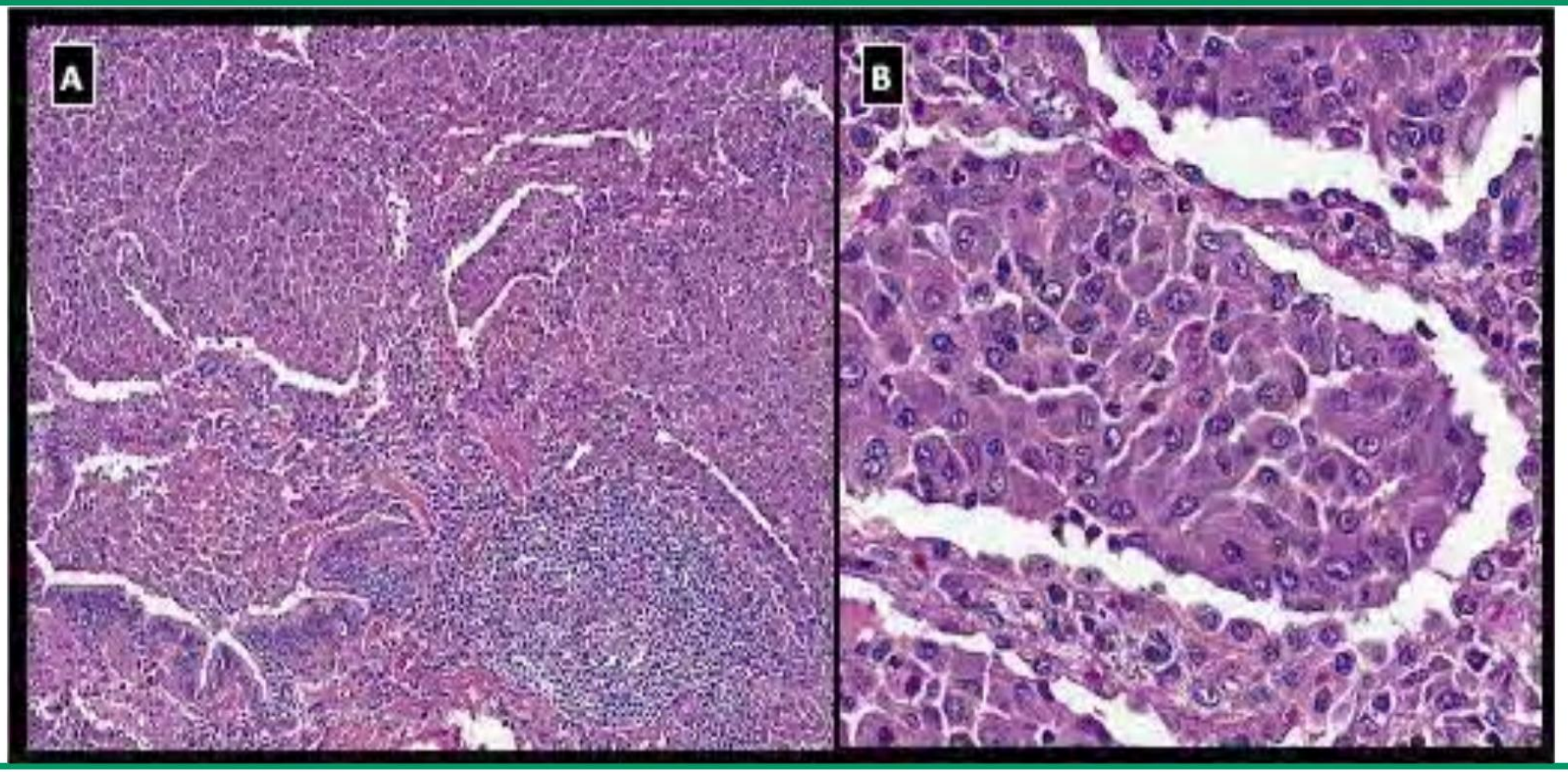
* مظهر تشريحي مشترك : بالعات كبيرة محملة بالصباغ
* ارتشاح البالعات الكبيرة المصطبغة في القصيبات التنفسية و حولها هو RBILD *
ارتشاح البالعات الكبيرة المصطبغة بشكل سنخي منتشر هو DIP

Respiratory bronchiolitis in patient with respiratory bronchiolitis-associated interstitial lung disease



Faintly pigmented alveolar macrophages fill the lumen of this respiratory bronchiole and the surrounding airspaces. There is a mild thickening of the wall of the respiratory bronchiole.

Desquamative interstitial pneumonia pattern



(A) The alveolar spaces are diffusely involved by marked alveolar macrophage accumulation and there is mild interstitial thickening. (B) The alveolar walls are mildly thickened by fibrous connective tissue and a few chronic inflammatory cells. The alveolar spaces are filled with macrophages.

التهاب القصيبات التنفسية مع ذات رئة خلالية & ذات الرئة التوسفية RBILD & DIP

- **العلاج :**
  - *** إيقاف التدخين ← الشفاء**
  - *** الكورتيكوستيرويدات : 3 أشهر**
  - *** إيقاف التدخين & الكورتيزون في RBILD : شفاء %**
  - *** DIP : الاستجابة للكورتيزون 60 %**
- **الانذار : جيد ، البقيا : 70 % لخمس سنوات**
  التليف الرئوي و RBILD غير موجود

TABLE 10 Pathologic Classification and Distinguishing Radiographic Features of the Idiopathic Interstitial Pneumonia

Histologic Pattern	Microscopic Findings	Radiographic Correlate
Idiopathic pulmonary fibrosis	Patchy, heterogeneous disease	Lower lobe reticulation
	Subpleural honeycomb fibrosis	Subpleural honeycombing
	Proliferating fibroblast foci	Traction bronchiectasis
	Minimal inflammation	
Nonspecific interstitial pneumonia	Uniform disease activity	
	Intense interstitial inflammation	Lower lobe reticulation
	Fibrosis, if present, more temporally uniform than idiopathic pulmonary fibrosis	Ground-glass infiltrates
Desquamative Interstitial pneumonitis/ respiratory bronchiolitis interstitial lung disease	Uniform disease activity	Ground-glass infiltrates,
	Distal airspaces filled with pigmented macrophages	No honeycomb change
	Peribronchiolar inflammation with little fibrosis	Few or no signs of architectural distortion
Acute interstitial pneumonia	Diffuse alveolar damage	Dense bilateral infiltrates
	Alveolar hyaline membranes	Ground-glass infiltrates
	Proliferating type II cells	Air bronchograms
	Collapse of alveoli spaces	
Cryptogenic organizing pneumonia	Bronchiolocentric inflammation	Focal, patchy consolidations
	Airspaces plugged by granulation tissue	Ground-glass infiltrates
		Bronchiolocentric nodules

19.80 Conditions which mimic interstitial lung diseases

Infection

- Viral pneumonia
- *Pneumocystis jirovecii*
- *Mycoplasma pneumoniae*
- TB
- Parasites, e.g. filariasis
- Fungal infection

Malignancy

- Leukaemia and lymphoma
- Lymphatic carcinomatosis
- Multiple metastases
- Bronchoalveolar carcinoma

Pulmonary oedema Aspiration pneumonitis