Diffuse Parenchymal Lung Disease: Diagnosis and Management

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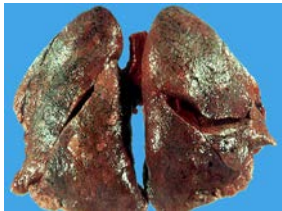
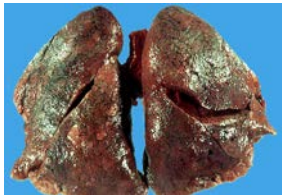


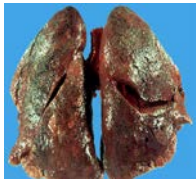
Case : 1

- A 65-year-old banker presented with progressive exertional dyspnoea with dry cough for 12 m
- Ex-smoker of 15 pack-year history
- No significant environmental exposures to mould, birds, dust & on irbesartan
- No features of CTD
- His resting SpO_2 was 96%, which dropped to 87% with sit-to-stand exercise



contd.

- He had
  - Marked digital clubbing
  - Fine bibasilar velcro-like crepitations
  - no evidence of cor pulmonale
- Spirometry: restrictive pattern
  - ⬇ FEV_1, ⬇ FVC & normal spirometric ratio
- No improvement with inhaled bronchodilator

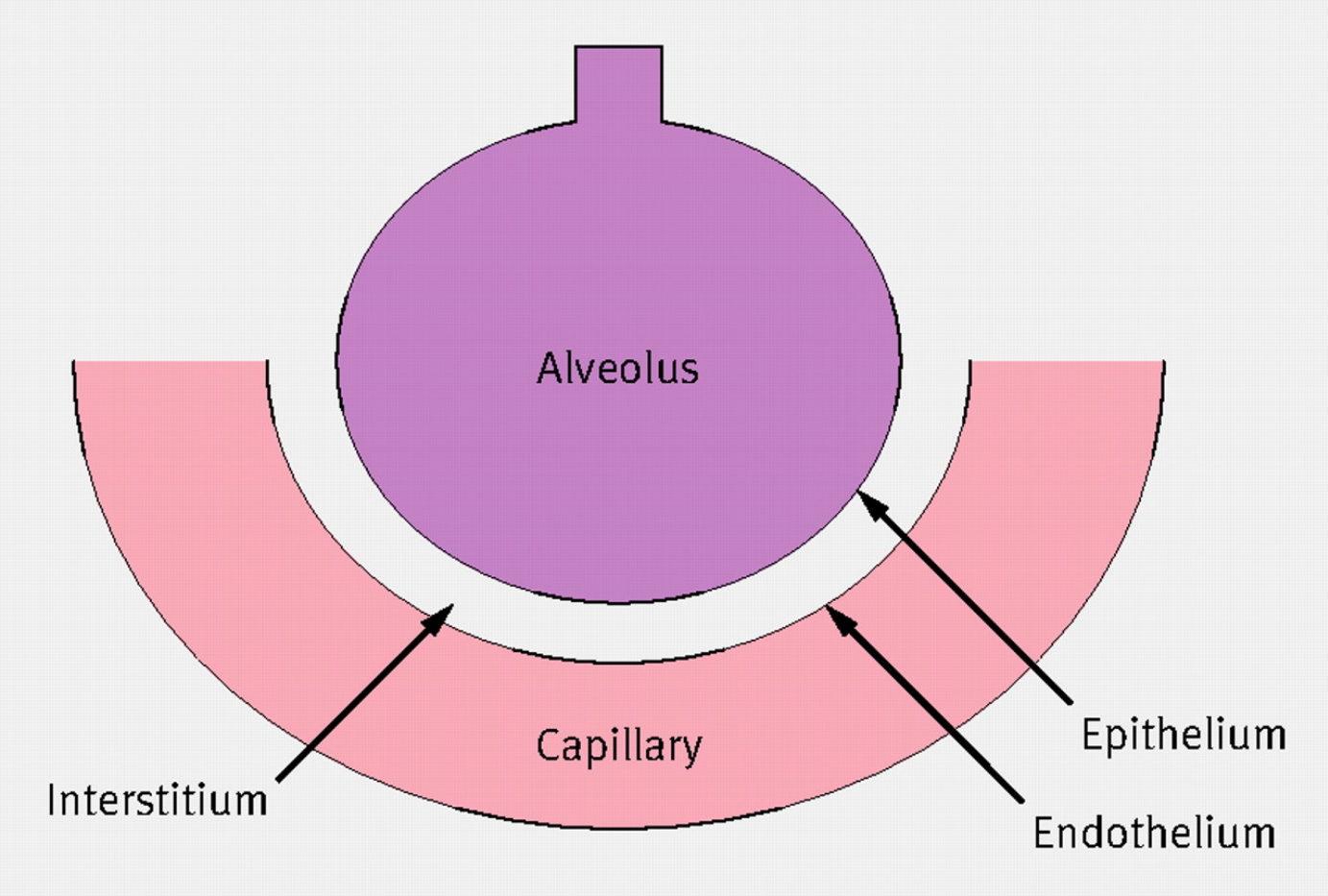


- What is the diagnosis?

What is DPLD?

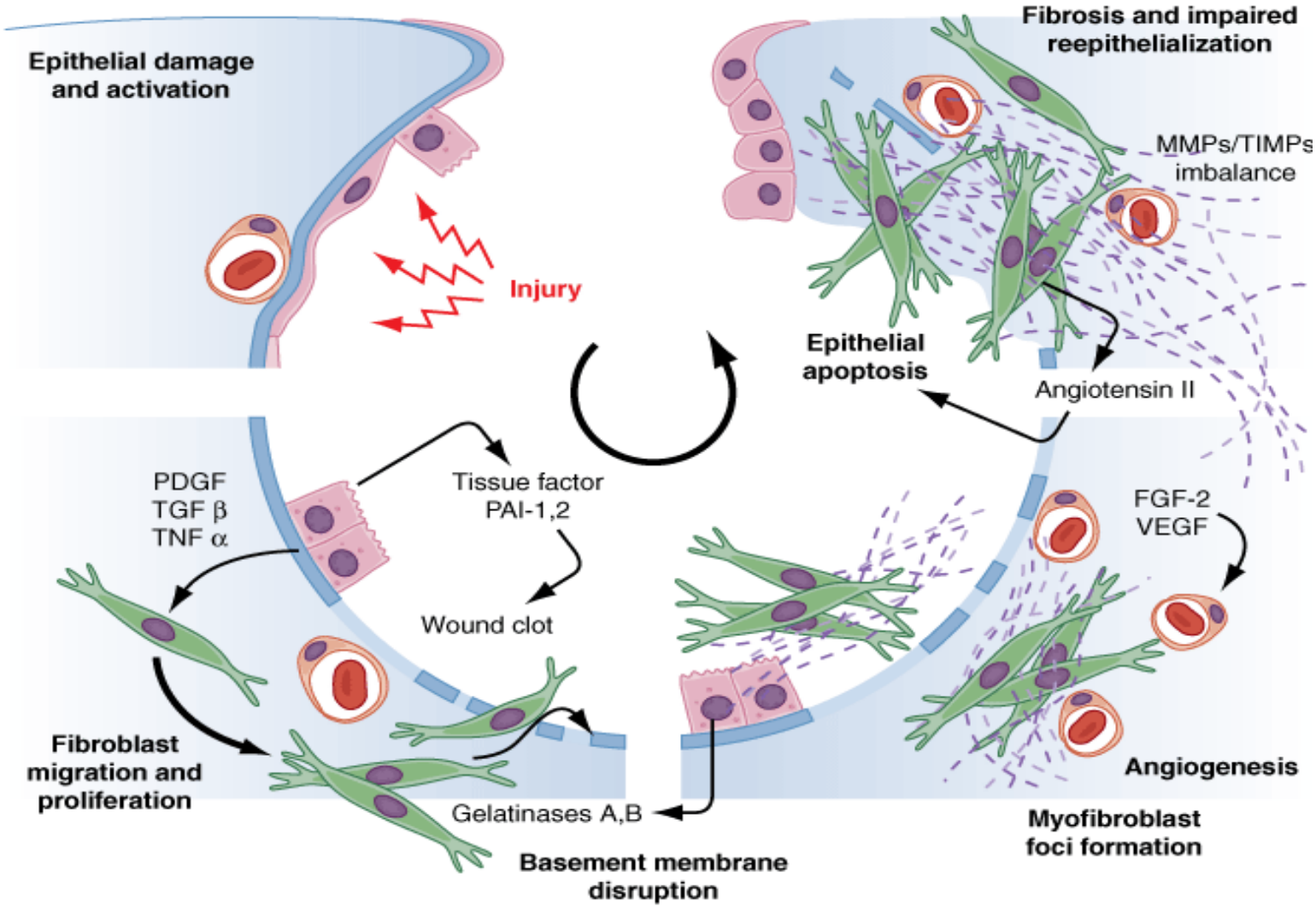
- DPLDs are
  - a group of >200 disorders
  - affect pulmonary interstitium
  - present with breathlessness, chronic cough, inspiratory crackles and
  - abnormal spirometry
- Incidence
  - Males 31.5/100,000
  - Females 26.1/100,000

Fig 1 The Pulmonary Interstitium



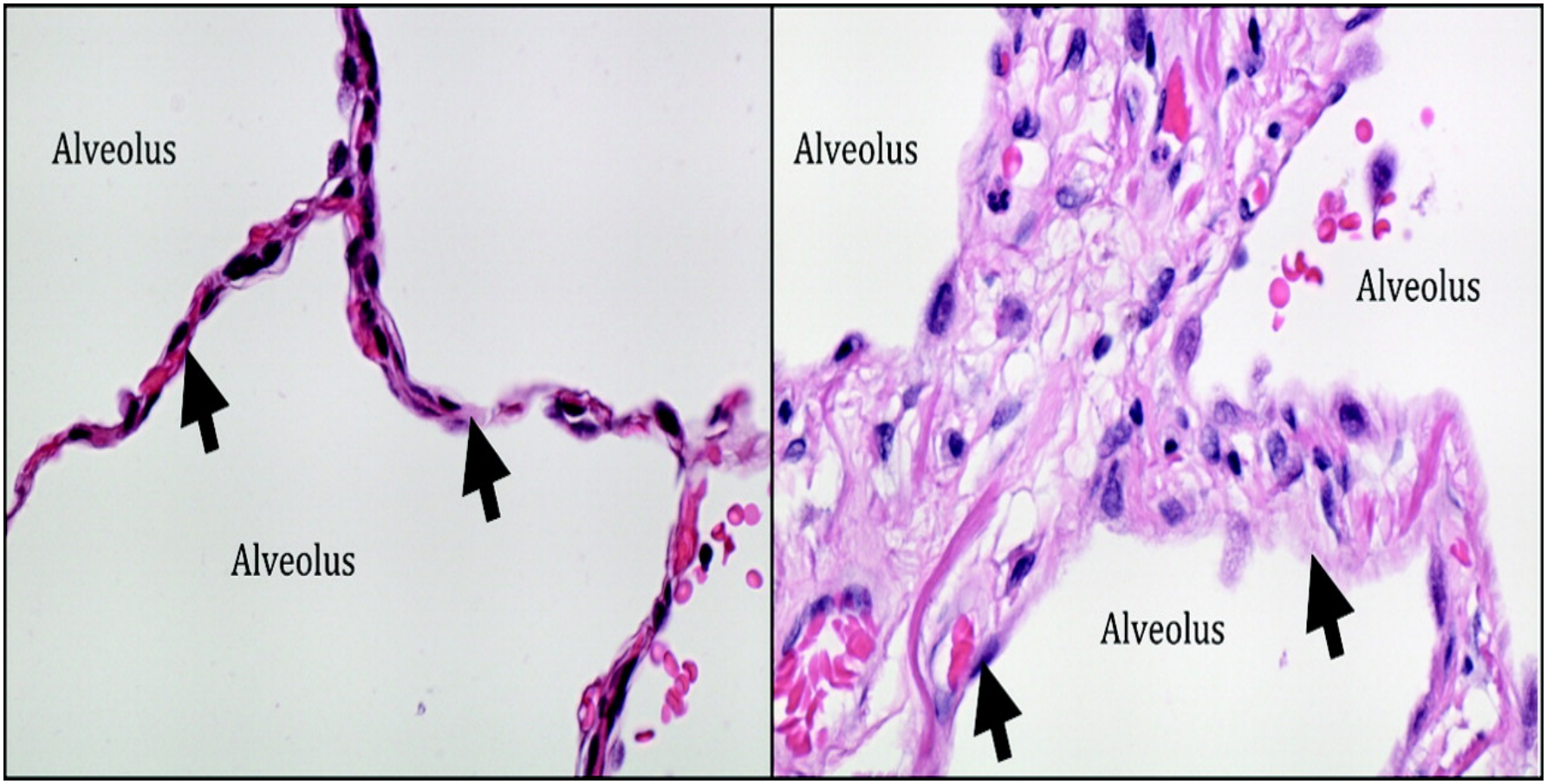
Dempsey, O. J. et al. BMJ 2010;340:c2843

Pathogenesis



Harrison 18th Ed

Fig 2 Arrows indicate pulmonary interstitium in (left) healthy lung and (right) pulmonary fibrosis.



Dempsey, O. J. et al. BMJ 2010;340:c2843

BMJ

Diffuse Parenchymal Lung Disease

- DPLD of known cause (e.g. drugs, dust exposure, collagen vascular disease)
- Idiopathic interstitial pneumonias
  - Idiopathic pulmonary fibrosis (IPF)
  - IIP other than idiopathic pulmonary fibrosis
    - Desquamative interstitial pneumonia (DIP)
    - Respiratory bronchiolitis/ Interst. lung dis. (RBILD)
    - Acute interstitial pneumonia (AIP)
    - Cryptogenic organising pneumonia (COP)
    - Nonspecific interstitial pneumonia (NSIP)
    - Lymphocytic interstitial pneumonia (LIP)
- Granulomatous DPLD (e.g. sarcoidosis)
- Other forms of DPLD (e.g. LAM, HX, eosin. pneum. etc.)

ATS 2002

Updated classification of IIP- ATS/ERS 2013

- Major IIP
  - IPF
  - NSIP
  - RB-ILD
  - DIP
  - COP
  - AIP
- Rare IIP
  - Lymphocytic interstitial pneumonia
  - Idiopathic pleuroparenchymal fibroelastosis (IPPF)
- Unclassifiable IIP

Table 255-2 Estimated Relative Frequency of the Interstitial Lung Diseases

Diagnosis	Relative Frequency, %
Idiopathic interstitial pneumonias	40
Idiopathic pulmonary fibrosis	55
Nonspecific interstitial pneumonia	25
Respiratory bronchiolitis—ILD and desquamative interstitial pneumonia	15
Cryptogenic organizing pneumonia	3
Acute interstitial pneumonia	<1
Occupational and environmental	26
Sarcoidosis	10
Connective tissue diseases	9
Drug and radiation	1
Pulmonary hemorrhage syndromes	<1
Other	13

Source: From DB Coultas, R Hubbard, in JP Lynch III (ed): *Lung Biology in Health and Disease*. New York, Marcel Dekker, 2004; and S Garantziotis et al: J Clin Invest 114:319, 2004.

Harrison 18 th ed

Diagnostic approach

- ATS/ERS
  - Integrated clinical
  - radiological and
  - pathological approach

DPLD History:

1. AGE:

- 20-40 years: Sarcoidosis, CTD, LAM, EG
- 50 years: IPF

2. GENDER:

- Female predominant:

  ILD associated with CTD, LAM

- Male predominant:

  ILD associated with RA

  Pneumoconiosis

DPLD History contd. :

3. Smoking:

- **associated with** smoker:
  - DIP, RB- ILD, EG, Histocytosis X
- **less likely** to be seen in smoker:
  - Hypersensitivity pneumonitis
  - Sarcoidosis

DPLD History contd. :

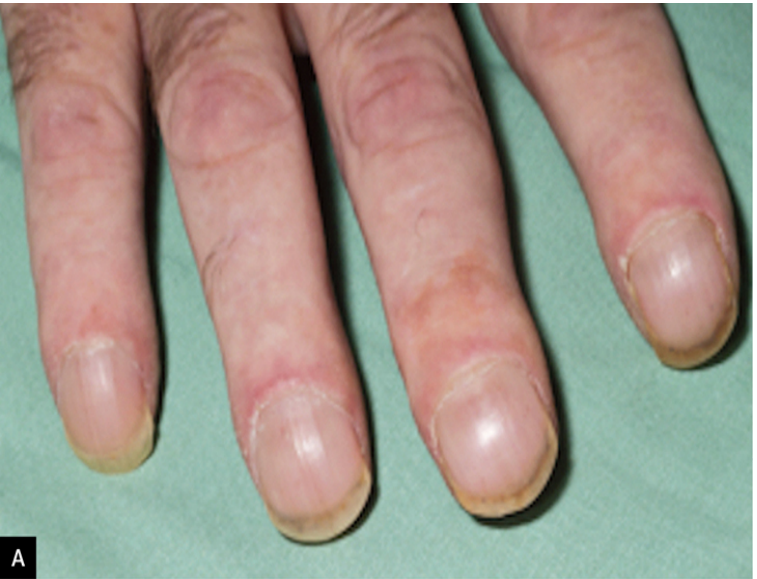
4. *Onset of symptoms:*
   - *Acute:* AIP, eosinophilic pneumonia, BOOP
   - *Sub-Acute/Chronic:* IPF, silicosis/ asbestosis
5. Co morbidity – CTD, IBD
6. Drug exposure - http://www.pneumotox.com
7. H/o. Occupation/ social/leisure
   - avian, animal, fish proteins, fungal spores
   - asbestos, silica, cobalt, beryllium, etc

SYMPTOMS OF DPLD

1. **Dyspnea**
2. **Cough:** dry and non productive
3. **Wheezing:** uncommon, may present in
   - Chronic eosinophilic penumonia
   - Churg-Strauss syndrome
   - RB- ILD
4. **Weight loss:** COP or BOOP
5. **Features of CTD**

Examination

- Dry bibasilar crackles
- Inspiratory high-pitched rhonchi (“squeaks”): bronchiolar disorders
- Clubbing (most common in IPF)
- PH/ Right heart failure
- Signs of underlying CTD

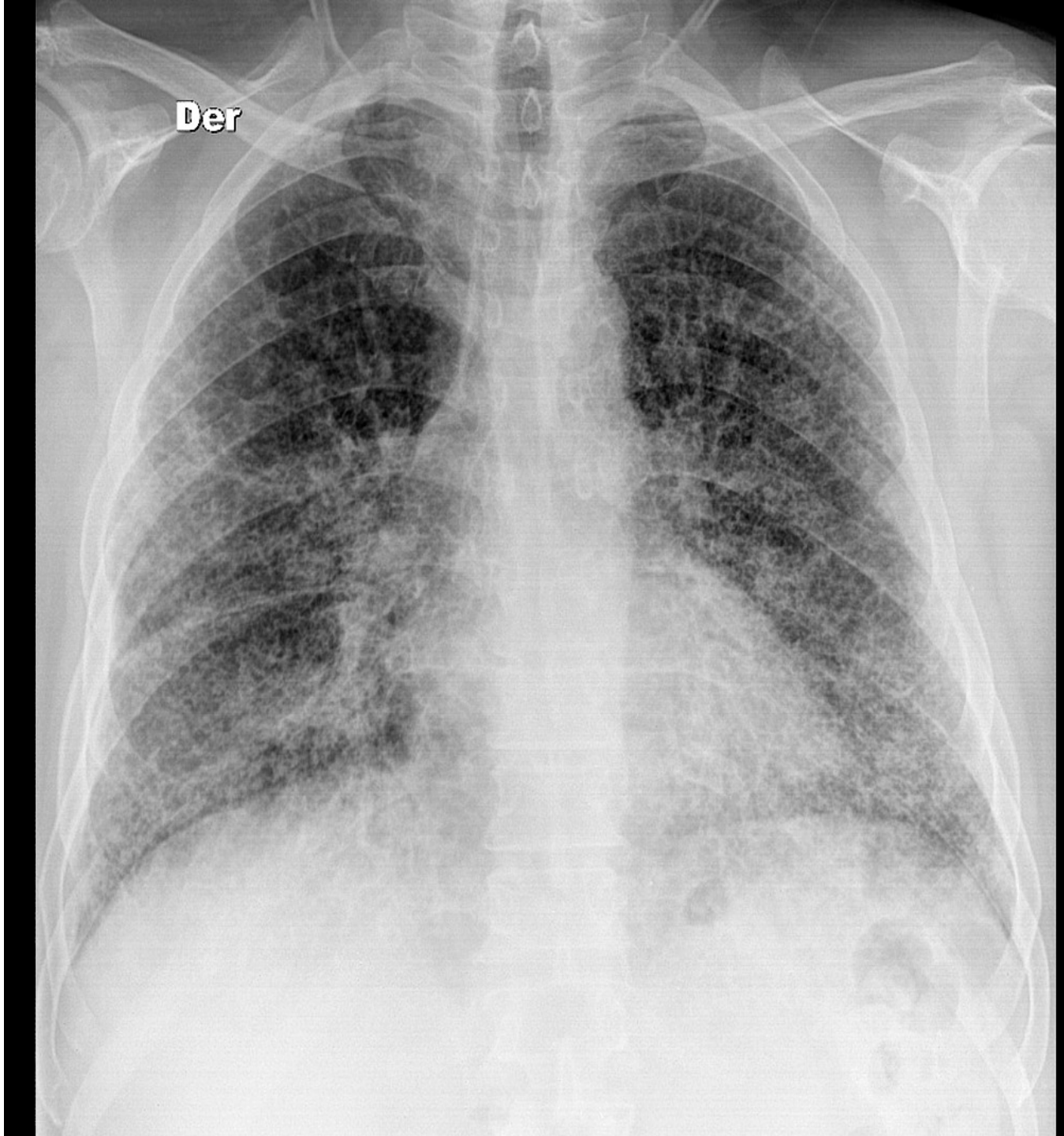


DPLD investigations. RACGP2015; 44(8):546-552.

	Investigation	Possible findings
Routine at baseline and follow up	•Chest X-ray	•Non-specific infiltrates
	•HRCT scan	•Nodules •Cysts •Ground glass change •Honeycomb change •Traction bronchiectasis •Intralobular septal thickening
	•Pulse oximetry/ ABG	•Low SpO_2, Low PaO_2

X- ray

IPF



DPLD investigations. RACGP2015; 44(8):546-552.

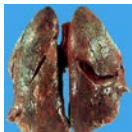
	Investigation	Possible findings
Routine at baseline and follow up	•Connective tissue disease serology	• ANA, ENA, RF, myositis antibodies, ANCA
	•Lung function tests	•FEV_1, FVC: ↓ •FEV_1/FVC ratio: N or ↑ •Lung volumes: ↓ •DLCO: ↓
	•6-minute walk test	•Reduced walk distance •Oxygen desaturation

Table 1. DPLD investigations. RACGP2015; 44(8):546-552.

	Investigation	Possible findings
Occasional	•Bronchoscopy with lavage	• Frequently normal
	•Surgical lung biopsy	•Variable and specific for diagnosis
	•Echocardiogram	•Pulmonary hypertension •RV dysfunction
	•Right heart catheter	•Confirmation of PH

- The ATS/ERS/JRS/ALAT 2011 guidelines: HRCT features for **“UIP”, “possible UIP” and “inconsistent with UIP”** patterns

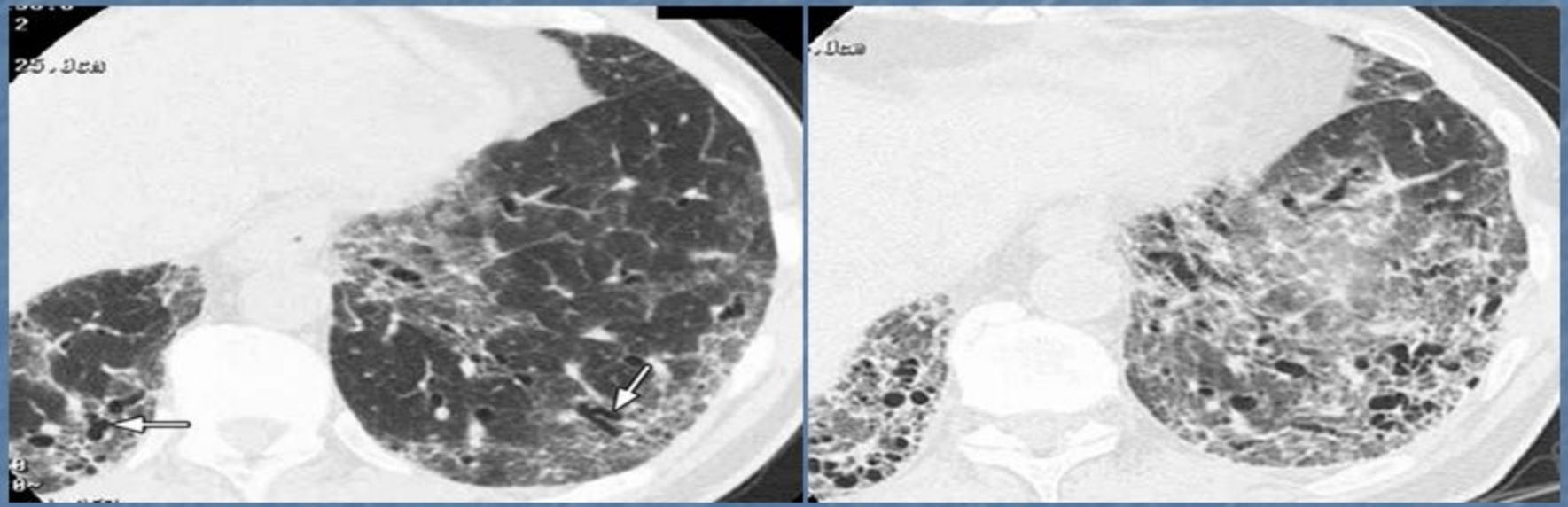
- In the appropriate clinical setting, HRCT pattern of UIP obviates a diagnostic SLB



HRCT criteria for UIP pattern

UIP Pattern (All 4 Features)	Possible UIP Pattern (All 3 Features)	Inconsistent with UIP Pattern (any of the 7 Features)
■ **Subpleural, basal** predominance	■ Subpleural, basal predominance	■ **Upper or mid-lung** predominance
■ **Reticular** abnormality	■ Reticular abnormality	■ **Peribronchovascular** predominance
■ **Honeycombing ± traction bronchiectasis**	■ Absence of features as inconsistent UIP	■ Extensive **ground glass** (>reticular) abnormality
■ Absence of features as inconsistent with UP		■ Profuse **micronodules** (bilateral, predominantly upper lobes)
Am J Respir Crit Care Med. 2011;183(6):788–824.		■ **Discrete cysts** (multiple, bilateral, away from areas of honeycombing)
		■ Diffuse **mosaic attenuation/air-trapping** (bilateral in ≥ 3 lobes)
		■ **Consolidation** in broncho-pulmonary segment(s)/lobe(s)

CT features of UIP



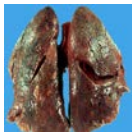
- Left: left lower lobe shows peripheral ground-glass opacity and reticular patterns with traction bronchiectasis (arrow)
- Right: same patient two years later with progression of ground-glass to reticular pattern and honeycombing and progression of traction bronchiectasis

Images from Lynch et al., 2005

Table 1: Clinical conditions associated with UIP pattern

- IPF/cryptogenic fibrosing alveolitis
- Collagen vascular disease
- Chronic hypersensitivity pneumonitis
- Asbetosis
- Drug toxicity

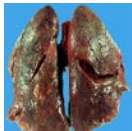
- ***Respir Res. 2013; 14(Suppl 1): S2***



Bronchoalveolar lavage (BAL)

- Before initiation of Rx
- Diagnostic of
  - hypersensitivity pneumonitis
  - sarcoidosis
  - infection
  - malignancy

Thorax 2008;63(Suppl V):v1–v58



Diagnostic features of BAL in ILD

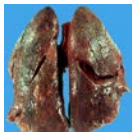
Disease category	Examples	Findings in BAL fluid
Malignancy	Lymphangitic carcinomatosis, Bronchioloalveolar cell ca, Pulmonary lymphoma	Malignant cells
Due to inhaled (exogenous) material	Asbestosis	Ferruginous bodies
	Silicosis	Dust particles by polarized microscopy
Inflammatory	Diffuse alveolar hemorrhage	Large numbers of erythrocytes, Hemosiderin-laden macrophages
	Chronic eosinophilic pneumonia	Eosinophils ≥40 percent
	Acute eosinophilic pneumonia	Eosinophils ≥25 percent
	Pulmonary Langerhans cell histiocytosis (Histiocytosis X)	Monoclonal antibody (T6) + ve histiocytes, CD1 positive Langerhans cells >5 %, Birbeck granules in macrophages

BAL Cytology in ILD

Disease	Macrophage	Lympho	Eosino	Neutrphil
IPF		↑	↑	↑↑
NSIP		↑	↑	↑↑
COP		↑↑	↑	↑
Sarcoidosis		↑↑	→	→
HP	Foamy appearence	↑↑↑	↑	→
AIP		↑	↑	↑↑
Pneumoconiosis	Inclusion particles	↑	↑	→
Eosinophilic pneumonia		↑	↑↑	→
Drug induced ILD	Foamy appearence	↑↑	↑↑	↑

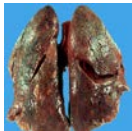
IPF:

- Histological appearance of UIP
- Incidence 5-10/1 million
- Median survival 2.9-5 yrs at diagnosis
- Unknown etiology
- 2-5% in families, usually in younger age, even in children



IPF-Risk Factors

- Cigarette smoking
- Drugs-antidepressant
- GERD
- Environmental exposure- wood dust and metal dust (steel, brass, lead, pine wood)
- Infectious agents-EBV, CMV, HIV



Clinical Feature-IPF

- **Symptoms**:
  - Age 50-70 y
  - M>F=3:2
  - Progressive dyspnea
  - Nonproductive cough: may be paroxysmal
  - **Constitutional symptoms - unusual**
- **Signs**:
  - Clubbing 25-50%, cyanosis
  - End inspiratory creps in 90%
  - PH, Right heart failure- late

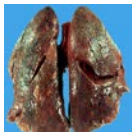


Table 2 ATS/ERS criteria for diagnosis of idiopathic pulmonary fibrosis (IPF) in the absence of surgical lung biopsy*†

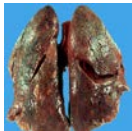
Major criteria	Minor criteria
► Exclusion of other known causes of ILD such as certain drug toxicities, environmental exposures and connective tissue diseases	► Age >50 years
► Abnormal pulmonary function studies that include evidence of restriction (reduced VC, often with an increased FEV_1/FVC ratio) and impaired gas exchange (increased $P(A–a)o_2$, decreased Pao_2 with rest or exercise or decreased T_{LCO})	► Bibasilar, inspiratory crackles (dry or "Velcro"-type in quality)
► Bibasilar reticular abnormalities with minimal ground glass opacities on HRCT scans	► Insidious onset of otherwise unexplained dyspnoea on exertion
► Transbronchial lung biopsy or BAL showing no features to support an alternative diagnosis‡	► Duration of illness >3 months

BAL, bronchoalveolar lavage; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; HRCT, high resolution computed tomography; ILD, interstitial lung disease; $P(A–a)o_2$, difference between alveolar and arterial pressure; Pao_2, arterial oxygen tension; T_{LCO}, carbon monoxide transfer factor; VC, vital capacity.

BTS 2008, AUSTS, NEZTS, IRISH TS

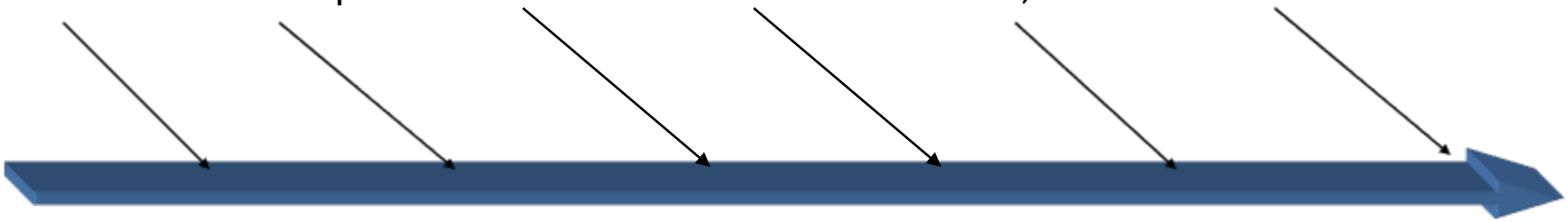
IPF-Rx

- The optimal medical therapy has yet to be identified
- Pros, cons, risks, benefits, and alternatives must be considered



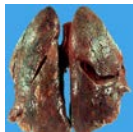
The Evolution of IPF therapy

- Steroids Azathioprine anti-oxidants anti-fibrotic ERA's,anti-TNF ??????



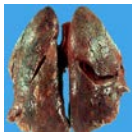
1950s

2004



N-Acetyl Cysteine

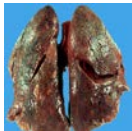
- Restores glutathione
- Reduces fibroblasts
- Decreases ECM components
- Inhibits proinflammatory & profibrotic cytokines



IFIGENIA trial

(Idiopathic Pulmonary Fibrosis International Group Exploring *N*-Acetylcysteine I Annual)

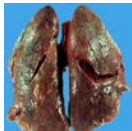
- 155 patients: (prednisone, azathioprine, and acetylcysteine: 600mg t.i.d)
- 1º endpoint at 12 months
  - 15% Δ VC
  - 20% Δ DLCO
- Result: Preserved pulmonary function better than a two-drug regimen of azathioprine plus prednisone



PANTHER-IPF

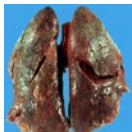
(Prednisone, Azathioprine, and NAC: A Study that Evaluates Response in IPF)

- The PANTHER-IPF study: could **slow disease progression and improve lung function** in people with moderate IPF or not?
- In October 2011, triple-therapy arm stopped, because **more people died (11% vs. 1%), were hospitalized (29% vs. 8%) and had serious adverse events (31% vs. 9%)**
- The NAC and placebo arms will continue on



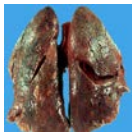
N-Acetyl Cysteine

- Randomized Trial of Acetylcysteine in Idiopathic Pulmonary Fibrosis
- No benefit
- N Engl J Med 2014; 370:2093-2101



Interferon Gamma (INF-γ 1b)

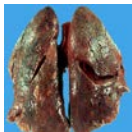
- Anti-fibrotic, anti-infective, anti-proliferative, and immunomodulator
- Raghu G 2004: R, MC, PC, DB; 330 patients
  - SC 200 µg 3 times/ wk, 58 wk follow up
  - Did not significantly affect progression-free survival, pulmonary function, or QOL
- In 2009: effect on survival (INF-γ 15% vs placebo 13% died)
- Rx- Not recommended
- Am J Respir Crit Care Med 2008; 78(9): 948-55



Etanercept- anti TNF

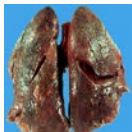
- TNF–α, a cytokine with inflammatory and fibrogenic properties
- Raghu G 2008: R, MC, DB, PC 48-week trial,
- [Etanercept (25 mg twice weekly sc)]
- Result: well tolerated
- No differences in the predefined endpoints & disease progression

- Am J Respir Crit Care Med *2008*;177:75–81



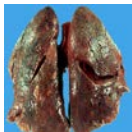
Bosentan

- BUILD I (IPF)
  - R, MC, DB, PC, 158 pt
  - 1º endpoint at 12 months: 6 MWT
  - 2 º endpoint: mortality, lung function, QOL
  - not superior in 1º outcome, but had better 2º outcome
- BUILD III (IPF): 616 patients
  - to demonstrate delay disease worsening or death in patients: no difference
- Should not be treated with bosentan



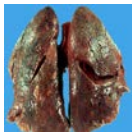
Sildenafil,

- Sildenafil, a PDE -5 Inhibitor
- MC, DB, RCT, PC trial
- 1º endpoint at 12 weeks: 20% improvement of 6 MWT (20mg tds)
- No significant difference of 1º outcome
- Statistically significant differences in change in dyspnea, PaO_2, DLCO and QOL



Pirfenidone:

- Antifibrotic agent
  - Decreases fibroblast proliferation
  - Decreases ECM production
  - Inhibits TGF-β collagen synthesis
  - Inhibits mitogenic effect of PDGF
  - Ameliorated fibrosis in a hamster model of bleomycin lung
- Orally active, Safe

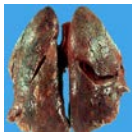


Pirfenidone

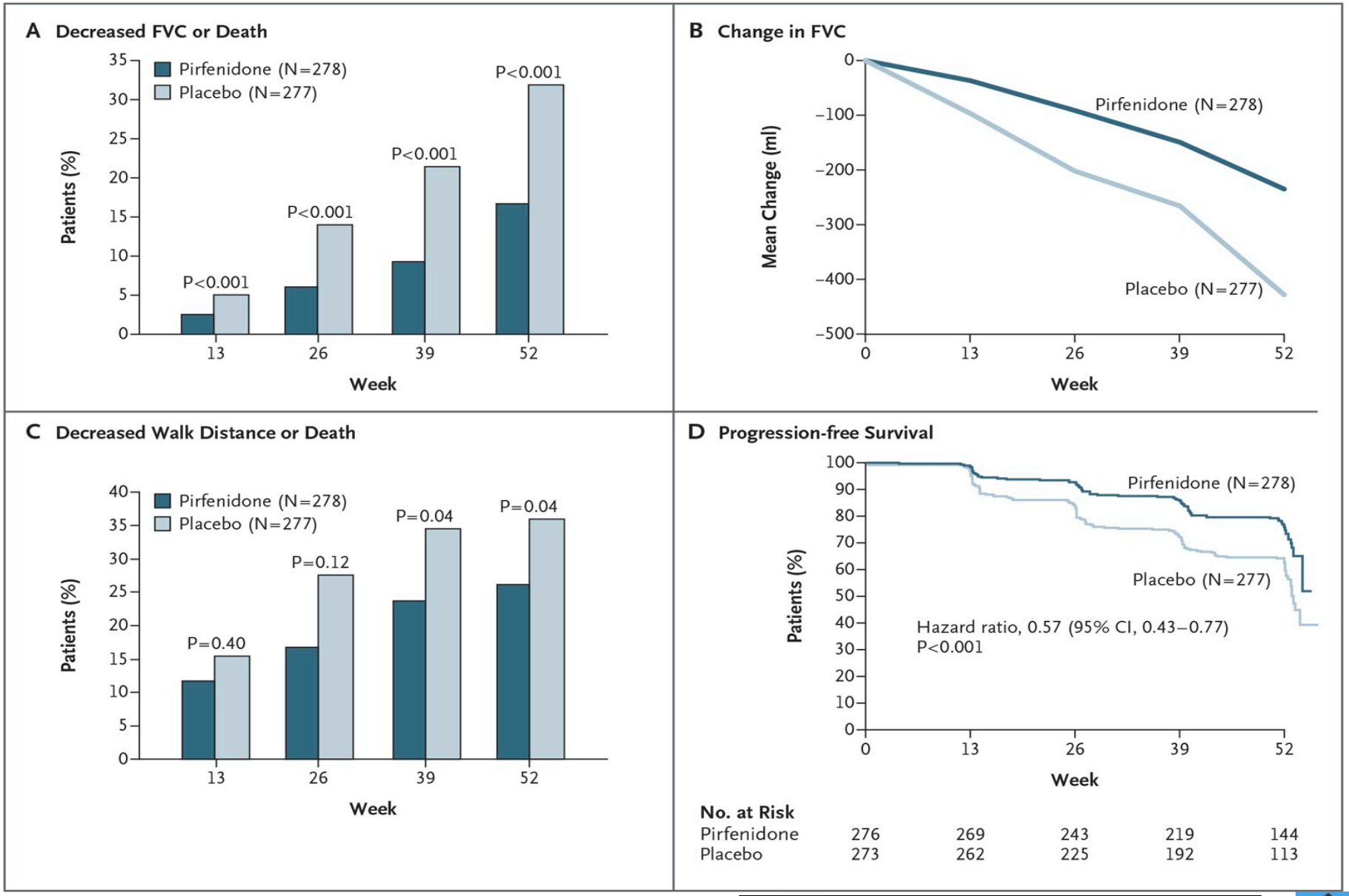
- The CAPACITY programme (studies 004 and 006):

  " Whether Pirfenidone reduces deterioration in lung function in patients with IPF or not?"
- The ASCEND (Assessment of Pirfenidone to Confirm Efficacy and Safety in Idiopathic Pulmonary Fibrosis)

- Result: use of pirfenidone in patients with IPF slows rate of loss in FVC than the use of placebo



1º and Key 2º Efficacy Outcomes during the 52-Week Study Period (The ASCEND)



TE Jr et al. N Engl J Med 2014;370:2083-2092

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Mortality in the ASCEND and CAPACITY Trials.

Table 2. Mortality in the ASCEND and CAPACITY Trials.*

Variable	Pirfenidone	Placebo	Hazard Ratio (95% CI)†	P Value‡
ASCEND trial				
No. of patients	278	277		
Death — no. (%)				
From any cause	11 (4.0)	20 (7.2)	0.55 (0.26–1.15)	0.10
Related to idiopathic pulmonary fibrosis§	3 (1.1)	7 (2.5)	0.44 (0.11–1.72)	0.23
Pooled data from ASCEND and CAPACITY trials				
No. of patients	623	624		
Death — no. (%)				
From any cause	22 (3.5)	42 (6.7)	0.52 (0.31–0.87)	0.01
Related to idiopathic pulmonary fibrosis§	7 (1.1)	22 (3.5)	0.32 (0.14–0.76)	0.006

* Data from the two CAPACITY studies[8] were censored at 1 year to standardize the follow-up for the three studies.
† Hazard ratios are for the pirfenidone group, as compared with the placebo group, and were calculated with the use of the Cox proportional-hazards model.
‡ P values were calculated with the use of the log-rank test.
§ Death related to idiopathic pulmonary fibrosis was defined as death that occurred during the period from randomization to 28 days after the last dose of the study drug. This category was evaluated in a blinded fashion by an independent mortality-assessment committee in the ASCEND trial and by clinical investigators in the CAPACITY trials.

TE Jr et al. N Engl J Med 2014;370:2083-2092

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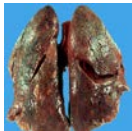
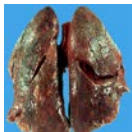
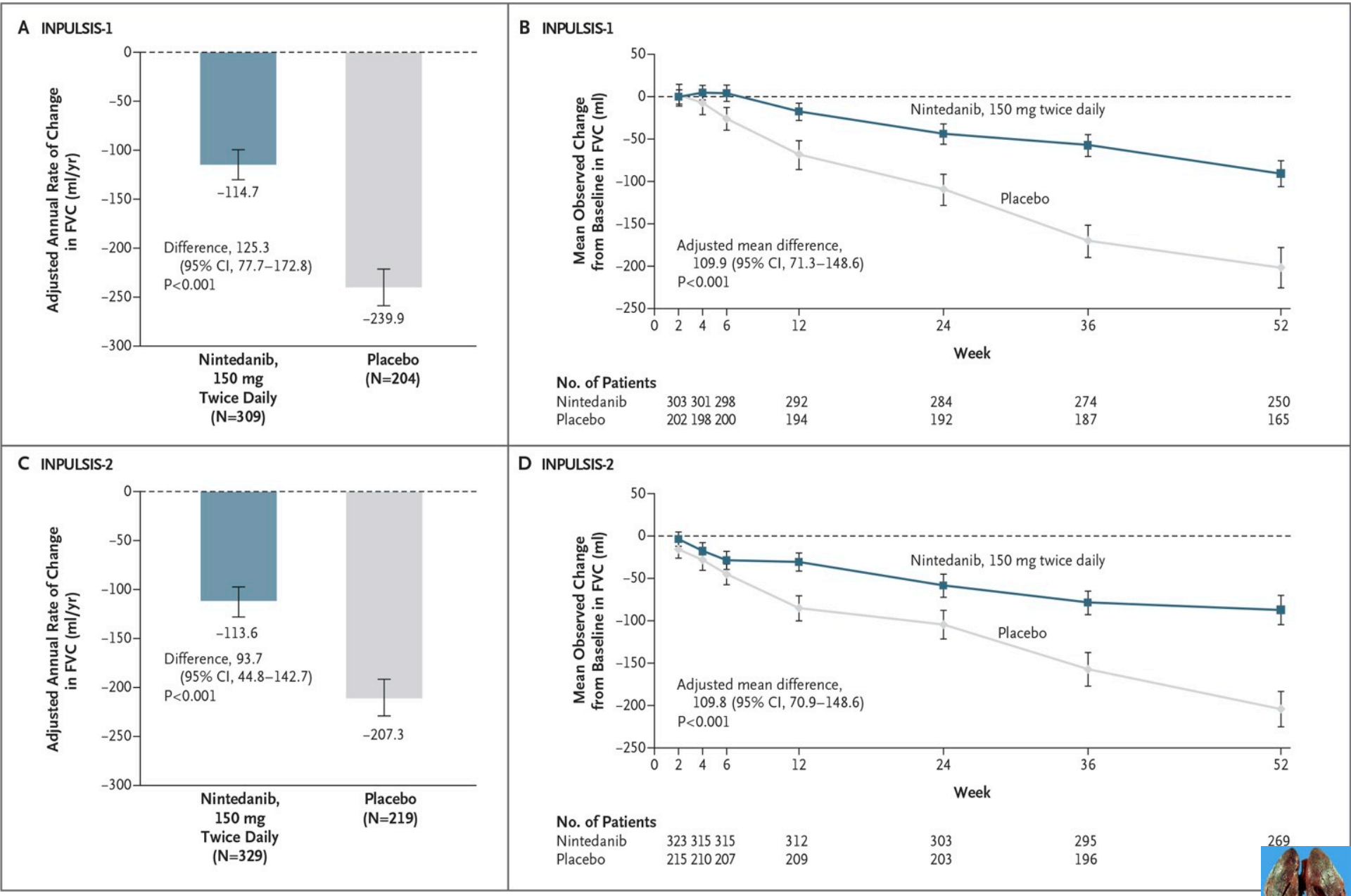


Nintedanib

- Tyrosine kinase inhibitor
- Targets PDGF receptors α & β
- VEGF receptors 1, 2, & 3
- FGF receptors 1, 2 & 3



Annual Rate of Decline and Change of FVC in INPULSIS-1 and INPULSIS-2



Richeldi L et al. N Engl J Med 2014;370:2071-2082

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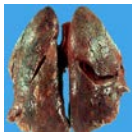
Antacid

- "Antacid therapy and disease outcomes in idiopathic pulmonary fibrosis: a pooled analysis". Lancet Respir Med 2016;4(5): 381-9.

- INTERPRETATION:
  - did not improve outcomes
  - associated with an increased risk of infection in those with advanced disease



Comparison of 2015 and 2011 ATS- IPF Guidelines- New and revised recommendations

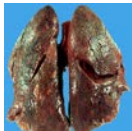
Agent	2015 Guideline	2011 Guideline
Anticoagulation (warfarin)	Strong recommendation against use*	Conditional recommendation against use‡
Prednisone + azathioprine + N-acetylcysteine	Strong recommendation against use†	Conditional recommendation against use†
Selective endothelin receptor antagonist (ambrisentan)	Strong recommendation against use†	Not addressed
Imatinib, a tyrosine kinase inhibitor with one target	Strong recommendation against use*	Not addressed
Nintedanib, a tyrosine kinase inhibitor with multiple targets	Conditional recommendation for use*	Not addressed
Pirfenidone	Conditional recommendation for use*	Conditional recommendation against use†
Dual endothelin receptor antagonists (macitentan, bosentan	Conditional recommendation against use†	Strong recommendation against use*
Phosphodiesterase-5 inhibitor (Sildenafil)	Conditional recommendation against use*	Not addressed

Comparison of 2015 and 2011 ATS- IPF Guidelines- Unchanged recommendations

Agent	2015 Guideline	2011 Guideline
Antacid therapy	Conditional recommendation for use‡	Conditional recommendation for use‡
N-acetylcysteine monotherapy	Conditional recommendation against use†	Conditional recommendation against use†
Antipulmonary hypertension therapy for idiopathic pulmonary fibrosis-associated pulmonary hypertension	Reassessment of the previous recommendation was deferred	Conditional recommendation against use†
Lung transplantation: single vs. bilateral lung transplantation	Formulation of a recommendation for single vs. bilateral lung transplantation was deferred	Not addressed
*⊕⊕⊕⊖, moderate confidence in effect estimates	† ⊕⊕⊖⊖, low confidence in effect estimates.	‡ ⊕⊖⊖⊖, very low confidence in effect estimates.

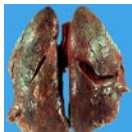
RB-ILD

- In 4th & 5th decades with >30 pack-years
- HRCT: diagnostic
  - patchy ground glass opacity
  - upper lobe centrilobular emphysema
  - central airway thickening
- Improves after cessation of smoking
- Progression to diffuse pulmonary fibrosis- not reported



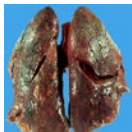
DESQUAMATIVE INTERSTITIAL PNEUMONIA (DIP)

- In 4th & 5th , M:F=2:1, Clubbing (50%)
- Pathology: accumulation of macrophages in alveolar spaces
- HRCT:
  - widespread patchy ground glass opacification
  - lower zone predilection &
  - honeycombing in <1/3
- BAL: increased no of alveolar macrophages
- Prognosis: improve with smoking cessation and corticosteroids & survival is 70% after 10 yrs



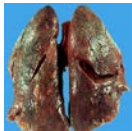
CRYPTOGENIC ORGANIZING PNEUMONIA (COP)

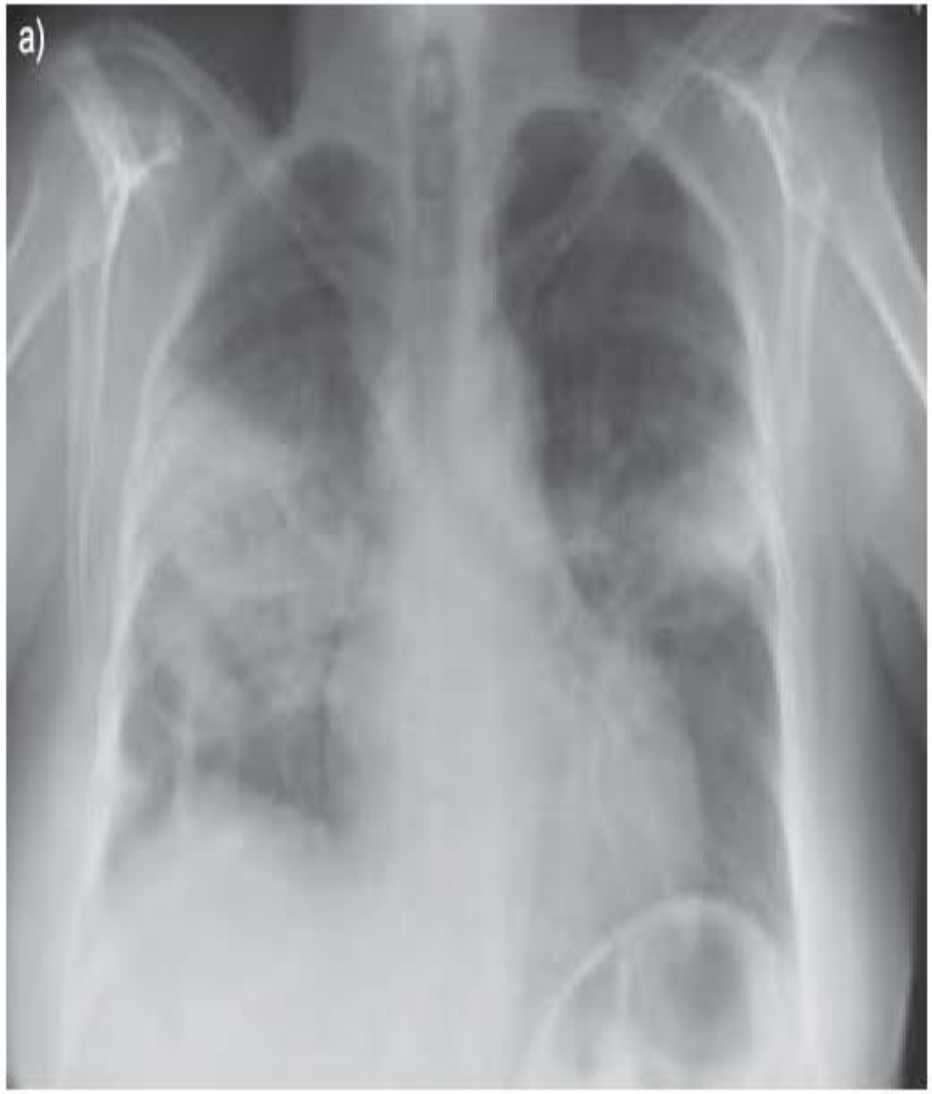
- M=F, 50–60 yrs.
- C/F:Mild flu-like illness, dyspnoea, anorexia, wt. loss, chest pain, night sweats & arthralgia
- No finger clubbing
- Signs:
  - Localized or widespread crackles
  - rarely features of consolidation

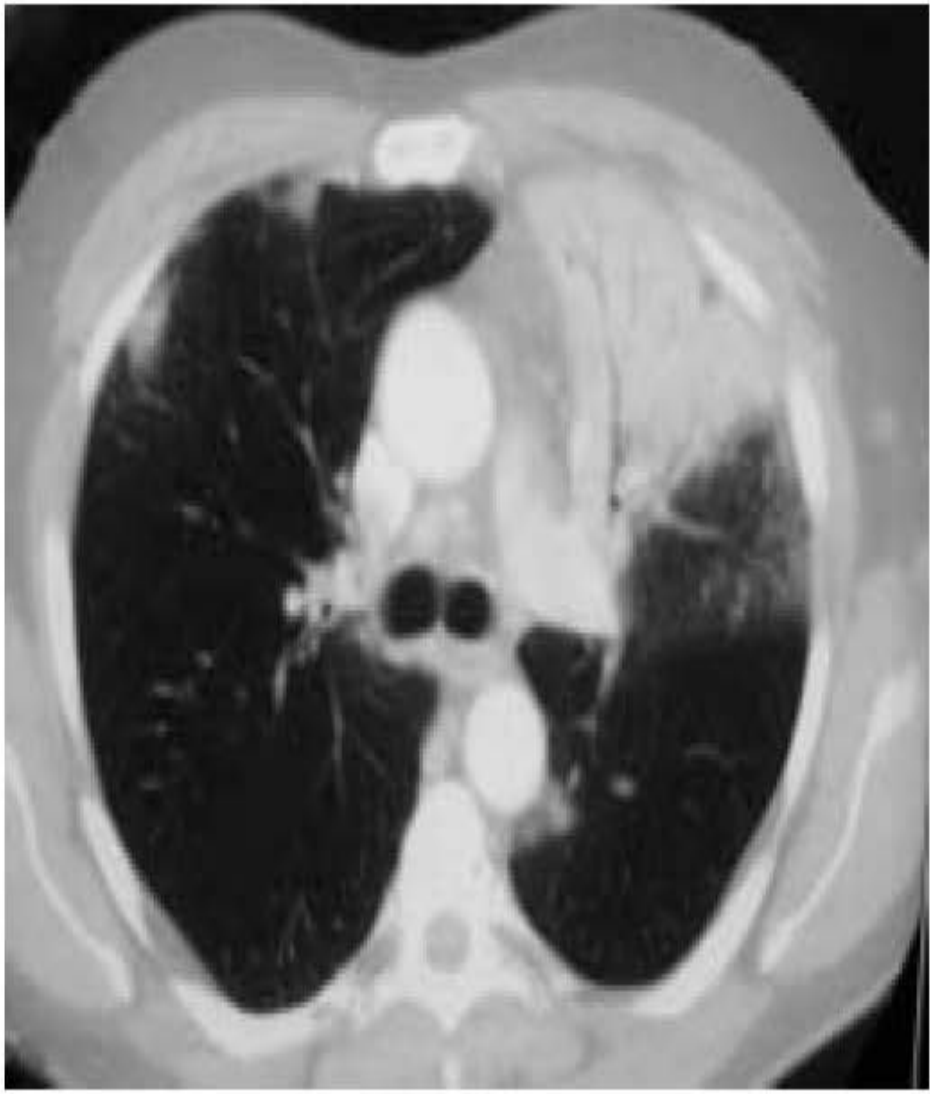


Investigations

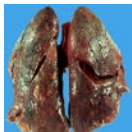
- CBC: N↑, ESR/CRP↑
- PFT: a restrictive pattern
- CXR: consolidation, reticulonodular opacity
- HRCT:
  - consolidation with air bronchogram,
  - nodules, ground glass opacity
- TBLB: intraluminal organizing fibrosis in distal airspaces





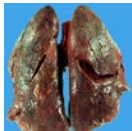


Typical COP with consolidation in the left-upper lobe with an air bronchogram.
Two small contralateral subpleural opacities



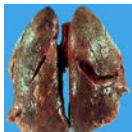
Treatment

- Corticosteroid: rapid clinical improvement
- Prednisone:
  - 0.75 mg/kg daily ➡ 0.5 mg/kg ➡ 20 mg for 4 wks each ➡ 10 mg for 6 weeks ➡ 5 mg for 6 weeks before they were stopped
  - In severe cases, i.v. boluses of methyl prednisolone 500-1000 mg/day for the first 3 days
  - Relapses at <20 mg daily were treated by increasing prednisone to 20 mg only, then decreasing as above



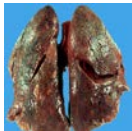
NSIP

- Insidious onset
- Age 50-55 yrs
- M:F =1:1
- C/F: like IPF, clubbing uncommon
- Prognosis- cellular NSIP median survival >10 yrs, fibrotic NSIP 6-8 yrs



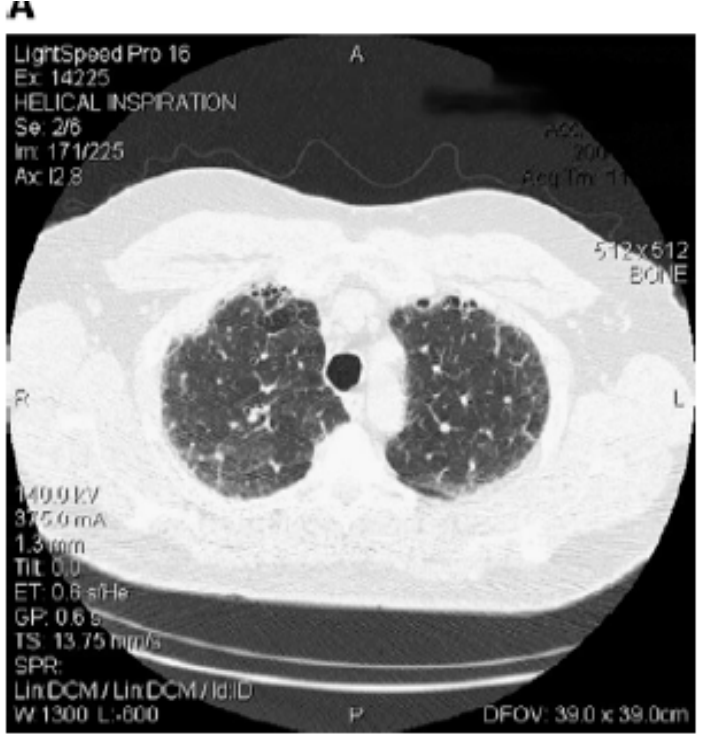
NSIP- types

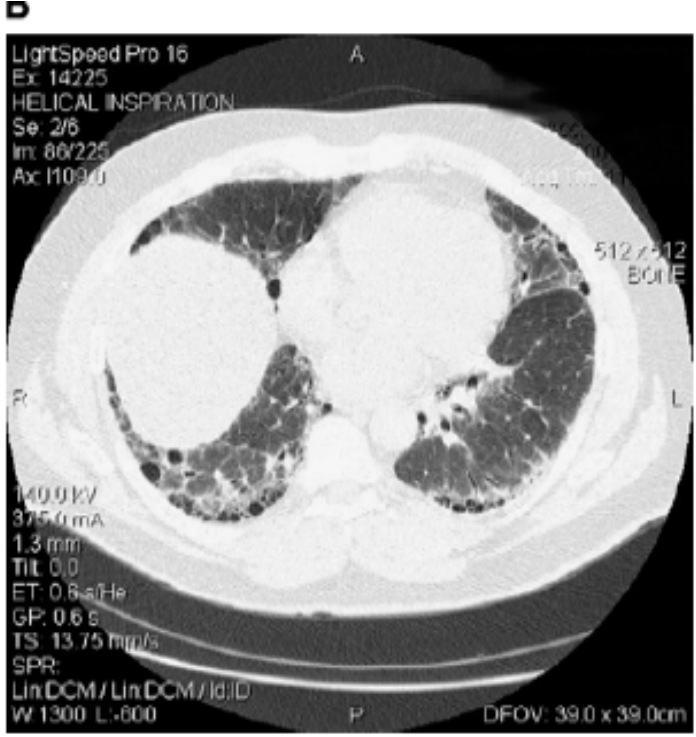
- Confirmed by surgical biopsy
- Histology: homogeneous interstitial fibrosis with inflammatory infiltrate
- **Classification:** NSIP was sub classified as
  - **Cellular NSIP (type I):** interstitial inflammatory infiltrate with little or no fibrosis
  - **In mixed disease (type II):** both
  - **Fibrosing NSIP (type III):** interstitial thickening by uniform fibrosis

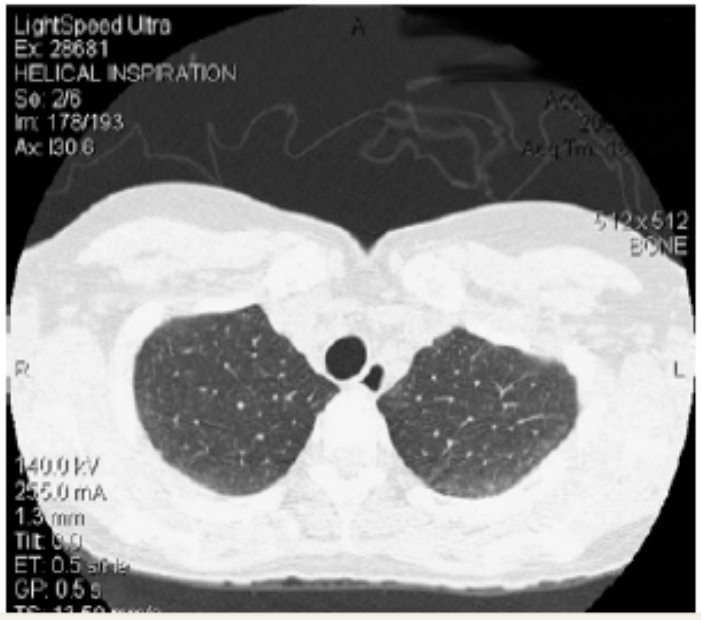


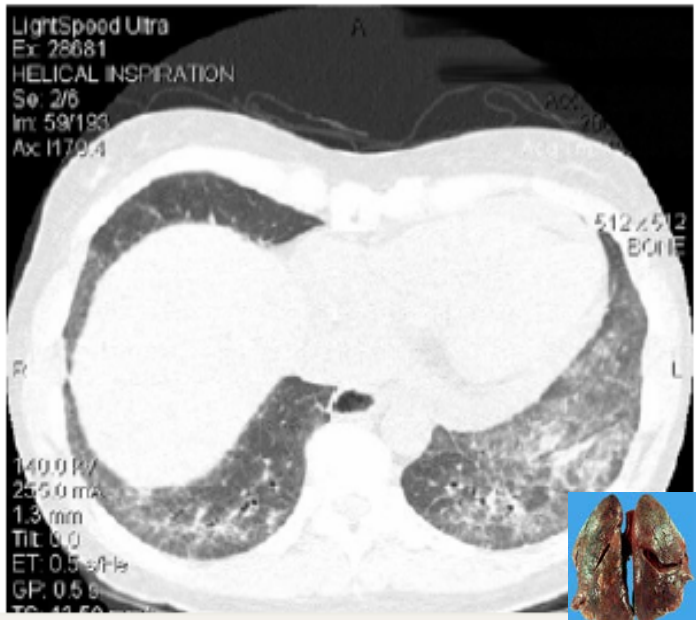
(*A*, *B*) UIP: upper lobe septal thickening and basilar predominant, subpleural honeycomb change.

(*C*, *D*) NSIP: the basilar predominant ground glass opacity with traction bronchiectasis



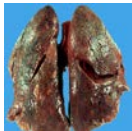






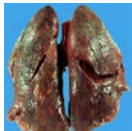
Treatment-NSIP

- Corticosteroids, with or without immunosuppressive agents: mainstay of treatment
- *Azathioprine, cyclophosphamide* and *colchicine:* most widely used
- *Cyclosporin, methotrexate*, *chlorambucil* also tried in isolated cases



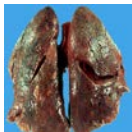
AIP

- Mod to sev hypoxemia with respiratory failure
- **CXR:** bilateral consolidation
- **HRCT:** consolidation, ground glass attenuation, bronchial dilatation
- **BAL:** RBC, neutrophils
- **Rx:** IV methylprednisolone & cyclophosphamide
- Mortality rate: >60%, most pts within 6 m



LYMPHOID INTERSTITIAL PNEUMONIA (LIP)

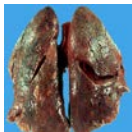
- Benign lympho-proliferative disorder
- Diffuse infiltration of the alveolar septa by dense collections of lymphocytes admixed with plasma cells
- F>M, mean age 5th decade
- Crackles and lymphadenopathy is present in some cases
- Associated with RA, Sjögren's syndrome , Hashimoto's disease, pernicious anemia, chronic active hepatitis , SLE, AHA , PBC, in children with AIDS etc



Sarcoidosis

- NO Rx for asymptomatic stage I disease [B]
- NO Rx for asymptomatic stage II or III disease with mildly abnormal lung function and stable disease [D]
- Oral corticosteroids: progressive disease, significant symptoms or extra-pulmonary disease [B]
- Prednisolone (or equivalent) 0.5 mg/kg/day for 4 weeks, then reduced to a maintenance dose for a period of 6–24 months [D]
- Other: Methotrexate is the treatment of choice [C]

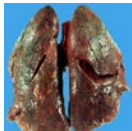
- BTS guideline 2008



CTD-associated ILD

- **In non SSc-associated ILD:** oral prednisolone 0.5–1 mg/kg, maintenance dose of 10 mg/day or less, often with an immunosuppressive agent (usually oral or intravenous cyclophosphamide or oral azathioprine) [C]

- **In SSc-associated ILD:**, if required, low-dose oral steroids (10 mg/day) and/or cyclophosphamide (oral or intravenous) [C]



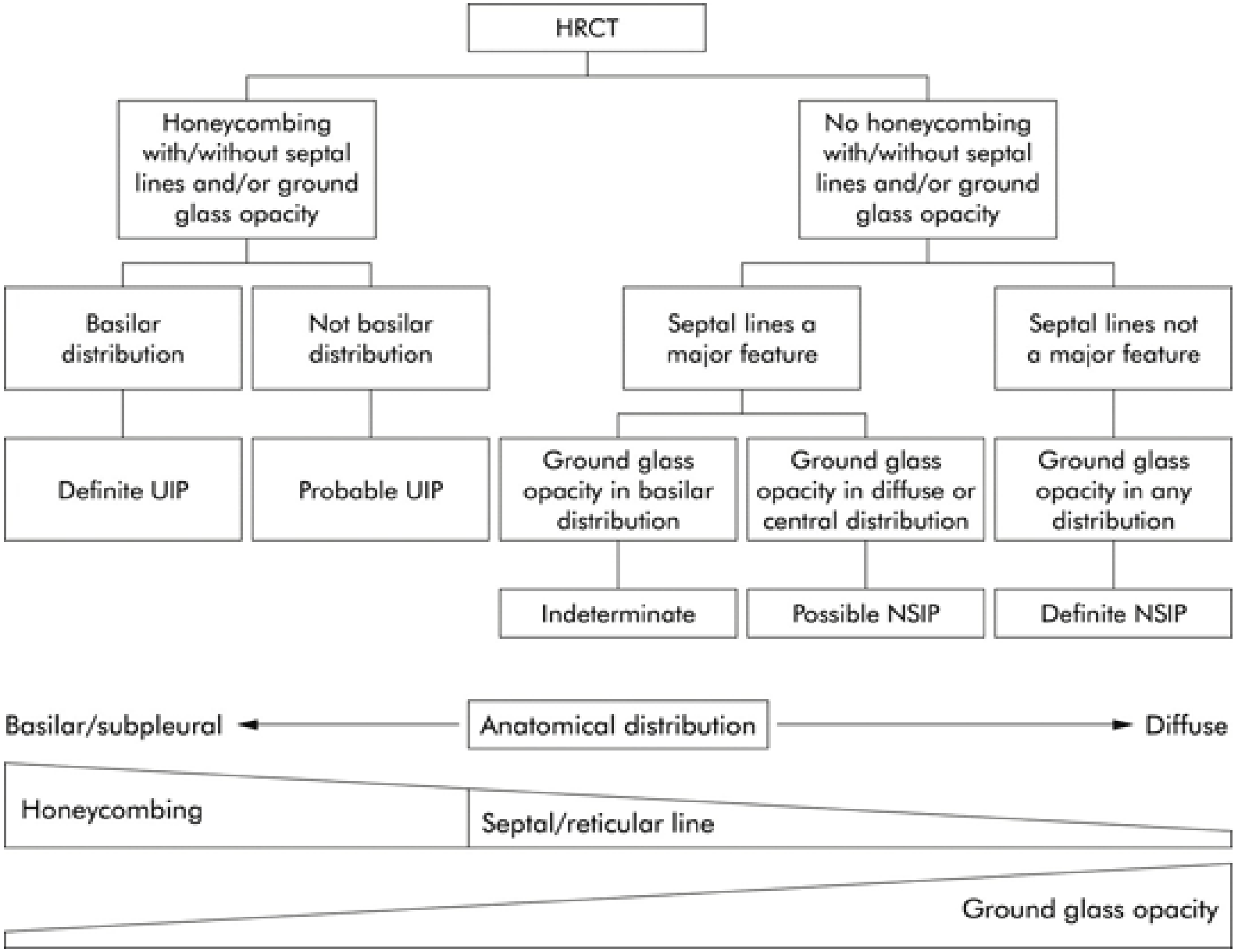
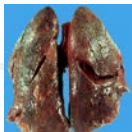

HRCT
Honeycombing with/without septal lines and/or ground glass opacity
No honeycombing with/without septal lines and/or ground glass opacity
Basilar distribution
Not basilar distribution
Septal lines a major feature
Septal lines not a major feature
Definite UIP
Probable UIP
Ground glass opacity in basilar distribution
Ground glass opacity in diffuse or central distribution
Ground glass opacity in any distribution
Indeterminate
Possible NSIP
Definite NSIP
Basilar/subpleural
Anatomical distribution
Diffuse
Honeycombing
Septal/reticular line
Ground glass opacity

TABLE 2. CLINICAL, RADIOLOGIC, AND HISTOLOGIC FEATURES, TREATMENT, AND PROGNOSIS OF THE IDIOPATHIC INTERSTITIAL PNEUMONIAS

	Idiopathic Pulmonary Fibrosis	NSIP	DIP, RB-ILD	Cryptogenic Organizing Pneumonia	Acute Interstital Pneumonia	Lymphocytic Interstitial Pneumonia
Duration of illness	Chronic (> 12 mo)	Subacute to chronic (mo to yr)	Subacute (wk to mo);	Subacute (< 3 mo)	Abrupt (1 to 2 wk)	Chronic (> 12 mo)
HRCT	• Peripheral, subpleural, basal predominance • Reticular opacities • Architectural distortion • Traction bronchiectasis/ bronchiolectasis • Honeycombing	• Peripheral, subpleural, basal, symmetric • Ground-glass attenuation • Consolidation (uncommon) • Lower lobe volume loss • Subpleural sparing may be seen	• DIP: diffuse ground-glass opacity in the middle and lower lung zones • RB-ILD: bronchial wall thickening; centrilobular nodules; patchy ground-glass opacity	• Subpleural or peribronchial • Patchy consolidation • Nodules	• Diffuse, bilateral • Ground-glass opacities often with lobular sparing	• Diffuse • Centrilobular nodules, • Ground-glass attenuation, • Septal and bronchovascular thickening, • Thin-walled cysts
Treatment	Poor response to corticosteroid or cytotoxic agents	Corticosteroid responsiveness	Smoking cessation, effectiveness of corticosteroid unknown	Corticosteroid responsiveness	Effectiveness of corticosteroid unknown	Corticosteroid responsiveness
Prognosis	5-yr mortality, 80% (median survival 2–3 yr)	Cellular NSIP: 5-yr mortality < 10% (median survival > 10 yr) Fibrotic NSIP: 5-yr mortality 10% (median survival 6–8 yr)	RB-ILD: no deaths reported DIP: 5-yr mortality < 5%	5-yr mortality < 5% (deaths rare)	60% mortality in < 6 mo	Limited data, not well defined

Definition of abbreviations: NSIP = nonspecific interstitial pneumonia; RB-ILD = respiratory bronchiolitis–interstitial lung disease.



Common co-mrobidities in ILD. RACGP2015; 44(8):546-552.

Co-morbidity	Potential implications	Management
GERD	Acceleration of lung fibrosis	•PPI/ H_2- blockers •Prokinetic agents •Surgery in selected cases
Osteoporosis	Vertebral and rib # : restrict breathing, as well as QOL	•Vitamin D repletion •Surveillance of BMD •Bisphosphonates

Common comrobidities in ILD. RACGP2015; 44(8):546-552.

Co-morbidity	Potential implications	Management
Infections	Accelerate decline in lung function	•Influenza and pneumococcal vaccinations •Timely antibiotic therapy
Sleep-disordered breathing	pulmonary hypertension	•Nocturnal oxygen • CPAP
Pulmonary hypertension	Increased mortality	• O_2 therapy •Diuretics (for RHF) •Vasodilator therapy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