Epidemiology and classification of the idiopathic interstitial pneumonias

Interstitial Lung Disease congress, Prague, June 2014

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AUW has received consultancy fees from Actelion, Almirali, Boehringer Ingelheim, Centocor, Encysive, Genentech, Gilead, Intermune, MedImmune, Novartis, Takeda

Plan

- **Revised classification of IIPs**
- **Key epidemiologic data, relevant to clinical diagnosis**

Histologic and clinical classification of idiopathic interstitial pneumonias (ICCILD) 2002

HISTOLOGIC PATTERNS	CLINICAL DIAGNOSIS
UIP	Idiopathic Pulmonary Fibrosis Cryptogenic Fibrosing Alveolitis
DIP (Alveolar Macrophage Pneumonia)	DIP (Alveolar Macrophage Pneumonia)
Respiratory Bronchiolitis (RB)	Respiratory Bronchiolitis Interstitial Lung Disease (RBILD)
Organizing Pneumonia (OP)	Cryptogenic organizing Pneumonia (*BOOP)
Diffuse Alveolar Damage (DAD)	Acute Interstitial Pneumonia (AIP)
Non-Specific Interstitial Pneumonia (NSIP)	*Non-Specific Interstitial Pneumonia (**Provisional)*
Lymphoid Interstitial Pneumonia (LIP)	Lymphoid Interstitial Pneumonia

The idiopathic interstitial pneumonias

Major Idiopathic Interstitial Pneumonias
Idiopathic pulmonary fibrosis
Idiopathic nonspecific interstitial pneumonia
Respiratory bronchiolitis interstitial lung disease
Desquamative interstitial pneumonia
Cryptogenic organizing pneumonia
Acute interstitial pneumonia

Rare Idiopathic Interstitial Pneumonias
Idiopathic lymphoid interstitial pneumonia
Idiopathic pleuropulmonary fibroelastosis

Unclassifiable idiopathic interstitial pneumonias

Travis WD et al. Am J Respir Crit Care Med 2013; 188:733-48

CATEGORIZATION OF MAJOR IDIOPATHIC INTERSTITIAL PNEUMONIAS

†DIP can occasionally occur in nonsmokers;

CATEGORY	CLINICAL-RADIOLOGIC- PATHOLOGIC DIAGNOSES	ASSOCIATED MORPHOLOGIC PATTERNS
Chronic Fibrosing IP	Idiopathic Pulmonary Fibrosis	Usual Interstitial Pneumonia
	Idiopathic Nonspecific Interstitial Pneumonia‡	Nonspecific Interstitial Pneumonia
Smoking-related IP †	Respiratory Bronchiolitis Interstitial Lung Disease	Respiratory Bronchiolitis
	Desquamative Interstitial Pneumonia	Desquamative Interstitial Pneumonia
Acute/subacute IP	Cryptogenic Organizing Pneumonia	Organizing Pneumonia
	Acute Interstitial Pneumonia	Diffuse Alveolar Damage

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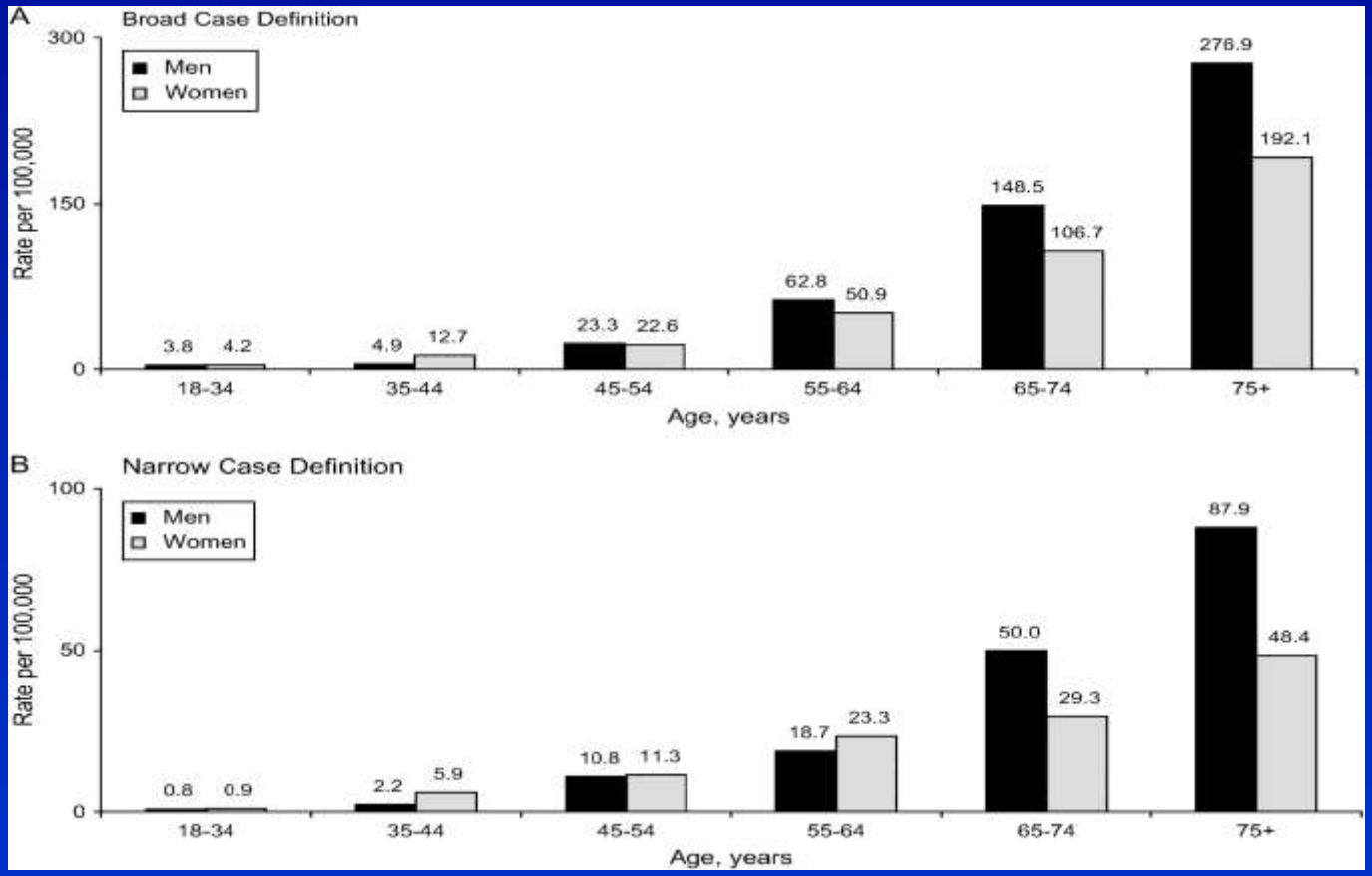
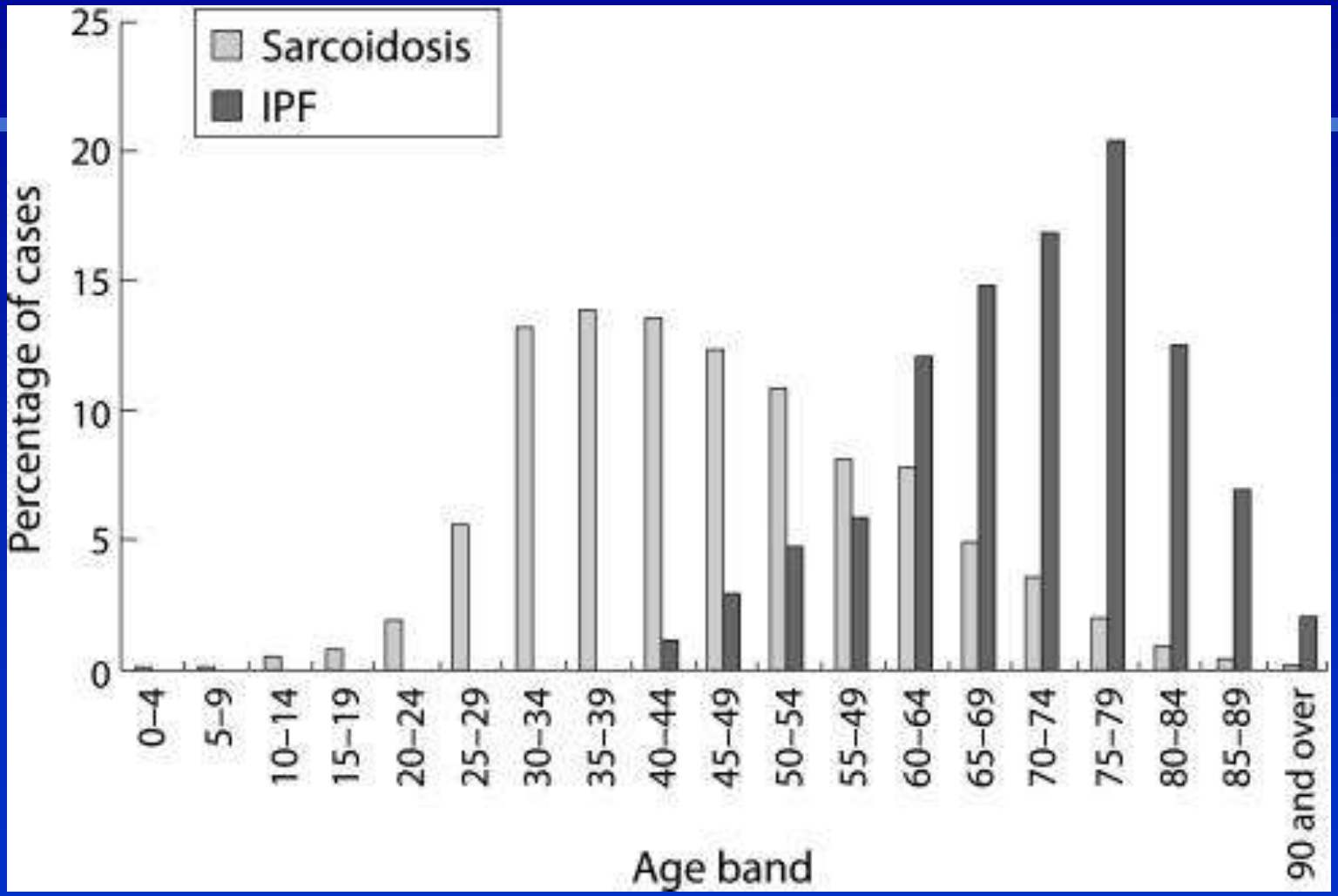
Epidemiology of idiopathic pulmonary fibrosis

- Diagnostic purity (referral centre) versus spectrum of disease with looser definition
- Probably best to work with the latter but same broad conclusions in any case
- Peak incidence in eighth decade, males>females, incidence >5/100,000, may be as high as 10/100,00
- Most detailed work in the last decade in the UK

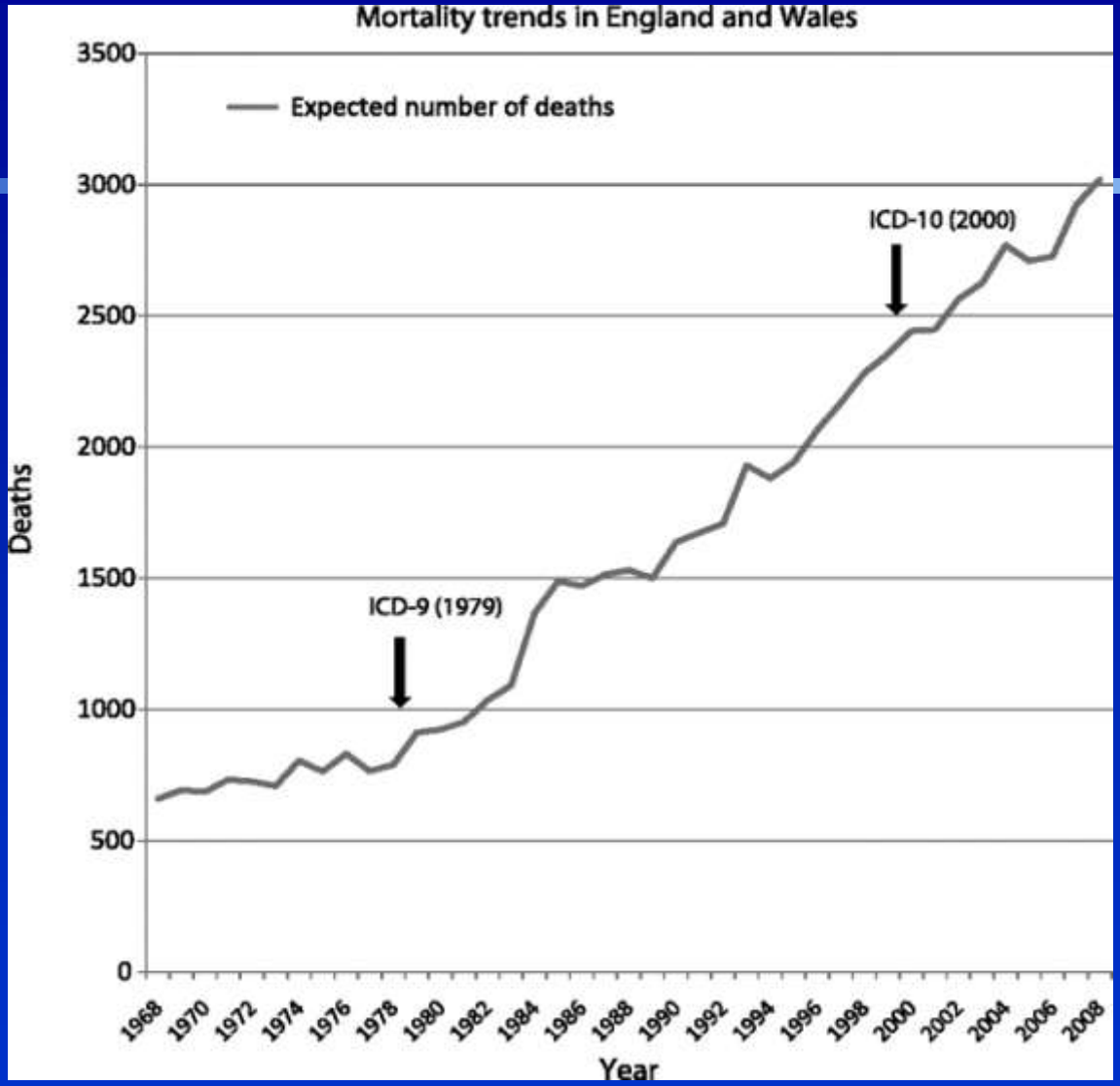


Raghu G et al. Am J Respir Crit Care Med 2006; 174:810-6

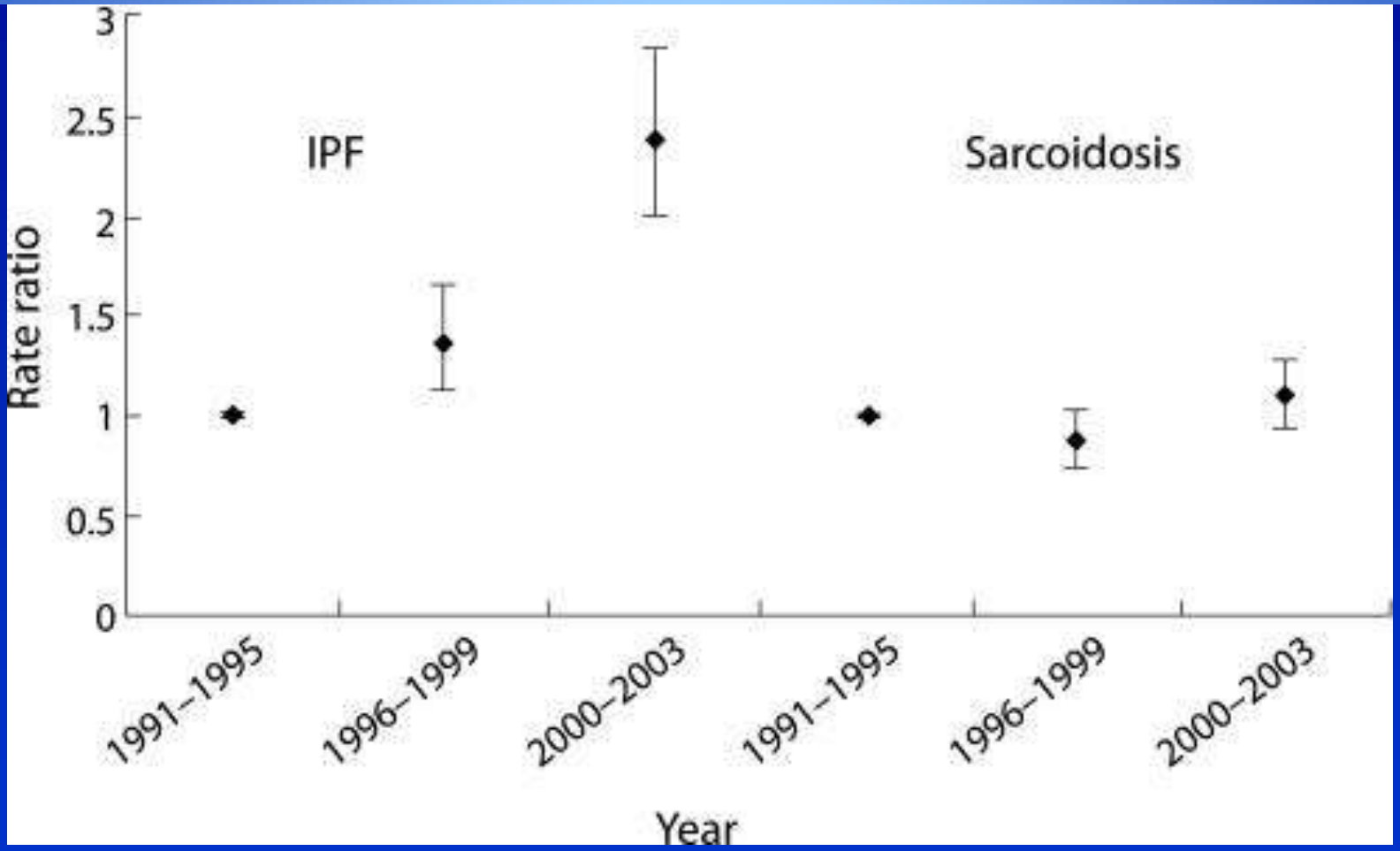


Gribben et al. Thorax 2006; 61:980-5

Navartnam V et al. Thorax 2011; 66:462-7



Navartnam V et al. Thorax 2011; 66:462-7

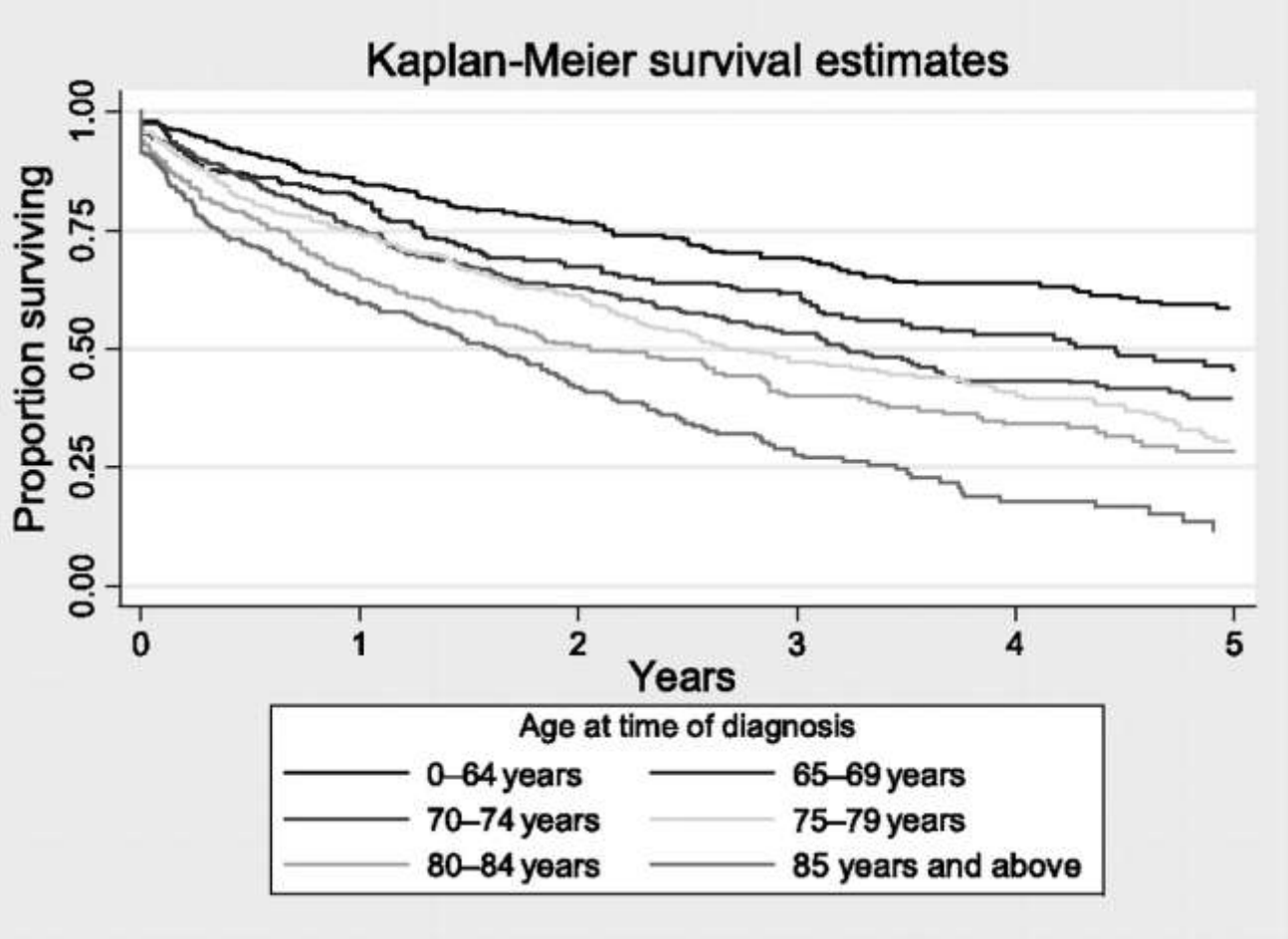


Gribben et al. Thorax 2006; 61:980-5

Table 3 Survival analysis for patients with IPF

	Mutually adjusted hazard ratios (95% CI)
Sex	
Women	1.00
Men	1.40 (1.15 to 1.70), p = 0.001
Calendar period	
1991–1995	1.00
1996–1999	0.86 (0.67 to 1.11)
2000–2003	0.92 (0.71 to 1.19), p = 0.6*
Age group (years)	
<55	1.00
55–64.9	2.25 (1.30 to 3.91)
65–74.9	3.30 (1.96 to 5.56)

Gribben et al. Thorax 2006; 61:980-5



Navartnam V et al. Thorax 2011; 66:462-7

Risk factors

- Amalgamtingall series, smoking has an odds ratio of approximately 2.0
- Weak associations with a number of air-borne factors including various dusts, especially wood dust, coal smoke.
- No cardinal association

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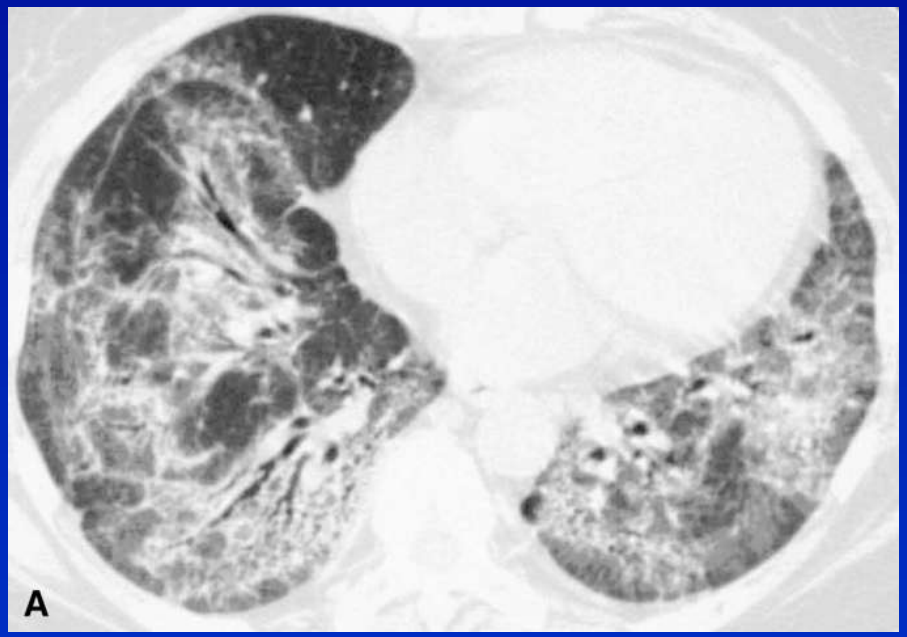
Idiopathic NSIP: a true clinical entity?

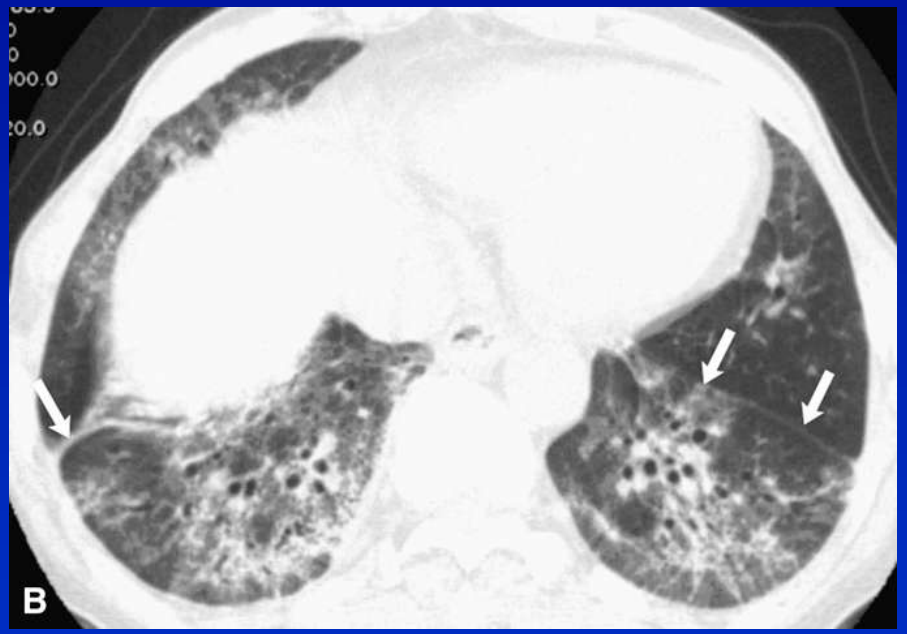
- Idiopathic NSIP designated a “provisional” entity in ATS/ERS 2002
- Important divergences between series in HRCT features, BAL findings and outcome data
- Overlap in clinical and HRCT features increasingly observed with HP, IPF and COP

Report of an American Thoracic Society workshop

- Idiopathic NSIP exists and has typical clinical and HRCT features
- The diagnosis requires a dynamic integrated multi-disciplinary approach because of overlap with other disorders
- If your pathologist reports NSIP at biopsy, the chances are high (>65%) that an expert multidisciplinary group will assign an alternative diagnosis
- Usual alternative diagnoses: IPF, HP, COP

Travis WD et al. *Am J Respir Crit Care Med 2008; 177:1338-1347*





Epidemiology: "occurs most often in middle-aged women who are never-smokers"

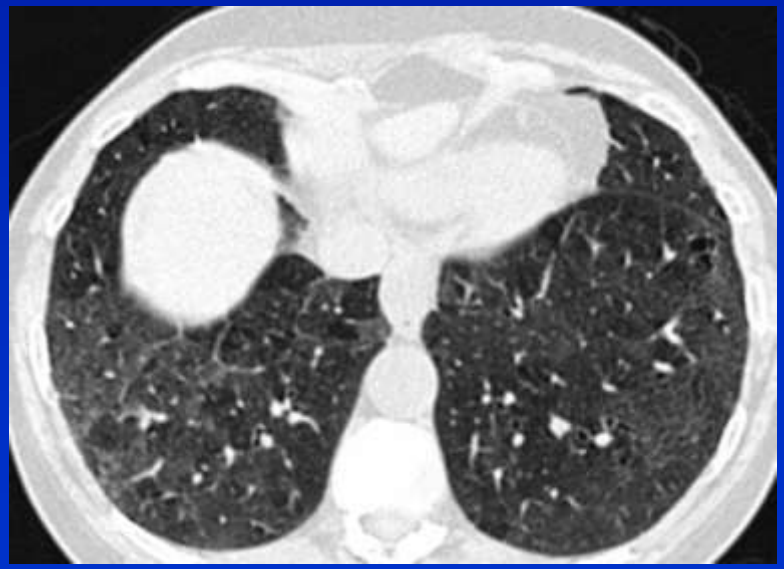
Travis WD et al. *Am J Respir Crit Care Med 2008; 177:1338-1347*

Does it really matter?

- Should DIP and RB-ILD be in an IIP classification?
- Serious disagreement on that point
- They should be because they are! Overlap with other IIPs
- DIP increasingly seen in non-smokers. Both DIP and RBILD very rare in smokers

Respiratory bronchiolitis with associated ILD

- Third to sixth decade usually
- No gender predilection above smoking
- Exclusively in smokers
- Prevalence???



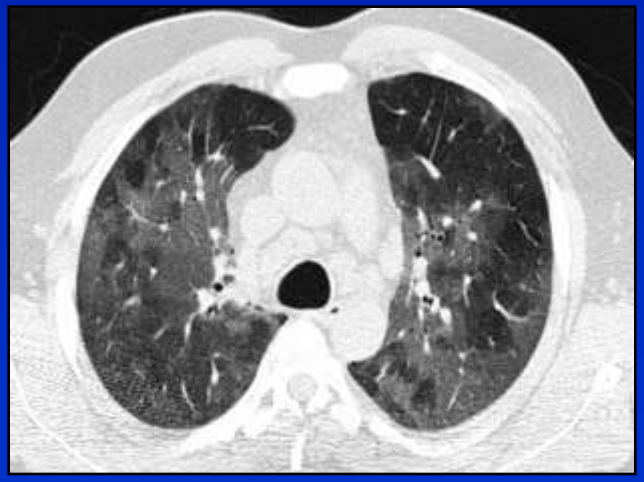
- The issue is confusion between RB and RB-ILD

RB vs RBILD

- Respiratory bronchiolitis is a physiologic response to smoking
- No histologic difference between RB and RB-ILD. This applies equally to spectrum of morphologic abnormality and to severity
- The diagnosis of RB-ILD is made when RB is severe enough to be regarded clinically as an ILD, based upon symptoms, imaging features and PFTs
- This judgement is NOT standardised and is complex when there is associated emphysema
- Any more detailed epidemiologic statement is truly unrealistic!

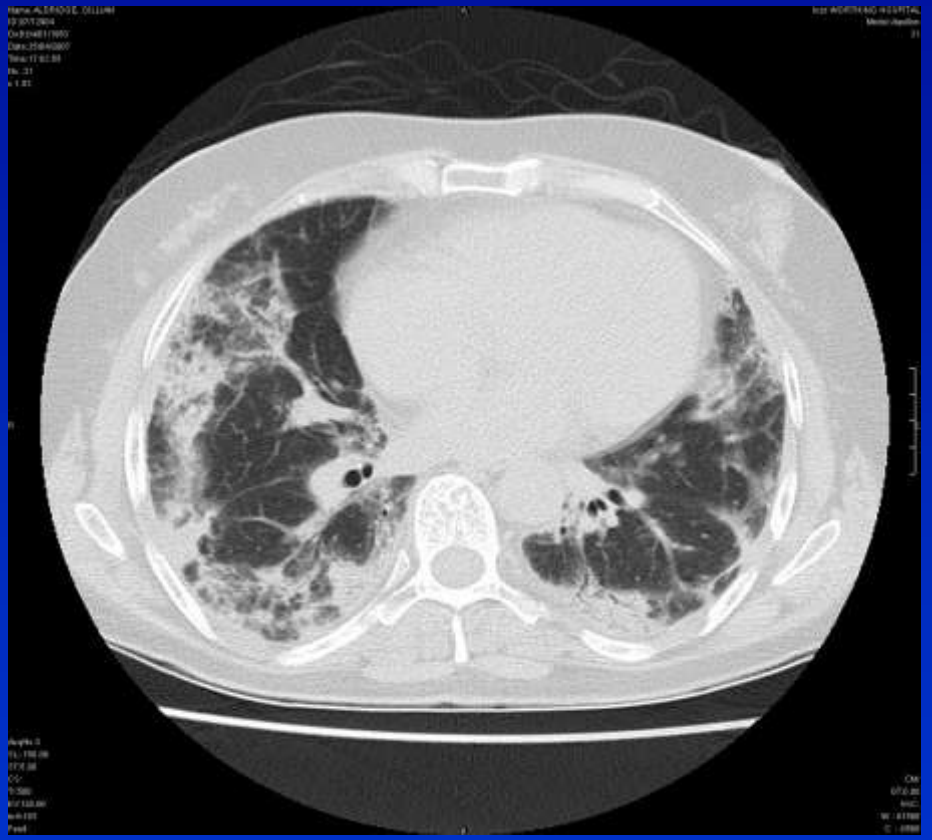
Desquamative interstitial pneumonitis

- Rare!! Fourth to sixth decade usually. No clear gender predilection beyond smoking.
- A smoking history once the rule – but as smoking decreases in prevalence, proportion of life-long non-smokers has risen.
- Less than 200 cases in literature
- Treatment responsive in 70%
- True incidence and prevalence?



Cryptogenic organizing pneumonia

- Another rare disorder
- Exact incidence?
- Mean age 55
- M=F

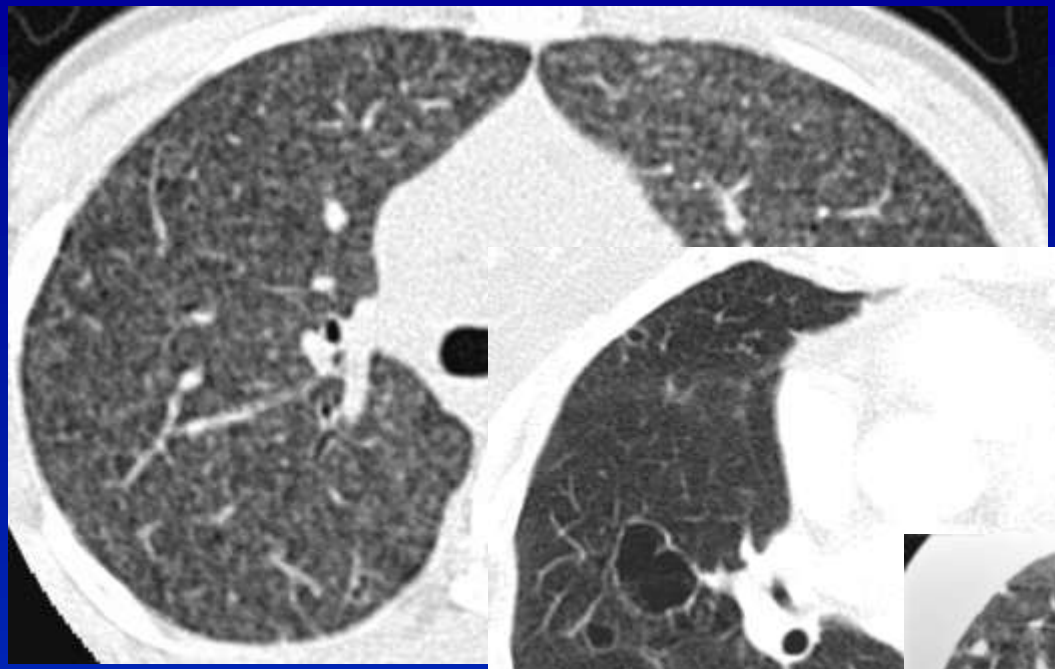


- Two thirds are non smokers, aspiration a recently recognised risk factor

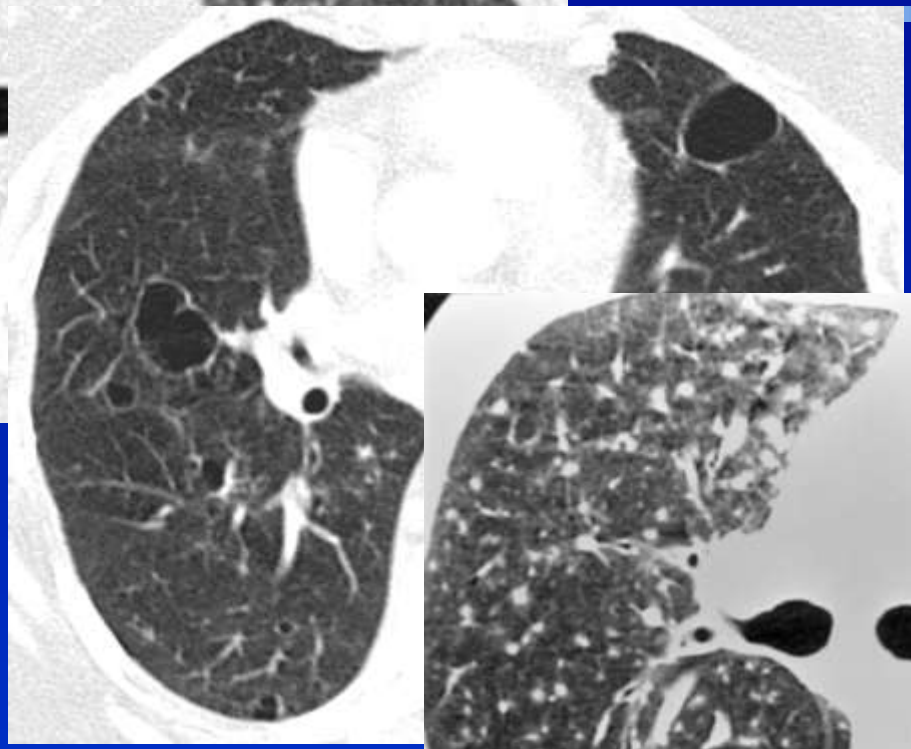
Acute interstitial pneumonitis

- Essentially, idiopathic DAD
- Prodrome of viral symptoms
- Mean age 50
- No gender predilection
- No smoking link

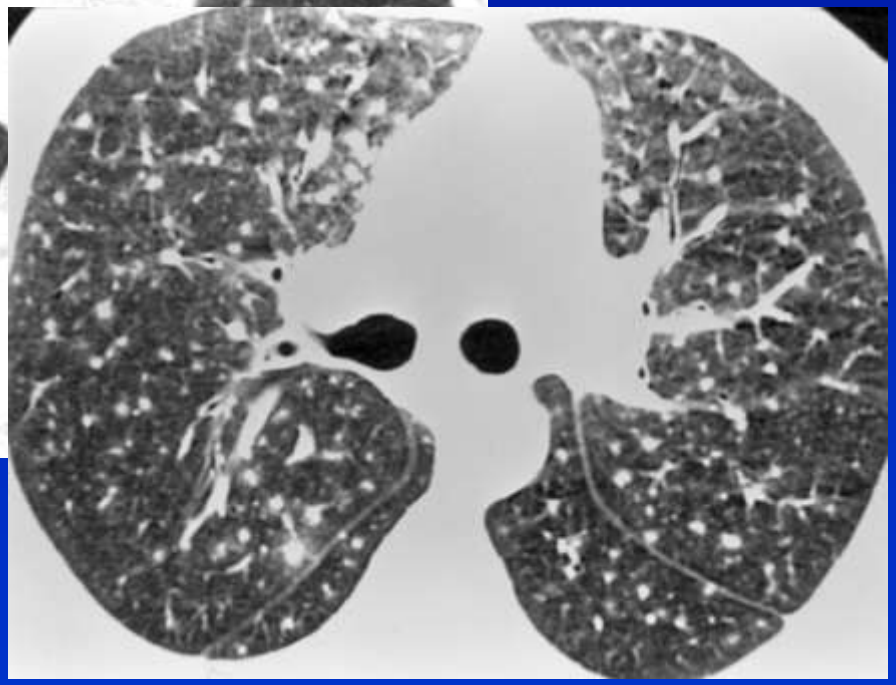
Creatures “rich and strange”



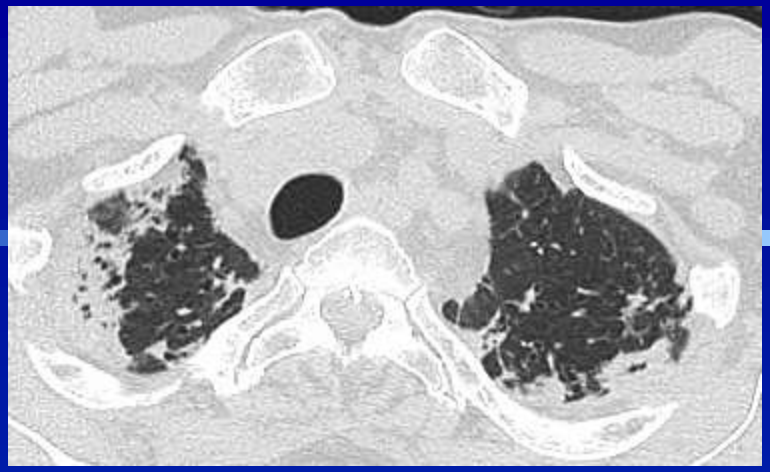
LIP

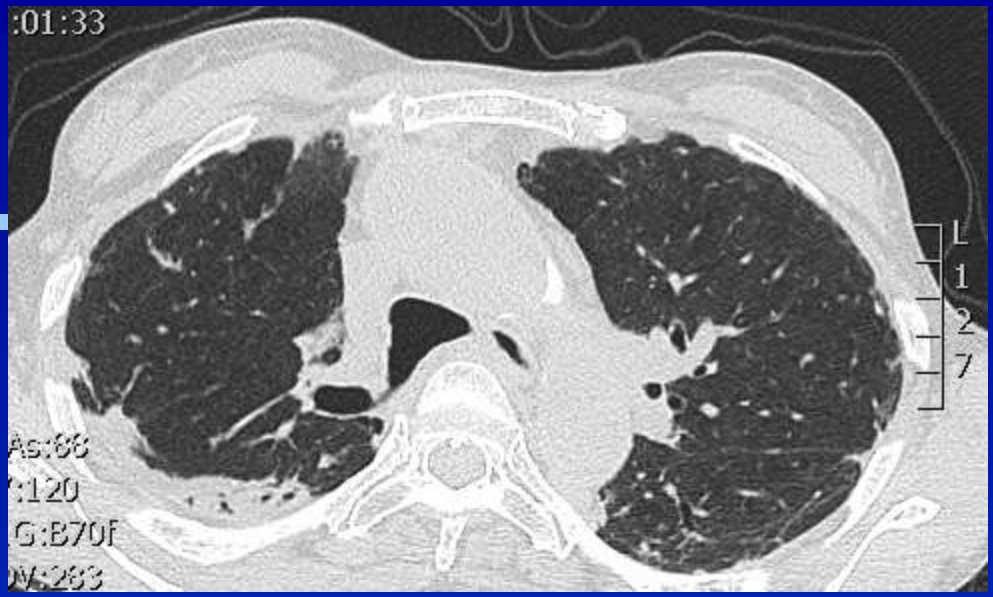


LIP!



Women, fifth decade *LIP!!*

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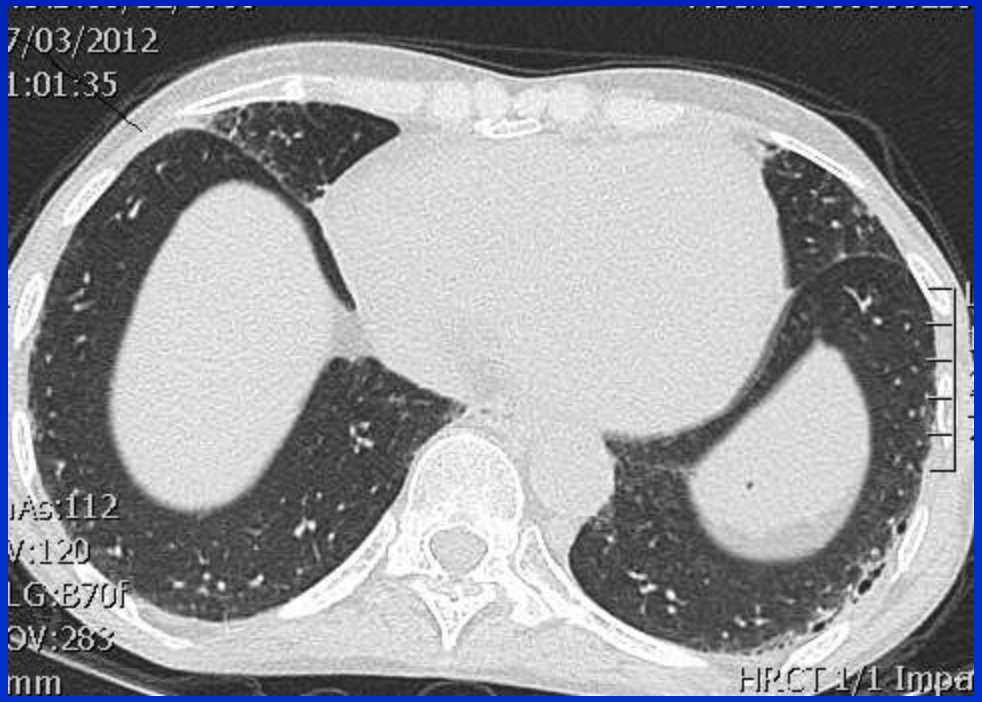
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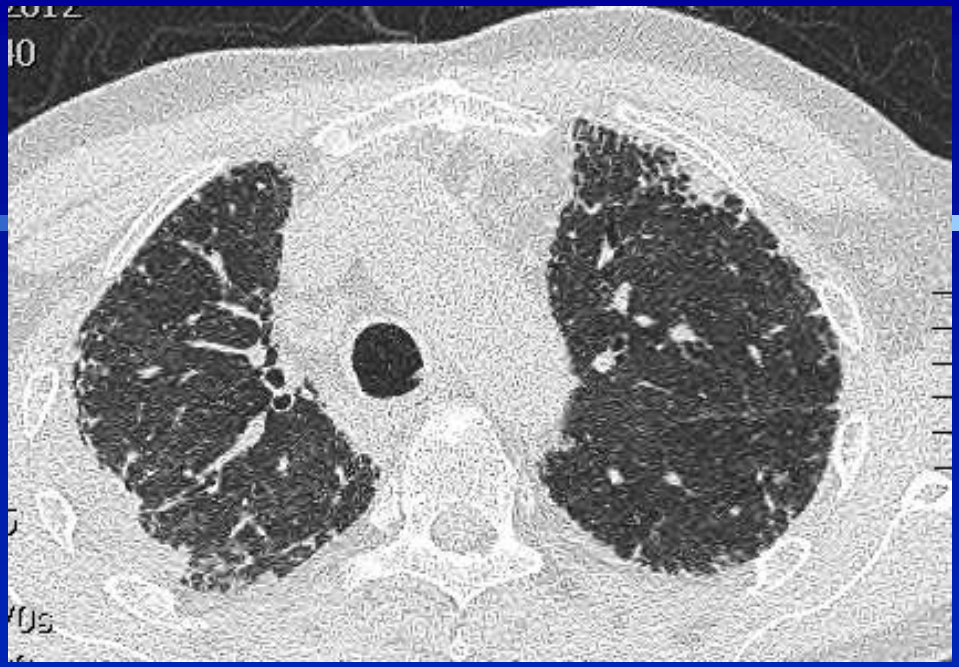
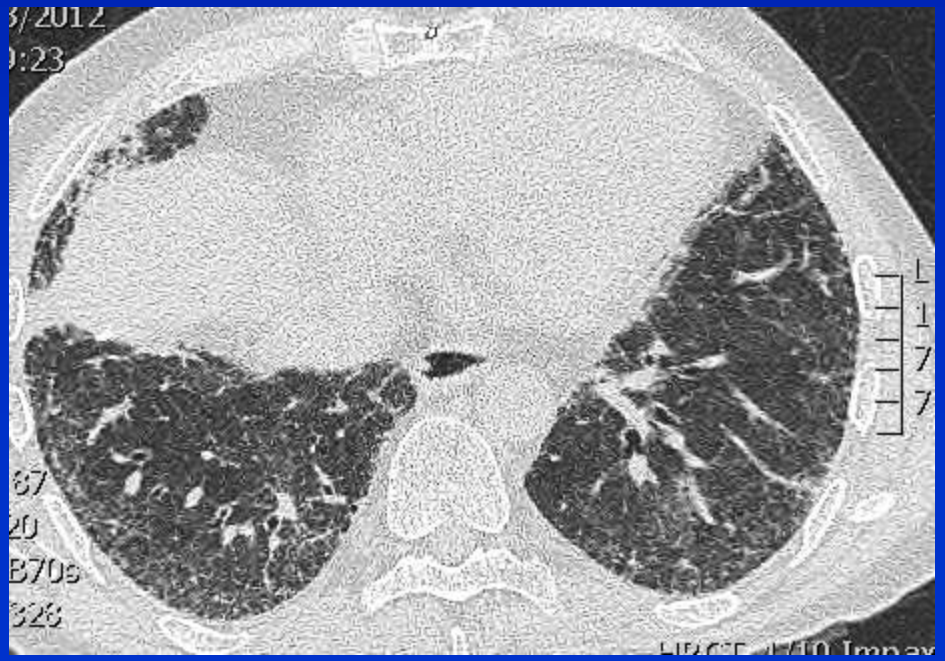
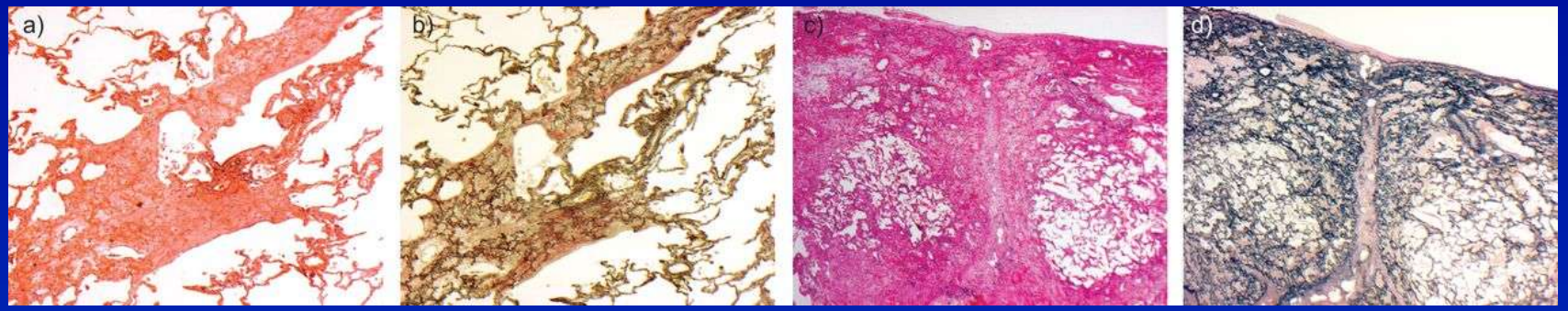






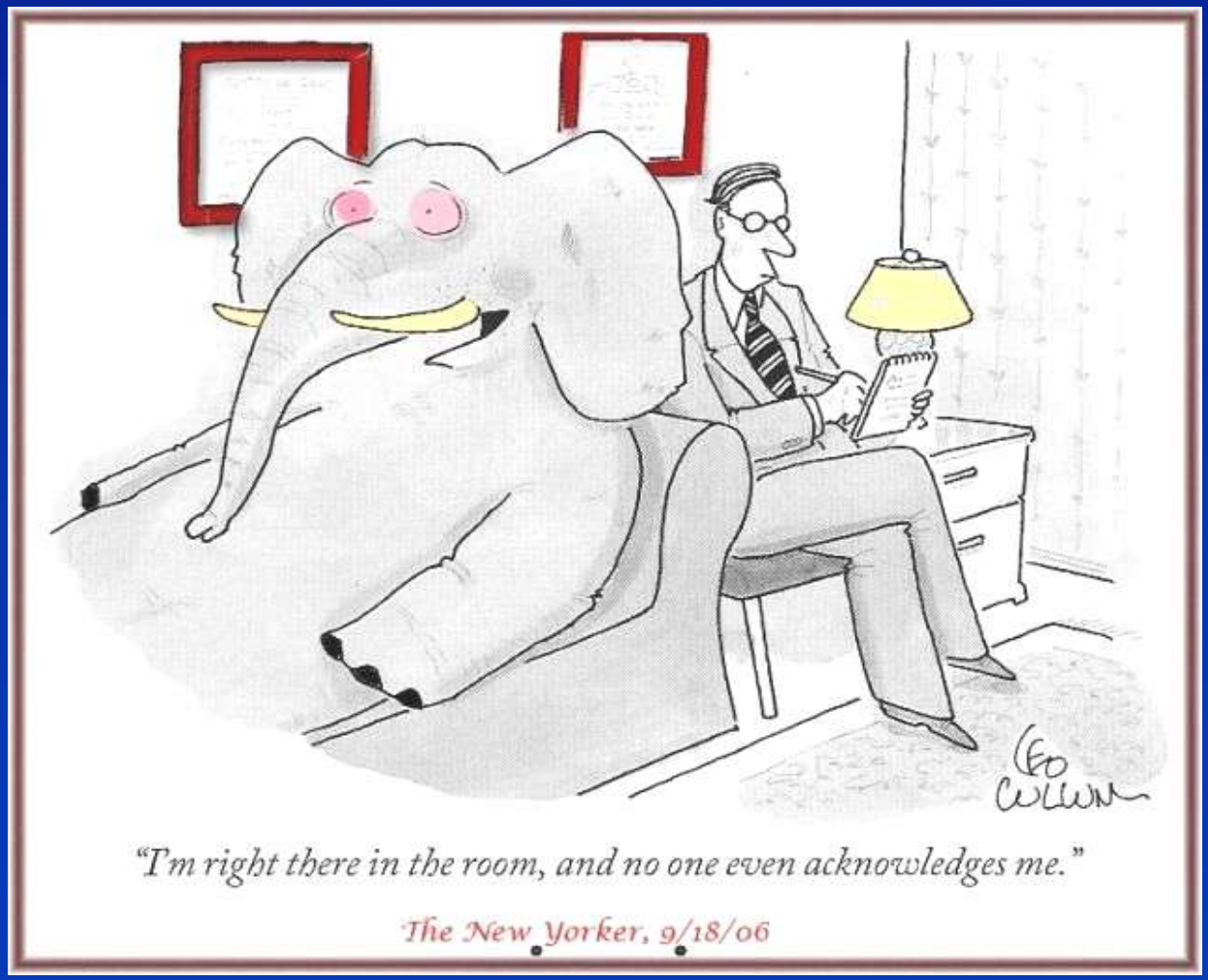
a, b) Intra-alveolar fibrosis distant from the pleura shows a peribronchiolar distribution, extending to surround an alveolar duct (top right). c, d) Other areas shows a more perilobular distribution as the intra-alveolar fibrosis extends away from the pleura. Staining: &a,c) a, c) haematoxylin and eosin; b, d) elastic Van Gieson. Magnification: a, b) 100× c, d) 20×.

Idiopathic pleuroparenchymal fibroelastosis (IPPFE)

- More prevalent than LIP
- A second interstitial lung disease frequent
- When isolated, highly variable course
- Seen also post marrow transplant and in CTD

- Often represents an abnormal response to infection
- Recurrent bacterial or chronic fugal infection
- Beware of overenthusiastic immunosuppression
- Low dose prednisolone, hydroxychloroquine, prophylactic azithromycin +/- anti-fungal therapy

The elephant in the room: patients who do not fit into a classification



Unclassifiable disease

- What is it?
- How common is it?
- How important is it?
- How should it be managed?

“Unclassifiable disease”

- **Low confidence:** tentative first choice diagnosis, no clear differential diagnosis
- **Overlapping disorders:** IPF/HP, IPF/NSIP, HP/NSIP
- No plausible first choice diagnosis

Common to all three scenarios…..

- Diagnosis not clear (using current diagnostic classification)
- As a result, major uncertainties regarding prognostic evaluation and/or optimal management

ORIGINAL ARTICLE
INTERSTITIAL LUNG DISEASE

Prevalence and prognosis of unclassifiable interstitial lung disease

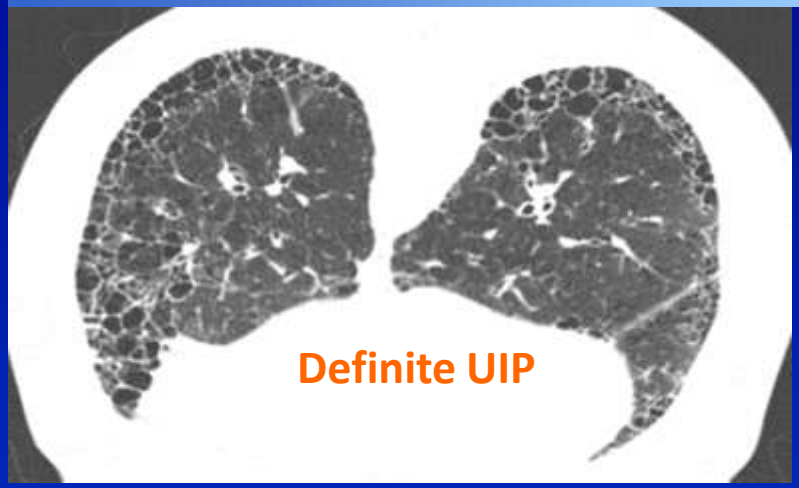
Christopher J. Ryerson[1], Thomas H. Urbania[2], Luca Richeldi[3], Joshua J. Mooney[4], Joyce S. Lee[4], Kirk D. Jones[5], Brett M. Elicker[2], Laura L. Koth[4], Talmadge E. King Jr[4], Paul J. Wolters[4] and Harold R. Collard[4]

Eur Respir J 2013; 42: 750–757 | DOI: 10.1183/09031936.00131912

Features of series

- **Large retrospective series of 1370 patients**
- **Disease unclassifiable in 10% of cases**
- **Unclassifiable disease the fourth most prevalent entity**
- ***This series built with an ethos of routine diagnostic biopsy, pre MD diagnosis***

The CT spectrum of IPF



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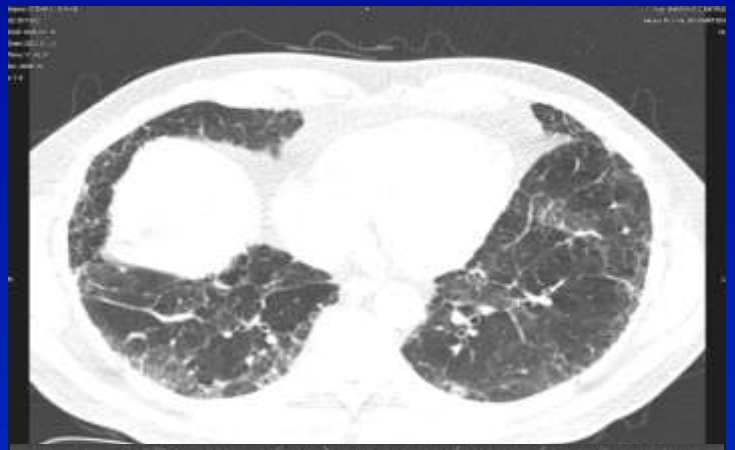

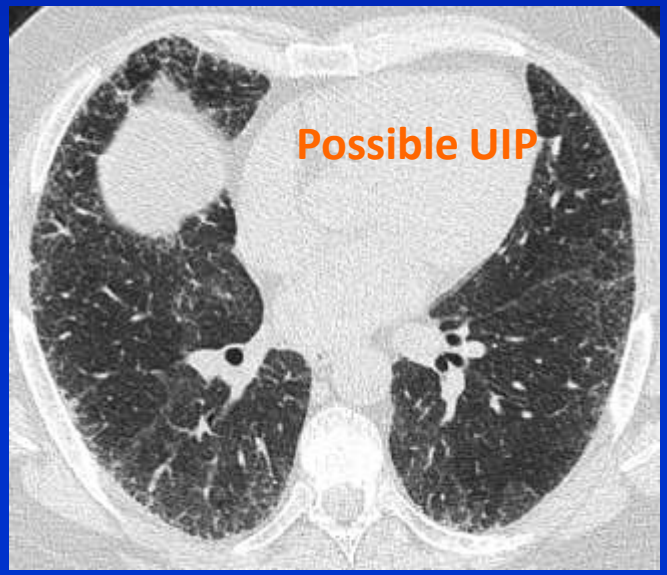

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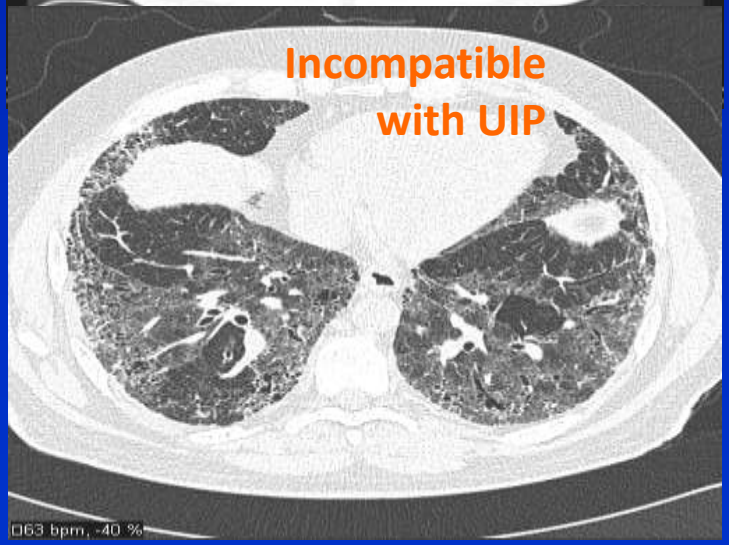

5-10%

2011 IPF guideline

- IPF patients with possible UIP on HRCT who do not have a biopsy have unclassifiable disease based on the 2011 IPF guideline recommendations
- This is a very frequent scenario which has probably doubled the frequency of unclassifiable disease
- Major management dilemmas
- Unclassifiable disease is more important than ever before

Summary

- Diagnosis/classification of the IIPs now driven by the mutidisiplinary process
- NSIP now viewed as a clinical entity
- LIP has been demoted into a “rare” category, accompanied by IPPFE
- Other entities essentially unchanged
- Birth of a disease behaviour classification