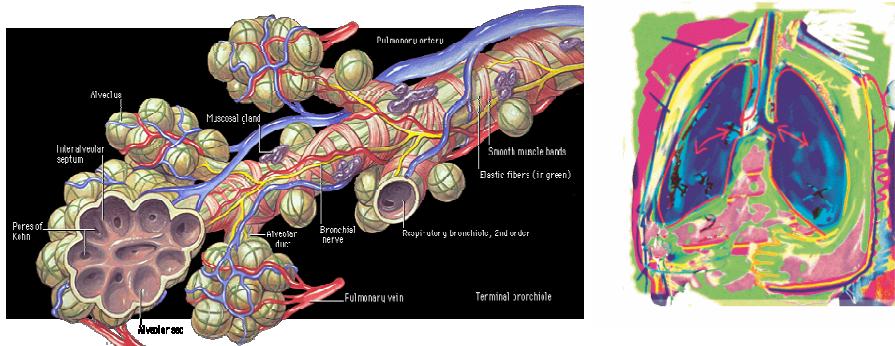


## Patologia Polmonare Idiopatica: Possibile ruolo dell'esposizione professionale



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## *Occupational Respiratory Diseases*

- I materiali inalati sul posto di lavoro possono causare tutte le maggiori malattie polmonari
- A causa di differenze nel metabolismo e suscettibilità dell'ospite, un agente occupazionale può causare diverse malattie. Al contrario una malattia polmonare può avere numerose cause occupazionali

## *Occupational Respiratory Diseases*

➤ Il riconoscimento di cause occupazionali può essere reso difficile dalle risposte ritardate che avvengono a domicilio dopo il lavoro o dagli anni di latenza tra l'esposizione lavorativa e il manifestarsi della malattia

## Gheorghita A.

- Donna di 34 anni, non fumatrice, proveniente dalla Moldavia.
- Nel 2004 per 2 anni lavora come operaia in industria tessile di jeans
- Da 2 anni lavora come badante
- Anamnesi Patologica Remota: ndd

## Anamnesi patologica prossima

- Da 1 anno dispnea da sforzo ingravescente e tosse secca, calo ponderale di 5 Kg
- Gennaio '07 ricovero c/o H della Liguria: in considerazione di un quadro nodulare all'Rx torace e della Mantoux positiva iniziava terapia antitubercolare ex adivantibus per 2 mesi senza beneficio
- Successivamente comparsa di PNX bilaterale per cui viene nuovamente ricoverata e trattata con drenaggio pleurico e pleurodesi chirurgica

## Esami di laboratorio (Febbraio '08)

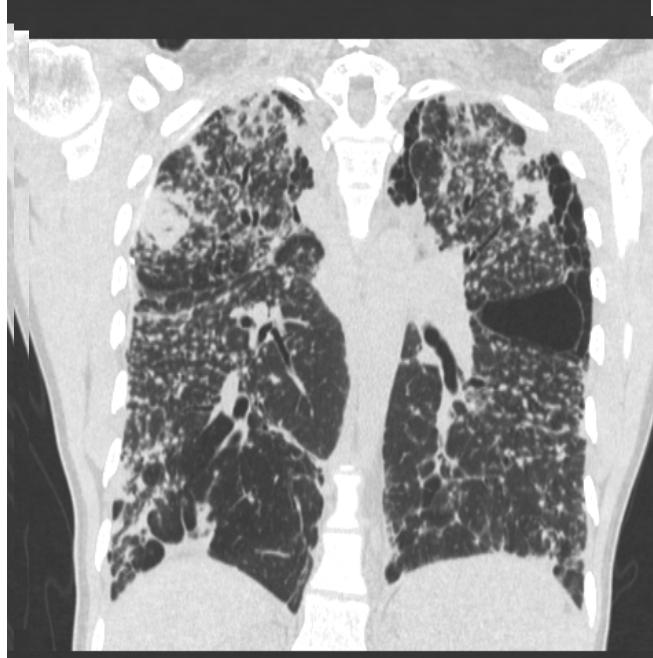
Tutto nella norma eccetto:

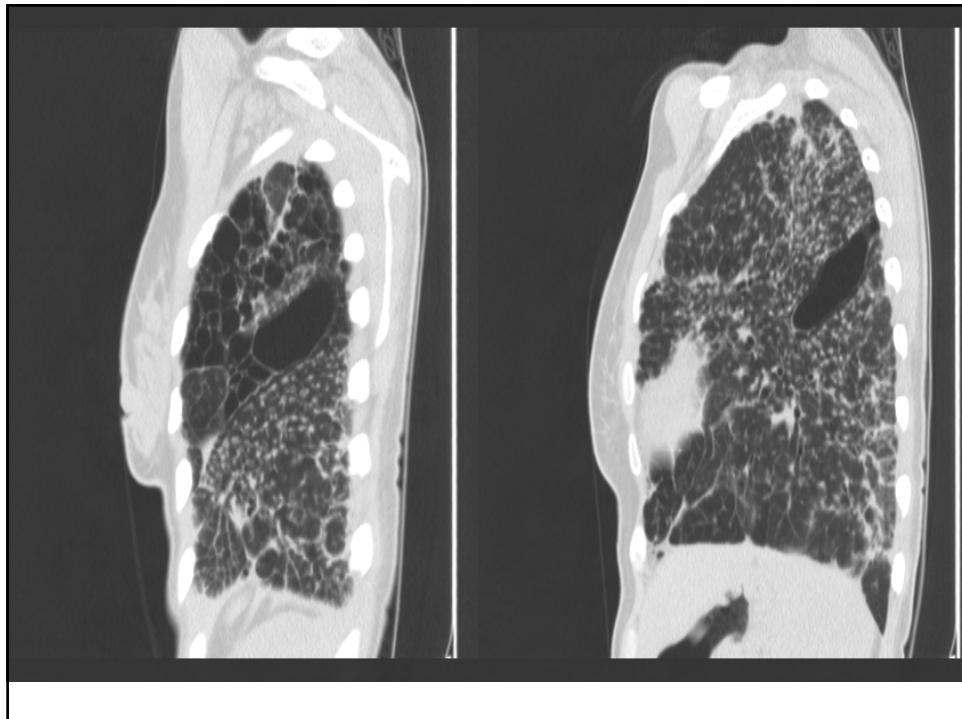
- VES 66 1° h
- ANA positivi, pattern omogeneo, titolo 1:160

## Test di Funzionalità Polmonare

- 6 min walking test: desaturazione (O<sub>2</sub> Sat inizio 96%- O<sub>2</sub> Sat fine 81%)
- Spirometria:

	VC	%	TLC	%	TIFFENAU	DLCO%	Sat%
Lug '07	1,81	52	2,98	70,7	81	?	97
Feb'08	1,27	37	3,42	71	64	37	96

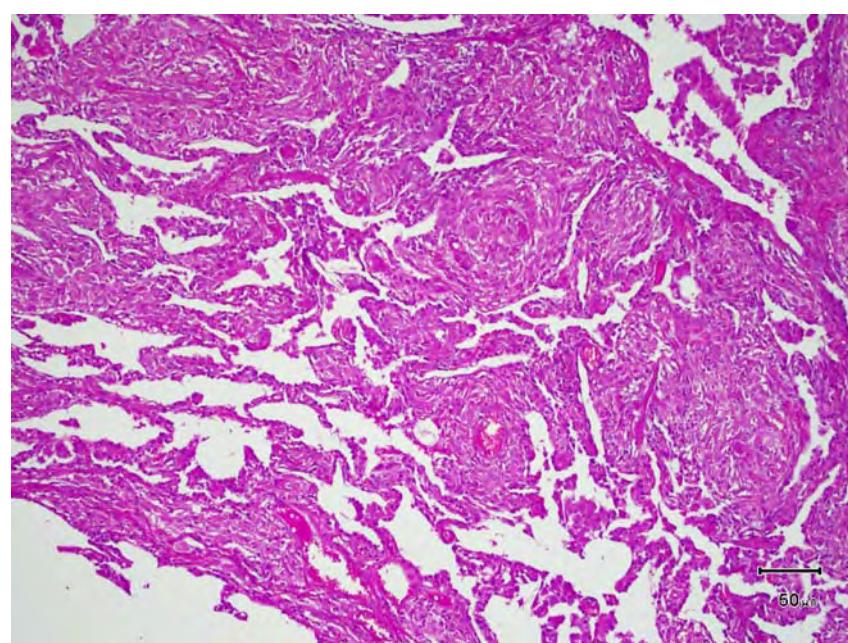
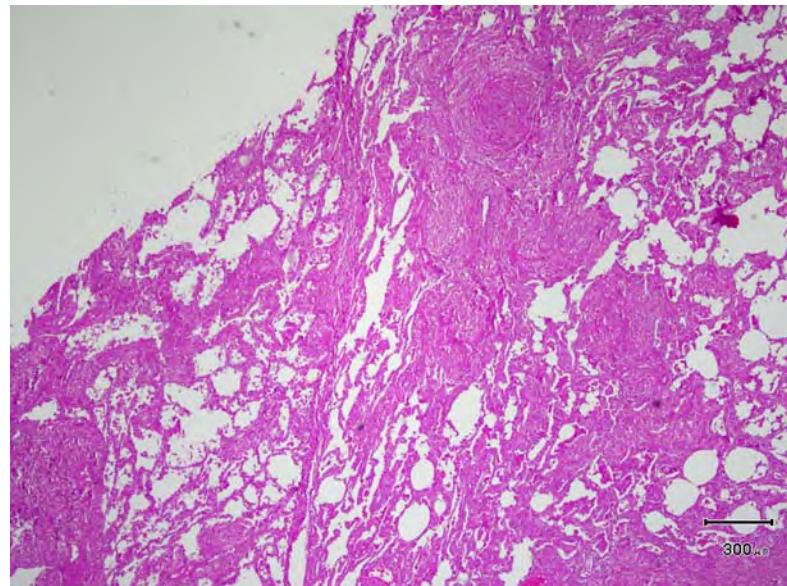


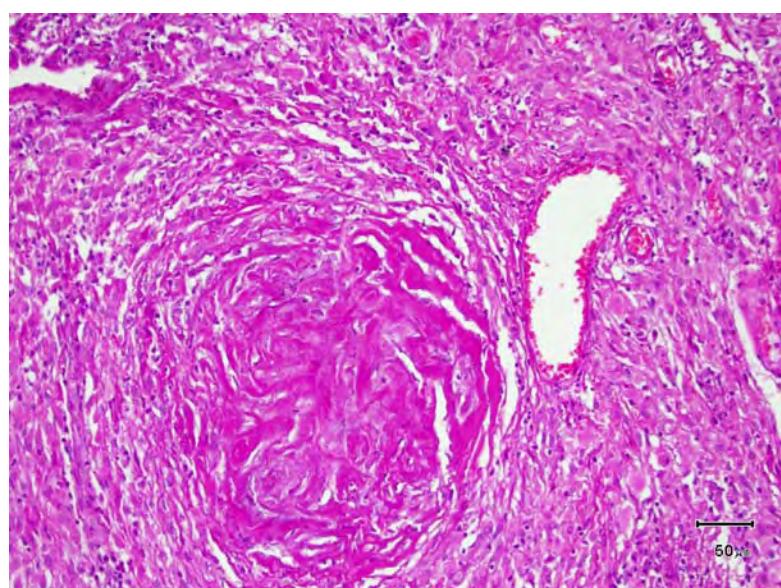
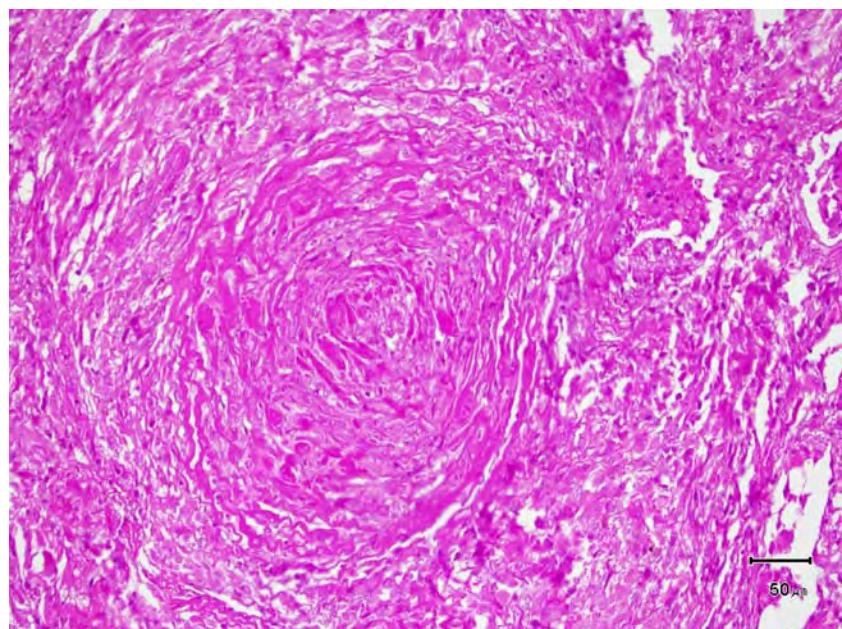


*Ipotesi Diagnostica  
Radiologica:*

- *Sarcoidosi ?*
- *Pneumoconiosi ?*
- *Tuberkulosi ?*
- *Granulomatosi ndd ?*

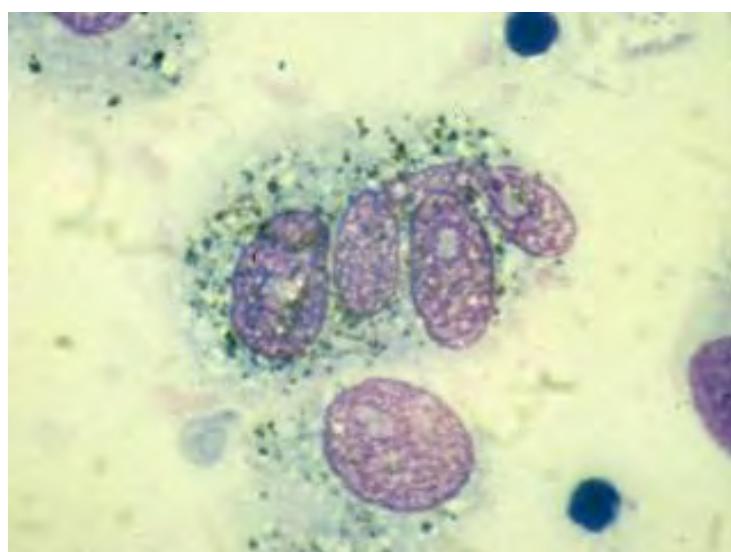
Revisione materiale asportato  
chirurgicamente per pleurodesi





## Fibrobroncoscopia

- Imbocco del bronco lobare medio che appare stirato e ridotto di diametro come da fenomeni retrai
- Broncoaspirato: CTM, colturale per flora comune, miceti, Legionella, BAAR, Pneumocystis e CMV negativi
- BAL: conta cellulare: macrofagi 77%, neutrofili 5%, linfociti 18%





Eur Respir J 2008; 32: 1295–1303  
DOI: 10.1183/09031936.00093507  
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## An epidemic of silicosis among former denim sandblasters

M. Akgun\*, O. Araz\*, I. Akkurt#, A. Eroglu†, F. Alper‡, L. M. Gorguner\* and B. Nemery†

**TABLE 1** Demographic and exposure characteristics, and pulmonary function test results in subjects with previous experience in sandblasting

Subjects n	157
Age yrs	23 ± 6 (15–44)
Age at first exposure to sandblasting yrs	17 ± 6 (10–38)
Total exposure duration months	36 ± 25 (1–120)
Duration since the last exposure months	43 ± 28 (10–144)
Latency period* months	79 ± 35 (12–192)
Number of places of work	3 ± 2 (1–12)
Number of sandblasting devices at the workplace	4 ± 1 (2–12)
Smokers or ex-smokers	106 (67.5)
Smoking in smokers pack-yrs	7.3 ± 4.4 (1–23)
Sleeping at the workplace	129 (82.2)

All subjects were male, with a mean (range) age of 23 (15–44) yrs. They had worked for a mean (range) of 36 (1–120) months, starting employment at a 17 (10–38) yrs of age. Most subjects (83%) had respiratory symptoms, especially dyspnoea (52%) but also chest pain (46%). Radiological evidence of silicosis (ILo score 1/0 or higher) was present in 77 (53%) out of 145 subjects with interpretable chest radiographs. These subjects had lower forced expiratory volume in one second and forced vital capacity. The risk of silicosis correlated with seniority (i.e. working as a foreman), exposure duration and number of places of work.

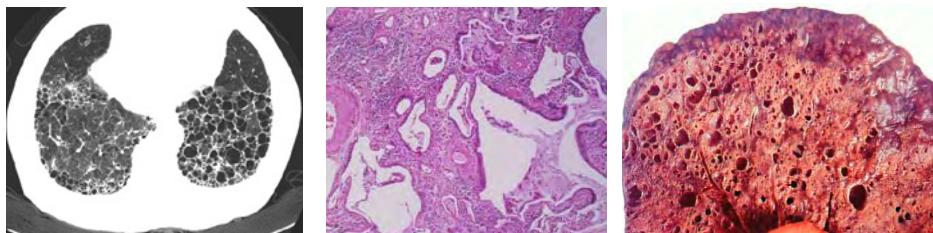
\*stated. FEV1: forced expiratory volume in one second; % pred: % predicted; FVC: forced vital capacity. \*: time elapsed since the beginning of exposure.



	VC	%	TIFFENAU	DLCO%	Sat%
Luglio 2007	1,81	52	81	?	97
Febbraio 2008	1,27	37	64	37	96
Maggio 2008	1,48	43	71	39	93
Giugno 2009	1.2	36	72	37	94
Dicemb. 2009	1.62	47	75	40	95
Maggio 2010	1.56	46	73	38	96

## *Definizione*

- La Fibrosi Polmonare Idiopatica (IPF) è una polmonite interstiziale cronica fibrosante da causa sconosciuta ed è associata ad un pattern istologico di polmonite interstiziale usuale (UIP)



## **Is Idiopathic Pulmonary Fibrosis an Environmental Disease?**

- In experimental or occupational settings, exposure to fibrogenic dusts, fibers, and fumes have long been recognized as causing fibrotic lung diseases

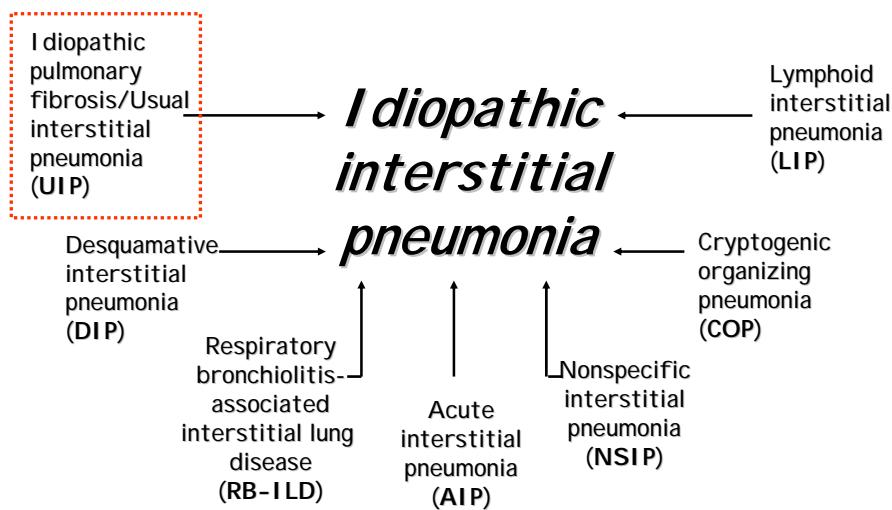
Glazer CS, Newman LS. Occupational interstitial lung disease. *Clin Chest Med* 2004;25:467-478

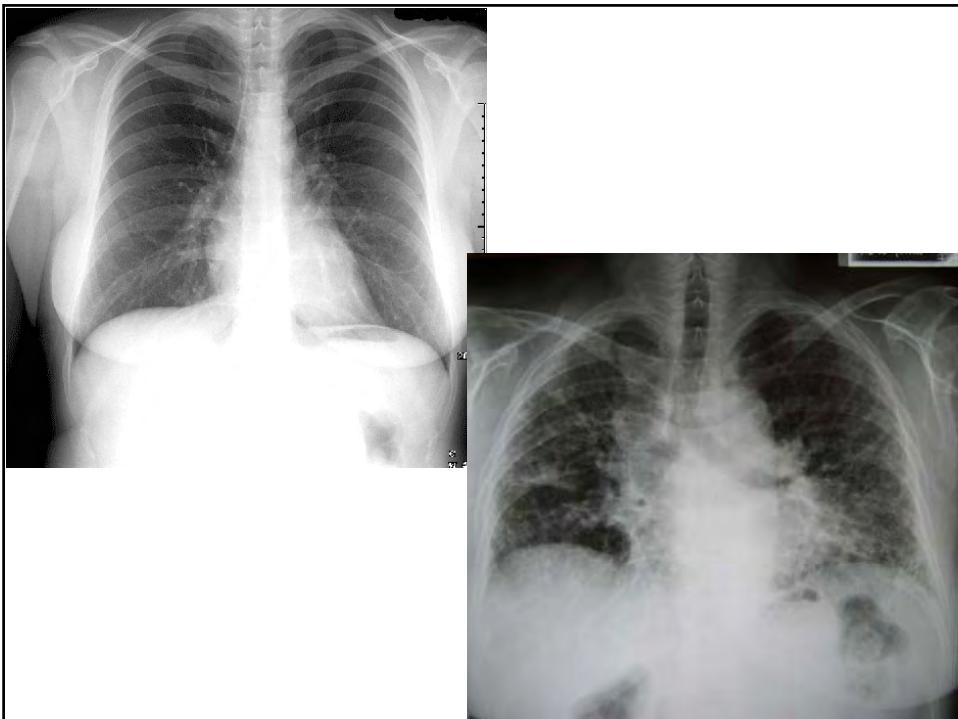
## FACTORS LIMITING RECOGNITION OF ENVIRONMENTAL AGENTS CAUSING IPF

- Diagnostic misclassification,
- Infrequent occurrence of IPF,
- Exposure misclassification (patient and/or clinician)
- Variation in susceptibility to exposures

Glazer CS, Newman LS. *Clin Chest Med* 2004;25:467-478  
Armstrong BG. *Occup Environ Med* 1998;55:651-656

## *New Classification of Idiopathic Interstitial Pneumonia*

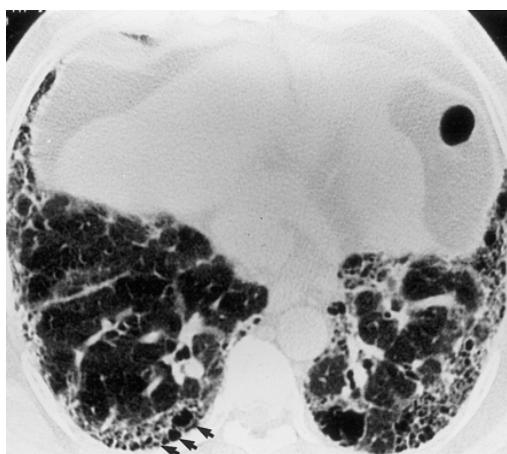




Fibrosi Polmonare Idiopatica

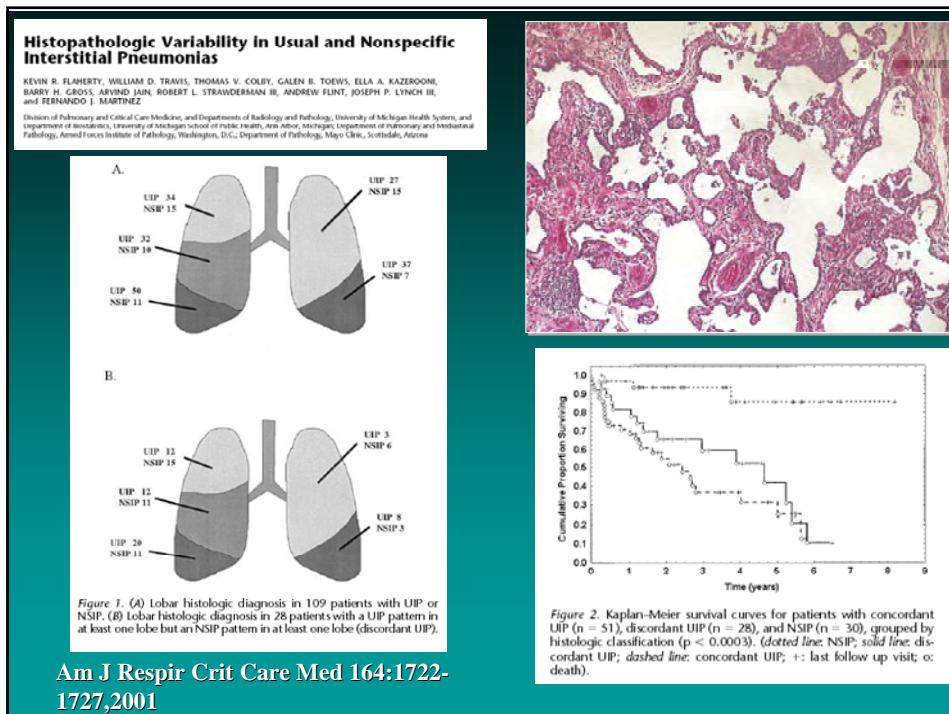
## *TAC ad Alta Risoluzione (HRCT)*

- Segni di fibrosi: I spessimento interstiziale intralobulare, irregolarità delle interfacce, bronchioli intralobulari visibili, honeycombing, bronchiectasie da trazione
- Opacità a vetro smerigliato (poco estese)
- Predominanza delle lesioni in sede periferica, subpleurica, ai campi polmonari inferiori e posteriori



## Fibrosi Polmonare Idiopatica

# *TAC ad Alta Risoluzione (HRCT)*



Am J Respir Crit Care Med 164:1722-1727, 2001

## FACTORS LIMITING RECOGNITION OF ENVIRONMENTAL AGENTS CAUSING IPF

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### Incidence and Prevalence of Idiopathic Pulmonary Fibrosis

Ganesh Raghu, Derek Weycker, John Edelsberg, Williamson Z. Bradford, and Gerry Oster

Am J Respir Crit Care Med Vol 174. pp 810-816, 2006

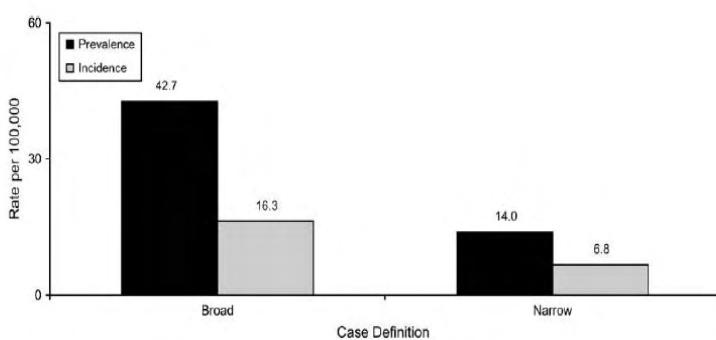
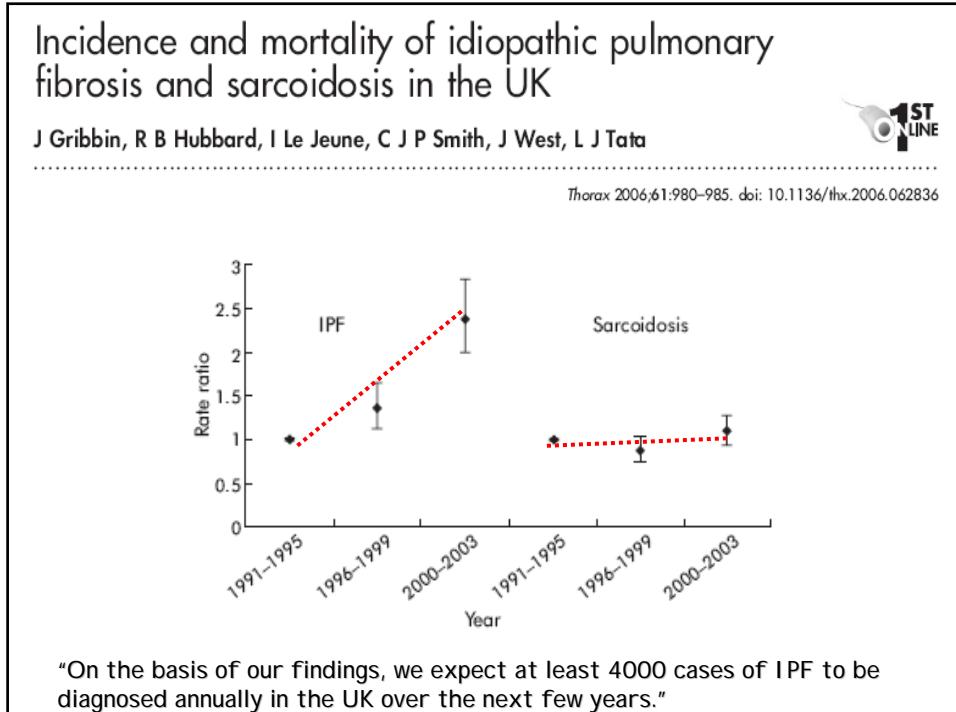
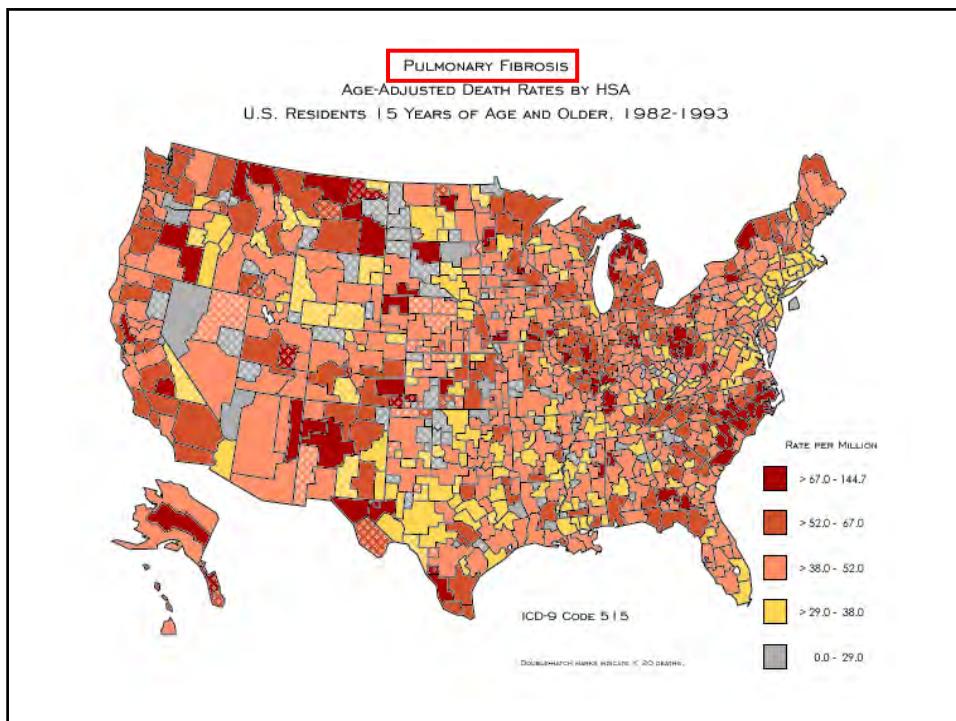


Figure 3. Prevalence of IPF, by age, sex, and case definition. Broad definition includes persons with a diagnosis of idiopathic pulmonary fibrosis (ICD-9-CM 516.3) and no subsequent diagnoses of other interstitial lung diseases; narrow definition includes all persons meeting broad definition who also had evidence of a prior diagnostic test (including surgical lung biopsy, transbronchial lung biopsy, or computed tomography of the thorax).

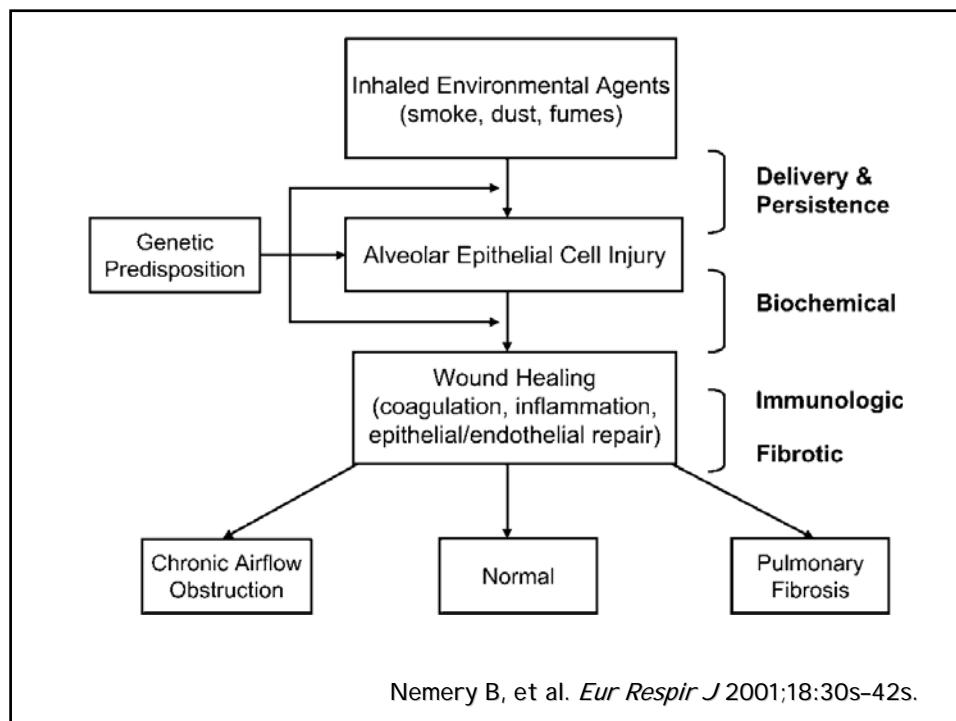
From January 1996 to December 2000



## FACTORS LIMITING RECOGNITION OF ENVIRONMENTAL AGENTS CAUSING IPF

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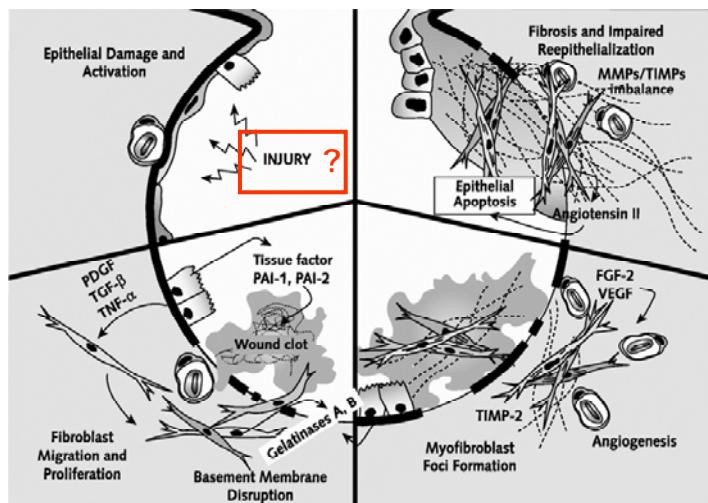


## *SOURCES OF EVIDENCE*

- Studies of Pathogenesis
  - Asbestos, beryllium, silicates, hard metals...
  - Animal models
  - Particle dimension, persistence, biochemical, immunologic and fibrotic response...
- Observational Studies

Fibrosi Polmonare Idiopatica

## *Patogenesi*



## **SOURCES OF EVIDENCE**

- Studies of Pathogenesis
- Observational Studies

### **CASE-CONTROL STUDIES OF OCCUPATIONAL AND ENVIRONMENTAL RISK FACTORS FOR IDIOPATHIC PULMONARY FIBROSIS**

Exposure	United Kingdom		United States		Japan	
	England/Wales Scott and Colleagues, 1990 (45) (40/106)*	Trent Region Hubbard and Colleagues, 1996 (46) (218/569)*	Mullen and Colleagues, 1998 (50) (17/94)*	Baumgartner and Colleagues, 2000 (48) (248/491)*	Iwai and Colleagues, 1994 (43) (86/172)*	Miyake and Colleagues, 2005 (51) (102/59)*
Agriculture/Farming				1.60 (1.0–2.5)	3.01 (1.29–7.43)	
Livestock	10.89 (1.24–96.0)			2.70 (1.30–5.50)		
Wood dust	2.94 (0.87–9.9)	1.71 (1.01–2.92)	3.3 (0.42–25.8)	1.60 (0.80–3.30)		6.71 (0.37–123.59)
Textile dust	0.9 (0.24–3.44)	1.80 (1.10–2.96)		1.90 (0.80–4.40)		
Mold			16.0 (1.62–158)			
Metal dust	10.97 (2.34–52.4)	1.68 (1.07–2.65)		2.00 (1.00–4.00)	1.34 (1.14–1.59)	0.98 (0.48–2.01)
Stone/sand/silica	1.59 (0.52–4.79)	1.76 (1.01–3.07)	11.0 (1.05–115)	3.90 (1.20–12.70)		9.55 (1.68–181.12)
Wood fires	12.55 (1.40–114.0)			0.80 (0.40–1.60)		
Smoking	1.11 (0.13–1.40)	1.57 (1.01–2.43)		1.60 (1.10–2.40)	2.94 (1.37–6.3)	3.23 (1.01–10.84)

Values are shown as odds ratios (95% confidence intervals).

\* Numbers in parentheses represent number of cases/number of controls.

Taskar VS and Coultas DB. Proc Am Thorac Soc 2006;3:293

## META-ANALYSIS OF RISK FOR IDIOPATHIC PULMONARY FIBROSIS ASSOCIATED WITH ENVIRONMENTAL AND OCCUPATIONAL EXPOSURES

Exposure	No. Studies (Reference)	Cases Exposed/ Not Exposed, n (%)	Controls Exposed/ Not Exposed, n (%)	Summary Estimates*	Population- Attributable Risk Percentage
Agriculture/farming	2 (43, 48)	86/334 (25.7)	115/663 (17.3)	1.65 (1.20–2.26)	20.8
Livestock	2 (45, 48)	30/288 (10.4)	30/597 (5.0)	2.17 (1.28–3.68)	4.1
Wood dust	5 (45, 46, 48, 50, 51)	58/625 (9.3)	67/1319 (4.9)	1.94 (1.34–2.81)	5.0
Metal dust	5 (43, 45, 46, 48, 51)	82/694 (11.8)	75/1397 (5.4)	2.44 (1.74–3.40)	3.4
Stone/sand/silica	4 (45, 48, 50, 51)	28/407 (6.9)	26/750 (3.5)	1.97 (1.09–3.55)	3.5
Smoking	5 (43, 45, 46, 48, 51)	460/694 (66.3)	784/1,397 (56.1)	1.58 (1.27–1.97)	49.1

\* Values are shown as odds ratios (95% confidence intervals).

Taskar VS and Coultas DB. Proc Am Thorac Soc 2006;3:293

- In a population-based study of the occurrence of IPF, the disease was most common in older men who are most likely to work in dust-exposed occupations \*
- and in the United Kingdom there is an excess mortality from IPF in regions associated with the manufacturing industry\*\*

\*Coultas DB, et al. *Am J Respir Crit Care Med* 1994;150:967

\*\* Johnston I, et al. *BMJ* 1990;301:1017

- A number of case reports link IPF to various occupations that involve dust or fume exposure, including diamond polishing, industrial car cleaning , dairy work, welding, gold extraction, and technical dental work
- Lung mineralogic analysis of patients with IPF has revealed that these patients have an excess of silica and metals, including iron and nickel

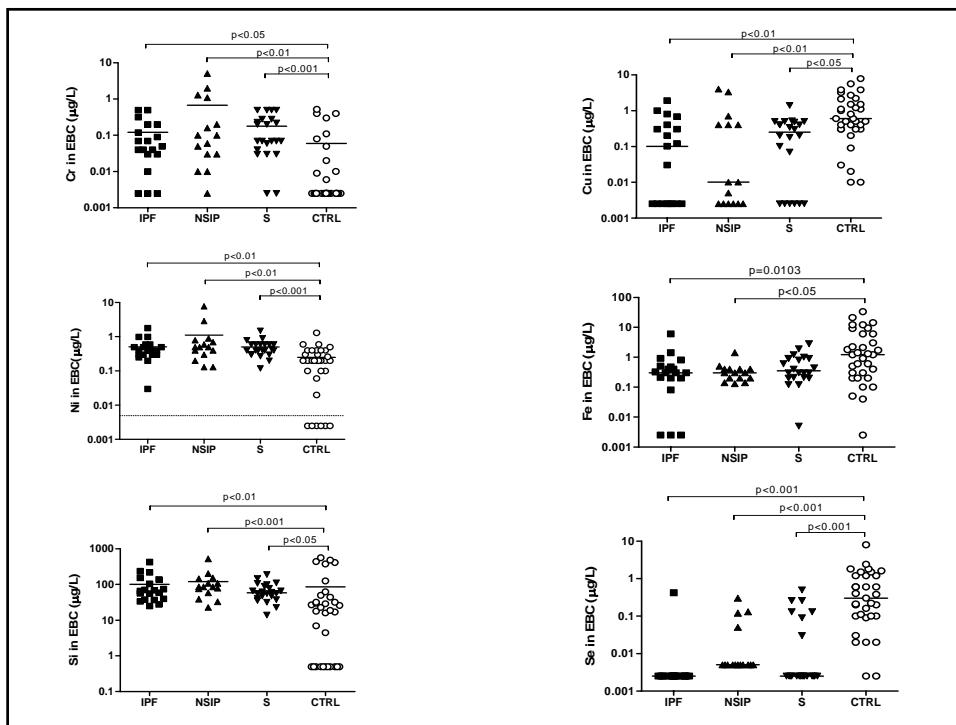
Taskar VS and Coulas DB. Proc Am Thorac Soc 2006;3:293

#### METALLIC ELEMENTS IN EXHALED BREATH CONDENSATE OF PATIENTS WITH INTERSTITIAL LUNG DISEASES

M Corradi, O Acampa, M Goldoni, E Adami, P Apostoli,  
G de Palma, A Pesci, A Mutti, in press

	IPF	NSIP	Sarcoidosis	Controls
No. of subjects (M/F)	19 (14/5)	15 (9/6)	22 (14/8)	33 (25/8)
Age	68±0.78	65.3±9.7	53.5±13.9	55±10.80
Ex-smokers/non-smokers	13/6	10/5	16/6	0/33
Pack/years	24.5 (16.5-38.5)	26.4 (15.0-42.5)	16.5 (5.3-20.0)	0
FVC, L	2.3±0.9	2.6±0.9	3.5±0.9	4.8±0.9
FVC % of predicted	67.8±19.2	80.8±18.1	94±12.5	108±10.5
TLC, L	3.8±1.2	4.4±1.4	5.4±1.1	5.6±1.3
TLC % of predicted	62.0±13.5	75.2±16.4	89.6±11.4	85±2.3
FEV <sub>1</sub> /FVC %	84.1±7.4	78.8±8.6	79.7±7.8	79±7.4
DLCO %	46.4±17.6	59.7±19.5	76.3±18.8	81±17.1

Mean values ± SD, or median values (25<sup>th</sup> – 75<sup>th</sup> percentile)



- In conclusion, assessing the elemental composition of EBC in patients with different ILDs seem to provide useful information.
- We found higher levels of Ni, Cr and Si in ILD patients than in controls, and lower levels of some trace elements involved in the oxidant/anti-oxidant balance; this depletion may be due to the oxidative stress and chronic inflammation characterizing ILDs.
- Furthermore, the pattern of some metallic elements seemed to be able to differentiate controls and patients.

## *Conclusions*

- Together, the available evidence strongly suggests that the term “IPF” may be a misnomer and multiple environmental agents may be causing pulmonary fibrosis in susceptible individuals