
ČPFS
AIPO
ASSOCIAZIONE ITALIANA PNEUMOLOGI OSPEDALIERI
ERS
FIBROSING INTERSTITIAL LUNG DISEASES OF IDIOPATHIC AND EXOGENOUS ORIGIN. PHENOTYPE APPROACH.
Conference, Postgradual and Scientific Course
PRAGUE
CZECH REPUBLIC
JUNE 19TH – 21ST 2014
HOTEL ARTEMIS
U SLUNCOVÉ 14, PRAGUE 8
Rare exogenous ILDs. (ILDs caused by metals, organic dusts toxic syndrome, et al).

Fibrosing interstitial lung diseases of idiopathic and exogenous origin.
Prague – 20.06.2014

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Organic dust toxic syndrome (ODTS)

- Acute febrile reaction following single heavy exposure to (mould contaminated) organic dust
  - “silo unloader’s syndrome”
  - “pulmonary mycotoxicosis”
  - grain fever
  - (cotton) mill fever
  - intensive pig farming

= non infectious, non allergic “toxic alveolitis”

≠ acute Hypersensitivity Pneumonitis

≠ acute Extrinsic Allergic Alveolitis, i.e. ≠ ILD !

ODTS

- 4 to 8 h after exposure:
  - flu-like symptoms
    - fever
    - malaise
    - muscle & joint aches
    - (moderate) respiratory symptoms
  - massive influx of polymorphonuclear cells in BAL
  - peripheral leukocytosis

ODTS

- spontaneous resolution in 24 to 48 h
- cause: bacterial endotoxin ?
- tolerance
  - does not occur in chronically exposed
  - occurs after exposure-free period
- no sequelae (?)
- frequent, but unreported, overlooked or misdiagnosed

ODTS

- all jobs or circumstances with potential heavy exposure to organic dusts or bioaerosols
  - agriculture & horticulture
  - transportation, storage & handling of food stuffs
  - textile & wood industry
  - garbage treatment, sewage & composting
  - old buildings, archives, ...
  - humidifiers
  - swimming pools, ...

“Inhalation fevers”

- Organic Dust Toxic Syndrome (ODTS)
- Metal Fume Fever (MFF)
- Polymer Fume Fever (PFF)

Metal fume fever

- Single exposure to high concentrations of <u>some</u> metal oxides (ZnO, CuO, ...)
  - smelting
  - welding (galvanized metal)
  - galvanizing
  - brazing
  - metallizing (gun-spraying Zn)

  in enclosed spaces or poorly ventilated conditions

! CdO, Os_3O_4, V_2O_5, MnO: more severe pneumonitis (life-threatening pulmonary oedema)

Polymer fume fever

- Exposure to heated F-containing polymers,
  typically: polytetrafluoroethylene (PTFE) > 300°C
  - PTFE resin moulding & extrusion
  - welding of PTFE-coated metal
  - high-speed machining of PTFE
  - smoking cigarettes contaminated with PTFE
- also heated Cl-containing polymers (PVC) ?
- also heated polymers containing Br-based flame retardants ?

! May be severe (pulmonary oedema → †)

- No tolerance, possible sequelae (fibrosis)

Inhalation fevers

- 4 - 8 h after exposure influenza-like reaction
  - fever, chills, malaise, g-i upset, muscle pains
  - [metallic taste]
  - mild respiratory symptoms
  - chest x-ray: transient infiltrates possible
    + features of pulmonary oedema if severe
  - LFT: VC (↓), DLco (↓), PaO_2 (↓)
  - pmn ↑↑ in blood and BAL
- self-limited: usually resolution in 24 - 48 h
- tolerance (“Monday fever”), except in PFF

Inhalation fevers

- pathogenesis:

  non allergic

  non infectious

  massive influx of pmn in lung

➢ “toxic alveolitis”

- activation of cytokine networks

  macrophages - epithelium ?

- switch-off mechanism? tolerance?

- long-term effects ? “no sequelae”

Zinc Fume Fever

- Blanc *et al.* *Ann. Int. Med*. 1991, 114, 930-6; *ARRD* 1993, 147, 134-8
  - 26 volunteers welding on galvanized steel (15-30 min)
  - BAL 3, 8 or 22 h later
  - pmn 2%, 12 % , 37 % // ZnO in air
  - ↗ TNF (↑↑ 3 h), (IL-1), IL-6, IL-8

ODTS

- Larsson *et al.* *AJRCCM* 1994, 150, 973-7
  - 14 previously unexposed volunteers weighing swines in swine-confinement building (700 pigs) for 2-5h
  - BAL 2 wk before & after 24 h
  - total BAL cells x4
  - BAL pmn x 75 (1% → 28%)

    ↑ // dust & endotoxin
  - blood WBC & CRP

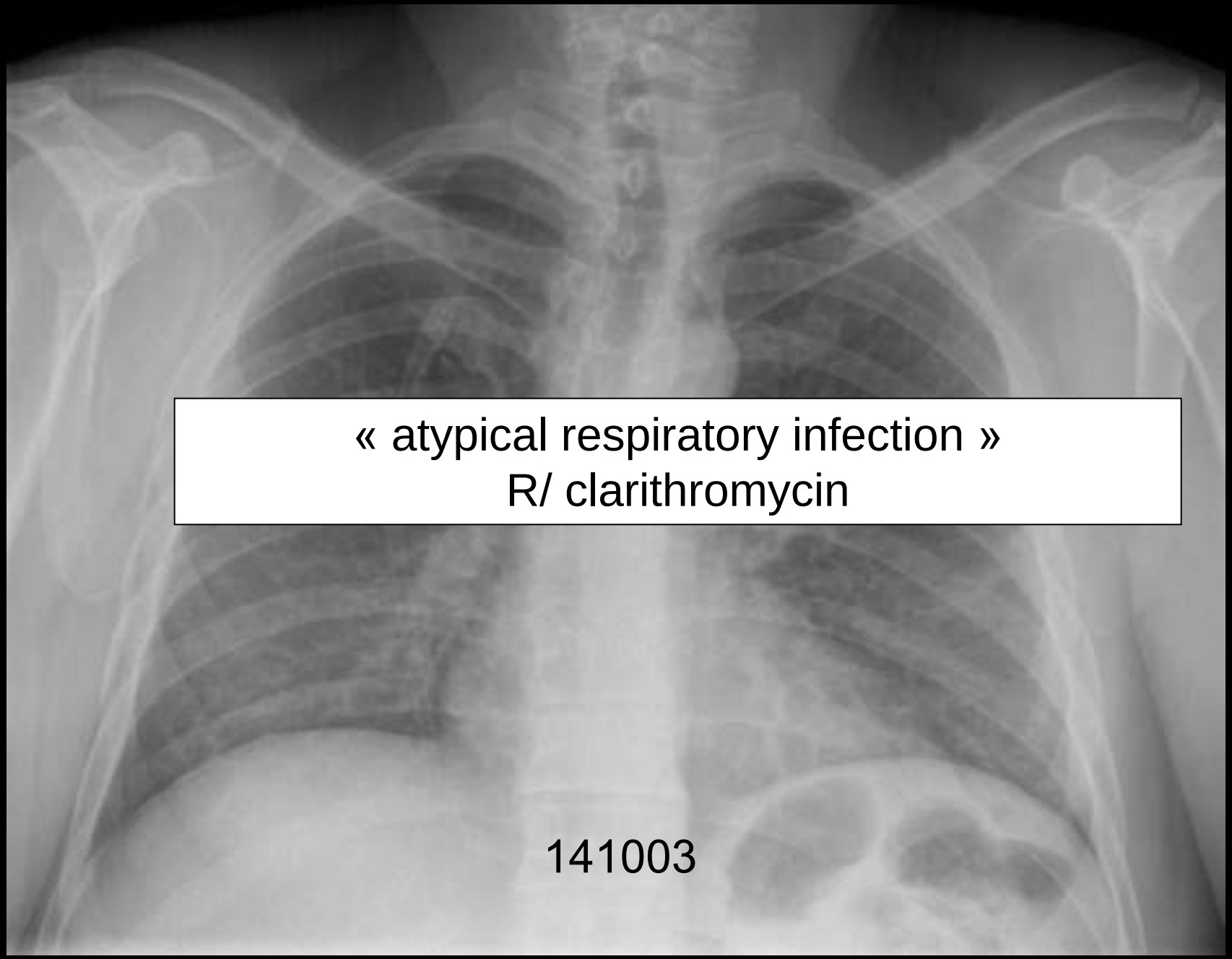
Inhalation fevers

Differential diagnosis

- Other causes of FUO
- Infections (viral, ...)
- Pulmonary oedema (CdO, PTFE, ...)
- Hypersensitivity pneumonitis
- Occupational asthma

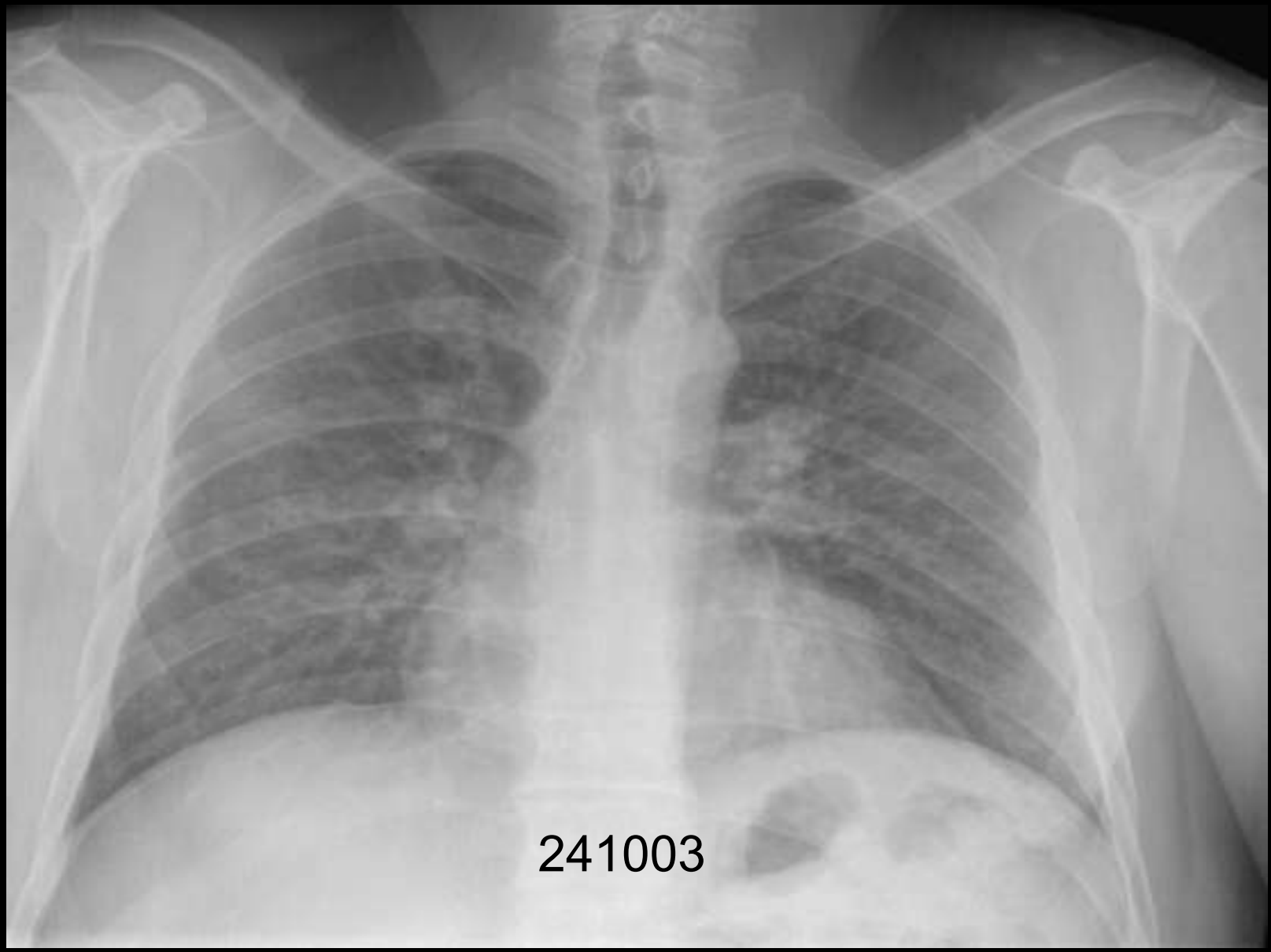
Case

- Man, 43 y, smoker, no previous disease
- Visit to Emergency Department:
  - fever, malaise, dry cough, dyspnoea
  - evening: WBC 17,200 (82% pmn), CRP 7 mg/L
  - morning: WBC 11,800 (69% pmn), CRP 53 mg/L, PaO_2 63 mmHg
  - Chest X-ray:

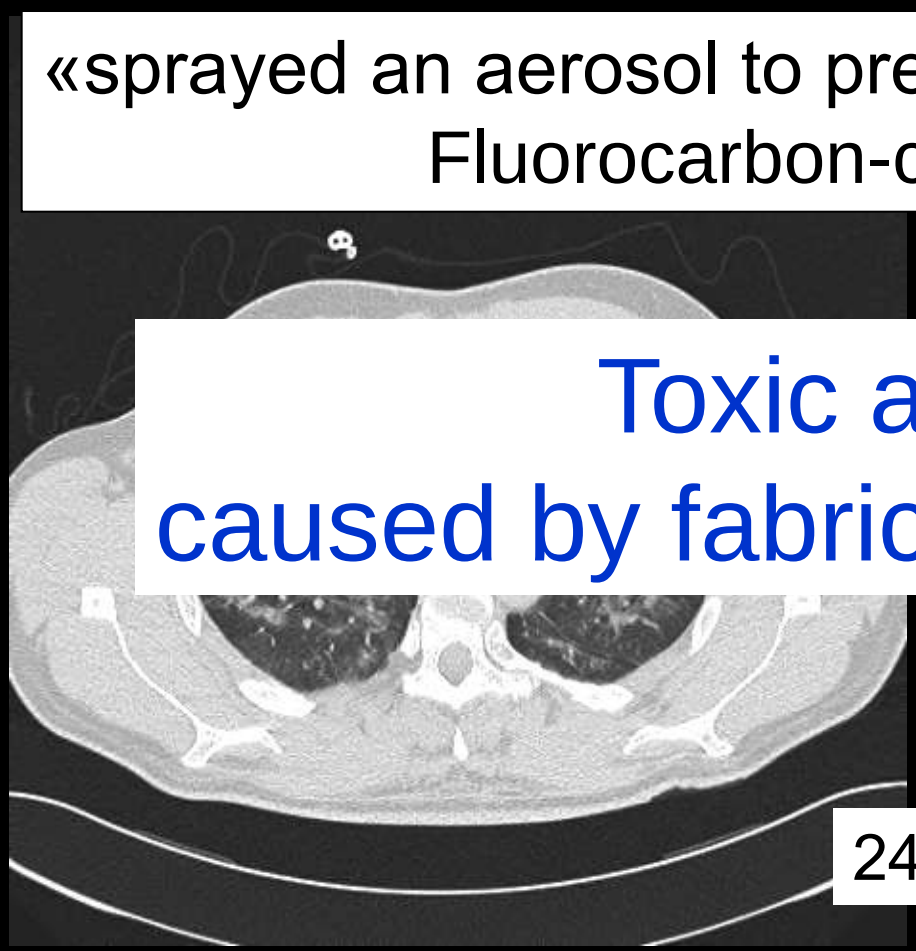

« atypical respiratory infection »
R/ clarithromycin
141003

Case

- Second visit to ED 10 days later:
  - similar symptoms
  - WBC 21,400 (81% pmn), CRP 11 mg/L, PaO_2 74 mmHg
  - Chest X-ray and HRCT


241003

«sprayed an aerosol to prepare new cars (1 can/car)»
Fluorocarbon-containing spray

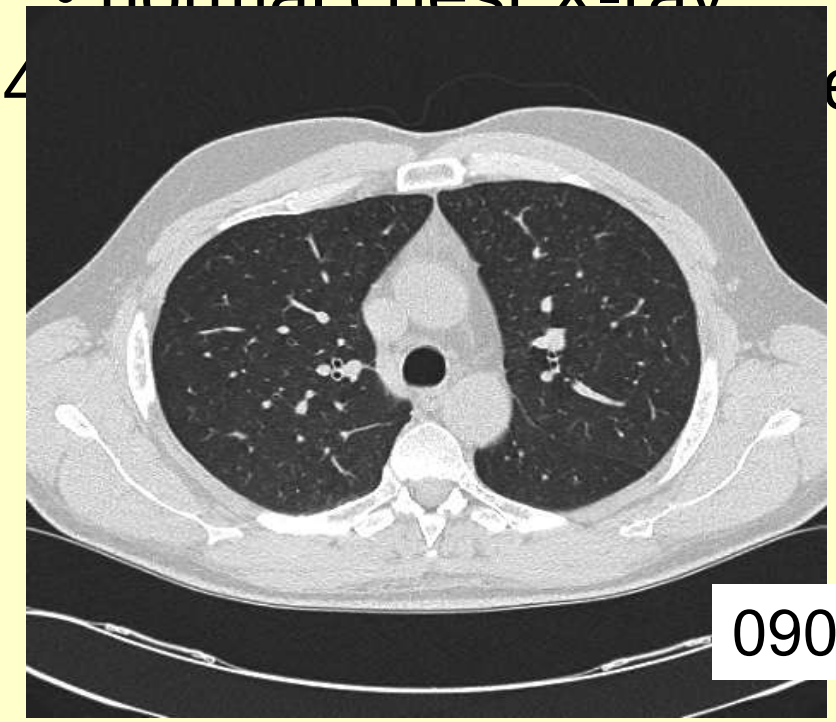


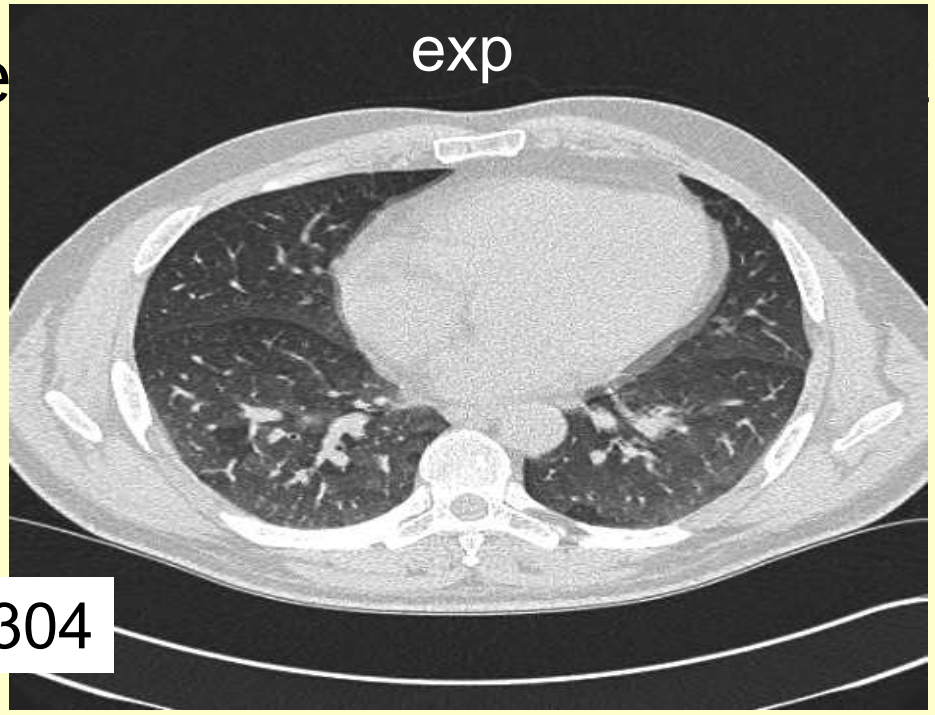
Toxic alveolitis
caused by fabric protection spray

24100

Case

- no infectious organisms detected
- R/ methylprednisolone
- rapid improvement, discharged after 5 days
  - normal pulmonary function, including DLco
  - normal chest X-ray
- 4





Fabric protection sprays

- Sprays for impregnation of leather or fabrics (shoes, jackets, furnishings, …) (water/dirt repellant, waterproofing, “anti-rain”, …)
  - Fluorine-containing hydrocarbons
  - + propellant (organic solvents)

➢ severe pulmonary damage in consumers, domestic animals, workers

- Burkhart *et al*. Pulmonary toxicity following exposure to an aerosolized leather protector. *Clin Toxicol* 1996;**34**:21-24.
- Jinn *et al*. Acute lung injury after inhalation of water-proofing spray while smoking a cigarette. *Respiration* 1998;**65**:486-488.
- Bracco & Favre. Pulmonary injury after ski wax inhalation exposure. *Ann Emerg Med* 1998;**32**:616-619.

Fabric protection sprays

- 2002-2003 reports of (severe) pulmonary injury in users of fabric & leather protection sprays
- The Netherlands

  Bonte *et al*. *Ned T Geneesk*, 2003, 147, 1185-8
  - Rotterdam, 5 patients [~70 cases reported to PCC]
- Switzerland

  Heinzer *et al*. *Thorax*, 2004, 59, 541-2
  - Lausanne, 6 patients [153 cases reported to PCC]

  Vernez *et al*. *J Occup Environ Hyg* 2006, 3, 250-61
  - Switzerland: 102 cases
- Belgium
  - Leuven, 3 men (36-43 y)

Change in propellant
(solvent with more pleasant smell)

Take home messages

- Not all clinical pictures of acute respiratory infection are due to infection
- Acute lung injury may occur following use of commonly available consumer products
- Old materials in new formulations!
- Take an occupational history in all patients!

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Exposure to metals

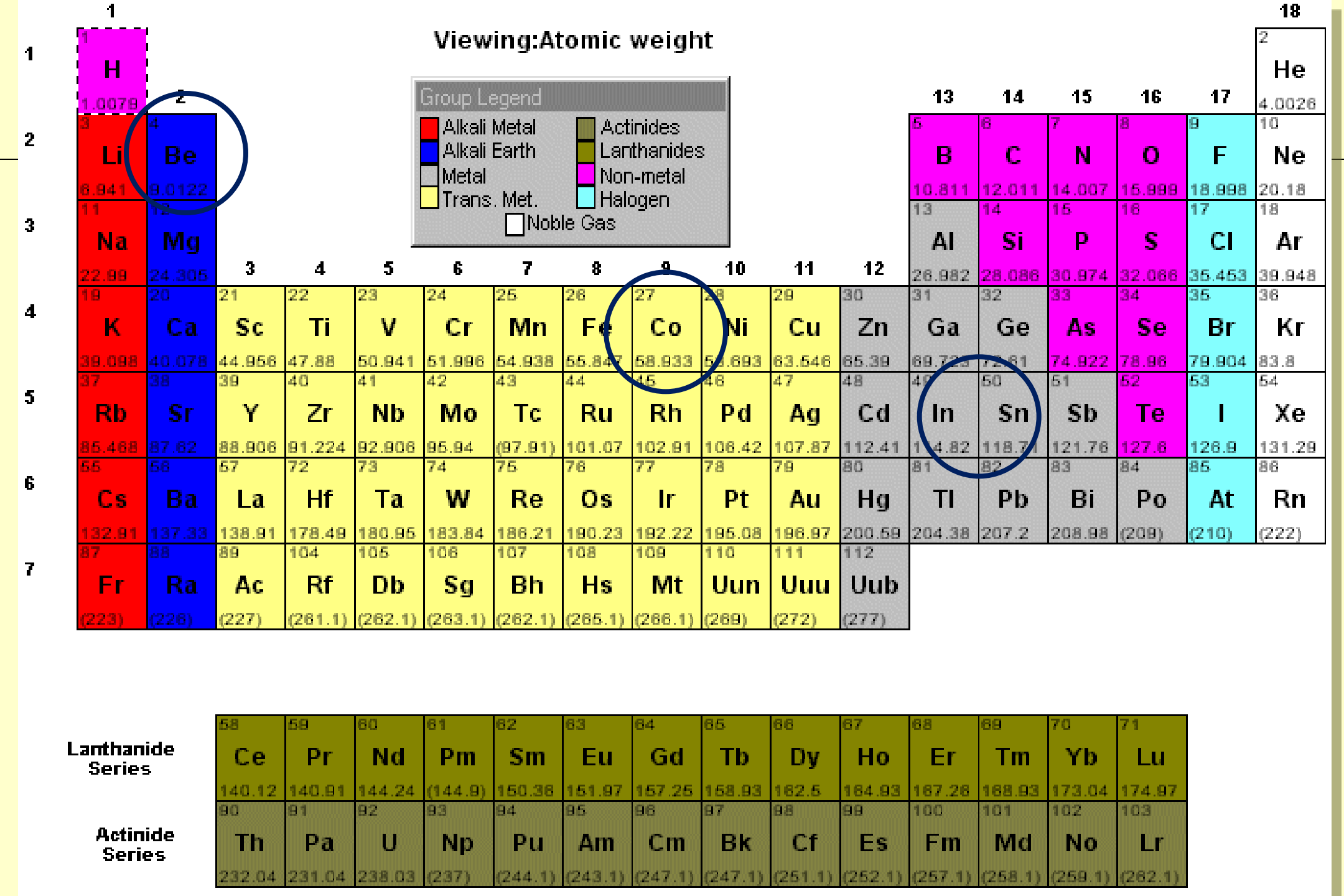
- is not confined to metal mining and metallurgy
- the respiratory tract is not necessarily the primary target
- respiratory disease in metal-exposed workers may be due to non-metallic agents
  - other minerals (crystalline SiO_2, asbestos, …)
  - gaseous agents (CO, SO_2, NO_x, …)
  - organic chemicals (solvents, resins, …)
  - Metal Working Fluids (= mineral oil + water + …)
  - microbiological agents (mycobacteria, fungi, …)




“Pneumoconioses” caused by metals

- Siderosis & welders’ pneumoconiosis (Fe)
- Dental technician’s pneumoconiosis
  - SiO_2, Be, Vitallium (Cr-Co-Mo), …
- Aluminium (Al)
  - “aluminosis” is rare and controversial
  - granulomatous reactions (DD sarcoidosis)
- Stannosis (Sn)
- Barytosis (Ba)
- Rare earth / cerium pneumoconiosis (Ce, lanthanides)
- Carborundum pneumoconiosis (SiC)

Metals and diseases of the lung parenchyma (3 specific examples)


Viewing:Atomic weight
Group Legend
Alkali Metal
Alkali Earth
Metal
Trans. Met.
Actinides
Lanthanides
Non-metal
Halogen
Noble Gas
1 H 1.0079
2 He 4.0026
3 Li 6.941
4 Be 9.0122
5 B 10.811
6 C 12.011
7 N 14.007
8 O 15.999
9 F 18.998
10 Ne 20.18
11 Na 22.99
12 Mg 24.305
13 Al 26.982
14 Si 28.086
15 P 30.974
16 S 32.066
17 Cl 35.453
18 Ar 39.948
19 K 39.098
20 Ca 40.078
21 Sc 44.956
22 Ti 47.88
23 V 50.941
24 Cr 51.996
25 Mn 54.938
26 Fe 55.847
27 Co 58.933
28 Ni 58.693
29 Cu 63.546
30 Zn 65.39
31 Ga 69.723
32 Ge 72.61
33 As 74.922
34 Se 78.96
35 Br 79.904
36 Kr 83.8
37 Rb 85.468
38 Sr 87.62
39 Y 88.906
40 Zr 91.224
41 Nb 92.906
42 Mo 95.94
43 Tc (97.91)
44 Ru 101.07
45 Rh 102.91
46 Pd 106.42
47 Ag 107.87
48 Cd 112.41
49 In 114.82
50 Sn 118.71
51 Sb 121.76
52 Te 127.6
53 I 126.9
54 Xe 131.29
55 Cs 132.91
56 Ba 137.33
57 La 138.91
72 Hf 178.49
73 Ta 180.95
74 W 183.84
75 Re 186.21
76 Os 190.23
77 Ir 192.22
78 Pt 195.08
79 Au 196.97
80 Hg 200.59
81 Tl 204.38
82 Pb 207.2
83 Bi 208.98
84 Po (209)
85 At (210)
86 Rn (222)
87 Fr (223)
88 Ra (226)
89 Ac (227)
104 Rf (261.1)
105 Db (262.1)
106 Sg (263.1)
107 Bh (262.1)
108 Hs (265.1)
109 Mt (266.1)
110 Uun (269)
111 Uuu (272)
112 Uub (277)
Lanthanide Series
58 Ce 140.12
59 Pr 140.91
60 Nd 144.24
61 Pm (144.9)
62 Sm 150.36
63 Eu 151.97
64 Gd 157.25
65 Tb 158.93
66 Dy 162.5
67 Ho 164.93
68 Er 167.26
69 Tm 168.93
70 Yb 173.04
71 Lu 174.97
Actinide Series
90 Th 232.04
91 Pa 231.04
92 U 238.03
93 Np (237)
94 Pu (244.1)
95 Am (243.1)
96 Cm (247.1)
97 Bk (247.1)
98 Cf (251.1)
99 Es (252.1)
100 Fm (257.1)
101 Md (258.1)
102 No (259.1)
103 Lr (262.1)

Beryllium (Be)

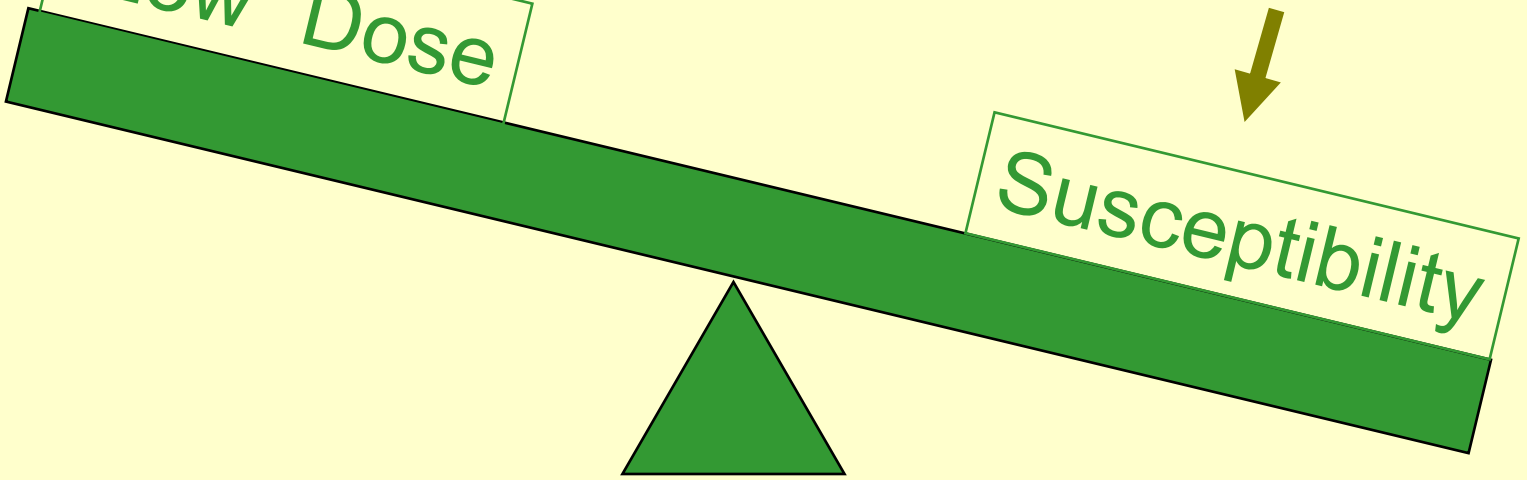
ILD due to “hypersensitivity”

low “intrinsic” toxicity

x

“Low” Dose

immune sensitization



Susceptibility

Chronic Beryllium lung Disease (CBD, Berylliosis)

- Be used in (light) alloys (aerospace, electronics, dental, …), ceramics, nuclear weapons, …

➢ granulomatous lung disease (= sarcoidosis)

- cellular (type IV) immune response to Be

➢ diagnosis: Be Lymphocyte Proliferation Test

ex vivo incubation of lymphocytes with Be salt

if proliferation (SI > 3): proof of sensitization to Be

- high susceptibility if HLA-DPß1 glu69
- Also other metals: Zr, Al, Ti, Cr?

Sarcoidosis and CBD

Müller-Quernheim *et al. ERJ* 2006, 27, 1190-5

- 84 sarcoidosis patients with possible exposure to Be were re-evaluated for Be exposure (1997-2005; Borstel, Freiburg, Tel Aviv)
  - detailed occupational history
  - 2 Be-LPT with blood lymphocytes

➢ 34 diagnosed with CBD

Müller-Quernheim *et al. ERJ* 2006, 27, 1190-5

TABLE 2 Workplaces and occupational settings with beryllium exposure identified by occupational case history

Occupational beryllium exposure	CBD	Exposed sensitised healthy	Exposed nonsensitised healthy	Sarcoidosis exposed
Individuals	34	7	6	50
Dental technician/dentist	13 (7/6)	1 (1/0)	4 (4/0)	10 (6; 4)
Engine development/mechanics/ automobile industry	2 (1/1)	2 (2/0)	1 (1/0)	7 (7/0)
Brass alloys, beryllium-containing alloys[#]	4 (4/0)	1 (1/0)		14 (8/6)
Metallurgic factory	2 (1/1)			4 (1/3)
Aircraft production and maintenance	3 (2/1)			2 (2/0)
Nonsparking tools	1 (1/0)		1 (1/0)	1 (1/0)
Radiation shielding	1 (0/1)	1 (1/0)		
Military vehicle armour	2 (1/1)			
Fluorescent lamps	2 (1/1)			
Microelectronics/electrical relays	1 (1/0)	1 (1/0)		8 (6/2)
Chemical industry[¶]	1 (1/0)			
Engraving of gems	1 (1/0)			
Ore mining	1 (1/0)			1 (1/0)
Grinding of optical lenses for precision instruments		1 (1/0)		1 (1/0)
Indirect[+]				2 (2/0)

Data are presented as total n (patients in Germany/patients in Israel). CBD: chronic beryllium disease. [#]: galvanic industry, ship yards, metal processing; [¶]: additive to glass, ceramics, plastics/catalyst; [+]: *i.e.* contaminated garments.

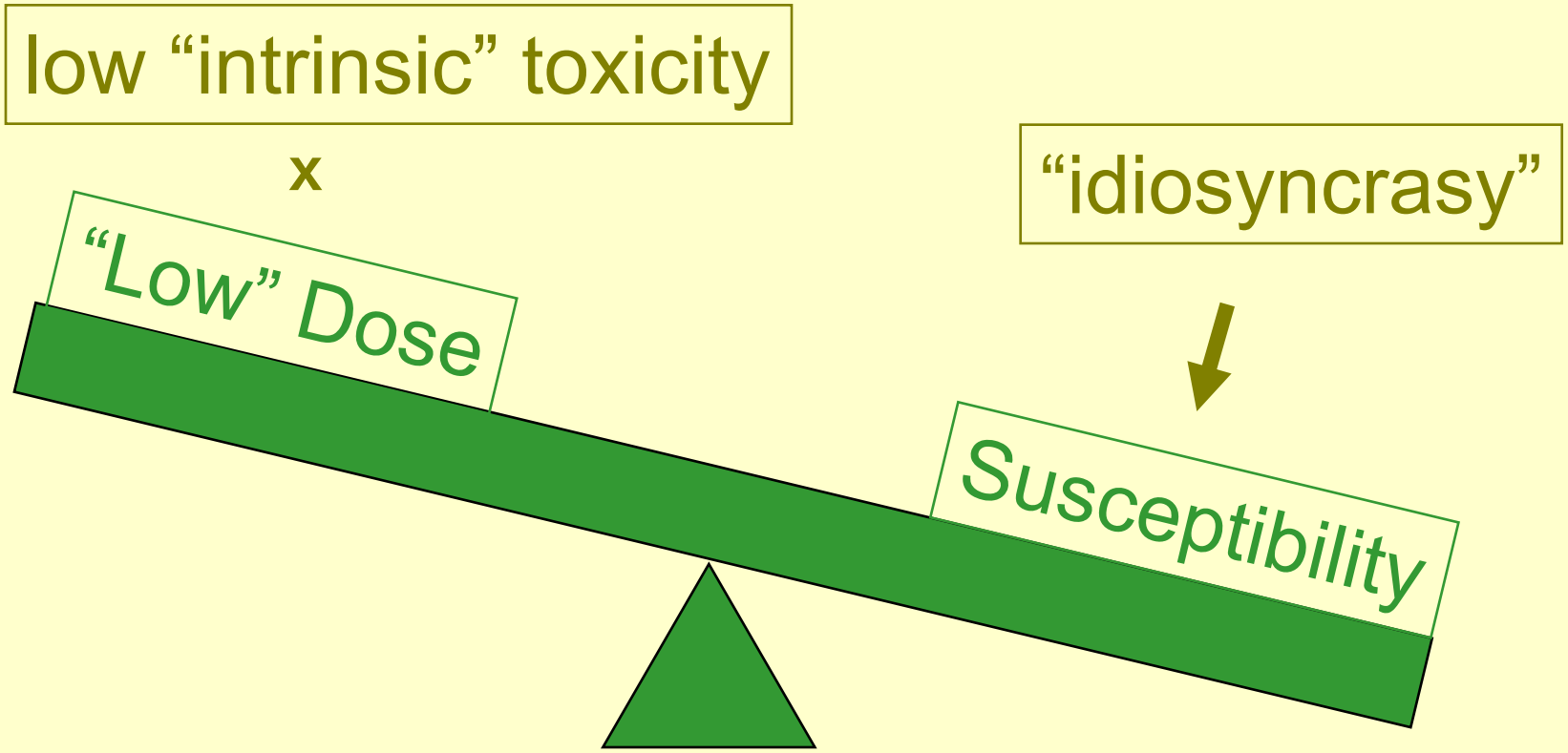
Take home message

- Sarcoidosis is a diagnosis of exclusion!
- always evaluate the possibility of an exogenous cause
  - silica
  - talc
  - beryllium (Be-LPT)
  - other metals (aluminium, zirconium, …)
  - “inorganic particles” (WTC)
  - atypical mycobacteria

Newman KL, Newman LS. Occupational causes of sarcoidosis. *Curr Opin Allergy Clin Immunol.* 2012, 12(2):145-50.

Cobalt (Co)

ILD due to “hypersensitivity”



“Hard metal”

- Man-made composite material
  - 85-95% tungsten carbide (WC) + 5-15% Co

    + Ni, Cr, carbides of Ta, Ti, Nb

  ➢ “cemented carbides” or “cermets”

  - produced by sintering

    = conversion of compacted powder into a polycrystalline material

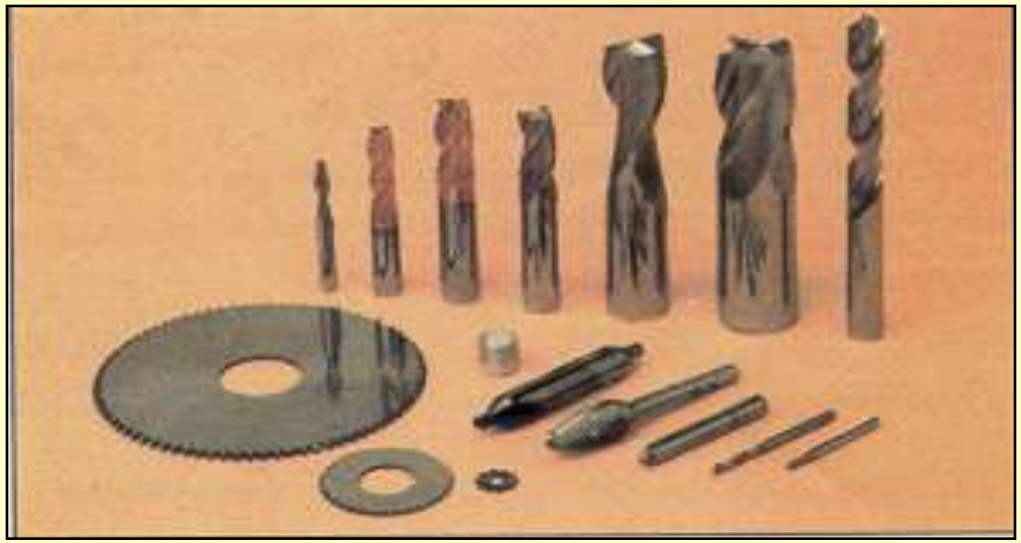
  ➢ “sintered carbides”

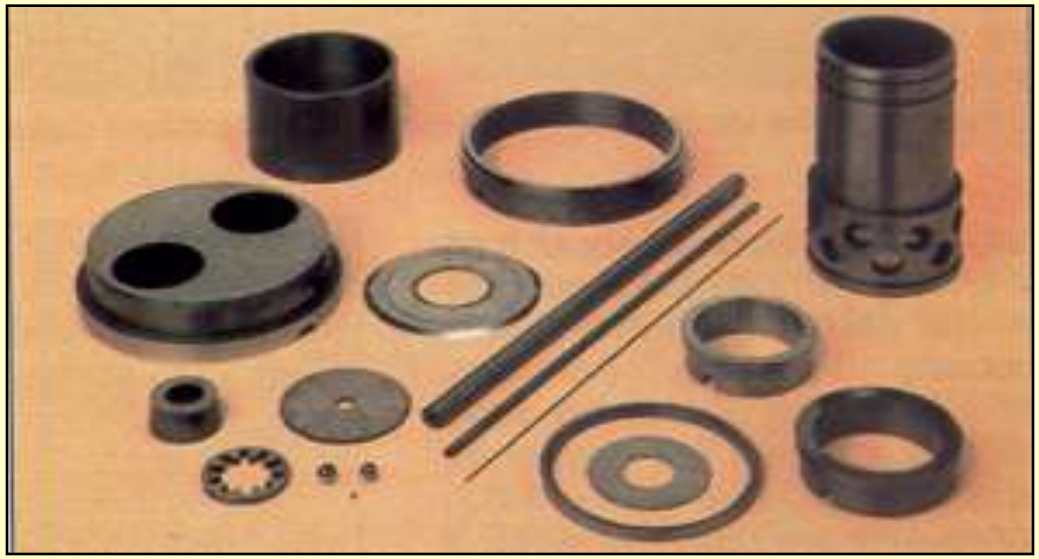
≠ “heavy metal” (Cd, Pb, Hg)

“Hard metal”

- Properties
  - high heat resistance → hardness almost like diamond (“Widia”)
- used for
  - drilling rocks, cement, bricks, glass, ...
  - cutting wood, ceramics, foodstuffs, …
  - machining, grinding, polishing metals, etc
  - specialised tools & machine parts

Hard metal





Cobalt News 96/4

Diamond-cobalt

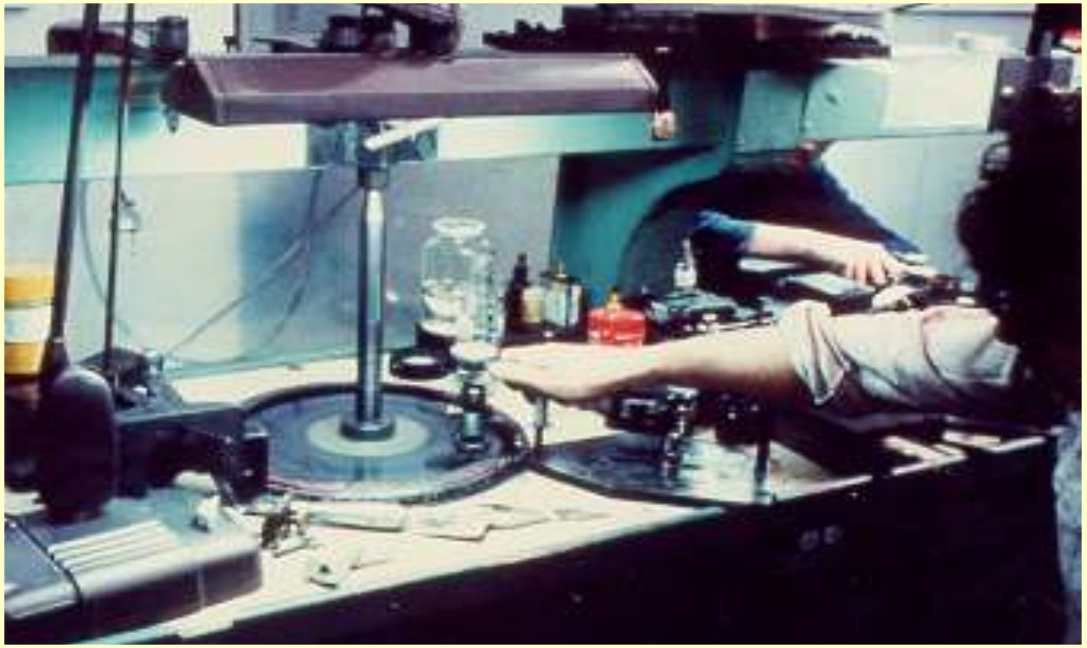
- “Diamond tools”
  - microdiamonds bonded with Co (up to 90%) (also other metals used for bonding)
- used for
  - cutting stone, marble, glass, crystal, roads, …
  - grinding & polishing various materials
  - polishing (faceting) diamonds

Diamond tooling

HRD

Cobalt News 93/2

Diamond polishing with diamond-cobalt disks



Hard metal lung disease
Cobalt lung
Giant Cell Interstitial Pneumonia
(GIP)

Nemery *et al*. Sem. Respir. Med. 2001, 22, 435-447

Clinical presentation

± similar to hypersensitivity pneumonitis

- subacute alveolitis

  ± work-related:

  - dry or productive cough
  - dyspnoea, chest tightness
  - flu-like symptoms

  + asthenia, fatigue, weight loss

  + nasal & upper airway symptoms

  possibly **+** asthma

Clinical presentation

± similar to hypersensitivity pneumonitis

- fibrotic lung disease

  with or without prior subacute manifestations:

  - gradual dyspnoea
  - weight loss
  - digital clubbing
  - cyanosis
  - fine crackles

  ➢ cor pulmonale

Clinical presentation

± similar to hypersensitivity pneumonitis

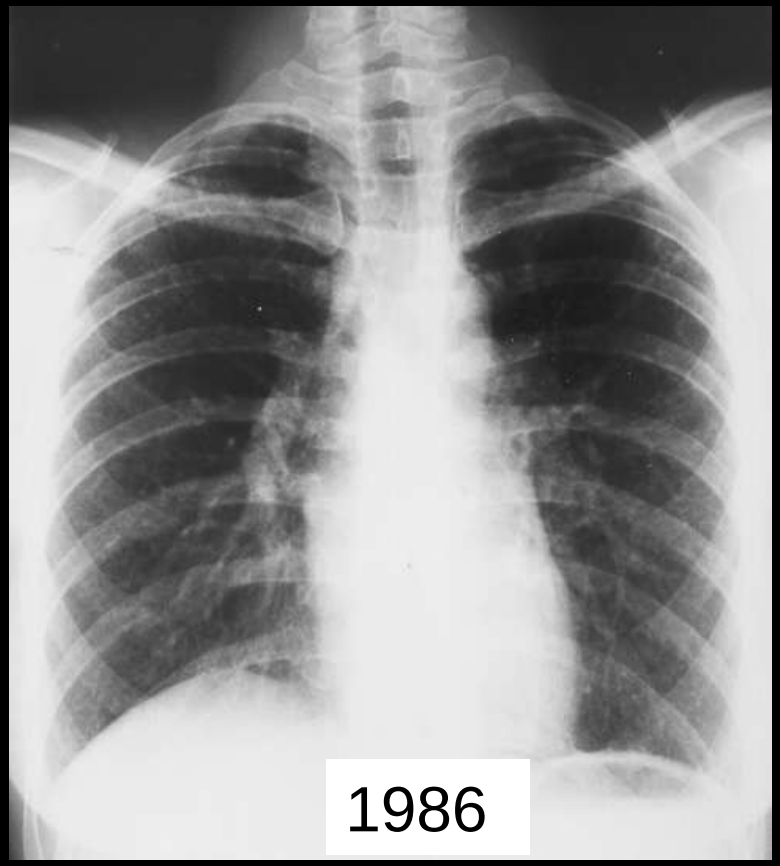
- fibrotic lung disease

  with or without prior subacute manifestations:

  - gradual dyspnoea
  - weight loss
  - digital clubbing
  - cyanosis
  - fine crackles

  ➢ cor pulmonale

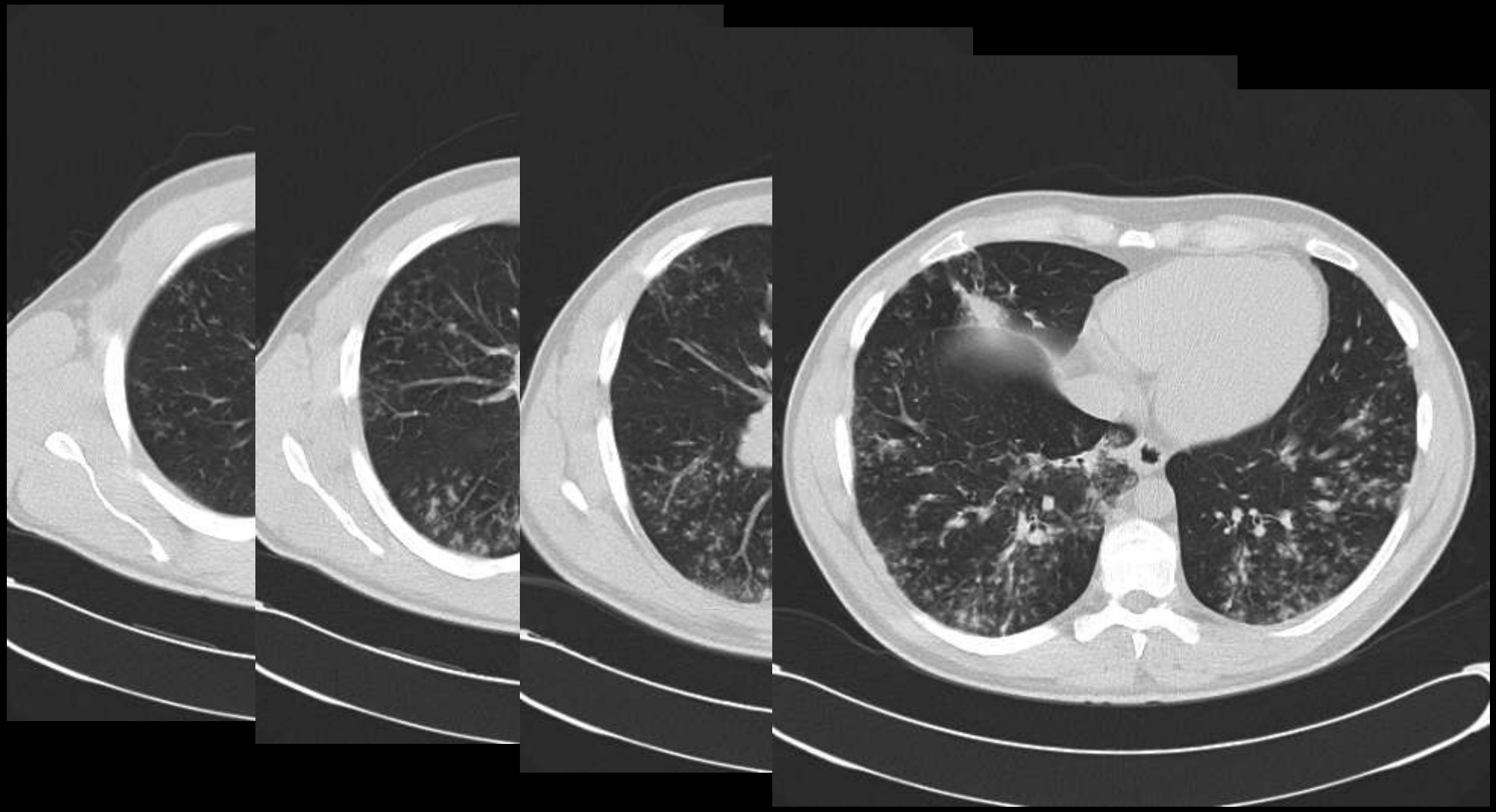
F- 24 y - NS
diamond polisher
TLC 49% pred
DLco 27% pred



Thermal spraying of hard metal

Hard facing

Case



13-09-2006

Case

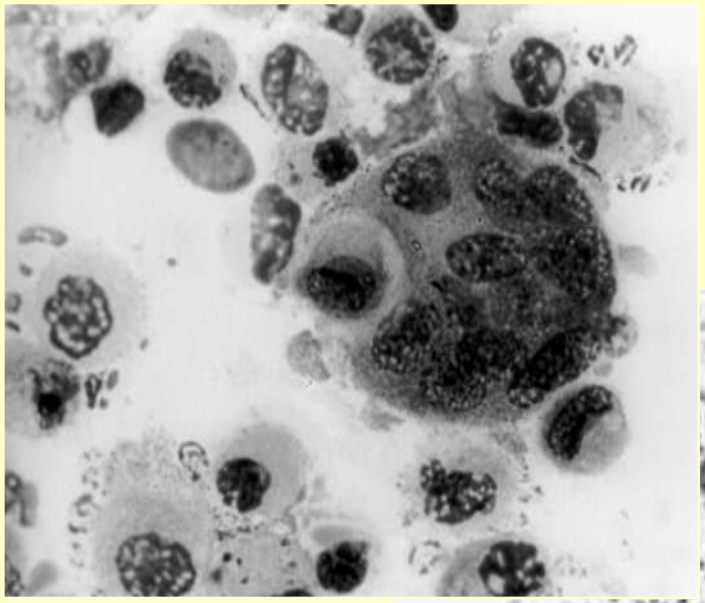
13-09-2006

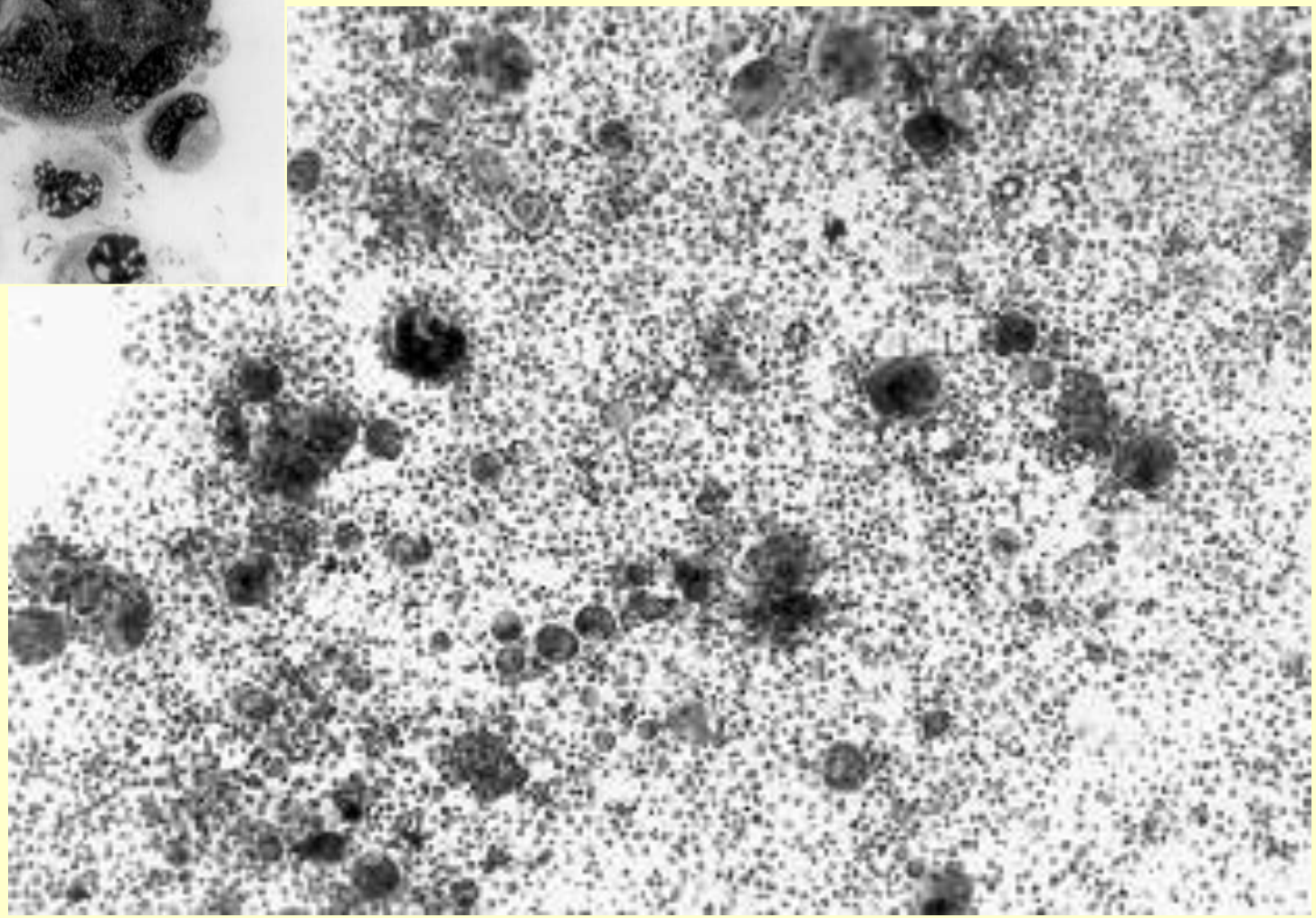
Pathology

Ohori *et al.* Am J Surg Pathol 1989, 13, 581-7

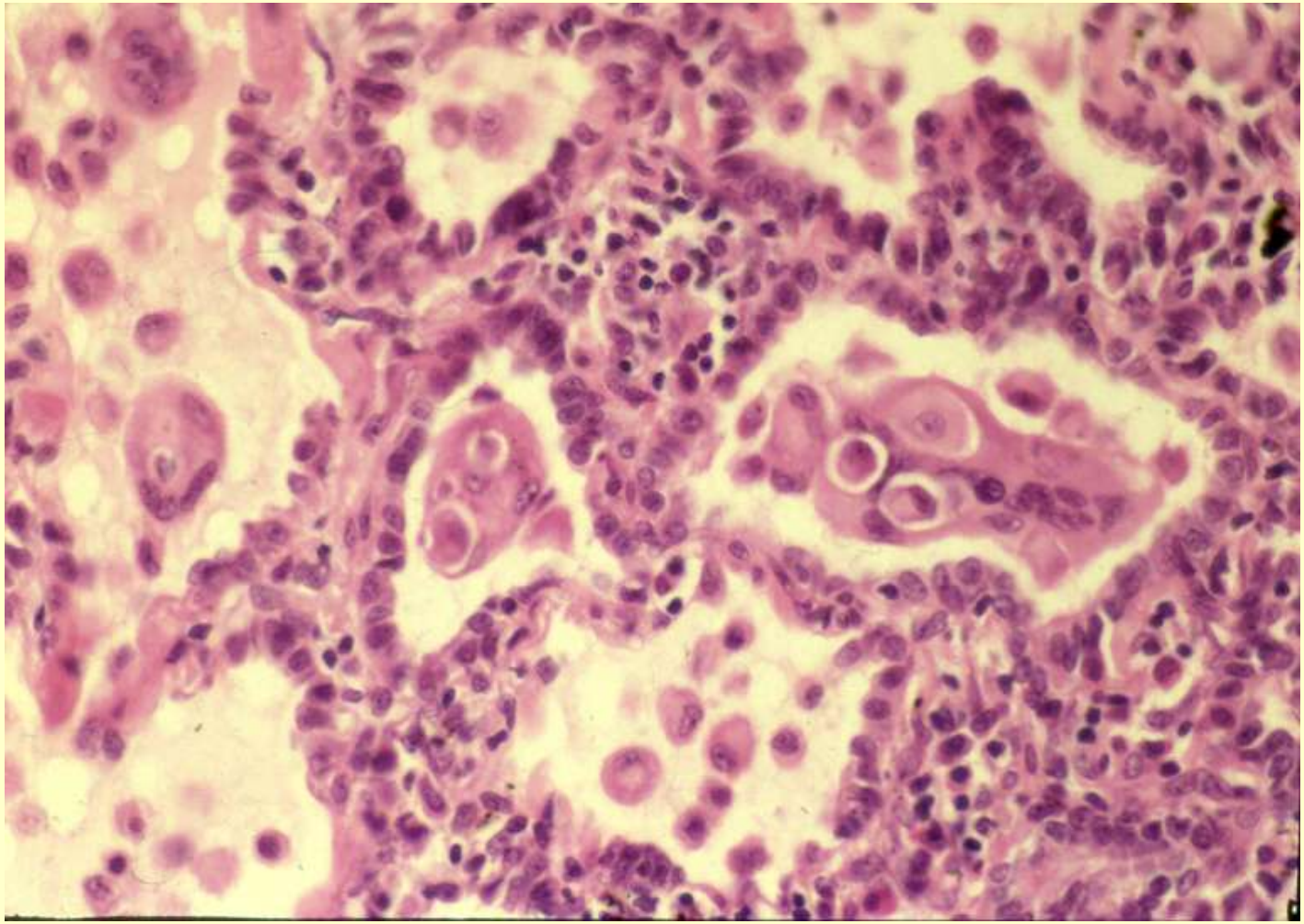
- giant cell interstitial pneumonia (GIP) = specific feature of HMD, but not always present
- also other features:
  - lymphoplasmocytic infiltration (no granulomas)
  - hyperplasia alveolar epithelium
  - cell desquamation in alveoli (DIP)
  - BOOP pattern possible
- bronchiolocentric distribution
- various stages: normal / inflammation / fibrosis

BAL





GIP - cobalt lung



E.K. Verbeken

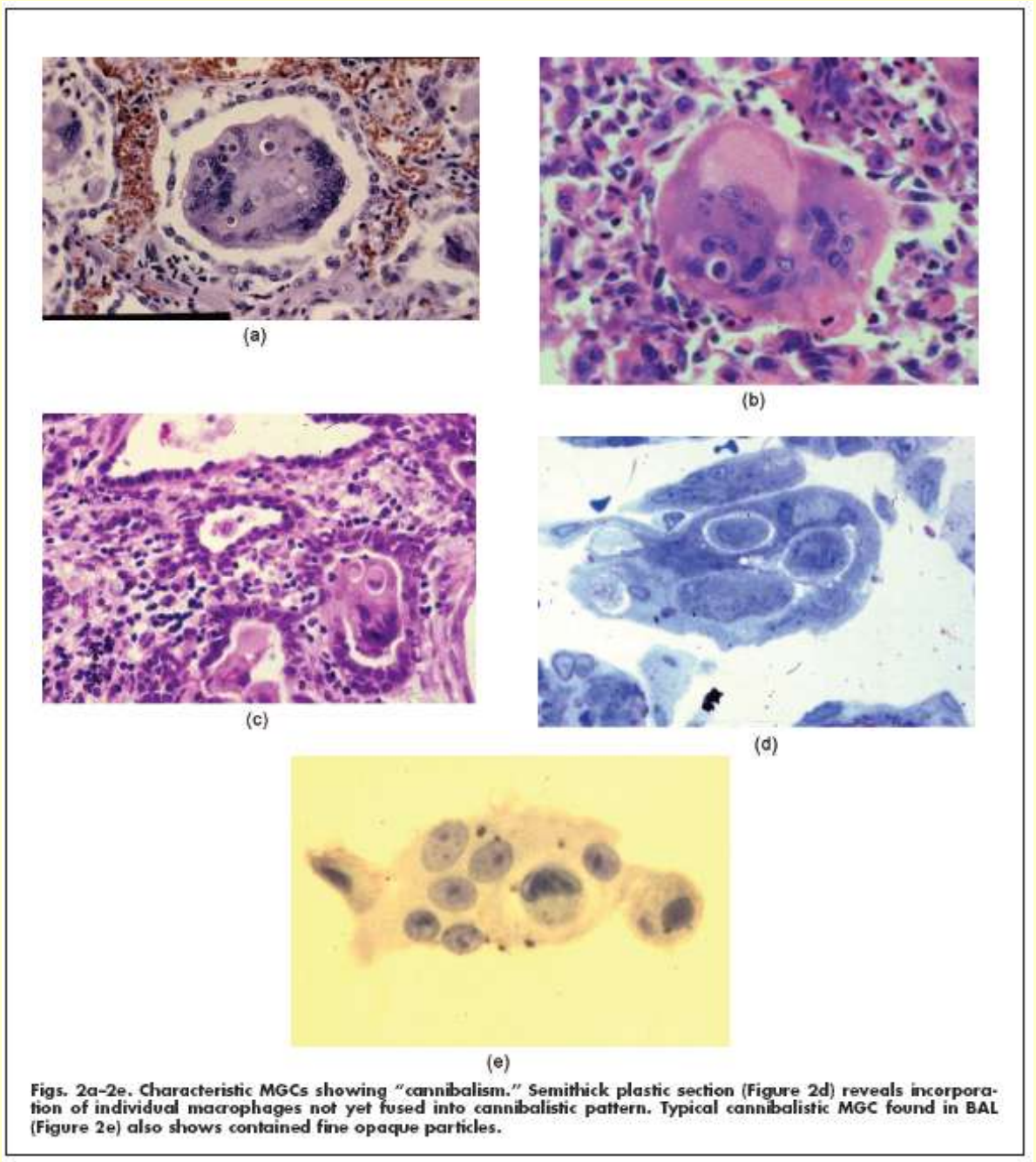
Pathology

Naqvi *et al.* Pathologic spectrum and lung dust burden in Giant Cell Interstitial Pneumonia (Hard Metal Disease/ Cobalt pneumonitis). Arch Environ Occup Health 2008, 63, 51-70

- 100 cases of HMD (1958-2002)
  - 59 with GIP
  - 41 with > 2.10^6 particles containing W /cm^3 lung (SEM/EDS)
  - Co detected in only 6%

Multinucleated giant cells showing cannibalism

Naqvi *et al.*
Arch Environ Occup Health 2008, 63, 51-70



Figs. 2a–2e. Characteristic MGCs showing "cannibalism." Semithick plastic section (Figure 2d) reveals incorporation of individual macrophages not yet fused into cannibalistic pattern. Typical cannibalistic MGC found in BAL (Figure 2e) also shows contained fine opaque particles.

GIP

Naqvi *et al.*
Arch Environ Occup Health
2008, 63, 51-70

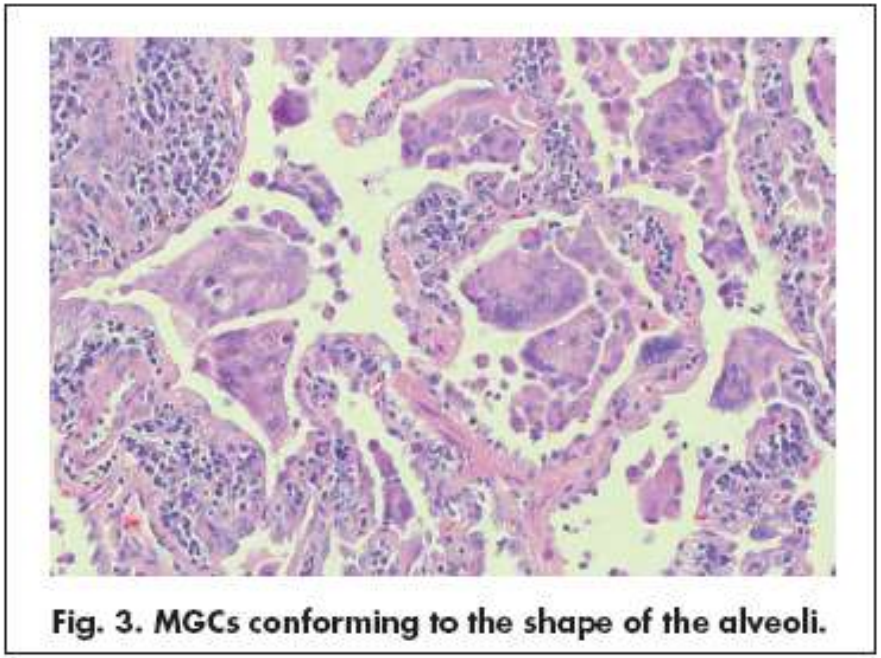
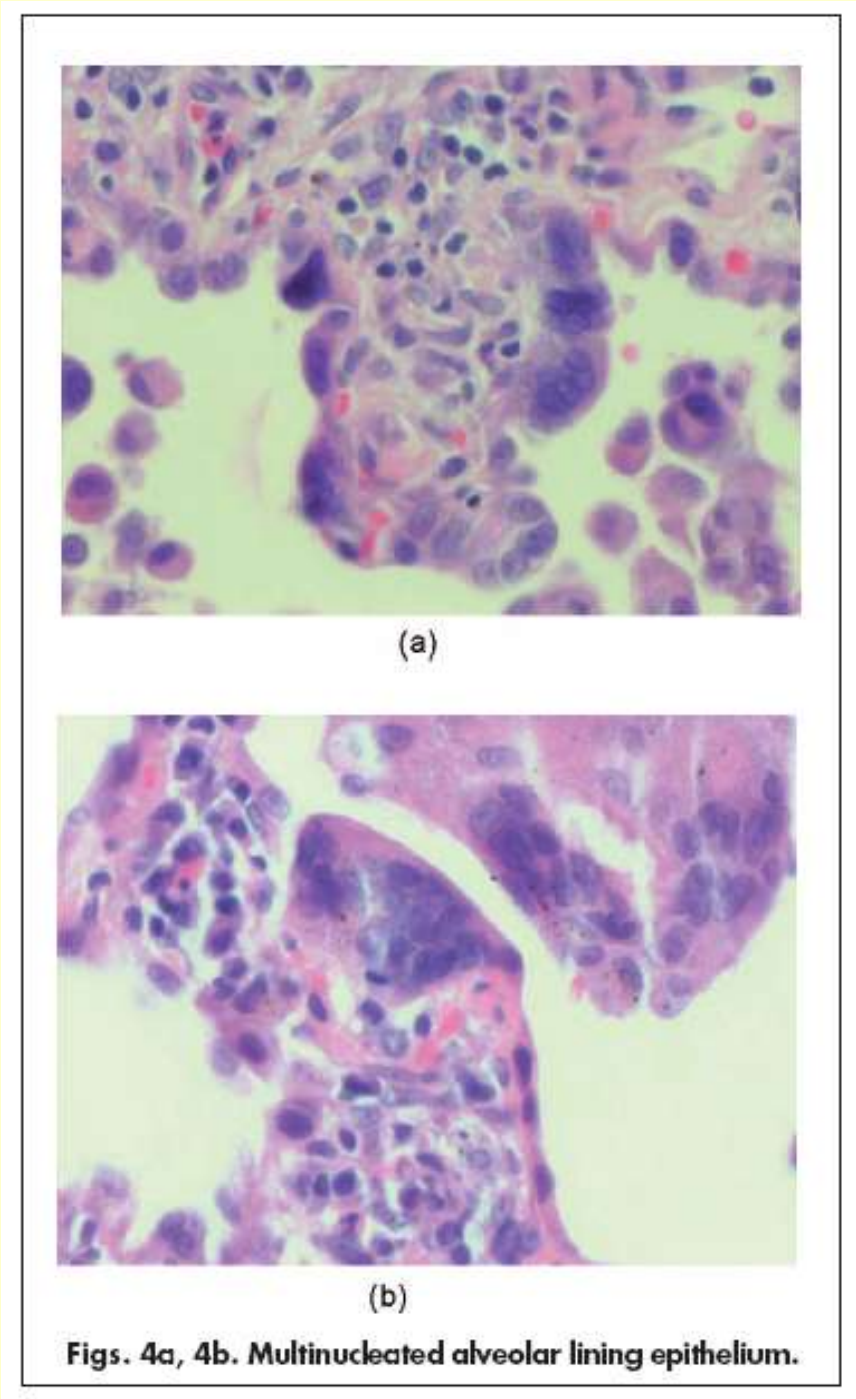


Fig. 3. MGCs conforming to the shape of the alveoli.



(a)

(b)

Figs. 4a, 4b. Multinucleated alveolar lining epithelium.

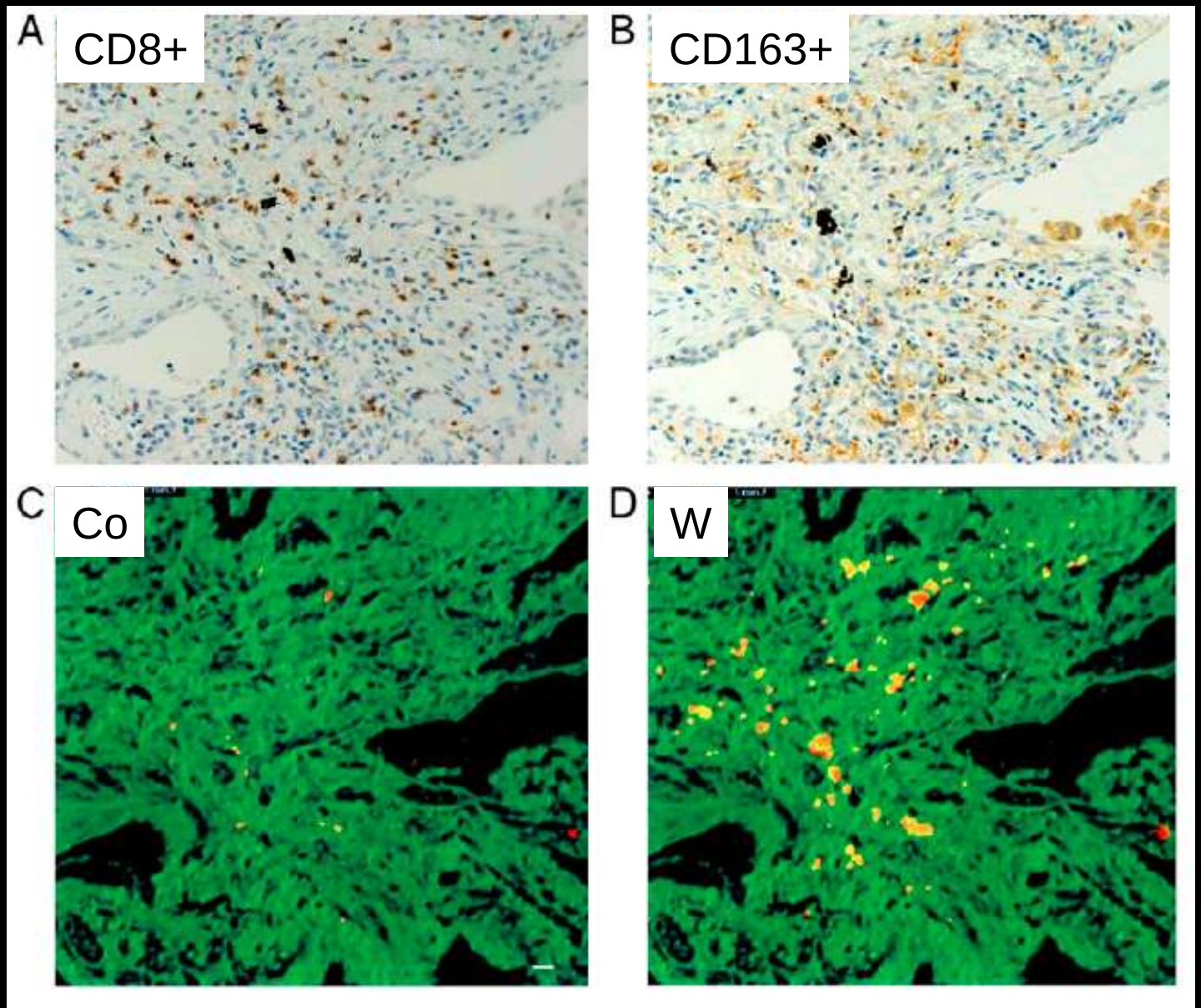
Pathology

Moriyama *et al.* Two-dimensional analysis of elements and mononuclear cells in hard metal lung disease. AJRCCM 2007, 176, 70-77

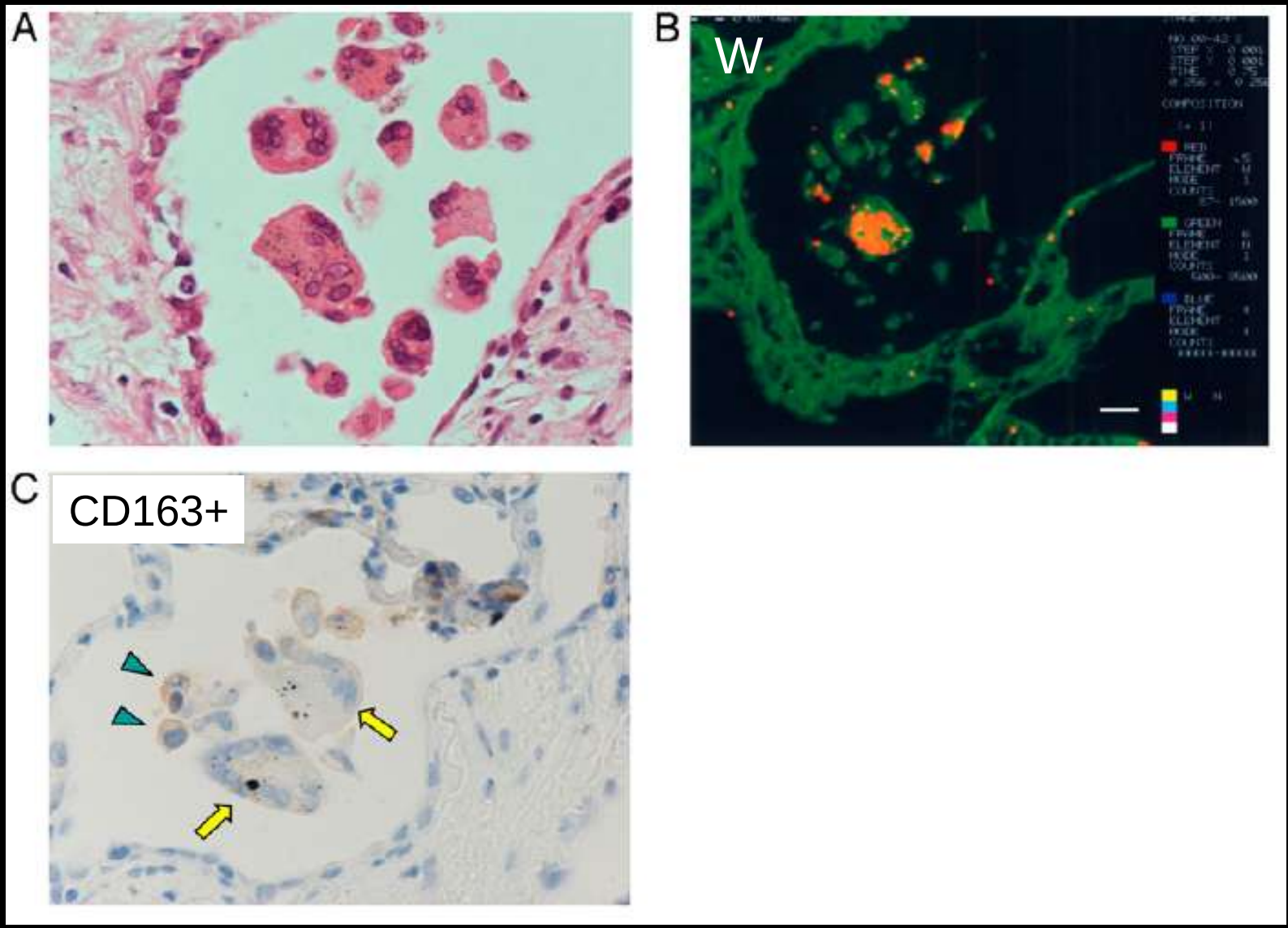
- 17 patients with HMLD (13 GIP, 4 “atypical” GIP)
- Electron probe microanalysis (EPMA) with wavelength-dispersive spectrometry (WDS)
- Immunohistochemistry ($CD8^+$, $CD163^+$)

[+ editorial by Nemery & Abraham]

Moriyama *et al.* AJRCCM 2007, 176, 70-7



Moriyama *et al.* AJRCCM 2007, 176, 70-7

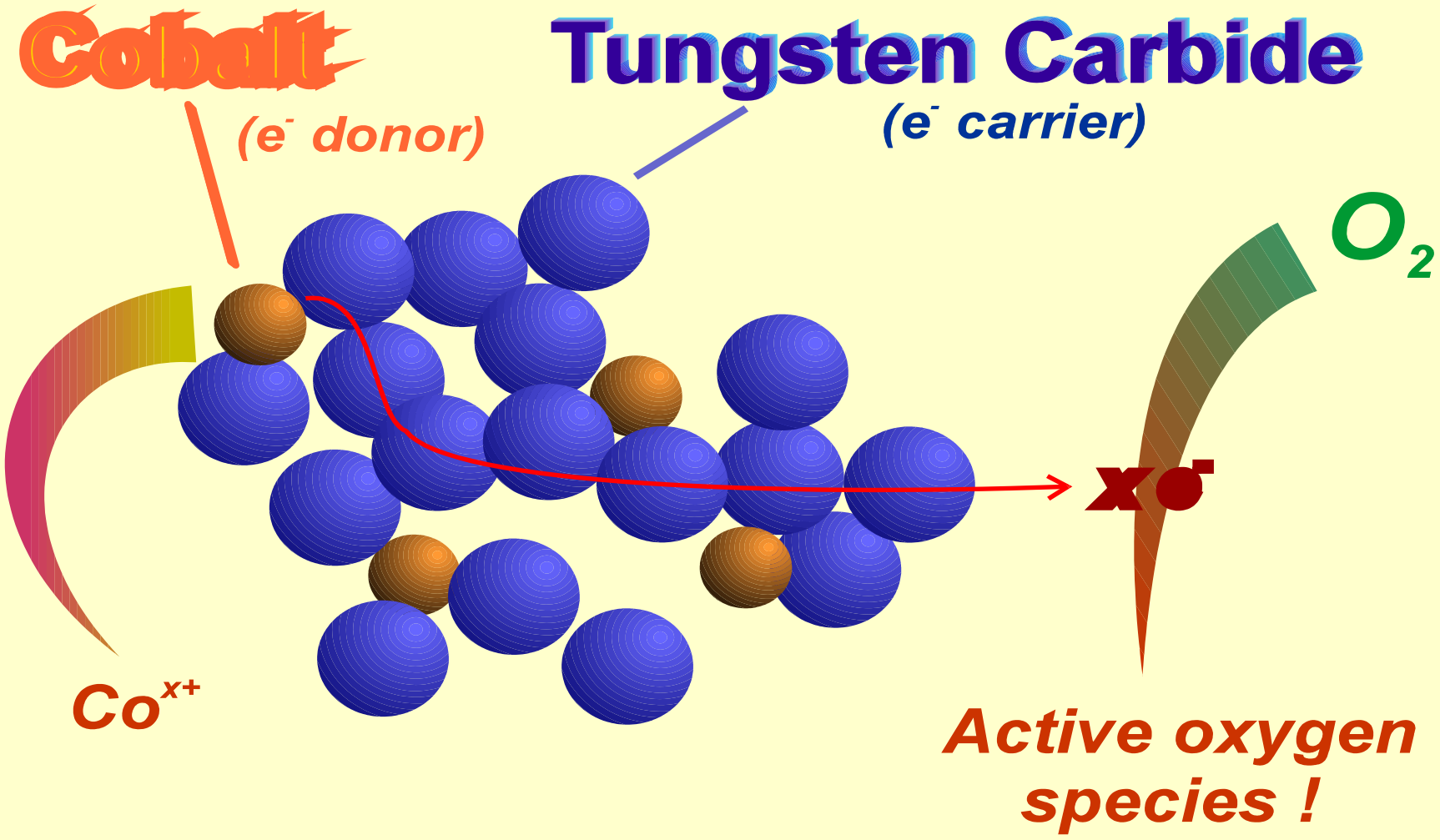


Pathogenesis ?

- immunologic mechanisms ?

+ genetic susceptibility ? HLA-DPβ glu69
  - Potolicchio *et al*. Eur J Immunol 1997, 27, 2741-3; 1999, 29, 2140-7

- synergy Co + other particles (WC)
  - no ILD reported if exposure to Co only
    - Swennen *et al.* Br J Ind Med 1993, 50, 835-42
  - animal studies & *in vitro* studies
- pro-oxidant mechanisms ?



Lison et al. Chem. Res. Toxicol. 8 : 600-606 (1995)

Indium - Tin Oxide (ITO)

Indium-Tin Oxide (ITO)

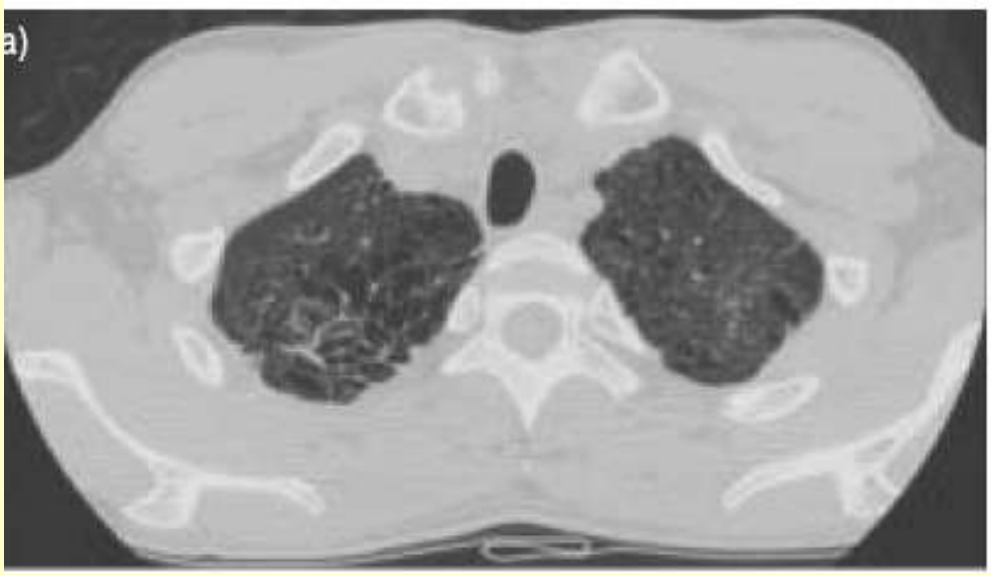
Homma S. *et al*. Pulmonary fibrosis in an individual occupationally exposed to inhaled indium-tin oxide. *ERJ* 2005, 25, 200-4

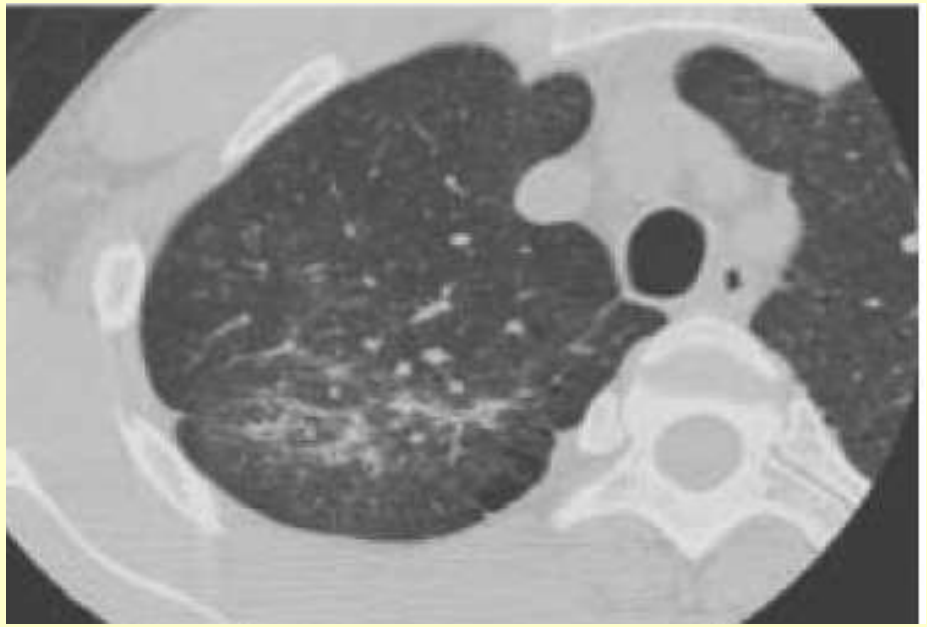
- Man, 30 y, light smoker (3 cig/d for 3 y)
- Exposure for 4 y to ITO (90% In_2O_3 / 10% SnO_2)
  - Manufacture of flat-panel displays (LCD, plasma screen)
- Dry cough and exertional dyspnoea; normal PFT
- Chest x-ray: reticulonodular shadows (right upper f)

Indium-Tin Oxide (ITO)

Homma S. *et al*. *ERJ* 2005, 25, 200-4

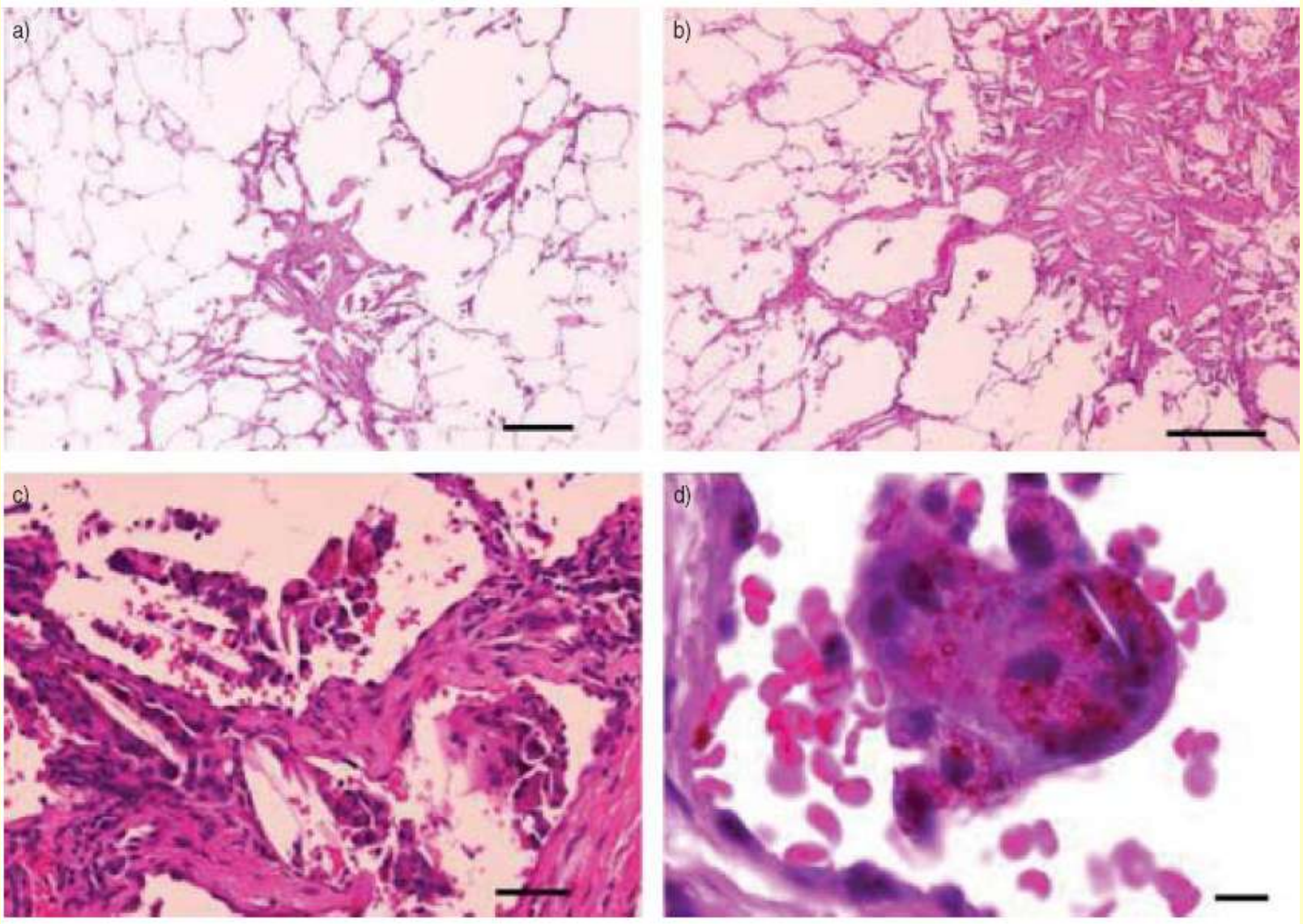
- CT





Homma S. *et al*. *ERJ* 2005, 25, 200-4

- VATS

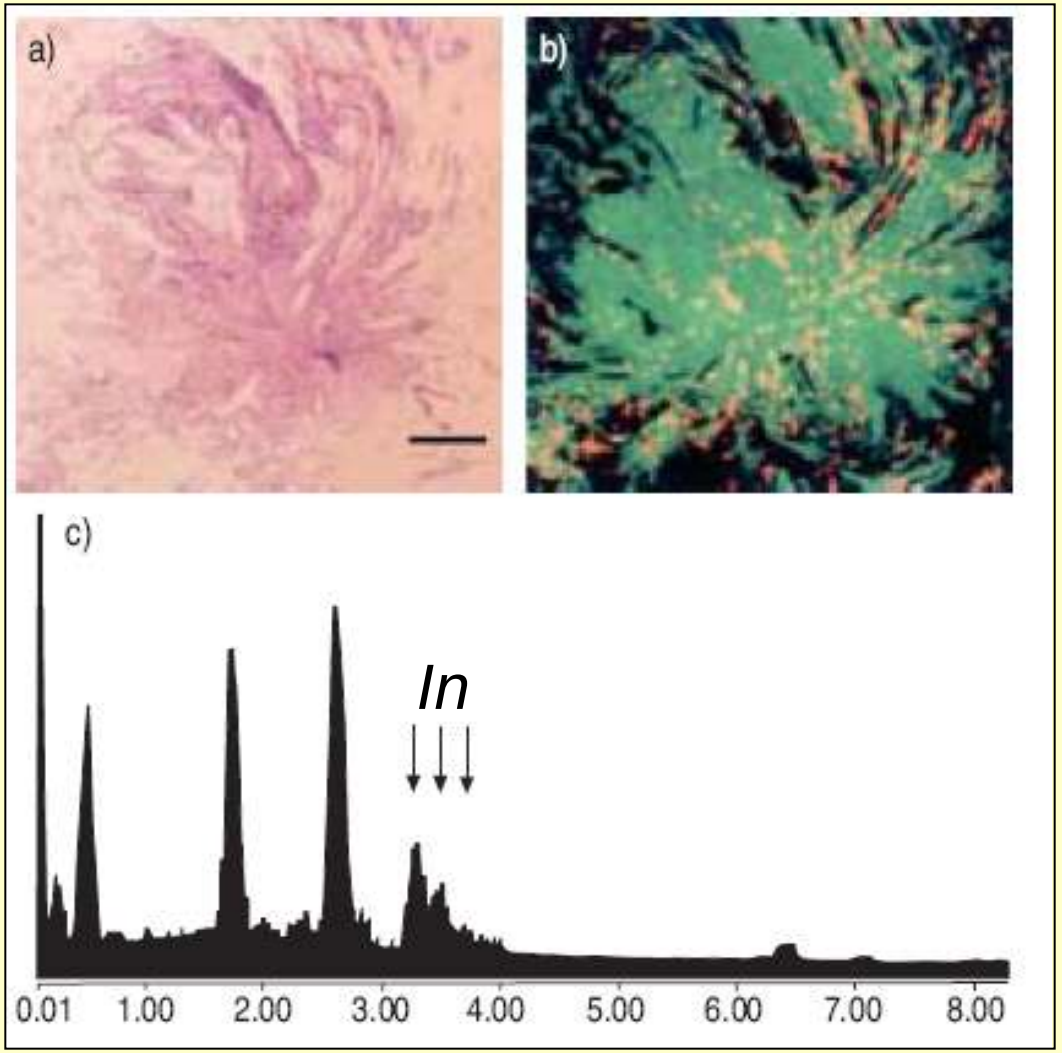


Homma S. *et al*. *ERJ* 2005, 25, 200-4

- Electron probe X-ray microanalysis

+ SEM with EDX

In 61%, Sn 4%



Chonan T. *et al*. *ERJ* 2007, 29, 317-24

- ITO plant
  - 108 male workers (24 ex-workers)
  - mean age: 34 y [20-60 y]
  - mean duration of exposure: 3.6 y [0.8-17 y]
  - serum Indium: GM 8 ng.mL^{-1} [0-127] ↑ with exposure duration;
    (control: GM 0.3 ng.mL^{-1})
  - exposure to Indium: GM 0.01 – 0.05 mg.m^{-3} (max: 0.36);
    (particles Ø 2.5 µm [0.1-11 µm])
  - ➢ HRCT: interstitial changes in 23 subjects
  - ➢ Serum KL-6 > 500 U.mL-1 in 40 subjects

    Related to serum Indium

    More disease in wet-surface grinding of ITO

Cummings *et al*. AJRCCM 2010, 181, 458-64

- Facility producing ITO (USA) (~ 15 workers)
- 2 cases of Pulmonary Alveolar Proteinosis

A. Male, nonsmoker, 49 y
   - September 2000 (after 9 month): dyspnea + dry cough
   - Diagnosis of PAP (HRCT, pathology)
   - October 2006: death in respiratory failure

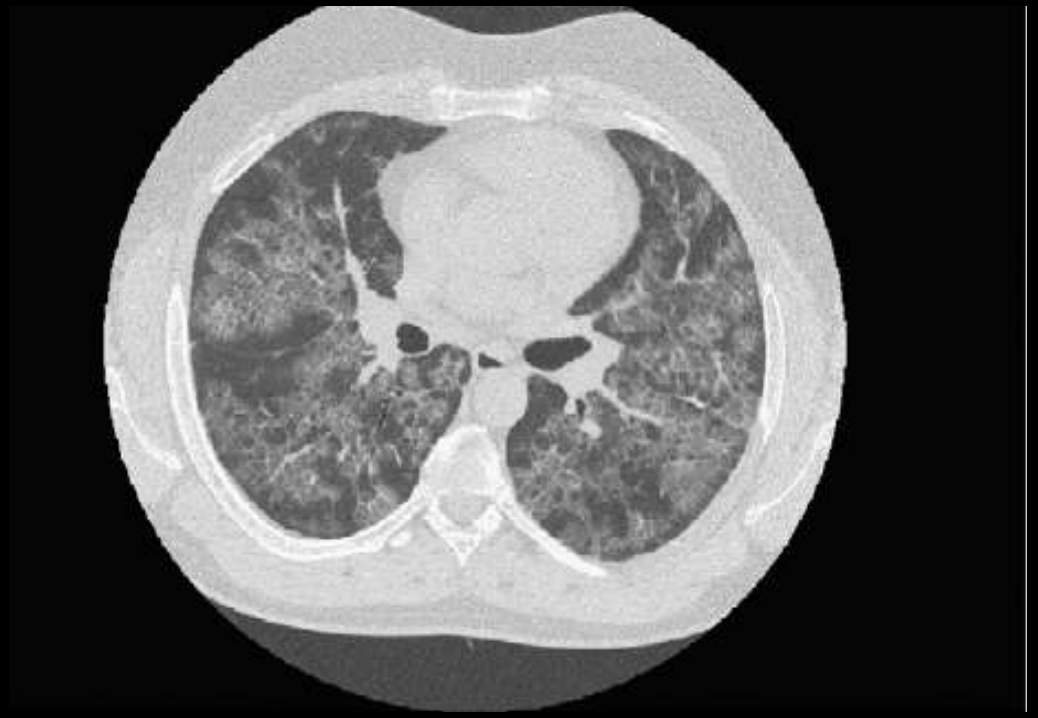
B. Male, smoker, 39 y
   - 2005 (6 to 9 months after hire): dyspnea, dry cough, chest tightness
   - Diagnosis of PAP (HRCT, pathology)
   - 2009: partial improvement after bilateral whole lung lavage; autoAB against GM-CSF +

Cummings *et al*. AJRCCM 2010, 181, 458-64

HRCT

A

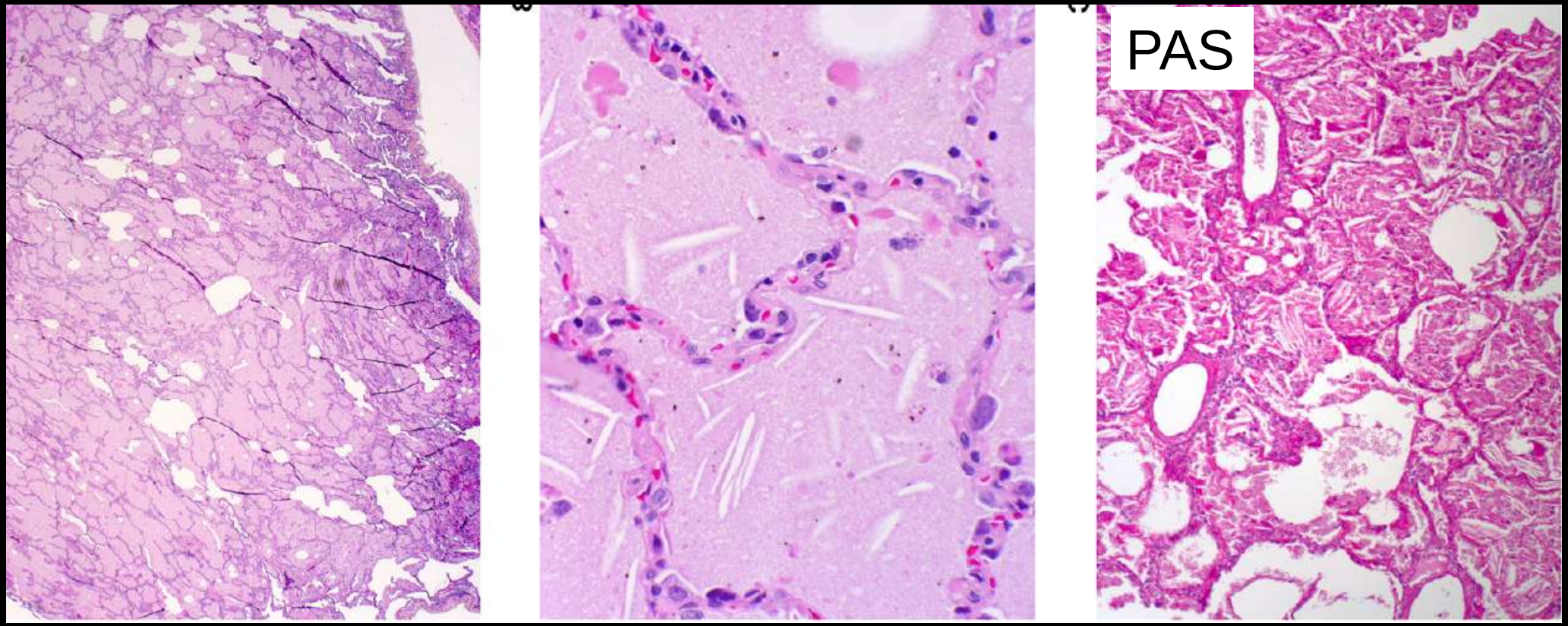
B



Cummings *et al*. AJRCCM 2010, 181, 458-64

Pathology

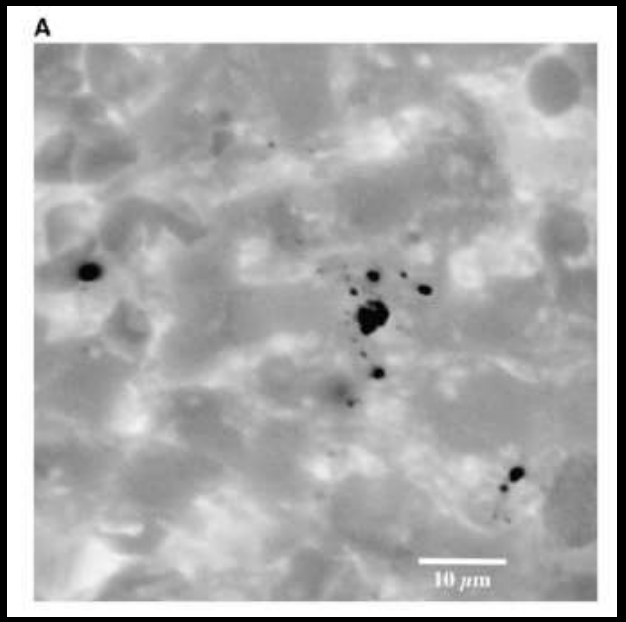
A

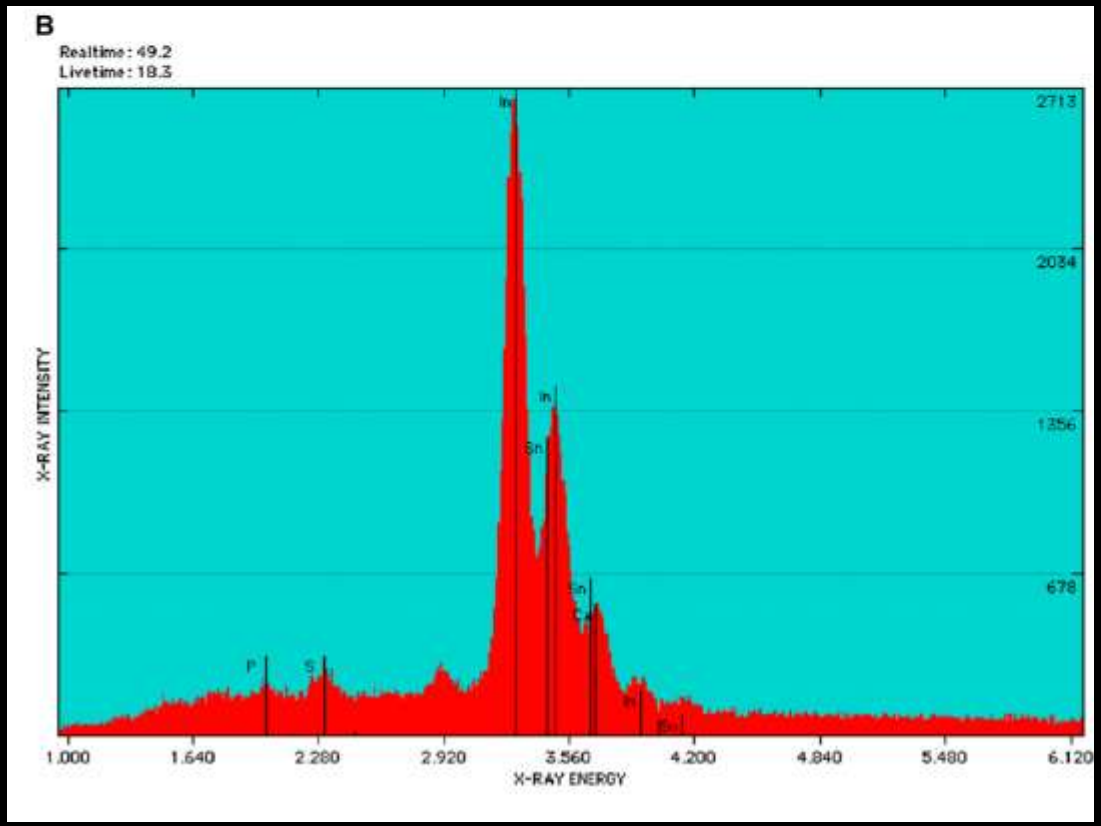


Cummings *et al*. AJRCCM 2010, 181, 458-64

em + EDXA

A

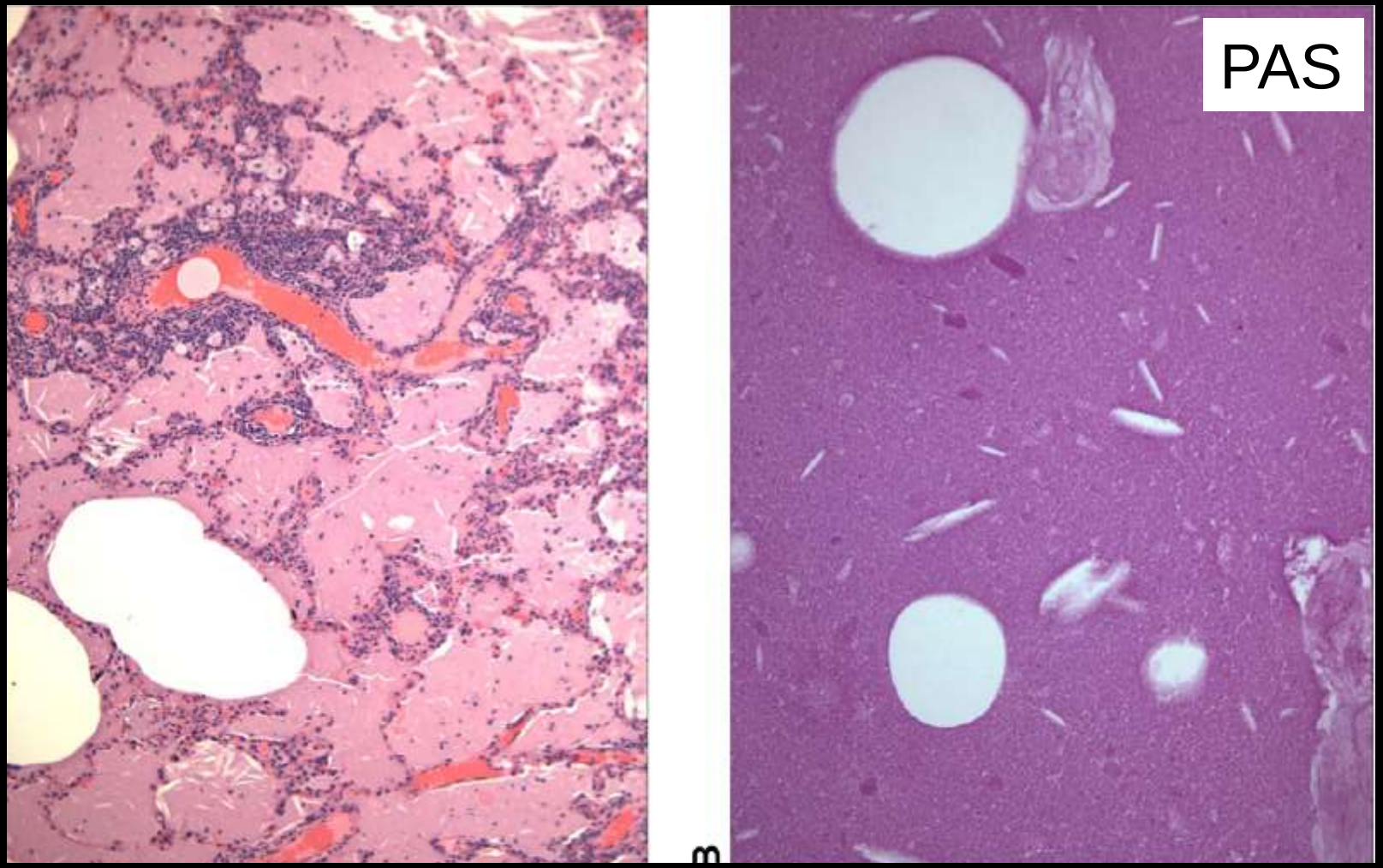




Cummings *et al*. AJRCCM 2010, 181, 458-64

Pathology

B



Cummings *et al*. Indium lung disease. (Review). *Chest* 2012, 141, 1512-21

Background: Reports of pulmonary fibrosis, emphysema, and, more recently, pulmonary alveolar proteinosis (PAP) in indium workers suggested that workplace exposure to indium compounds caused several different lung diseases.

Methods: To better understand the pathogenesis and natural history of indium lung disease, a detailed, systematic, multidisciplinary analysis of clinical, histopathologic, radiologic, and epidemiologic data for all reported cases and workplaces was undertaken.

Results: Ten men (median age, 35 years) who produced, used, or reclaimed indium compounds were diagnosed with interstitial lung disease 4-13 years after first exposure (n = 7) or PAP 1-2 years after first exposure (n = 3). Common pulmonary histopathologic features in these patients included intraalveolar exudate typical of alveolar proteinosis (n = 9), cholesterol clefts and granulomas (n = 10), and fibrosis (n = 9). Two patients with interstitial lung disease had pneumothoraces. Lung disease progressed following cessation of exposure in most patients and was fatal in two. Radiographic data revealed that two patients with PAP subsequently developed fibrosis and one also developed emphysematous changes. Epidemiologic investigations demonstrated the potential for exposure to respirable particles and an excess of lung abnormalities among coworkers.

Conclusions: Occupational exposure to indium compounds was associated with PAP, cholesterol ester crystals and granulomas, pulmonary fibrosis, emphysema, and pneumothoraces. The available evidence suggests exposure to indium compounds causes a novel lung disease that may begin with PAP and progress to include fibrosis and emphysema, and, in some cases, premature death. Prospective studies are needed to better define the natural history and prognosis of this emerging lung disease and identify effective prevention strategies.

CHEST 2012; 141(6):1512–1521

Take home message

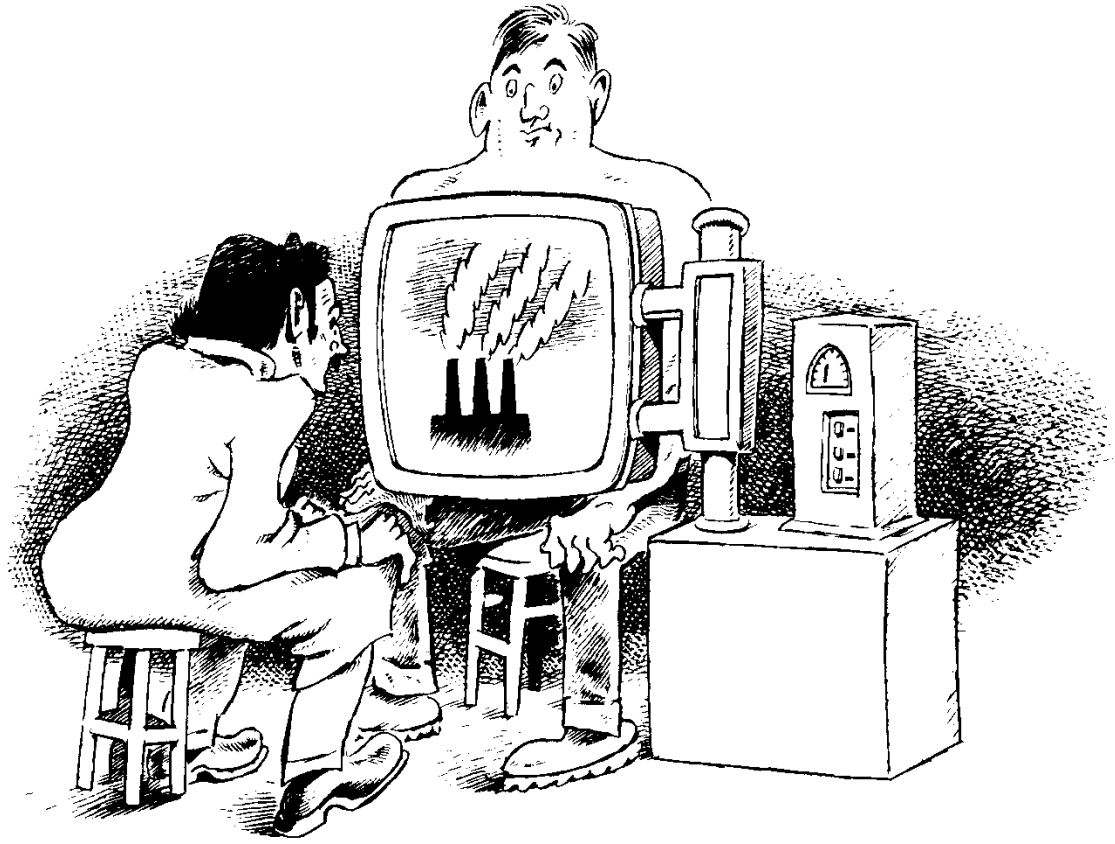
- Indium Tin Oxide is a new cause of pulmonary alveolar proteinosis (in addition to SiO_2, ...)
- Hi-tech materials are not necessarily produced or applied with hi-tech safety and hygiene!

Final Take Home Messages

Clinicians, radiologists, pathologists,

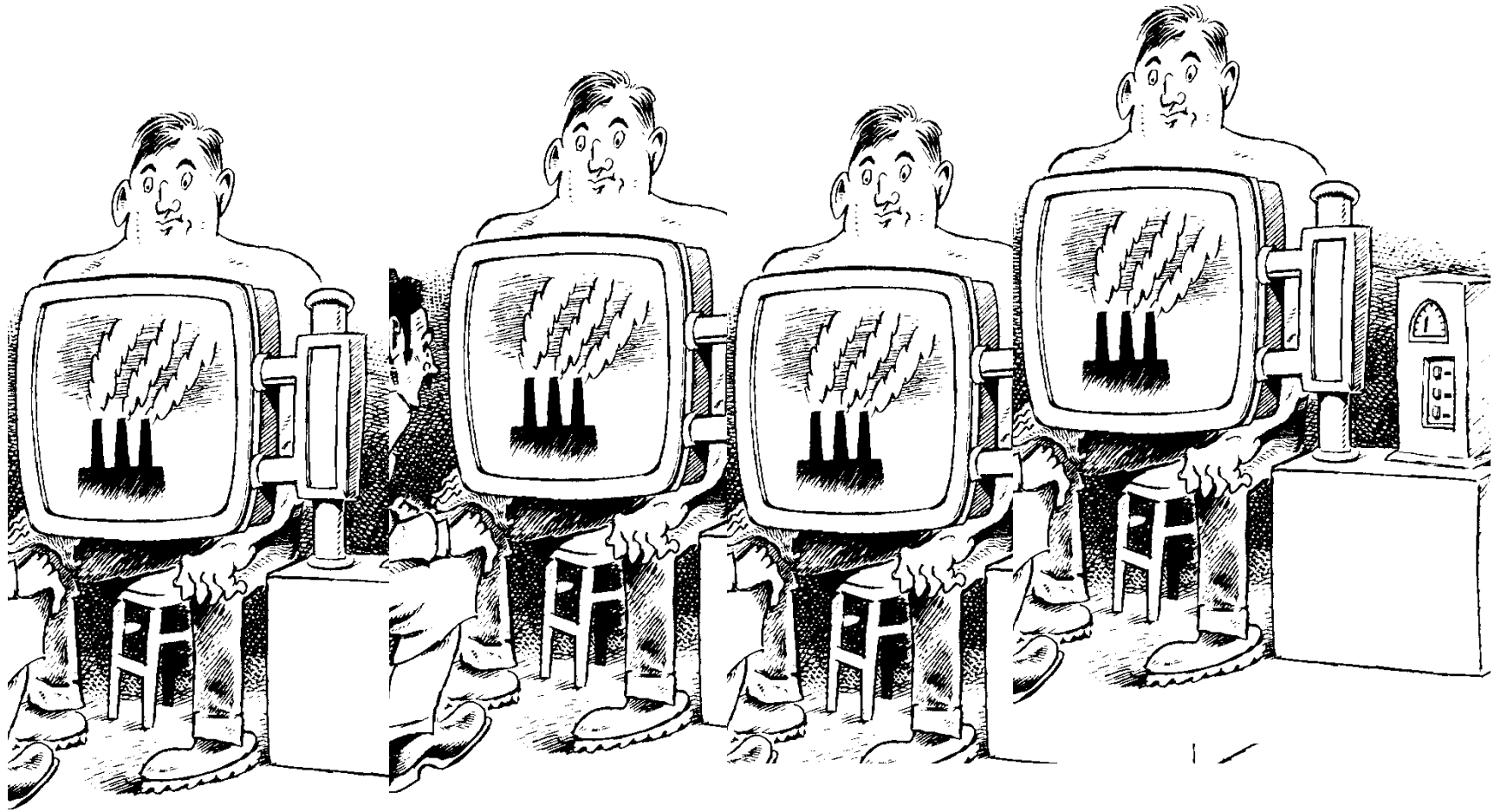
- Use « idiopathic » or « cryptogenic » with care (diagnosis of exclusion)
- Keep searching for possible environmental causes of lung disease
- Ask advice from experts

Old and new causes of disease may occur even in modern industry



Contrary to this drawing, there is no simple test.
The suspicion and the determination of work-relatedness depend primarily on a careful occupational history

From LEVY BS, WEGMAN DH. Occupational health (3d ed), p.60



When you find one case of occupational disease, there are likely more around ...

In occupational medicine, n is nearly always >1

Modified From LEVY BS, WEGMAN DH. Occupational health (3d ed), p.60

Thank you for your attention

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