KU LEUVEN

21 nov 2025 – Heijermanslezing

Occupational exposure and auto-immune diseases with example cases from the clinic

Steven Ronsmans

Raadpleging voor beroeps- en milieugebonden aandoeningen, Pneumologie, UZ Leuven

Centrum Omgeving en Gezondheid, Departement Maatschappelijke Gezondheidszorg en Eerstelijnszorg, KU Leuven

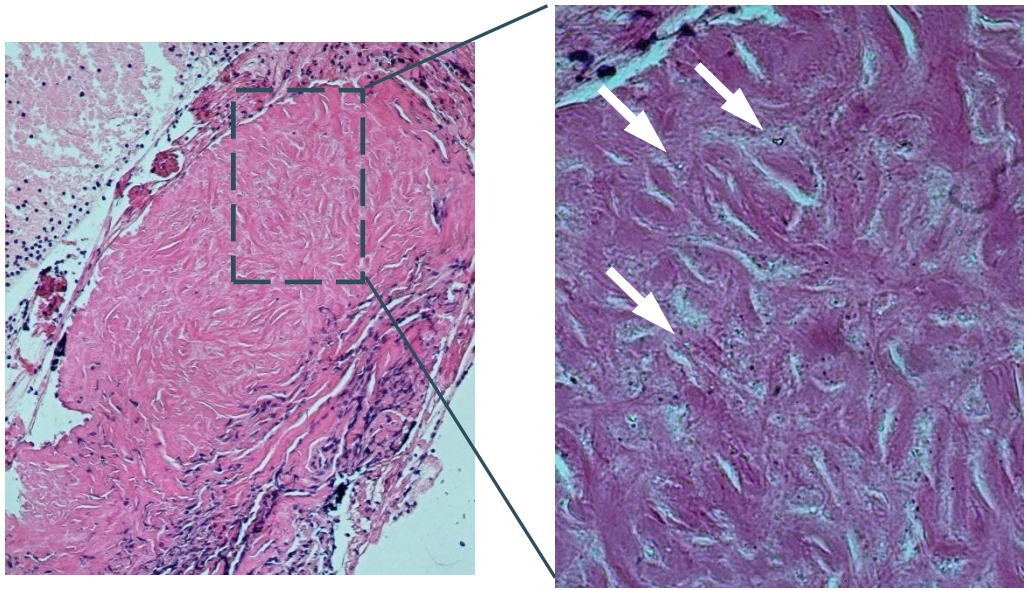
steven.ronsmans@kuleuven.be

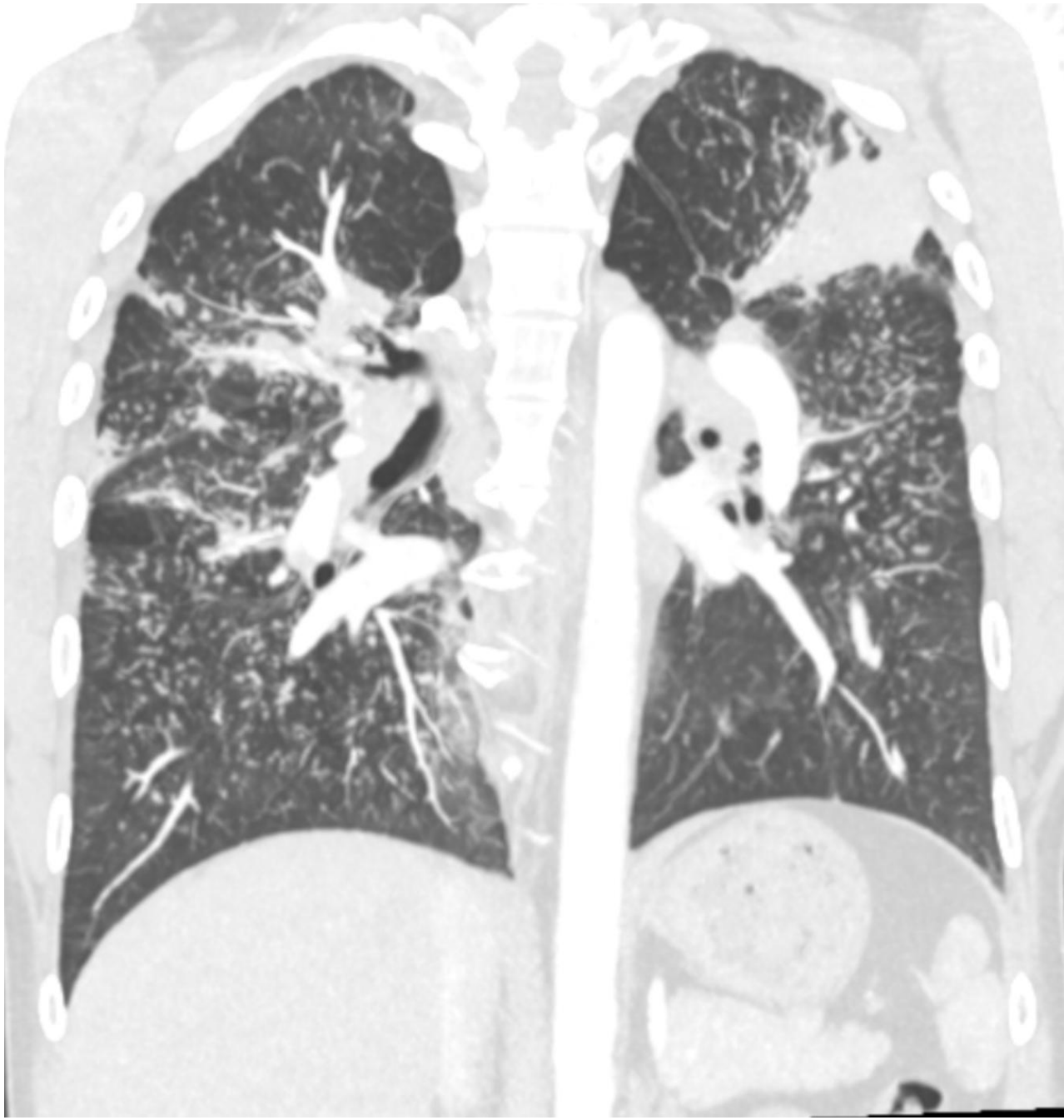
Overview

- Recent outbreak of silicosis
- Case of systemic sclerosis
- Case of rheumatoid arthritis
- Spectrum of autoimmune diseases related to silica exposure
- Outbreak of “sarcoidosis”

Case

- Man, 38y
- Former smoker (stop 2011, 12 packyears)
- In the past 2 years: cough, exertional dyspnee
- Lung function:
  restrictive pattern with low diffusing capacity



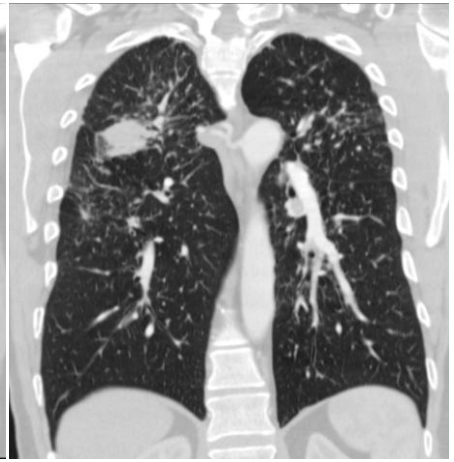
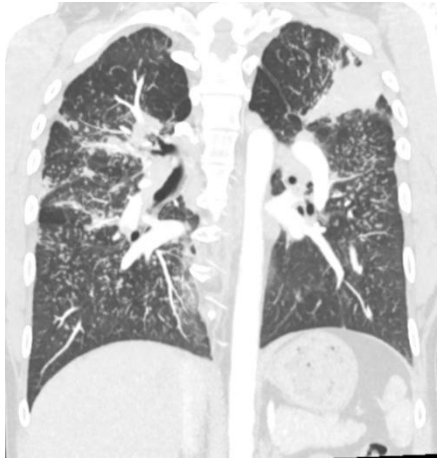


Case with silicosis

- Company X (Belgium), production of skirting boards for food/pharma industry (10 workers)
  - Mixing polyester resin, quartz powder, quartz sand, dolomite
  - After curing: dry finishing of the stones
  - Since 2019: respiratory protection

Respirable crystalline silica
1080 µg/m³ (limit value 100 µg/m³)

Outbreak of silicosis in workers producing a novel application of silica-based composites

Worker	1	2	3	4	5 (index case)
Diagnosis	Enlarged lymph nodes	Simple silicosis	Simple silicosis and emphysema	Progressive massive fibrosis	Progressive massive fibrosis
Age at diagnosis	42 y	56 y	59 y	47 y	38 y
Years working at the company	8 y	30 y	11 y	16 y	10 y
Chest CT at diagnosis					

"Classical" silicosis can still occur (also in "modern" industries)

Ronsmans et al, Chest. 2022

"Old" risks in new applications – Outbreaks of silicosis in artificial stone workers worldwide

The world is failing on silicosis

Lancet Respir Med 2019
Published Online
March 11, 2019

Silica-associated lung disease: An old-world exposure in modern industries

Respirology (2019)
doi: 10.1111/resp.13695

Severe Silicosis in Engineered Stone Fabrication Workers — California, Colorado, Texas, and Washington, 2017–2019

Morbidity and Mortality Weekly Report
September 27, 2019

Artificial stone-associated silicosis in Belgium

Occup Environ Med 2019;**76**:133–134.

Prohibition on the use of engineered stone

Safe Work Australia
August 2023

Populair materiaal voor aanrechtbladen veroorzaakt stoflong bij arbeiders

DE TIJD DONDERDAG 8 AUGUSTUS 2024

Artificial stone
70–95% silica

Silicosis is not the only health effect of silica exposure

Allergy
EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

REVIEW ARTICLE | Free Access

Silica-related diseases in the modern world

Ryan F. Hoy, Daniel C. Chambers

First published: 27 January 2020 | https://doi.org/10.1111/all.14202

Silicosis
Chronic simple silicosis
Chronic complicated silicosis (progressive massive fibrosis)
Accelerated silicosis
Acute silicosis (silicoproteinosis)
Other pulmonary conditions
Lymphadenopathy
COPD
Pulmonary fibrosis
Sarcoidosis
Lung cancer
Caplan's syndrome
Mycobacterial disease
Pulmonary tuberculosis
Autoimmune disease
Systemic sclerosis
Systemic lupus eryth.
Rheumatoid arthritis
ANCA-assoc. vasculitis
Renal disease
Chronic renal disease

Overview

- Recent outbreak of silicosis
- **Case of systemic sclerosis**
- Case of rheumatoid arthritis
- Spectrum of autoimmune diseases related to silica exposure
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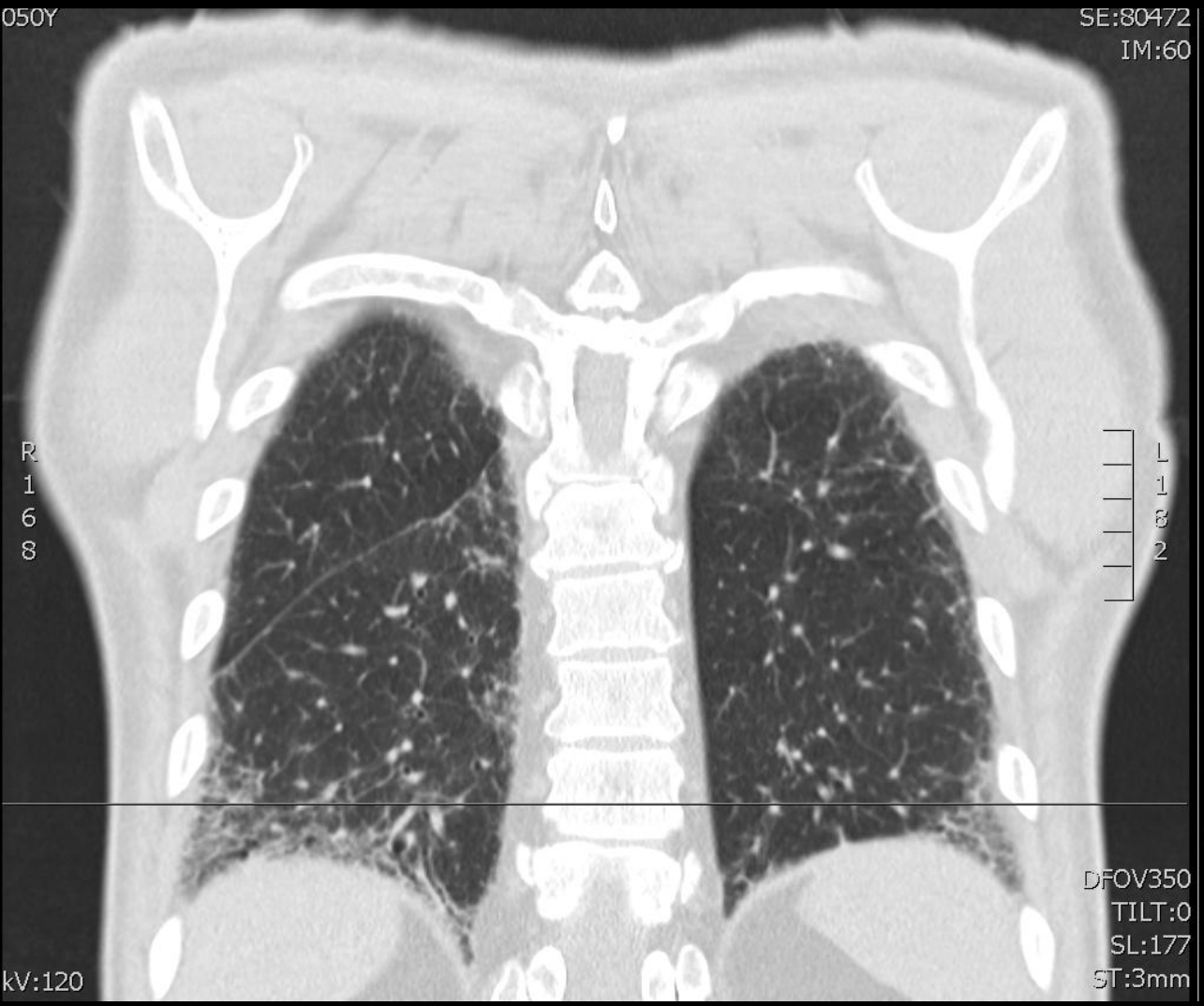
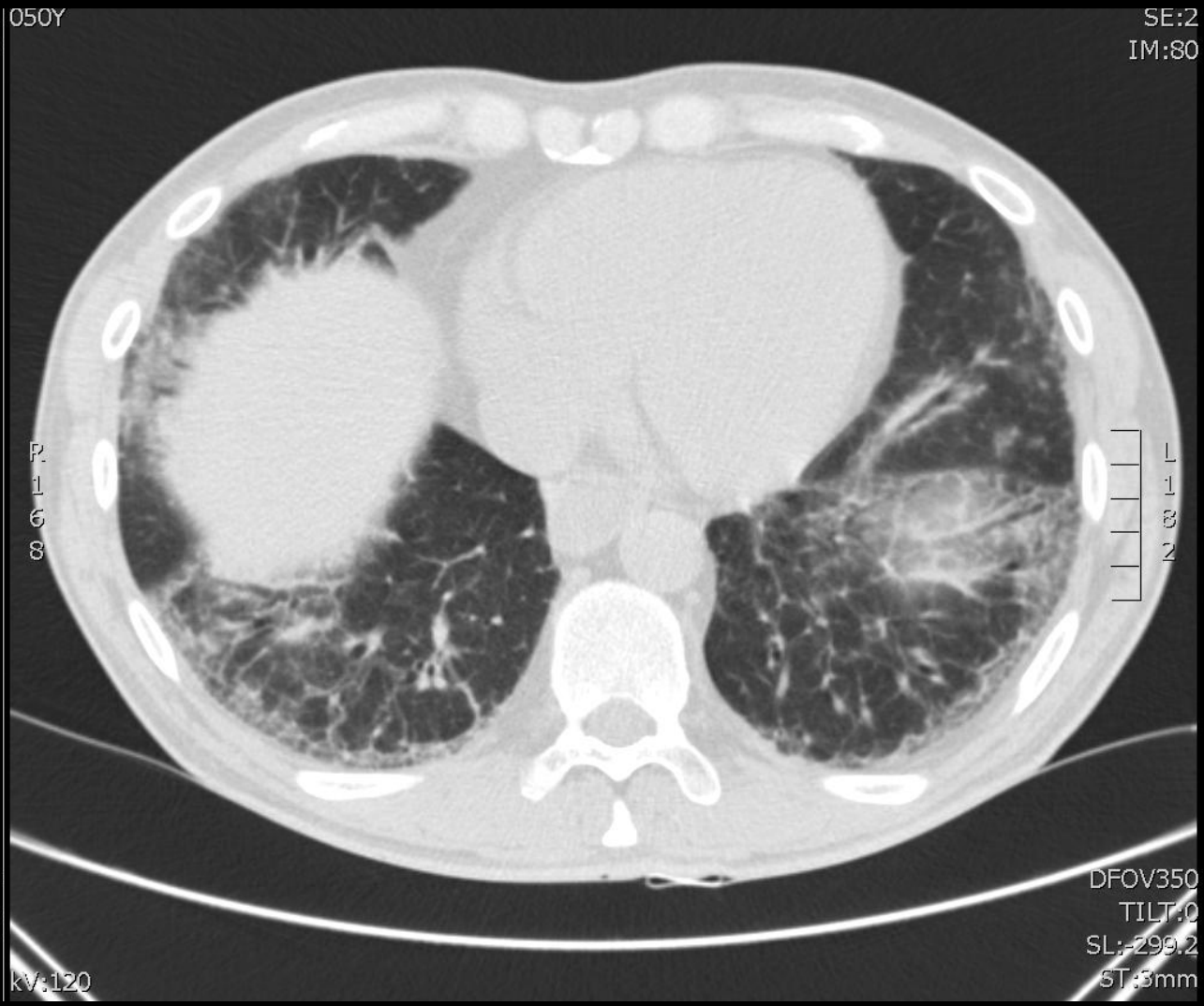
Case — ‘Artificial marble’

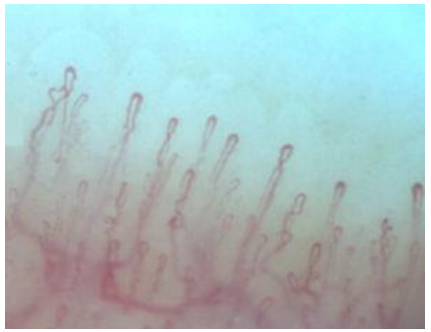
- M, °1961
- Job history
  - 1977 – 1991: making and installing stairs
    - Made ‘artificial marble’ stairs themselves
    - = marble chips, gravel, quartz (‘as fine as possible’) bound together with cement or resin, and colorants
    - First years: **dry** finishing
  - 1991 – 2014: administrative job in same company
- 2011:
  - Dry cough, lost 10 kg in 6 months
  - Lung function
    - FVC: 3.57L (83.7%)
    - FEV_1: 2.69L (77.7%)
    - RV: 111%
    - TLC: 82.8%
    - $D_{L_{CO}}$: 63.8%

Chest CT: fNSIP-pattern + Enlarged lymph nodes (No silicosis)





Case — ‘Artificial marble’



normal pattern

megacapillaries

- Histology lymph node (EBUS-TBNA):
  - no malignancy, no granuloma, no silicotic nodules, “**black pigment**”

- Tightening of the skin of arms and face
- Anti-nuclear antibodies (ANA): cytoplasmic speckled 1/1280, anti-SSA/U1RNP +
- Megacapillaries on capillaroscopy
- Oesophageal dysmotility
- ECG first degree AV block
- **Diagnosis:**
  Diffuse cutaneous systemic sclerosis

Clinical Rheumatology
https://doi.org/10.1007/s10067-018-4045-y

BRIEF REPORT

CrossMark

High prevalence of occupational exposure to solvents or silica in male systemic sclerosis patients: a Belgian cohort analysis

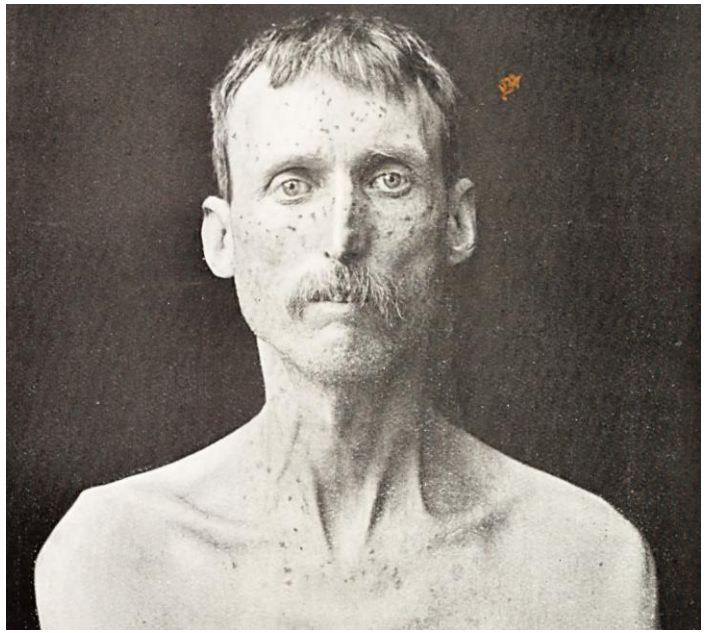
Evelien De Decker[1] · Marie Vanthuyne[2] · Daniel Blockmans[3] · Frederic Houssiau[2] · Jan Lenaerts[1] · Rene Westhovens[1] · Benoit Nemery[4] · Ellen De Langhe[1,5]

Received: 22 November 2017 / Revised: 11 February 2018 / Ac

55/103 male systemic sclerosis patients had a history of silica exposure

Silica & systemic sclerosis

1914: Bramwell: ‘Diffuse sclerodermia’
(Edinburgh Medical Journal):



No.	Initials.	Age.	Sex.		Occupation.
			M.	F.	
1	Miss F.	65		1	None.
2	D. K.	36	1		Stone-mason.
3	D. M.	43	1		Stone-mason.
4	A. H.	44	1		Coal-miner.
5	R. M.	35	1		Stone-mason.
6	J. M‘I.	57	1		Merchant.
7	J. D.	26	1		Stone-mason.
8	J. L.	46	1		Coppersmith.
9	J. S.	55	1		Stone-mason.

1957: Erasmus’ study in gold-miners (S-Africa): first link silica – systemic sclerosis

1960 – 2014 (Rubio-Rivas 2017 meta-analysis)

- 15 case-control studies: overall **OR 2.81** [1.86–4.23]
- 4 cohort studies: overall **RR 17.52** [5.98–51.37]

Recognized as occupational disease:

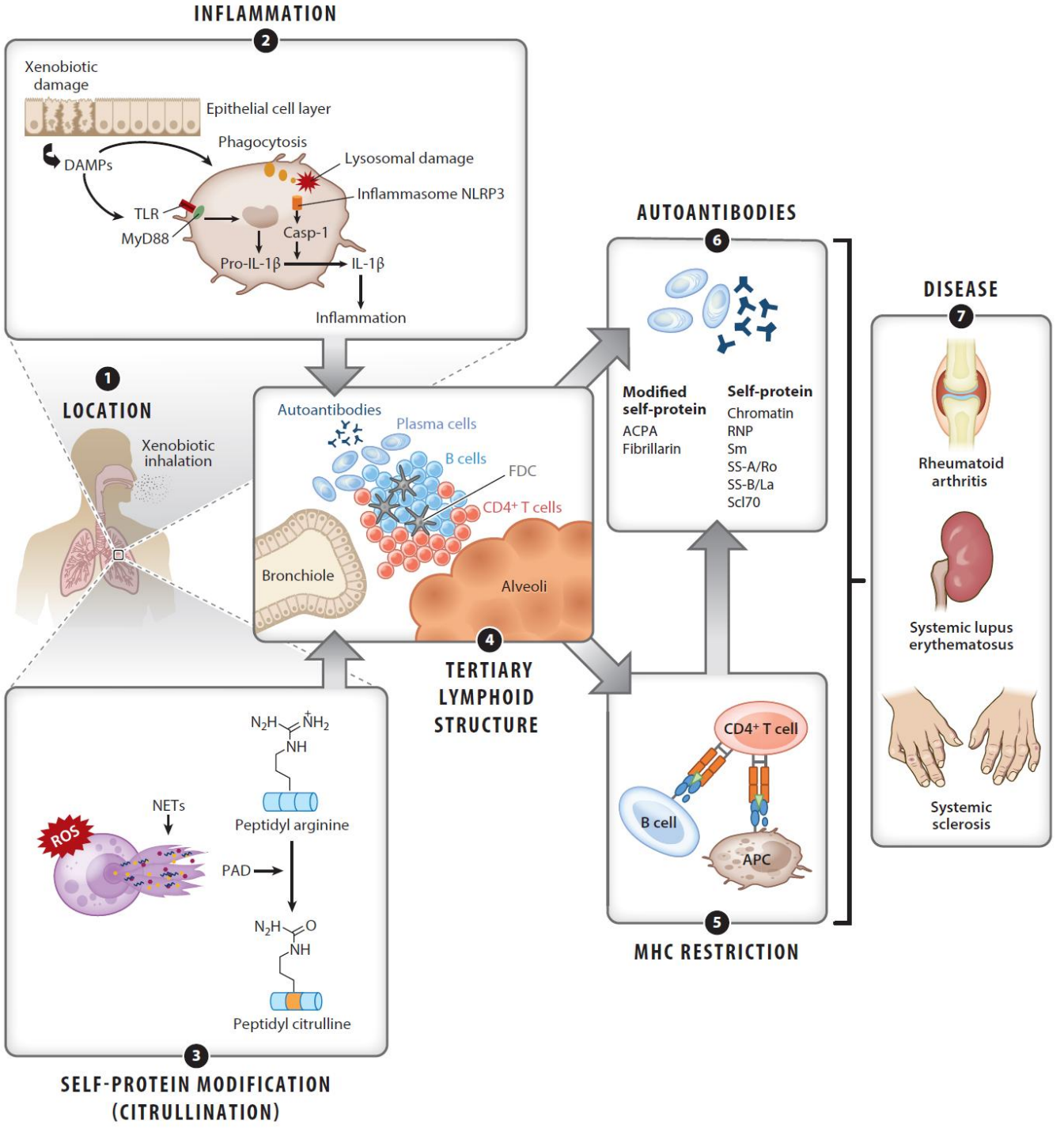
1974: South-Africa (miners)
1979: German Democratic Republic (GDR)
1992: France (in workers with silicosis)
1990s: Ontario, Canada
2000: France (silica exposed)
2022: Belgium

Mechanisms of Environment-Induced Autoimmunity

K. Michael Pollard,[1] David M. Cauvi,[2]
Jessica M. Mayeux,[1] Christopher B. Toomey,[3]
Amy K. Peiss,[1] Per Hultman,[4] and Dwight H. Kono[5]

Annu. Rev. Pharmacol. Toxicol. 2021

Hypothesized steps leading to autoimmunity or autoimmune disease following xenobiotic exposure



Overview

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- **Case of rheumatoid arthritis**
- Spectrum of autoimmune diseases related to silica exposure
- Outbreak of “sarcoidosis”

Case — Silica mining

- M, 40y, never-smoker
- **Since 2000: maintenance technician** @ silica mining and processing plant
    - Yearly chest X-ray and spirometry normal
- Clinical
    - **Joint pains and swelling**: hands (PIPs++) → wrists, feet, ankles, hips, knees, shoulders
    - Morning stiffness until 2 pm
- Lung function: normal
- CT Thorax:
    - No signs of interstitial lung disease
    - Enlarged mediastinal and hilar lymph nodes
- Lab
    - CRP ↑, ESR ↑
    - **Anti-citrullinated protein antibodies (ACPA) +, Rheumatoid factor (RF) +**
    - Anti-nuclear antibodies (ANA) −

- Diagnosis: **Rheumatoid arthritis**

Association between rheumatoid arthritis (RA) and silica exposure – with or without pneumoconiosis

- Meta-analysis: 10 studies 1966 – 2002 [Miller, 2012]: **RR 3.43**
- Some studies after 2002
  - Stolt et al. 2005: case-control: 276 male RA cases, 276 controls (Swedish general pop): **OR = 2.2**, adjusted for age, smoking
  - Blanc et al. 2015: cohort of 240,983 male construction workers (1997-2010): **RR = 1.33**, adjusted for age, smoking
  - Vihlborg et al 2017: cohort of 2187 male workers in iron foundries: **Incidentie ratio (IR) = 2.59**
  - Boudigaard et al. 2021: Danish working population 1979-2010 (3 million workers): **Incidence rate ratio = 1.57**

Thorax (1955), **10**, 9.

PATHOLOGICAL STUDIES OF MODIFIED PNEUMOCONIOSIS IN COAL-MINERS WITH RHEUMATOID ARTHRITIS (CAPLAN'S SYNDROME)

BY

J. GOUGH, D. RIVERS, AND R. M. E. SEAL

From the Department of Pathology and Bacteriology, Welsh National School of Medicine, Cardiff

"These rheumatoid pneumoconiotic nodules contain necrotic collagen and dust"

Rheumatoid pneumoconiosis—Colinet 1950

Un cas de panarthrite engainante

par E. COLINET

Adjoint des Hôpitaux de Bruxelles

Acta Physiotherapica et Rheumatologica Belgica

Vol. 5, Juillet-Août 1950

Polyarthrite chronique évolutive et silicose pulmonaire

par E. COLINET (Bruxelles)

Acta Physiotherapica et Rheumatologica Belgica

Vol. 8, Mars-Avril 1953

Silicose pulmonaire et rhumatisme ou syndrome de Colinet-Caplan (*)

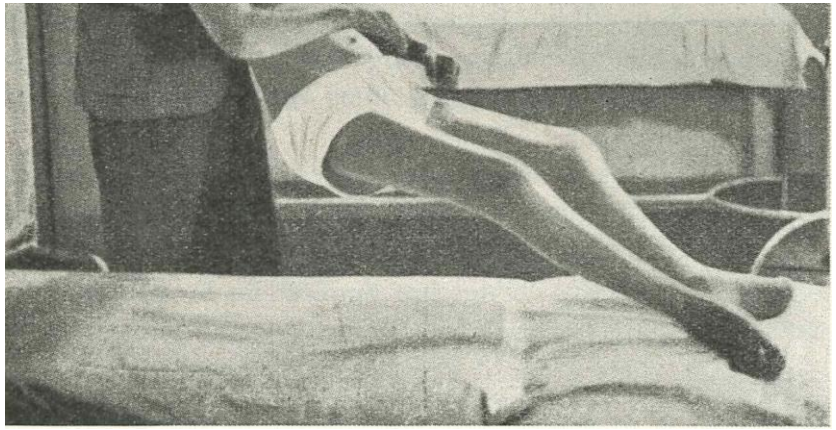
par le Dr J. CLERENS

Chef de Service des Hôpitaux

Archives Belges de Médecine Sociale, Hygiène, Médecine du Travail et Médecine Légale

Dec 1953

Two young women who had worked in a factory producing silica-based scouring powder developed severe **rheumatoid arthritis + pneumoconiosis**



Vim packing department at the Savonneries Lever Frères factory, Forest, Brussels (circa 1936)

[Ronsmans & Blanc. Annals of Internal Medicine. 2023;176:260–5]

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- **Spectrum of autoimmune diseases related to silica exposure**
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Silica & spectrum of autoimmune disease
Scouring powder factory (Sevilla)

"The SAN was filled by hand; the only protection was an ordinary cloth handkerchief brought from home. When transferring the hoppers with products, the dust rose and covered everything, so we left the workplace literally white" *[Autos nº 847/2000, Sentencia Nº 103/01; Ms AMG (factory operator 1961-1964) against Persan SA*]

Sanchez-Roman (1993):

- Grinding and handling scouring powder = 90% silica
- +/- 300 workers had been exposed

- 10 years after production had stopped
- **50** former workers traced (44 F, 6 M):
  - **18 silicotic pattern on chest X-ray**
  - **32 autoimmune manifestations** (of which 14 had silicosis)

[mean exposure duration 6.1y]

Systemic sclerosis (SSc)	5
Systemic lupus erythematosus (SLE)	3
Overlap syndrome (SLE/SSc)	5
Secondary Sjögren's syndrome*	6
Undefined collagen diseases†	19

Silica & spectrum of systemic autoimmune disease

Occupational Medicine 2015;**65**:444–450
Advance Access publication 12 June 2015 doi:10.1093/occmed/kqv073

Outbreak of autoimmune disease in silicosis linked to artificial stone

O. Shtraichman[1], P. D. Blanc[2], J. E. Ollech[1], L. Fridel[3], L. Fuks[1], E. Fireman[4] and M. R. Kramer[1]

Case series Israel (1997-2012):

- 40 artificial stone workers with silicosis referred to lung transplant centre
- **9/40** had autoimmune disease: systemic sclerosis, rheumatoid arthritis, mixed-connective tissue disease, Sjögren, polymyositis

International Journal of Epidemiology, 2021, 1–14

Occupational exposure to respirable crystalline silica and risk of autoimmune rheumatic diseases: a nationwide cohort study

Signe Hjuler Boudigaard ,[1]* Vivi Schlünssen,[2,3]
Jesper Medom Vestergaard,[1] Klaus Søndergaard,[4] Kjell Torén,[5]
Susan Peters ,[6] Hans Kromhout[6] and Henrik A Kolstad[1]

Cohort study of total Danish working population (DOC*X; 1979-2015; n ≈ 3 million workers)

Men exposed to high levels of respirable crystalline silica compared with nonexposed:

	Incidence rate ratio
• Systemic sclerosis	1.62 (1.08–2.44)
• Rheumatoid arthritis	1.57 (1.41–1.75)
• Systemic lupus erythematosus	1.46 (0.94–2.27)
• Small vessel vasculitis	1.34 (1.02–1.76)

Overview

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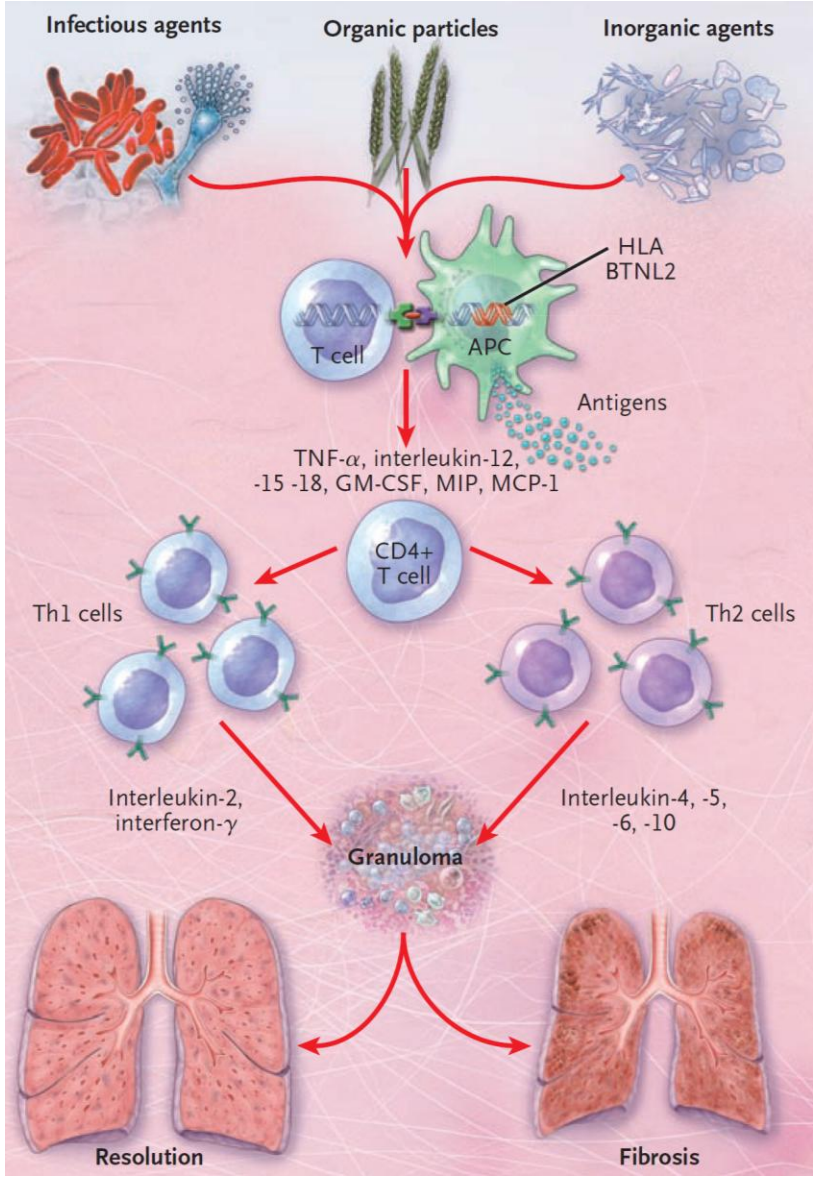
Sarcoidosis

- Development of immune granulomas in various organs
- Caused by an interaction between:
  - Genetic susceptibility
  - Exposure to 1 or more environmental factors

- **Metals**
  - Beryllium (chronic beryllium disease)
  - Other metals
    - Kucera et al. 2003: Metal workers: **OR 7.47** [1.19 - 47.06]
    - Newman, 2004: Car industry: **OR 8.00** [1.07-354.98]
    - Liu, 2006: Job in metal sector: **OR 1.41** [1.08-1.85]
- **Silica**
  - Vihlborg, 2017: 2187 workers in 10 iron foundries (1930 – 2013)
    Highest silica exposure (>0.048 mg/m³): **OR 3.94** [1.07-10.08]
  - Jonsson, 2019: Cohort: 297,917 construction workers
    Medium/high exposure: **RR 1.83** [1.14–2.95]
- **Organic dust**: moulds, ...



Iannuzzi et al; N Engl J Med 2007;357:2153-65.
Moller et al; Ann Am Thorac Soc. 2017 Dec;14(Suppl 6):S429-S436
Sverrild, et al; Thorax 2008;63:894-896.

Sarcoidosis

Case 1 — Man, °1986, ex-smoker

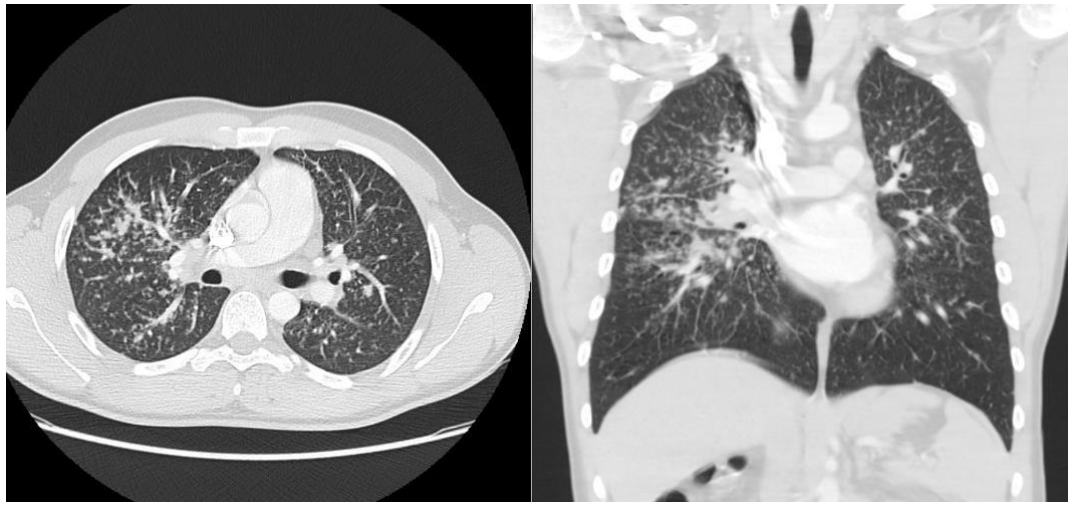
Medical history: nil

2013: Diagnosis of sarcoidosis

Work: Since 2005: operator at various places in lamp factory

Mainly in the workshop with 'special lamps' (~ 30 workers)

→ "One of my colleagues also has sarcoidosis"



Sarcoidosis

Case 1 — Man, °1986, ex-smoker

Medical history: nil

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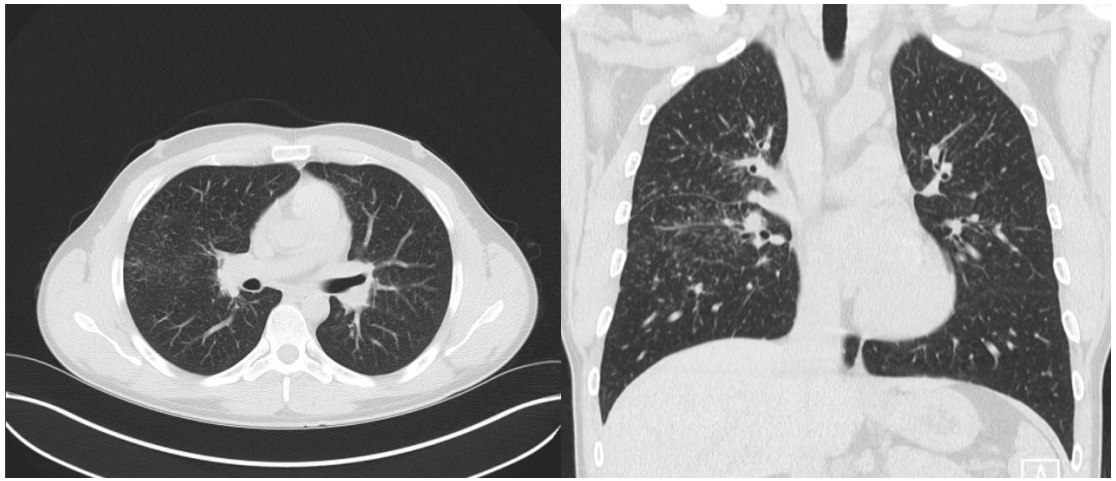
Mainly in the workshop with 'special lamps' (~ 30 workers)

Case 2 — Man, °1981, ex-smoker

Medical history: nil

2008: Diagnosis of sarcoidosis

Work: Since 2005: operator, same workshop as 1st case



Occupational exposure:

- Lamp tubes made of (amorphous) fused silica: heated + clipped
- X-ray powder diffraction of dust: mainly **amorphous silica** and some **cristobalite (crystalline silica)**
- Personal dust sampling during cleaning of machine (1h): total respirable dust: **6 mg/m³**
  → Occupational limit value respirable amorphous silica: **0.3 mg/m³**

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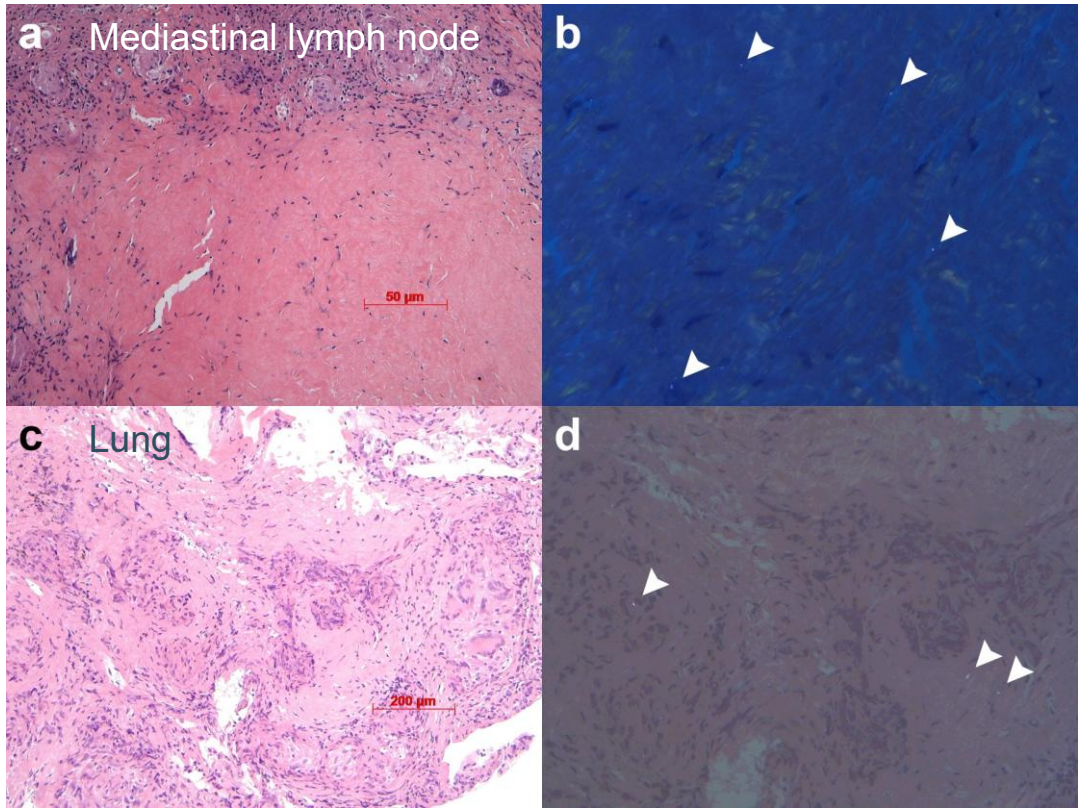

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Medical history: nil

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Mainly in the workshop with 'special lamps' (~ 30 workers)

Case 2 — Man, °1981, ex-smoker

Medical history: nil

2008: Diagnosis of sarcoidosis

Work: Since 2005: operator, same workshop as 1st case

Case 3 — Woman, °1972, never-smoker

2022: Diagnosis of sarcoidosis

Work: Since 2016: operator, same workshop as 1st + 2nd case

Arguments suggesting relation work - disease

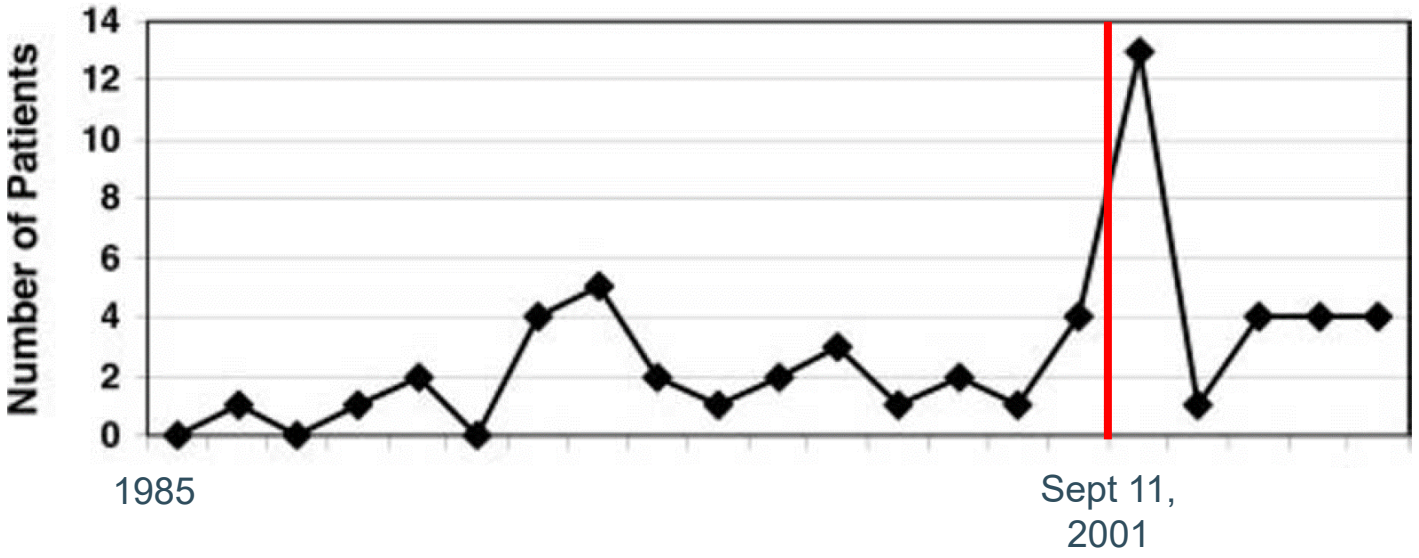
- 3 workers with “sarcoidosis” in small workshop (normal prevalence 4.7-64 / 100 000)
- Relevant exposure to fused silica dust (> limit value)
- Birefringent particles in relevant areas of lung or mediastinal lymph node
- Clinical improvement after removal from exposure

CHEST
Original Research
WORLD TRADE CENTER-RELATED PULMONARY DISEASE

Izbicki et al, Chest 2007; *131:1414–1423*

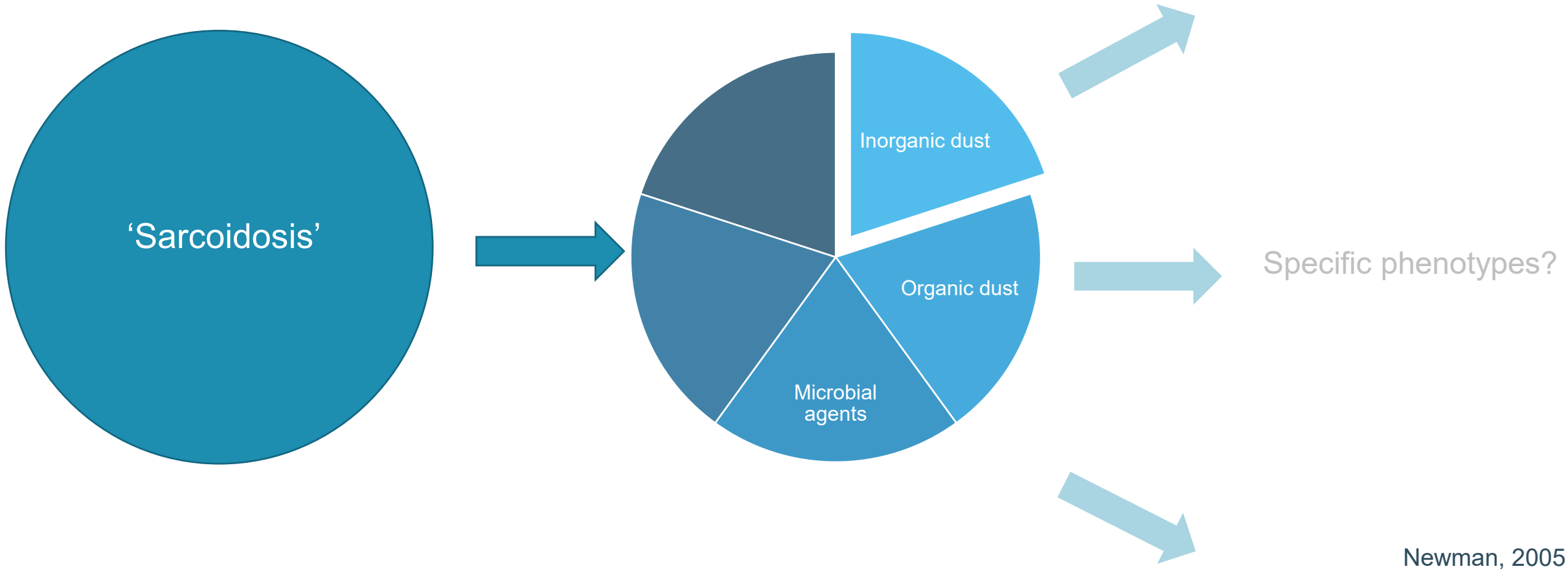
World Trade Center "Sarcoid-Like" Granulomatous Pulmonary Disease in New York City Fire Department Rescue Workers*

Cohort: n = 15,048



Incidence (biopsy-proven)

Sarcoidosis: 1 disease?



Newman, 2005
Judson, 2018
Ronsmans, 2021

Conclusion

- Silicosis is not the only health effect of silica exposure
- Although a contribution of occupational and environmental exposures is suspected, for most of the diseases discussed, the causes are still largely unknown
- The acceptance by clinical medicine that certain exposures might induce diseases generally regarded as “idiopathic” is slow