Prof. F. Rasmussen

"Environment."

Everything outside the body
that interacts with humans.

Specific sense:
only (natural or manmade) agents encountered by humans in their daily life, upon which they have no or limited personal control

British Medical Bulletin 2003; 68: 71–94

- The lungs and skin (including nose and eyes) are the organs of first contact for most environmental exposures (excluding ingestion).

THE RESPIRATORY SYSTEM

- Lungs that receive prolonged &/or repeated exposure to air contaminants eventually cannot keep up with the rate of deposition &/or constant irritation.
- Result: contaminants accumulate contributing to the development of Occupational Lung Diseases.

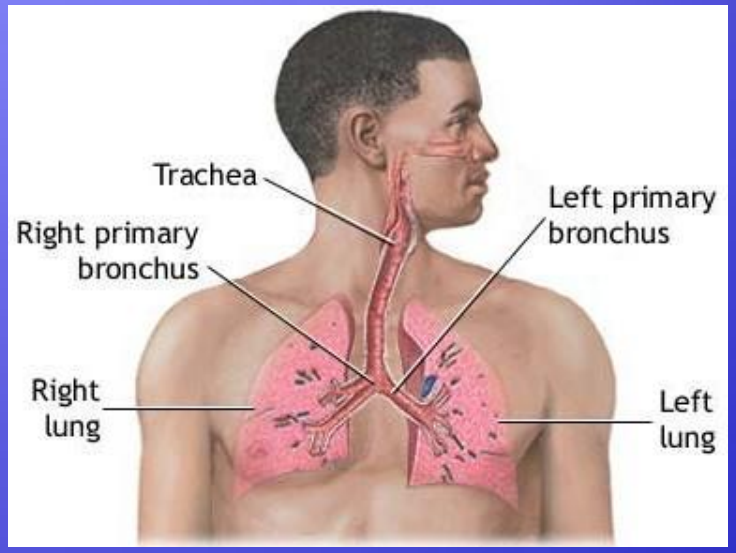


Diagram- black asbestos fibers- exposure standards to be less than 1 fibre/cm3 for 8 hr exposure

Primary prevention
- The best but always not possible

- Reduce exposure
- Pre-employment screening
  - Atopy
  - Genetic factors
- Education
- Screen for potential respiratory sensitizers

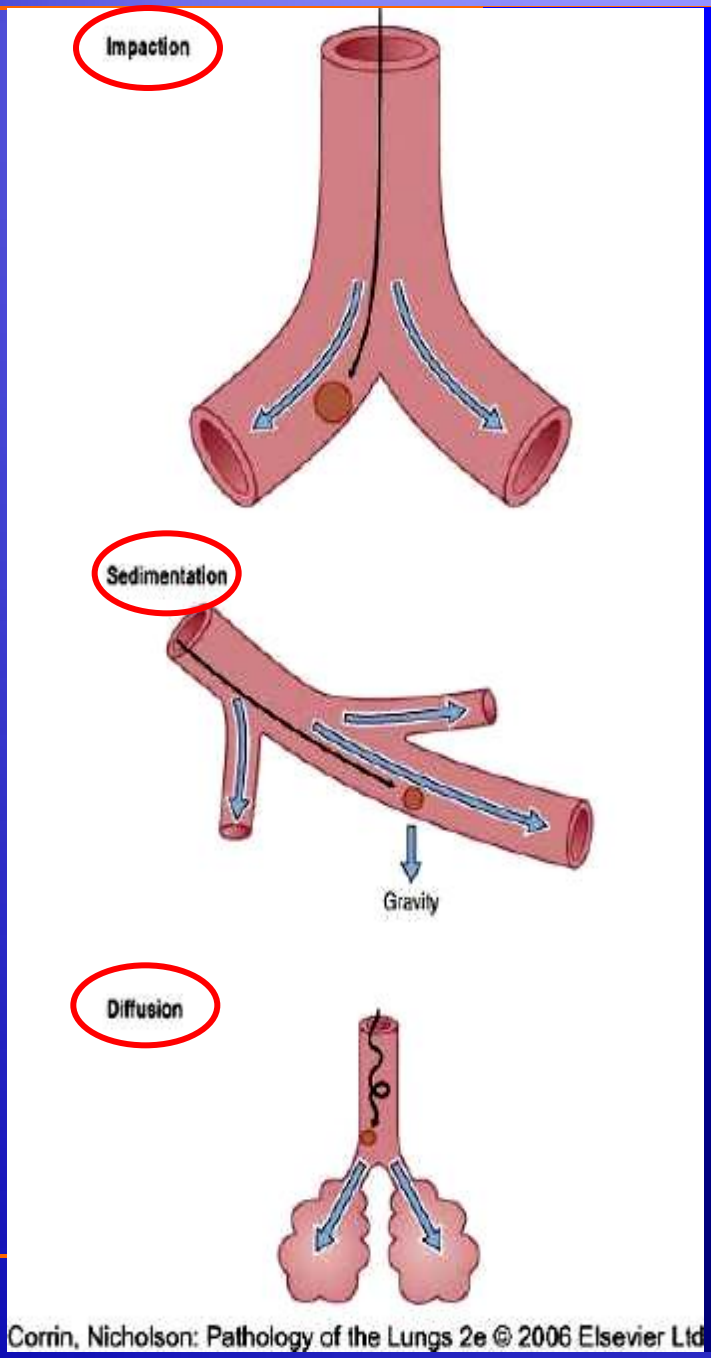
Indoor and outdoor air pollution affects health

Key points

- Recent epidemiological studies have clearly shown that outdoor and indoor air pollution affects respiratory health worldwide, causing an increase in the prevalence of respiratory symptoms/diseases (*i.e.* COPD, asthma, hay fever, lung function reduction) and of mortality, both in children and in adults.
- Rapid industrialisation and urbanisation have increased air pollution and, consequently, the amount of exposed people.
- Conservative estimates show that between 1.5 and 2 million deaths per year could be attributed to indoor air pollution in developing countries.
- The abatement of the main risk factors for respiratory diseases and the support of health care providers and general community to public health policy for improving outdoor/indoor air quality can achieve huge health benefits.

Table 1. Major outdoor pollutants and related health effects

Pollutant	Major sources	Health effects
Particulate matter	Vehicular traffic Wood stoves Organic matter/fossil fuel combustion Power plants/industry Wind-blown dust from roads, agriculture and construction Bush fires/dust storms	Lung cancer Premature death Mortality from cardiorespiratory diseases Reduced lung function Lower airways inflammation Upper airways irritation
Nitrogen dioxide	Vehicular traffic Power plants/industry	Exacerbation of asthma Airway inflammation Bronchial hyperresponsiveness Increased susceptibility to respiratory infection
Ozone	Sunlight: chemical reaction between other pollutants Vehicular traffic Power plants/industry Consumer products	Lung tissue damage Reduced lung function Reduced exercise capacity Exacerbation of asthma Upper airway and eye irritation
Carbon monoxide	Organic matter/fossil fuel combustion Vehicular traffic Wood stoves	Death/coma at very high levels Headache, nausea, breathlessness Confusion/reduced mental alertness Bronchial hyperresponsiveness
Sulphur dioxide	Coal/oil burning power plants Industry/refineries Diesel engines Metal smelting	Exacerbation of respiratory diseases including asthma Respiratory tract irritation



Mechanisms of Particle Deposition in the Respiratory Tract

Influenced by particle
- Size
- Shape
- Density

Stoke's diameter: size of an irregular particle relative to that of a sphere of unit density

Particle Clearance
- Mucociliary action
- Alveolar macrophages
- Pulmonary lymphatics

Ancient times

- Egypt, Greece and Rome
  - Mining one of the oldest industries
  - miners – slaves, criminals
  - work = punishment
  - manual trades – inferior
  - miners used bags, sacks, animal bladders as masks to decrease dust exposure

ILO List of Occupational Diseases

- Diseases caused by agents
  - Chemical, physical, biological
    - e.g. Beryllium
- Diseases by target organ system
  - Respiratory, skin, musculoskeletal
    - e.g. Pneumoconioses
- Occupational cancer
  - Cancer caused by the following agents
    - e.g. radiation

What to focus on ?

Exposure History	Medical History
• Work history • Source, intensity, duration, and frequency of exposure • Time elapsed since first exposure • Workplace dust measurements or description of exposure scenario • Use of personal protective equipment • Paraoccupational exposures • Sources of environmental exposure	• History of smoking • History of other conditions

http://www.atsdr.cdc.gov/HEC/CSEM/csem.html

Occupational Respiratory Diseases

Size, Location, Outcome

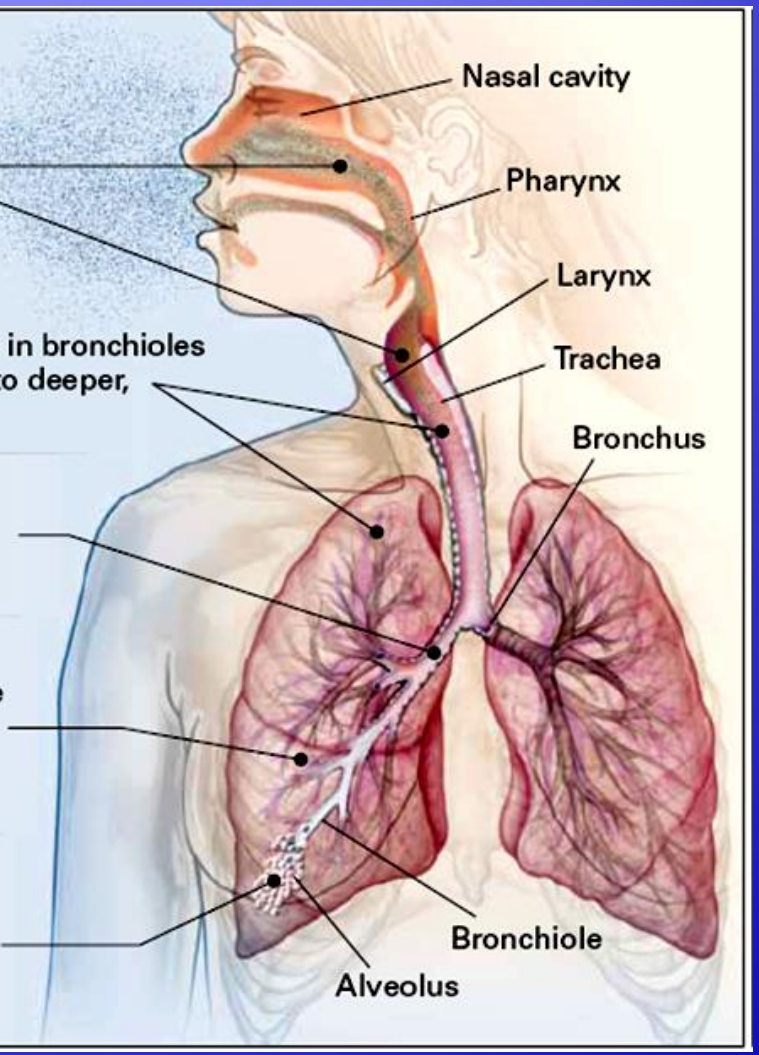
Rhinitis and laryngitis
Large particles are deposited in the nose, pharynx, and larynx. More soluble gases (e.g., sulfur dioxide) are absorbed by upper respiratory tract mucous membranes, causing edema and mucus hypersecretion.

Tracheitis, bronchitis, and bronchiolitis
Large particles (more than 10 μm in diameter) are deposited and then cleared by cilia. Small particles and fine fibers are deposited in bronchioles and bifurcations of alveolar ducts. Less soluble gases penetrate to deeper, small airways.

Asthma and chronic obstructive pulmonary disease
Allergens and irritants are deposited in large airways by turbulent flow, causing chronic inflammatory changes.

Cancer
Carcinogens (asbestos and polycyclic aromatic hydrocarbons) come into contact with bronchial epithelial cells, causing mutations in proto-oncogenes and tumor-suppressor genes. More than one such contact results in malignant transformation.

Interstitial disease
Small particles (less than 10 μm in diameter) and fibers are deposited in terminal bronchioles, alveolar ducts, and alveoli. Penetration to the interstitium results in fibrosis and the formation of granulomas.



NEJM 2000

How much adult asthma is occupationally related?

- Attributable risk estimates (median)
  - All studies 9% (IQI: 5%-19%)
  - Published AR 9%
  - Derived AR 25%
  - Highest scores (n=12) 15%
  - Conclusion: "≈1 in 10-20 cases"

Blanc PD. Am J Med 1999; 107: 580

Occupational Asthma (OA)

- No difference between “normal” asthma and OA in symptoms and diagnosis of asthma but:
- OA: Onset of asthma after entering the workplace.
- OA: Association between symptoms and work.
  - One or more of the following:
  - (Workplace exposure to agent known to give rise to OA).
  - Work-related changes in FEV1, PEF, or bronchial responsiveness.(15% change)
  - Positive response to specific inhalation challenge.
  - Onset of asthma clearly associated with symptomatic exposure to an inhaled irritant agent in the workplace.

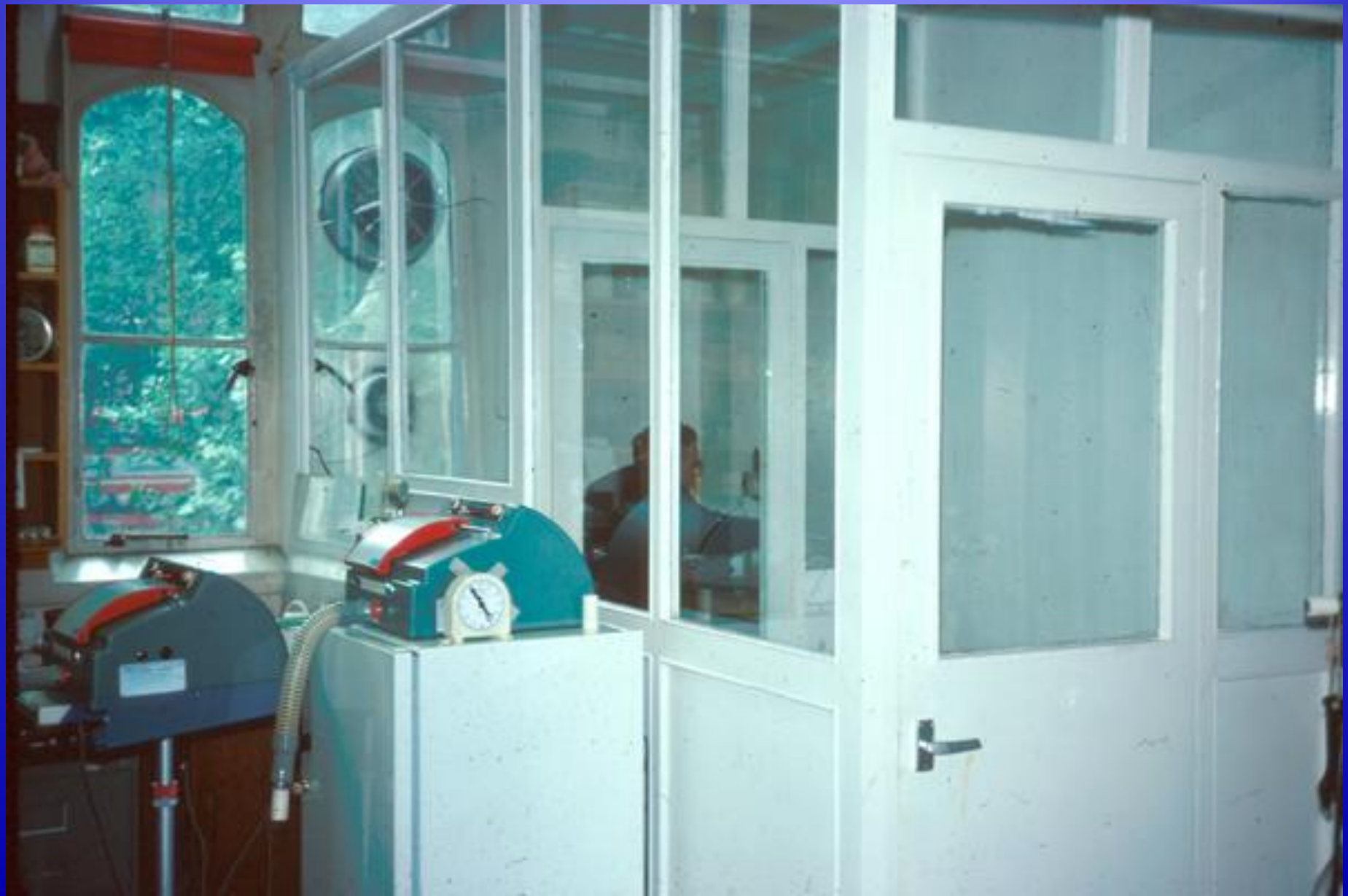
Occupational Asthma: Diagnosis

- Symptoms
  - Wheezing, cough, dyspnea
  - Relationship to work
- Evidence of airway reactivity
  - Bronchodilator response
- Workplace challenge
  - Serial peak flow measurement
  - Serial spirometry

Monitoring of PEF - How to do it ?

- At least **2 weeks at work and off work**
  - ✓ (often longer...)
- At least 4 times daily, preferably every 2 hours
- Medication allowed:
  - ✓ keep constant & at minimum dose...
  - ✓ beta-2 agonist on demand only
  - ✓ continue inhaled steroids/theophylline
  - ✓ avoid, if possible, long-acting beta-2-agonist

Exposure chamber



Selected Common Causes of Occupational Airway Disease - *Asthma with latency*

- Acid anhydrides (used in epoxy adhesives and paints, coatings, circuit boards, polymers, polyesters, plasticizers)
- Aldehydes
- Acrylates (used in paints and adhesives)
- Animal proteins (in laboratory animals, farming, and veterinary medicine)
- Cobalt (used in carbide-tipped tools)
- Dusts from flours and grains (found in bakeries)
- Dusts from wood (used in furniture making and cabinetry)
- Ethylenediamine, monoethanolamine, and other amines

NEJM 2000 Volume 342 Number 6

Selected Common Causes of Occupational Airway Disease - *Asthma*

- Formaldehyde and glutaraldehyde (used in sterilizing medical instruments)
- Isocyanates (hexamethylene diisocyanate, diphenylmethane diisocyanate, and toluene diisocyanate) used in polyurethane paint (used in auto-body repair) and the manufacture and application of foam (used in roofing foams)
- Latex (used in health care facilities)
- Asthma without latency (irritants that cause reactive airway dysfunction syndrome - RADS)
- Contaminants in metalworking fluids
- Chlorine gas (pulp from paper mills)
- Bleach (sodium hypochlorite)
- Strong acids

Reactive Airways Dysfunction Syndrome (RADS)

- No preceding complaints
- Onset after a single exposure incident
- Exposure to a gas, smoke, fume or vapor with irritant properties; in very high concentrations
- Symptoms of asthma: cough, wheeze, dyspnea
- Airflow obstruction on PFTs
- Nonspecific bronchial hyper-responsiveness
- Other pulmonary diseases ruled out

Table 1. Possible causes of toxic tracheo-bronchitis or pneumonitis

Irritant gases
- High water-solubility: NH_3, SO_2, HCl, *etc.*
- Moderate water-solubility: Cl_2, H_2S, *etc.*
- Low water-solubility: O_3, NO_2, $COCl_2$, *etc.*

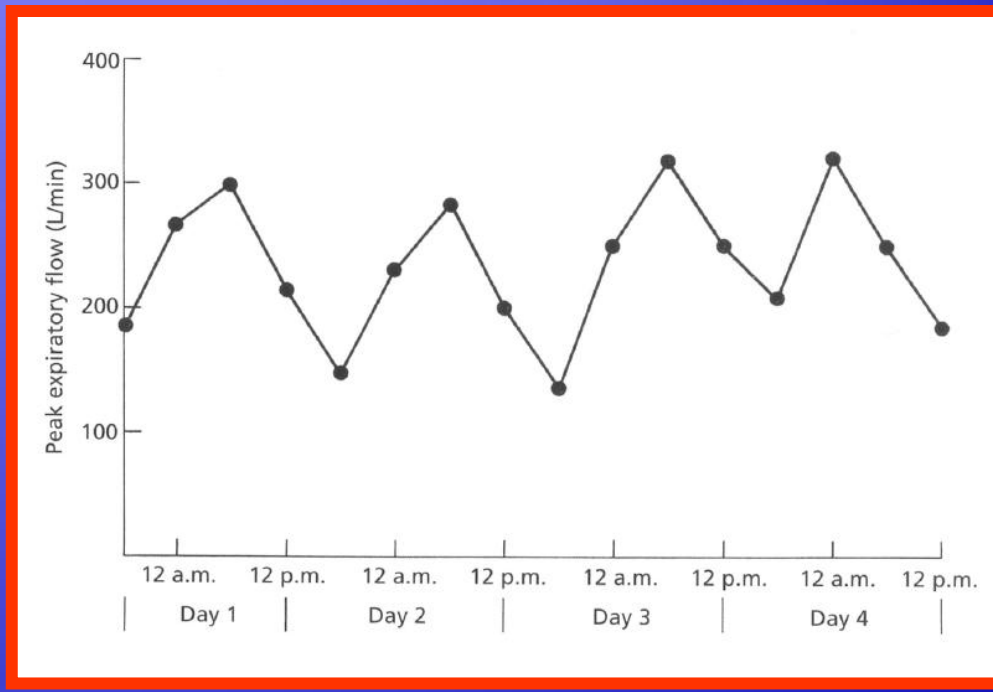
Organic chemicals
- Organic acids: acetic acid, *etc.*
- Aldehydes: formaldehyde, acrolein, *etc.*
- Isocyanates: methylisocyanate (MIC), toluene diisocyanate (TDI)
- Amines: hydrazine, chloramines, *etc.*
- Riot control agents (CS) and vesicants (mustard gas)
- Organic solvents
- Leather treatment sprays
- Some agrochemicals (paraquat, cholinesterase inhibitors)

Metallic compounds
- Mercury vapours
- Metallic oxides: CdO, V_2O_5, MnO, Os_3O_4, *etc.*
- Halides: $ZnCl_2$, $TiCl_4$, $SbCl_5$, UF_6, *etc.*
- $Ni(CO)_4$
- Hydrides: B_2H_5, LiH, AsH_3, SbH_3

Complex mixtures
- Fire smoke
- Pyrolysis products from plastics
- Solvent mixtures
- Spores and toxins from microorganisms

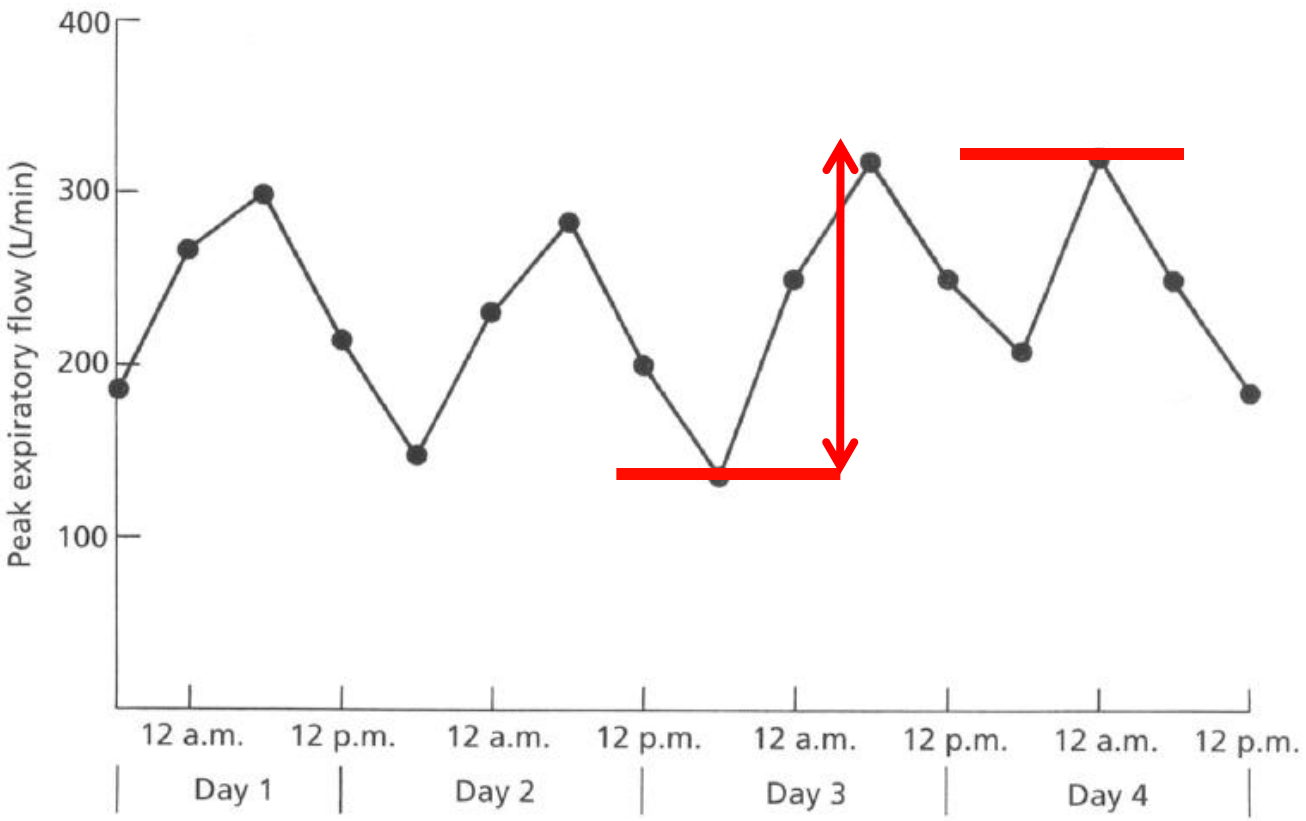
Based on these serial measurement of peak expiratory flow (PEF) which statement is true given that PEF is correctly measured?

1. The patients has definitive Occupational asthma
2. The patient does definitive not have Occupational asthma
3. The patient has asthma but there is not enough information given to determine if it is Occupational asthma
4. None of above



Question 1: Is it asthma: Yes

Serial measurement of peak expiratory flow (PEF)



Variability calculation (Fast): Highest-lowest/Average

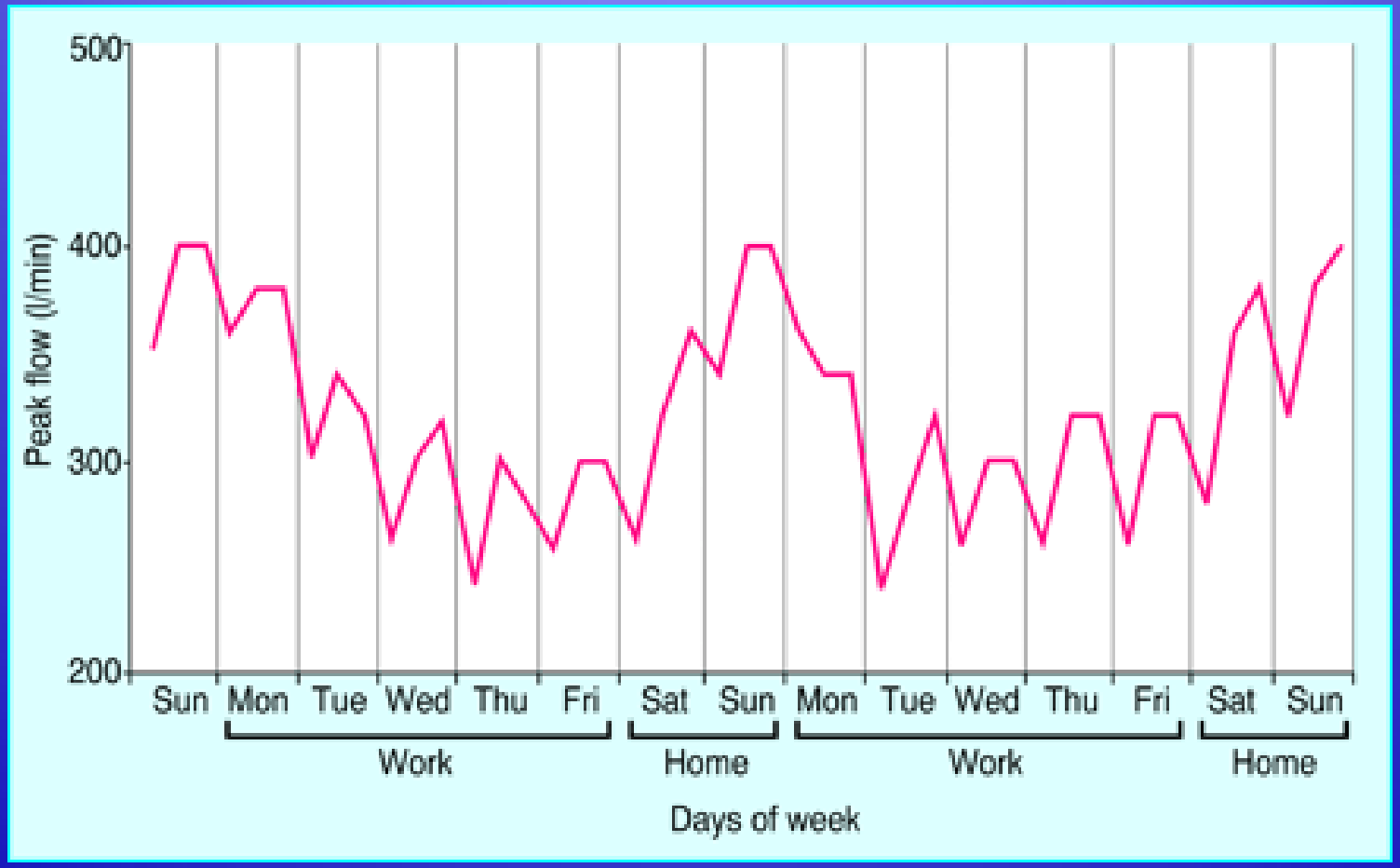
310-140/225

76% variability =asthma

But if it OA we do not know yet!!

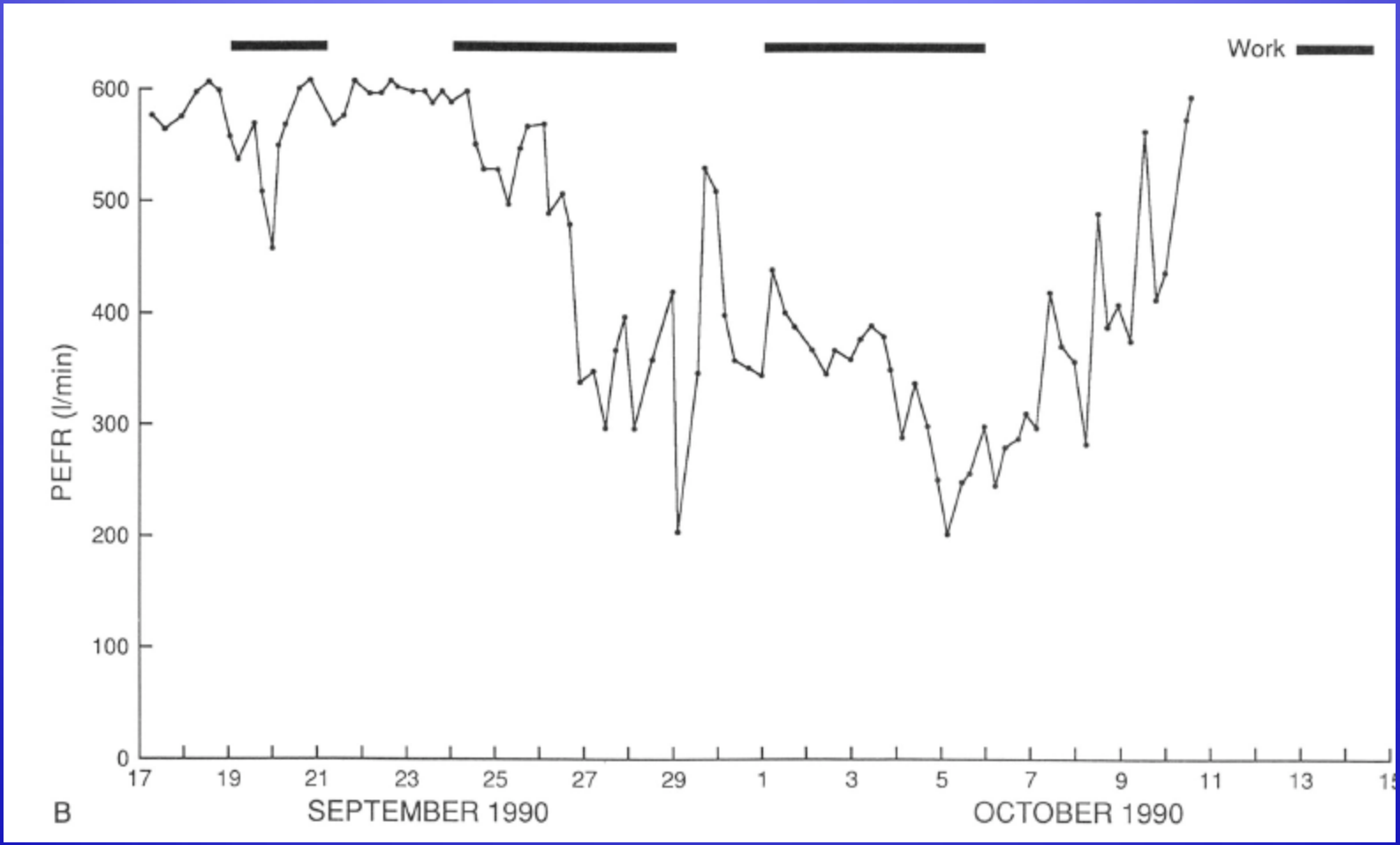
Seaton 2000

Question 2: Has it anything to do with working hours ?



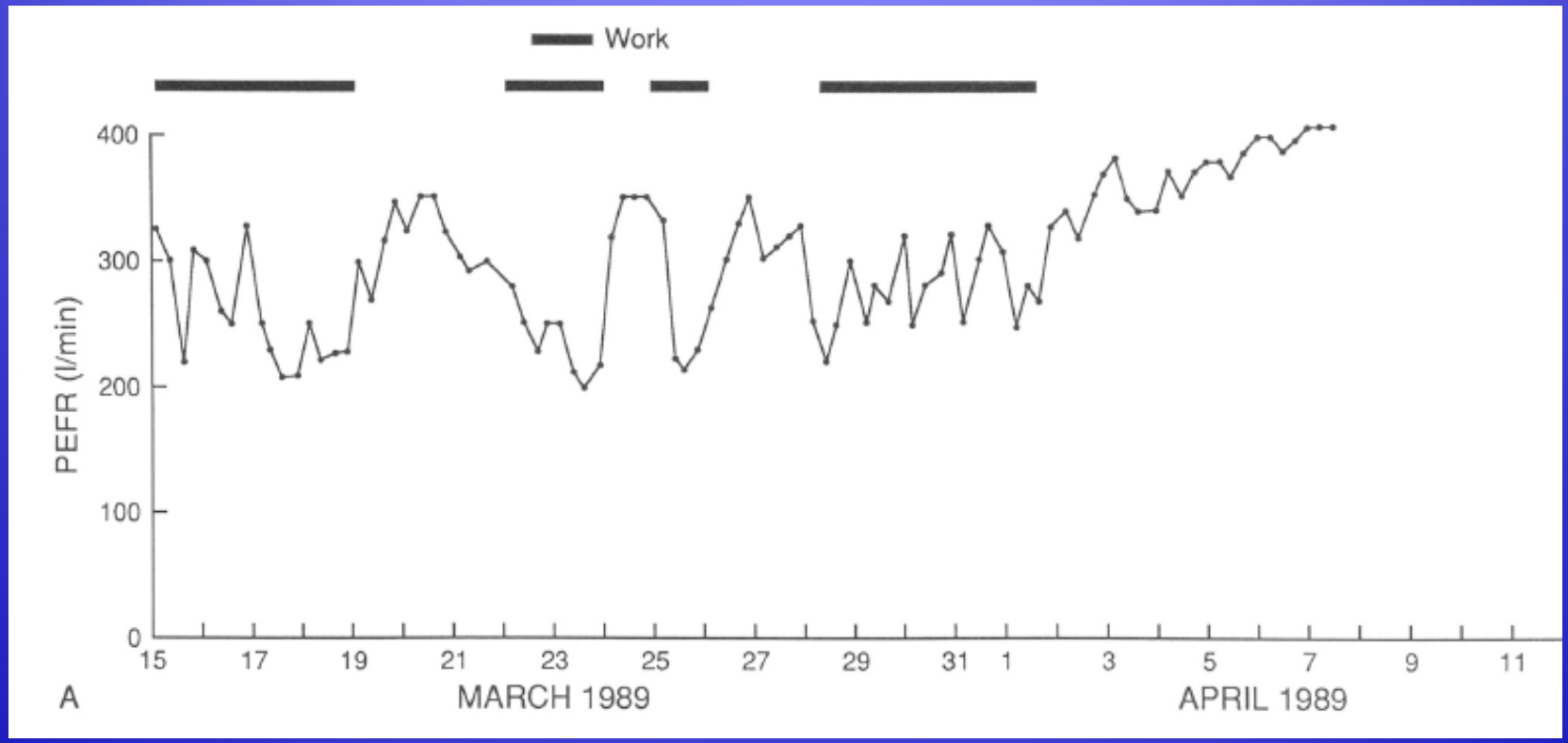
Madan 1996

Question 2: Has it anything to do with working hours ?
Occupational asthma



Rosenstock and Cullen 1994

Question 3: Does it disappear when work stops ?
Occupational asthma



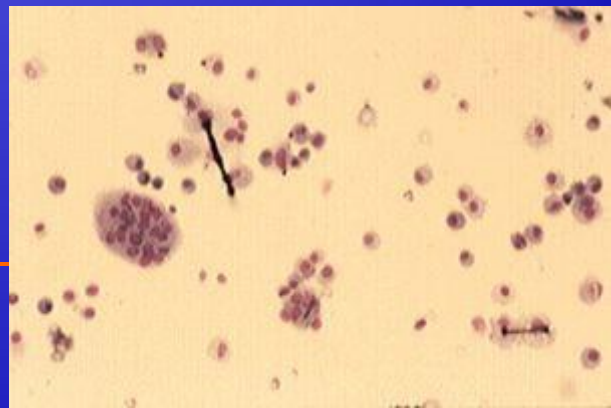
Rosenstock and Cullen 1994

Pneumoconiosis

- Non-neoplastic (i.e. excludes cancer) reaction of the lungs to inhaled mineral or inorganic dust and the resultant alteration in their structure.
- It also excludes diseases mainly of the airways like asthma, bronchitis and emphysema (although destruction of alveoli as in emphysema can be caused by dusts).

3 important pneumoconioses exsists

- Coal workers pneumoconiosis
- Asbestosis
- silicosis.



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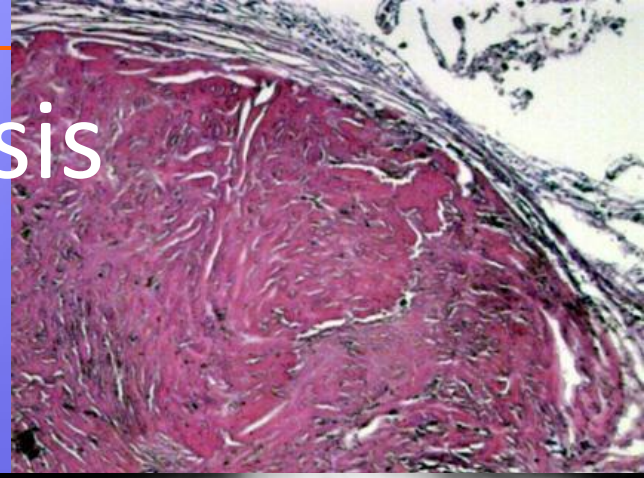
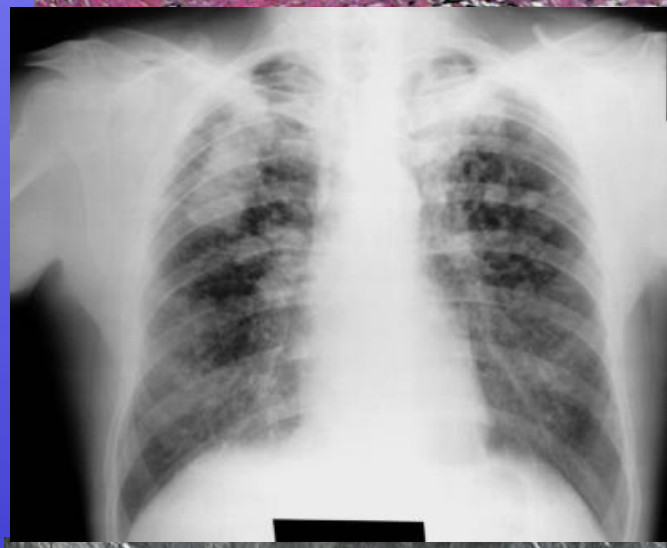
Coal workers pneumoconiosis

- Coalworkers' pneumoconiosis (cwp) is a pneumoconiosis caused by inhalation of coal dust and is more prevalent in underground workers exposed to higher concentrations of dust than in surface workers. The lung is destroyed by fibrosis and emphysema.

Pneumoconiosis - Silicosis

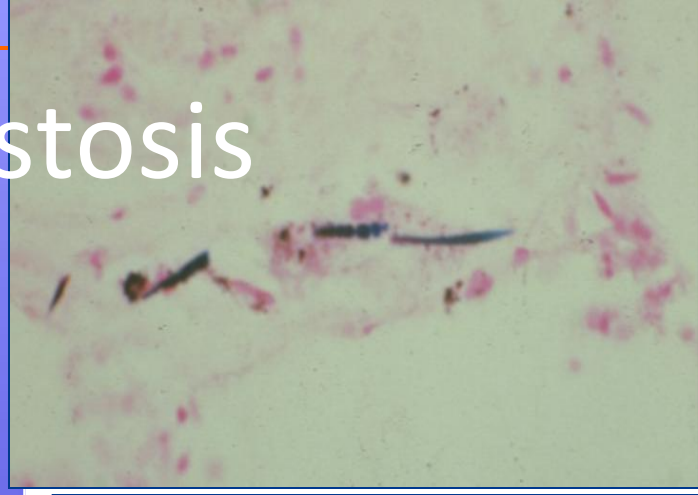
- Caused by inhalation of quartz (or some other crystalline forms of silicon dioxide) which is lethal to macrophages that ingest it and releases their enzymes.
- In its early stages it is similar to Coalworkers' pneumoconiosis but the nodules in the lung tend to be denser.
- It is a serious and progressive disease.
- A number of exposures such as grit / sand-blasting with silica have essentially been banned because of the risk of this serious condition.

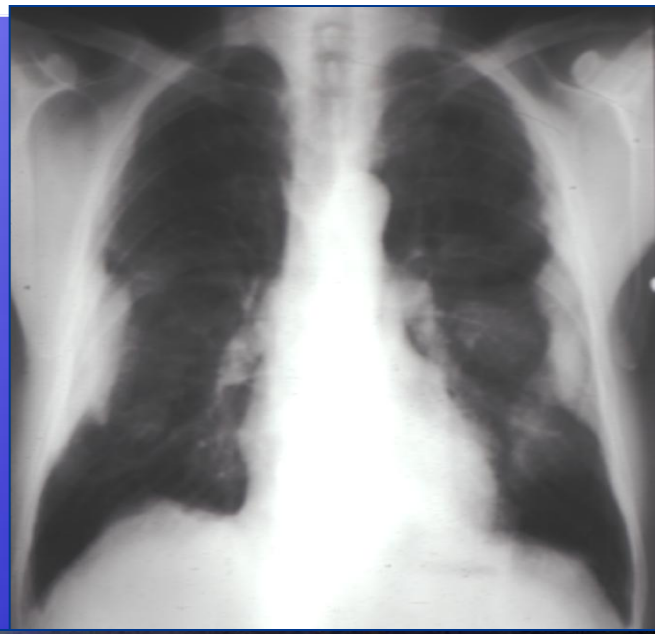




Pneumoconiosis- asbestosis

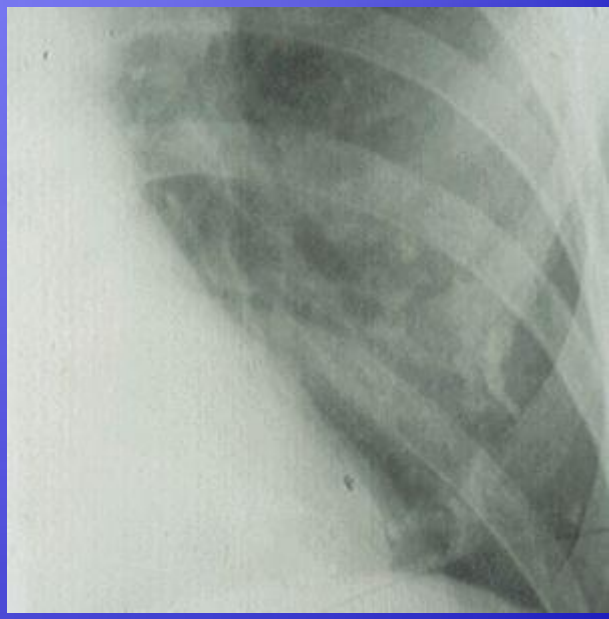
- Caused by inhalation of asbestos fibers
- Asbestos fibers induce pathogenic changes via:
  - Direct interaction with cellular macromolecules
  - Generation of reactive oxygen species (ROS)
  - Other cell-mediated mechanisms
- These changes can lead to cell injury, fibrosis, and possibly cancer
- Asbestos is genotoxic and carcinogenic

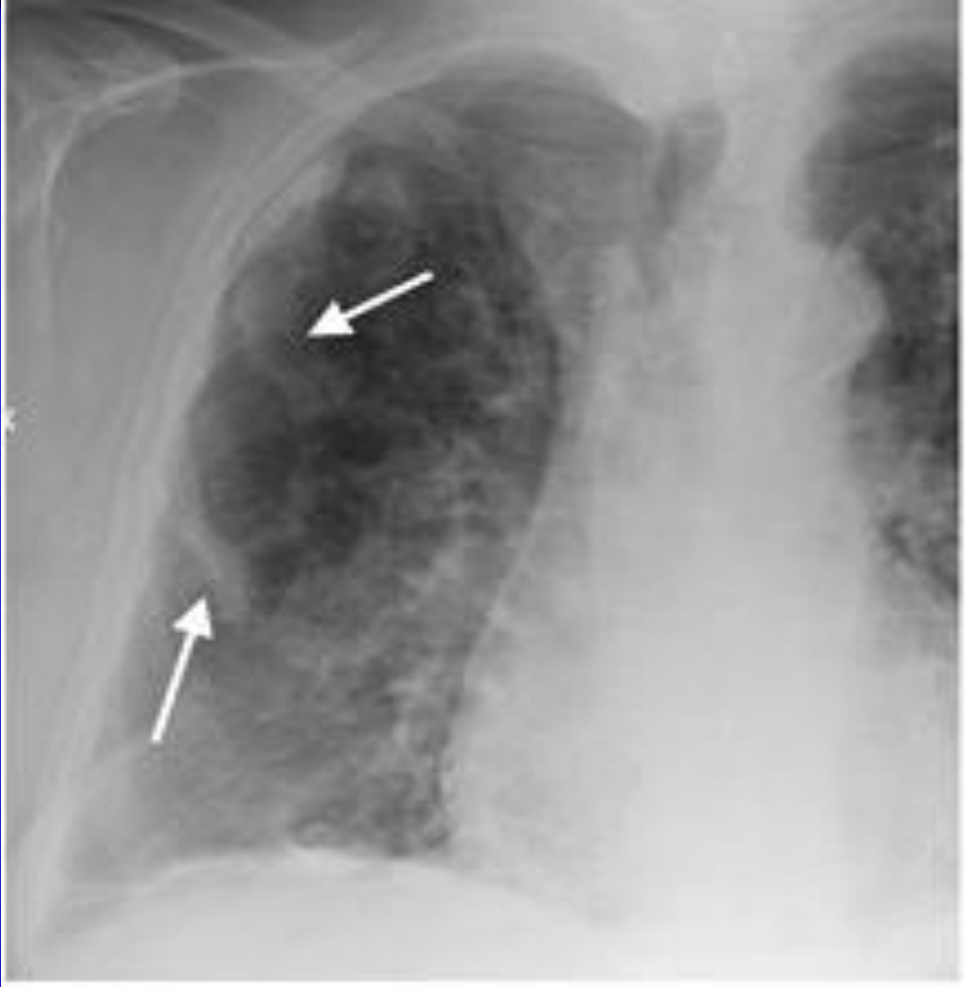


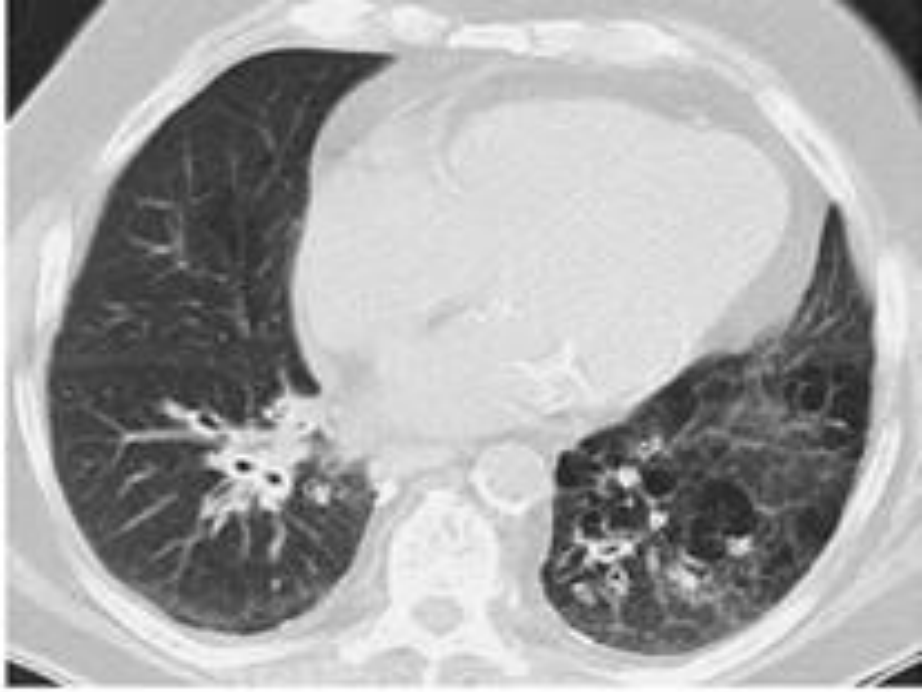


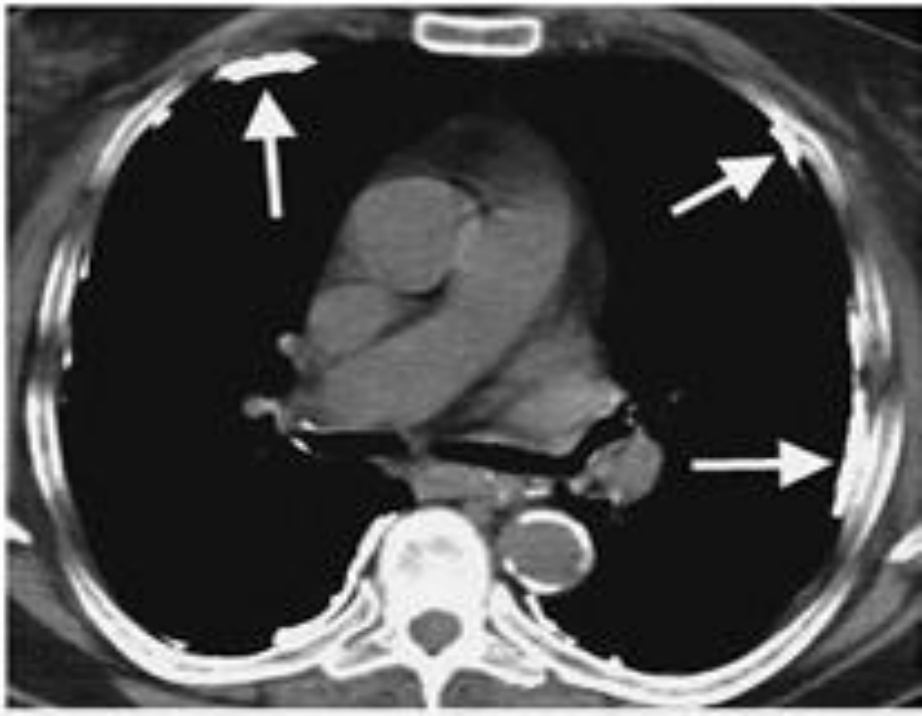
Asbestos -Associated Diseases

- Respiratory diseases:
  - Parenchymal asbestosis
  - Asbestos-related pleural abnormalities
  - Lung carcinoma
  - Pleural mesothelioma
- Nonrespiratory diseases:
  - Peritoneal mesothelioma
  - Possibly, other extrathoracic cancers
  - Rarely, cor pulmonale or constrictive pericarditis







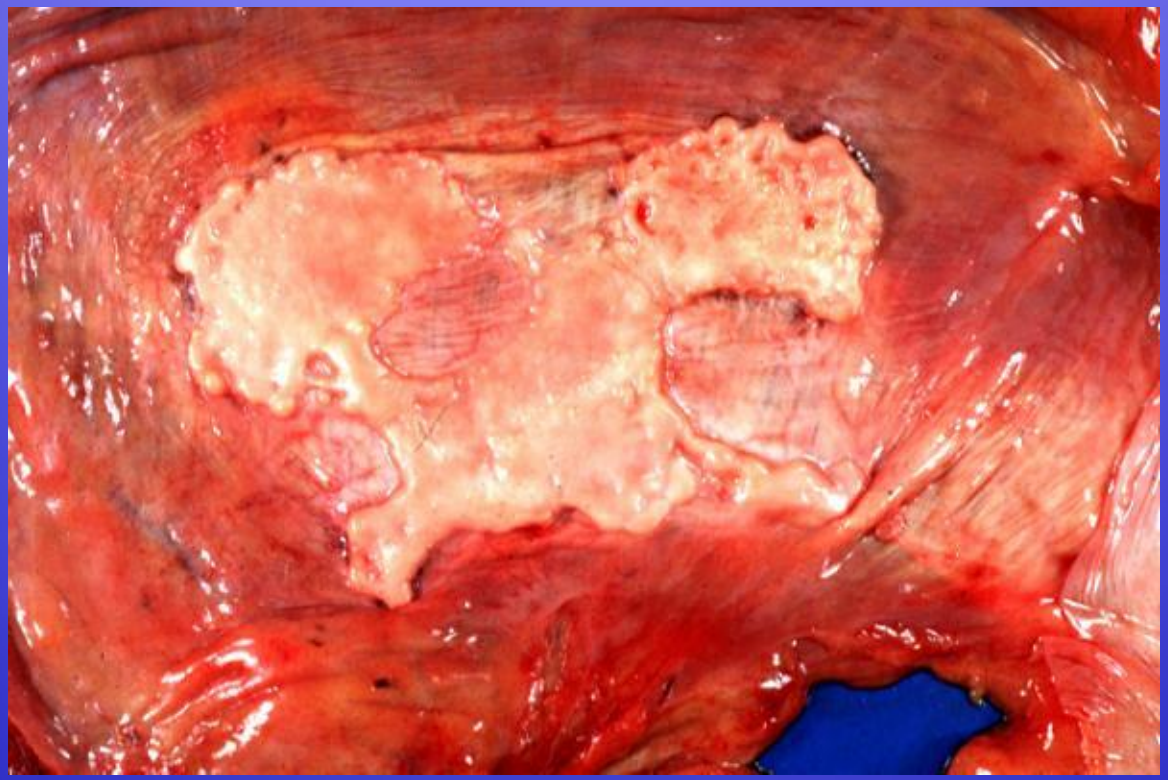


Asbestos-related pleural disease and asbestosis

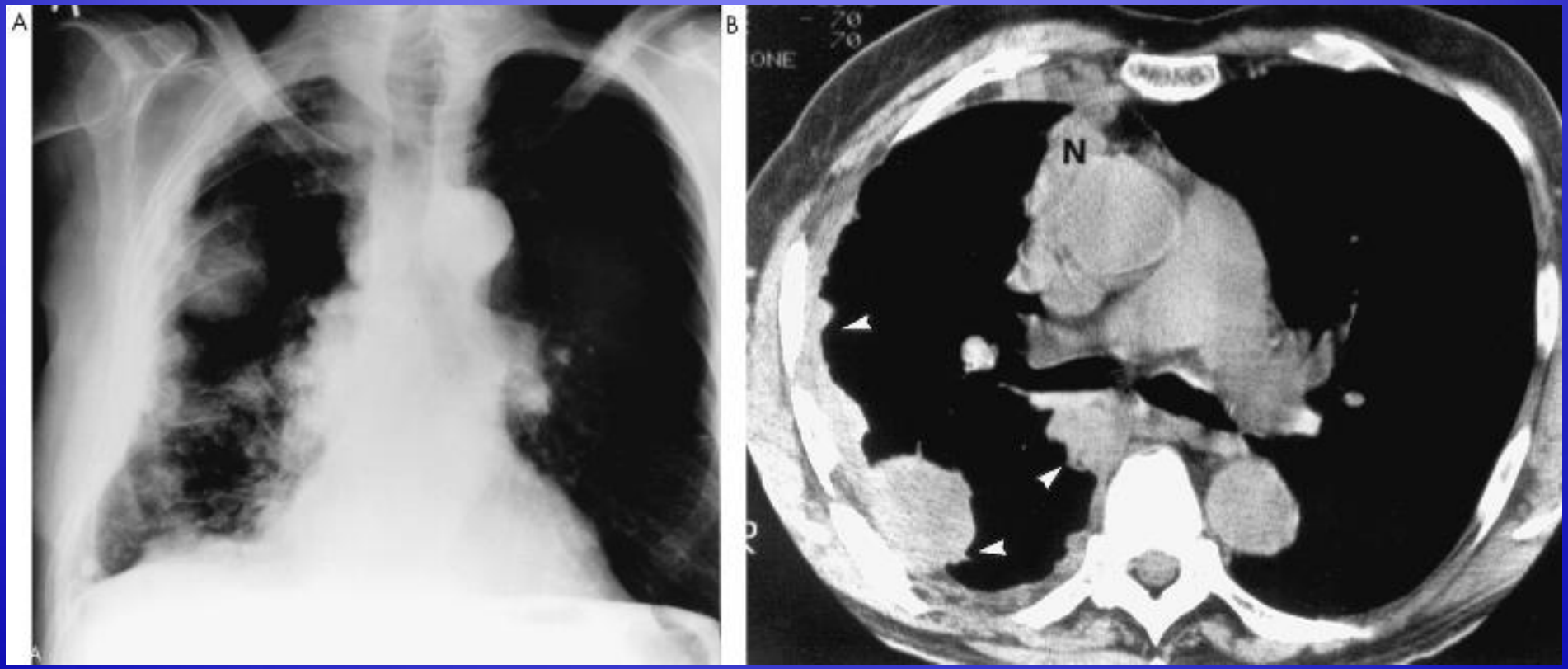
Asbestos -Associated Diseases

- Diffuse interstitial fibrosis with:
  - Restrictive pattern of disease on pulmonary function testing (but can see mixed pattern)
  - Impaired gas exchange
  - Progressive exertional dyspnea
- Radiographic changes: >10 years
- Latency period: 20-40 years

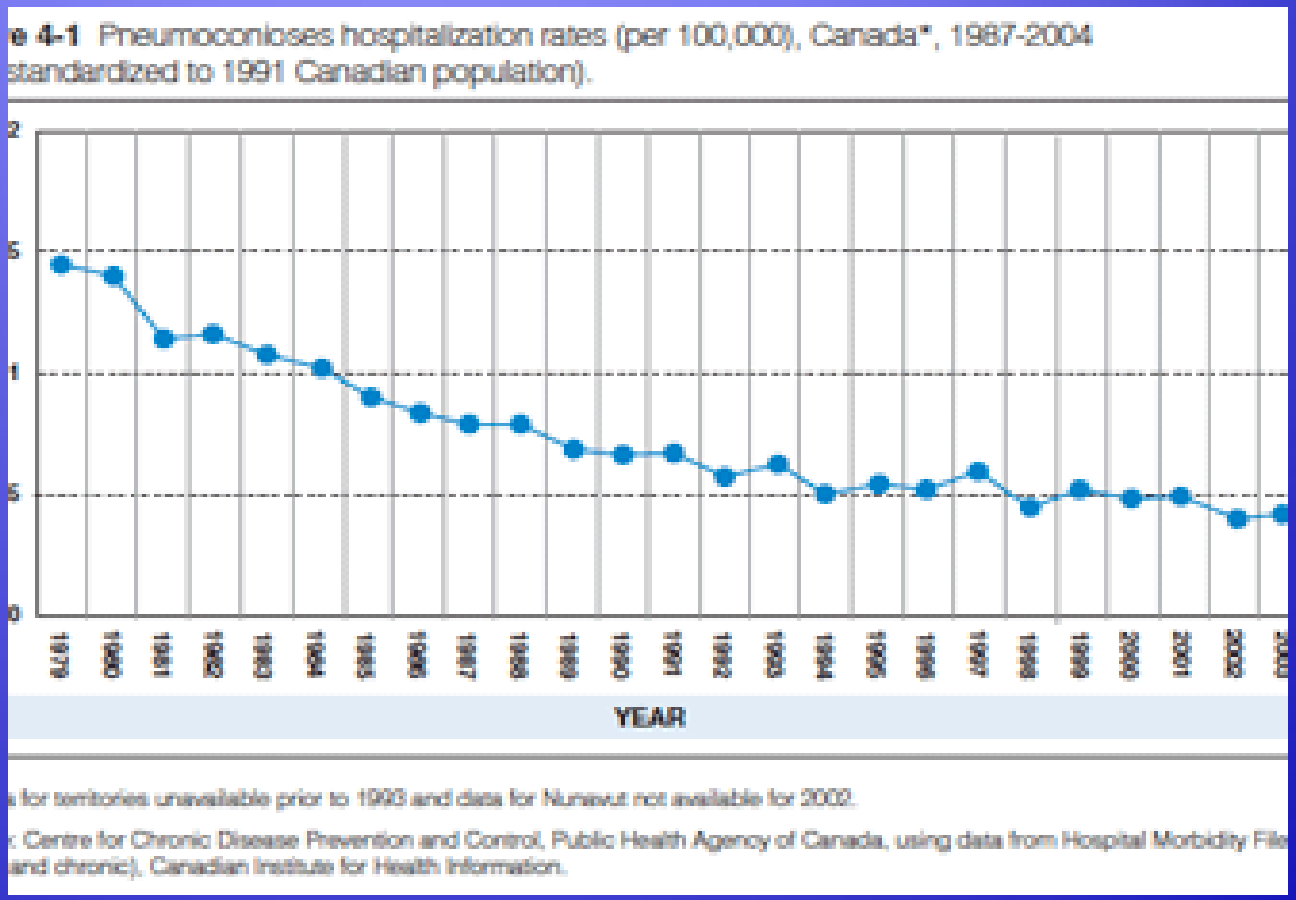
Diaphragmatic Pleural Plaque Asbestosis



Asbestosis Pleural Thickening



PNEUMONCONIOSES



Lung disease from inhaling inorganic dust in mines & other workplaces has declined over past 30 years.

Selected Common Causes of Occupational Upper Respiratory Tract Disease- *Rhinitis and Laryngitis†*

- *Rhinorrhea*
  - Cold air
  - Certain pesticides (carbaryl, malathion, parathion, mevinphos, pyrethrum)
- *Nasal ulceration and perforation of septum*
  - Arsenic
  - Chromic acid and chromates
  - Copper dusts and mists

Selected Common Causes of Occupational Airway Disease - *Bronchitis*

- Sulfur dioxide (used in chemical manufacturing)
- Rock and mineral dusts (used in road construction and digging of foundations)
- Cement dust
- Smoke from welding or cutting with acetylene torch

Selected Common Causes of Occupational Airway Disease-b*ronchiolitis*

- Acetaldehyde
- Ammonia (used in farm-crop preservation)
- Chlorine gas
- Hydrogen fluoride
- Hydrogen sulfide (used in oil refining)
- Nitrogen dioxide (generated by freshly stored hay in silos)
- Nitric acid, nitrous acid, and nitric oxide
- Phosgene (used in chemical manufacturing)

Selected Common Causes of Occupational Airway Disease

COPD and Chronic Airflow Limitation

- Coal dust (causes emphysema with nodular fibrosis)
- Crystalline silica (causes chronic airflow limitation)
- Cotton dust (causes chronic airflow limitation)
- Cadmium (causes emphysema)

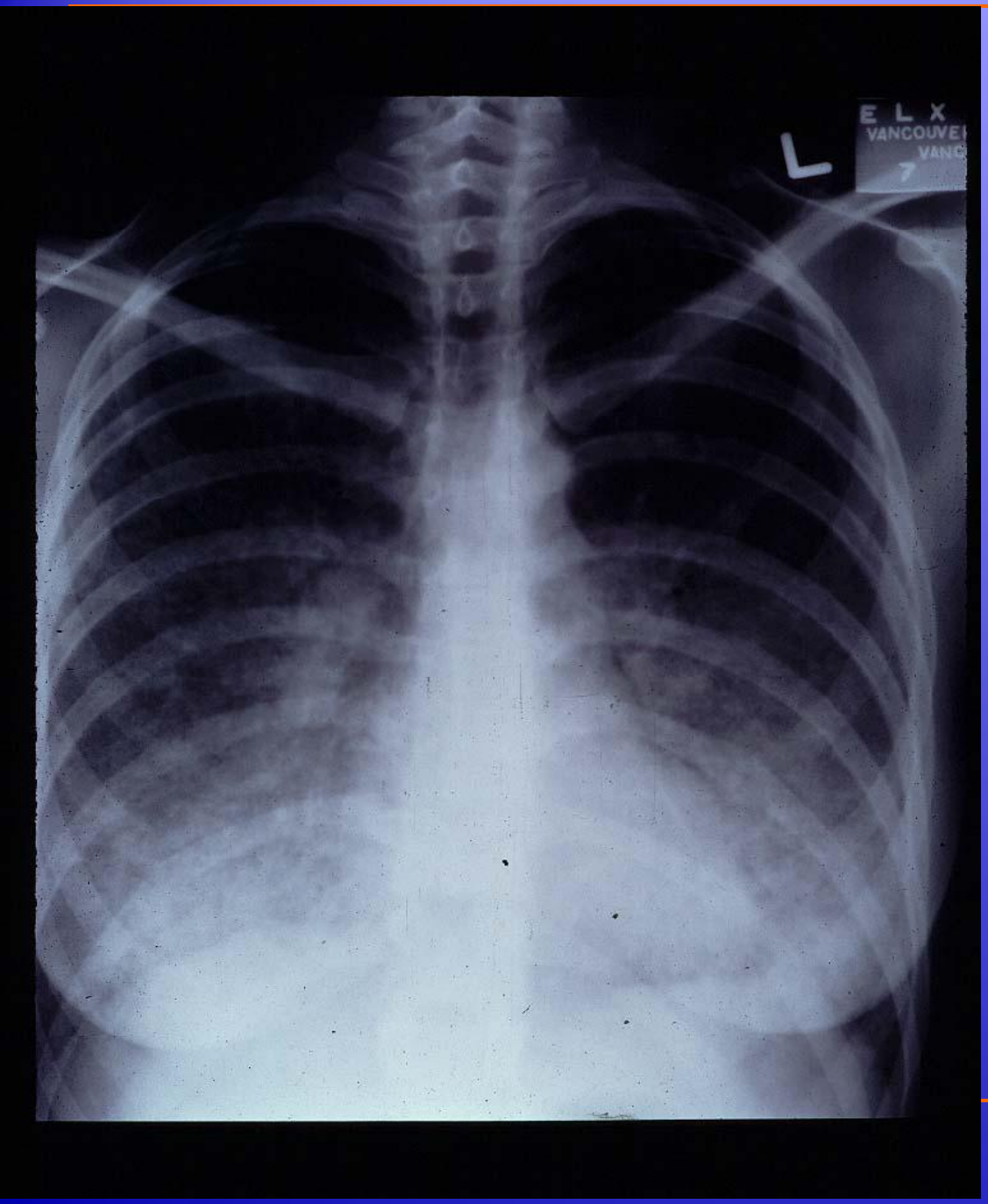
  (used in electronics, metal plating, and batteries)
- Toluene diisocyanate (causes chronic airflow obstruction)

Hypersensitivity pneumonitis-definition

Hypersensitivity pneumonitis is a spectrum of granulomatous, interstitial, and alveolar-filling lung diseases that result from repeated inhalation of and sensitization to a wide variety of organic dusts

Extrinsic allergic alveolitis

- Extrinsic allergic alveolitis can be caused by sensitisation to many organic dusts mainly fungal spores, e.g. farmer's lung and malt worker's lung.
- **Industries:** Agriculture, manufacturers (furniture/ drugs), millers, bakers, chemists
- Normally reversible if treated in time
- It tends to affect the respiratory units of the lung rather than the conducting airways and may have 'flu' like symptoms in addition.



Mushroom Workers' Lung

(Thermoactinomyces vulgaris)

Acute onset of fever, malaise, and shortness of breath after spawning
Chest- diffuse crackles

Hypersensitivity pneumonitis (HP) Diagnosis

Diagnosis of HP:

- Compatible clinical picture (symptoms, chest x-ray or CT, lung function changes) of HP
- Presence of precipitating antibodies
- Bronchoalveolar lavage
- Lung biopsy

Objective testing to establish work-relatedness:

- Returning to work induce similar symptoms and signs
- Specific challenge tests – more difficult to do

- That’s all for this session
  - Questions?