Recognizing and preventing Occupational asthma and lung diseases

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Diseases associated with occupational exposure

Clinical manifestations of lung diseases are the same irrespective of the etiology

Airway diseases
  Asthma (reversible)
  Chronic obstructive lung disease (irreversible)
  Cancer

Parenchymal diseases
  Hypersensitivity pneumonitis (reversible)
  Diffuse fibrosis (irreversible)
  eg. silicosis, asbestosis
Occupational asthma

Disease characterized by variable airflow obstruction and/or airway hyperresponsiveness due to causes and conditions attributable to a particular working environment and not to stimuli encountered outside the workplace.
% occupational asthma in occupational lung diseases

<table>
<thead>
<tr>
<th></th>
<th>UK</th>
<th>BC, Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>26.4</td>
<td>52.0</td>
</tr>
<tr>
<td>Pneumoconiosis</td>
<td>15.4</td>
<td>17.8</td>
</tr>
<tr>
<td>Others</td>
<td>58.2</td>
<td>30.2</td>
</tr>
<tr>
<td>Source of Data</td>
<td>AR</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>Population-based studies</td>
<td>15 (2-20)</td>
<td></td>
</tr>
<tr>
<td>Medical practice data</td>
<td>9 (2-33)</td>
<td></td>
</tr>
<tr>
<td>Surveillance or registry data</td>
<td>4 (2-17)</td>
<td></td>
</tr>
<tr>
<td>Medicolegal data</td>
<td>5 (3-8)</td>
<td></td>
</tr>
<tr>
<td><strong>Overall Median</strong></td>
<td>9 (2-45)</td>
<td></td>
</tr>
</tbody>
</table>

Blanc and Toren 1999
Recognise and establish work-relatedness

- Aware and suspect
- Occupational history
- Medical history suggesting work-relatedness
  - Symptoms started after employment
  - Improvement of symptoms during weekends and holidays
  - Worsening of symptoms on returning to work
- Objective testing
History

• A history suggestive of work-relatedness is very sensitive but…:
  • Predictive value of questionnaire
    • positive = 63% / negative = 83%

• A history of asthma at work, even in the presence of a known sensitizer, does not confirm the diagnosis of occupational asthma

• The diagnosis needs to be confirmed objectively
Objective testing to confirm work-relatedness

- Pre and post-shift measurement of lung function
- Monitoring of PEF at and off work, each for a period of 2 weeks with and without measurement of NSBH
- Specific inhalation challenges or occupational type of exposure tests - "gold standard"
Exposure to nickel dust
Spirometry

- at and away from work
- cross-shift

<table>
<thead>
<tr>
<th></th>
<th>FEV₁ (L)</th>
<th>FVC (L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Away from work 3 months</td>
<td>3.70</td>
<td>4.54</td>
</tr>
<tr>
<td>After one week of work</td>
<td>2.85</td>
<td>3.61</td>
</tr>
<tr>
<td>Pre-shift 6:45 a.m.</td>
<td>3.20</td>
<td>4.20</td>
</tr>
<tr>
<td>Post-shift 3:00 p.m.</td>
<td>2.40</td>
<td>3.60</td>
</tr>
</tbody>
</table>

Exposure challenge testing
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
Serial monitoring of PEF in the diagnosis of OA
PEF monitoring

False positive
- Subject not exposed during monitoring
- Poor compliance

False negative
- Change in medication (inhaled steroids)
- Bronchitis
- Malingering (falsification of results)
Serial monitoring of PEF in the diagnosis of OA
Exposure chamber
Methods - exposure testing

Flour
Typical patterns of response
Skin tests & serology

• Valid for HMW allergens (eg. baker’s asthma) & rarely for LMW agents (eg. diisocyanates)
• Requires good allergen extracts
• Frequently not available commercially
• When positive, means presence of sensitization
Algorithm for investigation of occupational asthma

Compatible clinical history and exposure
  Skin testing and/or specific IgE (if possible)
  Assessment of NSBH

Normal
  Subject still at work
  Laboratory challenge tests
    Positive
      Consider return to work
    Negative
      Workplace challenge tests
        PEF monitoring, or both
          Positive
            
          Negative
            
Increased
  Subject no longer at work
  Laboratory challenge tests
    Positive
      Consider return to work
    Negative
      No asthma

Subject still at work
  Laboratory challenge tests
    Positive
      Consider return to work
    Negative
      Occupational asthma

Non occupational asthma

Use of other means (induced sputum, exhaled NO)

Chan Yeung M, Malo JL. NEJM 1995; 333:107
### Occupational agents known to cause OA


<table>
<thead>
<tr>
<th>Agents</th>
<th>Occupation</th>
<th>Reference</th>
<th>Subjects</th>
<th>Prevalence (%)</th>
<th>Skin (%)</th>
<th>Specific IgE test</th>
<th>Other Immunologic test</th>
<th>Broncho-provocation test</th>
<th>Other evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High molecular weight agents</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Animal-derived antigens</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laboratory animal</td>
<td>Laboratory workers</td>
<td>(1)</td>
<td>296</td>
<td>13</td>
<td>17% +</td>
<td>34% of 255 +</td>
<td>ND</td>
<td>ND</td>
<td></td>
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<tr>
<td>Cow dander</td>
<td>Agricultural workers</td>
<td>(2)</td>
<td>5</td>
<td>NA</td>
<td>100% +</td>
<td>100 % +</td>
<td>neg precipitin</td>
<td>100% +</td>
<td></td>
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<tr>
<td>Monkey dander</td>
<td>Laboratory workers</td>
<td>(3)</td>
<td>49</td>
<td>NA</td>
<td>100%</td>
<td>ND</td>
<td>Immunoblotting</td>
<td>ND</td>
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<tr>
<td>Deer dander</td>
<td>Farmer</td>
<td>(4)</td>
<td>2</td>
<td>NA</td>
<td>2 +</td>
<td>2 +</td>
<td>ND</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>Mink urine</td>
<td>Farmer</td>
<td>(5)</td>
<td>1</td>
<td>NA</td>
<td>+</td>
<td>ND</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Chicken</td>
<td>Poultry workers</td>
<td>(6)</td>
<td>4</td>
<td>NA</td>
<td>+ to feathers</td>
<td>ND</td>
<td>ND</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Pig</td>
<td>Butcher</td>
<td>(7)</td>
<td>1</td>
<td>NA</td>
<td>+</td>
<td>ND</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Frog</td>
<td>Frog catcher</td>
<td>(8)</td>
<td>1</td>
<td>NA</td>
<td>+</td>
<td>neg precipitin</td>
<td>ND</td>
<td>ND</td>
<td></td>
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<tr>
<td>Lactoserum</td>
<td>Dairy industry</td>
<td>(9)</td>
<td>1</td>
<td>NA</td>
<td>+</td>
<td>ND</td>
<td>basophil</td>
<td>+</td>
<td></td>
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<tr>
<td><strong>Bovine serum albumin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laboratory technician</td>
<td></td>
<td>(10)</td>
<td>1</td>
<td>NA</td>
<td>+</td>
<td>ND</td>
<td>+ conjunctival</td>
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<tr>
<td>Lactalbumin</td>
<td>Chocolate candy</td>
<td>(11)</td>
<td>1</td>
<td>NA</td>
<td>+</td>
<td>ND</td>
<td>+</td>
<td></td>
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<tr>
<td>Casein (cow's milk)</td>
<td>Tanner</td>
<td>(12)</td>
<td>1</td>
<td>NA</td>
<td>+</td>
<td>ND</td>
<td>+</td>
<td></td>
<td></td>
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<tr>
<td>Egg protein</td>
<td>Egg producers</td>
<td>(13)</td>
<td>188</td>
<td>7</td>
<td>34% +</td>
<td>29% +</td>
<td>ND</td>
<td>ND</td>
<td>PEF, 7% +</td>
</tr>
<tr>
<td>Endocrine glands</td>
<td>Pharmacist</td>
<td>(14)</td>
<td>1</td>
<td>NA</td>
<td>+</td>
<td>ND</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bat guano</td>
<td></td>
<td>(15)</td>
<td>7</td>
<td>NA</td>
<td>+</td>
<td>RAST inhibition</td>
<td>ND</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ivory dust</td>
<td>Ivory worker</td>
<td>(16)</td>
<td>1</td>
<td>NA</td>
<td>neg</td>
<td>ND</td>
<td>+</td>
<td>FEV1 at work</td>
<td></td>
</tr>
<tr>
<td>Nacre dust</td>
<td>Nacre buttons</td>
<td>(17)</td>
<td>1</td>
<td>NA</td>
<td>+</td>
<td>ND</td>
<td>neg precipitin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sericin</td>
<td>Hairdresser</td>
<td>(18)</td>
<td>2</td>
<td>NA</td>
<td>1/1 +</td>
<td>ND</td>
<td>ND</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Crustaceae, seafoods, fish</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crab</td>
<td>Snow-crab processors</td>
<td>(19)</td>
<td>303</td>
<td>16</td>
<td>22% +</td>
<td>ND</td>
<td>+</td>
<td>72 % of 46 + PEF, PC20</td>
<td></td>
</tr>
<tr>
<td>Prawn</td>
<td>Prawn processors</td>
<td>(20)</td>
<td>50</td>
<td>36</td>
<td>26% +</td>
<td>16% +</td>
<td>ND</td>
<td>2/2 +</td>
<td></td>
</tr>
<tr>
<td>Hoya</td>
<td>Oyster farm</td>
<td>(21)</td>
<td>1413</td>
<td>29</td>
<td>82% of 511</td>
<td>89% of ~ 180</td>
<td>89% of 511 with asthma +</td>
<td>29% of 180 with asthma +</td>
<td></td>
</tr>
<tr>
<td>Clam and shrimp</td>
<td>Food processors</td>
<td>(22)</td>
<td>2</td>
<td>4%</td>
<td>+</td>
<td>RAST inhibition</td>
<td>+</td>
<td>PC20</td>
<td></td>
</tr>
<tr>
<td>Lobster and shrimp</td>
<td>Fishmonger shop</td>
<td>(23)</td>
<td>1</td>
<td>NA</td>
<td>+</td>
<td>ND</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gammarus shrimp</td>
<td>Fishfood factory</td>
<td>(24)</td>
<td>1</td>
<td>NA</td>
<td>+</td>
<td>SDS-Page</td>
<td>+</td>
<td>PC20</td>
<td></td>
</tr>
<tr>
<td>Scallop and shrimp</td>
<td>Restaurant seafood</td>
<td>(25)</td>
<td>1</td>
<td>NA</td>
<td>+</td>
<td>ND</td>
<td>+</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Identifying a novel agent suspected for causing occupational asthma
Thuja plicata
Western red cedar
Inhalation challenge test with dust of Western red cedar induced a late asthmatic reaction.
### COMPONENTS OF EXTRACTIVES OF WESTERN RED CEDAR (after Gardner, 1963)

#### Volatile Components

- Methyl thujate
- Thujic acid
- Tropolones
  - α-thujaplicinol
  - δ-thujaplicin
  - β-thujaplicin
  - γ-thujaplicin

#### Non-volatile components (water soluble)

- Phenolic-fraction - plicatic acid
  - plicatin
  - lignans
- Non-phenolic fraction - pectic acid
  - starch
  - hemicellulose
  - simple sugars
Inhalation challenge with aqueous Western red cedar extract and with plicatic acid induced biphasic asthmatic reaction
PLICATIC ACID
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.
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
# Hypersensitivity pneumonitis - microorganisms (1)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Source</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farmer’s Lung</td>
<td>Hay, straw</td>
<td>Micropolyspora faeni</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thermoactinomycetes spp</td>
</tr>
<tr>
<td>Mushroom worker’s lung</td>
<td>Compost</td>
<td>Thermoactinomycetes spp</td>
</tr>
<tr>
<td>Woodworker’s lung</td>
<td>Wood pulp</td>
<td>Alternaria spp</td>
</tr>
<tr>
<td>Malt worker’s lung</td>
<td>Whiskey maltings</td>
<td>Aspergillus spp</td>
</tr>
<tr>
<td>Sequoiosis</td>
<td>Redwood</td>
<td>Aureobasidium pullulans</td>
</tr>
<tr>
<td>Bagassosis</td>
<td>Bagasse</td>
<td>Thermoactinomycetes spp</td>
</tr>
</tbody>
</table>
Hypersensitivity pneumonitis - microorganisms (2)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Source</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sewage worker’s lung</td>
<td>Sewage</td>
<td>Cephalosporium</td>
</tr>
<tr>
<td>Maple bark stripper’s lung</td>
<td>Maple</td>
<td>Cryptostroma corticale</td>
</tr>
<tr>
<td>Suberosis</td>
<td>Cork</td>
<td>Penicillium frequentens</td>
</tr>
<tr>
<td>Paprika splitter’s lung</td>
<td>Paprika</td>
<td>Mucor stolonifer</td>
</tr>
<tr>
<td>Detergent worker’s lung</td>
<td>Detergents</td>
<td>Bacillus subtilis</td>
</tr>
<tr>
<td>Humidifier lung</td>
<td>Water in humidifier</td>
<td>Thermophilic organisms</td>
</tr>
</tbody>
</table>
### Hypersensitivity pneumonitis – (3)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Source</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Animal source</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wheat weevil lung</td>
<td>Grain dust</td>
<td>Sitophilus granarius</td>
</tr>
<tr>
<td>Pigeon breeder’s lung</td>
<td>Excreta</td>
<td>Pigeons</td>
</tr>
<tr>
<td>Furrier’s lung</td>
<td>Hair</td>
<td>Animal furs</td>
</tr>
<tr>
<td>Fish-meal worker’s lung</td>
<td>Meal</td>
<td>Fish</td>
</tr>
<tr>
<td>Rodent handler’s lung</td>
<td>Urinary protein</td>
<td>Rodents</td>
</tr>
<tr>
<td><strong>Plant source</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coffee worker’s lung</td>
<td>Coffee bean</td>
<td>Coffee</td>
</tr>
<tr>
<td>Woodworker’s lung</td>
<td>Wood dust</td>
<td>Gonystylus bacanus</td>
</tr>
</tbody>
</table>
Bronchiolitis obliterans

• Narrowing of the small airways as a result of inhalation of toxins
• Patients present with progressive shortness of breath on exertion over a period of weeks or months
• Lung function tests show irreversible airflow obstruction
• Chest x-ray normal
Clinical bronchiolitis obliterans in workers in a microwave-popcorn plant - Kreiss et al

- May 2000, eight former employees of a microwave-popcorn plant were reported to have severe bronchiolitis obliterans (between 1993-2000)
- A survey was carried out in the plant
- 117/135 took part
Workers in the popcorn plant had significantly higher prevalence of symptoms than expected irrespective of smoking habit.
**Table 2. Levels of Diacetyl and Respirable Dust According to Work Area in the Microwave-Popcorn Plant in November 2000.***

<table>
<thead>
<tr>
<th>Work Area</th>
<th>No. of Samples</th>
<th>Diacetyl Level (ppm)</th>
<th>Respirable Dust Level (mg/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plain-popcorn packaging line, bag-printing areas, warehouse, offices, or outside</td>
<td>14</td>
<td>0.04 (≤0.25)‡</td>
<td>33</td>
</tr>
<tr>
<td>Quality control or maintenance</td>
<td>5</td>
<td>0.56 (0.33–0.89)</td>
<td>15</td>
</tr>
<tr>
<td>Microwave-popcorn packaging lines</td>
<td>22</td>
<td>1.88 (0.26–6.80)</td>
<td>72</td>
</tr>
<tr>
<td>Mixing room</td>
<td>12</td>
<td>32.27 (1.34–97.94)</td>
<td>18</td>
</tr>
</tbody>
</table>

*Levels of analytes are expressed as means, with ranges given in parentheses.

†Measurements of respirable dust included both 54 area samples and 84 personal samples.

‡At its minimum, the analyte was undetectable (diacetyl, less than approximately 0.01 ppm; respirable dust, less than 0.005 mg per cubic meter).
Strong relation between the quartile of estimated cumulative exposure to diacetyl (butter-flavouring agent) and the frequency and extent of airway obstruction.
Difficulties in recognizing disease related to work exposure

• No distinct episode of over-exposure that preceded the onset of symptoms
• No temporal relationship existed between working at the plant and the severity of symptoms over the course of the workday or workweek
• Association of this disease with exposures in the workplace was largely unsuspected by the workers, their physicians and the plant managers
Clinical bronchiolitis obliterans in workers in a microwave-popcorn plant- Kreiss et al

- Distribution of health-related conditions among workers and over time;
- Excess prevalence of respiratory disease in the current workers
- Estimated cumulative exposure to diacetyl direct inverse correlation with lung function
- Rats exposed to diacetyl levels of 352 ppm had damage to respiratory epithelium, higher level damage the area below the epithelium
Chronic obstructive pulmonary disease (COPD)

COPD is a disease characterized by airflow obstruction that is not reversible. The airflow obstruction is usually progressive and associated with abnormal inflammatory response of the lungs to noxious particles and gases.

COPD should be considered in any patient presenting with cough, sputum production and breathlessness. The diagnosis is confirmed by spirometry. The presence of post bronchodilator FEV1 of < 80% the predicted and FEV/FVC of <70% confirms the presence of airflow limitation that is not reversible.

GOLD 2001
### Occupational contribution to the burden of COPD

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>No of studies</th>
<th>No of subjects</th>
<th>PAR %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic bronchitis</td>
<td>8</td>
<td>&gt; 38,000</td>
<td>15 (4-24)</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>6</td>
<td>&gt; 25,000</td>
<td>13 (6-30)</td>
</tr>
<tr>
<td>Airflow obstruction</td>
<td>6</td>
<td>&gt; 12,000</td>
<td>18 (12-55)</td>
</tr>
</tbody>
</table>

ATS position statement 2003
Occupational exposure and chronic obstructive pulmonary disease (COPD)

Long-term exposure to

• Inorganic dust
• Organic dust
• Chemicals - vapors, irritants, fumes
Area sampling of grain elevators 1974-1989
Respiratory symptoms in grain workers and controls

![Graph showing respiratory symptoms in grain workers and controls.](image)
Cumulative exposure and lung function in grain workers

FEV1, Grain and Civic Workers

- All workers
- Hired since 78 only

(* p<.05, compared to civic and lowest grain dust group)
Lung function of retired grain and civic workers
Establish work-relatedness of COPD

- Mostly based on epidemiological evidence
- In an individual patient, work-relatedness of COPD is difficult to establish
- Diagnosis is by exclusion, easier if patient is a nonsmoker
- In a smoker, it is often not possible to apportion effect of smoking from effect of occupational exposure
Prevention of occupational lung disease
Primary prevention of OA

- Reduce exposure
- Pre-employment screening
  - Atopy
  - Genetic factors
- Education
- Screen for potential respiratory sensitizers
Accepted claims for diisocyanate-induced and other types of OA in Ontario, 1980-93

Annual incidence of incident reports and allergy clinic visits of hospital staff relating to perceived NRL allergy

Tarlo and Liss 2002
% Atopic subjects in occupational asthma

- Animal handiers
- Detergent enzyme
- Bakers
- TDI
- Red cedar
- Colophony

%
# HLA and occupational sensitizers

<table>
<thead>
<tr>
<th>Agent</th>
<th>HLA class</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Western red cedar</td>
<td>DQB1 *0501</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>DQB1 *0302</td>
<td>4.9</td>
</tr>
<tr>
<td>Diisocyanates</td>
<td>DQB1 *0501</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>DQB1 *0503</td>
<td>9.8</td>
</tr>
</tbody>
</table>

*Horne et al ERJ; 2000*

*Bignon et al ARJCCM; 1994*
Structure of the occupational agent

Some agents are potent respiratory sensitizers:

- **HMW** – those with enzymatic activity eg. detergent enzymes
- **LMW compounds** – those with N=C=O eg. isocyanates
Summary

• Awareness of occupational exposure as a cause of disease is important
• Occupational history is mandatory
• To establish a work relationship, objective evidence of exposure and occurrence of symptoms or changes in lung function is necessary
• Reduction of exposure is the key to prevention
Asbestos exposure and recognition of asbestos-related diseases

- Asbestososis
- Lung cancer
- Mesothelioma
- Other cancers

Start of commercial production of:
- Chrysotile
- Crocidolite
- Amosite
- Anthophyllite
Employment based risk factors

- Size of business
- Region
- Age of employees most at risk
- Income
Sensitivity and specificity of various diagnostic methods – specific challenge test as gold standard
Improvement of PEF when away from work and deterioration of PEF on returning to work
Cases of OA in selected countries

![Graph showing the number of cases of OA from 1980 to 1998 in Germany, Finland, and Quebec.](image-url)

- **Germany**: The number of cases has increased significantly from around 400 in 1980 to over 1400 in 1998.
- **Finland**: The number of cases has also increased, starting from around 200 in 1980 and reaching over 600 in 1998.
- **Quebec**: The number of cases has seen a steady increase, starting from around 100 in 1980 and reaching over 200 in 1998.

The chart illustrates the trend in OA cases over the years for these three countries.
Atypical patterns of response

- Progressive
  - % change in FEV1
  - $n = 9$

- Square-waved
  - % change in FEV1
  - $n = 4$

- Prolonged immediate
  - % change in FEV1
  - $n = 2$
Improvement of PEF when away from work and deterioration of PEF on returning to work.
# Exposure-response relationships

<table>
<thead>
<tr>
<th>Substance</th>
<th>Lowest effective dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flour</td>
<td>1-2.4 mg/m³</td>
</tr>
<tr>
<td>Fungal amylase</td>
<td>0.25 ng/m³</td>
</tr>
<tr>
<td>Red cedar dust</td>
<td>1 mg/m³</td>
</tr>
<tr>
<td>Natural rubber latex</td>
<td>0.6 ng/m³</td>
</tr>
<tr>
<td>Cow dander</td>
<td>1-29 ug/g dust</td>
</tr>
<tr>
<td>Rat urine</td>
<td>0.1 – 68 u/m³</td>
</tr>
<tr>
<td>Acid anhydride - TMA</td>
<td>0.82 mg/m³</td>
</tr>
<tr>
<td>Isocyanates</td>
<td>5-10 ppb</td>
</tr>
</tbody>
</table>

Prevention of CAO

- Prohibition of smoking in the workplace
- Reduction of exposure
- Education
Grain elevator workers
5 cross-sectional study
1974-1989

.... Cross-sectional study
___ Longitudinal study
Changing trend in OA

Year


% Isocyanates

Latex

20 25 30 35 40 45

0 5 10 15 20
Probability of refinery workers remaining skin prick negative, by smoking and exposure categories.
FEV$_1$ slope according to smoking habits and occupational exposure

FEV$_1$ slope (ml/a)

- Non Smokers
- Ex-Smokers
- Moderate Smokers
- Heavy Smokers

Occupational exposure

No
Yes

No of men

() No of men

(31) (51) (20) (48) (88) (156) (48) (132)
Prevalence of respiratory symptoms in nonsmoking grain and civic workers 1974-1989
Dose-response relationship for sensitization to occupational allergens

![Graph showing the dose-response relationship for sensitization to occupational allergens. The graph plots log (allergen concentration) (ng/m³) on the x-axis and prevalence ratio on the y-axis. Data points are shown for wheat (Houba et al. 1998), fungal alpha-amylase (Houba et al. 1996), and fungal alpha-amylase (Nieuwenhuijsen et al. 1999).]
Prevalence of symptoms by dust concentration in cedar workers

Dust concentration mg/M^3

- Work-related asthma
- Persistent wheeze