Workplace indoor air quality and allergic disease

Monika Raulf

Disclosure

• In relation to this presentation, I declare no conflicts of interest.
Background

- Work processes and tasks that generate excessive dust and bio-aerosols contribute to the excessive exposure in several occupational settings.
- Occupational exposure to airborne allergens occurs through inhalation of dust, vapours and aerosolized proteins generated during working tasks.

The contact between the respiratory organ and the air containing the allergens is the key factor for the development of respiratory allergy.
Work-related asthma (WRA) phenotypes

Asthma caused by work = Occupational asthma (OA)
Asthma exacerbated by work = work-exacerbated asthma (WEA)

Irritant-induced asthma (IIA)
- Acute-single exposure RADS
- Non-acute multiple exposures

Allergic
- Non-IgE-dependent
- IgE-dependent

According to Moscato et al. 2011, Allergy
Workplaces with allergen exposure

<table>
<thead>
<tr>
<th>Industry</th>
<th>Allergen source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agriculture</td>
<td>Cattle hair, pollen, storage mites</td>
</tr>
<tr>
<td>Bakeries, mills</td>
<td>Wheat flour, rye flour, soy flour, α-amylase, xylanase, storage mites, insects</td>
</tr>
<tr>
<td>Fish processing</td>
<td>Fish allergens</td>
</tr>
<tr>
<td>Animal feed</td>
<td>Soy, phytase</td>
</tr>
<tr>
<td>Pharmaceutical industry</td>
<td>Gummi arabicum, enzymes</td>
</tr>
<tr>
<td>Laboratory animal care</td>
<td>Mouse allergens, rat allergens</td>
</tr>
<tr>
<td>Healthcare</td>
<td>Natural rubber latex</td>
</tr>
<tr>
<td>Detergent production</td>
<td>Enzymes: protease, cellulase, lipase, amylase</td>
</tr>
<tr>
<td>Woodworking</td>
<td>Wood dust</td>
</tr>
<tr>
<td>Composting plants</td>
<td>Moulds, bacteria</td>
</tr>
<tr>
<td>Many others</td>
<td>House dust mites, Moulds, ubiquities indoor allergens</td>
</tr>
</tbody>
</table>

Problem: How high is the allergen exposure at the workplaces??

- Assessment of the relationship between exposure and the work-related allergic diseases.
- Implementation of appropriate measures to reduce or avoid allergen exposure and monitoring of the outcome of the intervention.
Why is allergen exposure necessary?

Dust exposure ⟷ allergen exposure

It is necessary to quantify the allergens.
Aeroallergen monitoring is a stepwise process

Definition of objectives and setting

- Procedure
- Sampling methods
- Allergen quantification
- Conclusion

Sampling strategies

Main questions:

a) Which allergen exposure do you want to know: What is the specific objective of the requested and planned allergen monitoring?

b) Which procedures – choice of equipment, sampling and analytical methods give the best proxy of exposure?

Measured concentrations = Allergen exposure?

According to G. Doekes IRAS
Allergen monitoring in various, quite different settings

- clinical (individual patients, clusters)
- experimental (allergen challenge test)
- population dose – response studies (allergo-epidemiology)
- intervention (pre and post) studies/allergen avoidance
- routine monitoring: compliance with recommended TLVs?

home (indoor) – work – outdoor environment

---

Diagnosis and management of individual/cluster patients

1. development of tailored IgE test
2. IgE inhibition tests
3. if necessary development of more sensitive tests

**most likely and relevant exposure route and the type of exposure (single peak, permanent or frequently) should be taken into account in relation to the symptoms (acute, sub-acute or chronic)**

Raulf et al Allergy 2014
Population studies on exposure – response relationship

Epidemiology
Aim: exposure-response-relation
Study design depends on the health outcome
Outcome: IgE-sensitization (as a result from chronic exposure)

Routine Monitoring/Health surveillance programs
Aim: safe and healthy workplace

Domestic environment
proxy: allergen levels in dust reservoirs
single personal measurement

Workplaces
screening of intervention
airborne personal measurement (repetition)

Options for allergen monitoring in occupational and environmental settings

Allergen-Monitoring

Occupational
Indoor
Outdoor

Environmental
Outdoor
Indoor

Stationary aerosol sampling with flow-regulated pumps

Short term exposure
• Personal sampling with pumps on filters (e.g. during job task/cross shift)

Long term exposure
• Settled airborne dust
• Reservoir dust (rarely used)

Short term exposure
• Personal sampling with pumps on filters (rarely used)

Long term exposure
• Settled airborne dust
• Reservoir dust

Rauf et al Allergy 2014
Air sampling
GSP/filter sampling
Gravikon VC 25

Reservoir dust sampling
Vacuum cleaning of a surface;
sampling on cellulose or glass
fiber filters or in nylon bags

Settled dust sampling
Electrostatic dust collector (EDC)
Aluminum foil-covered pizza boxes

Allergen analysis: Sandwich enzyme immunoassay (EIA)
### Measurement of allergens

A range of assays have been described, but only few of them are commercially available (selection)

<table>
<thead>
<tr>
<th>Detected Allergens</th>
<th>Standard Test Antigen</th>
<th>Type of assay</th>
<th>Antibodies</th>
<th>Detection limit</th>
<th>Company/Institute</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheat flour</td>
<td>Wheat flour protein mix</td>
<td>Inhibition-ELISA</td>
<td>Human IgG4 or rabbit IgG</td>
<td>20 ng/ml</td>
<td>IRAS</td>
</tr>
<tr>
<td>Wheat flour</td>
<td>Wheat flour protein mix</td>
<td>Sandwich-ELISA</td>
<td>pAb</td>
<td>0.2 ng/ml</td>
<td>IRAS</td>
</tr>
<tr>
<td>Rye flour</td>
<td>Rye flour protein mix</td>
<td>Sandwich-ELISA</td>
<td>pAb</td>
<td>0.2 ng/ml</td>
<td>IPA</td>
</tr>
<tr>
<td>Soy hull</td>
<td>Soy hull protein mix</td>
<td>Sandwich-ELISA</td>
<td>pAb</td>
<td>0.04 ng/ml</td>
<td>Laboratorios Clinicos Barcelona (IRAS)</td>
</tr>
<tr>
<td>Pollen - <em>Olea eurpaea</em> Ole e 1</td>
<td>Ole e 1</td>
<td>Sandwich-ELISA</td>
<td>mAb</td>
<td>0.1 ng/ml</td>
<td>Bial-Aristegui</td>
</tr>
<tr>
<td>Pollen - <em>Ambrosia artemisiifolia</em> Amb a 1</td>
<td>Amb a 1 (short ragweed extract)</td>
<td>Sandwich-ELISA</td>
<td>pAb</td>
<td>0.002 U/ml</td>
<td>Indoor Biotechnologies</td>
</tr>
<tr>
<td>Latex - Hev b 1</td>
<td>Hev b 1 (puriﬁed)</td>
<td>Sandwich-ELISA</td>
<td>mAb</td>
<td>2 ng/ml</td>
<td>IPA</td>
</tr>
<tr>
<td>Latex - Hev b 1</td>
<td>Hev b 1 (puriﬁed)</td>
<td>Sandwich-ELISA</td>
<td>mAb</td>
<td>1.2 ng/ml</td>
<td>Indoor/Quattromed</td>
</tr>
<tr>
<td>Fish (whiff and hake)</td>
<td>Fish protein mix</td>
<td>Inhibition-ELISA</td>
<td>human IgE pool</td>
<td>200 µg/ml</td>
<td>Indoor Biotechnologies</td>
</tr>
<tr>
<td>Allergen mixture</td>
<td>mites, cat, dog</td>
<td>Multiplex assay</td>
<td>MARIATM-P5</td>
<td>mAb</td>
<td>0.02 ng/ml</td>
</tr>
</tbody>
</table>

### Outcome: Allergen concentration

- **Airborne concentration via (active) measurement**
  - pg or ng/m³

- **Reservoir dust sampling**
  - ng/m²
  - ng/g dust

- **Settled dust (e.g. via EDC)**
  - pg/ml or ng/tissue or ng/m²
Cow dander allergen exposure

![Box plot showing allergen concentration (µg/m²) for different settings and samples.](image1)

- **Cow stable:** n = 32, 100% positive, median 46683 µg/m²
- **Changing room:** n = 29, 100% positive, median 109.7 µg/m²
- **Living rooms rural:** n = 101, 100% positive, median 15.9 µg/m²
- **Living rooms urban:** n = 35, 63% positive, median 0.2 µg/m²

Houba et al. 1996, Am J Respir Crit Care Med. 154:130

Dose-response relation for α-amylase in bakeries

![Bar chart showing percentage of bakers with positive skin prick test for different exposure levels.](image2)

- **All:** 0%
- **Atopic:** 20%
- **Non-Atopic:** 20%

Houba et al. 1996, Am J Respir Crit Care Med. 154:130
Exposure Prevention: Granulation of enzymes
(α-amylase since 90ies, Baking granulate Novo)

⇒ Reduces exposure by inhalation of enzyme dust
⇒ Aim: no sensitization to enzymes
⇒ Aim: no allergies to enzymes

Particles instead of
200 - 400 μm
5 - 50 μm

Résumé

➢ There are a few internationally recognized occupational exposure limits for allergens in the workplace, that have been recommended (e.g. ACGIH, TLVs) to protect against the development of sensitization or allergic reactions.
➢ Environmental control/exposure assessment is the cornerstone of prevention strategy.
➢ However, due to the lack of standards, reduction of allergen exposure using appropriate risk management and exposure control strategies is advocated to be best practice.
➢ In some occupational settings exposure could be reduced by changing the formulation of products (e.g. encapsulation or dissolved enzyme formulation) and/or optimizing work practices thereby decreasing the associated risks.
References: