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# Workplace indoor air quality and allergic disease

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

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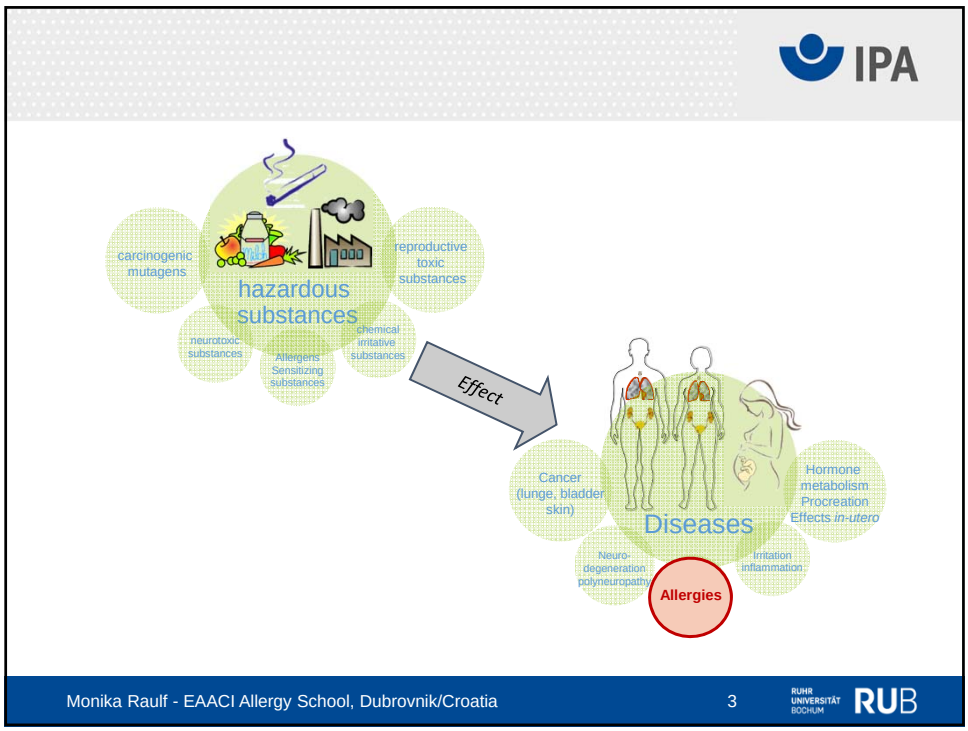
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carcinogenic mutagens
reproductive toxic substances
hazardous substances
neurotoxic substances
chemical irritative substances
Allergens Sensitizing substances
Effect
Cancer (lunge, bladder skin)
Hormone metabolism Procreation Effects in-utero
Diseases
Neuro-degeneration polyneuropathy
Irritation inflammation
Allergies
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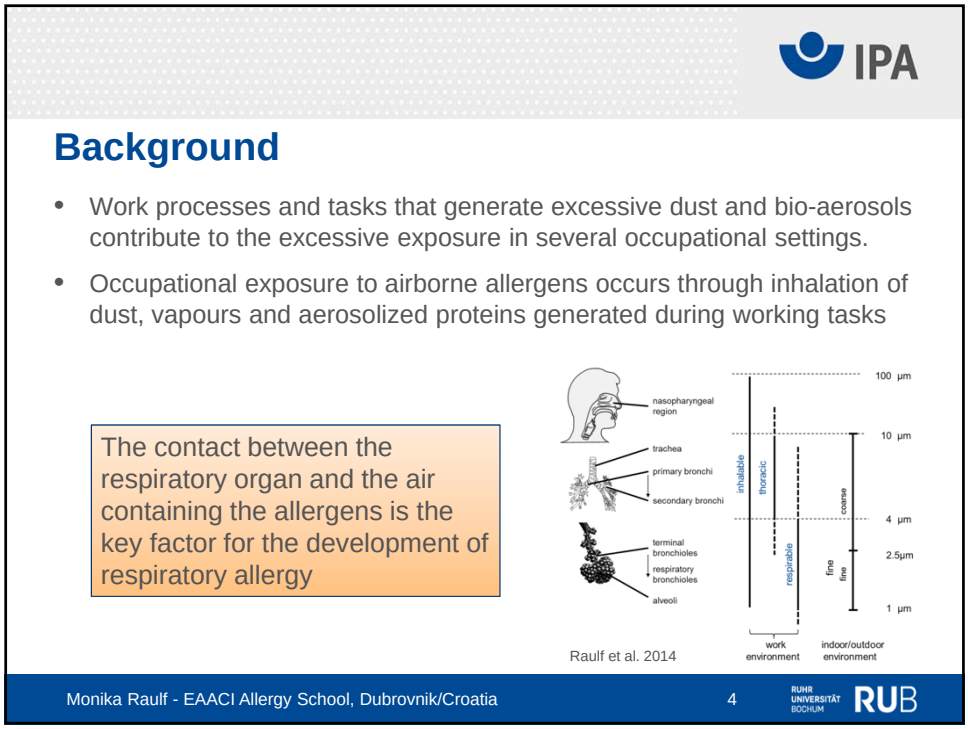
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Background
• Work processes and tasks that generate excessive dust and bio-aerosols contribute to the excessive exposure in several occupational settings.
• Occupational exposure to airborne allergens occurs through inhalation of dust, vapours and 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
nasopharyngeal region
trachea
primary bronchi
secondary bronchi
terminal bronchioles
respiratory bronchioles
alveoli
inhalable
thoracic
respirable
coarse
fine
fine
100 µm
10 µm
4 µm
2.5µm
1 µm
work environment
indoor/outdoor environment
Raulf et al. 2014
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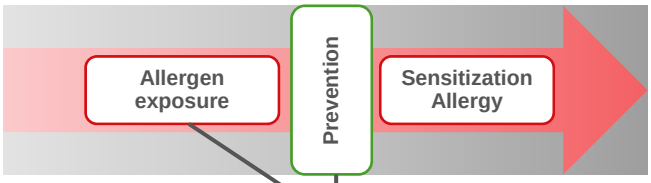
**Postulation: Keep the workplaces as healthy places**

predisposition

case history, background




Allergen exposure assessment



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## 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

high-molecular weight inducers

low-molecular weight inducers

According to Moscato et al. 2011, Allergy

## Workplaces with allergen exposure

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



## 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**

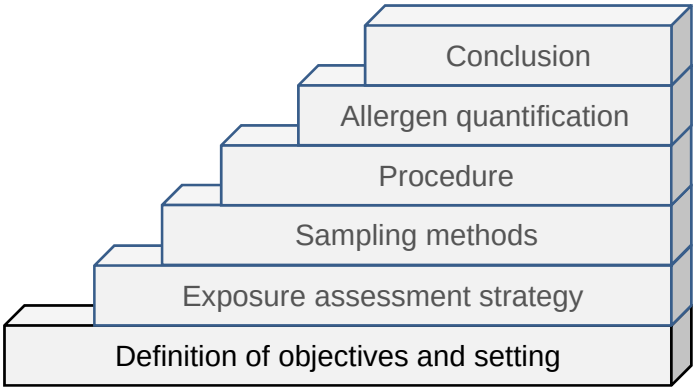


## Dust exposure ≠ allergen exposure

| Empty urine contaminated cages | Fill of clean cages with bedding |
|---|---|
| High dust exposure | High dust exposure |
| High allergen exposure ☹ | No allergen exposure ☺ |

It is necessary to quantify the allergens

## Aeroallergen monitoring is a stepwise process




Raulf et al.: Monitoring of occupational and environmental aeroallergens-EAACI Position Paper. Allergy 2014; 69: 1280-1299



## 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

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## 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



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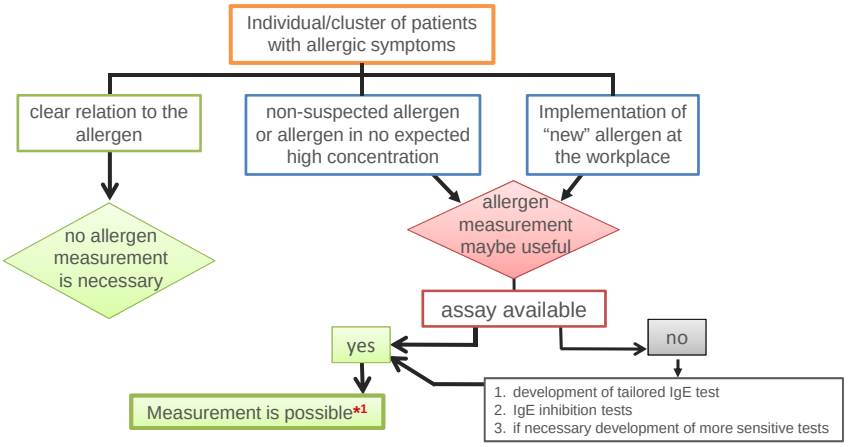
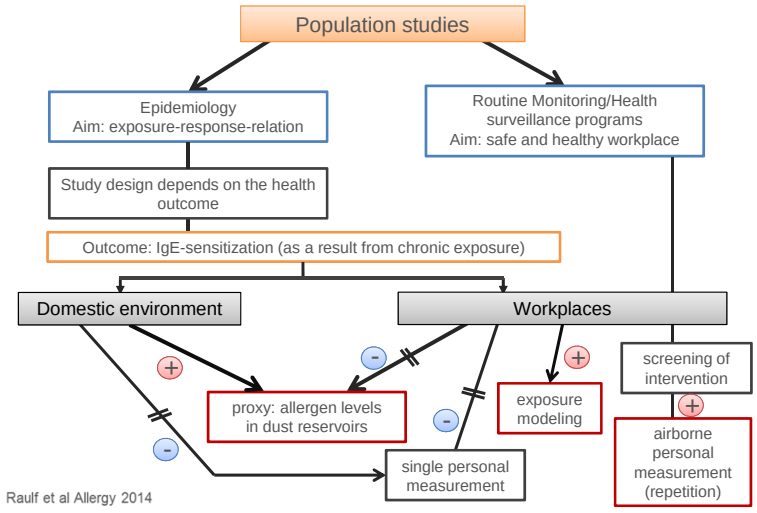
## Diagnosis and management of individual/cluster patients




*1most 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)

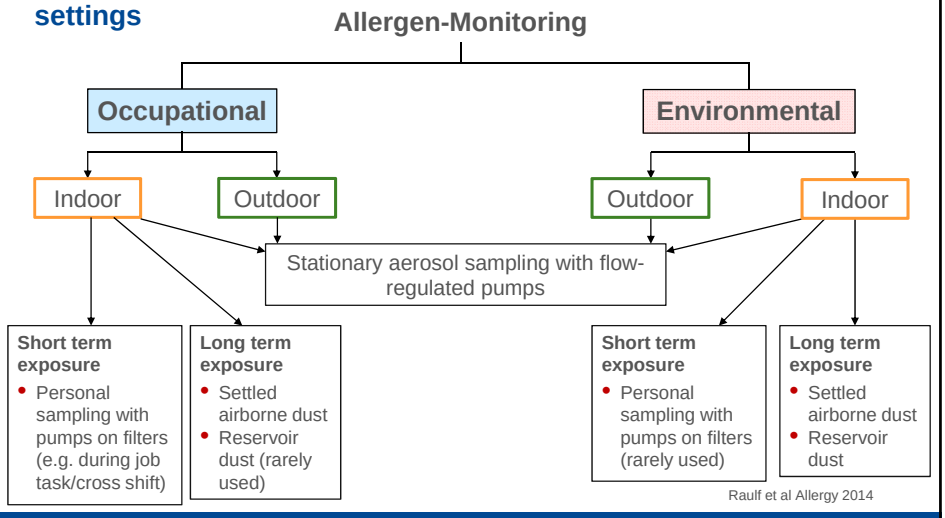
Raulf et al Allergy 2014

## Population studies on exposure – response relationship






## Options for allergen monitoring in occupational and environmental settings




Raulf et al Allergy 2014

## Air sampling

GSP/filter sampling
Gravikon VC 25

## Reservoir dust sampling

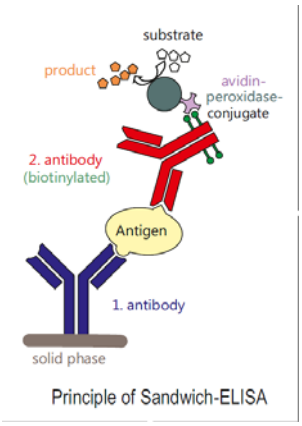
Vacuum cleaning of a surface;
sampling on cellulose or glass
fiber filters or in nylon bags

## Settled dust sampling

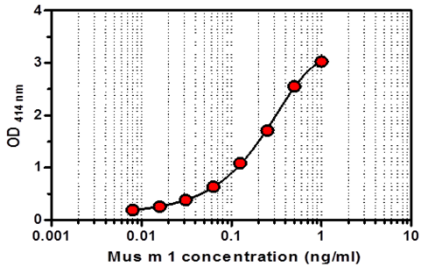
Electrostatic dust collector (EDC)
Aluminum foil-covered pizza boxes



## Allergen analysis: Sandwich enzyme immunoassay (EIA)



Principle of Sandwich-ELISA



## Measurement of allergens

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

| Detected Allergens | Standard Test Antigen | Type of assay | Antibodies | Detection limit | Company/ Institute |
|---|---|---|---|---|---|
| Wheat flour | Wheat flour protein mix | Inhibition-ELISA | "human IgG4 or rabbit IgG" | 20 ng/ml | IRAS |
| Wheat flour | Wheat flour protein mix | Sandwich-ELISA | pAb | 0.2 ng/ml | IRAS |
| Rye flour | Rye flour protein mix | Sandwich-ELISA | pAb | 0.2 ng/ml | IPA |
| Soy hull | Soy hull protein mix | Sandwich-ELISA | pAb | 0.04 ng/ml | Laboratorios Clinicos-Barcelona (IRAS) |
| Pollen - *Olea europea* Ole e 1 | Ole e 1 | Sandwich-ELISA | mAb | 0.1 ng/ml | Bial-Aristegui |
| Pollen - *Ambrosia artemisiifolia* Amb a 1 | Amb a 1 (short ragweed extract) | Sandwich-ELISA | pAb | 0.002 U/ml | Indoor Biotechnologies |
| Latex Hev b 1 | Hev b 1 (purified) | Sandwich-ELISA | mAb | 2ng/ml | IPA |
| Latex Hev b 1 | Hev b 1 (purified) | Sandwich-ELISA | mAb | 1.2 ng/ml | Indoor/Quattromed |
| Fish (whiff and hake) | Fish protein mix | Inhibition-ELISA | human IgE pool | 200 µg/ml | |
| Allergen mixture mites, cat, dog | Der p 1, Der f 1, Der p 2, Fel d 1, Can f 1 | Multiplex assay MARIA™-P5 | mAb | 0.02 ng/ml | Indoor Biotechnologies |



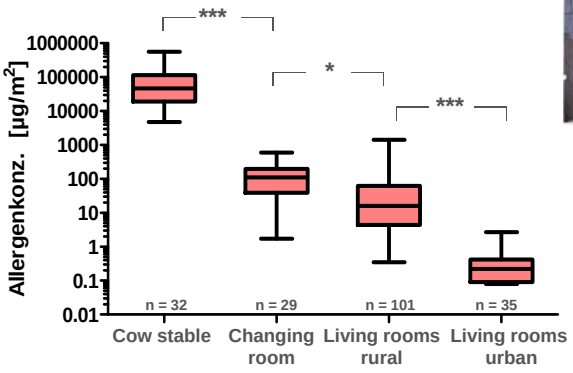
## Outcome: Allergen concentration

Airborne concentration via (active) measurement
→ pg or ng/m$^3$

Reservoir dust sampling
→ ng/m$^2$
→ ng/g dust

Settled dust (e.g. via EDC)
→ pg/ml or ng/tissue or ng/m$^2$

## Cow dander allergen exposure

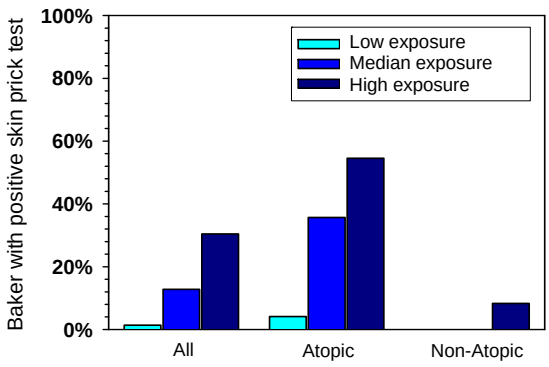



| | | | | |
|---|---|---|---|---|
| **Positive Samples:** | 100% | 100% | 100% | 63% |
| **Median in µg/m²:** | 46683 | 109.7 | 15.9 | 0.2 |

Zahradnik..Raulf-Heimsoth, 2011



## Dose-response relation for α-amylase in bakeries




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 | 200 - 400 µm |
| instead of | 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.

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