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69. Asthma and COPD at work: what are the effects of exposure and risk factors?

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Evolution of immunological occupational asthma depending on the continuation or end of exposure

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Introduction: It is generally agreed that the best treatment after diagnosis of occupational asthma (OA) is avoidance of exposure to the causal agent. However, recent meta-analyses have raised doubts about this conclusion. The aim of the present study is to assess the evolution of OA depending on whether or not the patient avoids exposure.

Methods: Multicentre, cross-sectional clinical follow-up study in patients diagnosed with OA using a specific inhalation challenge (SIC) between January 2000 and December 2009. Patients with this diagnosis received the following examinations on the same day: clinical interview, physical examination, forced spirometry, methacholine test and determination of total IgE and IgE specific to the causal agent. Clinical improvement, deterioration or no change were defined according to the changes seen in the GINA severity scale at the time of diagnosis.

Results: Of the 73 patients finally included, 55 had totally ended exposure and 18 continued. The mean time elapsed since diagnosis was 48 months (range: 12 – 123). Forty-two per cent of patients who avoided exposure improved clinically, 38% presented no change, and 14% deteriorated. In the patients who did not avoid exposure improvement was recorded in 22%, deterioration in 17% and no change in 61%. No significant differences in methacholine PC20 or FEV1 were detected between both groups.

Conclusions: Avoiding exposure to the causal agent in patients with OA does not seem to improve prognosis in this disease.

Project partially funded by Ciber de Enfermedades Respiratorias (CibeRes).

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Transfer of wheat allergen and fungal α -amylase from workplace to home by bakersNara Tagiveva, Siti Anua, Sean Semple, Dick Finlay, Graham Devereux. *Applied Health Sciences, University of Aberdeen, United Kingdom*

Background: Exposure to flour dust is a leading cause of occupational asthma. Paternal occupational exposure to flour has been associated with childhood asthma, raising the possibility of 'take-home' exposure.

Aim: To establish whether workplace contamination of skin/clothing with wheat flour allergen (WFA) and fungal α -amylase (FAA) is associated with increased levels of these allergens in bakers' homes.

Methods: Bakeries in north-east Scotland were invited to participate. Controls were recruited from staff/students at the University of Aberdeen. Exposure assessment was carried out in bakeries, bakers' cars and bakers'/controls' homes using surface wipe and vacuum sampling; samples were analysed for total protein, FAA and WFA.

Results: 164 wipe and 49 vacuum samples were collected from 38 bakers (5 bakeries) and 10 controls. Compared to non-bakers, bakers had higher median levels of WFA and FAA in house vacuum samples; the difference was statistically significant for WFA/total protein (516×10^{-6} vs 164×10^{-6} , $p=0.031$), FAA/total protein (1.5×10^{-6} vs 0.04×10^{-6} , $p<0.001$) ratios and FAA loading (median 1.2 pg/cm^2 vs 0.1 pg/cm^2 , $p<0.001$). We found positive correlations between WFA contamination of the bakers' foreheads and cars ($r_s 0.57$, $p=0.028$), foreheads and houses ($r_s 0.46$, $p=0.025$), shoes and houses ($r_s 0.45$, $p=0.029$); and between FAA contamination of shoes and houses ($r_s 0.46$, $p=0.023$), and cars and houses ($r_s 0.70$, $p=0.008$).

Conclusions: This work demonstrates pathways for 'take home' exposure of occupationally sourced flour. Taken with our previous work, showing that bakers' children are more likely to have asthma, this supports the need for workplace intervention trials to prevent asthma in bakers' children.

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Incident rhinitis is related to dust and rye exposure among baker's apprenticesTorben Sigsgaard¹. ¹Section of Occupational and Environmental Medicine, Institute of Public Health, Aarhus University, Aarhus, Denmark; ²Dept of Pulmonary Med, Aarhus University Hospital, Aarhus, Denmark

Background: Baker's asthma and rhinitis are related to occupational exposure with an exposure-response relationship for prevalence and incidence. This study was a prospective study to estimate: The dose response relation between new onset asthma and rhinitis and the exposure to personal dust and allergens in baker apprentices during their apprenticeship.

Methods: Participants were recruited from baker schools. Baker apprentices without previous occupational exposure to flour, was followed for 1 (n=187) to 36 month (n=86).

They were examined every 4th month. Personal (n = 79) exposure to dust, rye- and wheat antigen were performed 1 or 2 times in each bakery. Cox proportional methods were used to estimate the hazard ratio (HR).

Results: We found 42 new cases of rhinitis and 27 of asthma like symptoms. The dust and allergen levels were: dust Mean (SD) 1.9 (1.6), rye 0.8 (0.7) and wheat 0.8 (0.5) mg/m^3 .

The HR for high exposure to personal dust controlling for atopy was increased for rhinitis, table 1.

Table 1. Cox proportional hazard modelling of Rhinitis with exposure

Rhinitis during apprenticeship	Hazard ratio	95.0% CI
Personal dust Lowest half		1
Personal dust 3rd quartile	1.27	0.431, 3.722
Personal dust 4th quartile	3.07	1.20, 7.87
Sex (Male = 0)	2.57	1.11, 5.96

We found no association to wheat exposure, but for rye exposure an increased HR for rhinitis symptoms with exposure highest for the 3rd quartile, 2.9 (1.2-7.5) vs 1.6 (0.5-4.8) in the 4th quartile. Only 4 persons developed positive SPT to flour and two to α -amylase during the study.

Conclusions: In baker apprentices followed for 36 months, a dose dependent HR for rhinitis symptoms with exposure to dust and rye antigen was seen.

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Lung function among workers exposed to endotoxins in coffee processing factoriesGloria Sakwari^{1,2,3}, Simon H.D. Mamuya², Magne Bråtevit¹, Bente E. Moen¹. ¹Department of Public Health and Primary Health Care- Section for Occupational and Environmental Medicine, University of Bergen, Hordaland, Norway; ²Department of Occupational and Environmental Health, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania, United Republic of; ³Centre for International Health, University of Bergen, Hordaland, Norway

Background: Occupational exposure to endotoxins causes airway diseases and impairs lung function.

Objectives: To measure personal total dust and endotoxins levels and to examine lung function among coffee workers in relation to exposure.

Methods: All 159 production workers from four Tanzanian factories processing Arabica and Robusta coffee were invited to participate. Personal total dust was sampled throughout the shift using Sidekick Casella pumps (n=193). Cumulative dust was calculated as mean dust exposure multiplied with the number of years of work in the respective coffee factories. Lung function test were carried out using a portable spirometer (SPIRARE3). Differences in groups were tested by independent t-tests. Linear regression was done to adjust for confounders; age, height and smoking.

Results: Robusta (n= 74) and Arabica (n=66) coffee workers had a mean age of 33 years and 38% were current smokers. Total dust levels and endotoxins were significantly higher in the Robusta factories (geometric mean 3.42 mg/m^3 and 10800 EU/m^3 , respectively) than in the Arabica coffee factories (2.10 mg/m^3 and 1400 EU/m^3). Mean cumulative dust in both groups was 17 mg/m^3 . Arabica coffee workers had worked longer in the coffee factories (AM 7years vs. 3.5 years) and had lower forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC) and FEV_1/FVC ratio than Robusta coffee workers, though not significantly different. When the groups were merged, FEV_1 correlated negatively with cumulative dust. After adjusting for confounders there was a decrease in FEV_1 of 3 ml per mg/m^3 per year ($p=0.053$).

Conclusion: Exposures to dust and endotoxins in coffee processing factories are high and might cause decreased lung function.

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Occupational exposure and lung function in a Dutch general population cohortKim de Jong^{1,2}, H. Marika Boezen^{1,2}, Hans Kromhout³, Roel Vermeulen³, Dirkje S. Postma^{4,2}, Judith M. Vonk^{1,2}. ¹Department of Epidemiology, University of Groningen, University Medical Center Groningen, Netherlands; ²GRIAC Research institute, University of Groningen, University Medical Center Groningen, Netherlands; ³Division of Environmental Epidemiology, Institute for Risk Assessment Sciences (IRAS), University of Utrecht, Netherlands; ⁴Department of Pulmonary Diseases, University of Groningen, University Medical Center Groningen, Netherlands

Background: Occupational exposure to vapors, gases, dusts, fumes (VGDF) has been associated with lower lung function, with more pronounced effects in smokers. Less is known about occupational exposure to pesticides, solvents and heavy metals in relation to lung function. We assessed whether these agents negatively affect lung function in a general population cohort.

Methods: We included 8,128 subjects aged 18-89 from the LifeLines cohort study (43% males). Occupational exposures (no/low/high) for current or last held job were estimated with the ALOHA+ Job Exposure Matrix. Associations between exposure and FEV_1 were assessed using linear regression, adjusted for sex, age, height, weight, and smoking. Additionally we stratified for gender and smoking status.

Results: Males were more often exposed than females. VGDF and pesticides had a negative dose-response effect on FEV_1 (table 1). Effects were more pronounced in males and ever smokers.

Table 1. Associations between exposures and FEV_1 (ml) (reference = no exposure)

Exposure	b (95% CI)	
	Low	High
Biological dust	-15 (-40; 10)	-85 (-141; -29)
Mineral dust	-40 (-70; -9)	-102 (-155; -49)
Gases/Fumes	-21 (-44; 2)	-65 (-122; -17)
VGDF	-8 (-32; 15)	-94 (-131; -58)
Pesticides	-90 (-154; -25)	-227 (-346; -108)
Herbicides	-128 (-235; -22)	-413 (-640; -185)
Insecticides	-93 (-164; -22)	-227 (-345; -108)
Aromatic solvents	6 (-34; 46)	-55 (-172; 61)
Chlorinated solvents	15 (-31; 62)	-26 (-110; 58)
Other solvents	18 (-9; 44)	-40 (-121; 41)
Metals	13 (-39; 65)	-73 (-146; 0)

Conclusion: This study confirmed current knowledge on the detrimental effects of occupational VGDF exposure on lung function, especially in males and ever smokers. Additionally we show negative effects of pesticide exposure on lung function.

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Cross-shift change and subsequent longitudinal changes in FEV_1 in a 6 year follow-up study of wood dust exposed workersGitte Jacobsen^{1,2}, Vivi Schlünssen¹, Inger Schaumburg³, Torben Sigsgaard¹. ¹Department of Public Health, Section of Environmental and Occupational Medicine, Aarhus University, Aarhus, Denmark; ²Department of Occupational Medicine, Herning Hospital, Herning, Denmark; ³Neuro Centre, Aarhus Sygehus, Aarhus University Hospital, Aarhus, Denmark

Objective: Cross-shift lung function (LF) changes might predict an accelerated decline in LF. This study investigates the association between cross-shift and annual changes in FEV_1 among woodworkers in a 6-yr follow-up study.

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Methods: 817 woodworkers and 136 controls participated with cross-shift changes of FEV₁ at baseline and FEV₁ and FVC at follow-up. Height and weight were measured and questionnaire information on respiratory symptoms, employment and smoking habits were collected. Wood dust exposure was assessed from 3,572 personal dust measurements at baseline and follow-up. Cumulative wood dust exposure was assessed by a study-specific job exposure matrix and exposure time. **Results:** The median (range) of inhalable dust at baseline and cumulative wood dust exposure was 1.0 (0.2-9.8) mg/m³ and 3.8 (0-7.1) mg*year/m³ respectively. Mean (SD) for %ΔFEV₁/workday and ΔFEV₁/year was 0.2 (6.0)%, and -29.1 (41.8)ml. Linear regression models adjusting for smoking, sex, age, height and weight change revealed no association between cross-shift and annual change in FEV₁ (table 1). Including different exposure estimates, atopy or cross-shift change dichotomized or as quartiles did not change the results.

Table 1. Linear regression on the association between longitudinal and cross-shift change in FEV₁

	Longitudinal ΔFEV ₁ (ml yr ⁻¹)	
	β ± SE	p
Cross-shift ΔFEV ₁ , %	-0.38 (0.22)	0.08
Wood dust exposure mg·yr·m ⁻³ †	-1.54 (0.72)	0.03
Smokers	-10.48 (2.67)	0.00

N=881, Model is adjusted for sex, age, height and weight-gain. †Cumulative wood dust exposure.

Conclusion: This study among low exposed woodworkers does not support an association between cross-shift changes and accelerated LF decline.

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Associations between occupational exposure and quantitative computed tomography (qCT) measures of emphysema

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Rationale: There is limited knowledge of the effect of occupational exposure on quantitative CT measures of emphysema.

Objectives: To examine the effect of occupational exposure assessed by a job exposure matrix (JEM) on qCT measures of emphysema.

Methods: In the Norwegian GenKOLS study 2003-05, 951 ever-smokers (49% with COPD) aged 40-85 years performed spirometry and CT examination. 941 of them completed a full occupational history. In the current study a JEM was used to assess occupational exposure, and CT measured emphysema (% low-attenuation areas, %LAA) was the main outcome. Quantile regression analyses were used for the multivariate analyses, adjusting for sex, age, smoking, inflation level and FEV₁% of predicted.

Results: Quantile regression analyses showed significant associations between occupational exposure to gas/fumes and mineral dust, and %LAA. The unadjusted regression coefficients for %LAA for subjects with occupational exposure in the longest held job, were 0.95 and 1.21 for low and high exposure to gas/fumes, and 1.16 and 1.98 for low and high exposure to mineral dust. For those with low and high exposure to gas/fumes and mineral dust in their latest job, the regression coefficients were 0.90, 1.19, 1.09 and 1.51 respectively. After adjustments, the association's only remained statistically significant for subjects exposed to high levels of gas and fumes in their latest held job.

Conclusions: Subjects with high levels of occupational exposure to gas/fumes in their latest job were found to have higher levels of CT measured emphysema compared to subjects with low or no exposure. A dose-response relationship was suggested.

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Anti-IgE treatment: An alternative for severe allergic occupational asthma

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Severe work-related asthma remains a difficult problem and new alternative treatment must be evaluated to obtain asthma control and ideally the sustain of the occupational activity.

During 2 years we have enrolled 10 occupational asthmatics (8 men, 2 women, mean age 37, suffering of asthma from 0.5 to 8 years. They were all severe uncontrolled asthma (GINA recommendations). The mean dose of inhaled corticosteroids was 3200 µg/day of beclomethasone equivalent. All patients had 2 to 8

severe exacerbations/year. Six patients were allergic to a high molecular weight agent (wheat flour: 2, cat: 1, rabbit: 1, storage mites: 1, *Alternaria*: 1). In 4 patients the causative agent was a low molecular weight compound (isocyanates in 2 cases, acrylates one case, perchlorethylene one case). Total IgE levels were always above 30 U/mL. The follow-up was performed from 6 to 48 months. Asthma parameters and the occupational status were registered every 6 months.

Results showed a reduction of severe exacerbations in 9 patients. Only one patient was "non responder" after 6 months of treatment. In the 9 "responders" an optimal control could be obtained in 4 patients. Oral daily corticosteroids could be decreased in the 5 (mean initial dose 8,6 mg/day to 1,2 mg/day of equivalent prednisone). Days off-work because of asthma were reduced in the 9 "responders". 7 could continue to work with amendment of the working place. We suggest that omalizumab could be a potential treatment for severe uncontrolled work-related asthma in 3 conditions, patients who were unable to avoid allergen exposure, persistent asthma after cessation of the offending exposure and work-aggravated asthma symptoms in workers with pre-existing allergic asthma.