

Nasal indices of eosinophilic and exudative inflammation in bakery-workers

Torgeir Storaas¹, Laila Årdal², Thien Van Do³, Erik Florvaag³, Sverre K. Steinsvåg¹, Ågot Irgens², Tor B. Aasen² and Lennart Greiff⁴

¹Department of Otolaryngology/Head & Neck Surgery, ²Department of Occupational Medicine, and ³Department of Laboratory of Clinical Biochemistry, Haukeland University Hospital, Bergen, Norway, and ⁴Department of Otorhinolaryngology, Head & Neck Surgery, Lund University Hospital, Lund, Sweden

Summary

Correspondence

Torgeir Storaas, MD, Department of Otolaryngology/Head & Neck Surgery, Haukeland University Hospital, N-5021 Bergen, Norway
E-mail: torgeir.storaas@helse-bergen.no

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Aims: Rhinitis symptoms frequently occur in bakery-workers. Yet, little is known about the pathophysiology of this condition. The objective of the present study was to examine nasal indices of inflammation in relation to occupational dust exposure, occupational rhinitis according to defined criteria, rhinitis symptoms associated to the workplace, and occupational sensitization in bakery-workers.

Methods: Bakery-workers ($n = 197$) were subjected to interviews, questionnaires, workplace dust measurements, allergy tests, and nasal lavages with and without histamine. α_2 -Macroglobulin and eosinophil cationic protein (ECP) were measured in saline lavages as indices of plasma exudation and eosinophilic activity, respectively. Histamine lavages were employed to explore the nasal exudative responsiveness.

Results: α_2 -Macroglobulin and ECP increased significantly by increased workplace dust exposure ($P \leq 0.035$). Furthermore, the exudative responsiveness to histamine increased significantly by such exposure ($P \leq 0.016$). Similar patterns were seen in workers with occupational rhinitis and in subjects with rhinitis symptoms associated to the workplace, but not in workers with occupational sensitization.

Conclusions: We conclude that occupational dust exposure in bakery-workers is associated with nasal eosinophilic exudative inflammation. In contrast, occupational sensitization is not a discriminating factor with regard to indices of eosinophilic, exudative inflammation in the present material.

Introduction

In a previous analysis of the present material, we observed that >50% of workers in the Bergen bakery industry presented rhinitis symptoms (Storaas et al., 2005). While occupational allergens were identified as likely causative factors in many of these subjects, we failed to identify specific sensitization in 55–62% of the cases, depending on diagnostic criteria for occupational rhinitis (OcR) (Storaas et al., 2005). To better understand the pathophysiology of OcR in bakery-workers, it is important to examine the relationship between exposure to occupational factors and nasal mucosal indices of disease.

In a previous study, Brisman et al. (1998) demonstrated increased nasal lavage levels of myeloperoxidase (MPO), indicating neutrophilic activity, in bakers reporting rhinorrhea (c.f. bakers who did not report this symptom). In contrast, no differences were observed in levels of eosinophil cationic protein (ECP), indicating eosinophil activity, and albumin,

reflecting plasma exudation. Accordingly, Brisman et al. (1998) concluded that flour-dust exposure may produce a non-allergic, neutrophilic nasal inflammation. The lack of eosinophilic activity may be surprising considering observations that many patients with OcR have identifiable occupational allergic causes (Storaas et al., 2005), and since symptomatic allergic rhinitis usually is characterized by increased eosinophil activity (Ahlstrom-Emanuelsson et al., 2004).

Plasma exudation is a feature of airway inflammation, and this process can be monitored by analysis of plasma proteins in nasal lavages (Greiff et al., 2001). Whereas low molecular weight plasma proteins such as albumin (69 kD) may be present in nasal surface secretions in high concentrations under physiological conditions, this is not the case for larger proteins. Thus, plasma proteins such as α_2 -macroglobulin (720 kD) may be used to detect plasma exudation with greater sensitivity than albumin. Accordingly, the observation by Brisman et al. (1998) on similar levels of albumin in nasal lavage fluids from rhinitic and non-rhinitic bakery-workers

may not exclude a true difference in plasma exudation between these groups.

In the present study, we have monitored levels of α_2 -macroglobulin and ECP in nasal lavage fluids obtained from bakery-workers. Furthermore, we have employed histamine lavages and monitored the ability of histamine to produce plasma exudation. Increased exudative responsiveness to histamine has previously been demonstrated in allergic rhinitis (Svensson et al., 1995). We have examined the relationship between lavage fluid indices of inflammation and occupational dust exposure, a diagnosis of OcR, presence of rhinitis and chest symptoms, and occupational sensitization.

Methods

Study design

In this cross-sectional study subjects working in six bakeries in Bergen, Norway were recruited. Following interviews, questionnaires and workplace dust measurements, the workers were subjected to nasal saline and histamine lavages. The study was conducted throughout the year, but the nasal lavages were carried out outside the pollen season. Demographic and clinical data of the study material have been reported elsewhere (Storaas et al., 2005).

Subjects

Out of 197 employees, 181 were interviewed, 180 answered the questionnaire and 172 completed the nasal lavage procedure. The mean age was 38 (range 16–66), and a male/female ratio of 2:1. The median number of years in the bakery industry were 10 (range 1–44). Allergy tests including SPT, specific IgE, and histamine release were performed with occupational allergens [wheat, α -amylase, oat, barley, rye, soybean, storage mites (*A. Siro*, *L. Destructor*, *T. Putrescentiae*) and cockroach (*B. Germanica*)] as well as on common aeroallergens [house dust mites (*D. Pteronyssinus*), mould (*C. Herbarium*), cat, dog, timothy and birch]. A subject was considered sensitized to an occupational allergen if any of the above tests turned out positive for any of the above occupational allergens. The study was approved by the Regional Committee for medical research ethics in western Norway (REK-Vest) and written informed consent was obtained.

Interview

An otolaryngologist (T.S.), who was blinded for occupational dust exposure data, carried out standardized interviews focusing on previous diseases, prevalence of allergy, medication, smoking and work-related symptoms. The diagnostic criteria for OcR was based on the International Report on the Diagnosis and Management of Rhinitis in which rhinitis is defined as 'Two or more nasal symptoms (discharge, blockage or sneeze/itch) for >1 h on most days' and OcR as 'Rhinitis caused by exposure to an agent at work' (International Consensus Report 1994). The

work relationship was further established by at least one of the following features: an occupational trigger factor (i.e. information reported by the worker on a factor at the work-place that either started or worsened nasal symptoms), improvement during vacations or weekends, and no history of nasal problems before start of employment.

The following categories of OcR were defined:

OcR-I:

- Two or more symptoms of rhinitis as defined above.
- Symptoms for >1 h on most days.
- Relation to work.

OcR-II:

- One or more symptoms of rhinitis as defined above.
- Symptoms for >1 h on most days.
- Relation to work.

Questionnaire

A self-administered questionnaire was used to obtain information on family history, occupational symptoms, smoking habits and prevalence of allergy and atopic dermatitis/eczema. In addition, a work task scheme with information on main and secondary work task was completed. Questions on nasal symptoms were adopted from the ISAAC questionnaire (Asher et al., 1995). Questions focusing on trigger factors (Do your nasal symptoms start or worsen when you are in contact with: Flour dust? Baking improvers? Cinnamon? Other ingredients?) as well as on improvement during vacations/weekends were added. The criteria for a questionnaire based diagnosis of OcR were: OcR-QI: Two or more symptoms of rhinitis as defined above and relation to work. OcR-QII: One or more symptoms of rhinitis as defined above and relation to work.

Questions on asthma and chest symptoms were adopted from the European Community Respiratory Health Survey (Burney et al., 1994; Svanes et al., 1998). 'Asthma symptom complex' was defined as wheeze with breathlessness when not having a cold. Specific work related asthma symptoms were also assessed. 'Work related asthma symptom complex' was thus defined as wheeze with breathlessness at work when not having a cold. Chest symptoms were assessed by the question: Have you ever had wheezing, shortness of breath, or cough in the evening/night or at work.

Dust exposure

Exposure to occupational dust was measured using the closed face Gelman total dust sampler (Gelman Sciences, Ann Arbor, MI, USA) equipped with a 25 mm polytetrafluoroethylene filter (Millipore, pore size 1 μ m) and a sampling pump (2 l min⁻¹). The amount of dust was determined gravimetrically. Before dust sampling, a mapping had been done in each bakery to assess the organization of the production, the possible sources of exposure and the different job titles involved.

In each bakery a number of workers, altogether 58, wore dust samplers to obtain representative measurements of dust expo-

sure in all job titles present (dough makers, bread formers, oven staff, packers, confectionary workers, administration and cleaning workers).

In addition, in four of the six bakeries, stationary measurements were carried out in areas with anticipated homogenous and low flour dust exposure. The stationary equipment was placed in the same height as the workers' breathing zone. Specific localizations were Bakery B: four in the administration. Bakery C: two in the lunch-room. Bakery E: three in the bakery selling area. Bakery F: five in the oven-room, ten in the packing area. In total, 235 observations were made (211 personal and 24 stationary), 230 of 235 as whole shift measurements.

The exposure measurements made it possible to assign an exposure level to each of the 35 combinations of job title and bakery found in the six bakeries. The results of the exposure measurements indicated that both the job title and bakery had to be considered. In addition, in one of the bakeries (Bakery A), a day-night difference in exposure levels made it necessary to consider whether dough makers worked day or night shifts.

The 35 bakery-job title combinations were collapsed into broader exposure categories. On the basis of the 'work task scheme' (see previously under 'Questionnaire'), on information about which bakery the subjects worked in, and (for dough-makers in Bakery A) on information about working shifts, it was possible to allocate all workers into one of four exposure groups: $<1.0 \text{ mg m}^{-3}$: packers, oven workers and administration, $1.0\text{--}1.9 \text{ mg m}^{-3}$: mainly confectionary workers and bread formers, $2.0\text{--}3.9 \text{ mg m}^{-3}$: mainly dough-makers, and $>3.9 \text{ mg m}^{-3}$: mainly dough-makers. The transport workers were assigned the lowest category. The categorization was meant to reflect the approximate day-to-day, week-to-week exposure level that each individual was subjected to.

Nasal challenge and lavage

Nasal lavages with and without histamine were carried out using a pool-device (Greiff et al., 2001). The volume of the pool-fluid was 14 ml. Isotonic saline was instilled into the nasal cavity for 5 min followed in sequence by a 30 s saline lavage (carried out to produce a low baseline and discarded) and by histamine challenge/lavage ($400 \mu\text{g ml}^{-1}$) kept in the nasal cavity for 5 min. Most workers had been at work for at least 2 h before on the day all the lavages were performed. The recovered fluid was centrifuged and aliquots of the supernatant were frozen (-80°C).

Analysis of α_2 -macroglobulin and ECP

α_2 -Macroglobulin was measured using a radioimmunoassay (detection limit 7.8 ng ml^{-1}). Rabbit anti-human α_2 -macroglobulin (Dakopatts, Copenhagen, Denmark) was used as anti-serum and human serum (Behringwerke, Marburg, Germany) as standard. Human α_2 -macroglobulin (Cappel-Organon, Turnhout, Belgium) was iodinated using the lactoperoxidase method. Tracer and sample were mixed with anti-serum before

adding goat anti-rabbit anti-serum (AstraZeneca, Lund, Sweden). The bound fraction was measured using a gamma counter (Pharmacia, Uppsala, Sweden). The intra- and inter-assay coefficients of variation are between 3.8–6.0% and 3.1–7.2%, respectively. ECP was measured using the CAP system (Pharmacia). The intra- and inter-assay coefficients of variation for this test are, according to the supplier, $<10\%$.

Statistics

Statistical analyses were performed using the SPSS 11.0 software package for Windows XP (SPSS, Chicago, IL, USA). Odds ratios and 95% confidence intervals (CI) were calculated for relationships between dust exposure and prevalence of OcR and chest symptoms using multiple logistic regression adjusted for the potential confounders age or working years, gender and smoking. Differences in levels of α_2 -macroglobulin and ECP between groups were examined by the Kruskal–Wallis test and the Mann–Whitney U-test. Differences in levels of α_2 -macroglobulin between observations at saline and histamine challenge were examined using the Wilcoxon signed rank test. Data are presented as medians with inter quartile ranges.

Results

The amount [geometric mean (range)] of dust recorded in the different work tasks in the bakeries, i.e. dough making, bread forming, confectionary, oven work, packing and administration were 3.14 ($0.93\text{--}16.56$), 1.51 ($0.26\text{--}9.15$), 1.35 ($0.41\text{--}5.35$), 0.54 ($0.17\text{--}1.87$), 0.29 ($0.02\text{--}1.81$) and 0.06 ($0\text{--}0.26$) mg m^{-3} , respectively.

The prevalence of OcR increased with increasing workplace exposure to dust (Table 1). For example, the OR for such a diagnosis based on a structured interview (i.e. OcR-II) was 4.88 ($2.31\text{--}10.30$) when an exposure level of $\geq 1 \text{ mg m}^{-3}$ was compared with an exposure of $<1 \text{ mg m}^{-3}$. Furthermore, workplace dust exposure was associated with chest symptoms and improvements during vacations (Table 1).

We also looked for differences between current ($n = 37$), former ($n = 33$) and never ($n = 112$) dough-makers. Former and current dough-makers had an increased OR for a diagnosis of occupational rhinitis (i.e. OcR-QI) compared with never dough-makers: 3.14 ($1.30\text{--}7.58$) and 3.31 ($1.40\text{--}7.80$), respectively.

In the study group as a whole, saline lavage fluid levels of α_2 -macroglobulin, as marker of plasma exudation, increased significantly and dose-dependently by dust exposure in the range up to 4.0 mg m^{-3} (Fig. 1a). Histamine induced significant plasma exudation responses in all exposure groups ($P \leq 0.013$). The exudative responsiveness to histamine increased significantly by increased dust exposure (Fig. 1b). Nasal saline lavage fluid levels of ECP also increased by dust exposure (Fig. 2).

Nasal saline lavage fluid levels of α_2 -macroglobulin and ECP as well as the exudative responsiveness to histamine were

Table 1 Percentage (number) of workers with interview- and questionnaire-derived diagnosis of occupational rhinitis, questionnaire-derived lower respiratory symptoms and asthma symptom complex in relation to exposure of dust ($n = 183$).

	Occupational dust exposure				OR (95% CI) $\geq 1.0 \text{ mg m}^{-3}$ vs. $<1.0 \text{ mg m}^{-3}$
	$<1.0 \text{ mg m}^{-3}$ ($n = 107$)	$1.0\text{--}1.9 \text{ mg m}^{-3}$ ($n = 33$)	$2.0\text{--}3.9 \text{ mg m}^{-3}$ ($n = 24$)	$>3.9 \text{ mg m}^{-3}$ ($n = 19$)	
OcR-I	11 (12)	38 (12)	38 (9)	50 (9)	4.78 (2.09–11.00)
OcR-II	15 (16)	53 (17)	54 (13)	50 (9)	4.88 (2.31–10.30)
OcR-QI	22 (24)	46 (15)	46 (11)	69 (11)	2.93 (1.45–5.92)
OcR-QII	27 (29)	64 (21)	63 (15)	75 (12)	4.06 (2.02–8.14)
Asthma symptom complex	14 (15)	27 (9)	17 (4)	38 (6)	2.17 (0.99–4.75) ^a
Work related asthma symptom complex	10 (11)	24 (8)	25 (6)	19 (3)	2.66 (1.13–6.23) ^a
Chest symptoms + vocational improvement	14 (15)	36 (12)	25 (6)	50 (8)	3.48 (1.50–8.10)

Odds ratios (OR) for comparisons between exposure level $\geq 1 \text{ mg m}^{-3}$ and exposure below this level. OcR-I and II, occupational rhinitis, interview based; OcR-QI and QII, occupational rhinitis, questionnaire based.

^aAdjusted for working years, gender and smoking.

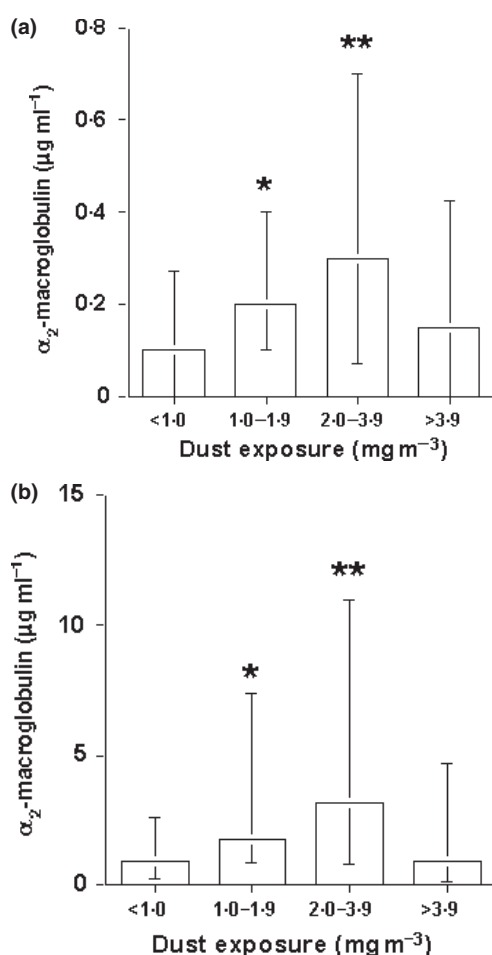


Figure 1 Levels of α_2 -macroglobulin in nasal saline lavages (a) and histamine lavages (b) in the study population as a whole. Increased workplace exposure to dust was associated with significantly increased levels of α_2 -macroglobulin (c.f. $<1 \text{ mg m}^{-3}$) (except for the highest exposure group). Furthermore, the ability of histamine to produce plasma exudation (α_2 -macroglobulin) was significantly increased by increased work dust exposure (c.f. $<1 \text{ mg m}^{-3}$) (a) * $P = 0.010$; ** $P = 0.008$. (b) * $P = 0.016$; ** $P = 0.009$.

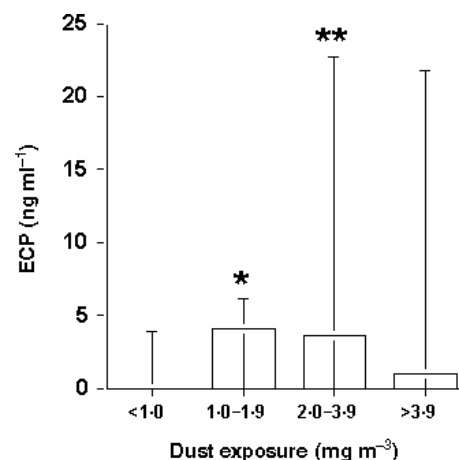


Figure 2 Levels of ECP in nasal saline lavages in the study population as a whole. Increased workplace exposure to dust was associated with significantly increased levels of ECP (c.f. $<1 \text{ mg m}^{-3}$) (* $P = 0.035$; ** $P = 0.004$).

significantly increased in seven of twelve comparisons between those with OcR, defined either as OcR-I, OcR-II, OcR-QI or OcR-QII, and those without (Table 2). The difference was particularly clear for OcR defined as OcR-II and OcR-QII.

In subjects with workplace associated nasal symptoms, i.e. a trigger factor or improvement during vacations, saline lavage fluid levels of α_2 -macroglobulin as well as ECP were increased (c.f. subjects without nasal symptoms) (Table 2). Moreover, subjects with workplace associated nasal symptoms featured an increased exudative responsiveness to histamine (Table 2).

Sensitization to common aeroallergens was a significant discriminating factor between low and high levels of α_2 -macroglobulin in contrast to sensitization to occupational allergens (Table 2).

Discussion

The present study has demonstrated that exposure to occupational dust per se, as well as a diagnosis of OcR and rhinitis

Table 2 Levels of α_2 -macroglobulin ($\mu\text{g ml}^{-1}$) in nasal saline and histamine lavages and levels of ECP (ng ml^{-1}) in saline lavages by the subgroups OcR-I, OcR-II, OcR-QI and OcR-QII, by nasal symptoms associated with occupational trigger factor or improvement during vacations, and by sensitization.

	Saline			Histamine		
	α_2 -Macroglobulin		ECP	α_2 -Macroglobulin		
OcR-I						
Yes, n = 34	0.2 (0.1–0.4)	P = 0.173	2.51 (0–6.79)	2.0 (0.8–5.8)	P = 0.023	
No, n = 128	0.1 (0–0.4)		0 (0–4.87)	1.0 (0.2–3.3)		
OcR-II						
Yes, n = 47	0.6 (0.2–1.6)	P = 0.013	3.27 (0–6.43)	2.3 (0.9–6.6)	P = 0.001	
No, n = 115	0.1 (0–0.3)		0 (0–4.30)	0.9 (0.2–2.6)		
OcR-QI						
Yes, n = 51	0.2 (0–0.4)	P = 0.296	2.23 (0–7.30)	1.8 (0.3–7.8)	P = 0.115	
No, n = 109	0.1 (0–0.4)		2.15 (0–4.58)	1.1 (0.3–3.1)		
OcR-QII						
Yes, n = 67	0.2 (0–0.4)	P = 0.020	2.77 (0–7.79)	2.0 (0.6–7.4)	P = 0.001	
No, n = 93	0.1 (0–0.3)		0 (0–4.13)	0.9 (0.2–2.2)		
Nasal sympt. + workplace trigger						
Yes, n = 55	0.2 (0.2–0.5)	P = 0.002	2.77 (0–7.30)	2.0 (0.8–8.0)	P = 0.003	
No, n = 105	0.1 (0.2–0.4)		0 (0–4.29)	0.9 (0.2–2.4)		
Nasal sympt. + vocational improvement						
Yes, n = 57	0.2 (0.1–0.7)	P = 0.001	3.86 (0–10.20)	1.9 (0.7–7.9)	P = 0.002	
No, n = 103	0.1 (0–0.3)		0 (0–4.02)	0.9 (0.2–3.1)		
Sensitization to common aeroallergens						
Yes, n = 44	0.2 (0.1–0.6)	P = 0.026	2.45 (0–8.14)	1.8 (0.8–6.3)	P = 0.014	
No, n = 118	0.1 (0–0.3)		0 (0–4.50)	0.9 (0.2–3.1)		
Occupational sensitization						
Yes, n = 45	0.2 (0–0.4)	P = 0.305	2.27 (0–5.53)	1.7 (0.6–4.7)	P = 0.073	
No, n = 117	0.1 (0–0.4)		0 (0–5.14)	1.1 (0.2–3.8)		

Data are presented as medians with inter quartile ranges.

OcR-I and II, occupational rhinitis, interview based; OcR-QI and QII, occupational rhinitis, questionnaire based.

symptoms associated to the workplace, is associated with plasma exudation, increased eosinophil activity and exudative hyper-responsiveness to histamine in bakery workers. In contrast, occupational sensitization was not a significant discriminating factor between high and low levels of indices of inflammation. The observations are of interest in terms of the pathophysiology of OcR and also in terms of monitoring this condition.

In the present study, the prevalence of OcR as defined by a structured interview was 30% (i.e. OcR-II). This is consistent with figures reported by others (15–40%) (Houba et al., 1998). In contrast to previous nasal lavage studies in OcR, nearly all (172/197) of the present employees working in the six bakeries were examined. Thus, the lavage material represents samples from individuals subjected to all levels of dust and from subjects with and without symptoms of rhinitis. Our analysis has included the whole study population as well as logical subgroups, e.g. subjects with and without nasal symptoms.

The Gelman particle-trap was used to collect dust from various workplace settings in a standardized manner, but we have not quantified specific allergens. However, we regard it as likely that the present overall dust exposure also reflects exposure to occupational allergens as previously reported by Nieuwenhuijsen and Cullinan (Nieuwenhuijsen et al., 1994; Cullinan et al., 2001). The present study subjects were allocated

to specific exposure levels in the relevant workplace setting. We regard it as likely that these dust levels reflect individual exposure.

In the present study, α_2 -macroglobulin was employed as a plasma exudation tracer. We have previously shown that lavage-fluid levels of this particular protein accurately reflect plasma exudation at nasal airway inflammation (Greiff et al., 2003). The present saline lavage levels of α_2 -macroglobulin increased dose-dependently by increased workplace dust exposure except for the group with the highest level of exposure. We suspect that the low response to occupational dust in this group of individuals may be due to a 'healthy worker effect'. Significantly higher levels of α_2 -macroglobulin were also observed in workers classified as having OcR and in workers with nasal symptoms associated to the workplace. While our findings are in contrast to those of Brisman et al. (1998), who reported similar lavage-fluid levels of albumin in bakery workers with rhinitis symptoms c.f. without symptoms, they are in agreement with reports on an increased 'permeability index', i.e. nasal lavage albumin/total protein, following occupational allergen challenge (Gorski et al., 1998; Walusiak et al., 2004). That Gorski et al. (1998) succeeded in showing plasma exudation may be explained by the fact that the challenge was given to selected, sensitized subjects, and that care was taken to establish a low

baseline level by performing repeated saline lavages before the challenge. That we could demonstrate plasma exudation at workplace exposure is likely explained by the fact that we employed a very sensitive plasma exudation tracer. Taken together, our findings indicate that OcR is characterized by plasma exudation. In turn, this observation indicates a degree of active nasal airway inflammation.

It has previously been shown that nasal histamine challenge induces plasma exudation (Greiff et al., 2003). In the present study, this effect of histamine was confirmed. Also, it was demonstrated that the ability of histamine to induce plasma exudation was significantly increased by increased occupational dust exposure. Moreover, workers classified as having OcR and subjects reporting nasal symptoms associated with the workplace (as trigger factor or improvement during vacations) presented increased exudative responses to histamine. Such an exudative hyper-responsiveness has previously been shown to be a feature of nasal airway inflammation in allergic rhinitis (Greiff et al., 2001). An increased responsiveness to histamine was also reported by Gorski et al. (1998) in their study where subjects with OcR responded with greater increases in the 'permeability index' (above) compared with healthy subjects. Accordingly, available information indicates that bakery-workers with OcR feature an exudative hyper-responsiveness.

Nasal lavage fluid levels of ECP were employed as an index of eosinophilic activity. The levels of ECP increased significantly by dust exposure and, as for α_2 -macroglobulin, increases in ECP were observed in workers with OcR. Again, our finding correspond with the observations by Gorski et al. (1998). They reported increased nasal lavage fluid levels of ECP following allergen challenge as well as increased numbers of eosinophils (c.f. baseline). Taken together, our observations indicate that OcR in bakery workers as a group is associated with an active eosinophilic inflammation. An important difference is that we have examined individuals in a workplace setting.

In the present study, we observed significantly higher levels of α_2 -macroglobulin in workers sensitized to common aeroallergens, in contrast to the cohort sensitized to occupational allergens. The allergy work-up in the present study was comprehensive and the prevalence of occupational sensitization in the study material is one of the highest reported from the bakery industry (Storaas et al., 2005). If specific occupational allergens had a uniquely discriminating impact on the prevalence of nasal airway inflammation, we would have expected workers with such sensitization to feature abnormally high levels of the presently monitored nasal lavage fluid indices. This was not the case, and from this, in combination with our observation that <46% of the study subjects with OcR had identifiable occupational sensitization (Storaas et al., 2005) we suggest, in agreement with Brisman et al. (1998) that OcR might be driven by non-IgE mediated mechanisms (in addition to IgE mediated mechanisms in sensitized subjects). In many cases, the disease promoting factor may thus be exposure to workplace dust *per se* rather than exposure to specific allergens.

Brisman et al. (1998) reported increased nasal lavage levels of MPO specifically in subjects answering yes to the question: 'Do you have a runny nose' (c.f. workers answering no). As they did not find increased levels of ECP in these symptomatic bakers, they concluded that flour-dust exposure produced a non-allergic, neutrophilic inflammation. In the present study, no attempts were made to monitor neutrophilic activity, since our focus was to monitor a cellular index that would characterize allergic, eosinophilic airway inflammation (ECP). However, even if OcR in bakery-workers is characterized by increased eosinophilic activity, as indicated by the present study, increased neutrophilic activity may also occur. For example, in seasonal allergic rhinitis, acute allergen exposure can be associated with a mixed granulocyte response (Bascom et al., 1988). Conversely, in common cold, the neutrophilic inflammation may also feature increased eosinophilic activity (Greiff et al., 2002).

In conclusion, occupational dust exposure is associated with rhinitis and chest symptoms in bakery-workers. Dust exposure *per se*, as well as a diagnosis of OcR and rhinitis symptoms associated with the workplace, is characterized by eosinophilic, exudative inflammation and exudative hyper-responsiveness. In contrast, occupational sensitization is not a discriminating factor between high and low levels of the present indices of inflammation in the present study. Our findings suggest that non-allergic mechanisms may be involved in the pathophysiology of OcR in bakery-workers, in addition to situations where specific allergens can be identified and IgE dependent mechanisms likely contribute. We suggest that nasal lavages and the employment of indices of inflammation may be used to monitor OcR, e.g. following workplace interventions.

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