

Prevalence of and relationship between rhinoconjunctivitis and lower airway diseases in compost workers with current or former exposure to organic dust

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Abstract

Introduction and objective. The relationship between allergic rhinitis and allergic asthma is well characterized. However, it remains unknown whether an association exists between symptoms of upper and lower airway diseases and occupational bioaerosol exposure beyond the scope of allergy.

Materials and methods. The current cross-sectional study focuses on 190 current and 59 former compost workers exposed to bioaerosols. Work-related symptoms indicative of conjunctivitis, rhinitis and lower airway irritation were assessed and compared with 38 non-exposed control subjects. Allergic asthma was diagnosed using a calculated score, and chronic obstructive pulmonary disease (COPD) was spirometrically determined.

Results. 12 current, 8 former and 5 non-exposed subjects were diagnosed with allergic asthma and excluded from further analysis. Multivariate logistic regression models suggested that cough and chronic bronchitis in current compost workers were associated with eye irritation (OR 2.75 (0.93–8.07); OR 7.22 (1.12–46.5)). Chronic bronchitis in former workers was strongly associated with work-related eye irritation (OR 38.6 (1.33- >1000) and nose irritation (OR 25.0 (1.21–513)).

Conclusions. After excluding allergic asthmatics, there was no evidence that eye or nose irritation was due to an underlying atopic disease, but rather to non-allergic mucous membrane irritation syndrome. Therefore, the higher incidence of chronic bronchitis in former compost workers may reflect a chronic irritative process triggered by exposure to bioaerosols.

Key Words

mucous membrane irritation, chronic bronchitis, bioaerosol

INTRODUCTION

Adverse health effects have been reported in workers exposed to bioaerosols in composting plants [1, 2]. The currently available health information arises from bioaerosol exposure characterized from a variety of components in different human populations with a range of susceptibility to effects [3, 4]. To date, there has been relatively little investigation on the effects arising from composting waste.

Bioaerosol exposures can cause infectious, toxic, and allergenic effects [5]. Many fungal species are known to be potential inducers of sensitization and immunoglobulin E (IgE) antibody production [6]. However, allergic diseases caused by fungi are not considered a major problem in occupational medicine [7]. Another potential source of allergens is plant material or airborne pollens sticking to organic waste delivered for composting processes. Conversely, results from a previous study showed no significant differences in allergen-specific IgE concentrations in compost workers compared to controls who were not previously exposed to organic dust [8]. Apart from their allergic and infectious

properties, bacteria and fungi can induce inflammatory responses via inhalation of endotoxin or β -glucans [9, 10]. Furthermore, the respiratory symptoms observed in bioaerosol-exposed workers are thought to be mainly based on non-allergic inflammatory reactions [11]. This disease entity – the so-called mucus membrane irritation syndrome (MMIS) – is often caused by exposure to mould, dust, or chemical vapours [2]. MMIS can present as conjunctivitis, rhinitis when present in the upper respiratory tract, whereas cough and phlegm are signs of lower respiratory tract irritation. Reports indicate that in the field of recycling, an increased number of workers exhibit symptoms of eye or nose irritation, accompanied by a (productive) cough [1, 8]. However, the symptoms are relatively non-specific and may reflect different respiratory diseases, e.g. asthma, chronic bronchitis or chronic obstructive pulmonary disease (COPD). In this respect, the pathophysiologic features of asthma, as well as COPD, are based on (ongoing) airway inflammation resulting in similar symptoms, including airflow limitation [12]. Additionally, smoking-related symptoms are common, and especially related with workers age. Smoking, as well as pre-existing respiratory conditions (atopy, asthma), may modify the development of bioaerosol-related symptoms. In this respect, lifestyle, together with environmental and/or occupational exposures, can have an additive or a synergistic impact.

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The authors have previously reported that exposure during composting is associated with an elevated prevalence of chronic cough, and lower values for FEV₁ % predicted and FVC % predicted, compared to controls. However, no association was seen between lung function parameters and duration of employment [8]. The presented study focuses on non-allergic adverse health effects in compost workers, in which individuals with a high probability of allergic asthma were identified and excluded. Prevalence of cough, chronic bronchitis, COPD, rhinitis and conjunctivitis was assessed with respect to smoking habits, atopy and occupational history as a compost worker.

OBJECTIVES

The aims of these in-depth analyses were: 1) to validate the hypothesis that compost workers suffer more frequently from non-allergic respiratory health complaints, and 2) to test the hypothesis that an association exists between MMIS of the upper and lower airways.

MATERIALS AND METHODS

In 2009, 190 'currently-exposed' compost workers were examined at 31 composting plants in northwestern Germany. In addition, 59 former compost workers who had stopped working for various reasons, and a reference group without occupational bioaerosol exposure (38 white-collar workers) were studied from the end of 2009 to the beginning of 2010 using the same study protocol as recently described [8]. Briefly, the protocol included a questionnaire, in combination with a physical examination by an occupational physician which included lung function measurement, serologic parameters, and a differential cell count of induced sputum. The study was approved by the Ethics Committee of the Ruhr-University in Bochum, and all participants gave written informed consent.

Smoking habits. Smoking habits were assessed by the questionnaire and justified by cotinine concentrations in urine according to Xu et al. [13], with some modifications. Assigned non-smokers or former smokers with concentrations above 100 µg/L were reclassified as current smokers.

Chronic bronchitis and COPD. Based on the intensity and quality of the reported symptoms, subjects were categorized according to no symptoms, cough, and chronic bronchitis. Chronic bronchitis was diagnosed in subjects who experienced 'cough and phlegm 3 months or more per year during two consecutive years' [14]. Lung function, in terms of spirometry, was performed with a portable spirometer (MasterScope, Viasys Health Care, Germany) prior to work shifts. Each protocol was verified in terms of acceptability and reproducibility according to the recommendations of the American Thoracic Society (ATS) [15]. Forced expiratory volume in 1 sec (FEV₁) and forced vital capacity (FVC) of the best spirogram fulfilling these criteria were used for further analyses.

A diagnosis of COPD was based on objective evidence acquired for airflow limitation. With respect to the guidelines provided by the Global Initiative for Obstructive Lung Disease (GOLD) [14], airflow limitation is assumed if the FEV₁/FVC

ratio is less than 0.7. Besides this, with a fixed FEV₁/FVC ratio of 0.7 provided by GOLD, there is evidence indicating that the respective age-corrected predicted values might model airway limitation more accurately [16]. Therefore, the FEV₁/FVC ratio percent predicted for assuming airflow limitation was used. COPD was defined by the 5% lower limit of the normal (LLN) FEV₁/FVC ratio according to reference values provided by Brändli et al. [17]. Referring to GOLD, COPD was further divided into the following four stages – Stage I: FEV₁ ≥80% predicted; stage II: FEV₁ 50 – 80% pred; stage III: FEV₁ 30 – <50%pred; and stage IV: FEV₁ <30% pred [14].

Immunologically-based illness. Atopy describes the tendency to become sensitized and produce specific (IgE) antibodies in response to everyday exposures to ubiquitous allergens. The atopy status of the workers was determined serologically using the specific IgE measurement to a variety of environmental allergens (sx1 Phadiatop, ThermoFisher Scientific (formerly Phadia), Uppsala, Sweden). According to a dichotomous view, a positive atopic status is assumed when sx1 > 0.35 kU/L. Presently, analytic sensitivity is as low as 0.1 kU/L, but the relevance of values between 0.1 and 0.35 kU/L remains unclear [18]. In cases where intermediate values for sx1 were measured, additional information, such as total serum IgE with a cut-off > 100 kU/L or a positive familial disposition to atopic diseases, was considered before deciding on the atopic status.

Subjects were clinically examined and information provided in the questionnaire was cross-checked by a physician experienced in the field of occupational medicine. Asthma was defined as experiencing shortness of breath, an asthma attack, or the use of asthma medication [19].

The probability of allergic asthma was derived from a score that included information from:

- 1) the questionnaire;
- 2) a physician-based diagnosis of asthma;
- 3) exhaled nitric oxide (FeNO) with cut-offs stratified by smoking habits as previously reported (never-smokers 31 ppb, ex-smokers 26 ppb and current smokers 22 ppb) [20];
- 4) the percentage of eosinophils in induced sputum with a 2% cut-off based on published data for eosinophils from healthy subjects [21];
- 5) an allergy to any inhalation allergen (house dust mites, animals, pollen);
- 6) atopy.

Results meeting the criteria were rated 1, except for the questionnaire which was rated 2. The score ranged from 0 – 7. A person was diagnosed as suffering from allergic asthma with a score ≥ 4.

Rhinitis and conjunctivitis. Subjects were asked via the questionnaire to report their work-related symptoms, indicating irritation of eyes or nose [8]. Questions comprised watering eyes, burning eyes, and itching eyes or runny nose, nasal congestion, and restriction of olfactory sense. Answers to the questions were rated 0 (no) or 1 (yes). Affirmative answers were integrated into an additive symptom score in the range from 0 – 3. A symptom score of 2 or more was considered to be indicative of conjunctivitis or rhinitis.

Data analysis. Data were expressed as mean with range or median with interquartile range (25th; 75th percentile). The D'Agostino & Pearson omnibus normality test was used to

assess value distributions. Fisher's exact test or Chi-square test was used for categorical variables. Multivariate logistic regression models were applied to evaluate the influence of several variables on respiratory illness and MMIS. A p-value below 0.05 was considered statistically significant for all analyses, and all tests were performed 2-sided. Data were analyzed using SAS Software 9.2 (Cary, NC, USA), and visualized with GraphPad Prism version 5.01 for Windows (GraphPad Software, San Diego, CA, USA).

RESULTS

Study characteristics and prevalence of asthma bronchiale. The study groups consisted of 190 current and 59 former workers exposed to bioaerosols, as well as 38 non-occupationally exposed control subjects [8]. A score-based diagnosis of allergic asthma was less common in the current (12/190; 6.3%) compared to former compost workers (8/59; 13.6%), and to the control subjects (5/38; 13.2%) (For results for asthma scoring see supplemental Table). Altogether, 25 subjects previously diagnosed with allergic asthma were excluded from further analysis of work-related impairment. From these excluded subjects, one former worker and one subject from the control group were diagnosed with chronic bronchitis in addition to being classified as asthmatic. After accounting for asthma, further analyses were based on 178 current workers, 51 former workers, and 33 white-collar workers. Study characteristics are presented in Table 1. In summary, the average age of the workers in the different groups differed significantly from one another, with current workers being the youngest ($p < 0.0001$). In addition, duration of employment was different among the groups with members of the reference group who were not occupationally exposed to bioaerosols, being the longest employed ($p < 0.0001$). There were more current smokers among the compost workers, but no differences in anthropometric data or prevalence of atopic condition were observed.

Supplemental Table. Probability of asthma based on a multivariate score

Asthma-Score	Compost workers (n = 190)		Former worker (n = 59)		Reference group (n = 38)	
	n	(%)	n	(%)	n	(%)
0	67	(35.3)	13	(22.0)	21	(55.3)
1	56	(29.5)	14	(23.7)	1	(2.6)
2	31	(16.3)	14	(23.7)	8	(21.1)
3	24	(12.6)	10	(17.0)	3	(7.9)
4	10	(5.3)	7	(11.9)	4	(10.5)
5	2	(1.1)	1	(1.7)	1	(2.6)
6	0	(0.0)	0	(0.0)	0	(0.0)
7	0	(0.0)	0	(0.0)	0	(0.0)

Asthma-Score was based on: 1) a questionnaire; 2) a physician-based diagnosis of asthma; 3) exhaled nitric oxide (FeNO); 4) eosinophils in induced sputum; 5) an allergy to any inhalation allergen; 6) atopy. Results meeting the criteria were rated 1, except for the questionnaire which was rated 2.

Prevalence of cough, chronic bronchitis and COPD. According to the replies in the questionnaire, subjects suffering from chronic bronchitis were separated from those who reported coughing. Prevalence of cough among the

Table 1. Characteristics of 178 currently exposed compost workers, 51 former compost workers and 33 non-exposed control subjects (without asthma)

	Compost workers	Former workers	Reference group	P
Study group (n):	178	51	33	
Age (yrs): median (IQR)	46 (40–51)	51 (43–60)	57 (53–63)	<0.0001*
Height (cm): median (IQR)	179 (173–186)	180 (172–186)	179 (171–181)	0.652*
Weight (kg): median (IQR)	87 (75–98)	89 (78–100)	86 (75–95)	0.613*
BMI (kg/m ²): median (IQR)	26.7 (24.6–30.1)	27.0 (25.7–30.0)	26.9 (23.8–29.9)	0.661*
Smoking status				
Never smokers: n (%)	55 (30.9%)	22 (43.1%)	14 (42.4%)	0.431 [§]
Ever smokers: n (%)	67 (37.6%)	17 (33.3%)	14 (42.4%)	0.698 [§]
Current smokers: n (%)	56 (31.5%)	12 (23.5%)	5 (15.2%)	0.118 [§]
Atopic: n (%)	53 (29.8%)	15 (29.4%)	5 (15.2%)	0.219 [§]
Employment: yrs (median, IQR)	12.3 (6.3–17.4)	9.0 (5.0–12.0)	30.2 (23.9–34.4)	<0.0001*

*Chi-square test [§]Kruskal-Wallis test

compost workers was 14.6% in the current and 15.7% in the former workers, and 3.0% in the control subjects ($p = 0.172$). The prevalence of cough among the compost workers (current vs. former) was similar, but less frequent, compared to the control subjects (active: $p = 0.087$; former: $p = 0.082$).

The prevalence of chronic bronchitis was highest among individuals who had previously left the composting plants. More specifically, chronic bronchitis was reported by 25.5% of the former workers, 4.5% of current workers, and 9.1% of the control subjects ($p < 0.0001$). The prevalence of chronic bronchitis in active compost workers did not statistically differ from the control subjects ($p = 0.384$).

For COPD, no obvious difference was observed with respect to LLN among the study groups (active compost workers 12.9%, former workers 21.6%, and control subjects 18.2%; $p = 0.281$). However, an increased percentage of subjects presented with severe airflow limitation, e.g. stage GOLD 2 and 3 in former workers (former workers 15.7%, current compost workers 6.6%, references 9.1%, $p = 0.091$) (data not shown). Concomitant chronic bronchitis and COPD was most apparent in former workers (former workers 13.7%, current compost workers 0.6%, control subjects 3.0%, $p < 0.0001$) (Tab. 2).

Risk factors for cough, chronic bronchitis and COPD. The respective odds-ratios for the study groups after adjusting for the effect of age, smoking habits, BMI and atopy by multivariate logistic regression analyses, are depicted in Table 3. After adjustment, there were obvious associations between smoking habits and respiratory diseases. Compared to never smokers, prevalence of chronic bronchitis (3.79; 1.16 – 12.33), as well as COPD (6.44; 2.32 – 17.88), was significantly higher in current smokers who also tended to cough more frequently (2.16; 0.84 – 5.57). An increased risk for COPD was also observed in ever smokers (2.65; 0.93 – 7.50). In

Table 2. Relation between chronic bronchitis and COPD with occupational exposures and by smoking habits

CB	COPD	Compost workers (n=178)			Former workers (n=51)			Reference group (n=33)		
		NS	ES	CS	NS	ES	CS	NS	ES	CS
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
-	-	50 (28.1)	55 (30.9)	43 (24.2)	17 (33.3)	13 (25.5)	4 (7.8)	12 (36.4)	11 (33.3)	2 (6.1)
+	-	2 (1.1)	3 (1.7)	2 (1.1)	3 (5.9)	2 (3.9)	1 (2.0)	1 (3.0)	0 (0.0)	1 (3.0)
-	+	3 (1.7)	9 (5.1)	10 (5.6)	1 (2.0)	1 (2.0)	2 (3.9)	1 (3.0)	3 (9.1)	1 (3.0)
+	+	0 (0.0)	0 (0.0)	1 (0.6)	1 (2.0)	1 (2.0)	5 (9.8)	0 (0.0)	0 (0.0)	1 (3.0)

Stratification by smoking habits: NS – never smokers; ES – ever smokers; CS – current smokers; CB – chronic bronchitis; COPD – spirometrically determined chronic obstructive pulmonary disease.

Table 3. Multivariate logistic regression analyses of associations between occupational exposure and prevalence of cough, chronic bronchitis and airflow limitation by subject characteristics

Variable	n	Cough		Chronic bronchitis		Airflow limitation	
		OR	(95%CI)	OR	(95%CI)	OR	95%CI
Working group							
Reference group	33	1		1		1	
Compost worker	178	4.11	(0.49–34.34)	0.42	(0.09–2.05)	0.65	(0.21–2.02)
Former worker	51	6.75	(0.75–60.79)	4.10	(0.95–17.77)	1.50	(0.44–5.08)
Age							
< 50 years	144	1		1		1	
≥ 50 years	118	0.75	(0.33–1.67)	1.25	(0.45–3.50)	1.53	(0.70–3.31)
Smoking habits							
Never smokers	91	1		1		1	
Ever smokers	98	1.14	(0.45–2.94)	0.94	(0.28–3.18)	2.65	(0.93–7.50)
Current smokers	73	2.16	(0.84–5.57)	3.79	(1.16–12.33)	6.44	(2.32–17.88)
BMI							
BMI < 25	72	1		1		1	
25 ≤ BMI < 30	125	1.54	(0.61–3.89)	0.19	(0.35–4.05)	0.69	(0.30–1.60)
BMI ≥ 30	65	0.96	(0.31–2.95)	1.65	(0.46–6.00)	0.53	(0.19–1.45)
Atopy							
No	189	1		1		1	
Yes	73	0.61	(0.25–1.48)	1.13	(0.40–3.18)	0.82	(0.36–1.85)

addition, compared to the reference group, the OR for chronic bronchitis was elevated among the former workers, though not significantly different (4.10; 0.95–17.77). In addition, there was an association between lifetime occupational bioaerosol exposure and cough (active compost worker OR 4.11, former worker OR 6.75), although also not statistically significant.

Eye and nose irritation during time of employment in a composting plant. Diagnosis of conjunctivitis and rhinitis were derived from respective symptom-scores of the workers. After excluding subjects with allergic asthma, compost

workers suffered more often from work-related irritation of the eyes than control subjects (active 34/178; 19.1%, former 13/51; 25.5% vs. reference group 1/33; 3.0%). In relation to the reference group, differences in prevalence reached statistical significance (former workers; $p=0.030$), or were close to being statistically significant (active workers; $p=0.060$). Furthermore, compared to the reference group (5/33; 15.2%), current workers exhibited less nasal irritation (19/178; 10.7%); whereas, the former workers had a higher prevalence (12/51; 23.5%). Differences in prevalence between current and former compost workers were near to significance (active workers; $p=0.071$). Only subjects who were ever previously occupationally exposed to bioaerosols reported concomitant irritation of both eyes and nose. The prevalence was similar in both active ($n=10$; 5.6%) and in former workers ($n=3$; 5.9%).

Overall, irritation of either nose or eyes was quite common. Among the currently-exposed subjects who showed symptoms of rhinoconjunctivitis, 23.3% could be categorized as atopic and 18.6% reported an allergy to ubiquitous aero-allergens. The prevalence of atopy and allergy in former workers were 22.7% and 26.1%, respectively. No control subject with irritation of eyes or nose was atopic, but 16.7% reported an allergy to ubiquitous aero-allergens.

Influences on prevalence of cough and chronic bronchitis in compost workers. The results from multivariate logistic regression analyses on cough and chronic bronchitis of current and former compost workers are shown in Table 4. Duration of employment in a composting plant (2.61; 0.91–7.48), together with irritation of nose (3.51; 1.07–11.6) or eyes (2.75; 0.93–8.07), seemed to be associated with cough in workers who are currently exposed to bioaerosols. Duration of employment (9.18; 0.83–101) and irritation of eyes (7.22; 1.12–46.8) was also associated with chronic bronchitis. In addition, current compost workers identified as atopic demonstrated a significantly enhanced OR for chronic bronchitis (6.25; 1.19–32.9).

Irritation of eyes as well as nose at the time of bioaerosol exposure emerged as strong predictors of chronic bronchitis, as reported by former compost workers (eyes OR 38.6, nose OR 25.0). While there were no associations between spirometrically-determined airflow limitation (COPD) and cough (1.50; 0.42–5.34) or chronic bronchitis (0.94; 0.07–12.1) in the current compost workers, a relevant relationship could be described for the former workers (cough 375 (0.98->1000); chronic bronchitis 286 (1.49->1000)).

Table 4. Demographics, smoking, occupational exposure and symptoms among current and former compost workers (multivariate logistic regression)

Variables	Current compost worker					Former worker				
	n	OR	Cough (95% CI)	Chronic bronchitis OR (95% CI)		n	OR	Cough (95% CI)	Chronic bronchitis OR (95% CI)	
Age										
< 50 years	118	1		1		25	1		1	
≥ 50 years	60	0.55	(0.19 – 1.57)	0.66	(0.12 – 3.79)	26	0.22	(0.01 – 3.44)	0.17	(0.01 – 4.96)
Smoking habit										
Never smoker	55	1		1		22	1		1	
Ever smoker	67	0.95	(0.31 – 2.87)	1.07	(0.13 – 8.61)	17	35.3	(0.26 – >1000)	4.44	(0.19 – 103)
Current smoker	56	1.24	(0.39 – 3.96)	2.04	(0.22 – 18.8)	12	6.04	(0.24 – 154)	5.68	(0.12 – 264)
Atopy										
No	125	1		1		36	1		1	
Yes	53	0.67	(0.21 – 2.10)	6.25	(1.19 – 32.9)	15	14.9	(0.24 – 923)	1.0	(0.02 – 43.7)
Employment										
< 10 years	67	1		1		31	1		1	
≥ 10 years	111	2.61	(0.91 – 7.48)	9.18	(0.83 – 101)	20	0.03	(0.00 – 2.31)	0.54	(0.02 – 15.1)
MMI of eyes										
No	144	1		1		38	1		1	
Yes	34	2.75	(0.93 – 8.07)	7.22	(1.12 – 46.8)	13	48.0	(0.22 – >1000)	38.6	(1.33 – >1000)
MMI of nose										
No	159	1		1		39	1		1	
Yes	19	3.51	(1.07 – 11.6)	1.30	(0.13 – 12.7)	12	4.76	(0.11 – 210)	25.0	(1.21 – 513)

DISCUSSION

There is evidence that occupational exposure to bioaerosols can contribute to the development of chronic airway disease [1, 2, 3, 4, 8]. Definitions of airway diseases are differentially based on clinical, functional or anatomic conditions which may overlap and affect discrimination [12]. The definition of COPD in different guidelines is mostly based on non-fully reversible airflow limitation, independent of clinical symptoms [22]. In the presented study, COPD was defined with respect to 5% LLN of FEV₁/FVC, which has been suggested to provide a less age-biased estimate [16]. This definition was especially relevant in the current analysis of groups demonstrating statistically different mean ages. Post-bronchodilator spirometry was not performed. In order to avoid an overestimation of COPD prevalence, subjects having a high probability of allergic asthma, as reported previously [23, 24], were excluded.

The presented study focused on the prevalence of and relationship between symptoms of upper and lower airways. As rhinitis is common among allergic asthmatics, subjects suffering from rhinitis would bias the current evaluations where an attempt was made to link non-specific upper and lower airway disease in compost workers [25]. Therefore, the aim was to identify asthma, e.g. allergic asthma, using multimodal criteria including non-invasive diagnostic tools [21]. Thus, the group of spirometrically-determined COPD subjects may also include non-allergic asthmatics. However, there is no general consensus on whether chronic non-allergic asthma and COPD represent a single disease with different phenotypes, or represent distinct diseases that share common characteristics [26].

Assessment of prevalence in a working population using a cross-sectional study design is usually biased by healthy-worker effects. First, subjects choosing a physically challenging job may be in better shape than white-collar workers, and secondly, workers with health complaints, especially in the case of work-related illness, may leave their jobs. Therefore, in addition to excluding asthmatic subjects, in this study, special emphasis was placed on recruiting former compost workers as well as a group of non-occupationally exposed office workers who were similarly evaluated. There were fewer current smokers in the reference group, and smoking is a known risk factor for airway inflammation leading to chronic (obstructive) bronchitis. Adjusted odds ratios confirmed that smoking had a dramatic impact on the incidence of chronic bronchitis and spirometrically-determined COPD, with the highest prevalence occurring in current smokers. This is a reasonable finding in view of data reported in the literature [27].

Multivariate logistic regression analyses were hampered by the low number of subjects in the respective subgroups, which is the major limitation of the presented study. Some p-values for certain parameters that were just below the level of significance may have gained significance with a larger sample size. Though not statistically significant, additional conclusions could be drawn after adjustment for, e.g. age, smoking habits and atopy. Indeed, the presented results demonstrate a lower prevalence of chronic bronchitis in current compost workers, and a higher prevalence that is close to significance in former workers when compared to white-collar workers. First, these data confirm a healthy-worker effect in the current study. Second, compost workers with respiratory symptoms even after quitting the job suggest

that these workers were already beyond the 'point of no return'. This observation supports a recent study showing that symptoms persist and/or progress even after allergen withdrawal [28]. Additionally, in the current study it was found that non-chronic cough was more common in workers who were exposed to bioaerosols. In contrast, no obvious differences were observed between the study groups with respect to airflow limitations. The overall prevalence of spirometrically-determined COPD was 15.3%, which is consistent with recently aggregated epidemiologic data [29].

Respiratory symptoms reported by current compost workers were not associated with COPD. These results are consistent with previous reports on the relationship between respiratory symptoms and spirometric values after stratification for asthma [30]. Chronic bronchitis is one clinical phenotype of COPD [14], but has to be considered as an independent entity, especially with respect to other underlying causes [31]. The underlying mechanism by which respiratory symptoms related to chronic bronchial mucus hypersecretion appear during structural changes in the lung leading to COPD remains unclear; the respiratory symptoms may precede or follow airflow limitation [32]. In former compost workers, it was observed that airflow limitation and cough, as well as chronic bronchitis, were closely associated. Occupational exposures in composting plants pose hazards to the workers due to substances with irritant and/or allergic together with infectious properties [5]. Due to the process of composting, biological waste is usually contaminated with fluctuating levels of microorganisms, predominantly bacteria and moulds. Emission rates of the microorganisms vary depending on conditions of cell growth, e.g. weather conditions and duration of processing cycles. Release of microorganisms and related components is especially enhanced when composting material is moved [3]. Bacteria levels fluctuated between 10^4 CFU/m³ – 10^7 CFU/m³, actinomycetes were measured at approximately 10^5 CFU/m³, and endotoxin concentrations were up to 1,000 EU/m³. Reported fungal concentrations at compost sites range from about 10^4 – 10^7 CFU/m³ and beta (1→3) glucan concentrations to approximately 5,000 ng/m³ [4].

The different tasks are associated with significantly different exposure intensities, which are modulated by technical or personal means of protection. The municipal waste management companies under investigation had only a limited number of employees fulfilling all job tasks without special preference. Therefore, in the presented study, a job exposure matrix was not employed but associations were explored between health effects and duration of employment. Age is associated with certain cumulative lifetime occupational or environmental exposures, allowing for longer exposures to hazards. Nevertheless, after adjusting for age and smoking habits, cough and chronic bronchitis were found more often in current workers who had been employed for more than 10 years in a compost facility. The difference, however, did not reach statistical significance. This may be due to, as described above, the low number of subjects in the different subgroups that limit the power to detect significant associations.

Atopic status and sensitization represent a pathophysiologic basis for the development of immunological diseases such as rhinoconjunctivitis and asthma [25]. After excluding allergic asthmatics, irritation of nose or eyes was still frequently reported in workers who were currently or previously employed

in composting plants. Irritation due to an underlying atopic disease could be suggested only in few workers. Therefore, in the current study nasal and ocular irritation symptoms were defined in terms of MMIS. Furthermore, the higher incidence of chronic bronchitis in former compost workers may reflect a chronic irritative process of airway linings triggered by exposure to bioaerosols. In contrast, subjects never exposed to bioaerosols demonstrated no association between cough and rhinoconjunctivitis. Endotoxins and β -glucans are especially present in bioaerosols [9, 10] and known to play a major role in triggering non-allergic inflammatory processes. A strong association between exposure to fungal spores and irritation symptoms was previously shown in farmers [11]. A previous report was not able to demonstrate marked differences in specific IgE to environmental allergens and moulds in compost workers, compared to non-exposed control subjects [8]. There is evidence that non-allergic inflammatory reactions may be important for symptoms arising from bioaerosol exposure. Endotoxin, a known airway irritant, has been shown to induce chronic bronchitis in animal models [33]. However, the current analysis was not aimed at drawing conclusions on which a specific special agent of exposure may be responsible for morbidity.

The presented results, although limited by study size resulting in a broad 95% CI and an obvious healthy worker effect [34], suggest correlations between irritation of nose and respiratory symptoms due to exposures to bioaerosols in composting plants. Multivariate logistic regression analyses reveal that the prevalence of cough in current workers and of chronic bronchitis in former workers is associated with nasal irritation, where the symptoms are common and usually reversible, and thus not considered a serious condition. The presented results indicate the development of chronic inflammation in the upper airways associated with an increased risk of lower airway disease. Therefore, the current data support a united airway concept, also relevant for non-allergic diseases. Whether work-related nasal irritation could be regarded as a predictor for lower airway disease needs to be confirmed in longitudinal studies evaluating incidences of respiratory diseases. Chronic bronchitis was most common in former workers and strongly associated with airflow limitation. Although this is a cross-sectional study, the data presented support the idea that chronic bronchitis does not necessarily regress when exposure is discontinued.

CONCLUSION

Exposure to bioaerosols is a common health risk for workers in the composting industry and has been reported to be associated with a higher prevalence of respiratory symptoms and illness. Interpretation of the presented multivariate analyses should be undertaken with caution in view of the relatively small number of cases of cough, chronic bronchitis and COPD. Particularly, with respect to the association of work-related MMIS of eyes and nose and lower respiratory tract, analysis of longitudinal studies would be valuable for proving the predictive value of rhinoconjunctivitis. Taking this correlation into consideration may contribute to a better understanding of enhanced exposure or to identify susceptible subjects. Finally, in the long-term, this could reduce the incidence of chronic respiratory diseases while employed at composting facilities.

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REFERENCES

- Domingo JL, Nadal M. Domestic waste composting facilities: a review of human health risks. *Environ Int.* 2009; 35(2): 382–389.
- Schlosser O, Huyard A, Cartnick K, Yañez A, Catalán V, Quang ZD. Bioaerosol in composting facilities: occupational health risk assessment. *Water Environ Res.* 2009; 81(9): 866–877.
- Swan JRM, Kelsey A, Crook B, Gilbert EJ. Occupational and Environmental Exposure to Bioaerosols from Composts and Potential Health Effects: A Critical Review of Published Data, Research report 130, Health and Safety Executive, Norwich, United Kingdom, 2003 <http://www.hse.gov.uk/research/rrpdf/rr130.pdf> (access: 2014.03.13).
- Searl A. Exposure-response relationships for bioaerosol emissions from waste treatment processes, Defra Project: WR0606. Institute of Occupational Medicine (IOM), Edinburgh, United Kingdom, 2008 <http://www.iom-world.org/news-events/news/2010/health-effects-associated-with-bioaerosols-from-waste-handling-processes/> (access: 2014.03.13).
- Bru-Adan V, Wéry N, Moletta-Denat M, Boiron P, Delgènes JP, Godon JJ. Diversity of bacteria and fungi in aerosols during screening in a green waste composting plant. *Curr Microbiol.* 2009; 59(3): 326–335.
- Eduard W, Heederik D, Duchaine C, Green BJ. Bioaerosol exposure assessment in the workplace: the past, present and recent advances. *J Environ Monit.* 2012; 14(2): 334–339.
- Bünger J, Schappler-Scheele B, Hilgers R, Hallier E. A 5-year follow-up study on respiratory disorders and lung function in workers exposed to organic dust from composting plants. *Int Arch Occup Environ Health.* 2007; 80(4): 306–312.
- van Kampen V, Deckert A, Hoffmeyer F, Taeger D, Brinkmann E, Brüning T, et al. Symptoms, spirometry, and serum antibody concentrations among compost workers exposed to organic dust. *J Toxicol Environ Health A.* 2012; 75(8–10): 492–500.
- Rylander R. Organic dust induced pulmonary disease – the role of mould derived beta-glucan. *Ann Agric Environ Med* 2010; 17(1): 9–13.
- Liebers V, van Kampen V, Bünger J, Düser M, Stubel H, Brüning T, et al. Assessment of airborne exposure to endotoxin and pyrogenic active dust using electrostatic dustfall collectors (EDCs). *J Toxicol Environ Health A.* 2012; 75(8–10): 501–507.
- Eduard W, Douwes J, Mehl R, Heederik D, Melbostad E. Short term exposure to airborne microbial agents during farm work: exposure-response relations with eye and respiratory symptoms. *Occup Environ Med.* 2001; 58(2): 113–118.
- Guerra S. Overlap of asthma and chronic obstructive pulmonary disease. *Curr Opin Pulm Med.* 2005; 11(1): 7–13.
- Xu X, Iba MM, Weisel CP. Simultaneous and sensitive measurement of anabasine, nicotine, and nicotine metabolites in human urine by liquid chromatography-tandem mass spectrometry. *Clin Chem.* 2004; 50(12): 2323–2330.
- Global Initiative for Chronic Obstructive Lung Disease (GOLD), “Global Strategy for the Diagnosis, Management and Prevention of COPD,” 2011, available from: <http://www.goldcopd.org/> (access: 2014.03.13).
- American Thoracic Society (ATS). Standardization of spirometry (1994 update). *Am J Respir Crit Care Med.* 1995; 152(3): 1107–1136.
- Hansen JE, Sun XG, Wasserman K. Spirometric criteria for airway obstruction: Use percentage of FEV₁/FVC ratio below the fifth percentile, not < 70%. *Chest.* 2007; 131(2): 349–355.
- Brändli O, Schindler C, Leuenberger PH, Baur X, Degens P, Künzli N, et al. Re-estimated equations for 5th percentiles of lung function variables. *Thorax.* 2000; 55(2): 173–174.
- Linden CC, Misiak RT, Wegienka G, Havstad S, Ownby DR, Johnson CC, et al. Analysis of allergen specific IgE cut points to cat and dog in the Childhood Allergy Study. *Ann Allergy Asthma Immunol.* 2011; 106(2): 153–158.
- Janson C, Anto J, Burney P, Chinn S, de Marco R, Heinrich J, et al. The European Community Respiratory Health Survey: what are the main results so far? *European Community Respiratory Health Survey II.* *Eur Respir J.* 2001; 18(3): 598–611.
- Malinowski A, Backer V, Harving H, Porsbjerg C. The value of exhaled nitric oxide to identify asthma in smoking patients with asthma-like symptoms. *Respir Med.* 2012; 106(6): 794–801.
- Quirce S, Lemièrre C, de Blay F, del Pozo V, Gerth Van Wijk R, Maestrelli P, et al. Noninvasive methods for assessment of airway inflammation in occupational settings. *Allergy.* 2010; 65(4): 445–458.
- Lindberg A, Jonsson AC, Rönmark E, Lundgren R, Larsson LG, Lundbäck B. Prevalence of chronic obstructive pulmonary disease according to BTS, ERS, GOLD and ATS criteria in relation to doctor's diagnosis, symptoms, age, gender, and smoking habits. *Respiration.* 2005; 72(5): 471–479.
- Eduard W, Pearce N, Douwes J. Chronic bronchitis, COPD, and lung function in farmers: the role of biological agents. *Chest.* 2009; 136(3): 716–725.
- de Marco R, Accordini S, Marcon A, Cerveri I, Antó JM, Gislason T, et al.; European Community Respiratory Health Survey (ECRHS). Risk factors for chronic obstructive pulmonary disease in a European cohort of young adults. *Am J Respir Crit Care Med.* 2011; 183(7): 891–897.
- Boulay ME, Boulet LP. The relationships between atopy, rhinitis and asthma: pathophysiological considerations. *Curr Opin Allergy Clin Immunol.* 2003; 3(1): 51–55.
- Sunyer J, Antó JM, Kogevinas M, Soriano JB, Tobias A, Muñoz A. Smoking and bronchial responsiveness in nonatopic and atopic young adults. Spanish Group of the European Study of Asthma. *Thorax.* 1997; 52(3): 235–238.
- Forey BA, Thornton AJ, Lee PN. Systematic review with meta-analysis of the epidemiological evidence relating smoking to COPD, chronic bronchitis and emphysema. *BMC Pulm Med.* 2011; 14(11): 36. doi: 10.1186/1471-2466-11-36.
- Broding HC, Frank P, Hoffmeyer F, Bünger J. Course of occupational asthma depending on the duration of workplace exposure to allergens – a retrospective cohort study in bakers and farmers. *Ann Agric Environ Med.* 2011; 18(1): 35–40.
- Rycroft CE, Heyes A, Lanza L, Becker K. Epidemiology of chronic obstructive pulmonary disease: a literature review. *Int J Chron Obstruct Pulmon Dis.* 2012; 7: 457–494.
- Sunyer J, Basagaña X, Roca J, Urrutia I, Jaen A, Antó JM, et al. Relations between respiratory symptoms and spirometric values in young adults: the European community respiratory health study. *Respir Med.* 2004; 98(10): 1025–1033.
- de Oca MM, Halbert RJ, Lopez MV, Perez-Padilla R, Tálamo C, Moreno D, et al. The chronic bronchitis phenotype in subjects with and without COPD: the PLATINO study. *Eur Respir J.* 2012; 40(1): 28–36.
- Lamprecht B, McBurnie MA, Vollmer WM, Gudmundsson G, Welte T, Nizankowska-Mogilnicka E, et al.; BOLD Collaborative Research Group. COPD in never smokers: results from the population-based burden of obstructive lung disease study. *Chest.* 2011; 139(4): 752–763.
- Harkema JR, Hotchkiss JA. Ozone- and endotoxin-induced mucous cell metaplasias in rat airway epithelium: novel animal models to study toxicant-induced epithelial transformation in airways. *Toxicol Lett.* 1993; 68(1–2): 251–263.
- Bünger J, Antlauf-Lammers M, Schulz TG, Westphal GA, Müller MM, Ruhnau P, et al. Health complaints and immunological markers of exposure to bioaerosols among biowaste collectors and compost workers. *Occup Environ Med.* 2000; 57(7): 458–464.