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# COURSE OF OCCUPATIONAL ASTHMA DEPENDING ON THE DURATION OF WORKPLACE EXPOSURE TO ALLERGENS – A RETROSPECTIVE COHORT STUDY IN BAKERS AND FARMERS

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**Abstract:** The management of occupational asthma requires valid information about prognostic factors. The present study therefore investigates the importance of exposure duration, work cessation, and confounding factors on allergic obstructive airway disease in bakers and farmers. Patients with confirmed allergic occupational airway disease registered in a German Occupational Health Inspectorate received a mailed questionnaire on their respiratory health and employment status. Relations between duration of exposure and course of disease were analysed by multifactorial logistic regression under consideration of confounding variables. 178 patients (65 [36.5%] farmers and 113 [63.5%] bakers) aged between 24 and 74 (mean 42.0 ± standard deviation 12.7) years of age were included in the analysis. Farmers had much more severe respiratory complaints than bakers, and a significantly larger proportion of them (77.5%) had been employed for over 10 years (bakers: 36.6%). Unlike in bakers (Odds-Ratio for a sum score of more than 4 points 6.48 [95%CI 2.04–20.56]), among farmers (OR 1.47 [95%CI 0.30–7.29]) the duration of work under exposure did not independently explain the severity of respiratory complaints. The multivariate statistical analysis confirms the prognostic value of the cessation of work in occupational asthma; this remedy, however, is often not available for farmers.

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**Key words: allergen induced asthma, occupational exposure/adverse effects, prognosis, time factors.**

## INTRODUCTION

Occupational asthma is the most common occupational airway disease in developing and industrialized countries with a proportion of roughly 15% of all asthma cases and an annual incidence of up to 18/100,000. Despite intensive efforts towards prevention, there is no compelling evidence for a decline in its frequency [9, 10, 13]. This may be partly explained by the introduction of new, potentially allergenic substances in production and processing that undo the effect of preventive measures taken previously [5]. Occupational asthma is internationally under-estimated, poorly diagnosed and managed, as well as inadequately compensated. Interactions between allergen exposure, genetic susceptibility, concomitant smoking, and co-morbid diseases hugely complicate both diagnosis and prevention [17].

Occupational asthma is an airway disease caused by workplace exposure to airborne allergens in terms of dusts, gases or aerosols [6]. The occupations and industries associated with an increased risk of developing work-related

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asthma show a marked regional and socio-economical variation. Exposure to isocyanates, cereal flour/grain dust, wood dust and hairdressing chemicals being the most common asthma causes in industrialised countries [11]. While allergic occupational asthma is in principle reversible at the beginning, prolonged exposure leads to chronic, structural changes in the airway system that eventually sustain even after allergen withdrawal [4, 10]. As a result, remnants of occupational asthma are responsible for up to 20% of cases of chronic obstructive pulmonary disease (COPD) [18].

While the prognostic value of allergen withdrawal is not unchallenged [12], patients with occupational asthma are generally advised to avoid further allergen exposure [14]. Furthermore, duration of employment in exposed workplaces has been shown to be positively associated with the severity of symptoms of airway diseases [19]. Despite certain advances in development and application of protective gear [9], the only way to avoid exposure is often relocation within the workplace or, almost invariably, a change of occupation [14]. The economical impact of this is severe, both for the patient and the respective social institution funding the change of occupation. In Germany, the Employers' Liability Insurance Association (Berufsgenossenschaft) subsidizes the vocational re-training of employees with confirmed occupational asthma. Under the recent economical pressures of increasing compensations, a certain tendency towards avoiding this can be observed [3]. Since 1993, the German insurance association for the food industry, for instance, has attempted to leave bakers with occupational asthma in the same employment under close medical scrutiny and improved working conditions, rather than paying for their re-training.

Another profession that is particularly at risk for developing occupational asthma are farmers who inhale several types of organic matter commonly referred to as 'organic dust'. Organic dust contains particles (e.g. grain, soil, animal faeces, hair) as well as moulds and other microorganisms, and can evoke immuno-allergic reactions such as rhinitis, asthma and extrinsic allergic alveolitis [1, 7, 15, 16]. For farmers, the system of re-training subsidy is basically the same; however, farmers are mostly self-employed and run their farms as a family enterprise, making a change of occupation not feasible and/or desirable in many cases.

This socio-economical difference provides an opportunity to assess the value of discontinuation of work in an allergen-burdened workplace: Considering the underlying mechanisms of occupational asthma in bakers and farmers – including the allergens – are fairly similar, a change of occupation occurs much more frequently and/or easier, as well as earlier, in bakers then in farmers. Hence, we compared the prevalence and severity of respiratory symptoms in a cohort of bakers and farmers with occupational asthma confirmed by the Occupational Health and Safety Inspectorate physicians, and investigated the influence of the duration of employment under exposure to common allergens.

## MATERIALS AND METHODS

**Study sample.** All cases of occupational obstructive airway disease that had been officially registered in the region of northern Bavaria (Occupational Health and Safety Inspectorates Regensburg, Würzburg and Nuremberg) between 1995–2003 were examined for confirmed allergic occupational asthma, diagnosed by certified occupational health practicioners. Out of a total of 2,693 scrutinized files, 729 (27.1%) met the confirmed diagnosis of occupational asthma in bakers or farmers. After giving their written consent to take part in the study, the participants received a standardized self-administered questionnaire regarding their current and past employment and their current health status by the Occupational Health and Safety Inspectorate. The questionnaire was returned in usable form by 257 patients (35.3% response rate) – 65 farmers (25.3%) and 113 bakers (44.0%). 79 participants were working in several other professions (such as health care workers, florists, hairdressers, painters and joiners) who were not included in the analysis. Thus, the study sample consisted of 178 patients whose basic data are displayed in Table 1.

**Questionnaire.** The questionnaire included questions regarding health and occupation-related topics:

- (1) Presence of lower airway complaints (asthma, constriction, dyspnea), (2) upper airway complaints (sneezing, rhinorrea, blocked nose), or (3) coughing and expectoration without the presence of a common cold;
- (4) Consultation of a physician because of respiratory symptoms;
- Step 1 to Step 5 medication (according to the WHO GINA scheme [8]) because of respiratory symptoms;

**Table 1.** Basic data of the study sample (valid cases).

| | All subjects | Farmers | Bakers |
|---|---|---|---|
| Respondents | 178 (100%) | 65 (36.5%) | 113 (63.5%) |
| Age (mean ± SD) | 42.0±12.7 | 51.1±12.8 | 37.2±10.9 |
| Up to 40 years | 93 (54.4%) | 15 (23.8%) | 78 (72.2%) |
| Over 40 years | 78 (45.6%) | 48 (76.2%) | 30 (27.8%) |
| No response | 7 subjects | 2 subjects | 5 subjects |
| Male | 113 (63.8%) | 38 (58.5%) | 75 (67.0%) |
| Female | 64 (36.2%) | 27 (41.5%) | 37 (33.0%) |
| No response | 1 subject | | 1 subject |
| Duration of work under allergen exposure (mean ± SD) | 14.9±13.0 | 23.9±13.7 | 11.3±11.8 |
| Up to 10 years | 63 (48.1%) | 11 (22.5%) | 52 (63.4%) |
| Over 10 years | 68 (51.9%) | 38 (77.5%) | 30 (36.6%) |
| No response | 47 subjects | 16 subjects | 31 subjects |
| Smoker | 45 (25.6%) | 11 (17.2%) | 34 (30.4%) |
| Non-Smoker | 131 (74.4%) | 53 (82.8%) | 78 (69.6%) |
| No response | 2 subjects | 1 subject | 1 subject |

SD – standard deviation

**Table 2.** Frequency of respiratory symptoms and therapeutic interventions in the different profession groups.

| Symptom | Farmers | Bakers | Significance |
|---|---|---|---|
| Lower airway complaints | 48 (73.8%) | 51 (45.1%) | $p<0.001$ |
| Upper airway complaints | 53 (81.5%) | 65 (57.5%) | $p<0.01$ |
| Coughing/expectoration | 45 (69.2%) | 41 (36.3%) | $p<0.0001$ |
| Physician consulted | 46 (70.8%) | 43 (38.1%) | $p<0.001$ |
| Medication | | | $p<0.0001$ |
| None | 14 (21.5%) | 75 (66.4%) | |
| Step 1 | 6 (9.2%) | 9 (8.0%) | |
| Step 2 | 12 (18.5%) | 7 (6.2%) | |
| Step 3 | 20 (30.8%) | 18 (15.9%) | |
| Step 4 | 13 (20.0%) | 4 (3.5%) | |
| Step 5 | – | – | |
| Medication, step > 2 | 33 (50.8%) | 22 (19.5%) | $p<0.0001$ |
| Sum score (mean±SD) | 5.5±2.4 | 3.0±2.8 | $p<0.0001$ |
| ≤4 points | 23 (35.4%) | 78 (69.0%) | $p<0.0001$ |
| >4 points | 42 (64.6%) | 35 (31.0%) | |

SD – standard deviation

- Smoking status;
- Sick-leave because of respiratory symptoms;
- Occupation, past and current, and employment status, changes of employment status due to occupational asthma.

Respiratory health status was assessed with a sum score consisting of one point for the health-related questions 1–4 and each medication step; the sum score was employed for statistical analysis.

**Data analysis.** All statistical analyses were performed using the SPSS statistical package (version 14.0, SPSS Inc., Chicago, IL). Categorical variables were evaluated with the $\chi^2$-test, and the between-groups difference in metric variables was assessed with the non-parametric U-test since data was not normally distributed. The possible influence of confounding variables such as age, sex and smoking status was evaluated with the logistic regression analysis [2]. This method allows for estimation of the relative risk of a disease in retrospective studies ("Odds-Ratio, OR") and adjustment of the OR for confounding variables. Age (≤ *vs.* > 40 years) and employment duration (≤ *vs.* > 10 years) were dichotomized for this analysis. Statistical significance was stated for $p<0.05$.

## RESULTS

Farmers were significantly older than bakers (51.1±12.8 years *vs.* 37.2±10.9 years, $p<0.0001$) and had been employed significantly longer (23.9±13.7 *vs.* 11.3±11.8 years, $p<0.0001$); the proportion of farmers employed for over 10 years was 77.5%, compared to only 36.6% in bakers ($p<0.0001$).

Practically all patients in the sample had given up their profession because of occupational asthma (167 of 178, 93.8%), and only few individuals were still employed in their occupation. This fraction was significantly higher in farmers than in bakers (12.3 *vs.* 2.7%, $p=0.010$).

Respiratory symptoms and therapeutic interventions were frequent in the study sample. Individuals reported lower airway complaints in 55.6%, upper airway complaints in 66.3%, coughing and expectoration in 50.0% (all in the absence of a common cold), airway-related consulting a physician in 50.0%, any medication in 50.0%, and stage 2 or higher medication in 30.9% of the cases, respectively. The average sum score was 3.92±2.90 (median, 4) points, and 43.3% of patients had a score of more than 4 points. Table 2 shows the frequency of symptoms in the different professions. Complaints were consistently much more common in farmers than in bakers, and these differences were statistically significant in all instances ($p<0.001$ for lower and $p<0.01$ for upper airway complaints, respectively, $p<0.0001$ for coughing, medication and the sum score, and $p<0.001$ for physician consultation). Whereas two-thirds of the farmers had a sum score of more than 4 points, the ratio in bakers was almost exactly reciprocal. Farmers were 4 times more likely to have a sum score of over 4 points than bakers (Unifactorial analysis: OR 4.03 [95%CI 2.13–7.66]).

Employing logistic regression analysis, the association between outcome and age, gender, duration of employment under exposure, smoking status and profession, respectively, was analyzed (Tab. 3). The only factor consistently and independently associated with more severe symptoms was an age above 40 years; duration of employment under exposure also had an influence on medication and the sum score. Being a farmer was consistently associated with more severe symptoms, but only independently with regard to coughing and medication.

In the subgroup of farmers, the only independent factor exerting an influence on respiratory symptoms was age. This was statistically significant for the occurrence of lower airway complaints (OR 6.58 [95%CI 1.71–25.31], $p=0.0052$), consulting a physician (OR 5.42 [95%CI 1.43-20.54], $p=0.0112$), step 2 or higher medication (OR 6.17 [95%CI1.42–26.72], $p=0.013$) and the sum score (OR 6.06 [95%CI 1.58–23.17], $p=0.007$; Tab. 4). Patients over 40 years of age were 6 times more likely to have a score over 4 points than those under 40. Neither sex, continuance in their work environment or smoking status had a significant influence on the sum score or the individual expression of symptoms.

In bakers, an influence of age was identified for lower airway complaints (OR 3.98 [95%CI 1.46–10.82], $p=0.0062$), coughing and expectoration (OR 3.57 [95%CI 1.29–9.94], $p=0.0136$), consulting a physician (OR 4.24 [95%CI [1.51–11.95], $p=0.057$), step 1 or higher medication (OR 3.62 [95%CI 1.33–9.80], $p=0.011$), and the sum score (OR 4.49 [95%CI 1.53–13.21], $p=0.006$) (Tab. 4). In

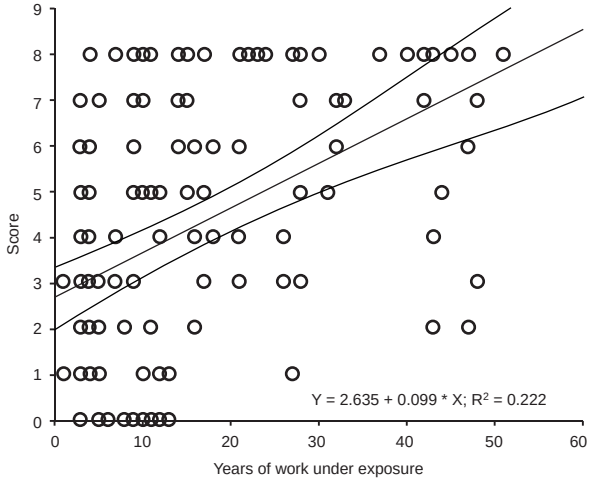


**Figure 1.** Regression between employment duration and symptom score. Regression function with 95% confidence bands for the mean.

contrast to the farmers, however, the continuance in their work environment also had a significant impact on respiratory symptoms. Bakers who had been working for more than 10 years quoted more often symptoms of the upper airways (OR 4.50 [95%CI 1.44–14.02], p=0.009), consulting a physician (OR 4.60 [95%CI 1.53–13.80], p=0.006), step 1 (OR 3.65 [95%CI 1.25–10.66], p=0.0017) and step 2 medication (OR 4.21 [95%CI 1.21–14.69], p=0.0226). In addition, smoking bakers reported cough and expectoration more often (OR 3.91 [95%CI 1.49–10.22]) than non-smoking bakers, an association that was absent in farmers. Female bakers were three times more likely to have a sum score over 4 than males (OR 2.99 [95%CI 1.05–8.48]) (Tab. 4).

**Table 4.** Odds-Ratio [95% CI] for multifactorial logistic regression analysis of influence of age, gender, duration of exposure and smoking status on respiratory sum score in farmers and bakers.

| | Farmers | Bakers |
|---|---|---|
| Age over 40 years | 6.06 [1.58–23.17] | 4.49 [1.53–13.21] |
| Female gender | 1.09 [0.33–3.62] | 2.99 [1.05–8.48] |
| On the job for over 10 years | 1.47 [0.30–7.29] | 6.48 [2.04–20.56] |
| Smoker | 0.55 [0.12–2.47] | 1.90 [0.66–5.45] |

The time of workplace exposure was significantly ($p<0.05$), but rather weakly ($R^2=0.222$) related to the symptom score. However, low scores after long employment duration where found as well as high scores after short duration (Fig. 1), which means, based on our data, that a direct 'dose'-dependency of symptoms or a certain threshold time after which certain effects can be expected, could not be established. Only 11 affected individuals (3 bakers and 8 farmers) in our sample had not given up working in their profession, analysis of this subgroup was therefore not possible.

**Table 3.** Odds-Ratio [95% CI] for multifactorial logistic regression analysis of influence of age, gender, duration of exposure, smoking status and occupation on respiratory symptoms (farmer *vs.* bakers).

| | Lower airway complaints | | Upper airway complaints | |
|---|---|---|---|---|
| | Odds Ratio [95%CI] | p-value | Odds Ratio [95%CI] | p-value |
| Age over 40 years | 4.62 [2.11–1013] | 0.0001 | 2.14 [0.95–4.80] | 0.0631 |
| Female gender | 1.74 [0.85–3.55] | 0.1260 | 1.76 [0.84–3.68] | 0.1285 |
| Occupied >10 yrs. | 1.09 [0.47–2.54] | 0.8321 | 2.11 [0.89–4.96] | 0.0861 |
| Smoker | 1.52 [0.69–3.33] | 0.2936 | 1.40 [0.64–3.08] | 0.3990 |
| Farmer | 1.82 [0.83–3.97] | 0.1319 | 1.83 [0.79–4.20] | 0.1535 |
| | Coughing | | Physician consulting | |
| | Odds Ratio [95%CI] | p-value | Odds Ratio [95%CI] | p-value |
| Age over 40 years | 2.85 [1.31–6.19] | 0.0077 | 4.34 [1.98–9.51] | 0.0002 |
| Female gender | 1.49 [0.73–3.04] | 0.2708 | 2.18 [1.04–4.58] | 0.0375 |
| Occupied >10 yrs. | 1.50 [0.64–3.49] | 0.3497 | 2.30 [0.98–5.39] | 0.0530 |
| Smoker | 2.76 [1.23–6.21] | 0.0132 | 1.02 [0.46–2.25] | 0.9705 |
| Farmer | 2.63 [1.21–5.72] | 0.0136 | 1.55 [0.71–3.39] | 0.2674 |
| | Medication, any step | | Sum score | |
| | Odds Ratio [95%CI] | p-value | Odds Ratio [95%CI] | p-value |
| Age over 40 years | 2.92 [1.33–6.41] | 0.0071 | 4.63 [2.09–10.27] | 0.0001 |
| Female gender | 1.49 [0.69–3.21] | 0.3007 | 1.91 [0.90–4.09] | 0.0913 |
| Occupied >10 yrs. | 3.15 [1.31–7.57] | 0.0097 | 2.70 [1.12–6.51] | 0.0256 |
| Smoker | 0.72 [0.31–1.69] | 0.4528 | 1,27 [0.55–2.92] | 0.5784 |
| Farmer | 3.59 [1.62–7.97] | 0.0015 | 1.60 [0.73–3.52] | 0.2366 |

## DISCUSSION

The course of occupational asthma is an issue with a major economical impact in industrialized countries. Most social security systems provide some means of funding the required re-training of affected employees who have to give up their jobs/work because of the offending exposure to workplace allergens. In Germany, it is the Employers' Liability Insurance Association that subsidizes vocational re-training. The prognostic value of removal from the workplace at a certain point in an individual's medical history has been subject of intensive debate for a long time. First of all, 3 basic models for the course of occupational asthma coexist at the moment, none of which can be confirmed or ruled out by available evidence:

1. The condition is generally *reversible*, i. e. symptoms improve after allergen withdrawal.
2. The condition is generally *irreversible*, i.e. symptoms persist (and/or progress) irrespective of allergen withdrawal.
3. The reversibility of symptoms *depends on the time of workplace exposure*.

Furthermore, certain occupational allergens are not restricted to workplaces but can also occur in people's private environment – quite possibly in a hidden form. Hence, allergen exposure may persist even after a change of workplace and/or profession. This influence may blur or entirely undo the beneficial effect of vocational re-training and has to be considered in studies dealing with occupational airway disease. Considering the economic backdrop of this issue, careful research is required.

The present study attempts to clarify this issue somewhat by comparing 2 groups of patients many similarities in the biological aspects of their disease, but distinct differences in their socio-economical background: bakers and farmers. The key difference between these two is the economical pressure that prevents them from following the suggestions of their medical advisors in cases of relevant occupational asthma. Whereas for bakers vocational re-training is mostly a feasible alternative, farming in Germany is mainly based on self-employment and family enterprises – an environment where, very often, the impact of a change of profession is only acceptable when there is no other alternative. This difference is clearly reflected in our study sample. More than twice as many farmers (roughly ¾) had been persistently working exposed to workplace allergens for over 10 years as compared to bakers, and the mean continuance in their work environment was twice as long (24 *vs.* 12 years).

Thus, it may be assumed that more severe symptoms are required to convince a farmer to give up his job, and this seems to be confirmed by our results. The proportion of farmers with a respiratory sum score of over 4 was twice as high in comparison to bakers.

Biological and allergological criteria alone can not explain the difference in the severity of symptoms. A different 're-training threshold' in bakers and farmers therefore seems to be the most probable interpretation of our results: in bakers, current symptom severity was independently and substantially influenced by the duration of their employment under allergen exposure; in farmers no such relationship was observed. Since the medical criteria for confirming occupational asthma and approving vocational re-training by the Occupational Health and Safety Inspectorates do not differ between bakers and farmers, the difference in actual symptoms is best explained by the course of disease after re-training rather than baseline differences.

Assuming that the third model mentioned previously (i.e., reversibility of symptoms depends on the time of workplace exposure) is appropriate, this would mean that farmers have stayed employed in their occupation beyond the 'point of no return', where is too late to benefit from allergen removal. In our view, this is the most convincing explanation of the results, but obviously not the only one. First of all, it depends on sufficient evidence for the relevance of time factors for the course of occupational asthma after cessation of exposure.

In conclusion, our results suggest – albeit do not prove – that cessation of work in an allergen-burdened environment is beneficial for the course of occupational allergic asthma. Indications of this are certain differences between farmers and bakers who are suffering from this disease:

1. Farmers had much more severe symptoms than bakers.
2. A significantly larger proportion of farmers had been employed in their occupation for over 10 years, as compared with bakers.
3. Unlike in bakers, in farmers, time of workplace exposure on its own did not explain the severity of respiratory symptoms.

Multivariate statistical analysis confirmed the prognostic value of cessation of work in occupational asthma that is, however, often not feasible for farmers who frequently own their own family enterprise.

Vocational re-training of affected patients should be generously subsidized in order to minimize the risk of irreversible obstructive airway disease and reduce the overall socio-economical expenditure on occupational asthma. Further research on the course of occupational asthma after cessation of work is required to confirm our results, for which a prospective study design is recommended. Responsible benefactors should generously subsidize vocational re-training of affected patients in order to minimize the risk of irreversible obstructive airway disease, and reduce the overall socio-economical expenditure on occupational asthma.

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