

Original article

Respiratory allergy in apprentice bakers: do occupational allergies follow the allergic march?

Background: This prospective study describes the incidence, risk factors and natural history of occupational respiratory allergy in apprentice bakers.

Methods: Two hundred and eighty-seven apprentice bakers were examined using a questionnaire, skin prick tests (SPTs) to common and occupational allergens, evaluation of total serum IgE level and specific anti-flour and α -amylase IgE, before, 1 year and 2 years after the onset of vocational training. To diagnose occupational respiratory disease, spirometry, histamine and allergen-specific inhalation challenge tests were performed.

Results: The incidence of work-related chest symptoms was 4.2% in the first year and 8.6% in the second year of exposure. Hypersensitivity to occupational allergens developed in 4.6 and 8.2% of subjects, respectively. The incidence of occupational allergic rhinitis was 8.4% after 1 year and 12.5% after 2 years, and that of occupational asthma/cough-variant asthma 6.1 and 8.7%, respectively. The latency period of work-related rhinitis symptoms was 11.6 ± 7.1 months and chest symptoms 12.9 ± 5.5 months. Only in 20% of occupational asthmatics could allergic rhinitis be diagnosed a stage earlier. In 21 out of 25 subjects with occupational asthma, chronic cough was the sole clinical manifestation of the disease. Stepwise logistic regression analysis revealed that positive SPT to common allergens was a significant risk factor of hypersensitivity to occupational allergens (OR = 10.6, 95% CI 5.27; 21.45), occupational rhinitis (OR = 3.9, 95% CI 1.71; 9.14) and occupational asthma (OR = 7.4, 95% CI 3.01; 18.04). Moreover, positive SPT to occupational allergens on entry to the training was a significant risk factor of asthma (OR = 6.9, 95% CI 0.93; 51.38).

Conclusions: The incidence of occupational asthma and rhinitis in apprentice bakers is high and increases with the duration of exposure. Skin reactivity to common and occupational allergens is the main risk factor of bakers' asthma. Most cases of work-related respiratory symptoms among apprentice bakers are related to a specific sensitization. In most subjects who developed occupational asthma, rhinitis occurred at the same time as the chest symptoms did.

**J. Walusiak¹, W. Hanke², P. Górski³,
C. Pałczyński¹**

¹Department of Occupational Diseases & Occupational and Environmental Allergy Centre;

²Department of Environmental Epidemiology, Nofer Institute of Occupational Medicine, Lodz;

³Department of Pulmonology and Allergology, Medical University of Lodz, Poland

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Jolanta Walusiak, MD, PhD
Department of Occupational Diseases
Nofer Institute of Occupational Medicine
8 Teresy St.
90-950 Lodz
Poland

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Baker's respiratory allergy is reported to be a major form of occupational allergy in many countries (1–4). Cross-sectional studies of bakers have shown the prevalence of allergic rhinitis ranging from 14 to 39% and that of asthma from 4.9 to 10% (3, 5–8). On the other hand, it was estimated that only about one-third of bakers with work-related symptoms are sensitized to occupational allergens (1). It remains of interest whether this may be due to nonallergic mechanisms or to methodological shortcomings of the cross-sectional studies (9). However, this observation was also confirmed by follow-up studies, e.g. Gautrin et al. reported that only three out of 30 apprentices with work-related symptoms of rhinoconjunctivitis had been sensitized to flour (10).

Although a number of studies have been performed on subjects exposed to high-molecular-weight (HMW) allergens (1, 3, 4, 8), the prospective studies in this population are much less common, especially those performed on bakers who were not exposed to flour prior to observation. Only Gautrin et al. and De Zotti and Bovenzi conducted studies on apprentice workers under exposure to high-molecular-weight allergens (11, 12). To our knowledge, none of the studies employed a specific challenge test that is the gold standard in the diagnosis of occupational respiratory allergy.

The aim of the present project was to evaluate the incidence, risk factors and natural course of occupational respiratory allergy in apprentice bakers. The baseline for our observation was the onset of vocational training.

Materials and methods

Subjects

The study group considered for final analysis comprised 287 apprentice bakers from three country districts of Poland. When enrolled for the study, they were in the first month of their vocational training. The initial cohort consisted of 461 trainees, but 174 subjects did not continue the training. All of them were interviewed by phone about the reasons for quitting the training and when possible, additional laboratory tests were performed. One subject who reported asthma and admitted to be on asthma medications was not enrolled for the study.

None of the other apprentice workers reported taking antihistamine or antiasthmatic medications. All the subjects were examined three times: on the entry to vocational training (stage I), after 1 year (stage II) and after 2 years (stage III) of training. A group of 47 subjects reporting the onset of work-related respiratory symptoms underwent additional laboratory assays.

The Regional Bioethical Committee approved the study protocol. All the participants gave their informed consent prior to the study.

Questionnaire

On the day of medical examinations, the subjects were administered a questionnaire that was an adaptation of the instrument developed by the International Union against Tuberculosis and Lung Disease (13). It included a history of physician-diagnosed allergic diseases, personal and family history of atopy, tobacco smoking status, exposure to pet allergens at home, housing conditions (new or old building) and area of residence (urban or rural). The questionnaire was always administered by a physician. The symptoms suggestive of asthma included wheezing, chest tightness, shortness of breath or cough under normal conditions or induced by exercise, exposure to cold air, smoke, dust or strong odours. The smoking status was denominated by three categories: current smokers, ex-smokers and nonsmokers. Smokers were defined as the subjects who reported smoking cigarettes at present. Ex-smokers were the subjects who used to smoke daily and gave up the habit since at least a month prior to the survey. Nonsmokers were those who had never smoked. Passive smokers were defined as nonsmokers who reported sharing a house with one or more smokers.

The incidence of respiratory work-related symptoms was defined as the onset of work-related nasal or chest symptoms during the follow-up. It was calculated separately for each year of follow-up – at stages II and III, and for the whole observation period (cumulative incidence).

Skin prick tests

Skin prick tests (SPTs) were performed on the volar part of the forearm with a standard battery of common allergens and bakery series, including tree and grass pollens, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, moulds, feathers, threshing, oatmeal, wheat, corn, barley and rye flour (Allergopharma, Reinbek, Germany), house dust and bakery dust (Stallergen, Antony, France). Negative control was allergen diluent and the positive one being 1 mg/ml histamine dihydrochloride solution. The largest wheal diameter was assessed after 15 min. Positive reaction was defined as a wheal diameter of at least 3 mm with no reaction to the diluent and a positive reaction to histamine. New specific SPT reactivity was defined as a change in skin reactivity to allergen from absent to present.

Total and specific IgE

Total serum IgE was evaluated at the onset and termination of the study, with the use of the Uni-CAP system (Pharmacia Diagnostics, Uppsala, Sweden). Total IgE level greater than 100 kU/l was regarded as elevated.

The presence of specific IgE antibodies against wheat, barley and rye flour and anti- α -amylase was demonstrated using allergen CAPS (Phadezym fx20, k87, Pharmacia Diagnostics, Uppsala, Sweden). The results were expressed quantitatively in kilounits per litre (kU/l), considered positive at values higher than 0.35 kU/l and also presented in classes (14). In all subjects, the detection of specific IgE was performed at stage III. Additionally, in subjects with positive SPT at the onset of the study and in randomly selected 20 other subjects, specific IgE was determined in samples collected at stage I.

Inhalation challenge tests

Provocation tests with wheat, rye, corn, barley or oatmeal flour were performed in a worksite simulation setting (room space 6 m³) with the patient's own samples. The patient was sifting approximately 100 g of each kind of flour and 10 g of bakers' additives for 30 min. Potato flour was used as placebo. The total dust concentration during the challenge was estimated to be 25 ± 5 mg/m³.

The number of sneezes and the degree of mucosal oedema, rhinorrhea and itching were evaluated. Total symptom score (SS) ranged from 0 to 8 and represented the sum of the scores for sneezing (0 sneezes, 0 point; one to four sneezes, 1 point; more than four sneezes, 2 points), rhinorrhea (none, 0 points; mild, 1 point; abundant, 2 points), mucosal oedema (none, 0 points; mild, 1 point; nasal block, 2 points) and itching (none, 0 points; itching of the nose or throat, 1 point; itching of the nose and throat, 2 points) (15).

Cellular and biochemical compositions of nasal washings were analysed. All the procedures were performed as in the 'nasal pool' method (16). Nasal washings were collected immediately before the provocation and 30 min, 4 h and 24 h later. The processing of nasal washings has been described in detail elsewhere (17).

Pulmonary function

Resting spirometry (Vicatest 2A, Mijnhardt, The Netherlands) was performed in all subjects reporting chest symptoms. Bronchial response was measured by serial monitoring of forced expiratory volume in 1 s (FEV₁) and peak expiratory flow rate (PEFR) before and 5 min, 30 min, 1 h, 2 h, 4 h, 6 h and 24 h after the provocation. All the subjects were instructed beforehand on how to use the peak flow meter for hourly PEF measurements.

Histamine challenge was performed according to Cockcroft et al. (18). Bronchial response was measured by FEV₁ monitoring. The nonspecific bronchial hyper-reactivity was evaluated on the day before specific challenge test and 24 h after the test.

Diagnostic criteria for occupational hypersensitivity, allergic rhinitis and bronchial asthma or cough-variant asthma

Hypersensitivity to occupational allergens has been defined as at least one positive result of SPT to occupational allergens or positivity of specific serum IgE assay (19). Diagnosis of occupational allergic rhinitis was based on questionnaire data and positive nasal response to provocation test, i.e. total score of more than 3 points (15) and a significant increase in the proportion of eosinophils and in the permeability index (17).

Occupational asthma/cough-variant asthma was recognized in subjects reporting work-related chest symptoms, for whom a specific challenge test induced significant bronchial response (at least a 20% decrease in FEV₁) – early or dual asthmatic reaction, or a threefold increase in nonspecific bronchial hyper reactivity.

Statistical analysis

Continuous variables were expressed as mean values $\pm$ standard deviations (SD), whereas the nominal variables as numbers and percentages. Chi-squared test was used to evaluate differences between the incidence of the study outcomes at subsequent stages.

The study outcomes were: hypersensitivity to occupational allergens, occupational allergic rhinitis and occupational asthma. Independent variables in the analyses were assessed at baseline: sex, history of conjunctivitis, seasonal or persistent rhinitis, respiratory symptoms suggestive of asthma under usual conditions, or such condition as cold air and exercise, physician-diagnosed asthma and other allergic diseases, family history of atopy, smoking status, contact with pets, housing conditions, residence area, positive results to at least one and to individual of common and occupational allergens, elevated total IgE level. The prevalence, i.e. the proportion of the group presenting the analysed factors on the entry into the study was calculated. To evaluate the risk factors of health outcomes under the study, the odds ratios (ORs) and their 95% confidence intervals (CI) were calculated using EPI INFO (CDC, Atlanta, GA, USA) program. Factors found to be significant in univariate analysis were included into the stepwise logistic regression model (EGRET statistical software). The analysis of the risk factors of hypersensitivity to bakers' allergens concerned the group of 51 subjects who developed occupational hypersensitivity during the follow-up period, and 231 persons who remained nonsensitized up to the end of the study (five subjects with positive SPT to occupational allergens at stage I were excluded). The analysis of the risk factors of occupational allergic rhinitis covered the group of 36 persons with disease and the remaining 251 persons. Analogical analysis was performed for 25 apprentices with occupational asthma and 262 disease-free subjects. The *P* value below 0.05 was adopted as the reference for selecting significant risk factors.

Results

The baseline characteristics are summarized in Table 1. The mean age of the subjects at the beginning of the study was 16.2 ± 0.5 years. The group consisted of 212 males and 75 females.

The rate of symptoms reported at the enrolment for the study and after 1 and 2 years of vocational training are presented in Table 2. The incidence of all symptoms was higher in the second year of training, but the differences were not statistically significant. Rhinitis was reported most frequently – 16.5% of subjects developed rhinitis symptoms during the observation period. All subjects reporting new respiratory symptoms at stages II and III considered these symptoms to be work-related. Moreover, 10/16 subjects who developed conjunctivitis and 17/20 who observed skin symptoms during the follow-up attributed their symptoms to occupational exposure.

Dyspnoea and chronic cough, according to the patients' history, developed after 13.7 ± 6.6 and

Table 1. Characteristics of the study population obtained from the survey of 287 apprentice bakers

	Stage I
Age (mean $\pm$ SD) (years)	16.19 $\pm$ 0.47
Sex	
Male	212 (73.9%)
Female	75 (26.1%)
Smoking status	
Active smokers	32 (11.2%)
Ex-smokers	0
Passive smokers	232 (80.8%)
Family history of atopy	38 (13.2%)
Pets at home	157 (54.7%)
Residence	
Rural	136 (47.4%)
Urban	151 (52.6%)
Housing	
Old	139 (48.4%)
New	148 (51.6%)

13.6 ± 4.3 months, respectively, which was almost after the same time as for rhinitis (13.5 ± 6.6 months), and only the latency period for wheezing was longer (15.1 ± 5.1 months).

During the 2 years of vocational training, 18.9% of apprentices developed hyper reactivity to at least one allergen, including 18.0% of subjects to common allergens and 12.4% to occupational allergens (Table 3). The incidence of skin reactivity to all individual allergens tested is presented in Table 3. At stage III, the most frequent allergens of skin reactivity were *D. pteronyssinus*, *D. farinae*, house dust and grass pollens. In 18 out of 38 subjects sensitized to flour, sensitization to grass pollens was also found.

The mean total IgE level, evaluated at the onset of vocational training, was 141.2 ± 309.8 kU/l and it was elevated in 81 subjects (28.2%). After 2 years of training, the mean total IgE level was 211.3 ± 105.1 kU/l and the proportion of subjects with elevated values approximated 32.4% (*n* = 93). At stage I, none of the examined subjects displayed the presence of allergen-specific IgE. Two years later, specific IgE was found in 47 subjects (16.3%): in 43 cases for antiwheat, barley and rye flour (10 in class 3, nine in class 2 and 24 in class 1) and in 31 cases for anti- α -amylase (nine in class 2 and 22 in class 1) (data not presented in tables).

Generally, during the 2 years of vocational training, 51 subjects (17.8%) developed hypersensitivity to occupational allergens. In 16 cases, the presence of specific IgE was the only marker of occupational sensitization. In 27 out of sensitized subjects (52.9%), the development of occupational hypersensitivity was preceded by skin reactivity to common allergen at an earlier stage.

Thirty-seven sensitized persons and 10 others reported work-related respiratory symptoms. All of them were subjected to additional laboratory assays, including inhalation challenge. Such testing confirmed occupational

Table 2. The baseline prevalence and the incidence of all reported symptoms of suspected allergic origin in apprentice bakers after 1 year and after 2 years of vocational training ($n = 287$)

Reported symptoms	Stage I [n (%)]	Incidence at stage II [n (%)]	Incidence at stage III [n (%)]	Cumulative incidence at stage III [n (%)]
Chest symptoms	7 (2.4)	12 (4.3)	23 (8.6)	35 (12.5)
Chronic cough	6 (2.1)	12 (4.2)	21 (7.8)	33 (11.7)
Wheezing	1 (0.3)	5 (1.7)	10 (3.6)	15 (5.2)
Dyspnoea	1 (0.3)	1 (0.3)	3 (1.1)	4 (1.4)
Rhinitis	9 (3.1)*	18 (6.5)	28 (10.8)	46 (16.5)
Conjunctivitis	8 (2.8)	4 (1.4)	12 (4.4)	16 (5.7)
Skin symptoms	8 (2.8)	7 (2.5)	13 (4.8)	20 (7.2)
Any symptoms	27 (9.4)	20 (7.7)	30 (12.5)	50 (19.2)

* In six subjects, seasonal allergic rhinitis was recognized due to grass pollens.

Table 3. Development of the hypersensitivity to common and occupational allergens in the group of 287 apprentice bakers

Positive SPT with:	Prevalence at stage I [n (%)]	Incidence at stage II [n (%)]	Incidence at stage III [n (%)]	Cumulative incidence at stage III [n (%)]
At least one allergen	55 (19.2)	20 (8.6)	24 (11.3)	44 (18.9)
Common allergens	54 (18.8)	19 (8.1)	23 (10.7)	42 (18.0)
House dust	8 (2.8)	17 (5.9)	21 (7.3)	38 (13.3)
<i>Dermatophagoides pteronyssinus</i>	30 (10.5)	8 (2.8)	12 (4.2)	20 (6.9)
<i>Dermatophagoides farinae</i>	23 (8.0)	7 (2.4)	19 (6.6)	26 (9.1)
Grass pollens	17 (5.9)	6 (2.1)	16 (5.6)	22 (7.7)
Tree pollens I*	8 (2.8)	11 (3.8)	9 (3.2)	20 (6.9)
Tree pollens II†	8 (2.8)	6 (2.1)	8 (2.8)	10 (3.5)
Moulds I‡	1 (0.4)	2 (0.7)	7 (2.4)	9 (3.1)
Moulds II¶	2 (0.7)	4 (1.4)	8 (2.8)	12 (4.2)
Feathers	5 (1.7)	1 (0.4)	9 (3.2)	10 (3.5)
Occupational allergens	5 (1.7)	13 (4.6)	22 (8.2)	35 (12.4)
Bakers dust	2 (0.7)	4 (1.4)	16 (5.6)	20 (6.9)
Wheat flour	2 (0.7)	13 (4.5)	19 (6.6)	32 (11.2)
Rye flour	1 (0.4)	3 (1.1)	16 (5.6)	19 (6.6)
Corn flour	0	5 (1.7)	9 (3.2)	14 (4.9)
Oatmeal flour	1 (0.4)	2 (0.7)	7 (2.4)	9 (3.1)
Barley flour	0	2 (0.7)	5 (1.7)	7 (2.4)
Threshings	0	2 (0.7)	6 (2.1)	8 (2.8)

* Alder, hazel, poplar, elm, willow.

† Bird, beech, oak, plane.

‡ *Alternaria tenuis*, *Botrytis cinerea*, *Cladosporium herbarum*, *Culvularia lunata*, *Helminthosporium*, *Fusarium moniliforme*.

¶ *Aspergillus fumigatus*, *Mucor mucedo*, *Penicillium notatum*, *Pullularia pullulans*, *Rhizopus nigricans*, *Serpula lacrimans*.

aetiology in 36 cases: in all of them positive nasal response was observed after the specific challenge test (Figs 1 and 2) and in 25 out of the same subjects the test induced significant bronchial response (early $n = 19$, dual asthmatic reaction $n = 6$). Two rhinitic patients with significant increase in the proportion of eosinophils and permeability index in the nasal lavage fluid after a specific challenge test had no laboratory signs of occupational sensitization. The increase in both analysed parameters was more pronounced in subjects with asthma and rhinitis than in those with isolated rhinitis (Figs 1 and 2). Allergic rhinitis due to occupational allergens was recognized in 36 subjects. Occupational bronchial asthma was recognized in 25 subjects (Table 4). Occupational asthma was always accompanied by allergic rhinitis. In 10

subjects reporting work-related cough (three sensitized to occupational allergens), specific inhalation challenge produced negative results and the symptoms were attributed to an irritant effect of the work environment. The incidence of occupational respiratory allergy in apprentice bakers increased with the duration of exposure and was found to be 4.5% after the first year and 8.4% after the second year of exposure. Allergic rhinitis due to occupational allergens developed more frequently than asthma – 4.5 and 2.8% in the first year and 8.4 and 6.1%, in the second year, respectively, although the values did not show significant differences (Table 4).

Sensitization to common allergens preceded occupational allergic rhinitis in 69% of cases and asthma in 64% (Table 5). Skin reactivity to occupational allergens

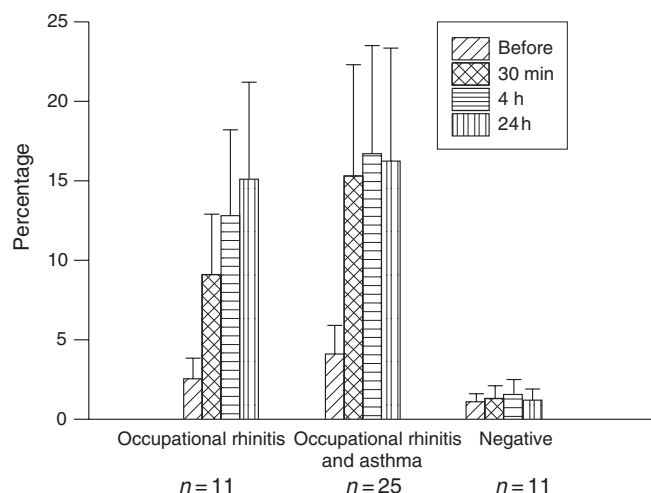


Figure 1. The changes in the proportion of eosinophils in the nasal lavage before and 30 min, 4 h and 24 h after the specific inhalative challenge test with flour in apprentices reporting work-related respiratory symptoms ($n = 47$). The data of subjects with occupational rhinitis and with occupational asthma and rhinitis are presented separately.

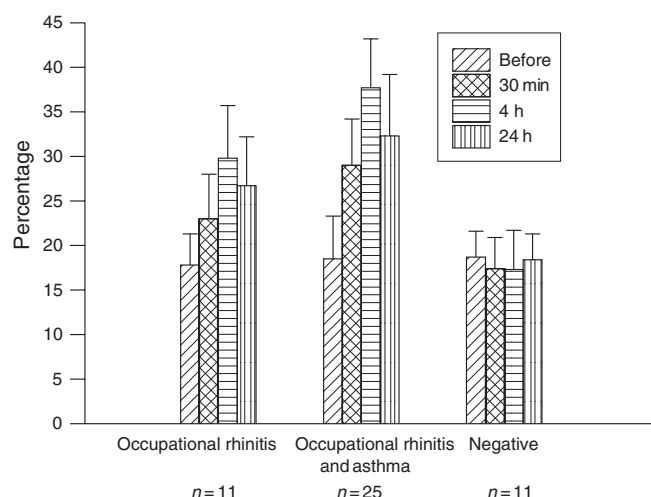


Figure 2. The changes in permeability index (albumin/total protein ratio) in the nasal lavage before and 30 min, 4 h and 24 h after the specific inhalative challenge test with flour in apprentices reporting work-related respiratory symptoms ($n = 47$). The data of subjects with occupational rhinitis and with occupational asthma and rhinitis are presented separately.

preceded rhinitis and asthma less frequently – 16.6% and 37.5%, respectively. Only in five cases (20%), bronchial asthma was preceded by allergic rhinitis found a stage earlier, of which four patients had seasonal rhinitis before the onset of vocational training.

Stepwise logistic regression analysis revealed that the history of skin symptoms and positive SPT to common allergens at the baseline were significant risk factor of

hypersensitivity to occupational allergens at stage III (Table 6). Positive SPT to common allergens was also found to be a significant risk factor of occupational allergic rhinitis and bronchial asthma. Moreover, positive SPT to occupational allergens before the vocational training reached the significance level in the stepwise analysis for risk factors of asthma development (Table 7).

The medical check-up of 104 subjects who did not continue vocational training after stage I revealed that three of them had to give up the training because of allergic rhinitis due to wheat flour and grass pollens. Moreover, four out of 70 subjects who did not take part in stage III of the study were found to suffer from allergic rhinitis induced by wheat flour and threshings; in two of them, concomitant hypersensitivity to grass pollens could be noted.

Discussion

The increasing prevalence of bakers' asthma (20, 21) makes it necessary to identify and evaluate the respective risk factors and determine the admission and rejection criteria for vocational training. The follow-up studies can provide the most valuable information. However, they are difficult to perform owing to the decreasing number of participants, which we could also observe during our study. Most of them quitted the training for reasons other than the work-related symptoms. Only nine of the apprentice workers stopped to continue the training because of allergic rhinitis. Thus, it seems that a health-based selection, i.e. the non-affected workers stay on the job more frequently than the affected ones, may not have been the case in our study. Although Monso et al. reported health-related self-selection in apprentice workers exposed to HMW agents, the finding concerned the students in animal health technology and dental hygiene (22). In the pastry-making programme, the age (above 20 years) was the only significant determinant.

To our knowledge, the present study is the first follow-up performed in apprentice bakers that includes a clinical verification of the reported symptoms and their relationship with hypersensitivity using specific challenge tests. In most of the prospective studies, the diagnosis of occupational asthma was based on the presence of hypersensitivity to occupational allergens and bronchial hyper-reactivity (23–25). Since allergic rhinitis is usually accompanied by nonspecific bronchial hyper-reactivity, the evaluation of asthma incidence based on these two tests might lead to overestimating the problem. On the other hand, in the present study, we had two symptomatic patients with negative results of SPT and specific IgE in whom a specific challenge test indicated occupational allergic rhinitis.

The present analysis was also carried out in apprentice bakers exposed to occupational allergens after a specified date. This approach makes it possible to reduce the bias

Table 4. Diagnosis of allergic respiratory diseases in apprentice bakers during the follow-up study ($n = 287$). The prevalence of that diseases on entry into the study, as well as the incidence of all cases of respiratory allergic diseases which developed during the observation period and of occupational diseases are presented

	Respiratory disease						
	Before	Developed during vocational training			Occupational		
	Stage I	Stage II	Stage III	All	Stage II	Stage III	All
Allergic respiratory disease	7 (2.4%)	16 (5.7%)	26 (9.8%)	42 (15.0%)	13 (4.5%)	23 (8.4%)	36 (12.5%)
Allergic rhinitis	6 (2.1%)*	15 (5.3%)	26 (9.8%)	41 (14.6%)	13 (4.5%)	23 (8.4%)	36 (12.5%)
Asthma	0	9 (3.1%)	17 (6.1%)	26 (9.1%)	8 (2.8%)	17 (6.1%)	25 (8.7%)
Coexistence of allergic rhinitis and asthma	1 (0.4%)	8 (2.8%)	17 (6.1%)	25 (8.7%)	8 (2.8%)	17 (6.1%)	25 (8.7%)
Irritant effect on respiratory tract	—	8 (2.8%)†	2 (0.7%)*	10 (3.5%)*	—	—	—

* All of these subjects developed sensitization to occupational allergens and cough-variant asthma.

† Work related.

Table 5. Natural history of occupational respiratory diseases recognized in apprentice bakers. For cases diagnosed at stage II, factors found at stage I are presented; for stage III, those at stages I and II are presented

Stage/disease	Number of cases	Found at previous stage(s)		
		Positive SPT to common allergens	Positive SPT to occupational allergens	Allergic rhinitis
Stage II				
Allergic rhinitis	13	54% (7/13)	8% (1/13)	—
Asthma/cough-variant asthma	8	75% (6/8)	25% (2/8)	25% (2/8)
Stage III				
Allergic rhinitis	23	78% (18/23)	22% (5/23)	—
Asthma/cough-variant asthma	17	59% (10/17)	24% (4/17)	18% (3/17)
All				
Allergic rhinitis	36	69% (25/36)	17% (6/36)	—
Asthma/cough-variant asthma	25	64% (16/25)	24% (6/25)	20% (5/25)

Table 6. Risk factors of hypersensitivity to occupational allergens* found to be significant by the stepwise logistic regression analysis. The analysis was performed in subjects with negative results of laboratory assays at the beginning of the study ($n = 282$)

Factor	n (%) of subjects presenting studied factor		OR (95% CI)	P
	Sensitized (n = 51)	Controls (n = 231)		
History of skin symptoms	5 (9.8%)	3 (1.3%)	6.3 (1.16; 34.22)	0.033
Positive SPT to at least one common allergen	27 (52.9%)	24 (10.4%)	10.6 (5.27; 21.45)	<0.001

* The following variables, found to be significant in univariate analysis (results given below), were included in the model: (1) history of conjunctivitis, OR 8.26, 95% CI (1.53; 54.43), (2) history of skin symptoms, OR, 8.26, 95% CI (1.53; 54.43). Positive SPT to: (3) at least one common allergen, OR 9.70, 95% CI (4.59; 20.64), (4) grass pollens, OR 10.31, 95% CI (3.24; 35.54), (5) trees pollens I, OR 15.27, 95% CI (2.59; 156.98), (6) trees pollens II, OR 15.27, 95% CI (2.59; 156.98), (7) *D. pteronyssinus*, OR 6.00, 95% CI (2.52; 14.34), (8) *D. farinae*, OR 1.35, 95% CI (1.35; 9.03).

that might occur if the cohort is assembled after some years of exposure. An important finding that supports the relevance of a follow-up study in subjects not previously exposed to occupational allergens is the fact that almost 2% of our apprentices were sensitized to bakers' allergens

when they started the training. If we made an assumption that these subjects developed their hypersensitivity during the training, then the incidence of sensitization attributed to occupational exposure would be overestimated.

In our study, after 2 years of vocational training, the incidence of reported rhinitis and chest symptoms was 6.5 and 4.2% after 1 year, and 10.8 and 8.6% after 2 years, respectively. For comparison, in the Cullinan et al. study, 22% of newly exposed bakers reported at least one new work-related symptom within the first 6 months of exposure; eye/nose symptoms were more frequent than the chest ones (17 vs 6%) (26). More recently, Cullinan et al. reported the incidence rates of 11.8 and 4.1 cases per 100 person-years for work-related eye/nose and chest symptoms, respectively (27). De Zotti and Bovenzi found that the incidence of work-related respiratory symptoms was 3.4% at 6 months and 4.8% at 18 months in bakery trainees (12).

It is worth noting that the chest symptom reported most frequently was chronic cough, not dyspnoea. Chronic cough may be the sole manifestation of bronchial asthma (28) and 'cough-variant asthma' has been used to categorize such patients. It is possible that these patients will eventually develop classical asthma, but the time of our study was too short to monitor this.

Table 7. Risk factors of occupational respiratory allergy – rhinitis* and asthma† found to be significant by the stepwise logistic regression analysis in the group of apprentice bakers ($n = 287$)

Factor	n (%) of subjects presenting studied factor		OR (95% CI)	P
	Occupational allergic rhinitis ($n = 36$)	Controls ($n = 251$)		
Positive SPT to at least one common allergen	20 (55.6%)	34 (13.5%)	3.9 (1.71; 9.14)	0.001
	Occupational asthma ($n = 25$)	Controls ($n = 262$)		
Positive SPT to at least one Common allergen	15 (60%)	39 (14.9%)	7.4 (3.01; 18.04)	<0.001
Occupational allergen	3 (12%)	2 (0.8%)	6.9 (0.93; 51.38)	0.058

* The following variables, found to be significant in univariate analysis (results given below), were included in the model: positive SPT to: (1) at least one common allergen, OR 7.89, 95% CI (3.54; 18.09), (2) grass pollens, OR 5.82, 95% CI (1.83; 18.30), (3) *D. pteronyssinus*2 OR 4.44, 95% CI (1.72; 11.35), (4) at least one occupational allergen, OR 11.32, 95% CI (1.23; 137.94).

† The following variables, found to be significant in univariate analysis (results given below), were included in the model: positive SPT to: (1) at least one common allergen, OR 8.58, 95% CI (3.33; 22.37), (2) feathers, OR 17.73, 95% CI (1.88; 217.86), (3) grass pollens, OR 5.21 95% CI (1.29, 17.81), (4) moulds II, OR 22.70, 95% CI (1.11; 1343.60), (5) *D. pteronyssinus*, OR 4.04, 95% CI (1.37; 11.67), (6) at least one occupational allergen, OR 17.73, 95% CI (1.88; 217.36).

Interestingly, most work-related symptoms were related to a specific sensitization. Unlike in our study, Gautrin et al. found that only a minority (3/30) of apprentices reporting work-related rhinoconjunctivitis symptoms developed SPT reactivity to flour as well (10). This could be partially explained by the differences in exposure. Our apprentices had been exposed to α -amylase, and almost 11% of them were sensitized to that agent, while in the Gautrin et al. study the flour used did not contain detectable amounts of this enzyme.

The incidence of skin sensitization to occupational allergens increased with the duration of exposure and was found to be 4.6% after 1 year and 8.2% after the 2 years. A prospective study, performed by De Zotti and Bovenzi on 125 apprentice bakers, revealed that the rate of positive results of SPT to occupational allergens at 18 and 30 months was 4.6 and 10.1%, respectively (12). In the Gautrin et al. study, the incidence of work-related sensitization (per person-year) was 4.2% in the pastry-making programme (11).

History of skin symptoms and positive SPT to common allergens were significant risk factors of occupational hypersensitivity. Gautrin et al. found association between atopy defined as hypersensitivity to at least two positive reactions to common inhalants and specific sensitization and between hay fever and the risk of sensitization to flour (11). Cullinan et al. observed that atopic workers were more likely to develop a positive SPT, but not the work-related symptoms (26). De Zotti and Bovenzi confirmed the significance of a personal history of allergic disease in the development of flour-induced symptoms in bakery trainees (12).

Moreover, in the stepwise logistic regression positive SPT to occupational allergens as a risk factor for occupational asthma reached the significance level. De Zotti and Bovenzi also reported that positive SPT to wheat flour or α -amylase was a significant risk factor of work-related respiratory symptoms (12). In addition,

Gautrin et al. confirmed the increased risk of immediate occupational allergy in persons with polyvalent hypersensitivity, including flour (11). It is difficult to explain the baseline sensitization to occupational allergens. Only in one subject this may be explained by cross-reactivity with grass pollen; indeed, he suffered from hay fever, was sensitized to grass pollens and wheat flour on entry and developed occupational asthma during the training. During the follow-up, the cross-reactivity was more frequent, in 18/38 subjects (47.4%) sensitized to wheat flour, positive SPT to grass pollens was also found, as compared to 8% among those with SPT negative to flour. Moreover, the six patients with seasonal rhinitis due to grass pollens on entry developed sensitization to occupational allergens and four out of them also the cough-variant asthma. It should be also noted that the confidence intervals for some variables were high. It is the effect of low number of subjects presenting analysed factors and means that significance of such result should be very cautiously interpreted. However, our results are in concordance with other studies. Thus, in our opinion the results fully justify postulation to perform SPT to common and occupational allergens in all apprentice bakers before starting the vocational training, which we try to establish in our country. Moreover, finding positive SPT to occupational allergens at the onset of vocational training further highlights the importance of obtaining information on baseline immunologic sensitization in prospective studies or when enrolling apprentices in a training programme. The high prevalence of atopy in the general population makes it impossible to exclude the atopics from vocation with a risk of sensitization. There is a general agreement that subjects with allergic disease should not be exposed to allergens in workplace. Thus, the pre-placement screening with SPT can be useful as a method for identifying such persons.

The natural course of respiratory allergy in the examined group appeared to be quite interesting in our

study. Allergic rhinitis is usually thought to precede bronchial asthma (29, 30). Contrary to the general opinion, the so-called 'allergic march' is not common. For instance, in the report by Danielsson et al., bronchial asthma developed only in 6% patients with allergic rhinitis during a 12-year observation period (31). Analysis of our questionnaire data revealed that dyspnoea and chronic cough had occurred almost at the same time as rhinitis and the latency period was longer only for wheezing. The above data were obtained from anamnesis, so it is possible that the patients could not have noticed rhinitic symptoms early enough, because they are less worrying than the chest symptoms. Nevertheless, the result of clinical testing showed that only in five patients occupational asthma was preceded by allergic rhinitis – in most cases, a seasonal one that existed before the vocational training had started. Sensitization to common allergens was often found as the first sign, but hypersensitivity to occupational allergens preceding respiratory disease was much less frequent.

In conclusion, the results of our study indicate that SPT to common and occupational allergens should be

performed in apprentice bakers before starting vocational training. It was also revealed that most of the work-related respiratory symptoms among trainees were related to a specific sensitization. Occupational respiratory allergy was usually preceded by sensitization to common allergens. However, the typical allergic march could not be observed in most cases. Chronic cough occurred at the same time or soon afterwards as rhinitis and frequently was the sole manifestation of asthma. Probably, these patients will develop a classical bronchial asthma, but this hypothesis requires a longer period of observation.

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