

Occupational Asthma after Withdrawal from the Occupational Allergen Exposure

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Abstract: Occupational asthma is characterised by airway inflammation, variable airflow limitation and airway hyperresponsiveness related causally to work. The aim of the study was to ascertain whether in patients with occupational asthma findings persist after withdrawal from occupational allergen exposure. A group of 37 patients with occupational asthma and a control group of 19 persons were examined. Results in asthmatics obtained during the first visit when occupational asthma was acknowledged, were compared with recent results about 6.5 yr on average after elimination of occupational allergen exposure. Recent findings in occupational asthma patients were compared with the control group. In patients with occupational asthma, no significant differences were found between results obtained at the first and recent visit. Symptoms of asthma persisted in as much as 86.5% of patients. During recent examination there were more positive results in asthmatic patients comparing with the control group in histamine challenge (61.3 vs. 5.3%, $p < 0.01$), eosinophile cationic protein (41.7 vs. 5.3%, $p < 0.05$), prick tests (45.9 vs. 10.5%, $p < 0.05$). Positive results of the present histamine challenge test and elevated eosinophils in sputum were more frequent ($p < 0.05$) in patients with occupational asthma due to high molecular weight allergens than to low molecular weight allergens.

Key words: Occupational asthma, Induced sputum, Bronchial hyperresponsiveness, Eosinophile inflammation

Introduction

Allergy is present not only in everyday life but it is also connected with workplace. Occupational allergies involve contact allergic dermatitis, occupational rhinitis and the most severe disease is occupational asthma. In many cases contact dermatitis and rhinitis precede the development of occupational asthma. In Czech Republic, 195 cases of occupational contact dermatitis have been acknowledged in the year 2004 (256 cases in 2003, 305 cases in 2002, 347

cases in 2001), 69 cases of occupational asthma in 2004 (36 cases in 2003, 44 in 2002, 41 in 2001), 6 cases of occupational asthma with rhinitis in 2004 (27 cases in 2003, 31 in 2002, 12 in 2001), and 44 cases of occupational rhinitis in 2004 (30 in 2003, 23 in 2002, 29 in 2001)^{1–4}.

Occupational asthma is a disease characterised by airway inflammation, variable airflow limitation and airway hyperresponsiveness causally related to work⁵. In adults, up to 15% cases of asthma may be attributed to workplace exposures⁶. Two types of occupational asthma have been described: immunologically mediated asthma, which appears after a latency period, and nonimmunologically mediated

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asthma which appears without a latency period⁷). Immunologically mediated asthma can be caused by high (HMW) or low molecular weight (LMW) allergens. Most high molecular weight agents as well as many low molecular weight agents are thought to induce asthma via a type I - IgE-mediated mechanism (immediate symptoms). Low molecular weight agents are also recognized as being able to induce late-phase responses⁷). Asthma without a latency period is illustrated by irritant-induced asthma (reactive airways dysfunction syndrome- RADS)⁸).

For the exact evaluation of the course of occupational asthma objective methods are needed⁹⁻¹¹). The diagnosis of occupational asthma involves the detailed patient's history and laboratory tests. The examination should include: blood eosinophils (their elevation may be the feature of presence of allergic disease), IgE (immunoglobuline E) —total and specific, skin prick test with environmental and occupational allergens (if available), pulmonary function testing (basic spirometry measurement, diurnal variation of peak expiratory flow, non-specific bronchial challenge test and specific bronchial challenge test with suspected occupational allergen, which is considered a "gold standard").

In Czech Republic, occupational asthma, rhinitis (allergic disease of upper airways) and allergic dermatitis caused by chemical, physical or biological elements are included in the List of Occupational Diseases (Appendix of Government Decree No. 290/1995). The notification of occupational disease to the National Register of Occupational Diseases is obligatory. The Czech Republic is divided into 18 regions and each region has the local centre for notification of occupational diseases. Diagnostics of some diseases (such as asthma) needs a special diagnostic instrumentation (for specific bronchoprovocation tests for example) and specialised medical staff. Our department performs specific provocation tests, the "gold standard" for diagnosis of occupational asthma and rhinitis for several regional centres for notification of occupational diseases in Czech Republic. Occupational hygiene evaluation of the workplace focused on possible occupational disease origin comes out from the Government Decree No. 342/1997. The occupational hygienists also collect materials (suspected allergens) for specific bronchoprovocation tests and sent them to our laboratory. Specific bronchoprovocation tests are recommended in Guidelines for Occupational Asthma of Czech Medical Association of Jan Evangelista Purkyně¹²).

For the notification of occupational disease, there are special registration forms, which are sent to the National Register of Occupational Disease, to the patient, his/her employer, occupational physician, general practitioner,

occupational hygienist, and health insurance. This form includes the identification data of the patient, his/her occupation, length of exposure, diagnosis, and the classification of the sensitizer¹³). Both the patient and the patient's employer have the right of appeal. The centres of notification make also decisions about the compensation for pain and suffering (at the time of diagnosis) and compensation for impaired life capacity (in a follow-up).

After confirmation of the diagnosis of occupational asthma, the patient must be withdrawn from the exposure of occupational allergen. He/she obtains one-off financial compensation for the occupational disease and also he can obtain a financial compensation for lost wages (if he/she has a decrease in wage at his new job position). Each patient is periodically examined (approximately every two years) by a physician specialized on occupational diseases. In case of health impairment due to an occupational disease he/she gets financial compensation again. This compensation in Czech Republic is relatively high, so the diagnosis of occupational disease must be very precise. However, several cases per year are finally resolved by the court. That is why the specific bronchial challenges with suspected occupational allergens are widely recommended for the confirmation of diagnosis of occupational asthma.

Asthmatic symptoms should theoretically disappear in patients with occupational asthma after elimination from occupational exposure to proven allergen. The early removal from occupational exposure is important for the prognosis of asthma. Individuals who are removed shortly after the onset of symptoms have better prognosis than those who continue to work. The prompt recognition is necessary to prevent long-term disability¹⁴). In previous studies, variable percentage of complete recovery was described. In Ontario, only 19% of occupational asthmatics had clearing of asthma and 47% had improvement at a mean follow-up time of 1.9 yr¹⁵). Other study reported that 71% of toluene diisocyanate-induced asthmatics had respiratory symptoms about 11 yr after withdrawal from exposure¹⁶).

The aim of our study was to find out, whether and to what extent the bronchial asthma persists after withdrawal from occupational exposure to proven allergen in patients, who were diagnosed occupational asthma at our department in Czech Republic. Financial benefits given to patients for their occupational asthma could lead to exaggeration of their subjective problems. Therefore, the purpose of this study was to examine the health condition by objective methods to learn more about the reversibility and severity of this occupational disease.

Materials and Methods

Thirty-seven persons with previously diagnosed occupational asthma after withdrawal from the occupational allergen exposure were examined. In all persons, occupational asthma was verified as immunological. The diagnosis of occupational asthma was made at the first hospitalisation in our department. The result of the specific bronchoprovocation test with occupational allergen was crucial for the decision about occupational aetiology of the disease.

Control group consisted of 19 persons, working as office or health care employees and having no current symptoms of asthma and/or allergic rhinitis.

The detailed demographic data about the occupational asthmatics' group and the control group are given in Table 1. Most asthmatic ex-smokers quit smoking at latest at the time of diagnosis of occupational asthma.

The average interval between first and last examination

of persons with occupational asthma was 6.5 yr (1–18 yr). The comparison of the length of work and the onset and duration of symptoms due to work with the occupational allergen in groups according to the allergen type (HMW, LMW) can be seen in Table 2.

Symptoms of asthma in the time of diagnosis of occupational asthma and their development until the recent hospitalisation were checked. The questions were focused on frequency of asthmatic attacks, types of attacks (during night or day, starters), frequency of using bronchodilators, dry cough with dyspnoea, exercise induced attacks.

The results of following tests obtained during the first hospitalisation in our department (when occupational asthma was diagnosed) and now, several years after withdrawal, were compared: blood eosinophils (absolute count and percentage), skin prick test reactivity (to environmental and specific allergens), immunoglobuline E (IgE) antibodies levels, spirometry, non-specific bronchial hyperresponsiveness. Some new parameters were examined

Table 1. Description of the group of occupational asthma patients and control group

Group	Occupational asthma			Controls		
	Total	Men	Women	Total	Men	Women
Number	37	14	23	19	7	12
Mean age (SD)	47.9 (9.4)	44.1 (12.3)	50.1 (5.99)	44.1 (14.6)	46.3(12.8)	42.8 (15.4)
Smoking: yes/ex/no	4/19/14	2/8/4	2/11/10	6/1/12	3/0/4	3/1/8
Exposure to HMW allergen in past	18	3	15	0	0	0
Exposure to LMW allergen in past	19	11	8	0	0	0
Current treatment: corticosteroids *	25	9	16	0	0	0
Current treatment: antihistaminics	17	3	14	0	0	0
Current treatment: bronchodilators	28	10	18	0	0	0
Current asthmatic symptoms	32	12	20	0	0	0

ex: ex-smoker, HMW: high molecular weight, LMW: low molecular weight, SD: statistic deviation.

*Two patients used systemic corticosteroids (1 patient for bronchial asthma, 1 patient for rheumatoid arthritis), 23 patients used inhaled corticosteroids.

Table 2. Comparison of the length of exposure to occupational allergen

	Total (yr)	HMW group (yr)	LMW group (yr)
Mean time-interval between first and last examination (SD)	6.51 (4.21)	5.11 (3.31)	7.84 (4.53)
Mean length of work to first onset of symptoms of allergy or asthma (SD)	8.55 (8.63)	8.88 (7.97)	8.22 (9.20)
Mean length of work with symptoms of allergy or asthma (SD)	2.64 (2.47)	3.49 (2.75)	1.83 (1.85)

HMW group: high molecular weight allergen exposed group, LMW group: low molecular weight allergen exposed group, SD: statistic deviation.

at the last visit: alpha-1-antitrypsine, eosinophile cationic protein (ECP) from blood, cell parameters in induced sputum. Parameters obtained during the last visit were also compared with the results of the control group.

ECP levels were obtained by chemiluminiscent immunoanalysis on Immulite 2000 (ECP kit DPC). Normal ECP levels in blood are in the range of 0–24 $\mu\text{g/l}$.

The level of alpha-1-antitrypsine was measured using nephelometry (normal range 0.9–2.0 g/l).

Skin prick tests were performed with the set of commercial extracts of environmental respiratory allergens: fungi, mites, mixture of several types of pollen, animal allergens—dog, cat (Sevapharma, Stallergenes) and also the suspected occupational allergen was included if it was available.

Spirometry and bodyplethysmography were performed at MasterLab and MasterScreen (Jaeger) according to European Respiratory Society recommendations¹⁷. FEV₁ (forced expiratory volume in one second) was used as a main marker for obstruction (less than 80% of a predicted value). Diurnal variation of lung function was classified as abnormal, when PEF (peak expiratory flow) was higher than 20%¹⁸.

Non-specific bronchial challenges were done via APS (Asthma Provocation System) Jaeger according to European Respiratory Society recommendations¹⁹. Tests were performed at the first hospitalisation with acetylcholine or histamine, at the last hospitalisation histamine challenge was performed as acetylcholine was no more available. The dosimeter method was used for these challenges. The Sandoz 1500 Nebulizer, with the particle size from 0.5 to 7.0 μl , was used for the APS unit. Aerosol mist was delivered discontinuously into the patient's inspiration. For each breath, with a nebulization time 0.6 s, APS generates an aerosol bolus of approximately 100 ml, which carries a fluid quantity of approximately 5 μl (the nebulizer pressure 160 kPa). The solution of acetylcholine was inhaled in increasing concentrations: 1 mg/ml, 2.5 mg/ml, 5 mg/ml, 10 mg/ml. Histamine test was performed by inhaling solution of histaminum dihydrochloridum in the concentrations: 1 mg/ml, 5 mg/ml, 10 mg/ml. A decrease in FEV₁ exceeding 20% was marked as a positive result.

Specific bronchial challenges were executed in our laboratory. Minimally one physician and one nurse with the first aid equipment for the possible asthmatic or allergic reaction or anaphylaxis assisted during tests performed in the exposure box. The specific challenges were done with materials from patients' workplace collected by occupational hygienists (physicians) from the Public health department. In case of necessity of performing the specific challenge in the workplace, the patient was transported to and back from

the workplace by ambulance and then monitored in our department for 24 h at least.

Patients simulated their work with collected materials from the workplace in a special exposure box for 30 min. If the work could not have been simulated in the laboratory, patients would have been exposed at their workplace for 2 h. Spirometry was measured before and after specific bronchoprovocation challenges during 24 h. The final diagnosis of occupational asthma at the first hospitalisation was based primarily on the result of specific challenge tests. Decrease of FEV₁ of 20%, decrease of mean expiratory flow at a specified lung volume (MEF 25%FVC, MEF 50%FVC, MEF 75%FVC) of 30% or increase of R tot of 40% was marked as a positive result of specific allergen challenge.

Sputum was induced by inhalation of 3%, 4%, 5% solution of hypertonic saline (NaCl) generated by a nebulizer Porta-Neb Sidestream (flow rate 6 l/min, output 0.46 g/min) with β_2 -agonist (salbutamol 200 μg) pretreatment. The whole sample was treated with the equal volume of dithiothreitol (Sputolysin Reagent, Calbiochem) freshly diluted with distilled water (1:10), shaken for 30 min (IKA M2S Minishaker) and then filtered. Sample was centrifuged at 1,200 rpm for 10 min. Cell mass was resuspended in phosphate buffer and after staining by May-Grünwald, Giemsa-Romanovski, the cell count was performed on 300 non-squamous cells^{20–23}.

All examinations and tests have been performed in accordance with the ethical standards and all subjects involved in this study signed their informed consent protocol.

Statistical Analysis

The McNemar test and paired t-test were used for the comparison of results obtained from the first and the last hospitalisation to correct for the fact that data obtained by repeated measurement of the same person tend to be correlated. Two sample t-tests and ordinary chi-square tests were used for the comparison of control and asthma groups (their measurements are independent of each other). For these tests, *p*-values are reported. The significance level was set at 5% (*p*<0.05) and 1% (*p*<0.01).

Results

In the group of occupational asthmatics, there were 18 persons with occupational asthma confirmed by specific bronchoprovocation tests provoked by HMW agents and

19 persons by LMW agents. HMW allergens included: 4× wheat flour, 2× hen feather, 2× grain meal, 1× grain dust, 1× cotton, 2× textile dust and fibres, 1× tea dust, 1× mouse hairs, 2× cow dust, 1× culture medium, 1× fungi. Among LMW agents there were: 3× polyurethane, 3× glue, 2× ostazin dye, 2× other dye, 2× 2,4-dichloro-5-chlorosulfonylbenzoic acid, 1× phenolformaldehyde resin, 1× epoxy resin, 1× platinum, 1× plastizol, 1× isocyanates, 1× sulphanyl acid and silicarbene, 1× disinfectant.

At the recent examination, symptoms of bronchial asthma were present in 32 persons (86.5%). Only five subjects had no asthmatic symptoms. Four of them were in the past exposed to occupational HMW allergen (cotton, grain dust, cow dust, textile dust) and one to LMW allergen (ostazin dye).

The results of examination and tests obtained at the first and at the last hospitalisation are presented in Tables 3 and 4; symptoms are in Table 5. Changes in the results between these hospitalisations were not significant.

The comparison of the results from the last hospitalisation of the asthmatics with the control group results is shown in Table 6. There were significant changes (i.e. more positive results or elevation above normal range in asthmatic group) for histamine challenge (61.3 vs. 5.3%, $p<0.01$), ECP in blood (41.7 vs. 5.3%, $p<0.05$), and prick tests (45.9 vs. 10.5%, $p<0.05$).

Average value of ECP was significantly ($p=0.001$) higher in asthmatic group (22.83 $\mu\text{g/l}$) than in control group (11.63 $\mu\text{g/l}$). Average values of alpha-1-antitrypsine were in normal range, however they were significantly ($p=0.0131$) lower in asthmatic group (1.48 g/l) than in control group (1.69 g/l).

When the group of asthmatic patients was divided into subgroups according to the past exposure to the occupational either HMW or LMW allergen, significantly ($p=0.0384$) more positive results of histamine challenge were seen in the subgroup of patients with occupational asthma due to HMW allergens.

A good quality sample of induced sputum was obtained in 24 persons with asthma (64.86% of all) and in 15 persons from the control group (78.95% of all). Sputum eosinophils were elevated in 6 patients (normal value $<2\%$). Three of them were treated with inhaled corticosteroids, two used only bronchodilators, and one person was asymptomatic without treatment. Increased eosinophils in induced sputum were found significantly more often ($p=0.0332$) in asthma patients exposed to HMW occupational allergens in past (45.45%, i.e. in 5 from 11) than in asthma patients exposed to LMW (7.69%, i.e. in 1 from 13). In the control group, no sample has shown elevated sputum eosinophils.

Discussion

The aim of our study was to ascertain whether in patients with occupational asthma the symptoms and findings persist after withdrawal from occupational allergen exposure. Theoretically asthmatic symptoms should disappear after ending of occupational allergen exposure. It is true that the prognosis of further development of occupational asthma depends on the early diagnosis and early withdrawal from occupational allergen exposure. The proportion of completely recovered persons (asymptomatic) after withdrawal from occupational allergen exposure in different studies varies considerably. Nineteen per cent of occupational asthmatics had clearing of asthma and 47% had improvement at a mean follow-up time of 1.9 yr in Ontario¹⁵. Seventy one per cent of toluene diisocyanate-induced asthmatics had respiratory symptoms about 11 yr after withdrawal from exposure (i.e. the recovery was 29%) according to Padoan¹⁶.

In our group the symptoms of asthma disappeared only in five persons (13.5%), that is much less than in reported studies, i.e. they persisted in as much as 86.5% of asthmatics. Complete removal from allergen exposure is sometimes impossible—especially for the high molecular weight allergens, for example flour, where the everyday contact with rolls, bread or flour during cooking is almost inevitable.

The airways' inflammation can be evaluated by several methods, which reflect the function of airways (spirometry, non-specific challenges) or by methods, which investigate airways directly. Sputum induction is relatively non-invasive method (comparing to bronchial wash or bronchoscopy) that is especially useful in patients who are not able to produce sputum spontaneously. Sputum cell analysis enables detecting the current airways inflammation. It can even serve as a measure of successful asthma treatment and inflammation control in patients treated with corticosteroids. Monitoring of cell parameters in induced sputum was recommended for the diagnostics of lung diseases by many authors^{20, 24–27}. Sputum eosinophilia is an important factor in asthma assessment. Raised eosinophils in sputum can reflect the poor control of allergic inflammation in the airways, recent exposure to allergen, non-compliance of patients and/or inadequate treatment^{24–27}. It is also useful in occupational patients, who have a tendency to exaggerate their symptoms. In our patients, the eosinophilic inflammation in induced sputum was present also more frequently in the HMW allergens' exposed group. In symptomatic patients it could mean that the inflammation in the airways is not well treated. In one asymptomatic patient the allergic inflammation persisted despite the asthmatic symptoms were absent.

Table 3. Occupational noxa and changes in skin prick tests in occupational asthmatic group between the first and the recent visit

Patient	Occupational noxa	Skin prick tests- before (positively tested agents)	Skin prick tests- after (positively tested agents)
1	Wheat flour	wheat and rye flour	wheat flour
2	Polyurethane	dust, mites, moulds, histamine	mites, feather, pollen: wood, ragweed, cat
3	Ostazin dye	dust, mites, upper airways bacteria, moulds, histamine	negative
4	Synthetic dye	dust, feather, mites, rye straw, rabbit, histamine	feather, mites
5	Phenolformaldehyd resin	dust, feather, mites, moulds, autumn pollen, histamine	dust, mites
6	Glue	mites, moulds, histamine	negative
7	Glue	negative	mites, grass pollen, spring pollen
8	Wheat flour	mites, wheat and rye flour	negative
9	Cotton	cotton	negative
10	Glue	moulds, upper airways bacteria	negative
11	Wheat flour	borderline autumn pollen, rye flour	rye flour
12	Grain meal	dust, mites, moulds, upper airway bacteria, rye straw, hay	moulds
13	2,4-dichloro-5- chlorsulfonylbenzoic acid	histamine	negative
14	2,4-dichloro-5- chlorsulfonylbenzoic acid	borderline spring pollen	negative
15	Textile dye	dust, mites	negative
16	Grain dust	dust, feather, mites, moulds, grass and spring pollen, rye straw	dust, mites, moulds, spring and grass pollen
17	Polyamide fibres	negative	negative
18	Hen feather	negative	negative
19	Wheat flour	dust, feather, mites, wheat and rye flour, histamine	mites, wheat flour
20	Ostazin dye	dust, feather, mites, histamine	negative
21	Epoxy resin	histamine	wood, herbs pollen
22	Polyurethane	dust, mites	negative
23	Platinum	dust, upper airways bacteria	negative
24	Plastizol	moulds, autumn and grass pollen	mites, moulds, spring, autumn and grass pollen, upper airways bacteria
25	Grain meal	negative	negative
26	Tea dust	dust, feather, mites, grass pollen, hay	dust, mites
27	Isocyanates	negative	negative
28	Mouse hairs	negative	negative
29	Cow dust	dust, mites, moulds, cow hairs, histamine	negative
30	Sulphanil acid, silicarbon	dust	negative
31	Hen feather	dust, feather, mites	feather, mites, spring pollen, cat, dog
32	Polyurethane	histamine	negative
33	Fungi "tree ear"	negative	negative
34	Cow dust	negative	cow hairs
35	Textile dust	dust, feather, mites, moulds, autumn pollen, upper airways bacteria, cotton	mites, grass, spring and autumn pollen, cotton
36	Disinfectant	mites, dust, feather, moulds, grass, spring and autumn pollen, upper airways bacteria	moulds, spring, autumn and grass pollen, upper airways bacteria, latex
37	Culture medium	mites, moulds, grass, spring and autumn pollen, upper airways bacteria	dust, mites, moulds, spring, autumn and grass pollen, upper airways bacteria

We did not find significant improvement in examined parameters several years after the withdrawal of exposure. Similar results described Merget in 1994 who followed the group of patients with occupational asthma, caused by platinum salts²⁸⁾. He did not find significant improvement

in bronchial responsiveness to methacholine, FEV₁, skin reactivity and bronchial responsiveness to platinum salt, but he found significant decrease in IgE.

Our study documents by a variety of methods the presence of allergic disease in our patients. According to our results,

Table 4. Changes in parameters in occupational asthmatic group between the first and the recent visit

Patient	IgE before mg/l *IU/ml	IgE after mg/l	Blood eo before ×10 ⁵	Blood eo after ×10 ⁵	Blood eo before %	Blood eo after %	Nonspecific BPT before	Nonspecific BPT after	FEV ₁ before %PV	FEV ₁ after %PV
1	46.0	105.0	0.310	0.160	5.8	3.0	ND	ND	98.3	80.9
2	232.3	286.0	0.168	0.110	3.3	1.7	ND	negative	106.0	112.0
3	32.7*	17.0	ND	0.300	3.9	5.8	ND	negative	106.0	99.5
4	ND	1195.0	ND	0.240	0	3.3	ND	positive	115.0	110.6
5	138.0*	222.0	0.200	0.160	3.1	1.9	positive	positive	82.6	81.0
6	30.3*	24.0	0.100	0.170	3.4	2.5	ND	negative	96.3	93.7
7	227.0*	278.0	0.159	0.210	2.9	3.0	positive	positive	121.0	96.6
8	937.0	1363.0	0.970	0.240	16.5	5.9	positive	positive	99.7	106.7
9	ND	73.0	0.186	0.160	2.2	2.0	ND	ND	88.1	75.7
10	ND	219.0	0.056	0.050	1.0	0.8	negative	negative	125.0	127.3
11	747.5	626.0	0.130	0.160	2.5	2.9	negative	positive	102.0	100.4
12	246.0*	482.0	0.530	0.440	8.4	6.9	negative	positive	103.0	104.6
13	693.0	262.0	0.210	0.120	7.0	2.8	negative	negative	118.0	126.5
14	102.0	53.0	0.260	0.200	4.7	2.9	positive	positive	95.7	94.1
15	ND	28.0	ND	0.200	3.0	1.7	ND	ND	79.0	71.0
16	ND	545.0	<0.700	0.290	ND	5.0	ND	negative	108.0	98.4
17	34.0	29.0	0.170	0.130	2.3	1.7	negative	positive	111.0	124.9
18	62.4*	241.0	0.100	0.190	2.1	2.4	positive	positive	101.0	89.0
19	83.6*	233.0	0.110	0.210	2.0	4.3	ND	positive	125.0	132.1
20	64.8*	81.0	0.215	0.320	2.2	3.7	ND	negative	118.0	102.8
21	ND	119.0	ND	0.120	2.0	1.6	ND	positive	95.0	97.9
22	ND	90.0	ND	0.310	1.0	5.1	negative	negative	102.0	128.4
23	ND	201.0	ND	0.280	10.0	2.8	ND	ND	45.0	63.0
24	633.0	617.0	0.370	0.500	4.7	5.3	negative	positive	87.4	82.9
25	451.0	389.0	0.160	0.230	2.4	3.1	positive	negative	74.6	80.1
26	285.0	206.0	0.140	0.100	1.1	1.2	positive	positive	87.9	72.9
27	166.0	137.0	0.060	1.130	1.4	13.4	positive	ND	84.3	50.3
28	ND	42.0	0.170	0.200	2.4	3.5	positive	ND	98.6	96.6
29	ND	175.0	<0.700	0.170	0	2.3	negative	negative	133.0	111.7
30	70.4	83.0	<0.700	0.130	0	1.7	ND	negative	100.0	104.4
31	573.0	463.0	0.200	0.280	2.3	3.4	ND	positive	106.0	108.0
32	ND	98.0	<0.700	0.220	0	3.7	negative	negative	105.0	95.2
33	28.0	47.0	0.070	0.020	2.3	0.4	positive	positive	67.2	96.0
34	ND	50.0	ND	0.230	ND	4.6	ND	positive	121.0	102.4
35	58.6	152.0	ND	0.230	4.6	3.4	ND	positive	105.0	113.0
36	202.6*	494.0	0.263	0.310	3.3	4.3	positive	positive	89.7	104.5
37	242.0	252.0	0.560	0.220	8.1	3.5	positive	positive	74.4	72.6

before: results from 1st visit, after: results from recent visit, BPT: bronchoprovocation test, IgE: immunoglobuline E, FEV₁: forced expiratory volume in one second, eo: eosinophils, %PV: percentage of predictive value, ND: not done. Specific bronchoprovocation test was positive in all patients at 1st visit.

the most important tests or parameters in which there were great differences between patients with formerly acknowledged occupational asthma and control subjects with no asthmatic symptoms, appear the histamine challenge, prick tests, and ECP in blood. Sputum cells analysis brings another supporting result in patients with occupational asthma.

Czech patients with occupational asthma can receive financial compensation for lost wages for many years. As

can be documented by the findings in our patients, their course of occupational asthma is not as benign as was previously supposed. This very complex study shows by objective methods, that reported persisting symptoms cannot be explained by the exaggeration of the patients.

Early diagnosis and removal from occupational exposure probably plays a key role. According to our results most cases of occupational asthma in spite of the elimination of

Table 5. Symptoms described in the first and the last visit

Patient	Symptoms (before)	Symptoms (after)
1	skin itching, rhinorrhoea, conjunctivitis, dyspnoea	moderate dyspnoea (physical exercise, weather changes)
2	dyspnoea, skin itching, rhinorrhoea	dyspnoea (physical exercise), cough, pollinosis
3	rhinitis, cough, dyspnoea	cough (dusty environment), dyspnoea (weather changes)
4	dyspnoea, rhinitis	dyspnoea (bad weather, smoky rooms, dusty environment)
5	cough, dyspnoea	dyspnoea- with treatment (ICS, LABA) stable
6	sneezing, rhinitis, dyspnoea	dyspnoea- 2×/wk
7	cough, dyspnoea	dyspnoea (bad weather, nighttime- 2–3×/wk)
8	sneezing, rhinorrhoea, conjunctivitis, cough, dyspnoea	dyspnoea (weather changes, dusty and irritant environment, nighttime), cough
9	cough, dyspnoea	none
10	cough, rhinitis	rare cough, dyspnoea (physical exercise)
11	dyspnoea, cough	permanent cough, dyspnoea
12	cough, dyspnoea	asthma attack 1–2×/yr
13	cough, sneezing, rhinorrhoea, dyspnoea	rare cough
14	rhinorrhoea, sneezing, dyspnoea	rhinorrhoea (dusty environment), dyspnoea (dusty, hot environment, bad weather)
15	cough, dyspnoea	dyspnoea (irritant, dusty environment, nighttime 2×/wk)
16	rhinorrhoea, cough, dyspnoea, dermatitis	none if contact with grain dust is avoided
17	dermatitis, dyspnoea, cough	rhinorrhoea, dyspnoea 2×/month, cough provoked by odour, stress
18	cough	rare cough, rare dyspnoea
19	rhinorrhoea, dyspnoea, cough	dyspnoea 2×/wk (physical exercise, worsening in autumn)
20	sneezing, rhinorrhoea, conjunctivitis, cough, dyspnoea, skin itching	none
21	dyspnoea, cough, rhinorrhoea	dyspnoea (physical exercise, dusty environment), rare cough
22	dyspnoea, cough	dyspnoea (2×/wk in winter, daily in summer, pollen season, nighttime)
23	dyspnoea, asthma attacks, rhinorrhoea, sneezing	frequent asthma attacks, permanent dyspnoea
24	dyspnoea, rhinorrhoea	rare dyspnoea, cough provoked by odour, rhinorrhoea
25	dyspnoea, cough, conjunctivitis	dyspnoea 3×/month (weather changes, odour, smoke, physical exercise)
26	cough, dyspnoea, rhinorrhoea, nasal blockage	cough in the morning, dyspnoea (physical exercise), pollinosis
27	dyspnoea, cough	rare dyspnoea, stable with treatment
28	cough, rhinorrhoea, conjunctivitis	rare cough, rhinorrhoea
29	dyspnoea, cough	dyspnoea (pollen season, bad weather, physical exercise)
30	dyspnoea, asthma attacks	dyspnoea (dusty environment, bad weather), asthma attacks 1×/month, in pollen season 2–3×/month, pollinosis
31	dyspnoea	dyspnoea, asthma attack 2×/wk in summer, nighttime 4–5×/wk, perennial rhinorrhoea, conjunctivitis in spring, rare cough
32	cough, dyspnoea	rare cough, dyspnoea (dusty environment, smoke, odours)
33	cough, dyspnoea	dyspnoea 2–3×/wk
34	cough, dyspnoea	none
35	cough, dyspnoea, rhinorrhoea	none
36	dyspnoea, cough, nasal blockage, rhinorrhoea, oedema of eyes, lips	rhinorrhoea (pollen season), dyspnoea and cough (physical exercise and irritative vapours), permanent nasal blockage
37	pollinosis, in work: cough, conjunctivitis, skin itching	dyspnoea (hot environment), night cough, nasal blockage in summer

before = symptoms in work or in connection with work before the elimination from occupational allergen, after = symptoms after the elimination from occupational allergen, LABA = long acting β_2 -agonists, ICS = inhaled corticosteroides.

Table 6. Comparison of results from the recent visit of the occupational asthmatic group with the control group. Percentage of subjects with indicated parameter is given

Parameter	Occupational asthma group	Control group	<i>p</i> values (statistics)
Elevated eosinophils (percentage) in blood	48.6%	26.3%	0.1077
Elevated eosinophils (absolute count) in blood	5.4%	0.0%	0.3021
Elevated IgE in blood	24.3%	10.5%	0.2185
Elevated ECP in blood	41.7%	5.3%	0.0047*
Positive skin prick tests	45.9%	10.5%	0.0080*
Positive histamine bronchoprovocation test (1)	61.3%	5.3%	0.0003**
FEV ₁ < 80%	16.2%	0.0%	0.0632
FVC < 80%	10.8%	0.0%	0.1369
Diurnal variation of PEF>20%	10.8%	not examined	not done

(1) not examined in 6 patients due to FEV₁ under 80% of predicted value, *significant $p < 0.05$, ** $p < 0.001$.

IgE: immunoglobuline E, ECP: eosinophilic cationic protein, FEV₁: forced expiratory volume in one second, FVC: forced expiratory capacity, PEF: peak expiratory flow.

the occupational allergen convert to “classical” asthma. The reason could be the long exposure and prolonged work with allergic symptoms in the workplace. Then the inflammation in the airways apparently does not resolve completely and can be sustained by common inhalation allergens. In patients with occupational asthma long life treatment is usually needed.

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