Trends in allergy to the 10 most frequent contact allergens in patients examined at the Nofer Institute, Lodz, Poland in 1996-2009

Marta Kieć-Świerczyńska, Beata Kręcisz, Dorota Chomiczewska, Wojciech Sobala

Dermatology Unit, Centre of Occupational Allergy and Environmental Health, Nofer Institute of Occupational Medicine, Lodz, Poland
Head: Assoc. Prof. Cezary Pałczyński MD, PhD

Post Dermatol Alergol 2012; XXIX, 1: 19–24

Abstract

Aim: The aim of the study was to analyse the trends of allergy to the 10 most frequent contact allergens and to assess age- and sex-dependent changes of the trends in patients examined in 1996-2009.

Material and methods: 4433 patients underwent patch tests with a set of allergens containing: potassium dichromate, nickel sulfate, cobalt chloride, 4-phenylenediamine, formaldehyde, thiuram mix, mercaptobenzothiazole, balsam of Peru, benzocaine and turpentine. We analyzed the trends of the frequency of sensitization to particular allergens and changes in the average age of the sensitized people. Also a comparison of the frequency of the allergy in males and females was performed.

Results: It was found that sensitization to at least one of the 10 tested chemicals was more frequent in females (42.5%) than in men (30.5%). Allergy to nickel (28.5%) and cobalt (13.6%) prevailed in women, while sensitization to chromium prevailed among the male patients (13.3%). Men were more frequently allergic to 4-phenylenediamine and mercaptobenzothiazole than women. Nickel was a more frequent sensitizer among younger women while balsam of Peru, chromates and thiurams were more frequent allergens among older women.

Conclusions: The analysis of the trend of contact allergy to 10 allergens showed a statistically significant decrease in prevalence of allergy to chromium, cobalt and formaldehyde and an increase in sensitization to nickel in the investigated group. After Poland accession to the European Union and the accompanying economic changes, the differences in the overall pattern of allergy in Poland have become less evident, although a few peculiarities are still present.

Key words: contact allergy, major allergens, gender, age.

Introduction

Allergic contact dermatitis is acquired eczematous dermatitis, caused by external chemical agents, usually of low molecular weight (haptens). The frequency of allergic contact eczema in the European Union is approximately 10% of the general population [1]. The type and frequency of contact hypersensitivity depend on many factors, especially the prevalence of allergens in the occupational and municipal environment, manufacturing process technology, automation and mechanization, type and severity of environmental pollution, habits, use of skin protection media, as well as on individual susceptibilities of people [2].

The data on this problem from different countries and regions differ; periodic changes in the frequency of allergy in the same locations are also observed.

Aim

The aim of our study was to evaluate the trends of sensitization to 10 basic contact allergens in the period from 1996 to 2009 and assess relevant gender- and age-related differences.

Material and methods

The study group comprised 4433 patients examined at the Nofer Institute of Occupational Medicine (NIOM) in Lodz for suspected allergic skin disease. Patch tests (the method recommended by the International Contact Dermatitis Group [3]) with a set of allergens from Chemotechnique Diagnostics (Sweden) containing, among others, 0.5% potassium dichromate, 5% nickel sul-

Address for correspondence: Prof. Marta Kieć-Świerczyńska MD, PhD, Laboratory of Dermatology, Center of Occupational Allergy and Environmental Health, Nofer Institute of Occupational Medicine, 8 Sw. Teresy, 91-348 Lodz, Poland, e-mail: marswier@imp.lodz.pl

fate, 1% cobalt chloride, 1% 4-phenylenediamine, 1% formaldehyde, 1% thiuram mix, 2% mercaptobenzothiazole, 25% balsam of Peru, 5% benzocaine and 0.3% turpentine were applied in all subjects. The allergens were suspended in vaseline, with the exception of formaldehyde (water) and turpentine oil (olive oil). The readings were recorded after 48 h and 96 h, and after 7 days.

We analyzed the trend of the frequency of sensitization to individual allergens in the years 1996-2009 and changes in the average age of the sensitized people. We also compared the frequency of the allergies in males and females. Linear regression and Fisher's exact test were used in the statistical analysis. The level of significance was set at $p = 0.05$.

Results

The study group of 4433 subjects comprised 2959 women (66.7%) and 1474 men (33.3%). Allergy to at least 1 of the 10 allergens was detected in 1709 subjects (38.6%). Women developed allergy more frequently (1259 – 42.5%) than men (450 – 30.5%) ($p < 0.001$) (Table 1).

Metals were the major causes of contact allergy. Hypersensitivity to nickel (28.5%) and cobalt (13.6%) dominated in women; it was also more frequent in them than in men ($p < 0.001$), while males were predominantly allergic to chromium (13.3%), more frequently than women ($p < 0.001$). The 4-phenylenediamine (PPD) is statistically more likely to sensitize men than women (6.4% vs. 4.1%); the same is true about mercaptobenzothiazole (1.4% vs. 0.5%) ($p < 0.001$). The frequency of allergy to balsam of Peru ($p = 0.053$) and formaldehyde ($p = 0.066$) was slightly higher in women than in men.

Mean age of subjects allergic to various chemicals was compared between women and men (Table 2).

The influence of age on the development of contact allergy was analyzed. Differences in age of people allergic to different allergens vs. the mean age was found in women and in the entire group of subjects. Younger women developed allergy to nickel ($p < 0.001$), while older women developed sensitivity to the balsam of Peru, chromium ($p < 0.001$) and the thiurams ($p = 0.001$). Age of men who were allergic to various chemicals did not differ from the average age of all men with contact allergy.

Moreover, the average age of the allergic women was compared with that of the allergic men. It was found that women who developed sensitivity to nickel ($p = 0.001$), cobalt ($p < 0.001$), 4-phenylenediamine ($p = 0.003$), mercaptobenzothiazole ($p = 0.057$) and turpentine ($p = 0.018$) were younger than men who developed sensitivity to those chemicals (Table 2).

We analyzed the trend of the frequency of allergy in total and to specific allergens in 1996-2009 in males and females (Figure 1). A statistically significant decrease in the frequency of allergy to chromium, cobalt and formaldehyde, and an increase in nickel allergy was found to occur in the whole group. The frequency of hypersensitivity to chromium, formaldehyde and thiurams in women dropped, while the frequency of allergy to 4-phenylenediamine became higher (Figure 2). In men,

Table 1. Sensitization to common 10 allergens in patients of the Institute of Occupational Medicine in Lodz in 1996-2009

Allergens	Women		Men		Total		Value of *p*
	Number of tested subjects = 2959		Number of tested subjects = 1474		Number of tested subjects = 4433		
	No. of allergic patients	%	No. of allergic patients	%	No. of allergic patients	%	
Allergy to at least 1 of 10 allergens	1259	42.5	450	30.5	1709	38.6	< 0.001
Nickel	844	28.5	111	7.5	955	21.5	< 0.001
Cobalt	403	13.6	140	9.5	543	12.2	< 0.001
Chromium	225	7.6	196	13.3	421	9.5	< 0.001
Formaldehyde	180	6.1	70	4.7	250	5.6	0.066
4-Phenylene diamine	121	4.1	95	6.4	216	4.9	< 0.001
Balsam of Peru	122	4.1	80	5.4	202	4.5	0.053
Thiuram mix	113	3.8	59	4.0	172	3.9	0.77
Mercaptobenzothiazole	14	0.5	21	1.4	35	0.8	0.001
Benzocaine	19	0.6	12	0.8	31	0.7	0.52
Turpentine	15	0.5	8	0.5	23	0.5	0.88

Table 2. Mean age of patients allergic to 10 common allergens, depending on gender

Allergens	Women mean age = 40.0	Value of *p*	Men mean age = 43.8	Value of *p*	Total mean age = 41.0	Value of *p*	Value of *p* Comparison between genders
Nickel	37.7	< 0.001	41.9	0.16	38.2	< 0.001	0.001
Cobalt	38.7	0.079	44.4	0.60	40.2	0.20	< 0.001
Chromium	43.1	< 0.001	44.6	0.45	43.8	< 0.001	0.18
Formaldehyde	42.4	0.013	43.0	0.60	42.5	0.062	0.68
4-Phenylene diamine	39.5	0.69	45.0	0.36	41.9	0.29	0.003
Balsam of Peru	46.4	< 0.001	46.7	0.054	46.5	< 0.001	0.89
Thiuram mix	43.8	0.001	44.7	0.29	44.1	< 0.001	0.30
Mercaptobenzothiazole	40.6	0.85	48.2	0.097	45.2	0.046	0.057
Benzocaine	47.6	0.007	47.0	0.36	47.3	0.004	0.89
Turpentine	37.3	0.21	47.4	0.41	40.8	0.69	0.018

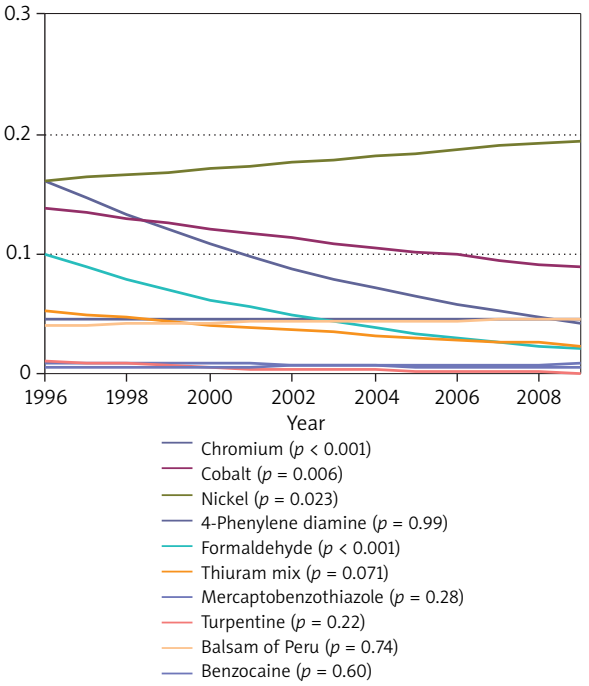

Figure 1. Trends in allergy to common allergens in the total study population, 1996-2009

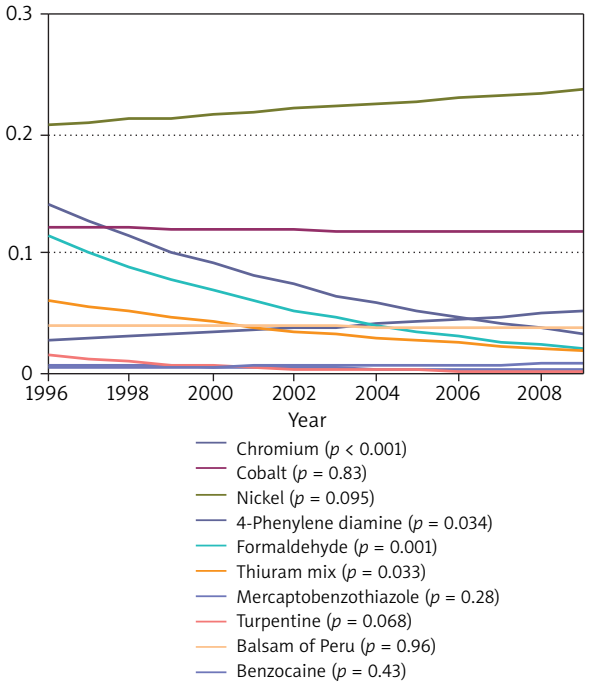

Figure 2. Trends in allergy to common allergens in women, 1996-2009

only decreasing trends in the frequency of sensitization were noted. The male subjects showed a reduced frequency in their sensitivity to chromium, cobalt and formaldehyde (Figure 3).

Discussion

Today, there are over 85 000 chemicals in the human environment. Nearly all of them can be irritants, and more than 3 700 compounds were identified as contact allergens. In the North America and Western Europe, 12.5% to 40.6% of the population (median: 21.2%) are allergic to at least one chemical [4].

In total, according to the data from most centres, allergy is caused most frequently by nickel. At the same time, allergy to chromates, rubber chemicals, formaldehyde, nickel and resins prevails in groups of patients with occupational dermatitis. Women are more often sensitive than

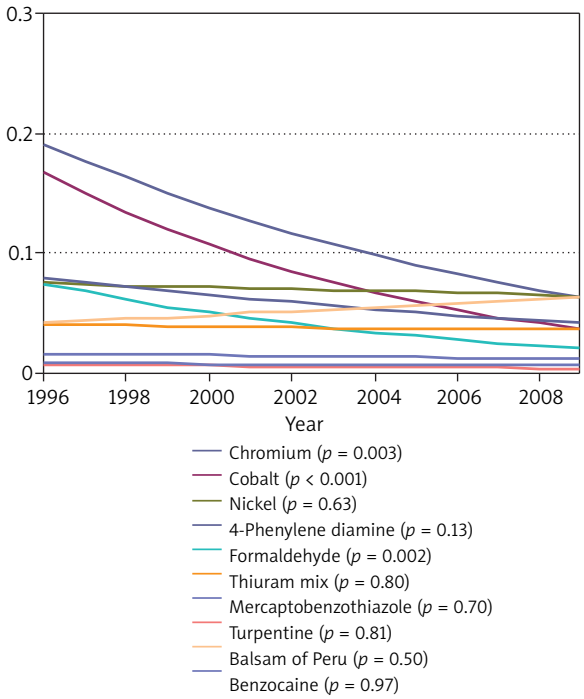

Figure 3. Trends in allergy to common allergens in men, 1996-2009

men (50.2% vs. 29.9%) [5]. Our results are in part consistent with these observations. As in other studies, women were in general more frequently sensitive than men (42.5% vs. 30.5%). However, our list of common allergens is slightly different. In our study, such allergy was caused by nickel, cobalt, chromium, formaldehyde, paraphenylenediamine, balsam of Peru and thiuram mix. In British studies, the list of 10 major allergens comprises nickel, perfume mix, balsam of Peru, cobalt, paraphenylenediamine, colophony and neomycin [6]. We have also noted some differences in the pattern of sensitization to individual allergens depending on gender. In our (NIOM) study, women were sensitive (in the descending order of frequency) to: nickel, cobalt, chromium, formaldehyde; in the British study, the corresponding order was: nickel, balsam of Peru, cobalt, 4-phenylenediamine. In our men, chemicals responsible most frequently for the allergy included chromium, cobalt, nickel, 4-phenylenediamine, while in the British study, the major allergens were: balsam of Peru, nickel, cobalt and thiurams [6].

Implementation, in the European Union, of the Nickel Directive (2001), intended to limit the quantities of nickel released from metal objects, resulted in some decrease in the frequency of the sensitivity. In Denmark, in children aged 0-18, the frequency of the allergy decreased from 24.8% to 9.2% over 12 years; in Germany, there was a drop in the frequency from 36.7% to 25.8% in women younger than 30 years during the 9-year follow-up [7, 8]. We have not noted a decline in the frequency of allergy to that metal during the recent 14 years. Instead, there is a slight upward trend of sensitization in the whole group of study subjects. In Poland, the Nickel Directive has been valid since 2004 and the effects of its implementation are likely to be evident only after some time. The fact that the contact hypersensitivity to nickel primarily concerns young people has been reported previously [6]. Our results confirm these observations in relation to both women and men.

In recent years, in Europe and the United States, the frequency of allergy to chromates has markedly decreased [9, 10]. A similar trend is observed in Lodz; however, the frequency is still higher than in other locations. In the EU, it is 0.5-1. 7% and about 2-4% in the U.S. [5, 10, 11], while the corresponding value resulting from the NIOM data is 9.5%. In Scandinavia, the decrease in the allergy to chromium is due, *inter alia*, to the inactivation of the sensitizing chromates in cement (for many years the main source of allergies to chromium). This decrease primarily relates to men since they perform jobs associated with exposure to chromium compounds (bricklayers, cement/concrete handling workers, painters, welders, etc.). As a result, in some countries, allergy to chromates is now even more common in women than in men. Such observations have been reported by German (sensitization of 1.5% in women and 0.7% in men) and Danish (2.5% vs. 2.4%, respectively) authors [5, 12]. In another analysis by the same Danish authors, no single case of allergy to chromium was recorded in men in 2006 [13]. Currently, they report chromate-tanned leather as the major source of chromium allergy [14]. In Lodz, allergy to chromates is still more frequent among men (13.3%) than women (7.6%), and the typical sources of allergy, such as cement, varnishes, paints, used lubricants and oils, leather tanning agents and laboratory reagents still prevail.

The frequency of allergy to cobalt decreased significantly in men, which is explainable by chromium/cobalt co-occurrence in cement. As a result of the major decline in the construction industry in Poland, and in particular in the prefabricated building construction industry, there has been a major decrease in exposure to cement, with the resultant drop in allergy to chromates and the sensitivity to cobalt, which is secondary to the previous hypersensitivity to chromium from the cement. On the other hand, we do not observe the downward trend of sensitization to cobalt in women. The sources of allergy to nickel and cobalt are similar. Cobalt usually occurs in the same metal products as nickel and at the moment there is no downward trend of nickel allergy in Poland. In our material, the frequency of allergy to cobalt is much higher than in the material of other authors. In studies by: Schäfer *et al*., it affected 3.4% of women and 1.4% of men in Germany [5]; Thyssen *et al*. – 0.4% of women and 0.1% of men in Denmark [13]; Garg *et al*. – 3.9% of women and 1.9% of men in the UK [6], while the corresponding proportions in our study were 13.6% and 9.5%, respectively.

So far, allergy to formaldehyde has occurred predominantly in the medical staff. In recent years, there has been

a decline in the frequency of the formaldehyde allergies. It seems reasonable to assume that the decline is linked to the withdrawal of most of the formaldehyde disinfectant preparations used in health care facilities for cold disinfection and replacing them with glutaraldehyde and glyoxal. This chemical causes also allergy among the workers of the textile industry (formaldehyde is a component of fabric finishing formulations) and metal working industry (formaldehyde and formaldehyde-releasing chemicals are included as preservatives in coolants used during metal cutting). The frequency of formaldehyde hypersensitivity in our material (5.6%) is higher than that reported by Schäfer *et al*. [5] in Germany (0.6%) and lower than that reported by the Finnish authors (6.3%) [11]. This frequency decreases both in women and men.

In the earlier years, thiurams were employed as major accelerators in the rubber used to manufacture surgical gloves. Since the late 1990s they have been replaced by less sensitizing thiocarbamates [15]. Chemical analysis done in 1992 showed that thiurams were still present in 4 popular types of gloves [16], while in 2000 – only in one [17], and in 2002, none of the commercially available surgical gloves contained thiurams [18]. Implementation of thiocarbamates in the production of rubber caused a decrease in the frequency of allergy to thiurams. This is confirmed in reports by Geier *et al.* [19], Nguyen *et al*. [10] and Gibbon *et al.* [20]. In our material, the decline was found to occur only in women. In our opinion, this results from a decreased frequency of allergy to the gloves in health care facilities that employ more women than men. In the presented material, allergy affected 3.9% of the subjects; this is a value similar to that obtained in studies performed in the United States (4.6%) [10]. In the European Union, this frequency is significantly lower (0.1%) [13].

The frequency of allergy to 4-phenylenediamine in the EU and the US ranges from 1.5% to 6.8% [5, 21]. The frequency in our material (4.9%) is within that range. Fashion for hair colouring, widespread among women and increasingly popular among men, youths and children, as well as fashion to apply permanent and temporary tattoos has increased allergies, as evidenced by reports from the UK [22, 23] and Germany [24]. We also observe an increasing trend of sensitization in women.

Many authors report more frequent sensitivity to 4-phenylenediamine among women than men, and the allergies were due to non-occupational agents (hair dyes) [9]. In our material, the frequency of allergies for many years has been higher in men than in women [25]. This indicates a significant contribution of occupational factors to the development of the hypersensitivity. Allergy to aromatic amines in men was attributable to contact with technical black rubber, fuel oil and grease, and the positive results of patch tests with PPD in most cases resulted from the cross-reactivity. In women, the sources of allergies were typical. The sensitization was primarily caused by hair dyes.

The average age was lowest in women with allergies to nickel, while it was highest in those susceptible to benzocaine and balsam of Peru. Age of men allergic to various allergens did not differ significantly, while it was highest in those sensitized to mercaptobenzothiazole, benzocaine and balsam of Peru. The sensitization to these allergens in the elderly people has been reported previously [26].

The pattern of contact allergy in Poland for several years has differed significantly from that prevailing in other countries. After Poland had become a European Union member state and after the resultant social and economic transformations, those differences became considerably less evident, but some peculiarities are still present.

Acknowledgments

Publication co-financed by the European Union under the European Social Fund, prepared as part of the project "Development of comprehensive programs intended to restore work ability." Project Number: POKL/Powroty/2008-2011/zad.3

Reference

1. Schnuch A, Uter W, Geier J, Gefeller O; IVDK study group. Epidemiology of contact allergy: an estimation of morbidity employing the clinical epidemiology and drug-utilization research (CE-DUR) approach. Contact Dermatitis 2002; 47: 32-9.
2. Klimańska M, Żmudzińska M, Jenerowicz D, et al. The importance of exposure to contact allergens in patients with allergic contact dermatitis. Post Dermatol Alergol 2011; 28: 203-11.
3. Fregert S. Manual of contact dermatitis. Munksgaard, Copenhagen 1981.
4. Thyssen JP, Linneberg A, Menné T, Johansen JD. The epidemiology of contact allergy in general population – prevalence and main findings. Contact Dermatitis 2007; 57: 287-99.
5. Schäfer T, Böhler E, Ruhdorfer S, et al. Epidemiology of contact allergy in adults. Allergy 2001; 56: 1192-6.
6. Garg S, McDonagh AJG, Gawkrodger DJ. Age- and sex-related variations in allergic contact dermatitis to common allergens. Contact Dermatitis 2009; 61: 46-7.
7. Johansen J, Menné T, Christophersen J, et al. Changes in the pattern of sensitization to common contact allergens in Denmark between 1985-86 and 1997-98, with a special view to the effect of preventive strategies. Br J Dermatol 2000; 142: 490-5.
8. Schnuch A, Uter W. Decrease in nickel allergy in Germany and regulatory interventions. Contact Dermatitis 2003; 49: 107-8.
9. Thyssen JP, Johansen JD, Menné T. Contact allergy epidemics and their controls. Contact Dermatitis 2007; 56: 185-95.
10. Nguyen SH, Dang TP, MacPherson C, et al. Prevalence of patch test results from 1970 to 2002 in a multi-centre population in North America (NACDG). Contact Dermatitis 2008; 58: 101-6.
11. The ESSCA Writing Group. The European Surveillance System of Contact Allergies (ESSCA): results of patch testing

the standard series, 2004. J Eur Acad Dermatol Venereol 2008; 22: 174-81.
12. Thyssen JP, Jensen P, Carlsen BC, et al. The prevalence of chromium allergy in Denmark is currently increasing as a result of leather exposure. Br J Dermatol 2009; 161: 1288-93.
13. Thyssen JP, Linneberg A, Menné T, et al. Contact allergy to allergens of the TRUE-test (panel 1 and 2) has decreased modestly in the general population. Br J Dermatol 2009; 161: 1124-9.
14. Zachariae CO, Agner T, Menné T. Chromium allergy in consecutive patients in country where ferrous sulphate has been added to cement since 1981. Contact Dermatitis 1996; 35: 83-5.
15. Wan Manshol bin Zin W. Radiation vulcanized natural rubber latex (RVNRL). Malaysian Rubber Seminar 1998; 28-31.
16. Knudsen BB, Larsen E, Egsgaard H, Menné T. Release of thiurams and carbamates from rubber gloves. Contact Dermatitis 1993; 28: 63-9.
17. Knudsen BB, Hametner C, Seycek O, et al. Allergologically relevant rubber accelerators in single-use medical gloves. Contact Dermatitis 2000; 43: 9-15.
18. Brehler R, Rütter A, Kütting B. Allergenicity of natural rubber latex gloves. Contact Dermatitis 2002; 46: 65-71.
19. Geier J, Lessmann H, Uter W, et al. Occupational rubber glove allergy: results of the Information Network of Dermatology (IVDK), 1995-2001. Contact Dermatitis 2003; 48: 39-44.
20. Gibbon Kl, McFadden JP, Rycroft RJG, et al. Changing frequency of thiuram allergy in healthcare workers with hand dermatitis. Br J Dermatol 2001; 144: 347-50.
21. Marks JG, Belisto DV, DeLeo VA, et al. North American Contact Dermatitis Group patch test results for the detection of delayed-type hypersensitivity to topical allergens. J Am Acad Dermatol 1998; 38: 911-8.
22. Søsted H, Hesse U, Menné T, et al. Contact dermatitis to hair dyes in a Danish adult population: an interview-based study. Br J Dermatol 2005; 153: 132-5.
23. Patel S, Basketter DA, Jefferies D, et al. Patch test frequency to p-phenylenediamine: follow up over the last 6 years. Contact Dermatitis 2007; 56: 35-7.
24. Uter W, Lessmann H, Geier J, Schnuch A. Contact allergy to ingrediens of hair cosmetics in female hairdressers and clients – 8-year analysis of IVDK data. Contact Dermatitis 2003; 49: 236-40.
25. Kieć-Świerczyńska M, Kręcisz B, Świerczyńska-Machura D. 10-year observation of contact allergy to paraphenylenediamine based on information collected by the Nofer Institute of Occupational Medicine in Lodz [Polish]. Med Pr 2007; 58: 215-22.
26. Wantke F, Hemmer W, Jarisch R, et al. Patch test reactions in childen, adults and the elderly. A comparative study in patients with suspected allergic contact dermatitis. Contact Dermatitis 1996; 34: 316-9.