

para-Phenylenediamine Hypersensitivity: A Report From Budapest, Hungary, 2007–2014

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Background: *para*-Phenylenediamine (PPD) is a potent allergen with frequent exposure through use of hair dyes or henna tattoos.

Objectives: We wished to determine if prevalence of PPD sensitivity is changing through time as trends in its use change.

Patients: A total of 3631 patients were patch tested consecutively with the environmental standard series between 2007 and 2014 to map the prevalence of PPD sensitivity and its distribution according to age, sex, and diagnosis.

Results: Two hundred nine patients (5.75%) were proven to be PPD sensitive. Most PPD-sensitive patients were approximately in their 60s in 2007, whereas in 2014, they were in their 20s and 30s. In 2014, 61.1% of the patients were younger than 35 years and 50% were younger than 25 years. Of 209 PPD-sensitive patients, 32.5% had present relevance related to hair dyeing and eyebrow or eyelash coloring procedures. All affected male patients were hairdressers. Adverse reaction to henna was detected in only 1 case after henna hair dye use.

Conclusions: The 5.75% prevalence of PPD sensitization in our study was higher compared with that in the European data. It is alarming that PPD hypersensitivity occurred even among teenagers. This may be mainly explained by hair dyeing at an early age.

Hair dyes have been used for thousands of years. During this time, the basic substances, compositions of ingredients, and methods of application have changed. Nowadays, *para*-phenylenediamine (PPD) seems to play the most significant role in the development of adverse reactions to hair dyes. Long-term consequences of sensitization influence the patients' quality of life, because substances with chemical structure similar to PPD may initiate cross-reactions. The significance of this allergen is demonstrated by the fact that PPD was chosen as the "Allergen of the Year" by the journal *Dermatitis* in 2006.^{1,2} Adverse reactions triggered by genuine natural henna are extremely rare, and

they are mainly caused by added compounds, for example, PPD ("black henna").^{3–10}

PATIENTS AND METHODS

A total of 3631 patients were patch tested consecutively with the environmental standard series between January 1, 2007, and December 31, 2014, at the Allergology Outpatient Unit of the Department of Dermatology, Venerology, and Dermato-oncology of the Semmelweis University, Budapest, Hungary. We studied the prevalence of PPD sensitivity and its distribution according to age, sex, and diagnosis of the patients.

Patch testing was performed on symptom-free patients because of suspected contact sensitization on the basis of their medical history. The antigens were applied on the dorsal skin, in a 48-hour occlusion. Evaluation of the test was performed at the 60th minute of the occlusion, then on D2, D3, D4, and D7. Reactions were taken as positive 1+ or more intense. Exclusion criteria of the test were the following: locally used steroids a week before the examination, taking antihistamines a week before and during the examination or systemic steroid treatment, UV radiation 6 weeks before the examination, acute or active skin symptoms, active rhinitis, pregnancy, and breastfeeding. Patch testing was performed using allergens dissolved in the nonirritating vehicle in internationally controlled and accepted concentrations (allergEAZE; Brial Allergen GmbH, Germany).

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The work has been approved by the ethical committees of the institution in which the study was performed, and the subjects gave informed consent.

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RESULTS

Two hundred nine (5.75%) of the 3631 patch-tested patients were proven to be PPD-sensitive. A total of 78.9% (165) were women and 21% (44) were men. During the 8-year-long examination period, the number of PPD-sensitive patients first significantly decreased and then stabilized (Table 1).

Patients were classified into the following 8 different age groups: 5 to 14, 15 to 24, 25 to 34, 35 to 44, 45 to 54, 55 to 64, 65 to 74, and 75 to 84 years. In 2007, most PPD-sensitive patients were around the age of 60. The proportion of younger age groups increased in the next years. Patients who were in their 40s in 2010 and in their 30s and 40s in 2011 dominated. In 2013, the age distribution was more balanced; in 2014, the younger generation became dominant (Fig. 1). In 2007, 20% of the PPD-sensitized patients were younger than 35 years. In 2012, 42.9% were younger than 35 and 28.5% younger than 25 years. Meanwhile, in 2014, 61.1% were younger than 35 years and 50% were younger than 25 years (Fig. 2).

The median age distribution of the patients tested positive for PPD for the examined period shifted toward younger groups as well (Fig. 3). Although the median age was 53 years in 2007, a moderate decrease was observed during the years and the median value was only 34 years in 2014.

Regarding diagnostic distribution of the PPD-sensitive patients, contact dermatitis was the most frequent diagnosis (81.8%, 171/209). It was followed by atopic dermatitis (13 patients, 6.2%), psoriasis (10 patients, 4.8%), dyshidrosis (6 patients, 2.8%), rosacea/perioral dermatitis (4 patients, 2%), chronic venous insufficiency (3 patients, 1.4%), and urticaria (2 patients, 0.9%).

Contact-related localization of skin symptoms occurred in the following order of frequency: scalp itching, dermatitis (23/68), periorbital contact dermatitis (19/68), and facial Quincke edema-like allergic contact dermatitis (16/68). The hands were also commonly affected (16/53; itching, contact dermatitis), typically in cases of occupational exposures (hairdresser, beautician, tattooist).

According to the anamnesis and localization of symptoms, of the 209 PPD-sensitive patients, 68 (32.5%) had present relevance related directly to hair dyeing or coloring procedures (symptoms were preceded by hair, eyebrow, or eyelash coloring, or occupations such as

hairdresser, beautician, tattooist). Out of the 68 patients, 63 were females (92.6%) and 5 were males (7.4%). All male patients were hairdressers. Adverse reaction to henna was detected in only 1 case after henna hair dye use. We did not find any data in the patients' medical history on previous temporary exposure to black henna tattooing.

DISCUSSION

The main source of PPD contact nowadays is hair dyeing; therefore, it means a significant risk to sensitization.^{3–17} Teenagers and adolescents are at special risk because hair dyeing performed at a very young age and influenced by unsafe fashion trends is also widely typical. *para*-Phenylenediamine is a strong sensitizer, and it is very irritating because of the ammonia released at destaining.^{7,10,15–18} Hair dyeing may provoke several adverse reactions; according to the literature, contact dermatitis is the most frequent reaction.^{4,8,12,15,16} Contact urticaria, bullous or edema-associated reactions, and erythema multiforme-type skin lesions have also been published in connection with hair and skin coloring procedures.^{9,12,18–28}

Local anesthetics, sulfonamides, anthraquinone-type purgatives, antihistamines, other ingredients of hair dyes, and certain food additives can give cross-reactions in sensitized patients, because these are compounds with chemical structure similar to PPD. Cross-reactive compounds simultaneously present in hair dyes may lead to synergistic immunological processes.^{4,13,14,16–19,21,27,29}

Adverse reactions triggered by genuine natural henna are extremely rare. However, the number of publications on reactions to temporary tattoos has increased in the past few years. Presumably, the newly recognized black henna is in the background, which is the result of other compounds added principally to the reddish brown henna. Such a compound is PPD, making the color of temporary tattoos darker and longer lasting as well as reducing the application time. The PPD concentration in black henna can reach even 15.7%, which is much higher than permitted in hair dye substances.^{3,4,6,7,10,11,13,14,19,30,31} Children and adolescents are at special risk^{7,15,16} because henna tattoos on the skin are frequent among them during summer holidays.

TABLE 1. Frequency of PPD Sensitivity, Mean Age of the PPD-Sensitive Patients, and the Youngest Patients With PPD Sensitivity 2007–2014

Year	Tested Patients/Year	No. PPD Sensitivity Cases	Total of Tested Patients, %	Age, PPD-Sensitive Patients, Mean	Youngest Patient With PPD Sensitivity, Age, y
2007	538	65	12.1	46	19
2008	514	34	6.6	43.3	22
2009	512	22	4.3	41.4	17
2010	480	15	3.1	29.3	15
2011	401	16	3.9	41.2	16
2012	413	21	5.1	44.2	19
2013	390	18	4.6	50.8	20
2014	383	18	4.7	33.7	19

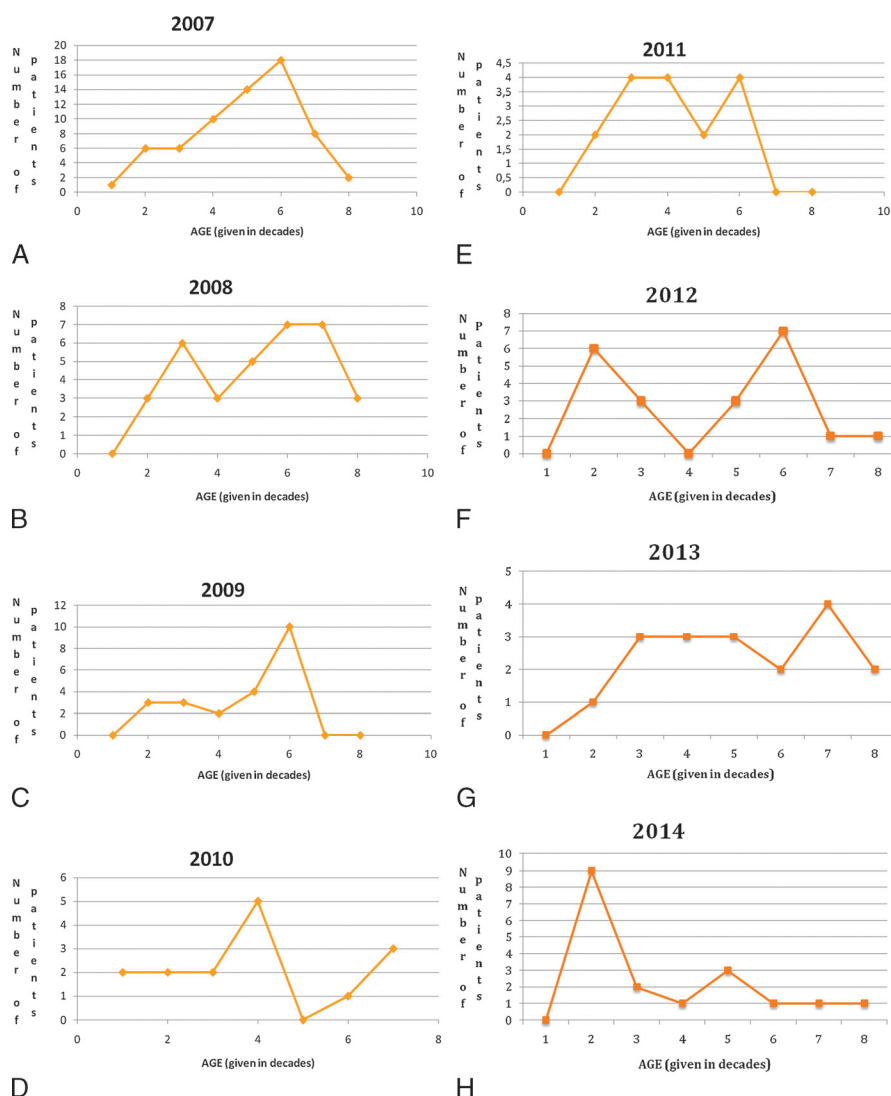


Figure 1. Age distribution of PPD-allergic patients.

Two thirds of the European PPD-allergic patients are women.^{14,19} The source of exposure so far has been mainly hair dyes.^{2,19} Skin symptoms mostly appear on the face and on the neck, although the trunk, hands, legs, and arms can also be affected.^{17,19} On the contrary, in Asia, most PPD-sensitized patients are men. The reason for this is that in Europe, women are most likely to dye their hair, generally every 1 to 6 months, whereas in Asia, men generally dye their beard every week. Accordingly, frequency of allergen exposure is also an important factor in sensitization.¹⁴

The prevalence of PPD sensitization in the general European population is between 0.0% and 2.5%.^{14,23,24} Among European hairdressers, PPD sensitization is quite frequent, because it can be as high as 20%.^{24,32} The prevalence is the lowest in the Scandinavian countries; however, hair dyes of lighter shade contain considerably less allergen.^{13,33}

The prevalence of PPD allergy among dermatitis patients was found to be 4.3% in Asia, 4% in Europe, 6.2% in North America,

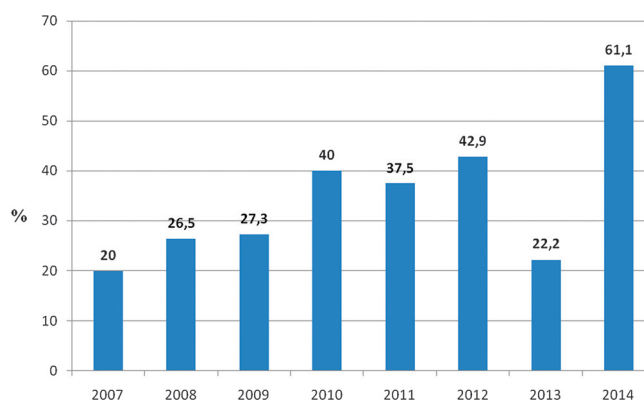


Figure 2. para-Phenylenediamine-allergic patients younger than 35 years.

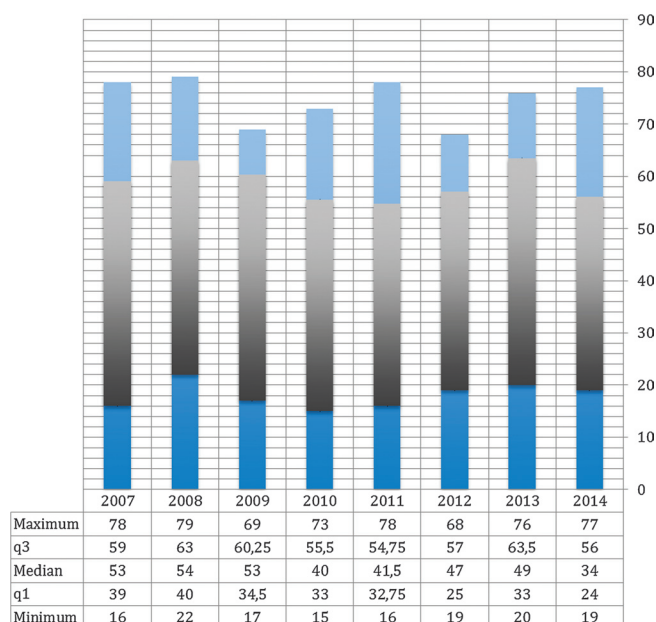


Figure 3. Age distribution of PPD-allergic patients (minimum, first quartile, median, third quartile, and maximum values).

and 2% in Australia.^{14,17} The rising prevalence of PPD sensitivity in elderly persons can be explained by hair dyeing for decades. In the younger age group, it may be associated with hair dyeing started very early and with the similarly popular but unregulated black henna tattoos. The very high PPD content of the latter ones (reaching even 15.7%) is almost 8 times more than the permitted concentration in hair dyes (2%). In younger age groups, severe reactions are likely to develop more frequently.^{2,3,9,14,18,27,31,34,35} Temesvári et al²⁰ found rather high (3.7%) PPD hypersensitivity among patients with periorbital dermatitis in a Hungarian study. It can be connected to the use of PPD for dyeing eyebrows and eyelashes by beauticians.

CONCLUSIONS

para-Phenylenediamine is a common and potent environmental allergen. The 5.75% prevalence of PPD sensitization found among our patients is higher compared with the European data. Age distribution of the sensitized patients has changed during the 8 years. On the contrary, the dominance of patients in their 60s observed in 2007, in their 30s and 40s in 2012, and in their 20s and 30s in 2014 was evident. In 2014, 61.1% of the PPD-sensitized patients were younger than 35 years and 50% were younger than 25 years. It is alarming that adverse reactions elicited by hair coloring occurred in very young patients, even among teenagers. The source of PPD hypersensitivity was hair dyeing. Adverse reaction triggered by henna hair dyeing was rare, only 1 case in our study, and we did not find any data in the patients' medical history about previous black henna tattooing. As to the occupations, it is important to emphasize that hairdressers have been exposed most of all to hair dyes since their apprenticeship.

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