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Japundžić, Iva; Vodanović, Marin; Lugović-Mihić, Liborija

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An Analysis of Skin Prick Tests to Latex and Patch Tests to Rubber Additives and other Causative Factors among Dental Professionals and Students with Contact Dermatoses

Iva Japundžić[a] Marin Vodanović[b, c] Liborija Lugović-Mihić[a]

[a]Clinical Department of Dermatovenereology, Sestre milosrdnice University Hospital Center, Zagreb, Croatia; [b]Department of Dental Anthropology, School of Dental Medicine, University of Zagreb, Zagreb, Croatia; [c]University Hospital Centre Zagreb, Zagreb, Croatia

Keywords
Dentists · Students · Contact dermatitis · Allergy · Latex gloves

Abstract
Background: Dental workers often experience unwanted allergic and nonallergic skin reactions resulting in different contact dermatoses (e.g., contact urticaria, irritant and allergic contact dermatitis) that are often attributed to rubber gloves. ***Objective:*** To examine allergic and nonallergic contact dermatoses by different methods amongst dental professionals and dental students, more specifically, reactions to natural rubber latex (NRL), rubber additives, and other causative factors. ***Methods:*** In this cross-sectional study we surveyed a total of 444 subjects (dentists, assistants, technicians, and students); 200 agreed to be tested to latex by the standard skin prick test (SPT) and prick-by-prick test, of whom 107 were patch tested to rubber additives (mercapto mix, thiuram mix, carba mix, and N-isopropyl-N-phenyl-4-phenylenediamine [IPPD]). ***Results:*** Skin lesions appeared significantly more frequently with longer work experience ($p = 0.002$; $V = 0.181$), frequent glove changes ($p < 0.001$; $V = 0.310$), and hand washing ($p < 0.001$; $V = 0.263$), and in subjects with a history of allergies (atopic dermatitis, allergic rhinitis, allergic conjunctivitis, and others) ($p < 0.001$; $V = 0.183$). Positive SPTs to latex occurred in 14/200 subjects (7%), of whom 5/14 subjects (35.7%) were also positive in prick-by-prick tests. Patch tests were positive in 5/104 subjects (4.8%) (mercapto mix 1%, thiuram mix 1.9%, and carba mix 1.9%). ***Conclusion:*** Only a small number of our subjects were allergic to latex (7%) or rubber additives (4.8%). Thus, self-reported contact dermatoses (during NRL product use) in dental professionals and students are not commonly caused by allergies to latex and rubber additives, as is often assumed, but by other factors.
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Introduction

Skin lesions due to professional exposure are frequently found in medical and dental workers, often explained by rubber material use, especially natural rubber latex (NRL) glove use [1–5]. In practice, the term "work-related dermatoses" refers to three types of reactions: IgE-mediated allergy (type I), irritant, nonallergic contact dermatitis (CD),

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E-Mail karger@karger.com
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Dr. Iva Japundžić
Clinical Department of Dermatovenereology
Sestre milosrdnice University Hospital Center
Vinogradska cesta 29, HR–10 000 Zagreb (Croatia)
E-Mail iva.japundzic@gmail.com

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Table 1. Questionnaire

Occupation: – dental student (year) ____ – dental professional (year of work) ____	
Have you observed work-related skin changes (itchy rash)? ____	How many times per day do you wash your hands? ____
Do you use latex gloves? (powdered or powder-free?) ____	Have you had any allergic conditions before and which? (multiple answers are possible)
How many pairs of gloves do you use per day on average? ____	Do you have hobbies that include long-term contact with liquids? ____

and allergic CD (type IV) [6]. Allergies to latex gloves are frequently reported, usually immediate-type allergies (contact urticaria) and delayed-type allergies (allergic CD) [1, 3, 7–10]. Often overlooked is nonallergic CD (irritant or toxic), common in healthcare workers due to frequent hand washing, glove changes, harsh soaps, disinfectants, detergents, etc. [5, 7, 11, 12]. Other factors can also contribute to the onset of irritant CD – perspiration from glove occlusion or prolonged contact with an alkaline, skin sensitivity, prior skin damage, or an atopy such as atopic dermatitis (AD) [13]. In diagnostics of rubber glove allergies, the most common tests are skin prick tests (SPTs) and/or latex-specific IgE assay to determine immediate-type allergies to *Hevea brasiliensis*, and patch tests to determine delayed-type allergies to rubber additives [1, 14, 15].

Since gloves are generally reported as the main factor for dermatitis onset, and since latex gloves are the most commonly used gloves in our country, Croatia, despite international recommendations (except in the cases of observed and proven reactions to latex gloves), we wanted to analyze allergy test results to latex and rubber additives. The aim of this study, in contrast to many previous studies, was to use a number of methods (questionnaire, SPT, patch test) to gain more thorough insight into various allergic and nonallergic factors that contribute to the onset of self-reported skin lesions among dental professionals and students.

Subjects and Methods

Research was carried out at the Clinical Department of Dermatovenereology, University Hospital Center Sestre milosrdnice, Zagreb, and the School of Dental Medicine, University of Zagreb, Croatia (May 2015 to May 2016) with approval from the Ethics Committee of the School of Dental Medicine (Ref. No. 05-PA-26-6/2015).

Subjects

The research included 444 subjects from several dental medicine institutions (employees from the Zagreb School of Dental Medicine and several dental clinics) – 301 dental professionals (261 dentists, 37 assistants, and 3 technicians) and 143 dental medicine students (33 second-year students not involved in dental work, 69 fourth-year students, and 41 sixth-year students). The subjects participated voluntarily and signed informed consent. The inclusion criteria were their lifetime use of latex gloves/materials; the exclusion criteria (for skin test interpretation) were dermographism and a negative reaction to histamine.

Methods

In this cross-sectional study, we included a questionnaire and skin tests (prick-by-prick test to latex, SPT to latex, and patch test to rubber additives). A total of 200 subjects underwent prick-by-prick tests to compare the results to SPTs. Among those, 104 agreed to undergo patch testing.

The questionnaire included questions about respondents' dental work habits, practices, and previous allergies (AD, allergic rhinitis, allergic conjunctivitis, and others) (Table 1). Some subjects (n = 200) filled it out when undergoing skin tests, while others (n = 244) completed it online.

SPTs were performed with a 2% latex allergen solution from the Institute of Immunology, Zagreb, Croatia [16]. A wheal ≥3 mm in diameter with a negative buffer solution and a positive reaction to histamine was considered a positive result.

Prick-by-prick tests correspond to SPTs, the difference being that the allergen was applied to the forearm directly from the source (latex gloves without talc Basic Plus; AMPRI GmbH, Germany) by using a lancet to prick through a piece of glove placed on the skin.

Patch tests to rubber additives were carried out by placing allergen patches (Curatest® Patch Test Strips; Lohman & Rauscher International, Rengsdorf, Germany) on the interscapular skin. Additives used were mercapto mix (2% petrolatum [pet.]), thiuram mix (1% pet.), carba mix (3% pet.), and N-Isopropyl-N-phenyl-4-phenylenediamine (IPPD) (0.1% pet.) from the Institute of Immunology, Zagreb, Croatia, and results were interpreted after 48 and 72 h according to European Society of Contact Dermatitis guidelines [17]. As this was a field research, our subjects could not, and did not, agree to further readings on following days.

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Table 2. The prevalence of self-reported work-related skin lesions in relation to the number of gloves used daily

	Frequency of glove pair changes					*p**	Cramer's *V*
	do not use (*n* = 21)	<5 pairs/day (*n* = 113)	5–10 pairs/day (*n* = 109)	>10 pairs/day (*n* = 201)	total (*n* = 444)		
Presence of skin lesions	5 (23.8)	42 (37.2)	60 (55.0)	142 (70.6)	249 (56.1)		
Absence of skin lesions	16 (76.2)	71 (62.8)	49 (45.0)	59 (29.4)	195 (43.9)	<0.001	0.310

Values are *n* (%). * χ^2 test.

Statistical analysis included the Fisher exact test, χ^2 test, and *z*-test with Bonferroni correction of *p* values for multiple comparisons. The effect size was quantified using ϕ and Cramer's *V*; Cohen's standards were used for its interpretation [18]. The connection between exposure to a certain factor and observing work-related dermatoses (based on surveys) was quantified by odds ratio (OR) and 95% confidence intervals (CI). The commercial statistics software IBM SPSS 21 (IBM Corp., Armonk, NY, USA) was used.

Results

Survey of Frequency of Skin Contact Reactions and Related Factors

Work-related skin changes were self-reported by 249 subjects (56.1%). Regarding the duration of professional work, lesions were most frequent in those with >30 years of experience (76.2%), much more frequent than in those with <10 years (51.3%) and 21–30 years (47.9%) (p = 0.002; V = 0.181) (Fig. 1).

Skin changes were significantly connected with the number of gloves used daily, ranging from 37.2% in those using <5 pairs/day to 70.6% in those using >10 pairs/day ($p < 0.001$; $V = 0.310$), with a large effect size (Table 2).

According to data from all 444 subjects, at the time of the survey 52.5% of participants were using powdered NRL gloves, 27.9% were using powder-free NRL gloves, and 9% reported they had stopped using any kind of NRL gloves because of their harmful effects. Of 249 participants who had noticed skin lesions, at the time of research 47% of them were using powdered NRL gloves and 61% were using powder-free NRL gloves (Fig. 2).

Hand-washing frequency had a significant impact on dermatoses prevalence ($p < 0.001$; $V = 0.263$), with a moderate effect size (Table 3). Dermatoses prevalence was significantly connected with subjects' personal allergy histories ($p < 0.001$; $V = 0.183$), with a small effect size (Table 4). Thus, dermatoses risk was 2.2 times higher in subjects with allergy histories (OR 2.2, 95% CI 1.5–3.3).

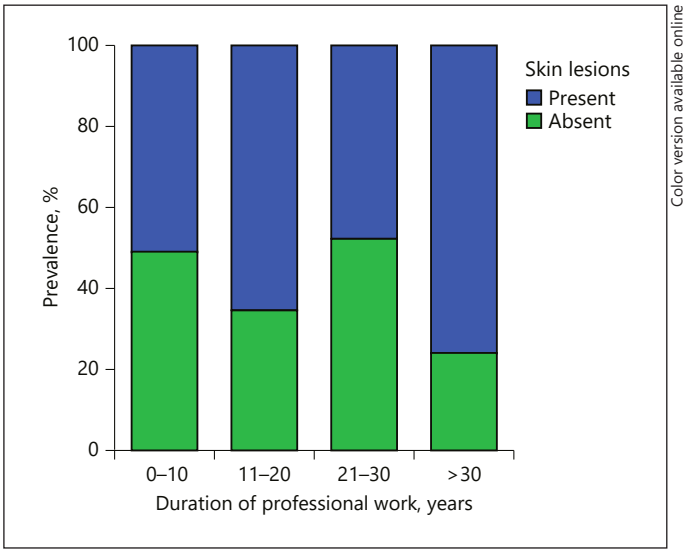

Fig. 1. The prevalence of self-reported work-related skin lesions in relation to duration of professional work.

Subjects reported various previous allergy frequencies (Table 5). Reported contact dermatoses risk was 2.5 times higher in AD subjects and 2 times higher in those with an allergic rhinitis history. Among subjects with an AD history, we confirmed a latex allergy by SPT in 21.4% of them and by prick-by-prick test in 14.3%. Prolonged contact with liquids outside work, reported by 13% of subjects, had no significant impact on lesion incidence (Table 6).

The Results of SPTs to Latex in Comparison to Prick-by-Prick Tests to Latex

Standard SPTs showed positive reactions in 14/200 tested subjects (7%), of whom 5/14 subjects (35.7%) were also positive in prick-by-prick tests. Similarly, prick-by-

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Table 3. The prevalence of self-reported work-related skin lesions in relation to daily hand-washing count

	Hand-washing frequency				*p**	Cramer's *V*
	<10× (*n* = 68)	10–20× (*n* = 234)	>21 (*n* = 142)	total (*n* = 444)		
Presence of skin lesions	24 (35.3)	121 (51.7)	104 (73.2)	249 (56.1)		
Absence of skin lesions	44 (64.7)	113 (48.3)	38 (26.8)	195 (43.9)	<0.001	0.263

Values are *n* (%). * χ^2 test.

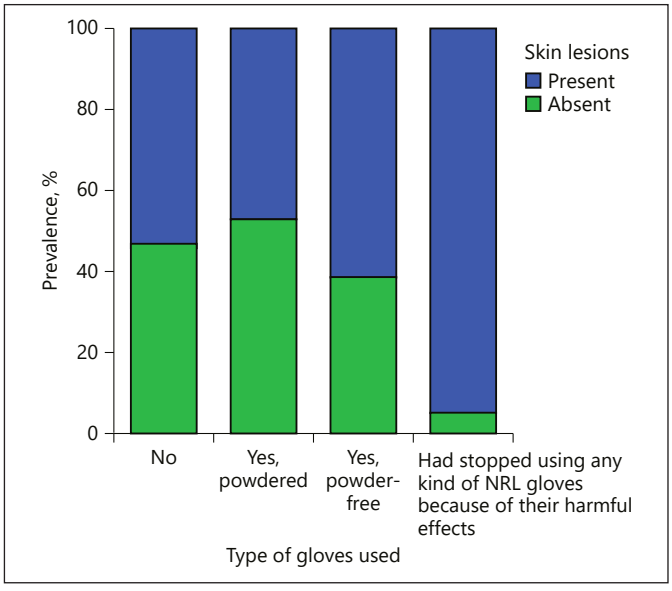

Fig. 2. The prevalence of self-reported work-related skin lesions in relation to the type of latex gloves used. NRL, natural rubber latex.

Color version available online

Table 4. Self-reported skin lesions in relation to previous allergic reactions

	Previous allergies			*p**	ϕ
	present (*n* = 294)	absent (*n* = 150)	total (*n* = 444)		
Skin lesions					
Present	184 (62.6)	65 (43.3)	249 (56.1)		
Absent	110 (37.4)	85 (56.7)	195 (43.9)	<0.001	0.183

Values are *n* (%). * Fisher's exact test.

prick tests were positive in 15/200 subjects (7.5%), whereas 5/15 (33.3%) were positive in both tests and 10/15 (66.7%) only in prick-by-prick tests.

Patch Test Results

Patch tests were positive in 5/104 subjects (4.8%) with confirmed allergies to mercapto mix (1%), thiuram mix (1.9%), and carba mix (1.9%).

Discussion

An earlier, extensive study on work-related contact dermatoses in various professions found the highest incidence among healthcare workers including dental workers (64%), midwives (67%), nurses (51%), and medical doctors (41%) [11]. Although skin lesions are often attributed to a latex allergy, studies have indicated that only 4–6% of dental workers are really allergic to latex (type I) [16, 19]. As reported in our previous study on dental workers, their clinical pictures were mostly erythema and dryness (66%), while localizations were predominantly on the hands and fingers (96%) [16]. According to the study by Minamoto et al. [12], 46.4% of dental workers reported a lifetime history of chronic hand eczema, which was commonly related to a history of AD, asthma/allergic rhinitis, dry skin, shorter duration of work, and hand washing (>10 times/day). Our results were somewhat similar and indicated peak lesion incidence at the beginning and end of a professional career. Their incidence significantly depends on the length of professional exposure (with a large effect size) and the number of gloves used daily (with a very large effect size) which implies that workers who change gloves more frequently have a higher working load and therefore longer exposure per day. Also, dental professionals with a long lifetime work exposure experience a growth in lesion incidence, likely due to increased skin dryness with age and cumulative exposure

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Table 5. Self-reported types of allergic reactions

Previous allergies	*n*	Self-reported skin lesions, %	*p**	ϕ	OR	95% CI
Allergic rhinitis	59	23.7	0.007	0.131	2.0	1.2–3.4
Atopic dermatitis	30	12	0.012	0.120	2.5	1.2–5.3
Allergic conjunctivitis	23	9.2	0.144	0.078	1.9	0.9–4.1
Others						
Penicillin	21	8.4	0.193	0.064	1.7	0.8–3.7
Latex	18	7.2	<0.001	0.165	15.1	2.0–114.3
Food	18	7.2	0.318	0.054	1.6	0.7–3.7
Metal	17	6.8	0.010	0.127	4.7	1.4–16.2
Asthma	16	6.4	0.202	0.064	1.8	0.7–4.6

* Fisher's exact test. Some subjects reported multiple reactions.

Table 6. The prevalence of self-reported work-related skin lesions in relation to prolonged contact with liquids outside work-related activities

	Contact with liquids			*p**	ϕ
	no (*n* = 386)	yes (*n* = 58)	total (*n* = 444)		
Presence of skin lesions	216 (56.0)	33 (56.9)	249 (56.1)		
Absence of skin lesions	170 (44.0)	25 (43.1)	195 (43.9)	1.000	0.006

Values are *n* (%). * Fisher's exact test.

to skin irritants over time. Further, frequent contact with water is also harmful, particularly in the case of dental workers who must wash their hands frequently and thoroughly, thus resulting in irritant CD.

When analyzing the results of SPTs to latex and type of gloves used, our results showed that out of 14 participants allergic to latex, 9 used powdered NRL gloves, and 5 used powder-free gloves. This association, observed in the majority of subjects, may indicate that powdered NRL gloves contain more latex protein and are more apt to cause immediate-type allergies because of contamination during the manufacturing process.

As lesions are common in those with <10 years of experience (51.3%), it is necessary that young professionals and dental students also pay particular attention and start taking protective measures as soon as they begin to work by avoiding frequent contact with harmful substances, applying protective creams, using sensitive-skin soaps, etc. [12]. Since a history of allergies is a risk factor, dental students should also be aware of that. According to the study by Vangveeravong et al. [20] of 617 dental students, latex allergies were found in 5% of subjects with different related risk factors – history of allergies, glove use (>18 h/week, >3 pairs of gloves/day), and many years of exposure. As our previous study (using SPTs to latex) supports similar results, in this study we additionally performed more methods to get more thorough information [16]. However, dental workers with an AD history should be aware of possible harmful effects of work-related activities to their skin, as they are more prone to irritant CD due to impairment of the skin barrier [8, 10, 21]. Also, as irritant CD predisposes to the occurrence of allergic CD, it is also important to recognize and examine a possible delayed allergy to rubber additives. According to the patch test results of Schwensen et al. [22] (thiuram mix, mercaptobenzothiazole, mercapto mix), this contact allergy was found in 3.1% (often to thiuram mix) and was significantly associated with occupational CD, hand and facial dermatitis, and age (>40 years). According to the patch testing of dental workers by Minamoto et al. [12], the most frequent occupationally relevant contact allergens were rubber chemicals and acrylates. Because of the

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limited conditions of our field study and its implementation, we did not research other common allergens in today's dental work environment (acrylates and methacrylates used in dental prostheses, dental restoration materials, antiseptic agents, and disinfectants, etc.), though we plan to include them in our future research.

Further, our study does not prove a connection to hobbies involving liquids or solvents as some previous studies have done [23]. Another possible contributing factor to contact dermatoses is a high level of skin sensitivity, as confirmed in a recent survey by Richters et al. [24] (n = 3,058 subjects) in which sensitive skin was reported by 41% of subjects, commonly associated with atopy (56%).

Of 41 subjects who reported dermatoses and agreed to all 4 of our research methods (questionnaire, SPT, prick-by-prick test, patch test), an allergic reaction to at least one rubber allergen (latex or rubber additive) was confirmed in only 2 subjects. Of the 41 aforementioned subjects, only 1 person was positive to latex by SPT and additionally positive to latex in the prick-by-prick test. A second person was positive to carba mix in the patch test. This shows that only these subjects (2/41 subjects who reported dermatoses) are truly allergic to something in rubber materials while the other 95.1% only have irritative reactions or allergies to something other than rubber materials. However, immediate allergies to natural rubber proteins have nowadays become rather rare in developed countries due to the reduced amount of proteins in gloves compared to 1 or 2 decades ago before current stricter EU regulations. Better manufacturing procedures and more generalized use of synthetic rubber gloves (e.g., nitrile gloves), particularly in dental personnel, also helps [25]. Thus, in Croatia, to keep up with current trends, we have begun to urge reduced latex use as opposed to the practice of general latex glove use.

To conclude, collecting data about CD prevalence in dental workers and the establishment of environmental and predisposing risk factors are necessary prerequisites for evaluating the efficacy of existing prevention programs concerning work-related skin diseases in high-risk occupations and for the planning and application of new prevention programs.

Statement of Ethics

This research adheres to the highest ethical standards with approval from the Ethics Committee of the School of Dental Medicine, University of Zagreb, Croatia (Ref. No. 05-PA-26-6/2015). Prior to the research, subjects were informed and written consents were obtained.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Iva Japundžić, DMD, associate professor Marin Vodanović, DMD, and associate professor Liborija Lugović-Mihić, MD, contributed equally to the conception of the work and interpretation of the data. They revised it critically for important intellectual content and approved this final version for publication. All questions related to accuracy of any part of the work were appropriately investigated and resolved.

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