Contact sensitization to metals in dental exposures in Bulgaria

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dental practice among students of dental medicine, students from a dental technician school, dental professionals and patients. A total of 128 participants: 28 dental professionals, 40 students of dental medicine, 38 students from a dental technician school and 22 patients without occupational exposure to metals, were patch tested with potassium dichromate, cobalt(II) chloride hexahydrate, copper(II)sulfate pentahydrate, palladium(II)chloride, aluminium(III)chloride hexahydrate, gold(I)sodium thiosulfate dehydrate, tin and nickel(II)sulfate hexahydrate. The main metal allergens for students of dental medicine were cobalt(II)chloride hexahydrate, gold(I)sodium thiosulfate dehydrate, nickel(II)sulfate hexahydrate and potassium dichromate; for students from the dental technician school – cobalt(II)chloride hexahydrate, nickel(II)sulfate hexahydrate and gold (I)sodium thiosulfate dehydrate; for dental professionals – cobalt(II)chloride hexahydrate, palladium (II)chloride and nickel(II)sulfate hexahydrate, and for dental patients – cobalt(II)chloride hexahydrate, nickel(II)sulfate hexahydrate and copper(II)sulfate pentahydrate. There was a significantly higher incidence of sensitization to potassium dichromate ($\chi^2 = 10.497, p = 0.012$), palladium(II)chloride ($\chi^2 = 5.381, p = 0.02$) and gold(I)sodium thiosulfate dehydrate ($\chi^2 = 6.347, p = 0.018$) in the group of students of dental medicine. Our findings confirm the importance of cobalt (II)chloride hexahydrate as contact sensitizer for all the studied groups. Students of dental medicine could be defined as a group of particular risk of contact sensitization with metals. We recommend that knowledge on the sensitizing properties of metals be provided at the very beginning of the course of practical education in dentistry, together with application of adequate preventive measures.

Introduction

Numerous chemical substances, many of which both allergens and irritants being ingredients of various dental materials and medicines impose serious health risk for both dental professionals and dental patients. The occupational exposure of dental professionals starts as early as during the course of their practical education in dentistry.

Contact sensitization to metals is a problem of growing importance for the overall population and its incidence is high: up to 17% of women and 3% of men are allergic to nickel and 1%–3%, to cobalt and chromium [1,2]. Environmental exposures are believed to be of main importance for the onset of sensitization to metals. The main sources of consumer exposure to metal allergens are jewelry, piercings, buttons, dental restorations, leather goods, etc. [1,2]. Nickel and cobalt are the most important contact allergens [1]. The incidence of contact sensitization to gold and palladium is also high [2]. Exposures to metals could be identified in numerous occupations, and health risk assessment of contact sensitization in such cases is of particular importance.

Sensitization to metals is a significant problem in dental exposures, for both dental patients treated with dental materials and for occupationally exposed dental professionals. The first case of metal allergy in dental practice, which occurred after placing of amalgam restorations in the oral cavity and with clinical manifestations of stomatitis and perioral dermatitis, was described in 1928 by Fleischmann [3]. During a routine dental treatment, the oral mucosa could be affected by about 10–15 different metals [4]. Students of dentistry are exposed to these materials from the very beginning of their practical education. Few studies have focused on the incidence of contact sensitization to metals among this part of the
population. Providing such scientific data would help to perform more efficient prevention activities and to reveal a protocol for early diagnosis. The purpose of the present study was to evaluate the incidence of contact sensitization to selected metals relevant for the dental practice, among students of dental medicine, dental professionals and patients in Bulgaria.

Subjects and methods

Study cohort

A total of 128 participants distributed into four groups were included in the study: dental professionals occupationally exposed to metals, students of dental medicine, students from a dental technician school and patients without occupational exposure to metals, serving as a control group. The gender characteristics of the studied subjects are presented in Table 1.

The study was approved by the Medical Ethics Board at Medical University of Sofia. All the participants were informed about the purpose of the study and gave their written informed consent before its commencement.

Skin patch testing

Skin patch testing with potassium dichromate (0.5% pet), cobalt(II)chloride hexahydrate (1.0% pet), copper(II)sulfate pentahydrate (2.0% pet), palladium(II)chloride (2.0% pet), aluminium(III)chloride hexahydrate (2.0% pet), gold (I)sodium thiosulfate dehydrate (2.0% pet), tin (50.0% pet) and nickel(II)sulfate hexahydrate (5.0% pet) – Chemotechnique Diagnostics, was performed according to the Jadassohn & Bloch classical methods for diagnosis of contact allergy, by placing the allergens in IQ-Ultra hypoallergenic patches of Chemotechnique Diagnostics (IQ Chambers®, Vellinge, Sweden). Lack of anti-allergic medication constituted a mandatory condition before placing the patches and during the testing. Patches with allergens were applied on the back of the tested individuals. Reading of the test was performed on day 2, several hours after removing the patches, with control revision on day 3.

The interpretation of reaction sites was based on the method and the interpretation key recommended by the International Contact Dermatitis Research Group (ICDRG) (Table 2).

Statistical methods

The statistical analysis was performed using SPSS 19.0. The following statistics available for cross-tabulation were used: Chi-squared test, Fisher exact test for statistical significance and probabilistic odds ratio (OR). Values of \( p < 0.05 \) were considered statistically significant.

Results and discussion

The distribution by gender was not uniform, with predominance of women in all the investigated groups, but without statistical significance \( (\chi^2 = 3.8, p = 0.187) \). The mean age of the studied population was 35 ± 13.22 years. Logically, the mean age in the groups of occupationally exposed dental professionals and the occupationally unexposed patients was significantly higher if compared to the groups of students. Individuals without a history of allergic pathology and skin complaints prevailed in all the studied groups, with no significant differences in the overall distribution.

Data concerning the incidence of sensitization to the investigated metals in the whole studied population are summarized in Figure 1. The highest incidence of

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**Table 1. Gender characteristics of the studied population.**

| Gender          |          |          |          |
|-----------------|----------|----------|----------|
|                 | Female [n (%)] | Male [n (%)] | Total [n (%)] |
|-----------------|----------|----------|----------|
| Occupationally exposed dental professionals | 18 (64.3%) | 10 (35.7) | 28 (21.9%) |
| Students from dental technician school | 29 (76.3%) | 9 (23.7) | 38 (29.7%) |
| Students of dental medicine | 25 (62.5%) | 15 (37.5) | 40 (31.3%) |
| Patients without occupational exposure | 17 (77.3%) | 5 (22.7) | 22 (17.2%) |
| **Total**       | 89 (69.5%) | 39 (30.5%) | 128 (100.0) |

**Table 2. Interpretation key of skin patch test results based on International Contact Dermatitis Research Group.**

| Symbol | Meaning                                      |
|--------|----------------------------------------------|
| –      | Negative reaction                            |
| ?      | Doubtful reaction                            |
| +      | Weak positive reaction (non-vesicular)       |
| ++     | Strong positive reaction (edematous or vesicular) |
| +++    | Extreme positive reaction (ulcerative or bullous) |
| IR     | Irritant reaction                            |

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Figure 1. Incidence of positive skin patch tests to the investigated metals in the whole studied population.
sensitization was that to cobalt(II) chloride hexahydrate, nickel(II) sulfate hexahydrate and gold(I) sodium thiosulfate dehydrate.

Data concerning the incidence of positive skin patch test reactions to potassium dichromate, palladium(II) chloride and gold(I) sodium thiosulfate dehydrate are presented in Table 3. The statistical analysis revealed a significantly higher incidence of sensitization to potassium dichromate in the group of dental students, constituting 54.8% of all sensitized subjects ($\chi^2 = 10.497$, $p = 0.012$). The incidence of positive skin patch test reactions to palladium(II) chloride in the group of dental students was also significantly higher (47.1%) among all sensitized to this agent ($\chi^2 = 5.381$, $p = 0.02$). There was a significantly higher incidence of positive skin patch test reactions to gold(I) sodium thiosulfate dehydrate again in the group of dental students: 46.3% of all sensitized ($\chi^2 = 6.347$, $p = 0.018$). Moreover, a significantly lower incidence of sensitization (4.9%) was found among the subjects from the control group ($\chi^2 = 6.36$, $p = 0.017$). There were no significant intra-group differences concerning the incidence of sensitization to the studied metals.

Figure 2 shows summarized data on the incidence of positive skin patch test reactions to the metals selected by us in the group of dental professionals. The main metal allergen for dental professionals was cobalt(II) chloride hexahydrate, followed by palladium(II) chloride and nickel(II) sulfate hexahydrate. The incidence of positive skin patch test reactions in the group of dental students is presented in Figure 3. Consistent with the results above, the main metal sensitizer was cobalt(II) chloride hexahydrate, followed by gold(I) sodium thiosulfate dehydrate, nickel(II) sulfate hexahydrate and, for this group – potassium dichromate. The incidence of sensitization to palladium was also high.

Similarly to the results above, in the group of students from the dental technician school, cobalt(II) chloride hexahydrate was an allergen of prominent importance, followed nickel(II) sulfate hexahydrate and gold(I) sodium thiosulfate dehydrate (Figure 4). Notably, in the group of students from dental technician school was established the highest incidence of sensitization to copper(II) sulfate pentahydrate, and the lowest one – to tin. In the group of dental patients (Figure 5), the highest incidences of positive skin patch test reactions were those to cobalt(II)

| Target group                      | Skin patch test reactions to potassium dichromate |       |       | Total |
|-----------------------------------|-----------------------------------------------|-------|-------|-------|
| Dental professionals              |                                               |       |       |       |
| Student from dental technician school |                                           |       |       |       |
| Students of dental medicine       |                                               |       |       |       |
| Occupationally unexposed patients |                                               |       |       |       |
| Total                             |                                               |       |       |       |

| Target group                      | Skin patch test reactions to palladium(II) chloride |       |       | Total |
|-----------------------------------|-----------------------------------------------|-------|-------|-------|
| Dental professionals              |                                               |       |       |       |
| Student from dental technician school |                                           |       |       |       |
| Students of dental medicine       |                                               |       |       |       |
| Occupationally unexposed patients |                                               |       |       |       |
| Total                             |                                               |       |       |       |

| Target group                      | Skin patch test reactions to gold(I) sodium thiosulfate dehydrate |       |       | Total |
|-----------------------------------|-----------------------------------------------|-------|-------|-------|
| Dental professionals              |                                               |       |       |       |
| Student from dental technician school |                                           |       |       |       |
| Students of dental medicine       |                                               |       |       |       |
| Occupationally unexposed patients |                                               |       |       |       |
| Total                             |                                               |       |       |       |

Figure 3. Incidence of positive skin patch test reactions in the group of dental students.
chloride hexahydrate and nickel(II)sulfate hexahydrate, followed by copper(II)sulfate pentahydrate.

Further, we analyzed the incidence of positive skin patch tests in male and female subjects. The statistical analysis revealed significantly higher incidence and OR of positive skin patch tests to palladium(II)chloride ($\chi^2 = 4.071, p = 0.044; \text{OR} = 2.303, \text{CI} = 1.014–5.231$) and to aluminium(III)chloride hexahydrate ($\chi^2 = 3.987, p = 0.046$) among men (Table 4).

There was statistical significance regarding the incidence of sensitization and manifestation of subjective skin symptoms only for nickel ($\chi^2 = 4.033, p = 0.045; \text{OR} = 2.151, \text{CI} = 1.012–4.571$). Traditionally, nickel, cobalt and chromium are considered to be the most important contact allergens [2]. However, the incidence of sensitization to gold and palladium is also high [1,2].

Cobalt is a strong skin sensitizer. Therefore, it is not surprising that cobalt allergy is common, affecting 6.2%–8.8% of dermatitis patients [5] and about 1% of the total population [6]. In 2016, cobalt was designated as ‘Allergen of the Year’ by the American Contact Dermatitis Society [7]. Today, cobalt is typically used to produce high-temperature corrosion-resistant super alloys for jet and gas turbine engines, magnetic alloys and high-strength steels. Furthermore, cobalt and its salts can be used as pigments and driers in paint, as catalysts and as additives in fertilizers and animal feed [8]. Deposition of cobalt on the hands of workers grinding hard metals is documented [9]. Cobalt allergy is thought to be a challenge in occupational exposure, despite the fact that, according to a British study, cobalt allergy accounts for only 4% of 22 184 cases of occupational contact dermatitis [10]. This low rate could be partly explained by the difficulties in identifying the sources of cobalt exposure.

In 1951, Rostenberg and Perkins [11] stated that nickel coating of consumer products is the most important cause of cobalt allergy in patients with dermatitis. Julander et al. [12] studied the release of cobalt, nickel, and chromium from some cobalt-containing hard metal alloys. They established that the concentration of released cobalt was high enough to elicit allergic contact dermatitis in cobalt-sensitized patients. As the materials are used in wear parts of hard metal tools, individuals with contact allergy to cobalt may develop hand eczema when handling such materials [12].

Most dental materials used for treatment with dental obturations, fixed and movable structures, orthodontic devices, etc. are intended for long-term use in the oral cavity and must strictly comply with biocompatibility specifications. In the Scandinavian countries, since the 1990s, national registers are monitoring the effects of dental biomaterials on oral mucosa associated with irritation and allergic reactions to specific materials [13].

The base metal alloy systems most commonly used in dentistry today include stainless steels, nickel-chromium, cobalt-chromium, titanium and nickel-titanium alloys [14]. Thyssen et al. [15] used the cobalt spot test to study cobalt ion release from cobalt-containing dental alloys as well as from mobile phones. Six of eight dental alloys released cobalt in the cobalt spot test, whereas none of 50 mobile phones gave positive reactions. Isolated patch test reactivity to cobalt was less associated with

![Figure 4](image_url) Incidence of positive skin patch test reactions in the group of students from the dental technician school.

![Figure 5](image_url) Incidence of positive skin patch test reactions in the group of dental patients.

### Table 4: Gender distribution of positive skin patch tests to palladium(II)chloride and aluminium(III)chloride hexahydrate.

| Gender | Skin patch test reactions to palladium(II)chloride |  | Gender | Skin patch test reactions to aluminium(III)chloride hexahydrate |  |
|---|---|---|---|---|---|
| | Women n (%) | Men n (%) | Total n | Gender | Women n (%) | Men n (%) | Total n |
| Negative reaction | 70 (78.7) | 24 (61.5) | 94 | OR = 2.303 | 77 (86.5) | 28 (71.8) | 105 |
| Positive reaction | 19 (21.3) | 15 (38.5) | 34 | CI = 1.014–5.231 | 12 (13.5) | 11 (28.2) | 23 |
| Total | 89 | 39 | 128 | 89 | 39 | 128 |
occupational dermatitis and hand eczema than patch test reactivity to cobalt in combination with other contact allergies. The authors concluded that it is often difficult to interpret the relevance of a positive patch test reaction to cobalt, and there is a need for further studies to determine sources of cobalt exposure [15]. Kettelarij et al. [16] quantified cobalt, chromium and nickel exposure on the skin and in the air in 13 dental technicians working with tools and alloys that may result in skin and respiratory exposure. According to the authors, cobalt skin doses may potentially elicit allergic contact dermatitis and cause sensitization [16].

Nickel is the most common sensitizer among metals [17]. In 1889, Goldman [18] reported the first case of nickel dermatitis. According to Wallenhammar et al., the most common allergens for dental professionals, along with methacrylates, are nickel sulfate and gold sodium thiosulfate [19]. Data published by Wrangsjö et al. [20] determine nickel, cobalt and palladium as main occupational metal sensitizers in dental practice.

The sensitization to palladium in dental practice is being intensively studied. Consumers are exposed to palladium primarily from jewelry and dental restorations. Palladium contact sensitization is almost always seen along with such to nickel, as palladium and nickel tend to cross-react [21]. In the field of biomedicine, palladium is mainly used as a component of denture alloys. Available data indicate palladium alloy as safe despite the concerns about harmful effects of low levels corrosion products in biomedical use. The mono-sensitization to palladium is considered to be rare but very often accompanies the sensitization to nickel [22].

Metal gold, including jewelry and dental gold alloys, is generally accepted as a non-sensitizing material. Therefore, contact dermatitis to gold is considered to be rare, as gold allergy is traditionally difficult to prove. However, in 1966, Kligman established that gold chloride is a strong sensitizer in maximization test in humans [23].

No data was found in the available literature on the incidence of sensitization to metals among students of dental medicine and students from dental technician schools. That is why in the present study we aimed to collect such information and to make comparative analysis on the incidence of positive skin patch tests to selected metals used in dental alloys between groups of occupationally exposed dental professionals, students of dentistry exposed during their course of practical education and dental patients without occupational exposure.

The results obtained in our study concerning the incidence of sensitization to metals among dental professionals to some extent confirmed the findings discussed above. Interestingly, we established the highest incidence of positive skin patch tests to cobalt(II)chloride hexahydrate in both this target group and in the whole studied cohort, the groups of dental students and the one of dental patients. This observation confirms the importance of cobalt as a contact sensitizer. However, we cannot give a definite statement on the leading role of occupational exposure in dentistry for the onset of sensitization. In the group of dental professionals, there were high sensitization rates to palladium(II)chloride and nickel(II)sulfate hexahydrate as well.

The group of students of dental medicine could be outlined as an especially vulnerable one regarding the sensitization to palladium. The results from the present study confirmed that sensitization to palladium often accompanies the sensitization to nickel, as well as the existence of concomitant reactivity to cobalt and nickel. We consider that the reason for the high sensitization rates is the occupational exposure to metals released from alloys used in dental practice.

The relatively lower incidence of positive skin patch test reactions to palladium(II)chloride among the group of students from the dental technician school, if compared with the sensitization rates to cobalt(II)chloride hexahydrate and nickel(II)sulfate hexahydrate, is difficult to explain, since no similar data were found in the available literature to compare with. This finding needs further confirmation, with more participants being tested. Interestingly, there was also high incidence of positive skin patch test reactions to gold(III)sodium thiosulfate dehydrate in the group of students from the dental technician school. Moreover, it was significantly higher in the group of students of dental medicine, and significantly lower among the subjects from the control group. We could suggest a leading role of the exposure in dentistry, with the groups with shorter duration of exposure (i.e. students) being more vulnerable. A possible manifestation of ‘hypo-sensitization’ with increasing of duration of exposure could be suggested.

According to our results, the exposure to potassium dichromate during the course of practical education in dental medicine seems to be of main importance for sensitization onset. Such high rates were not observed in the group of students from the dental technician school and the group of dental professionals.

The incidence of metal allergy among dental patients and the general population has been extensively studied. Kanerva et al. [22] collected information on the incidence of sensitization to dental allergens through a multicenter study involving 4000 individuals. The most common positive reactions were those to nickel (14.6%), mercury (13%), gold (7.7%), palladium (4.2%) and cobalt (4.1%) [22]. Raap et al. [23] patch tested 206 patients to metals used in dentistry. The highest incidence of positive reactions was attributed to gold sodium thiosulfate,
palladium chloride and nickel sulfate, as well as to amalgam, mercury and cobalt chloride [23]. Hosoki et al. [24] patch tested 212 dental patients with suspected metal allergy. Of these, 69.8% had one or more positive reactions, the most common allergens being nickel (25%), palladium (24%), chromium (16.7%), cobalt (15.9%) and tin (12.5%) [24].

Muris et al. [25] presented results from a multicenter study, where patch testing to palladium and nickel was performed in 906 patients. Of these, 24.3% exhibited positive reactions to palladium and 25.2% to nickel. Sensitivity to palladium was related to dental crowns [25]. Fall et al. [26] performed a retrospective comparative analysis of contact allergy trends in Sweden based on patch-test data from 1992, 2000 and 2009. Among the tested substances with sensitization rate above 2% in 2009, a significant reduction in the incidence of sensitization to nickel sulfate and cobalt chloride was observed. According to the authors, the changes in the sensitization incidence for the period 1992–2009 are likely to reflect the regulations on nickel content in a number of products and the decreased chromium content in cement [26]. Gündüz et al. [27] recently reported on some demographic characteristics and the occupation of patients from an occupational diseases clinic with early diagnosed occupational contact dermatitis. The most common allergens in both women and men were nickel sulfate and potassium dichromate. Women were most often engaged in household maintenance activities, and men, in industry [27].

Linauskienė et al. [28] presented data on the changes in the incidence of contact allergy to allergens included in the European baseline series among adults with suspected contact dermatitis in Lithuania. Among the metals relevant for dental practice, the highest incidence was that of sensitization to nickel sulfate (30.6%), potassium dichromate (6.1%) and cobalt chloride (6.1%) [28]. According to Vigneshkarthik et al. [29] nickel and cobalt are the most common allergens among women, while potassium dichromate, among men, with an occupation at particular risk being the one of bricklayers [29]. These data are confirmed by Kot et al. [30], who reported that the incidence of positive patch tests was the highest for nickel sulfate (26.2%), cobalt chloride (15.1%) and potassium dichromate (13.5%) [30].

Concerning the incidence of metal sensitization among the group of dental patients, the results obtained from the present study outline cobalt(II)chloride hexahydrate and nickel(II)sulfate hexahydrate as the most important contact sensitizers, with equal incidence of positive skin patch tests. We cannot underestimate the role of consumer exposure for sensitization onset. Moreover, copper(II)sulfate pentahydrate was ranked the third most important contact sensitizer for this study group. This could be due to the main role of environmental and consumer exposures (jewelry, agriculture and household products, etc.).

In the present study, men were identified as a group at higher risk of contact sensitization to palladium(II) chloride and aluminium(III)chloride hexahydrate. No similar data were found in the available literature, so further confirmations are needed to explain these results.

Conclusions

The results from the present study outlined cobalt(II)chloride hexahydrate as a sensitizer of paramount importance for all the studied groups. Other main metal allergens for dental professionals were nickel(II)sulfate hexahydrate and palladium(II)chloride; for students of dental medicine – gold(I)sodium thiosulfate dehydrate, as well as nickel(II)sulfate hexahydrate and potassium dichromate; for students from dental technician school – nickel(II)sulfate hexahydrate and gold(I)sodium thiosulfate dehydrate, and for dental patients – nickel(II)sulfate hexahydrate and copper(II)sulfate pentahydrate. Students of dental medicine could be defined as a group of particular risk of contact sensitization with metals, with significantly higher incidence of sensitization to potassium dichromate, palladium(II)chloride and gold(I)sodium thiosulfate dehydrate. On other hand, a significantly lower incidence of sensitization to gold(I)sodium thiosulfate dehydrate in the group of dental patients was observed. Due to the widespread–both consumer and dental–exposure to metals, it is difficult to give a categorical statement about the decisive role of exposure in dentistry for the onset of sensitization. Elucidating this would need further adequate information on the sensitizing properties of metals to dental students, dental patients, as well as to occupationally exposed dental professionals. We recommend application of adequate preventive measures as early as the beginning of the course of practical education of students of dentistry, with the role of Occupational Health Services being especially active.

Disclosure statement

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References

[1] Uter W, Amario-Hita JC, Balato A, et al. European Surveillance System on Contact Allergies (ESSCA): results with the European baseline series, 2013/14. J Eur Acad Dermatol Venereol. 2017; 31(9):1516–1525. DOI: 10.1111/jdv.14423.

[2] Thyssen JP, Menné T. Metal allergy - a review on exposures, penetration, genetics, prevalence, and clinical implications. Chem Res Toxicol. 2010;23(2):309–318.

[3] Fleischmann P. Zur Frage der Gefährlichkeit kleiner Quecksilbermengen [To the question of the danger of the smallest quantities of mercury]. Dtsch Med Wochenschr. 1928;54:304–307. German.

[4] Ditrichova D, Dobesova J, Kapralova S, et al. The most common contact allergens in the oral cavity and lips. Ces Stomatol. 2007;107:39–45. Czech.

[5] Uter W, Ramsch C, Aberer W, et al. The European baseline series in 10 European countries, 2005/2006 – results of the European Surveillance System of Contact Allergies (ESSCA). Contact Dermatitis. 2009;61(1):31–38.

[6] Thyssen JP, Linneberg A, Menné T, et al. The epidemiology of contact allergy in the general population – prevalence and main findings. Contact Dermatitis. 2007;57(5):287–299.

[7] Fowler JF Jr. Cobalt. Dermatitis. 2016;27(1):3–8.

[8] Lidén C, Bruze M, Thyssen JP, et al. Metals. In: Johansen JD, Lepoittevin JP, Frosch PJ, editors. Contact dermatitis. Berlin, Heidelberg, New York: Springer; 2011. p. 643–681.

[9] Julander A, Skare L, Mulder M, et al. Skin deposition of nickel, cobalt, and chromium in production of gas turbines and space propulsion components. Ann Occup Hyg. 2010;54(3):340–350.

[10] Athavale P, Shum KW, Chen Y, et al. Occupational dermatitis related to chromium and cobalt: experience of dermatologists (EPIDERM) and occupational physicians (OPRA) in the UK over an 11-year period (1993–2004). Br J Dermatol. 2007;157(3):518–522.

[11] Rostenberg A Jr, Perkins AJ. Nickel and cobalt dermatitis. J Allergy. 1951;22:466–474.

[12] Julander A, Hindsen M, Skare L, et al. Cobalt-containing alloys and their ability to release cobalt and cause dermatitis. Contact Dermatitis. 2009;60(3):165–170.

[13] Lygre GB, Gjerdet NR, Bjorkman L. A follow-up study of patients with subjective symptoms related to dental materials. Community Dent Oral Epidemiol. 2005;33(3):227–234.

[14] Roach M. Base metal alloys used for dental restorations and implants. Dent Clin North Am. 2007;51(3):603–627.

[15] Thyssen JP, Menné T, Lidén C, et al. Cobalt release from implants and consumer items and characteristics of cobalt sensitized patients with dermatitis. Contact Dermatitis. 2012;66(3):113–122.

[16] Kettelarij J, Nilsson S, Midander K, et al. Snapshot of cobalt, chromium and nickel exposure in dental technicians. Contact Dermatitis. 2016;75(6):370–376.

[17] Krecisz B, Chomiczewska D, Palczynski C, et al. Contact allergy to metals in adolescents: nickel release from metal accessories 7 years after the implementation of the EU Nickel Directive in Poland. Contact Dermatitis. 2012;67(5):270–276.

[18] Goldman L. Nickel eczema. Arch Dermatol Syphilol. 1933;28:686–696.

[19] Wallenhammar LM, Ortengren U, Andreasson H, et al. Contact allergy and hand eczema in Swedish dentists. Contact Dermatitis. 2000;43(4):192–199.

[20] Wrangsjö K, Swartling C, Meding B. Occupational dermatitis in dental personnel: contact dermatitis with special reference to (meth)acrylates in 174 patients. Contact Dermatitis. 2001;45(3):158–163.

[21] Faurouchou A, Menné T, Johansen JD, et al. Metal allergens of the 21st century - a review on exposure, epidemiology and clinical manifestations of palladium allergy. Contact Dermatitis. 2011;64(4):185–195.

[22] Wataha JC, Shor K. Palladium alloys for biomedical devices. Expert Rev Med Devices. 2010;7(4):489–501.

[23] Kligman AM. The identification of contact allergens by human assay. III. The maximization test: a procedure for screening and rating contact sensitizers. J Invest Dermatol. 1966;47(5):393–409.

[24] Kanerva L, Rantanen T, Aalto-Korte K, et al. A multicenter study of patch test reactions with dental screening series. Am J Contact Dermat. 2001;12(2):83–87.

[25] Raap U, Stiesch M, Reh H, et al. Investigation of contact allergy to dental metals in 206 patients. Contact Dermatitis. 2009;60(6):339–343.

[26] Hosoki M, Bando E, Asaoka K, et al. Assessment of allergic sensitization to Pd (metal)/Pd (compound) in Japan. Jpn J Oral Sci. 2008;59(3):267–273.

[27] Muris J, Goossens A, Gongnoo M, et al. Sensitization to palladium and nickel in Europe and the relationship with oral disease and dental alloys. Contact Dermatitis. 2015;72(5):286–296.

[28] Fall S, Bruze M, Isaksson M, et al. Contact allergy trends in Sweden - a retrospective comparison of patch test data from 1992, 2000, and 2009. Contact Dermatitis. 2015;72(5):297–304.

[29] Gündüz Ö, Aytekin A, Tutkun E, et al. Comparison of European standard patch test results of 330 patients from an occupational diseases hospital. Dermatol Res Pract. 2016 [cited 2017 Aug 15];2016:9421878. DOI: 10.1155/2016/9421878.

[30] Linasauskiene K, Malinauskienë L, Blazienë A. Time trends of contact allergy to the European baseline series in Lithuania. Contact Dermatitis. 2017;76(6):350–356.