

A 10-Year Retrospective Study on Palladium Sensitivity

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Background: Palladium has become an important contact allergen because of increased use in industry, jewelry, and dentistry.

Objective: To determine the frequency of palladium allergy in a US patch-test population tested to palladium.

Methods: A 10-year retrospective review (1997–2006) was performed on patients sensitive to palladium at the Department of Dermatology, Mayo Clinic, Rochester, MN.

Results: A total of 910 patients were tested to a series that included palladium chloride 2% in petrolatum. A palladium-positive patch-test result was noted in 110 patients (12.1%). Of the 106 patients sensitized to palladium who had records available for review, 15.1% had a diagnosis of lichen planus-like eruptions; 13.2%, burning mouth; 27.4%, stomatitis; and 29.2%, hand and body dermatitis.

Conclusion: Palladium sensitivity is more common in oral diseases than in skin. We describe a previously unknown high degree of co-reactivity of gold with palladium to the same degree as the known co-reactivity with nickel.

PALLADIUM is a precious metal used in the telecommunication and automotive industries, dental alloys, and jewelry. It is in group VII of the periodic table, with platinum and nickel. In the 1980s, with the rise in gold prices, demand for palladium increased, attributed to the metal's use in the automotive industry as a catalytic converter and to the growing popularity of white gold, which contains varying amounts of palladium.^{1–3} Dental alloys may contain up to 10% palladium; white gold may contain up to 20% palladium.^{1,3} Japan is the largest consumer of palladium, followed by the United States and then Europe.^{2,4}

The frequency of palladium allergy in patch tests was reported to be 8% in Austria,⁵ 9% in mainland United Kingdom,⁶ 9% in Turkey,⁷ 5.3% in Italy,⁸ 13% in an Israeli clinic,⁹ and 2% in Northern Ireland.¹⁰ To our knowledge, there are no studies from the United States that report the frequency of palladium sensitivity in a patch-test population.

The primary objective of our study was to determine the frequency of palladium allergy in a US patch-test

population. Our secondary objective was to determine the location and type of dermatitis and the metal co-reactants in palladium-sensitive patients.

Materials and Methods

This retrospective study was approved by the Mayo Clinic Institutional Review Board. Patients who underwent patch testing for suspected allergic contact dermatitis at Mayo Clinic from October 1, 1997, to December 31, 2006, were identified from an existing clinical database.

Patch testing was conducted in a standardized fashion using the same methods as previously described by our group.^{11,12} Testing was performed with Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster Aksjeselskap, Vennesla, Norway); patches were applied to the upper backs of patients and removed after 48 hours. Most allergens, including palladium in petrolatum, were purchased from Chemotechnique Diagnostics AB (Vellinge, Sweden). The other allergens were compounded by the Mayo Clinic pharmacy. Reactions were evaluated initially at 48 to 72 hours and again at 96 to 168 hours after application of the patch. Final patch-test reading, interpretation of results, and assessment of relevancy were performed by the ordering physician.

Patch-test reactions were interpreted with the following criteria: negative reaction, macular erythema or weak reaction (nonvesicular erythema, infiltration, and possibly papules), strong reaction (edematous or vesicular), and extreme reaction (spreading, bullous, ulcerative lesions). A

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positive allergic patch-test result was defined as a weak, strong, or extreme reaction at the last reading or as a macular erythema reaction if the result was relevant after irritant reactions had been excluded.

A total of 910 patients were identified who were patch-tested with palladium chloride 2% in petrolatum as part of the stomatitis, oral complete, or metal series. The medical records of these patients were reviewed individually to determine the patient's skin manifestation and dermatologic diagnosis at the time of the patch testing.

The associations between patient characteristics and palladium sensitivity (ie, yes or no) were assessed with the two-sided chi-square test and summarized through calculating odds ratios (ORs) and corresponding 95% confidence intervals (CIs). Analyses were performed with the *Statistical Analysis System* software package, version 9 (SAS Institute Inc., Cary, NC).

Results

A patch-test result positive for palladium chloride 2% was noted in 110 (12.1%) of the 910 patients. Among these patients, a weak reaction to palladium was noted in 34 patients (30.9%), a strong reaction in 50 (45.5%), and an extreme reaction in 26 (23.6%).

Of the 110 patients who were sensitive to palladium, only 106 had patient records available for review. Four patients were referred to our institution for patch testing only. Table 1 summarizes the characteristics of 106 palladium-sensitive patients. The ages ranged from 9 to 82 years; the mean age was 53.1 years. There were 98

female patients and 8 male patients. Statistical analysis showed that patients with palladium sensitivity were more likely to be female (OR, 3.5; 95% CI, 1.9–6.5; $p < .001$). Specifically, 98 (89.1%) of all palladium-sensitive patients were female, compared with 559 (69.9%) of the 800 (ie, 910 – 110) patients who were not palladium-sensitive. Sixteen patients (15.1%) had no skin manifestations but received patch testing for detection of metal allergy before surgical implantation of a metal prosthesis, referred to herein as a “preventive” patch test.

Most (55.7%) of the patients sensitized to palladium had oral disease diagnosed as lichen planus or lichenoid tissue reaction, stomatitis, or burning mouth, as compared with 31 patients (29.2%) with skin involvement diagnosed as dermatitis. Of the latter 31 patients, 17 were allergic to metal jewelry (mostly watches, earrings, and necklaces) and 4 were allergic to the frame of their eyeglasses.

The majority (101 [91.8%]) of the 110 patients were sensitive to more than one metal. Among the 110 patients, 9 (8.2%) had one positive reaction (to palladium only), 9 (8.2%) had two positive reactions, and 92 (83.6%) had three or more positive reactions. Of the 110 patients who were sensitized to palladium, 107 were also tested with nickel and cobalt; 61 (57.0%) of these 107 patients were sensitized to both palladium and nickel, and 33 (30.8%) were sensitized to palladium, nickel, and cobalt. Statistical analysis showed that patients with palladium sensitivity were more likely to have a nickel sensitivity (OR, 7.5; 95% CI, 4.9–11.6; $p < .001$). Specifically, 61 (57.0%) of the 107 palladium-sensitive patients who were also tested with nickel had a reaction to nickel, compared with 117 (15.0%) nickel-sensitive patients who did not have a palladium sensitivity. Patients with palladium sensitivity were more likely to be sensitized to gold than were patients without palladium sensitivity (OR, 5.5; 95% CI, 3.6–8.4; $p < .001$). In particular, 53 (48.2%) of the palladium-sensitive patients had a gold reaction, compared with 112 (14.5%) gold-sensitive patients who did not have a palladium reaction.

Nine (8.2%) patients were sensitized to palladium metal only. Of these patients, 4 had preventive patches, 2 had stomatitis, and the other 3 patients had lichen planus, burning mouth, and dermatitis, respectively. Sensitization to flavoring agents as nonmetal allergens was noted for the patient with lichen planus, and sensitization to flavoring agents plus colophony and phenol-formaldehyde resin was noted for the patient with dermatitis.

Table 2 summarizes the metal co-reactants of the palladium-sensitive patients. Sixty-one (57.0%) of the 107 patients who were tested with both palladium and nickel

Table 1. Characteristics of 106 Patients* with Palladium Sensitivity

Characteristic	Overall	Palladium Relevant
Age		
Mean (SD)	53.1 (14.9) yr	
Range	9–82 yr	
Female	98 (89.1%)	NA
Associated disease [†]	106 (100.0%)	74 (69.8%)
Oral disease	59 (55.7%)	53 (50.0%)
Burning mouth syndrome	14 (13.2%)	13 (12.3%)
Lichen planus-like eruptions	16 (15.1%)	15 (14.1%)
Stomatitis	29 (27.4%)	25 (23.6%)
Skin dermatitis	31 (29.2%)	21 (19.8%)
Preventive patch testing	16 (15.1%)	0 (0.0%)

NA = not applicable.

*Four of the 110 palladium-positive patients did not have medical records available to determine correct grouping.

[†]Eight patients had both oral disease and skin dermatitis.

Table 2. Metal Co-reactants in Patients with Palladium Sensitivity versus Patients without Palladium Sensitivity

<i>Metal Sensitivity</i>	<i>Patients Not Sensitive to Palladium*† (n = 800)</i>	<i>Patients Sensitive to Palladium*† (n = 110)</i>			
		<i>All Patients (n = 110)</i>	<i>Oral Disease (n = 59)</i>	<i>Skin Dermatitis (n = 31)</i>	<i>Preventive Patch Test (n = 16)</i>
Nickel	117 (15.0)	61 (57.0)	30 (50.8)	19 (63.3)	9 (64.3)
Gold	112 (14.5)	53 (48.2)	32 (54.2)	10 (32.3)	10 (62.5)
Cobalt	84 (10.5)	41 (37.6)	15 (25.4)	17 (54.8)	7 (46.7)
Chromium	25 (3.4)	11 (10.2)	5 (8.6)	4 (13.3)	1 (6.3)
Beryllium	36 (4.8)	12 (11.0)	11 (18.6)	0 (0)	0 (0)
Mercury	82 (10.3)	18 (16.4)	13 (22.0)	3 (9.7)	2 (12.5)

*Data are reported as numbers and percentages (in parentheses).

†Percentages are based on the number of patients who were patch-tested with both allergens.

(9 of whom were in the preventive-patch group) were sensitized to nickel. Thirty (50.8%) of 59 patients with oral disease were sensitized to nickel, compared with 19 patients (63.3%) in the group with skin dermatitis. Gold was the second most frequent co-reactant in all groups, its incidence ranking almost as high as that of nickel. In patients with oral disease, this incidence was as high as 54.2%, which was slightly higher than the incidence for nickel (50.8%). In patients with skin dermatitis, gold co-reactivity was considerably less than that of nickel (32.3% vs 63.3%). In all patients, beryllium was almost as common as mercury in its frequency as a co-reactant. No patient with skin involvement had co-reactivity to beryllium, as compared to an 18.6% incidence of co-reactivity in patients with oral disease. Table 3 shows the breakdown of metal co-reactants within the three categories of oral disease. Gold showed the highest frequency

as a co-reactant in patients with lichen planus and stomatitis—as high as 68.8% and 51.7%—when compared to patients with burning mouth syndrome (BMS) (42.9%).

Discussion

There are two key findings in our study. In the first, the frequency of palladium sensitivity in our US patch-test patients who were tested with palladium was 12.1%; a higher frequency was observed in patients with mucous membrane diseases. In the second, the incidence of co-reactivity of gold with palladium approached that of the co-reactivity of nickel.

Our frequency was higher than the sensitization rate found in European studies, which ranged between 8% and 10%, but was similar to the sensitization rate in the study from Israel, in which the investigators reported a rate of

Table 3. Characteristics and Metal Allergies of Palladium-Sensitive Patients with Oral Disease

<i>Characteristic</i>	<i>Patients with Oral Disease</i>		
	<i>Burning Mouth Syndrome (n = 14)</i>	<i>Lichen Planus–Like Eruption (n = 16)</i>	<i>Stomatitis (n = 29)</i>
Age, mean (range)	58.6 (33–82) yr	60.0 (43–69) yr	55.0 (33–79) yr
Female sex	14 (100.0%)	15 (93.8%)	25 (86.2%)
Metal sensitivity			
Gold	6 (42.9%)	11 (68.8%)	15 (51.7%)
Nickel	8 (57.1%)	6 (37.5%)	16 (55.2%)
Cobalt	5 (35.7%)	1 (6.3%)	9 (31.0%)
Chromium	1 (7.1%)	2 (12.5%)	2 (6.9%)
Beryllium	2 (14.3%)	2 (12.5%)	7 (24.1%)
Mercury	2 (14.3%)	5 (31.3%)	6 (20.7%)
Sensitivity to flavoring agents*	7 (50.0%)	10 (62.5%)	3 (10.3%)

*Balsam of Peru (*n* = 7), cinnamic aldehyde (*n* = 1), benzoic acid (*n* = 5), benzoyl alcohol or peroxide (*n* = 3), and fragrance (*n* = 3).

13%.⁹ The use of palladium in dental alloys in the United States is reportedly greater than its use in Europe,² which might account for the difference in sensitivity between European studies and our US-based study. However, to our knowledge, there is no indication of an increased use of palladium in jewelry produced in the United States as compared to Europe.⁴ Currently, there are no reports in the medical literature on the frequency of palladium sensitivity in a US patch-test population for comparison with our results.

No relevance data were available from any of the published series on palladium.^{5,6,8–10,13} Although we had a relevance of 54.7% as extracted from the histories, we found it difficult to verify this relevance in a large series of patients retrospectively, similar to other investigators. In one case in our series, the clinician tested the oral amalgam adjacent to the lichenoid lesions and found it to contain palladium and no gold. That patient had reaction to both metals; therefore, the palladium allergy was deemed valid and relevant. This difficulty of determining relevance is particularly true for a metal such as palladium, which is present in various concentrations and electrochemical configurations in many alloys^{3,14,15} and which co-reacts with many other metals. In addition, palladium is used in dentistry in the cores of crowns; hence, it may not be directly visible to the examining physician as a silver-colored filling. The solubility of palladium and other noble metals in the alloy has been the subject of extensive research and depends on the method by which the alloy is prepared, as well as the length of time the alloy is in the mouth and in contact with saliva, leading to corrosion.^{14,15} Garhammer and colleagues reported that deposition of metals (including gold, silver, and palladium) was noted in biopsy samples of affected mucosal skin directly adjacent to dental alloy.¹⁶ In 84% of cases, the investigators found the metal from lesional mucosa as opposed to unaffected mucosa. This finding indicated that metals do leach out of the alloy and may have a direct role in the skin disease. Because the patients may have had dental alloy from different manufacturers and may have had it applied at different times in their lives, the relevance data extracted from the charts may not be dependable. True relevance can be determined only by having information on the composition of the dental alloy (or obtaining a sample of the amalgam for analysis to confirm the presence of the metal) and by having an accurate history that tells when the alloy was placed in the mouth, neither of which were available to us in this study.

Exclusive palladium-only metal sensitivity is a rare phenomenon, and it is thought that these isolated cases

may help determine the true allergenic potential of the metal.⁹ In our study, 9 (8.2%) of 110 patients had palladium metal monosensitivity. Of these 9 patients, 4 had preventive patch tests and had no dermatologic complaints at the time of the patch testing. The other 5 patients consisted of 4 with oral involvement and 1 with skin dermatitis. A study in Italy reported a 7.2% (17 of 236 patients) occurrence of palladium monosensitivity.⁸ Only one patient in this study had an oral symptom, noted to be burning mouth, and the other 16 patients had dermatitis. Orion and colleagues reported a single dermatitis case in the Israeli study but did not specify the location of the dermatitis.⁹

The etiology of BMS is unknown but is thought to be multifactorial, possibly involving local and systemic factors. There have been controversial suggestions that contact hypersensitivity might have a role in BMS.¹⁷ In a study by Lamey and colleagues, as many as 65% of patients with positive patch-test reactions were reported to have intermittent BMS.¹⁸ A study by Dal Sacco and colleagues showed that 13% of patients with BMS had a relevant contact hypersensitivity.¹⁷ No studies in the literature have specifically linked palladium to the etiology of BMS. In a recent study by Torgerson and colleagues, 9.7% of 196 patients with BMS had patch-test results that were positive for palladium.¹⁹ Our study showed that 13.2% of palladium-sensitive patients had BMS, 1 patient having monosensitization to palladium. These findings raise the question of whether palladium sensitivity is related to BMS. Focused studies are needed to validate this association.

Our study showed that 15.1% of patients with sensitivity to palladium had oral lichen planus; of these patients, 6.3% had monosensitization to palladium. We found no US studies that reported the frequency of lichen planus in regard to palladium sensitivity; however, a study on palladium contact sensitivity indicated that lichenoid reactions are one of the common manifestations of palladium sensitivity in the clinical setting.¹⁰ A recent study from the Czech Republic noted a frequency of 12.9% for lichenoid reactions in the oral mucosa for palladium-sensitive patients, which ranked second to mercury and higher than gold in frequency.²⁰

Nickel allergy was found in 57.0% of patients sensitized to palladium. Our results are in line with those of previous studies, which have shown a co-reactivity as high as 94.1% between the two metals.^{1,9,13,21} This co-reactivity is thought to be either a cross-reaction (because both metals belong to group VIII of the periodic table)^{22,23} or a combined sensitization to both metals.¹⁰

The high incidence of co-reactivity of gold with palladium in our study has not been previously described. These two metals are far from each other in the periodic table, but both have been reported to cause lichenoid eruptions.^{1,24} In the oral mucosa, we found high gold co-reactivity, which is most likely related to the individual allergenicity of the two noble metals being present in the same alloy (either in jewelry or in oral dental alloys).

The high female preponderance of 92% in our study was noted in all groups of palladium-sensitive patients. The female preponderance in patients with BMS has been previously documented but is somewhat controversial in the other groups.^{19,25–28}

The limitations of our study include the retrospective nature of data retrieval and the difficulty in assigning relevance. In addition, our clinic is a referral center, and our patients may not be reflective of the general population.

Conclusion

The frequency of palladium sensitivity in a US patch-test population tested with palladium at a tertiary care center was 12.1%. Oral disease association was twice that of skin dermatitis and may be of particular significance in patients with BMS. Gold co-reactivity with palladium was almost as high as nickel co-reactivity, particularly in oral diseases. These preliminary findings raise many questions regarding the role of palladium in oral diseases and will need further validation in future studies.

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