

Clinically Relevant Patch Test Results in Patients With Burning Mouth Syndrome

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Background: Patients with a sore or burning mouth associated with clinically normal oral mucosa present a difficult diagnostic challenge.

Objective: The objective of this study was to assess the value of patch testing in patients with burning mouth syndrome.

Methods: We retrospectively reviewed the results of patch testing to an oral series in patients with burning mouth syndrome seen at Mayo Clinic, Rochester, Minnesota, between January 2000 and April 2006.

Results: Of 195 consecutive patients with a burning or sore mouth, 75 had patch testing to an oral series, and 28 of these patients (37.3%) had allergic patch test reactions. The most common allergens were nickel sulfate hexahydrate 2.5%, balsam of Peru, and gold sodium thiosulfate 0.5%. On follow-up, 15 patients reported improvement, 4 removed or avoided the offending dental metal, and 6 avoided the dietary allergen. Thirteen patients did not improve; 6 avoided identified allergens, but without improvement; 1 removed dental metals without symptom change; and 5 avoided test-positive dietary allergens but without improvement. The remaining 7 nonresponders had nonrelevant patch test results or did not avoid allergens.

Conclusions: Patch testing can identify patients who may be allergic to dental metals or dietary additives and who may benefit from removal or avoidance of these.

PATIENTS WITH a sore or burning mouth associated with clinically normal oral mucosa (burning mouth syndrome [BMS]) present a frequently difficult diagnostic challenge. Many potentiating or precipitating factors have been cited as initiating the burning sensation of the oral mucosa, including allergic contact stomatitis.¹⁻⁵

Most of the contributions to the literature on BMS and contact allergy are case reports or small case series of BMS patients. Allergens identified by patch testing have included prosthodontic materials,⁶⁻⁹ food additives,¹⁰ menthol and peppermint,¹¹ and dental restorative metals, namely, zinc, cobalt, and mercury,¹² mercury,^{13,14} mercury derivatives,¹⁵ gold,¹⁶ and palladium.¹⁷ One review¹⁸ suggested that BMS patients have a higher frequency of allergy to gold than to mercury.

The usefulness of patch testing in BMS patients has been debated. Some investigators¹⁹⁻²¹ have not recommended routine patch testing for BMS. Others^{12,22} have concluded that contact allergens do not play a primary role in BMS but recommended patch testing in select patients. Contact stomatitis is believed to

be rare²³; in a series of 8 patients, the investigators¹⁹ found no correlation between BMS and contact dermatitis.

We have previously reported the results of patch testing in BMS patients at our institution.³ In that study, 13% of patients had positive patch test results for allergens potentially relevant to their symptoms. Positive results were noted to flavorings or food additives such as cinnamic aldehyde, tartrazine, menthol, and peppermint. Interestingly, of the patients patch tested, none had a positive reaction to prosthodontic allergens or materials. We decided to update that report by describing our recent experience of patch testing BMS patients, with a view to identifying not only allergic patch test reactions in these patients but also patients who benefited from avoidance of identified allergens.

SUBJECTS AND METHODS

Definition of BMS

Burning, tingling, or stinging sensation of the oral mucosa has been accorded many names, including BMS, stomatopyrosis, stomatodynia, glossodynia, glossopyrosis, and oral dysesthesia. For the purposes of this retrospective medical record review, patients with normal oral mucosa who complained primarily of a sore or burning mouth were assigned the diagnosis of BMS.

The study was approved by the Mayo Clinic Institutional Review Board.

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TABLE 1. Standard and Preservative Series

Amidoamine 0.1% aqueous
Bacitracin 20%
Balsam of Peru 25%
Benzalkonium chloride 0.1% aqueous
Benzoic acid 5%
2-Bromo-2-nitropropane-1,3-diol 0.25%
Black rubber mix 0.6%
Budesonide 0.1%
2,6- <i>di-tert</i> -Butyl-4-cresol (BHT) 2%
4- <i>tert</i> -Butylphenol formaldehyde resin 1%
Carba mix 3%
Cetyl alcohol 5%
Chloroxylonol (PCMX) 1%
Cinnamic aldehyde 1%
Clobetasol-17-propionate 1%
Cobalt chloride 1%
Cocamidopropyl betaine 1% aqueous
Coconut diethanolamide (Cocamide DEA) 0.5%
Colophony 20%
Compositae mix 5%
Diazolidinyl urea 1%
Diazolidinyl urea 1% aqueous
Dimethylol dihydroxyethylene urea 4.5% aqueous
Disperse blue no. 106, 1%
Disperse blue no. 124, 1%
Disperse orange no. 3, 1%
DMDM (1,3-dimethylol-5,5-dimethyl) hydantoin 1%
DMDM hydantoin 2% in aqueous
Epoxy resin 1%
Ethyl acrylate 0.1%
Ethylene urea-melamine formaldehyde mix 5%
Ethylenediamine dihydrochloride 1%
Formaldehyde 1% aqueous
Fragrance mix 8%
Glutaraldehyde 0.2%
Glyceryl thioglycolate 1%
Gold sodium thiosulfate 0.25% in petrolatum
Hexylresorcinol 0.25%
Hydrocortisone 17-butyrate 1% alcohol
2-Hydroxy-4-methoxybenzophenone 3%
Imidazolidinyl urea 2% (in petrolatum)
Imidazolidinyl urea 2% aqueous
Isopropyl myristate 20%
Lidocaine 5%
MCI/MI (isothiazolinones) methylchlorisothiazolinone/ methylisothiazolinone 100 ppm aqueous
Mercapto mix 1%
Mercaptobenzothiazole 1%
Methyl methacrylate 2%
Methyldibromo glutaronitrile/phenoxyethanol 1.5%
Mixed dialkyl thioureas 1%
Natural fragrance mix 2%
Neomycin sulfate 20%
Nickel sulfate hexahydrate 2.5%
Paraben mix 16%

TABLE 1. (Continued)

Phenol formaldehyde resin 1%
Phenylenediamine 1%
Potassium dichromate 0.25%
Propylene glycol 10%
Quaternium 15 1%
Sesquiterpene lactone mix 0.1%
Sorbic acid 2%
Stearyl alcohol 30%
Thiuram mix 1%
Tixocortol 21 pivalate 1%
(+/-)- α -Tocopherol 100%
Toluenesulfonamide-formaldehyde resin 10%
Triamcinolone acetonide 1%
Triclosan 2%
Triethanolamine 2%
Wool alcohols (lanolin alcohol) 30%

TABLE 2. Oral Flavors and Preservatives Series

Anethole 5%
Ammonium persulfate 2.5%
Amyl cinnamaldehyde 2%
Benzoic acid 5%
Benzoyl peroxide 1%
Benzyl alcohol 1%
Bis-GMA (bisphenol A diglycidylether methacrylate) 2%
Citric acid 1% aqueous
Clove oil 2%
Dipentene (limonene) 1%
Dodecyl gallate 0.25%
Ethylene glycol dimethacrylate (EGDMA) 2%
Eucalyptus oil 2%
Eugenol 2%
Glutamic acid 1%
Isoeugenol 2%
Lemon oil 2%
Menthol 2%
Methyl salicylate 2%
Octyl gallate 0.25%
Orange oil 2%
Peppermint oil 2%
Propionic acid 3%
Propyl gallate 1%
R-(L)-carvone 5%
Resorcinol 1%
Sodium benzoate 5%
Sorbic acid 2%
Sorbitan sesquileate 20%
Spearmint oil 2%
Tartrazine yellow 0.1%
Triethylene glycol dimethacrylate (TREGDMA) 2%
Vanillin 10%

TABLE 3. Oral Complete Series

Aluminum powder 100%
Amalgam 5%
Ammonium persulfate 2.5%
Ammonium tetrachloroplatinate 0.25% aqueous
Amyl cinnamaldehyde 2%
Anethole 5%
Balsam of Peru 25%
Benzocaine 5%
Benzoic acid 5%
Benzoyl peroxide 1%
Benzyl alcohol 1%
Beryllium sulfate tetrahydrate 1% aqueous
Bis-GMA
2,2-bis(4-(2-hydroxy-3-methacryloxy-propoxyphenyl)propan) 2%
Bis-MA 2,2-bis(4-(methacryloxy)phenyl)propane 2%
Budesonide 0.1%
1,4-Butanediol dimethacrylate 2%
<i>n</i> -Butyl methacrylate 2%
Chromium chloride 5%
Citric acid 1% aqueous
Clove oil 2%
Cobalt chloride 1%
Cobalt sulfate 1%
Colophony 20%
Copper sulfate 2%
<i>N,N</i> -dimethylaminoethyl methacrylate 0.2%
Dipentene (limonene) 1%
Dodecyl gallate 0.25%
Ethyl acrylate 0.1%
Ethyl cyanoacrylate 10%
Ethylene glycol dimethacrylate (EGDMA) 2%
Eucalyptus oil 2%
Eugenol 2%
Ferric chloride 1% aqueous
Fluocinonide 1%
Fragrance mix 8%
Glutamic acid 1%
Gold chloride 0.5% alcohol
Gold sodium thiosulfate 0.25% in petrolatum
Gold sodium thiosulfate 0.5%
1,6-Hexanediol diacrylate 0.1%
Hydrocortisone 17-butyrate 1% alcohol
2-Hydroxyethyl methacrylate 2%
2-Hydroxypropyl methacrylate 2%
Isoeugenol 2%
Lemon oil 2%
Lidocaine 5%
Manganese chloride 2% aqueous
Menthol 2%
Mercuric chloride 0.1%
Mercury 0.5%
Mercury ammonium chloride 1%
Methyl methacrylate 2%
Methyl salicylate 2%
Molybdenum chloride 1%

TABLE 3. (Continued)

Natural fragrance mix 2%
Nickel sulfate hexahydrate 2.5%
Octyl gallate 0.25%
Orange oil 2%
Palladium chloride 2%
Peppermint oil 2%
Potassium dichromate 0.5%
Potassium dicyanoaurate 0.1% aqueous
Propionic acid 3%
Propyl gallate 1%
R-(L)-carvone 5%
Resorcinol 1%
Rhodium 1%
Silver nitrate 1% aqueous
Sodium benzoate 5%
Sorbic acid 2%
Sorbitan sesquileate 20%
Spearmint oil 2%
Tartrazine yellow 0.1%
Tetraethylene glycol dimethacrylate 2%
Tetrahydrofurfuryl methacrylate 2%
Tin 50%
Titanium alloy disk
Tixocortol 21 pivalate 1%
Triamcinolone acetonide 1%
Triclosan 2%
Triethylene glycol dimethacrylate (TREGDMA) 2%
Urethane dimethacrylate 2%
Vanillin 10%
Zinc 2.5%
Zinc chloride 2% aqueous

Patch Testing

Our institution uses 3 series in its approach to patch testing patients who complain of a sore, burning mouth. These are read at 48 and 96 hours. Patch tests to dental metals are also read at 1 week (day 7) and again at 2 weeks (day 14) to allow for delayed reactions to metals, which may occur as late as 14 days. All the patch test series are designed by the Mayo Clinic Contact Dermatitis Group.⁴ They are the Standard and Preservative Series (72 test substances) (Table 1), Oral Flavors and Preservatives Series (33 test substances) (Table 2), and the Oral Complete Series (86 test substances) (Table 3). Patients underwent patch testing if they had a history suggestive of contact allergy, including intermittent symptoms, known triggers, patient's own suspicion of allergy, or regular ingestion or use of a known oral allergen such as cinnamon or flavored chewing gum.

Patient Selection

We identified the medical records of all BMS patients evaluated in the Department of Dermatology, Mayo Clinic, Rochester, MN, by

the senior authors (A.J.B., R.S.R., and L.A.D) between 2000 and 2006. The electronic medical records were reviewed, and information from these consultations was extracted and analyzed.

The electronic records were examined to identify any improvement in symptoms with avoidance of allergens. If no follow-up visit had occurred with documentation or if no comment was noted in the record, a telephone follow-up was conducted by one of the senior authors (A.J.B. or R.S.R.).

RESULTS

Patients

Of the 195 consecutive patients evaluated for BMS, 75 (59 women, 16 men) had patch testing, and 38 of these had patch test reactions. Twenty-eight (37.3%) of the 75 patients tested demonstrated allergic patch test reactions; the remaining reactions were considered irritant patch test reactions. Thus, the study group comprised 28 patients with BMS who had allergic patch test reactions. The mean age of the study group (24 women, 4 men) at the onset of their symptoms was 60.5 years (range, 33–83 years).

Symptoms

Twenty-seven patients (96.4%) described their chief complaint as “burning”; the other patient complained of soreness of his gingivae. Sixteen patients (57.1%) had a subjective feeling of a dry mouth (xerostomia). Seven patients (25.0%) complained of a bad taste, and 1 of these patients also complained of decreased ability to taste. Four patients (14.3%) were smokers, 13 (46.4%) were former smokers, and 10 (35.7%) were nonsmokers. This information was not recorded for 1 patient.

The tongue was the most common site of burning, occurring in 18 patients (64.3%), followed by lips (9 patients [32.1%]) and palate (8 patients [28.6%]). Seven patients (25.0%) complained of burning of both their tongue and lips. Other sites included the gingivae (3 patients), throat (3 patients), and floor of the mouth (1 patient).

Factors That Exacerbated Burning and Soreness

Factors reported by patients that exacerbated the soreness and burning in the mouth included spices and spicy food (8 patients); tomatoes, acidic foods, and citrus fruits (4 patients); and candies and chocolate (3 patients), and 1 patient complained of reactions to each of the following: cheese, carbonated beverages, coffee, tea, cinnamon, strong smells, upper denture in situ, stress, vitamin supplements, and magnesium sulfate (Epsom salt).

Comorbid Conditions

Ten patients (35.7%) had controlled hypertension, 3 (10.7%) had diabetes mellitus, 5 (17.9%) had a history of hypothyroidism but were euthyroid on replacement therapy, 11 (39.3%) had a diagnosis of depression, 4 (14.3%) had a previous diagnosis of anxiety, and 13 (46.4%) had treated gastroesophageal reflux disease.

Physical Examination

No mucosal abnormality was noted on any of the patients' physical examinations, specifically, no evidence of inflammation, erythema, erosion, ulceration, or hyperkeratosis. Oral mucosal dryness affected 13 patients (46.4%), and 4 patients (14.3%) wore dentures. Oral dryness was treated with sialogogues and salivary replacements. Dietary factors were identified and eliminated, underlying vitamin deficiencies were corrected, and any associated candidiasis was treated before patch testing was pursued.

Allergens Identified

The positive allergens identified following patch testing are summarized in Table 4. The most common allergens were nickel

TABLE 4. Most Common Allergens Identified (Listed as Most to Least Common)

Allergen	No. (%)
Nickel sulfate hexahydrate 2.5%	8 (28.6)
Balsam of Peru 25%	8 (28.6)
Gold sodium thiosulfate 0.5%	8 (28.6)
Palladium chloride 2%	7 (25.0)
Dodecyl gallate 0.25%	5 (17.9)
Potassium dicyanoaurate 0.1% aqueous	5 (17.9)
Gold chloride 0.5% alcohol	3 (10.7)
Benzoic acid 5%	3 (10.7)
Cobalt chloride 1%	3 (10.7)
Fragrance mix 8%	3 (10.7)
Mercury 0.5%	3 (10.7)
Potassium dichromate 0.5%	3 (10.7)
Beryllium sulfate tetrahydrate 1% aqueous	2 (7.1)
Cobalt sulfate 1%	2 (7.1)
Octyl gallate 0.25%	2 (7.1)
Potassium dichromate 0.25%	2 (7.1)
Propyl gallate 1%	2 (7.1)
Mercury ammonium chloride 1%	1 (3.6)
Ammonium persulfate 2.5%	1 (3.6)
4- <i>tert</i> -Butylphenol formaldehyde resin 1%	1 (3.6)
Benzoyl peroxide 1%	1 (3.6)
Caine mix no. 3	1 (3.6)
Chromium chloride 5%	1 (3.6)
Cinnamic aldehyde 1%	1 (3.6)
Clove oil 2%	1 (3.6)
Colophony 20%	1 (3.6)
Copper sulfate 2%	1 (3.6)
Disperse blue no. 106	1 (3.6)
Disperse blue no. 124	1 (3.6)
Epoxy resin 1%	1 (3.6)
Eugenol 2%	1 (3.6)
Gold sodium thiosulfate 0.25%	1 (3.6)
Isoeugenol 2%	1 (3.6)
Phenol formaldehyde resin 1%	1 (3.6)
Propionic acid 3%	1 (3.6)
Sorbitan sesquioleate 20%	1 (3.6)
Terazol	1 (3.6)

TABLE 5. Outcome of Allergen Avoidance in 28 BMS Patients

Patient/Sex	Positive Patch Test Results	Outcome
1/F	Dodecyl gallate 0.25%, potassium dicyanoaurate, fragrance mix, gold sodium thiosulfate 0.5% and 0.25% in petrolatum	Not helpful
2/M	Gold sodium thiosulfate 0.5%, gold chloride 0.5% alcohol	Had gold in mouth, suggested removal, but patient did not comply because neither he nor his dentist considered the results clinically relevant
3/F	Fragrance mix 8%, cinnamic aldehyde 1%	95%–100% better, avoiding flavors and fragrances
4/F	Dodecyl gallate 0.25%, nickel sulfate hexahydrate 2.5%, sorbitan sesquioleate 20%	Nickel-containing crowns replaced with gold, substantial improvement
5/F	Gold chloride 0.5% alcohol, gold sodium thiosulfate 0.5%, potassium dicyanoaurate 0.1% aqueous	Much improvement after 3 gold crowns removed
6/F	Palladium chloride 2%, nickel sulfate hexahydrate 2.5%	Bridge lower left quadrant of 55% palladium; not removed as patient's symptoms improved, she preferred not to undertake cost and effort
7/F	Dodecyl gallate 0.25%, palladium chloride 2%	Avoiding preservatives in fatty/oily foods (dodecyl gallates) provided no relief; BMS improved spontaneously
8/M	Potassium dichromate 0.5%	Fixed chrome-containing bridge replaced; no improvement
9/M	Balsam of Peru 25%, gold sodium thiosulfate 0.5%	Patient had gold crowns and chewed gum; advised to stop gum and avoid flavored fragrance additive in diet, with almost 100% resolution
10/F	Ammonium persulfate 2.5%, octyl gallate 0.25%, benzoyl peroxide 1%	Avoidance of food additives/preservatives; no improvement
11/F	Palladium chloride 2%, cobalt chloride 1%, nickel sulfate 2.5%, copper sulfate 2%	Patient had previous reaction to jewelry (nickel, cobalt), had dental restorations; no avoidance but BMS in remission
12/F	Potassium dichromate 0.25%, mercury 0.5%, potassium dicyanoaurate 0.1% aqueous, fragrance mix 8%, isoeugenol 2%, eugenol 2%, clove oil 2%, balsam of Peru 25%	Planned dental implants, told to avoid balsam and cinnamon with no benefit; BMS persists
13/F	Benzoic acid	Switched toothpaste (benzoic acid) to baking soda; situation improved in early morning
14/F	Caine mix no. 3, potassium dichromate, balsam of Peru 25%, cobalt sulfate 1%, chromium chloride 5%, terazol, disperse blue no. 106 and no. 124	Avoided allergens that she felt were triggers; overall BMS improved
15/F	Nickel sulfate hexahydrate 2.5%, potassium dichromate 0.5%, potassium dicyanoaurate 0.1% aqueous, mercury 0.5%, gold sodium thiosulfate 0.5%, ammonium chloride 1%	Considered bridge removal; nothing done; BMS persisted unchanged
16/F	Nickel sulfate hexahydrate 2.5%, balsam of Peru 25%	Nickel-free diet with good improvement
17/F	Palladium chloride 2%	Dental restorations did not contain palladium; not helpful
18/M	Beryllium sulfate tetrahydrate 1% aqueous	Checked dental constituents; not helpful; BMS unchanged
19/F	Nickel sulfate hexahydrate 2.5%	Nickel-free diet recommended; no improvement
20/F	Balsam of Peru 25%, dodecyl gallate 0.25%	Told to avoid fragrances and relevant flavorings; no improvement
21/F	Benzoic acid 5%, balsam of Peru 25%	Dietary avoidance; no notable improvement
22/F	Propionic acid 3%, palladium chloride 2%, gold sodium thiosulfate 0.5%, propyl gallate 1%	Avoided irritant foodstuffs and margarine; somewhat improved
23/F	Balsam of Peru, dodecyl gallate	Dietary avoidance; no notable improvement
24/F	4-tert-Butylphenol formaldehyde resin 1%, phenol formaldehyde resin 1%, colophony 20%, gold sodium thiosulfate 0.5%	Suggested changing dental restorations especially teeth that had root canal treatment; not done
25/F	Benzoic acid, gallates	Dietary modification to avoid benzoic acid and gallates; partial improvement

(continued next page)

TABLE 5. (Continued)

Patient/Sex	Positive Patch Test Results	Outcome
26/F	2 forms of cobalt (chloride and sulfate), palladium, nickel	Dental work replaced; substantial improvement in left side of the tongue but not roof of mouth
27/F	Epoxy resin 1%, nickel sulfate 2.5%, cobalt chloride 1%, potassium dichromate 0.5%, gold sodium thiosulfate 0.5%, palladium chloride 2%, gold chloride 0.5% alcohol, potassium dicyanoaurate 0.1% aqueous, beryllium sulfate tetrahydrate 1% aqueous	Suggested to remove dental metals but did not do so; BMS improved with improved sugar control
28/F	Balsam of Peru	Improved but not clear if dietary modification helped

F indicates female; M, male.

sulfate hexahydrate, 2.5%; balsam of Peru, 25%; and gold sodium thiosulfate, 0.5%, each with 8 positive results. The mean number of allergens identified per patient was 3 (range, 1–9).

General Outcomes

Details on each of the 28 patients' allergens and the response of their BMS to avoidance are outlined in Table 5, and a summary of these results is shown in the flowchart (Fig. 1). Overall, BMS improved after patch testing in 15 patients; 3 had spontaneous improvement, and 12 improved after allergen avoidance, although 2 of these patients believed their improvement was unrelated to avoidance of the allergens.

Thirteen of the patients who had positive patch test results did not improve. Two of these tested positive for dental metals not present in their mouths, and therefore, these results were considered not relevant. Five patients had positive dental-metal reactions but elected not to remove the metal from their mouths, and 6 avoided allergens but without benefit. Five of the latter were all dietary allergens; 1 was a dental metal, but removal did not change symptoms (Fig. 2).

Dental-Metal Allergy

Twenty patients tested positive for dental-material allergy. Twelve patients did not intervene with their dental-metal allergies. Five were advised to change dental restorations but did not do so, and

their symptoms persisted. The reasons given were that either the patient or the patient's dentist did not believe the patch test results were clinically relevant or the cost and effort involved were prohibitive. Seven patients' symptoms improved without dental intervention or removal of dental metals. The response occurred spontaneously in 3 patients and in response to avoidance of other positive allergens in 4 patients.

Six patients intervened with their dental-metal allergies. Four patients reported symptom improvement after reducing exposure to the dental metal; 3 patients had improvement after changing dental restorations, and 1 improved by following a nickel-reduced diet. Two patients did not find elimination of the metal helpful; specifically, 1 patient had his chrome-containing fixed bridge replaced but without improvement; another patient adopted a nickel-reduced diet without improvement in his symptoms. Two patients had patch tested positive for metals that were not present in their mouth and hence not thought to be relevant allergens. Their symptoms persisted.

DISCUSSION AND REVIEW OF THE LITERATURE

Patch testing was a useful diagnostic tool in the evaluation of patients with BMS. Approximately one third of patients patch tested had positive allergic patch test reactions. Avoidance of allergens was associated with improvement in approximately half the patients with positive allergic patch test reactions. Patch testing was helpful in identifying patients who may be allergic to dental metals and who may benefit from removal of dental metals.

What Allergens Should Be Included in a Series for BMS Patients?

Over time, the array of allergens included in our patch test series has evolved. Initially, we tested to a standard series and an oral flavorings series. For patients with metal in their mouth, a metal series was included. For patients who had multiple dental amalgams, a dental series was included. We now have a defined oral series, which includes allergens we consider important in this setting (Table 3).⁴

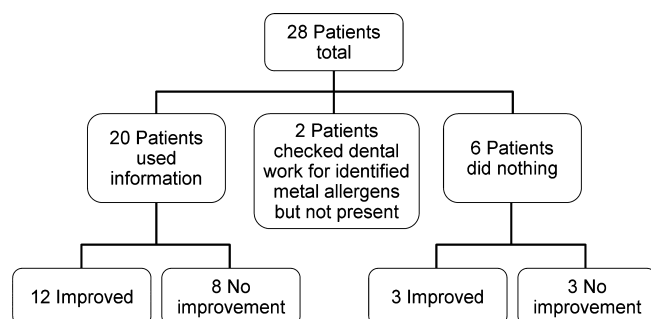


Figure 1. Summary of the 28 patients.

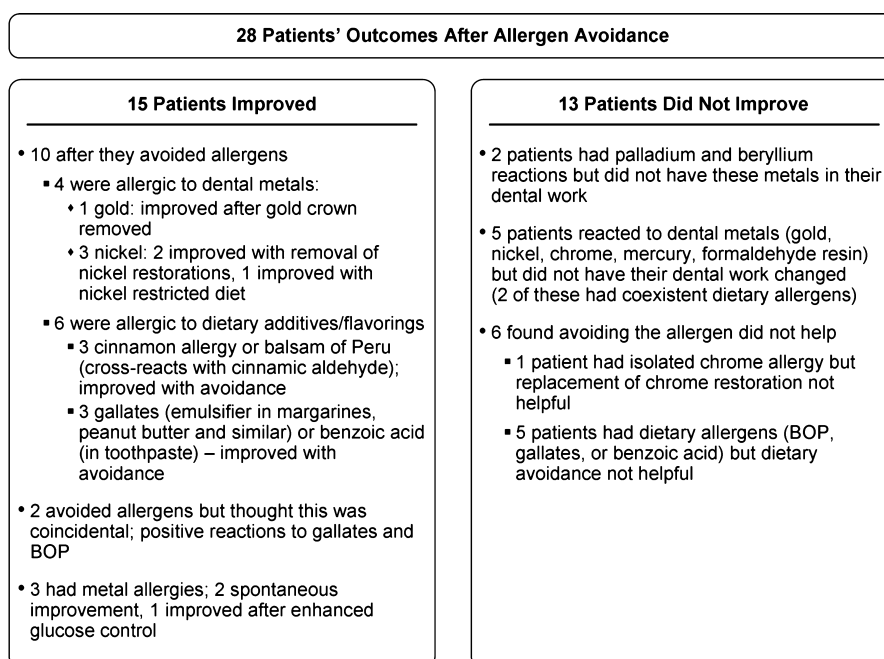


Figure 2. Outcomes of 28 patients with BMS based on allergen avoidance. BOP indicates balsam of Peru.

Identified Allergens

The allergens identified included those found in dental prostheses and dental-metal restorations and in foods and flavors. Of the top 6 identified allergens, 4 were metals found in dental materials and restorations—nickel sulfate hexahydrate (2.5%) and gold sodium thiosulfate (0.5%, most common [Table 4]), palladium chloride (2%, ranked fourth), and potassium dicyanoaurate (0.1% aqueous; ranked fifth)—and 2 were balsam of Peru 25% (also ranked first in Table 4), which is found in cinnamon, cinnamon-related compounds, vanilla, and the essential oil of orange, and dodecyl gallate 0.25% (also ranked fifth), which is an emulsifier present in fats, margarines, peanut butter, and other foods. Our previous study³ had suggested a possible association between food flavorings (fragrance allergy) and BMS; therefore, the balsam of Peru allergy identified in this current review is interesting to note.

Many of these patients improved either spontaneously or after avoidance of allergens. Of the patients who took a further step to remove offending dental metals, 3 of 4 experienced substantial improvement in their symptoms, with only 1 deriving no benefit from removal of a chrome bridge. Several patients whose symptoms remained unchanged did not follow the recommendation to replace their dental work. It would seem, therefore, on the basis of positive patch test results, that some patients' condition will improve either through avoidance of allergens or spontaneous remission (as in 15 of our 28 patients). This portends a better prognosis for BMS patients than is generally thought. Furthermore, it seems appropriate that if no benefit is derived from avoidance of clinically relevant dietary allergens, then it is reasonable in select patients to suggest replacement of allergenic dental metals.

It is also worth noting that, in patients with balsam of Peru allergy, avoidance of appropriate flavorings or a balsam of Peru-free diet may warrant a trial. We recognize that our numbers are very small to derive this conclusion, but in patients whose quality of life is severely affected, or in whom no other interventions have provided any relief, dental-metal replacement may provide relief. Larger studies are needed to explore this hypothesis and also to explore the relevance and potential role of fragrance allergy.

Previous Publications Describing Patch Test Results in BMS Patients

Two case reports have been published in the literature regarding allergens identified by patch testing and BMS and 12 case series of varying size. These are summarized in Table 6.

These studies identify isolated patients with clear-cut allergic causes for the BMS symptoms as demonstrated by dramatic improvement after avoidance of allergens. Similarly, in many of our patients, allergen avoidance led to improvement of the burning experienced by the patients.

Strength of This Study

This study is larger than any of the previously reported studies, although the number of patients studied thus far is still small. A major strength of this study is that we have follow-up on all 28 patients. Many studies showing positive patch test results had no follow-up to confirm clinical relevance. There is a difference between noting a positive allergic patch test reaction and

TABLE 6. Allergens Identified by Patch Testing for BMS: Review of the Literature

Source, Year	Report/ Series	Allergens	Outcomes
Pigatto et al ¹⁴ (2004)	Report	Mercury, amalgam	1 Patient with BMS and systemic allergic contact dermatitis; symptoms resolved after dental amalgam restoration removed
Koike ¹² (2005)	Report	Zinc, cobalt, mercury	1 Patient with burning sensation of oral cavity; symptoms resolved after removal of dental prosthesis
Kaaber et al ⁷ (1979)	Series	Denture-based materials, balsam of Peru	53 Partially dentate or edentulous patients with BMS; 12 substances tested: 14/53 tested positive for ≥ 1 allergens, 1/53 tested positive for balsam of Peru (11 of these 15 patients had mucosal inflammation so cannot be classified as BMS); 3/15 results not clinically relevant as tested positive for metals yet wore complete dentures (nonmetal); 6/15 had partial/complete resolution when alternative denture material was used or a substance was eliminated; patient with reaction to balsam of Peru had resolution after discontinuing use of the sensitizer (mouthwash)
van Joost et al ⁹ (1988)	Series	Denture-based materials (Luxene dentures), monomeric methyl methacrylate, epoxy resin	4 Patients with BMS; 2 patients reacted to constituents of Luxene dentures, 2 patients had reactions to monomeric methyl methacrylate and epoxy resin
Skoglund and Egelrud ²⁰ (1991)	Series	Nickel sulfate	24 Patients with oral lichenoid mucosal lesions and 24 with BMS patch tested using a battery of 35 dental test substances; 8 of lichenoid group tested positive for mercury ammonium chloride, none of BMS group tested positive; 5 BMS patients tested positive for nickel sulfate, and only 1 of lichenoid group tested positive for nickel sulfate
Dutree-Meulenberg et al ⁶ (1992)	Series	Various	22 Patients with BMS, 20 wore either partial or complete dentures; 6 patients (denture wearers) had a positive result to allergens used in the production of acrylate-based dentures; 6 patients had possibly relevant hypersensitivity to dental metals (4 to gold, 1 to nickel, 1 to cobalt)
Laeijendecker and van Joost ¹⁶ (1994)	Series	Gold	200 Patients with symptomatic oral mucosal or cutaneous lesions; patch tested with 20 dental materials (European standard series): 17 female patients (8.5%) tested positive for both 1% and 0.5% gold (tri)chloride; 6/17 patients diagnosed with BMS, 1/6 also had reactions to nickel and cobalt; resolution in symptoms of 2 patients after replacement of gold-containing alloys in 1 patient's dentures and nickel and cobalt in another's who did not have gold present
Lamey et al ¹⁰ (1994)	Series	Various food additives	Type 3* BMS patients; suggested that allergic reactions, especially to food additives, could be contributory
Helton and Storrs ¹⁹ (1994)	Series	Denture allergens	8 BMS patients who wore dentures; investigated to establish whether contact urticaria, allergic contact dermatitis, or pressure urticaria were of etiologic importance; battery of 25 possible denture allergens tested; no urticarial reactions and all patch tests negative
Bergdahl et al ¹³ (1994)	Series	Mercury, gold	25 Patients with burning mouth; 5 patients demonstrated hypersensitivity reactions to mercury; 2 of these 5 had resolution of symptoms after replacement of their restorations, 1 of these patients had reaction to gold also
Morton et al ¹¹ (1995)	Series	Menthol, peppermint	5/12 Cases reported were BMS patients; 3 tested positive for menthol (1 had resolution of symptoms through avoidance, 1 had no improvement, 1 lost to follow-up), 1 tested positive for peppermint (improved through avoidance), 1 to both (patient did not avoid sensitizers, no change)
Virgili et al ²² (1996)	Series	Various	15 Patients with BMS; 12 matched patients in control group; 6/15 and 3/12 had positive reactions

(continued next page)

TABLE 6. (Continued)

Source, Year	Report/ Series	Allergens	Outcomes
Larese Filon et al ¹⁷ (2003)	Series	Palladium chloride 1%	4446 Patients with suspected contact dermatitis; 10-y study looked at sensitization to palladium chloride 1%; 236 (5.3%) tested positive; 1.7% of this group “complained of BMS”
Mehulic et al ⁸ (2005)	Series	Chromium	32 Patients undergoing prosthodontic therapy had lichen planus, stomatitis, or stomatopyrosis; patch test–proven allergy to chromium more common in those with stomatopyrosis
Machet et al ¹⁵ (2008)	Series	Various	40 Patients with BMS patch tested; 16 patients (40%) had at least 1 positive result; total of 35 positive tests
Marino et al ²⁴ (2009)	Series	Various	124 Patients with BMS studied prospectively; 16 patients (13%) with positive patch test reactions
Present study (2011)	Series	Various	75 BMS patients patch tested; 38 had patch test reactions; 28 had allergic patch test reactions

*Type 3 is an intermittent burning sensation, not present every day as with types 1 and 2.

identifying a patient with burning mouth that can be attributed to identified allergens.

Limitations of This Study

Although the number of patients described is larger than that in other reports, the number reported is still small overall. In our cohort, there is follow-up on all patients, but it is still difficult to identify whether patients' improvement was attributable to allergen avoidance and not to other factors. Some patients did not avoid the identified allergens. The array of patch-tested allergens varied over the period studied. We also did not test for contact allergy.

CONCLUSIONS

Patch testing is a helpful tool in the investigation and management of patients with BMS. Approximately one third of BMS patients who had patch testing had positive allergic patch test reactions. Many of these reactions (65%) were clinically relevant, as evidenced by improvement in their condition with avoidance of the identified allergens. Patch testing can also identify patients who may be allergic to dental metals and who may benefit from removal of dental metals.

Overall, 12 of 75 patients derived direct clinical benefit from patch testing (ie, allergens were identified on testing, which when eliminated attenuated their BMS symptoms). Patch testing is an important part of the evaluation of BMS patients.

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