



Contact stomatitis

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Abstract Contact stomatitis occurs in up to 10% of the population. Mechanical or chemical irritation, ill-fitting dentures, and dental fillings can induce irritant contact stomatitis. Type I hypersensitivity and type IV hypersensitivity to dental products and foods are frequently responsible for the allergic types of contact stomatitis. We review the causal agents of contact stomatitis, the differential diagnoses, diagnostic testing, and potential treatment. © 2017 Published by Elsevier Inc.

Introduction

The oral mucosa reacts to either external irritations or allergens.^{1,2} Lips react more frequently than other parts of the oral cavity.^{3–5} The oral mucosa responds to irritants less strongly than the skin because of its anatomic and functional characteristics.⁶ Saliva washes away, dilutes, buffers, and digests both irritants and allergens. Both irritants and allergens are in contact with the oral mucosa for a very short period.¹ In addition, the abundant vasculature allows faster absorption and clearance of the irritants and allergens. These factors explain the immunologic tolerance of the oral cavity.

Some oral hygiene products and habits, as well as low-grade oral inflammatory conditions such as periodontitis, which produce inflammatory responses, play a role in allergic or irritant contact stomatitis.^{3,7} The prevalence of contact stomatitis ranges from 1% to 10% with a female predilection.¹

Irritant contact stomatitis

Irritant contact stomatitis is more common than the allergic variant. The onset depends on the irritant potential of the agent,

its penetration capacity, irritant concentration, duration and frequency of the contact, and patient's inflammatory response.

In irritant contact stomatitis, damage can be caused by mechanical irritation (ie, ill-fitting dentures or irregular dental fillings), as well as chemical or physical elements. Chronic mechanical irritation predisposes the area to injury by chemical irritants. Chemical irritants more frequently associated with contact stomatitis are foods, seasonings and flavors,⁴ oral hygiene products,⁸ dental restoration products (eugenol,^{9–11} formaldehyde, hydrogen peroxide), nicotine,⁶ dental metals, and chemicals.

Toothpastes and mouthwashes contain potential irritant substances such as detergents, moisturizers, binders, preservatives, sweeteners, flavorings, tartar-preventing agents, and whiteners.^{8,12,13} Thermal damage can cause irritant stomatitis as well. Hot oils on pieces of pepperoni can cause a burn of the palate and other mucosal surfaces.

The clinical presentation of irritant contact stomatitis can be very similar to allergic contact stomatitis; however, patch testing is negative in the setting of irritant contact stomatitis.

Allergic contact stomatitis

Allergic contact stomatitis is less frequent than irritant contact stomatitis.¹ A higher concentration of antigen is needed for an

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allergic response in oral exposures compared with the skin because of the effects of saliva and the vascularity of the oral mucosa.

If a patient is sensitized to an allergen through the skin, the oral mucosa may not develop allergic clinical manifestations; however, if sensitization occurs orally, it is highly probable that the patient will also develop cutaneous allergic signs and clinical manifestations. The allergic response of contact stomatitis may be mediated by type I hypersensitivity, which is very rare, or type IV hypersensitivity, which is most common. The most common causal agents are described in Table 1.

Type I allergic contact stomatitis

Type I hypersensitivity, an IgE-mediated reaction, is associated with the development of urticaria and angioedema, and in severe cases it can result in airway swelling and anaphylactic shock. In some cases, bullous and ulcerative lesions of the oral cavity have been reported.²

Latex allergy is the most common reaction in this group, especially in dental staff and sensitized patients. Latex is present in rubber gloves, dental dams, and rotating rubber tools. The powder in gloves spreads the allergen; therefore, the use of powder-free gloves decreases the occurrence of allergic reactions. The incidence of latex-positive prick test in dental workers has been reported up to 10%.^{14,15}

Metals such as nickel, cobalt, platinum, and palladium have been associated with type I allergies, such as contact urticaria and respiratory reactions.² Chlorhexidine is frequently present in mouthwashes. It can induce severe local and systemic allergic reactions when it is applied directly to the oral mucosa in high concentrations.^{12,13} Allergic reactions have been reported from application of local anesthetics, topical corticosteroids, propylene glycol, and topical antibiotics.

Immediate allergic reactions to acrylates have been observed among dental staff.

These patients are evaluated by performing prick testing¹⁵; however, the physician should consider the possibility of triggering an immediate allergic reaction. The radioallergosorbent test (RAST) is an alternative test to perform as it does not expose the patient to the allergen being studied; however, results may vary with patient’s comorbidities.

Although the severity of a type I hypersensitivity reaction can be variable, dentists should be aware of these reactions and to be prepared to manage the reactions. A detailed medical history is helpful to prevent the development of type I allergic reactions.

Table 1 Allergic contact stomatitis: common causal agents

Causal agents
Dental materials
Dental hygiene products
Foods and beverages
Drugs

Type IV allergic contact stomatitis

Patients with type IV allergic contact stomatitis present with clinical manifestations more frequently than significant physical findings.^{16–20} The lips and perioral tissues are frequently involved.^{4,5,21}

Clinical manifestations may be localized or diffuse and, in many cases, can be confused with vitamin deficiencies. The patient may have pain, burning sensations, taste loss, or dysesthesias.²² Clinical manifestations such as itching, dizziness, headache, gastrointestinal discomfort, and malaise are rare.

Physical examination may be negative for local signs. In some cases, edema, redness of the oral mucosa, vesicles, erosions, ulcers, white patches, or lichenoid lesions are observed.¹⁷ Lingual papillae may disappear. A well-defined demarcation between the area in direct contact with the allergen and the surrounding mucosa can be found in patients with allergic reactions to fillings^{16,23–26} or denture materials.^{16,27} Physical findings may include lip edema, scaling, fissuring, dryness, crusting, and angular cheilitis. The clinical manifestations are nonspecific and can be found in irritant contact stomatitis, actinic cheilitis, and vitamin deficiencies. The most common finding associated with allergic contact stomatitis to dental materials is oral lichenoid lesions.

A few studies have attempted to correlate the type of mucosal findings with the responsible agent.^{6,17,20,28–32} Metals are more frequently associated with oral lichenoid reactions (OLRs), oral lichen planus (OLP), burning mouth syndrome, nonspecific stomatitis, and perioral dermatitis.³³

Table 2 shows the dental materials that induce allergic contact stomatitis.

Reactions to dental materials including latex gloves and acrylates are described in up to 40% to 50% of dental personnel. Contact dermatitis of the hands caused by dental products occurs in 23% of women and 13.8% of men.

Metals

The oral cavity is exposed to fillings, orthodontic appliances, and prostheses (Table 3).

Table 2 Dental materials involved in allergic contact stomatitis

Causal agents
Metals
Dental alloys
Acrylates (resin-based composites)
Preservatives
Antiseptics
Anesthetics
Materials for dental impression
Toothpastes and mouthwashes
Adhesives for dental prosthesis

Table 3 Metals involved in allergic contact stomatitis

Causal agents
Mercury
Nickel
Chrome–cobalt
Gold (may contain nickel and/or cobalt)
Palladium
Platinum
Silver
Tin
Copper
Zinc
Dental alloys

Mercury is the main component of amalgam fillings.³⁴ It can be mixed with silver, tin, copper, and zinc. Modern amalgam preparations contain 40% to 50% mercury.

Amalgams have been used in dentistry since the 1830s. Amalgam fillings are the most commonly used fillings in the oral cavity, because they are inexpensive, resistant, and durable.

Mercury is released in the oral cavity by corrosion, tooth brushing, hot beverages, the use of chewing gum, and bruxism.³⁵ Attempts at producing amalgams containing gallium instead of mercury³⁶ have been made; however, studies showed that these alloys have poorer clinical properties than conventional amalgams. Since the 1990s, many publications have linked the appearance of oral lichenoid lesions in areas in direct contact with amalgams.^{24,25} A complete resolution can occur if the amalgams are removed.^{37–39}

Nickel is the most common cause of contact allergy, which is found in orthodontic appliances. Release of nickel allergen in the oral cavity is produced by condensation, mastication, and tooth polishing. Despite the large number of patients allergic to nickel, the frequency of allergic intraoral reactions is low.² Interestingly, prior exposure to nickel in orthodontic appliances reduces the risk of hypersensitivity to nickel-containing ear-piercing materials.^{40,41}

The use of chrome–cobalt alloy in the oral cavity is common. Cobalt and chrome allergy is usually associated with nickel cosensitization.²

Unlike metallic gold, gold salts are highly sensitizing. Oral lichenoid lesions are the most frequent manifestation of gold allergy. Gold alloys containing other metals can cause oral signs and clinical manifestations of contact stomatitis.^{30,31,41}

Palladium is used in orthodontic appliances; however, allergy to palladium is rare.⁴² A positive patch test to palladium is more likely to occur if concomitant sensitization to nickel is present.⁴³

Titanium and its alloys are used in biomedical devices. Titanium has high resistance to corrosion in a physiological environment and has excellent biocompatibility. In dental practice, pure titanium and titanium alloys are used preferentially for endosseous dental implants. Infection and overload are the main causes of dental implant failure. Allergy to titanium is another potential cause of implant failure,⁴⁴ although rare.

Acrylates

Resin-based composites and adhesives contain different acrylate-derived molecules. Acrylates are also used in temporary crowns, bridges, and removable dentures.^{45–47}

Methyl methacrylates are the most frequently used acrylates; methyl methacrylate, hydroxyethyl methacrylate, triethylene glycol dimethacrylate, and ethylene glycol dimethacrylate are all highly sensitizing.

Clinical manifestations of a sore, burning mouth are more commonly associated with allergy to methacrylates than metal-associated lichenoid contact stomatitis.⁴⁸ A positive patch test to acrylates is more frequent in dental workers than in patients.^{49,50}

Allergy to acrylates is increasing because of greater exposure of patients to acrylic materials such as acrylic nails. Formaldehyde and bisphenol-A can be released from resin-based composites as well.

Ceramics

Ceramics are inorganic materials. They are used in crowns, inlays, and copings. Although it is almost insoluble, degradation occurs in different pH environments or because of mechanical forces.

The allergenic potential of ceramics is very low. Practitioners should be aware that dental personnel can inhale dust during the finishing of dental ceramics. This is a risk for the development of silicosis.⁵¹

Eugenol

Eugenol is a flavoring agent derived from clove oil. It is used as a root canal sealer, temporary filling material, and an essence in cosmetics. Eugenol may cause irritant or allergic contact stomatitis.^{9–11} Cross-reaction with balsam of Peru can be seen in the patch test.

Toothpastes and mouthwashes

The ingredients in toothpastes and mouthwashes may vary depending on the country of manufacture. They can cause allergic or irritant contact stomatitis. Detergents, preservatives, antiseptics, and flavorings are frequently responsible for contact stomatitis.^{6,8,12,13} Common ingredients of toothpastes and mouthwashes are documented in [Table 4](#).

Foods and beverages

Flavors such as cinnamic aldehyde, menthol, and peppermint oil are associated with allergic reactions in the oral mucosa. Benzoic acid; benzoates; benzoyl peroxide; octyl, lauryl

Table 4 Toothpaste and mouthwash ingredients

Ingredients
Detergents (sodium lauryl sulfate)
Preservatives (sodium benzoate, propylene glycol, parabens, formaldehyde, dichlorophen)
Antiseptics (chlorhexidine, triclosan, benzalkonium chloride, formaldehyde, cetylpyridinium chloride, hydrogen peroxide)
Whiteners or abrasives (silica, pyrophosphates, aluminum oxide, calcium carbonate, calcium phosphate, hydrogen peroxide sodium bicarbonate, carbamide peroxide)
Moisturizers (glycerol, propylene glycol, sorbitol)
Binders (carrageenan, gum arabic, carboxymethylcellulose)
Fluoride
Abrasives (silica, alumina, calcium carbonate, calcium phosphate)
Sweeteners (saccharin, cyclamates, xylitol)
Flavorings (cinnamon oil, cinnamic aldehyde, menthol, clove oil)
Dyes (the same used in foods and beverages)
Alcohol
Tartar control (pyrophosphates)
Desensitizers (strontium chloride, sodium citrate, zinc chloride, potassium nitrate)

(dodecyl), and propyl gallates; propionic acid; propionates; and balsam of Peru are other food additives that can cause allergic contact stomatitis.⁴ Several food additives, such as preservatives, flavorings, and antioxidants, cause allergic contact dermatitis more often than immediate hypersensitivity allergic reactions of the oral mucosa.⁶

Oral lichenoid reactions

Oral lichenoid drug reactions are less common than cutaneous lichenoid drug reactions and may occur without skin involvement.^{17,26} Lesions develop weeks to months after the drug exposure (average of 2-3 months). Table 5 shows the drugs that are frequently associated with the occurrence of drug-induced OLRs. OLRs caused by contact stomatitis are similar to OLP, but the lesions tend to be unilateral or in apposition to the metal restoration to which the patient is allergic.^{17,26,52,53}

Workup

Patients should be evaluated by patch testing when allergic contact stomatitis is suspected and oral signs or clinical

Table 5 Drugs involved in contact stomatitis

Drug agent
Beta-blockers
NSAIDs
Thiazide diuretics
Hypoglycemic drugs
Antimicrobials
Gold
Penicillamine

manifestations are found supporting such a reaction. In case of suspected metal allergy, there should be a history of metal allergy and a chronological association between exposure and time of onset of signs or clinical manifestations.^{1,54}

Study methods

There are several tests to identify the causative agent for allergic contact stomatitis.

1. Elimination and provocation test: It is useful and easy to perform in patients with denture and food-induced contact stomatitis. Clinical manifestations usually subside 1 week after the cessation of the responsible agent.
2. Laboratory study:
 - a. Prick test is indicated for type I hypersensitivity such as latex allergy.¹⁵
 - b. Patch test is the gold standard for evaluation of type IV hypersensitivity.
 - c. Radioallergosorbent test (RAST) is used for diagnosis of IgE-mediated allergy.
 - d. Immunotoxicologic tests, including lymphocyte transformation test and memory lymphocyte assay immunostimulation, are not used as routine tests.
 - e. Analysis of metals in saliva and tissue specimens has little diagnostic value.

Patch testing

Patch testing is the main diagnostic tool for allergic contact stomatitis. It has a low risk of sensitization, and it should be used in patients suspected of allergic contact stomatitis.¹

Readings should be performed at days 3, 5, or 7 and 10 or 14; the later readings are important to detect late reactions, especially to metals.^{8,37,55,56}

One can expect to find positive patch tests to multiple agents when searching for the causative agents in allergic contact stomatitis.³³ A positive patch is not of diagnostic value if the patient does not have contact with the identified compound; however, a negative patch test does not rule out patient hypersensitivity to the allergen; sensitization to another compound that is not included in the test battery is possible.^{28,32,56} In the case of a negative patch test, a patch test of the suspected agent can be performed.

Differential diagnosis

Differential diagnoses of white reticulated plaques of the oral mucosa are OLP and OLR. OLP can be clinically indistinguishable from OLR. OLR can be caused by contact allergy, drugs (Table 5), or chronic graft-versus-host disease.¹⁷

In OLR, because of contact with dental materials, the lesions are in apposition to or very close (<1 cm) to the

suspected allergen, and absent where the suspected allergen is not present. The lesions of OLP are often bilateral and symmetrical. Typically, they are located at the lateral borders of the tongue and buccal mucosa.⁵⁷

Histology of OLR and OLP

In 1978, the World Health Organization published the clinical and histologic criteria for diagnosis of OLR. A 2006 report described OLR features, suggesting amalgam as an etiologic factor.⁵⁸

The following histopathologic findings suggest a diagnosis of OLR: deep and diffuse inflammatory infiltrates within the lamina propria and superficial submucosa (drug-induced OLR), focal perivascular neutrophilic infiltrates, significant increase of plasma cells in the connective tissue (in contrast with the characteristic lymphohistiocytic infiltrate in OLP), and an increase in the number of capillaries.^{23,26,37,58,59}

A biopsy may be useful in differentiating OLR from OLP and other diseases, although interobserver discrepancy with the diagnosis of these conditions is possible.

The differential diagnosis between OLR and OLP can be very difficult.

Treatment

The mainstay of treatment is elimination of the causative agent. This is followed by rapid improvement of signs and clinical manifestations.^{1,24,52,60,61}

Oral hygiene changes such as avoiding irritants (eg, toothpastes, mouthwashes, and dental prosthesis adhesives), correction of sharp edges and rough surfaces, and adjusting dental prostheses are important in irritant contact stomatitis. Patients should avoid consuming foods and beverages that contain irritant ingredients.⁴

In patients with lesions anatomically related to amalgam fillings, amalgam removal results in total or partial resolution after a few months.^{37,52,54,60,62–65} If the clinician is highly suspicious that oral lesions are caused by amalgams but patch testing is negative, obturation of amalgam can be useful to avoid direct contact with the mucosa; if improvement occurs, the amalgams should be replaced. It is recommended to use a rubber dam during replacement of restorations, because mercury vapors and dusts are released during the procedure and can become embedded in the surrounding soft tissues.

It is not always possible to avoid the causal agent; thus, topical immunomodulators, such as potent corticosteroids or tacrolimus, can be used.

Follow-up

Complete or partial response after elimination of the suspected agent ranges between 40.5% and 100%. Improvement is more evident in lesions in contact with amalgams and when patch tests are positive to amalgams or one of its components.^{38,39}

Conclusions

The clinical diagnosis of allergic contact stomatitis is not difficult. Identifying the irritants or allergens is more challenging. Patch testing is the gold standard for the diagnosis of type IV allergic contact stomatitis. Results should be interpreted cautiously and conform to the clinical findings. At this time, other testing methods for delayed hypersensitivity are unsatisfactory. In patients with OLR or OLP, amalgam removal is indicated only if the lesions are in close contact with oral lesions. Positive patch test reactions to the suspected dental metals can confirm the diagnosis and can aid in selection of replacement restorative metals to which the patient was not allergic at the time of patch testing.

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