

A review of the pathophysiology, diagnosis, and management of allergic reactions in the dental office

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Since more than 50 million people in the United States have allergies, knowledge of the management of allergic reactions in the dental office is extremely important. Appropriate care may range from a simple referral to a primary care physician to lifesaving measures implemented during acute anaphylactic reactions. The authors present a basic review of the pathophysiology of allergic reactions and provide information detailing the diagnosis and management of allergic reactions that may be encountered in the dental office. Utilizing this information, the dental practitioner and ancillary staff will have a thorough understanding of allergic reactions and be prepared to successfully identify and treat these reactions. (*Quintessence Int* 2011;42:149–156)

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It is estimated that more than 50 million people in the United States suffer from allergies to one or more substances.¹ These substances, including medications, micro-organisms, foods, fragrances, dust, pollen, latex, and many other antigens, may trigger an allergic attack with effects that range from minor discomfort and annoyance to life-threatening emergencies. Since many of these antigens such as latex and antibiotics are used during dental treatment and can therefore be encountered in the office of any dental practitioner, it is incumbent on every practitioner to be fully conversant with the potential antigens, pathophysiology, signs and symptoms, and management of allergic reactions. This article covers all aspects of the recognition and management of allergic reactions encountered in

dentistry. It also focuses on the management of anaphylaxis, a life-threatening reaction that requires immediate diagnosis and treatment.

PATHOPHYSIOLOGY OF ALLERGIC REACTIONS

An allergic reaction is an exaggerated response of the immune system to usually harmless substances (antigens) that trigger a host response. By definition, an allergy can be categorized as a type I or immediate hypersensitivity reaction. Common to all type I hypersensitivity reactions is the massive release of vasoactive amines and other mediators released from basophils and mast cells.² The result of this exaggerated inflammatory reaction is a rapid tissue response, with vascular permeability and smooth-muscle contraction occurring in the various affected organs.² Examples of type I hypersensitivity reactions include angioedema, hay fever, asthma, insect bites, food allergies, and anaphylaxis² (Figs 1 to 5).

When considering the cellular process that occurs with an immediate hypersensitivity reaction, there are two groups of medi-

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Fig 1 Angioedema of the orofacial region.



Fig 2 Uvular angioedema (Quincke disease).



Fig 3 Allergic reaction to fruit-flavored hard candy.



Fig 4 Allergic reaction to chocolate.

Table 1 Primary mediators of hypersensitivity reactions

Primary mediators	Physiologic responses
Histamine	Increased vascular permeability, vasodilation, broncho-constriction, increased mucus secretion
Adenosine	Bronchoconstriction, inhibited platelet aggregation
Chemotactic factors	Attraction neutrophils and eosinophils
Proteases	Generation of kinins and cleave complementation to produce additional chemotactic and inflammatory factors

ators that play a major role in the evolution of the inflammatory response. The primary mediators include histamine, adenosine, chemotactic factors, and proteases.² The secondary mediators include lipids, leu-

kotrienes (B₄, C₄, D₄), prostaglandin D₂, platelet-activating factor, and cytokines.² Included in Tables 1 and 2 are a brief summary of the physiologic responses during hypersensitivity reactions.



Fig 5 Various bee sting reactions. (a) Site of a bee sting. (b) Widespread hives. (c and d) Generalized ear redness after a bee sting.

Table 2 Secondary mediators of hypersensitivity reactions	
Secondary mediators	Physiologic responses
Lipids	Phospholipase A2 cleaves membrane phospholipids to produce arachidonic acid
Leukotriene B4	Highly chemotactic for neutrophils, eosinophils, and monocytes
Leukotrienes C4 and D4	Most potent vasoactive and spasmogenic agents
Prostaglandin D2	Intense bronchospasm and increased mucus secretion
Platelet-activating factor	Histamine release, bronchospasm, platelet aggregation, chemotactic for neutrophils and eosinophils
Tumor necrosis factor	Leukocyte adhesion, emigration, activation
Interleukin-4	Mast cell growth factor required to drive immunoglobulin synthesis by B cells
Interleukin-1, interleukin-5, interleukin-6	A variety of inflammatory cells recruited and activated

Although the focus of this article is on type I hypersensitivity reactions, for completeness, it should be mentioned that there are four hypersensitivity reactions. As mentioned, type I hypersensitivity reactions are considered an immediate hypersensitivity with a tissue response within seconds or minutes. Examples of these reactions include urticaria, food allergies, and anaphylaxis. Type II hypersensitivity reactions are antibody-dependent and result from antibodies directed against target antigens on the surface of cells or other tissue components.² Type II reactions can be complement-dependent (pemphigus vulgaris), antibody-dependent cell-mediated cytotoxicity (eosinophil-mediated killing of parasites), or antibody-mediated cellular dysfunction (myasthenia gravis).² Type III hypersensitivity reactions are immune complex-mediated. Antibodies bind antigens and cause large complexes that activate complement and lead to an accumulation of neutrophils.² The localized example is the Arthus reaction, and the systemic examples include serum sickness and systemic lupus erythematosus.² Finally, type IV hypersensitivity reactions are cell-mediated or delayed-type reactions, in which cell-mediated immune responses are carried out by specifically sensitized T cells.² These reactions typically take longer to peak (48 to 72 hours) for contact dermatitis and tuberculin reaction and 10 to 14 days for acute transplant rejection.²

CLINICAL APPLICATION

It is important for dental practitioners to be aware of common allergic reactions and their management should such an incident arise in the dental office. As mentioned, the most common antigens include dust, pollen, food, medications, and insect stings. Commonly encountered antigens in the dental office include latex, antibiotics, various restorative materials, local anesthetic preservatives, and other patient medications. Any of these potential antigens can be encountered on the way to an office visit or within the office itself. Even more appropriate for dental practice that the majority of a patient's symptoms will affect the head

and neck region. Common areas affected include the eyes, ears, nose, mouth, throat, airway, and sinuses, as well as the skin and gastrointestinal tract.² Although all type I hypersensitivity reactions share the same basic cellular response, the range of effects vary from itchy skin to life-threatening airway compromise. In addition, the presentation of symptoms and their progression varies among allergic reactions.

CLINICAL MANIFESTATIONS OF VARIOUS ALLERGIC REACTIONS

Allergy to latex

A latex allergy can present as either a type I or IV hypersensitivity reaction. The immediate reactions associated with type I are considered a natural rubber latex allergy, while those reactions associated with type IV are often due to the processing chemicals used in manufacturing the latex and may not appear until 48 to 96 hours later.³ Products commonly found in the dental office that contain latex include gloves, rubber dam, elastics, gutta-percha, blood pressure cuffs, stethoscope tubing, tourniquets, bandages, dressings, intervenous (IV) catheters, and syringes.^{4,5} The symptoms for an immediate reaction to latex can vary and may progress rapidly to include anaphylaxis. They include swelling of the affected area; sneezing; runny nose; headache; red, itchy, or tearing eyes; hives or welts; sore throat; hoarse voice; abdominal pain; tightness in the chest; and wheezing and shortness of breath.⁶ The treatment required for a latex allergy ranges from antihistamines and corticosteroids to full emergency management of anaphylaxis, beginning with administration of epinephrine and management of the airway. For cases of delayed hypersensitivity reaction, the reaction is usually localized to the area of exposure and the patient or practitioner develops a skin rash that is slightly elevated and red. Like allergic contact dermatitis, this type of reaction can be managed by avoiding the offending agent and topically or orally administering antihistamines and corticosteroids.

Allergy to medications

A thorough history concerning allergies to medications and the reactions that they elicit should be documented on every patient. This information must be periodically updated. Patients often report that they are allergic to a particular medication, but it becomes apparent with further questioning that their so-called allergy is actually a normal response or adverse effect of that particular medication. This is commonly seen with local anesthetics, analgesics, and antibiotics, three of the most commonly used medications in dental practice. A true allergy to an amide local anesthetic is extremely rare,⁷ and patients may have experienced tachycardia, hematoma formation, or a syncopal episode that they interpret as an allergy.

While an allergic reaction to an amide-type local anesthetic is extremely rare, an allergic reaction to the preservative in the local anesthetic cartridge, although also rare, is more likely than an allergy to the amide anesthetic. Sodium bisulfite and metabisulfite are included in all dental anesthetic cartridges that contain a vasoconstrictor.⁷ Bisulfites serve as antioxidants that prevent the breakdown of the vasoconstrictor.⁷ Sulfites are also found in wine and added to salad bars to preserve freshness. In the event a patient reports an allergy to sulfites, an amide anesthetic without a vasoconstrictor should be used, since it will be free of bisulfites.

Topical anesthetic agents also have the potential to provoke an allergic reaction. Most of the topical agents commonly used in dentistry contain ester compounds and are therefore much more likely to provoke an allergic reaction than amides.⁷ Some of the topical compounds do not penetrate mucosa and are unlikely to provoke anything more than a localized mucosal reaction.⁷ However, other topical formulations are systemically absorbed and more likely to provoke a generalized reaction. Additionally, many topical agents contain methylparaben, an agent known to cause systemic allergic reactions.⁷ Considering all of these variables regarding local anesthetics and allergic reactions, an accurate history becomes extremely important. If the patient reports a history that the clinician

feels is a true local anesthetic allergy, a referral to an allergist prior to dental treatment would be appropriate.

Allergies to analgesic medications can also occur. As with amide local anesthetics, the true incidence of allergic reactions to common pain-relieving medications is low.⁸ It is much more common for patients to experience an adverse effect of an analgesic that they then mistakenly term an allergic reaction. Such effects of analgesics, especially if they contain a narcotic component, include nausea, vomiting, constipation, drowsiness, and dysphoria.⁸ Therefore, the practitioner must distinguish between an adverse effect of an analgesic medication and a true allergic reaction when reviewing the patient's history.

The associated effects of antibiotics vary extensively, with the most common being nausea, vomiting, and diarrhea. A true allergic reaction to an antibiotic can range from a skin rash or hives to angioedema and anaphylaxis. Penicillin is one of the most commonly prescribed antibiotics in the management of odontogenic infections, and allergy to this medication is reported to be approximately 10%.⁹ In the United States, just 0.002% of patients will experience a fatal anaphylaxis reaction to penicillin.¹⁰ Treatment of an antibiotic allergy includes discontinuing the medication, administration of antihistamines for skin reactions, and prompt management of anaphylaxis. Complete management of anaphylaxis will be discussed later. If a patient has an allergic reaction to a penicillin-class antibiotic, antibiotics from a different class such as the lincosamide antibiotic clindamycin or the macrolide antibiotic erythromycin should be considered. It is important to note that when selecting an alternative antibiotic, cross-reactivity of approximately 10% between the penicillin class and first-generation cephalosporins has been reported.¹¹⁻¹³

In addition to the aforementioned allergic reactions to medications, a variety of other oral manifestations are associated with medications and the use of various dental restorative materials, including amalgam. These allergic reactions fall under the category of stomatitis medicamentosa and include the following patterns of oral mucosal disease: anaphylactic stomatitis, intra-

oral fixed drug eruptions, lichenoid drug reactions, lupus erythematosus-like eruptions, pemphigus-like drug reactions, and nonspecific vesiculoerosive or aphthous-like lesions.¹⁴ The number of medications capable of causing these types of reactions is vast and includes drugs and dental materials from many classifications and categories. However, complete discussion of the mechanism of action of these reactions and inclusion of all the drugs and materials implicated in these reactions is beyond the scope and purpose of this article.

Angiodema

Angioedema can be divided into two broad categories: hereditary and nonhereditary. The hereditary form is not considered an allergic response—rather, it is caused by a biochemical defect with a deficiency in C1 esterase inhibitor that results in the formation of vasoactive mediators and peptides that cause recurrent attacks of edematous swelling. Treatment for the hereditary form is administration of danazol, a synthetic androgen hormone.¹⁴

The more common form of angioedema is the nonhereditary or allergic type. This typical antigen-antibody reaction can be caused by multiple triggers or allergens, including foods, dyes, pollen, and dust, as well as medications (especially nonsteroidal anti-inflammatory drugs [NSAIDs] and angiotensin-converting enzyme [ACE] inhibitors), inhalants, and rubber dam.¹⁴ Typical signs and symptoms of angioedema include burning, painful, and swollen areas of the body that can include the eyelids, lips, tongue, throat, palms, soles, and genitalia¹⁴ (see Fig 1). Patients may also complain of more generalized complaints such as vomiting, abdominal pain, and diarrhea. Treatment for the nonhereditary allergic form depends on the severity of the reaction and includes a combination of antihistamines, epinephrine, and corticosteroids.¹⁴

Uvular angiodema

Uvular angioedema, or Quincke disease, is a localized form of angioedema that manifests as an isolated swelling of the uvula. The condition is named after Heinrich Quincke, a renowned German clinician of the late 19th century, who first described angioneurotic

edema in 1882.¹⁵ Precipitating factors of uvular angioedema include allergic reactions to nuts, medications, herbal agents, cocaine, inhalants, and direct thermal injury.^{15–18} This reaction can be encountered during routine dental treatment as a result of contact with latex, medication administration, and thermal injury. Additionally, a patient may first present to the dental office for treatment of this isolated form of angioedema because of its localization to the oral cavity. In some cases, the rapid onset and progression of uvular swelling may put patients at significant risk for airway obstruction and respiratory distress.¹⁵ In the event of a severe reaction, prompt diagnosis and effective treatment must be provided to prevent this medical emergency from becoming life-threatening.

Patients typically report a wide range of symptoms that can include an itching sensation of the soft palate; fullness, swelling, tightness, and pain of the throat; shortness of breath; difficulty swallowing; foreign-body sensation in the mouth; extreme gagging, drooling, and vomiting; and voice alteration that ranges from a slight difference to an inability to speak.^{15–18} The swelling of the uvula can be quite significant, with a rapid increase in size to two to three times its original (see Fig 2). The fullness in the oropharynx may lead to a state of generalized panic and distress in the patient, which further contributes to the patient's symptoms of respiratory distress. To provide anatomic relief, it is useful to have patients lean their head forward. This prevents the uvula from dropping back in the throat, thereby alleviating patient stress until definitive treatment can be rendered.¹⁶

Additional treatment for Quincke disease depends on the severity of the reaction. The treatment can range from antihistamines alone or require a combination of epinephrine, antihistamines, and corticosteroids. In the event of a severe reaction in the office, the dental practitioner will need to put the patient into the anatomical positional steps outlined above to maximize the patient's airway and administer the appropriate medications to treat the allergic reaction until the patient can be transported to an emergency room for further evaluation and treatment.

Table 3 Summary of management of allergic reactions

Degree of reaction	Signs and symptoms	Treatment
Mild	Latex reactions	1% hydrocortisone topical ointment Diphenhydramine 25–50 mg po q4–6 h Methylprednisolone 4–24 mg po qd tapered over 6 d
Moderate	Latex reactions Medication reactions Angioedema	Diphenhydramine 25–50 mg IM/IV q4–6 h Hydrocortisone 25–50 mg IM/IV q6 h
Severe	Latex reactions Medication reactions Angioedema Anaphylaxis	Epinephrine 0.3–0.5 mL 1:1,000 SC/IM q15 min Epinephrine 0.5–1.0 mL 1:10,000 IV slowly; repeat as needed Albuterol 0.5 mL 0.5% in 2.5 cc NS via nebulizer q15 min or albuterol MDI 2 puffs q15 min Diphenhydramine 25–50 mg IM/IV q4–6 h Hydrocortisone 100–200 mg IM/IV q6 h

Po, per OS; IM, intramuscular; IV, intravenous; NS, normal saline; MDI, metered dose inhaler; SC, subcutaneous.

Life-threatening conditions in the dental office (anaphylaxis)

The most serious and life-threatening allergic reaction is anaphylactic shock, which can be caused by a number of allergens, some of which include latex, penicillin, as well as foods and insect bites. Food allergies are thought to account for 35% to 50% of all cases of anaphylaxis.¹⁹ Regardless of the allergen responsible for the anaphylactic reaction, the course of the reaction is very similar. The reaction has a rapid onset, with its multisystem effects seen almost simultaneously throughout the body. Signs and symptoms include wheezing, constriction of the airway, tightness in the chest, flushing of the skin, hives, angioedema, hypotension, abdominal pain, vomiting, diarrhea, fainting, and loss of consciousness.⁸ The most critical step in management of this life-threatening condition is the administration of epinephrine, which works in a wide range of pharmacologic effects. Epinephrine has alpha-1, beta-1, and beta-2 receptor agonist activity. Each of these receptor activities helps to counter the anaphylactic reaction. Alpha-1 agonism causes peripheral vasoconstriction to elevate blood pressure and reduce glottal edema. Beta-1 agonism produces a positive chronotropic and inotropic effect to increase the rate and force of heart contraction, thereby further normalizing cardiac output and blood pressure. The beta-2 agonism produces relaxation of the smooth muscles

of the terminal bronchi, causing reduction in bronchial restriction, decreased bronchospasm, and wheezing and improved pulmonary ventilation and air exchange. Further management and treatment of anaphylaxis includes administration of antihistamines, corticosteroids, IV fluids, oxygen, and vasopressors. Following stabilization, any patient who suffers an anaphylactic reaction should be taken to the emergency room for further evaluation, monitoring, and additional treatment. Proper documentation of the incident, including the precipitating agent and the steps taken to manage the patient's condition in the office, as well as transportation to the emergency room, is imperative for medical considerations.

TREATMENT

The treatment of allergic reactions in the dental office varies depending on the severity of the presenting signs and symptoms (Table 3). Once any member of the treating team makes the diagnosis of a medical emergency, all treatment must be terminated immediately, the office emergency protocol must be activated, and the dentist in charge of the office must implement the required treatment appropriate for the severity of the reaction. Similarly, if a severe allergic reaction or anaphylaxis is diagnosed,

the office emergency medical protocol must be activated, appropriate medical treatment initiated, and the front desk instructed to call emergency medical services.

Mild cutaneous allergic reactions may be managed with a wide range of options, starting with observation to make sure the reaction does not progress further. Observation only, with referral to a physician for follow-up, may be all that is necessary for a mild allergic reaction involving primarily cutaneous areas of the body. For immediate management in an office setting, application of 1% hydrocortisone topical cream to the affected area or oral administration of an antihistamine (diphenhydramine) 25 to 50 mg would be appropriate.^{8,20} Following these measures, a follow-up with a physician may be advised.

Mild to moderate allergic reactions with only a cutaneous component, but more widely disseminated throughout the body should be managed with diphenhydramine 25 to 50 mg per os (po).^{8,20} If the respiratory system is involved as determined by the presence of wheezing and mild shortness of breath, the patient should be initially managed with an antihistamine. In such a case diphenhydramine 50 mg should be administered intramuscularly (IM) or IV.^{8,20} In addition, a beta-2 agonist (metaproterenol) inhaler should be considered if wheezing and shortness of breath become pronounced.^{8,20} Following the administration of these medications, the patient should be observed in the office until the acute signs and symptoms of the allergic reaction have resolved. Once stabilized, the patient should be referred to a physician for further evaluation and management.

Severe allergic or anaphylactic reactions usually present with rapid onset multisystem signs and symptoms. These include wheezing, tightening of the chest, difficulty breathing and shortness of breath, widespread cutaneous rashes, glottal edema, and hypotension and require immediate airway management and treatment with epinephrine 0.3 to 0.5 mL IM in 1:1,000 concentration or 3.0 to 5.0 mL IV in 1:10,000 concentration.^{8,20} Vital signs should be continuously monitored, oxygen administered, and legs elevated for hypotension. Continued attention must be given to integrity of the airway.

It must also be remembered that epinephrine has a very short half-life and may need to be administered more than once during the resuscitation effort. Once epinephrine has been administered, the next drug administered should be diphenhydramine 50 mg IV or IM if IV access has not been established.^{8,20} The third drug to be administered for an anaphylactic reaction is a corticosteroid (hydrocortisone) 100 mg IV or IM.^{8,20} This agent has a slow onset and is therefore not the first line of defense for anaphylaxis. However, it is useful to decrease edema and capillary dilation. While all this is being performed, vital signs should be monitored continuously, oxygen delivered, proper position of the patient maintained, and if possible an IV access started until paramedics arrive to transport the patient to the nearest hospital emergency department for continued management.

SUMMARY

Patients entering the dental office are exposed to a wide variety of potential allergens that may trigger an immune response. This response may vary from a mild cutaneous reaction that may not indicate treatment to a severe life-threatening anaphylactic reaction requiring prompt diagnosis and proper medical intervention. Dental practitioners and their office team must be prepared to diagnose and treat these reactions utilizing the appropriate modalities that include pharmacologic intervention, airway management, and general medical management principles. A patient's life may depend on the appropriate levels of drugs, equipment, and expertise available and the preparedness of the office team to quickly and correctly use these modalities.

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