Allergic Reactions in Dental Patients

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Faculty Disclosure
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The director has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience
This course is designed for all dental professionals who may encounter allergic reactions in their practice.

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Course Objective

The purpose of this course is to provide dental professionals with the information necessary to recognize, treat, and prevent allergic reactions in their patients.

Learning Objectives

Upon completion of this course, you should be able to:

1. Outline the importance of a patient's medical and dental history as a means of evaluating the potential for the development of an allergic reaction during dental treatment.
2. Describe the pathophysiology of the various types of allergic reactions.
3. Review the antibiotics, analgesics, and local anesthetics used in dentistry that may cause allergic reactions.
4. Discuss the materials used in dentistry that may cause allergic reactions in susceptible individuals.
5. Evaluate the recommended treatment protocols and emergency medications used to treat allergic reactions.

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

An allergy to any given substance is an abnormal or hypersensitive response by the immune system. Approximately 15% to 25% of all Americans have an allergy to at least one substance [1]. Allergic responses can range from watery eyes and congestion to life-threatening anaphylaxis.

This course will highlight allergic reactions that patients may experience as a result of exposure to medications and materials used during and for dental treatment. The pathophysiologic mechanisms that occur during the varied allergic responses, local and systemic manifestations, and emergency medications and treatment will be discussed.

PATIENT ASSESSMENT

Before the initiation of any dental treatment, a thorough medical history should be taken. The medical history should not be viewed as a static document; it should be updated regularly and should guide discussions between patients and clinicians. The presence of systemic illness(es), current medications, adverse reactions to medication(s), and any allergic responses warrant further investigation. It is essential to understand that an adverse reaction to a medication is not always an allergic reaction.

Adverse drug effects can be categorized as either type A or type B [2]. The most frequent adverse drug reactions (type A) are known pharmacologic effects of a medication. For example, many medications provide warnings about nausea or drowsiness as a potential adverse effect. Although type A reactions are known possibilities, they can be very serious, even life-threatening. In some cases, type A reactions may be incorrectly identified as "allergies," particularly by patients.

Type B adverse drug reactions occur less frequently than their type A counterparts and include allergic reactions. An allergic response occurs when the immune system develops a response to a noninfectious substance (i.e., an antigen).

When a patient indicates he or she has had an allergic response to a medication or material, it is important to obtain all of the pertinent details. It may be necessary to contact previous providers to determine the substance that caused the allergic reaction, the extent of systemic involvement, and emergency treatment provided, if applicable. Dental clinicians should not proceed with any dental treatment if there is inadequate information about the patient's allergy history.

PATHOPHYSIOLOGY AND CATEGORIZATION OF ALLERGIC REACTIONS

In 1975, Gell and Coombs developed a classification system to categorize the unique physiologic pathways of various hypersensitivity (allergic) reactions [3]. While this classification system has evolved, allergic reactions remain classified as type I through type IV.

Allergic reactions are associated with the production of immunoglobulin E (IgE) by specialized B-lymphocytes called plasma cells. Immunoglobulins, also known as antibodies, are proteins secreted against any of a myriad of antigens. This reaction is beneficial when the antibodies are directed against pathogenic micro-organisms (e.g., bacteria, fungi, viruses); however, this response becomes detrimental when IgE production is triggered against a nonpathogenic substance. In some cases, the immune response is strong enough to lead to serious morbidity or anaphylactic shock.

Plasma cells are concentrated in the skin, tonsils, and mucosa of the respiratory and gastrointestinal systems [4]. When the immune system recognizes an antigen, IgE binds to mast cells and basophils, which are stimulated to release compounds such as histamines, proteases, and chemotactic factors. The production of other mediators of an allergic response (e.g., prostaglandins, leukotrienes) is also enhanced. The systemic release of these substances leads to an increase in capillary permeability, vasodilation, spasms of the smooth muscles, and excessive secretion of mucus [5]. The degree to which these events occur varies considerably among patients. Extensive capillary permeability can lead to accumulation of interstitial fluids and swelling of the affected tissues. When this occurs in the laryngeal and tracheal areas, airway compromise can lead to asphyxiation. Spasms of the bronchiolar smooth muscles and excessive secretion of mucus can further exacerbate this problem.

TYPE I REACTIONS

Type I allergic reactions are immediate, with an onset of only a few minutes to a few hours. The most serious type I hypersensitivity reaction is anaphylaxis, the most serious degree of an allergic response. It is characterized by a set of symptoms that involves various organs and systems and occurs independently, simultaneously, or subsequently [6]. Initial symptoms often include widespread hives and progress rapidly to bronchospasm, respiratory arrest, and ultimately, cardiac arrest. Whether the anaphylactic reaction is of immune or nonimmune origin, the stimulation of mast cells and circulating basophils releases chemical mediators that begin the anaphylactic process. A rapidly escalating systemic reaction can occur only minutes after exposure to a specific antigen or onset may be delayed several hours [7]. In 1% to 20% of anaphylaxis cases, there will be a biphasic response, with recurrence of symptoms 8 to 12 hours later, after the individual had seemed to recover [8]. The interval between the initial reaction and the recurrence has ranged from 1 to 72 hours [9; 10].

Another type I hypersensitivity reaction is atopy. Atopy is a genetic predisposition to develop allergic rhinitis, asthma, and dermatitis [11]. Urticaria (hives) are the most common lesion associated with atopic reactions, although these lesions are not unique to atopy. An outbreak of urticaria can occur anywhere on the skin, and the classic presentation is a wheal—a raised area surrounded by an erythematous base. The cause of urticaria during an allergic reaction is the release of histamine from cutaneous mast cells coupled with other progenitors of inflammation. These substances cause the extravasation of fluids from surface capillaries, with subsequent swelling and redness. Urticarial lesions are intensely pruritic and blanch upon the application of direct pressure. Resolution of urticaria may take several weeks, during which the patient may experience moderate itchiness and discomfort.

TYPE II REACTIONS

Type II hypersensitivity reactions are mediated by IgG or IgM and are predominantly directed against erythrocytes, leukocytes, platelets, and their progenitor cells in the bone marrow. Hypersensitivity reactions in this category are cytotoxic reactions, the classic example of which is hemolytic transfusion reactions that occur when the transfused blood type is incompatible with the patient's blood type [12]. Although this is not a reaction that would occur in the dental office, it is important that normal laboratory values for the formed elements of human blood return to the normal range before any invasive dental procedure is performed.

TYPE III REACTIONS

Type III hypersensitivity reactions are immune complex mediated [13]. The unique feature of these reactions is the formation of antigen-antibody complexes in the blood vessels or tissues. Examples of disorders associated with type III hypersensitivity reactions include systemic lupus erythematosus, rheumatoid arthritis, serum sickness, and glomerulonephritis.

These diseases are chronic in nature, and patients may be taking immunosuppressive medications that can predispose them to the development of opportunistic infections. In addition, patients with these disorders may develop complications of xerostomia (dry mouth) and keratoconjunctivitis sicca (dry eyes).

TYPE IV REACTIONS

Type IV hypersensitivity reactions do not involve the immunoglobulins. Unlike type I hypersensitivity reactions, the clinical manifestations of type IV reactions are delayed for 48 to 72 hours following exposure to a given antigen [14]. These reactions are the result of the antigenic response of T-lymphocytes, monocytes, and macrophages. Contact dermatitis is a classic example of a type IV hypersensitivity reaction.

Contact Dermatitis

The most common triggers of contact dermatitis are rubber products, metals, and medications that are applied directly to mucosal or cutaneous tissues. There are two main forms: irritant contact dermatitis and allergic contact dermatitis.

Irritant contact dermatitis represents approximately 80% of the cases of contact dermatitis. It is characterized by a generalized inflammatory reaction to substances that come in direct contact with the skin [15]. Among dental professionals, irritant contact dermatitis may occur as a reaction to the chemicals in latex gloves, as will be discussed in detail later in this course [16]. Irritant contact dermatitis is limited to the area affected by the specific substance (e.g., the hands after wearing latex gloves) [17]. Treatment of irritant contact dermatitis involves identification and avoidance of the triggering substance. Oral antihistamines and topical corticosteroids may promote healing and alleviate symptoms.

Allergic contact dermatitis and irritant contact dermatitis have similar clinical presentations, but their pathogenesis differs considerably. The first phase of allergic contact dermatitis is hapten binding. Haptens are low-molecular-weight molecules capable of reacting with protein and peptide molecules recognized as antigens [18]. Hapten-specific T-cells develop in some individuals and produce a hypersensitivity response that results in cutaneous inflammation [19]. It is this specific T-cell mediated response that causes the tissue damage associated with allergic contact dermatitis.

The development of allergic contact dermatitis occurs over a period of time. There is a sensitizing (afferent) phase lasting weeks to months, during which repeated exposure to a particular substance stimulates the development and maturation of the hapten-specific T-cells. This is followed by the efferent or elicitation phase, during which the clinical manifestation of allergic contact dermatitis will recur with continued exposure to the same substance [20].

Identification of the substance causing allergic contact dermatitis requires patch testing. This involves the application of potential allergens to the patient's skin, usually on the back. The testing sites are evaluated after two days, and a positive reaction, characterized by swelling, redness, and blistering, identifies the offending substance(s).

Healing of allergic contact dermatitis can take several weeks. Severe cases may require the short-term use of oral corticosteroids (e.g., prednisone) to reduce the inflammation and the associated symptoms.

ALLERGIES TO MEDICATIONS USED IN DENTISTRY

Analgesics, antibiotics, and local anesthetics are the medications most commonly used in dental treatment, and allergic reactions, though infrequent, can occur with any of these.

LOCAL ANESTHETICS

Many dental procedures require the use of local anesthetics. Although these medications are generally very safe, allergic reactions can occur to any component of the formulations.

Local and topical anesthetics are chemically classified as either amides or esters. The most frequently used injectable local anesthetics today, including lidocaine, mepivacaine, and bupivacaine, are all amides. Articaine is also classified as an amide but has the unique feature of the inclusion of an ester group. Allergies to amide local anesthetics have been very rare; most allergic reactions occur in response to ester types. Ester-type local anesthetics are metabolized to para-aminobenzoic acid, which has allergenic properties [21]. While the ester anesthetic procaine is no longer used in North America, benzocaine is a widely used ester topical anesthetic applied to the oral mucosa prior to the injection of a local anesthetic. An allergic reaction to benzocaine is usually limited to the site of its application and can manifest as an area of erythema or ulceration.

It is important to remember that most adverse reactions to local anesthetics are not allergic reactions. More commonly, inadvertent intravascular injection of a local anesthetic can occur and is toxic to cerebral tissues. This can cause dizziness, slurred speech, seizures, and nausea. When a patient indicates he or she has had an allergic reaction to a local anesthetic, one should have a thorough discussion to determine if it was an adverse, but non-allergic, reaction or if an actual immediate (type I) or delayed-response (type IV) allergic reaction developed. A release of information should be obtained if input from a prior clinician is required to determine the nature of the reaction. If a patient reports a history of adverse or allergic reactions to a local anesthetic, dental treatment should be delayed until the origin of the problem has been identified and addressed. If necessary, consultation with a specialist in allergy and immunology should be sought.

Additives

Epinephrine is often added to local anesthetics to enhance the clinical dynamics. An allergy strictly to epinephrine does not exist. However, some patients may consider adverse transient reactions to be evidence of an "allergy" to epinephrine. If a patient's medical history lists an allergy to epinephrine, the clinician should discuss the nature and magnitude of the reaction with the patient.

The oxidation of epinephrine in local anesthetic solutions diminishes the potency and utility of this vasoconstrictor and will ultimately render it useless. So, preservatives such as sodium metabisulfite or potassium metabisulfite are added to prolong the lifespan of epinephrine by suppressing the oxidation process. Patients with allergies to sulfites may exhibit an allergic reaction to these sulfite-based preservatives. Among the general population, patients with asthma are at a greater risk for hypersensitivity to bisulfites, with the potential for a true allergic reaction if a local anesthetic with a vasoconstrictor is used [22]. Most patients are unaware that bisulfites are used as preservatives in local anesthetics and may not disclose a sulfite allergy in their medical history. As such, clinicians should inquire about allergies beyond obvious medications and materials used in dentistry, including sulfites, latex, and metals.

Local anesthetics such as mepivacaine and prilocaine are available in formulations that do not contain epinephrine, and these should be used for patients with sulfite allergy (provided no other allergy or contraindication exists). Without the vasoconstrictive qualities of epinephrine, the duration of anesthesia will be decreased, so clinicians should develop treatment plans that accommodate a shorter working time. The ability to obtain hemostasis during and after procedures such as oral surgery, periodontal surgery, and root planing and curettage will be more challenging in this shorter period. Clinicians should have adjunctive materials that promote hemostasis (e.g., oxidized cellulose) available. Longer procedures, such as full-mouth extractions or multiple quadrants of periodontal surgery or root planing and curettage, may need to be apportioned into smaller segments.

ANTIBIOTICS

The oral microflora consists of hundreds of microbial species, only a few of which cause dental caries and periodontal disease. Antibiotics used in dental treatment are generally chosen in order to treat and/or prevent odontogenic or systemic infection.

Beta-Lactam Antibiotics

Beta-lactam antibiotics are the most frequently used group in dentistry, as they display bactericidal activity against many of the pathogenic bacteria that cause odontogenic infections. The most commonly prescribed in dental practice include penicillin, amoxicillin, and ampicillin. However, generations of bacterial mutations have enabled bacteria to produce the enzyme beta-lactamase, which destroys the structural integrity of these antibiotics and renders them ineffective against some odontogenic infections.

Approximately 10% of the U.S. population has a reported allergy to penicillin, but only about 1% of the population has a true IgE-mediated allergic reaction [23; 51]. While most allergic reactions to penicillin and its derivatives result in skin rashes or urticarial lesions, medications in this group are among the most frequent causes of medication-induced anaphylaxis [24]. Type I reactions can progress to anaphylaxis in 0.04% to 0.2% of cases, with a 10% fatality rate [1]. Fortunately, most allergic reactions to penicillin are less severe but can still cause varying degrees of discomfort or morbidity.

Cross-reactivity among the beta-lactam antibiotics and the structurally similar cephalosporins (e.g., cephalexin) is a valid concern. The chemical structure of amoxicillin is very similar to penicillin, and patients who have IgE-mediated type I hypersensitivity reactions to penicillin have a markedly increased risk of a reaction to amoxicillin as well as cephalosporins and sulfonamides. There is a 20% chance of a reaction to cephalexin when a patient has had an allergic reaction to penicillin [25].

Clindamycin

The two antibiotics most likely to be prescribed when beta-lactams cannot be used are clindamycin and azithromycin. Clindamycin is derived from lincomycin, and its chemical structure varies from that of the beta-lactam antibiotics. At lower doses, it is a bacteriostatic medication that inhibits bacterial protein synthesis; at higher doses, it is bactericidal. It has excellent absorption from the stomach and is capable of penetrating infected tissues and bone. It has a minimum of adverse drug interactions, and type I and type IV hypersensitivity reactions are rare but possible [26]. There is no cross-reactivity between clindamycin and any other class of antibiotics [25].

The use of a broad-spectrum antibiotic such as clindamycin can be bactericidal to several bacterial species in the gastrointestinal tract and promote the overgrowth of *Clostridioides difficile*. *C. difficile* can then release toxins that cause *C. difficile*-associated diarrhea and pseudomembranous colitis. These adverse clinical manifestations, characterized by persistent abdominal cramps, watery or bloody diarrhea, and fever, may be misconstrued by patients as an allergy, but true allergy is very rare.

Azithromycin

Azithromycin is one of the few macrolide antibiotics used in dentistry. The base and ethylsuccinate forms of erythromycin, another macrolide, were the long-standing antibiotics of choice for acute odontogenic infections and for bacterial endocarditis prophylaxis. However, frequent issues with gastric intolerance and increased bacterial resistance have relegated them to infrequent use in dentistry. Azithromycin was approved for use in 1996, and unlike erythromycin, it is still in regular use for prophylaxis and dental treatment, typically for patients who cannot tolerate beta-lactam antibiotics or clindamycin. Hypersensitivity reactions to macrolide antibiotics are uncommon, occurring in 0.4% to 3% of patients [27]. There is cross-sensitivity among the macrolide antibiotics, so a patient who has had a hypersensitivity reaction to erythromycin or clarithromycin should not take azithromycin [25].

Tetracyclines

In dentistry, the primary use of tetracycline antibiotics is as a supplement to the definitive treatment of periodontal disease. In addition to oral formulations, this group of antibiotics is available as gels or microspheres that can be placed directly into the depth of a periodontal pocket.

The two tetracycline products most commonly used in the treatment of periodontitis are doxycycline periodontal gel (Atridox) and minocycline hydrochloride periodontal microspheres (Arestin) [28; 29].

Although these products are applied directly into the periodontal pocket, as opposed to being administered orally, a history of hypersensitivity to any tetracycline precludes the use of these agents, as there is cross-reactivity among all members of the class. Hypersensitivity reactions can occur even though these locally delivered tetracycline medications are not significantly absorbed into systemic circulation [30]. Localized tissue irritation can occur during the placement of these medications, but this does not constitute an allergic reaction.

ANALGESICS

Analgesic medications are used to relieve the pain associated with acute dental problems, oral and maxillofacial trauma, and tissue manipulation during dental procedures. These formulations are available over the counter or by a prescription. Although most analgesics used in dentistry have a short duration of action, a hypersensitivity reaction can occur, even with the initial dose.

Nonsteroidal Anti-Inflammatory Drugs

Ibuprofen and naproxen are the most common nonsteroidal anti-inflammatory drugs (NSAIDs) used in dentistry. Because they are available over the counter, patients may underestimate the potential for adverse effects with these drugs. Irritation and ulceration of the gastrointestinal tract is a known adverse effect with prolonged use, as is renal impairment.

In dentistry, the frequency of hypersensitivity reactions among NSAIDs is second only to those caused by beta-lactam antibiotics [31]. IgE-mediated reactions are rare, but when they do occur, they tend to develop soon after ingestion of either ibuprofen or naproxen and can feature urticaria, angioedema, respiratory distress, and anaphylaxis. Type IV (delayed) hypersensitivity reactions may also occur; manifestations can include cutaneous reactions such as maculopapular lesions, erythema multiforme, and Stevens-Johnson syndrome, any of which can take 24 to 72 hours to develop. Cross-reactivity among all NSAIDs is possible but infrequent, as the molecular structures of this group of medications can vary considerably [32]. However, if a patient indicates he or she has had an allergic reaction to ibuprofen, naproxen, or any other NSAID, it would be prudent to consult with the patient's physician before prescribing or administering any medication in this group. A hypersensitivity reaction to ibuprofen contraindicates its use when combined with other medications, such as hydrocodone. Patients who have had allergic reactions to ibuprofen or naproxen should also be advised to exercise caution when selecting over-the-counter analgesics.

Acetaminophen

Acetaminophen obtained initial approval in 1951 and is a widely available over-the-counter medication that is sold under many different brand names. It is also combined with opioid medications (e.g., codeine, hydrocodone, oxycodone) in prescribed medications. While a hypersensitivity reaction to acetaminophen is not dose-dependent, hepatic toxicity is a potentially serious adverse effect of excessive use of this medication.

Type I and type IV hypersensitivity reactions to acetaminophen are rare but can occur in reaction to any formulation of the medication [22]. Patients who have a history of hypersensitivity to acetaminophen should be advised to refrain from the use of any of the more than 600 formulations of this medication [33].

Opioids

Opioids are used in dentistry to alleviate moderate-to-severe postprocedural pain associated with oral surgery, periodontal surgery, and oral and maxillofacial trauma. These medications are used for the shortest possible duration due to the potential for tolerance and dependence. The opioids codeine, hydrocodone, and oxycodone are usually combined with a non-opioid component, such as acetaminophen or, less frequently, ibuprofen, for use in dental treatment.

Type I and type IV hypersensitivity reactions to opioid medications are very rare [34]. More commonly, adverse effects of opioids (e.g., nausea, constipation, sedation, pruritus) may be erroneously considered allergic reactions. The chemical structures of codeine, hydrocodone, and oxycodone are similar, and cross-reactivity is possible [35]. If a patient has a history of an allergic reaction to a combination medication, it is important to determine if the reaction was to the opioid, the non-opioid component, or both. If the source of the reaction cannot be determined, an alternative medication unrelated to any component of the combination medication should be prescribed.

ALLERGIC REACTIONS TO MATERIALS USED IN DENTISTRY

Various materials used in restorative and prosthetic dentistry can cause localized reactions of the oral tissues, as can ingredients in commercial oral hygiene products, such as toothpaste and mouth rinses. Some materials, such as latex gloves, can cause a hypersensitivity reaction in clinicians and/or patients.

NATURAL RUBBER LATEX

All healthcare professionals use Standard Precautions to prevent the transmission of communicable diseases, including bloodborne pathogens. This includes the use of personal protective equipment (e.g., masks, gowns, eye protection, gloves) during clinical procedures.

Natural rubber latex gloves have been used extensively due to their high level of comfort and ability to maintain good dexterity and tactile sensation. Natural rubber latex is derived from the milky sap harvested from rubber trees. Accelerators and other chemicals are used to manufacture latex products, and a hypersensitivity reaction may be in response to any of these components. With approximately 4.5% of the general population and 10% of healthcare workers developing varying degrees of sensitization to latex, alternative materials such as latex-free nitrile gloves are beginning to be used more frequently [36]. However, many clinicians still prefer the use of latex gloves.

Another possible source of natural rubber latex exposure is with rubber dams used in restorative dentistry and endodontics to provide isolation and to prevent salivary contamination of the tooth being treated. While rubber dams without latex are available, latex dams continue to be used.

Contact with natural rubber latex products can produce hypersensitivity reactions, including irritant contact dermatitis, allergic contact dermatitis, and type I (IgE-mediated) hypersensitivity. As discussed, irritant contact dermatitis is a non-allergenic reaction to latex and/or the chemicals incorporated into natural rubber latex products during the manufacturing process. It is the most common reaction to latex products, and it is characterized by an erythematous, cracked, and dry area confined to the immediate area in contact with the product. When this condition is caused by the use of latex gloves, it can be exacerbated by hand perspiration and frequent handwashing.

There are no systemic manifestations of irritant contact dermatitis, but the associated irritation and discomfort can preclude one's ability to practice dentistry until the area is healed. Because irritant contact dermatitis can disrupt the continuity of the skin, it may permit access of natural rubber latex molecules to deeper tissue layers and promote a progressive sensitization [37].

The clinical manifestations of latex-associated allergic contact dermatitis are more severe than those of irritant contact dermatitis, as the cutaneous areas involved can develop blisters that ooze and form a fragile crust that is easily disrupted. Pruritus is a common symptom of allergic contact dermatitis, but scratching will prolong the healing time. Discharge from open lesions can compromise the integrity of natural latex products and make wearing any gloves uncomfortable; clinicians should refrain from practice until the lesions are completely healed. Disruption of the epidermal surface that occurs during allergic contact dermatitis can also increase the risk of bacterial infection and sensitization to natural rubber latex components.

Clinicians who wear latex gloves and who develop symptoms of dermatitis should contact an allergist or dermatologist for skin patch testing to obtain a definitive diagnosis. (Interestingly, more than 50% of persons with latex allergy will also develop an allergy to certain fruit, most commonly avocado, banana, chestnut, and kiwi [38].) Initial treatment may include over-the-counter cortisone ointments, but severe cases of allergic contact dermatitis require the combined use of prescription topical cortisone preparations, antihistamines, and oral corticosteroids (e.g., prednisone). If staff or patients have a confirmed hypersensitivity to any component of natural rubber latex, these products should be avoided entirely in the office.

As with any allergic reaction, an IgE-mediated response to natural rubber latex is associated with the highest degree of morbidity [39]. A type I hypersensitivity reaction to latex can vary from a localized reaction (e.g., urticarial lesions at the site of contact) to a more generalized reaction with distal lesions, rhinitis, and conjunctivitis. The most severe reaction, anaphylaxis, is a possible but rare occurrence.

While direct contact to the skin or mucosa is the most common trigger of a reaction to latex, inhalation exposures are also possible. Natural rubber latex gloves often include powder on the interior to facilitate placement on the hands. This powder contains latex proteins, which can trigger an allergic response when inhaled by susceptible individuals. It is possible for these airborne particles to circulate and affect a sensitive patient or staff member in a completely different operatory.

A type I hypersensitivity reaction to natural rubber latex can occur without any prior hypersensitivity reaction, but there are certain indicators in a patient's medical history that should raise a "red flag" for a potential allergy. Patients with a history of irritant or allergic contact dermatitis can develop a progressive sensitization to natural rubber latex components. Subsequent exposure to any latex product can precipitate a hypersensitivity reaction in these individuals. Patients who have undergone multiple surgeries for any reason, particularly beginning in childhood, have likely been repeatedly exposed to natural rubber latex and can develop a progressive sensitization. Also, as discussed, persons with an allergy to certain fruits (e.g., banana, avocado) are at an increased risk for latex hypersensitivity. The basis of this cross-reactivity is the structural similarity between the protein-composed enzymes that the rubber tree uses to defend itself against microbial colonization, particularly fungal organisms, and the protein-based enzymes that perform the similar antimicrobial function in these fruit trees/vines [40].

Some dental offices have minimized or stopped the use of any product that contains latex in order to protect patients and staff members. Clinicians who use gloves, rubber dams, or any other product that contains latex should be vigilant about the potential for allergic reactions and should be ready to provide emergency medical treatment, if necessary.

MATERIALS USED IN RESTORATIVE AND PROSTHODONTIC DENTISTRY

Many materials are used to restore carious teeth and replace lost teeth. Most of these materials are biocompatible with the teeth, gingiva, oral mucosa, and bone, so hypersensitivity reactions are uncommon and usually manifest as a localized reaction in the contiguous tissue. Rarely, a type I hypersensitivity reaction will develop secondary to contact with a restorative or prosthodontic dental material.

Dental Amalgam

Dental amalgam is an alloy composed of mercury, silver, copper, and other trace metals that has been used to restore carious lesions for more than 150 years [41]. The primary controversy associated with dental amalgam has been the release of mercury vapor during mastication, removal of old amalgams, and placement of new amalgams. The U.S. Food and Drug Administration has reviewed extensive scientific research and considers dental amalgam safe for use in adults and children 6 years of age and older, as the mercury exposure from dental amalgam is considerably less than the levels associated with adverse health effects [42].

In the oral soft tissue, the most common hypersensitivity reaction to dental amalgam is a type IV response known as oral lichenoid lesions. These erythematous lesions develop on the oral mucosa in direct contact with an offending material (e.g., dental amalgam, epoxy resins, composite restorations, orthodontic appliances) [43]. It is a T-cell mediated response that develops over time as mercury salts or other ions penetrate through the epithelial lining and incorporate into the surface proteins of the basal keratinocytes [44].

The buccal mucosa and the mucosa of the lateral surface of the tongue are the most frequently involved areas. Partial or complete resolution of oral lichenoid lesions occurs upon removal and replacement of the amalgam (or other triggering substance). Given the extensive number of dental amalgam restorations in the general population, the prevalence of oral lichenoid lesions is extremely low. Therefore, clinicians should not assume that all lesions that develop proximate to an amalgam are hypersensitivity reactions; histopathologic and immunohistologic assays are required for a definitive diagnosis.

Oral lichenoid lesions should not be confused with the autoimmune disorder oral lichen planus. The lesions of oral lichen planus feature delicate white lines that are slightly elevated above the mucosal surface (i.e., Wickham striae). These lesions occur bilaterally, with a predilection for the buccal mucosa, and their formation is not in response to contact with any dental material.

Nickel

Nickel is a metal with multiple uses in dentistry, as a soft metal (e.g., gold) can be made harder when combined with nickel. The combination of nickel and titanium allows for strength and flexibility, and this alloy is used in endodontic files, non-precious metal crowns and bridges, and cast-metal partial denture frameworks.

Despite its widespread use, the American Contact Dermatitis Society named nickel the contact allergen of the year in 2008, and it is a common cause of allergic contact dermatitis [45]. Nickel allergy is much more common in women (10%) than men (1% to 2%), likely due to sensitization from nickel-containing jewelry [46]. It is extremely rare for a nickel-containing crown or cast-metal partial denture framework to cause an immediate type I hypersensitivity reaction; the usual manifestation is a delayed type IV reaction (specifically, allergic contact dermatitis).

The clinical presentation of a nickel allergy can vary depending on the severity and location of the exposure. When a non-precious metal crown extends to or below the gingival level, the adjacent tissue may appear erythematous and may bleed easily during brushing or flossing in hypersensitive patients. The erythema and inflammation cannot be resolved by meticulous hygiene or in-office scaling or root planing. Some patients may experience an itching or burning sensation at the site of the lesion. Patients who wear cast-metal partial denture frameworks may experience an erythematous reaction anywhere the partial denture overlies the oral mucosa. If testing by an allergist or a dermatologist reveals that the patient has a hypersensitivity to nickel or any other metal, the crown, bridge, or partial denture should be replaced with a more compatible prosthesis.

Titanium

One of the more recently identified metals to cause a hypersensitivity reaction is titanium. The use of titanium in prosthetic dentistry has increased dramatically, with most dental implants today composed of this material. Although generally safe, titanium is capable of causing type I or type IV reactions in susceptible patients, particularly patients with a hypersensitivity to other metals [47].

If a patient is at risk for or is suspected of having a hypersensitivity to titanium, he or she should be tested by an allergist prior to the surgical placement of the implant. When removal of an implant is necessary due to a patient's incompatibility with titanium, it negates the initial surgical placement, requires additional surgery to remove the implant, and may require a bone graft to replace the bone removed to place the original implant.

TREATMENT OF HYPERSENSITIVITY REACTIONS IN DENTAL PATIENTS

In a type I reaction, the release of histamine and bradykinins causes vasodilation and edema, while the release of prostaglandin D2 and leukotrienes results in bronchoconstriction [48]. These biochemical events can cause a transfer of as much as 50% of intravascular fluids to extracellular spaces [49]. A steep decline in blood pressure and cardiovascular collapse can ensue—anaphylaxis. Immediate emergency treatment and contact of emergency medical services is mandatory to save the patient's life.

While the patient is conscious, any dental materials in the patient's mouth must be removed to prevent their aspiration and further complication of efforts to treat the patient. The patient should be placed in a supine position with the legs slightly elevated to facilitate blood flow to the brain. The basics of airway, breathing, and circulation should be constantly monitored.

EVIDENCE-BASED PRACTICE RECOMMENDATION

To ensure adequate venous return, the European Academy of Allergy and Clinical Immunology recommends that patients experiencing anaphylaxis should lie flat with their legs raised. Where respiratory distress is the predominant presentation, patients may prefer to sit up with elevated legs. If pregnant, they can be placed on their left side with the bed in a head-down position. Where unconscious, patients can be placed in the recovery position. Avoid any abrupt change to a more upright posture.

(https://onlinelibrary.wiley.com/doi/full/10.1111/all.15032. Last accessed January 26, 2023.)

Strength of Recommendation: Expert Opinion/ Consensus Statement

Epinephrine remains the medication of choice to treat anaphylactic shock. Commercially prepared pre-loaded syringes of 0.3 mg of 1:1,000 epinephrine (usually referred to by their brand name, EpiPen) can be injected into the deltoid or vastus lateralis muscles or in the sublingual region. The highly vascular sublingual region can promote rapid absorption of the drug. Subcutaneous administration does not provide as much bioavailability of epinephrine as the intramuscular or sublingual routes [50].

Once absorbed, epinephrine targets the alpha and beta receptors of the cardiovascular system, inducing vasoconstriction and increasing the systolic blood pressure. Epinephrine also acts as a bronchodilator and can relieve the respiratory distress associated with anaphylaxis. The dose of 0.3 mg epinephrine can be administered every 5 to 15 minutes until hypotension and respiratory distress are stabilized. An intramuscular injection of a histamine blocker such as diphenhydramine can also help by reducing the effects of the histamine release from the mast cells [50].

Positive pressure oxygen delivered through a mask can provide supplemental oxygen. Some patients will exhibit severe pharyngeal and laryngeal swelling and require intubation for the proper exchange of oxygen. All patients with anaphylaxis should be transferred to a hospital for further treatment and observation, as some patients have a biphasic response and begin to display symptoms of anaphylaxis even after seemingly effective treatment. After recovery from the anaphylaxis reaction, the patient should consult with his or her physician or allergist to identify which substance(s) caused the event and to prevent recurrence.

In less severe cases of allergic responses, the usual treatment is removal or discontinuation of the triggering substance and avoidance of the material in the future. Clear documentation of any allergic responses is the best first step to prevent future occurrences.

CONCLUSION

This course has provided a brief overview of the complex issue of allergic reactions in dental patients and dental staff. Some of these reactions are minimally problematic, while others can lead to anaphylaxis and even death in a matter of minutes. Despite meticulous attention to a patient's medical history, allergic reactions can occur, even to medications or materials that a patient has previously tolerated.

Although it is rare for an anaphylactic response to occur in the dental office, appropriate training and preparedness should be a priority. In addition, clinicians should take steps to prescribe and use medications in a responsible fashion and to educate patients about the appropriate use and the potential adverse effects of over-the-counter medications. A dental staff with proper training, knowledge, and equipment can save a life.

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