Hypersensitivity Reactions and Dental Considerations- an Overview

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Abstract

Patients seeking dental treatment may have known or unknown underlying allergies. The manifestation of these immunological reactions may range from mild rashes to life threatening conditions such as laryngeal edema. A good understanding of the various drugs and dental materials which can cause these allergies are necessary to taking adequate precautions to prevent any untoward incidences. Apart from patients, allergic reactions to certain dental materials and substances can be also be seen in the dental health care providers.

Clinical relevance: This article describes the various hypersensitivity reactions and highlight the dental considerations in managing these hypersensitivity reactions that can been seen during dental practice.

Review (J Int Dent Med Res 2021; 14(1): 360-366)

Keywords: Anaphylaxis, Atopy, Contact Dermatitis, Dental Allergens, Latex Allergy.

Received date: 03 December 2020 **Accept date:** 03 January 2021

Introduction

Allergy is the response of the immune system to a foreign body referred to as an antigen. Hypersensitivity reaction is a type of harmful allergic immune response that causes injury to tissues with deleterious effects[1]. This immune reaction could be from an exogenous source like pollens resulting in hay fever or a pathogen or it could be endogenous. Based on etiology and timeline, in 1963, Gell and Coombs classified immune responses into four groups[2]. These include, type I (IgE mediated immediate) hypersensitivity, type II (antibody dependent cytotoxicity) hypersensitivity, type III (immune complex mediated) hypersensitivity and type IV (cell mediated delayed) hypersensitivity[3]. Even though these reactions are independent of each other, generally more than one hypersensitivity response can occur at a time.

In the field of dental practice, patients having known, or unknown underlying allergies may seek dental treatment. Certain materials used in dentistry can cause either immediate or late hypersensitivity reaction. Therefore, it is important for a dental clinician to have a thorough understanding of the various hypersensitivity reactions for prevention and management of untoward incidences in practice. This article aims to describe the various hypersensitivity reactions and highlight the dental considerations in managing patients with hypersensitivity reactions.

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Type I hypersensitivity reaction and its dental implications:

This type of hypersensitivity is seen in atopic hypersensitivity and anaphylaxis reactions. This represents the immediate allergic reactions, mediated chiefly by immunoglobulin E (IgE) [Fig 1a.]. For an individual to be prone to this type of reaction they must be sensitized to an antigen by an earlier exposure[1]. The reaction progresses rapidly within seconds to minutes after encountering the antigen. Common causative agents include antigens in food, dust, drugs or anesthetics resulting in diverse manifestations. The manifestations may range from mild symptoms like painless inflammation, urticaria, eczema, diarrhea with mild burning or itching sensation to serious angioedema and laryngeal edema leading to life threatening breathlessness[4].

Atopy: This term can be used to describe a familial or individual tendency to develop allergen specific IgE on exposure to environmental allergens like dust mite, and to suffer typical allergic symptoms such as asthma, rhino conjunctivitis or eczema/dermatitis[5]. This condition has greater prevalence in children with multifactorial etiology. It may have acute, subacute or chronic presentation with recurrent exacerbations. Allergic asthma can be triggered by fumes, monomer vapors, atopic dermatitis due to latex, acrylic, oral hygiene products, etc. that can be categorized under Type I and Type IV, but more towards Type I hypersensitivity reaction. Vaporized products that exasperate the respiratory tract include acrylic dusts, filling composites and disinfectant agents[6].

Diagnosis includes complete history and clinical examination. Elevated serum IgE levels can also indicate Type 1 hypersensitivity reaction. Skin prick test can be performed with adequate precaution to confirm sensitization to a specific allergen[7]. [Fig. 2] Treatment includes avoiding the allergen. Other treatment modalities include natural remedies like dry teas or essential oils. This could either cure certain individuals or can also decrease the severity of the condition. Allergic medications (antihistamines, corticosteroids, decongestants) and immunotherapy can also be considered.

Figure 2. Preparation for skin prick test on the arm using lancet.

Anaphylaxis/anaphylactoid reaction:

These terms are used depending on whether the reaction is Ig E mediated or not. If Ig E mediated, it is termed as anaphylaxis and termed anaphylactoid, if non-Ig E mediated [8]. Anaphylaxis is an acute life-threatening hypersensitivity reaction caused due to release of mediators from basophils, mast cells and inflammatory cells. Prevalence of anaphylaxis in dental setting is very low with a prevalence range of 0.004 to 0.015 cases/dentist/annum. In dentistry this reaction could be triggered due to local anesthesia, antibiotics, latex and topical povidone-iodine or chlorhexidine[9].

Hypersensitivity reaction to latex gloves increases with prolonged use among healthcare workers which has even led them to change their careers. Clinically it manifests either as delayed cell mediated contact dermatitis or immediate Type I reaction. Delayed cell mediated contact dermatitis reaction will be described at the end of this manuscript. Though immediate Type I reaction (referred to as true latex allergy) is rare, it is a more serious condition within minutes to hours of exposure which could prove fatal[10].

Drugs	Route of administration	Dosage
Adrenaline (epinephrine)	Intramuscularly	Adult Dose: 0.5 mg IM Above 12 years: 500 µg IM (0.5 mL), 6-12 years 300 µg IM (0.3 mL) Below 6 years: 150 µg IM (0.15 mL)
Antihistamines (Chlorphenamine)	Intramuscularly/ Intravenously	Above 12 years: 5 mg 6-12 years: 2.5 mg 6 months- 6 years: 250µg/kg Below 6 months: Diphenhydramine 50 mg or 1 mg/kg IV if necessary
Beta-agonists: patients on beta–blockers (as adrenaline will be less effective, give epinephrine) If the patient still fails to respond with further deterioration of the respiratory system, bronchodilators like salbutamol to be given Patients on beta –blockers and not responding to treatment	Inhalation /Intravenous Intravenous	Isoproterenol 1mg in 500 ml Atropine or Glucagon
Corticosteroids: After initial resuscitation steroids can be given and the dosage can be adjusted according to the patients age Alpha agonists like dopamine can be given if hypotension still exists	Intramuscularly/ Intravenously	Above 12 years: 200 mg 6-12 years: 100 mg 6 months to 6 years: 50 mg Below 6 months: 25 mg 5 µg/kg/min. Increased to 10-20 µg/kg/min

Table 1. List of emergency drugs for anaphylactic reaction.

The clinical manifestations appear within few minutes or hours after getting exposed to the agent. The signs and symptoms could manifest as slight increase in temperature, itching sensation and patient might start panicking followed by urticarial or red colored rashes, edema of face and neck, bronchospasm and laryngeal edema[11]. Urticaria and angioedema often represent the first symptoms. It usually starts locally and then shows general reaction referred to as anaphylactic shock, where patient has hypotension and severe bronchospasm[12]. The reaction could be biphasic, the recurrence

could occur anytime from 8-72 hours. Hence, a periodic examination should be done in patients who had experienced an episode of anaphylaxis[13].

Allergic reaction to local anesthesia is mostly attributed to ester anesthetics due to formation of the breakdown product p-aminobenzoic acid. Reactions can also be due to its components like methylparaben and metabisulphite. The reactions are commonly of Type 1 hypersensitivity type or Type IV delayed hypersensitivity. The former maybe severe and life threatening[14].

During a dental procedure if the patient is suspected to develop anaphylaxis, the operator should cease the treatment immediately, clear the airway and remove the triggering agent immediately. Watch if there is any sign of respiratory distress, check the vital signs and see if the patient is unconscious. Make the patient lie on a flat surface with legs slightly raised and pregnant patients in left lateral position if unconscious. The drugs used for managing anaphylactic reaction should always be a part of the emergency drug kit in the dental clinic. The details of this which are mentioned in Table 1[9,11,12].

Type II hypersensitivity reactions and its dental implications:

They are antibody dependent reactions. These reactions could be complement mediated antibody (IgG, IgM) reactions or complement independent (IgG, IgE) or due to phagocytosis. The antibodies are directed towards antigens in the extracellular matrix or against antigens in cell membrane. Goodpasture syndrome, Immune Thrombocytopenic Purpura and pernicious anemia are excellent examples of IgG mediated cell lysis and destruction[3].

ABO incompatibility or Erythroblastosis fetalis is a hemolytic disease of newborns caused due to fetal-maternal blood group incompatibility. In this, the fetus has a blood factor that its mother lacks, and the mother produces antibodies against that factor [15]. This depicts a response to a non-harmful antigen by an antibody or immunoglobulin [Fig 1b]. The teeth can appear green, brown or bluish in color due to the deposition of blood pigments in the enamel and dentine. Teeth may be affected by enamel hypoplasia especially at the incisal edges of anterior teeth and the mid portion of cuspid teeth in deciduous dentition. This ring like defect at the incisal edges was termed as 'Rh hump' by Watson [15].

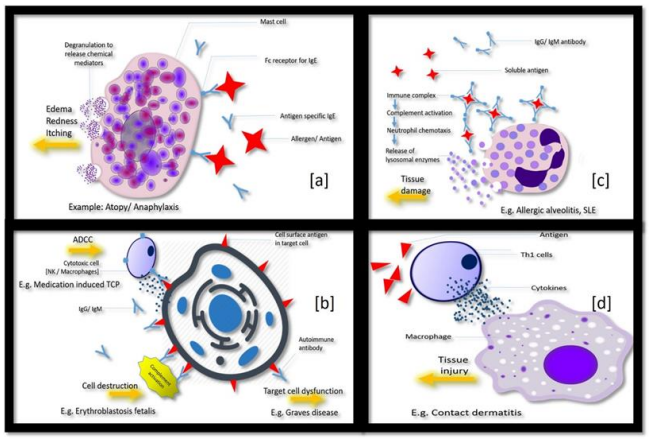

Figure 1. Mechanism of hypersensitivity (HS) reactions; [a] type 1: IgE mediated HS [b] type II: IgG/ IgM mediated cytotoxic HS [c] Immune complex mediated HS [d] Cell mediated HS.

Type V is an additional class of hypersensitivity reaction, where antibodies recognize and bind to cell surface receptors and impair cell signaling. Its mechanisms do not destroy target cells but results in induction of organ/tissue dysfunctions. Examples for this includes Graves' disease and Myasthenia gravis. These conditions are more often considered as a subcategory of Type II[16]. Graves` disease, an autoimmune disorder of thyroid described by the production of thyroid-stimulating IgG immunoglobulins gives rise to hyperthyroidism. In dentistry, identification of signs and symptoms of hyperthyroidism is crucial. A rise in thyroid hormone levels make the patient tremendously sensitive to epinephrine like sympathomimetic drugs used in local anesthesia and retraction cords during dental procedures due to its function as a vasoconstrictor. Dispensation of such drugs can cause hypertensive crisis, tachycardia, and/or dysrhythmia in the patient. These patients show resistance to the effects of CNS depressants such as diazepam and other anti-anxiety drugs. Therefore, the usual treatment for apprehension and stress reduction will not show any improvement, especially if they are undiagnosed or inadequately medicated[3,17].

Type III hypersensitivity reactions and its dental implications:

This is a consequence of deposition of circulating immune complexes and ensuant inflammation and tissue destruction at the site of

deposition of these complexes [Fig. 1c]. It commences after the administration of a drug (e.g., penicillin) or exposure to heterologous anti-serum or plasma. Clinically, it is characterized by skin rash, fever, arthralgias, or arthritis. Immune complexes mediate this complication, and it may affect many organs. Few examples include Serum sickness, Arthus reaction, Systemic lupus erythematosus as well as Erythema Multiform[3].
Erythema Multiforme (EM) is an acute drug reaction which affects various parts of the oral mucosa and extends to the vermillion border [Fig. 3].

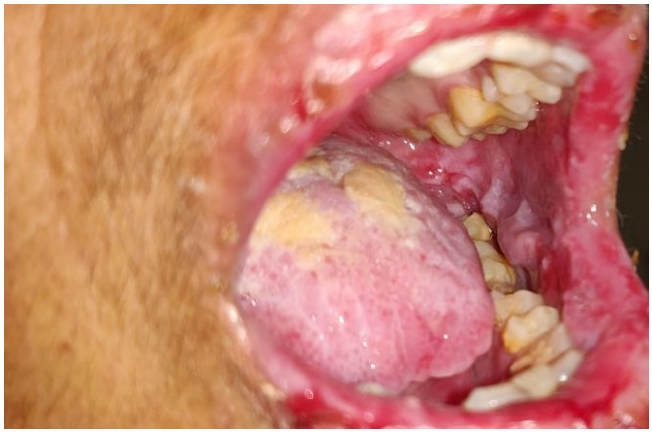

Figure 3. Patient with erythema multiforme affecting the oral mucosa.

It can also affect the skin genitalia and the conjunctiva[18]. The various drugs that cause erythema multiforme are antibacterials (such as Sulfonamide, Penicillin, Cephalosporins, Quinolones), anticonvulsants (Barbiturates, Hydantoins), analgesics, antifungals and cancer chemotherapeutics[19]. EM minor associated with recurrent HSV is Type III but EM major is more like Steven Johnson Syndrome which is Type IV[20].

Systemic lupus erythematosus (SLE) is a chronic, multisystemic disease of unknown etiology. It is depicted by the production of autoantibodies and immune complexes directing to variable systemic manifestations. More than 75 percent of patients exhibit signs and symptoms like xerostomia, burning mouth and oral ulcerations. The commonly affected areas are the vermilion, gingiva, buccal mucosa and palate. Patients also exhibit considerable xerostomia secondary to associated Sjögren's syndrome[21].

Dental technicians are at risk for allergic reactions as they are exposed to several chemicals in the form of dust and vapor. Pneumoconiosis is a disease rising from the accumulation of dust in the lungs. Silicosis is one such issue seen in dental laboratory technicians. This is a debilitating, sometimes fatal, yet preventable occupational lung disease caused by inhalation of respirable crystalline silica dust. An exposure to cobalt chromium molybdenum (CoCrMo) alloys containing cobalt, chromium, molybdenum, and traces of other metals, such as silicon and manganese cause a new type of dust-induced fibrotic lung disease known as dental technician pneumoconiosis. This is a complex pneumoconiosis or defined as mixed dust pneumoconiosis[22]. Extrinsic allergic alveolitis, lung damage due to irritant gases, fumes, and smoke comprises the occupational lung disease that affects the lung parenchyma [23].

Type IV hypersensitivity reactions and its dental implications:

In Type IV hypersensitivity reactions otherwise known as delayed type hypersensitivity reaction, the response takes about 12-24 hours to progress and remains for a longer period[4,5].

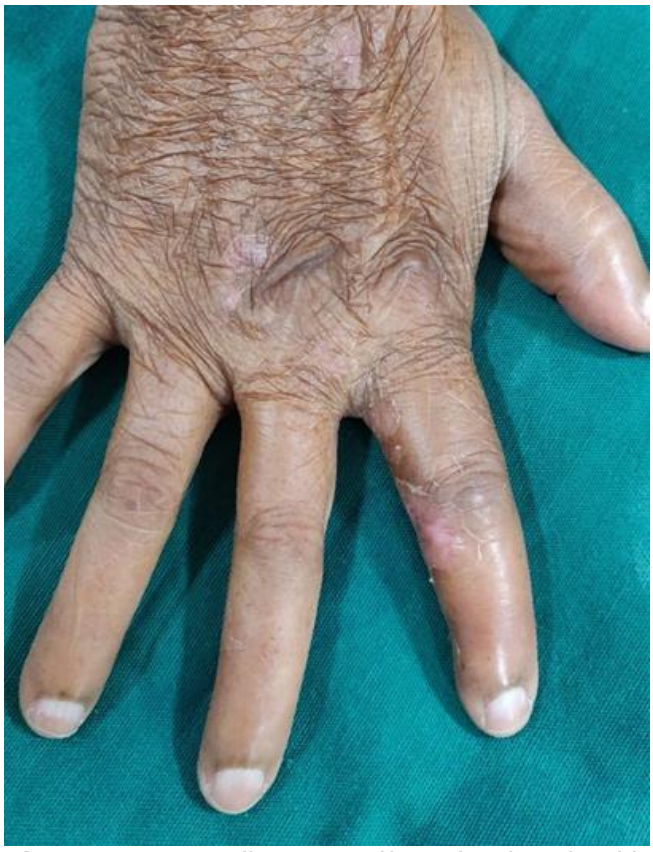

Figure 4. Latex allergy manifestation in a health care worker.

Allergic contact dermatitis (ACD) to latex products is an allergic reaction mediated by T cells commonly encountered among health care workers [Fig. 1d]. Common dental products that may contain latex include gloves, rubber dams, endodontic stoppers, anaesthetic cartridge, bite block, hoses, instrument bands, mixing bowls, polishing wheels, and orthodontic bands. The reaction invariably results from the thiuram (vulcanization accelerator) and mercaptobenzathiazole added during processing to natural latex[24]. Usually a rash develops within 24 to 48 hours and can progress to formation of urticarial skin blisters and peeling [Fig 4]. The gold standard for the diagnosis of contact dermatitis is patch-testing [Figure. 5].

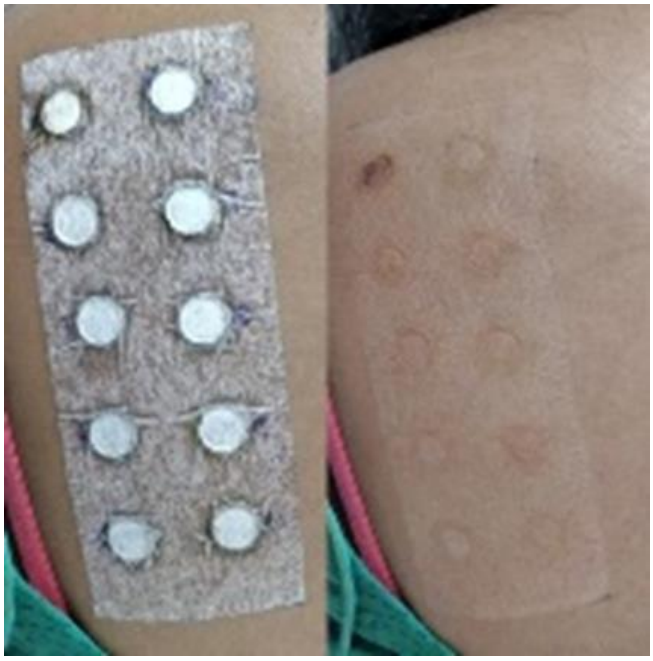

Figure 5. Allergy patch testing on skin.

The reproducibility and validity of this test is often challenged. Evaluation of the test also depends on experience and skill of the practitioner especially when evaluating weak positive results [25]. It can be managed with topical corticosteroid or by using latex free gloves[26]. However, patients with true latex allergy, as described in the type I hypersensitivity section, can have life threatening reactions [10]. Preparedness, if not prevention is the key in avoiding such a disaster.

Lichenoid reaction secondary to amalgam restoration although occurs less frequently is a delayed hypersensitivity reaction [Fig. 6].

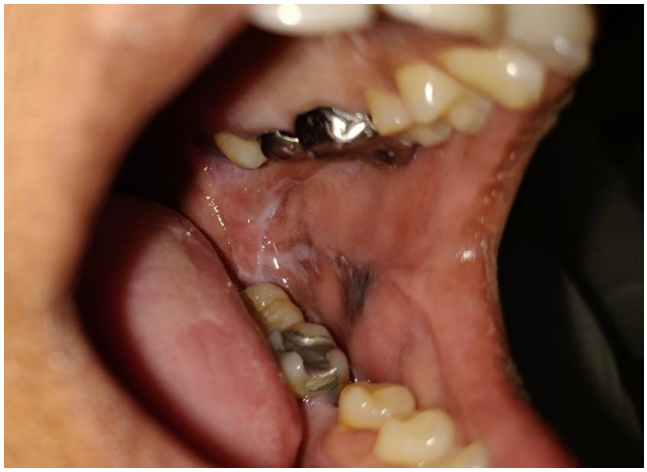

Figure 6. Clinical presentation of lichenoid reaction next to a restoration.

Gingival hyperplasia adjacent to amalgam restoration has also been attributed to allergic contact stomatitis caused by amalgam core preparation[27]. The allergen could either be mercury or components of amalgam alloy such as copper, tin or zinc. The oral manifestations are similar to lichen planus but its close proximity to the restoration helps us in the differentiation. Diagnosis can be done either by patch test or wait for the lesion to disappear on replacement of the amalgam restoration[28].

Nickel is the most common metal that causes allergic reactions in humans among other metals such as chromium, mercury, palladium, and cobalt. They could affect both the oral mucosa and the entire body and sometimes the skin of the extremities. The symptoms could present intraorally as any of the following i.e.: stomatitis. glossitis, glossalgia, cheilitis and lichen planus. Nickel maybe present in orthodontic brackets, arch-wires, bands, springs and ligature wires. It can also be present in endodontic instruments or restorations like crowns, fixed or removable partial denture. This can cause contact dermatitis and have intraoral manifestations[29].

Resins used in dentures can cause local irritation and sometimes it can also show systemic manifestations like soreness, itching, asthma, giddiness and swelling of the ankles. Methyl methacrylate, used in denture and in temporary crowns have been reported to cause tingling, burning or itching sensation associated with swelling[30,31]. Even after being considered safe, leaching out of constituents of resin based restorative materials can cause allergic contact

stomatitis and can manifest as mild erythema in the adjacent soft tissues. Treatment includes use of antifungal medication and replacement of existing restorations[32].

Mouth washes are known to cause allergic contact stomatitis (delayed or type IV hypersensitivity) and also type I reactions[33]. Various manifestations include epithelial peeling, mucosal ulceration, inflammation, gingivitis, petechiae and lip swelling[34]. Hypersensitivity reactions to toothpaste, although rare, is seen due to the ingredients used to prevent tartar formation and the flavouring agents. These are known to cause mucosal peeling of lips and tongue, edema, perioral dermatitis, angular chelitis, gingivitis and intraoral ulcers[35].

Berylliosis is a chronic beryllium disease that can also been seen in dental laboratory technicians due to prolonged exposure to beryllium in the workplace. This seems to be due to a delayed-type hypersensitivity reaction to beryllium [36]. Along with the use of corticosteroids, the treatment includes the removal of the diseased individual from any beryllium-containing workplace[37].

Thus, various agents encountered in dental practice can be a cause for delayed hypersensitivity reaction. Though not life threatening, these reactions can be an issue with regard to the quality of life for both patients as well as dental health care providers.

Conclusions

Allergic responses in dental patients to dental materials as well as drugs prescribed can sometimes be a medical emergency. As dental practitioners we should be prepared to handle such a situation. A detailed understanding of the probable dental allergens can also assist the dentist in diagnosing and managing certain oral conditions that could be a manifestation of an immunological response to the allergen. In addition to patients, dental practitioners as well as dental laboratory technicians can present with allergic reactions in response to certain allergens encountered in the dental health care setting. Therefore, the knowledge of etiology and management of allergic reactions and its dental considerations cannot be over emphasized.

Declaration of Interest

The authors report no conflict of interest.

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