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Research paper

Pediatric allergy: a common occurrence with multifarious implications

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Abstract

Pediatric professionals treat nature's most benevolent creation i.e., the child.
It is important to focus not only on oral health but also on the overall health of the pediatric patient because oral health is an integral part of total development.
There are various dental materials ranging from diagnosis to rehabilitation for the management of oral diseases that are not devoid of posing a potential risk of inducing allergic reactions to Pediatric patients in the dental setting.
Most importantly, a dental practitioner must be trained in medical emergencies and be capable of resuscitating a patient. Not only the dentist but also the assistants present in the clinic should be trained on how to manage any allergic emergency conditions in children in dental settings.
As some of these diseases have higher rates of morbidity and mortality, management of such conditions requires a multidisciplinary medical team approach consisting of physicians, dermatologists, Pediatric dentists, and ophthalmologists.
So, this review involves in-detail information regarding what is an allergy, history of allergy, allergic and immunological responses of the oral mucosa, dental materials prone to allergies, its diagnosis, and treatment modalities in child hoping that it will be helpful to every practicing pediatric professional.

Keywords: *Allergy; Children; Dental materials; Dental practitioner; Pediatric.*

1. Introduction

Allergy is described as altered bodily reactivity to an antigen in response to first exposure - Merriam Webster.[1]
The prevalence of allergic diseases worldwide is rising in both developed and developing countries. These diseases comprise asthma; rhinitis; anaphylaxis; drug, food, insect allergy; eczema; urticaria (hives), and angioedema. This increase is devastating for children, who are bearing a major brunt of the rising trend which has occurred over the last couple of decades.[2]
Over the last few years, due to the rise in the number of patients with allergies to different materials, the practicing pediatric dentists should know about documented allergies to known materials and thus circumvent such allergic manifestations in the dental clinic.

2. History

The concept of "Allergy" was originally introduced by the Viennese pediatrician Clemens von Pirquet in 1906. "Allergy" was derived from the Ancient Greek word allos meaning (other, different, and strange) + ergon (activity, to do).[3]
In 1911, Von Pirquet wrote his final piece on allergy, a monograph emphasizing his theory.[4]
Paradoxically, in 1913 when Richet received the Nobel Prize for his work on anaphylaxis, the term 'allergy' started appearing in various scientific articles and attracted the attention of clinicians and scientists.[5]

In the 1930s, a new medical subspecialty called allergology became established. In the late nineteenth century, physicians and patients in the USA had already established hay fever clinics and associations. [5]
Sure evidence of the triumph of the 'allergy' word was the creation in the USA in 1929 of an important journal: the Journal of Allergy.[5]
Specifically in 1963, Philip Gell and Robin Coombs made a new and groundbreaking classification of hypersensitivity diseases in their book Clinical aspects of immunology [6], which is still in use today with minor changes.[7]
Allergy in the 21st century
The extension of the idea of 'allergy' to the streets, which started in the 1930s as we showed above, has reached vast proportions. [5].

3. Working classification of allergic and immunologic diseases of the oral cavity (Fig.1) [8],[9],[10],[11]

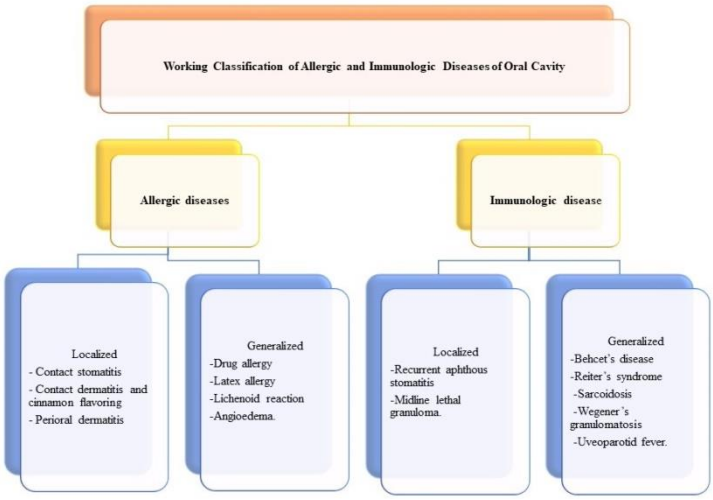

Fig. 1: Working Classification of Allergic and Immunologic Diseases of Oral Cavity.

4. Latex allergy

Natural latex is a derived product of the rubber tree, Hevia brasiliensis.
Allergic reactions may be a response to the NRL (Natural Rubber Latex) from which the glove is made or to other chemicals used in the manufacturing process.[12]
Latex is considered to be an occupational allergen as it can cause occupational asthma in people with the regular use of latex such as dental and medical professionals.

4.1. Adverse skin reactions due to latex gloves (Fig. 2) [13]

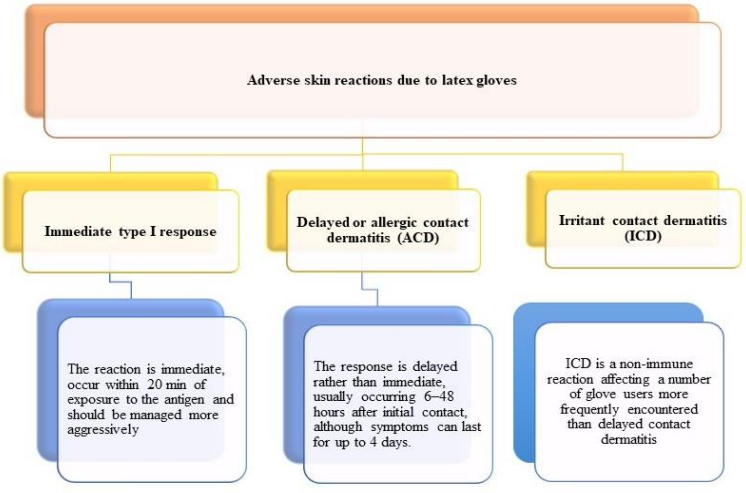

Fig. 2: Adverse Skin Reactions Due to Latex Gloves.

4.2. Alternative products for patients with latex allergy [14]

Product	Alternative
Latex gloves	Vinyl/Nitrile/Silicone gloves
Rubber dams	Non-latex(Polyvinyl-Chloride) dams
Latex bite blocks	Metallic/Silicone mouth props
Rubber file stops	Wax file stops
Injectable ampules (rubber plungers in syringe)	Injectable vials
Orthodontic elastics used for oral fixation	sterile wire to secure arch bars

Polishing cups	Non-latex toothbrushes
Rubber mixing cups	Silicone mixing cups
Penrose latex surgical drains	Silicone/Polyvinyl-Chloride Surgical drains
Containers with rubber droppers	Containers without rubber droppers

Patients with latex allergy should be immunologically tested for gutta-percha sensitivity also as gutta-percha is in the same botanical family as the rubber tree (Havea brasiliensis) as gutta-percha is derived from the juice of the Taban tree (lsonandra percha).[15]

4.3. Precautions [15]

1) Detail history
2) For emergency dental treatment, Use Nonlatex products.
3) The ambient air in the dental clinic should have a minimal level of powder contamination.
4) Schedule the appointment at the beginning of the office workday when the level of powder contamination in the air is at a minimum.
5) A thorough wipe-down of office equipment before the patient's appointment.
6) Patients with an extreme sensitivity to latex should consult with their physician regarding premedication with prednisone or Benadryl.
7) Prepare to manage an allergic reaction, including the use of epinephrine such as an EpiPen.

5. Allergy to eugenol

Eugenol is an active, primary aromatic liquid responsible for various pharmacological activities. It is routinely used with zinc oxide as a primary tooth obturating material in Pediatric dentistry and other forms such as impression pastes, periodontal dressings, cement, filling materials, endodontic sealers, dry socket dressings, as well as used as a flavoring agent in cosmetics and food items.[16][17]

5.1. Mechanism

The setting reaction between zinc oxide and eugenol produces zinc eugenolate, which is highly unstable in the existence of water. The surface of this material undergoes hydrolysis, releasing free eugenol, which has been reported to induce type IV hypersensitivity reactions as well as generalized anaphylactic symptoms. [18]

5.2. Clinical features [19]

According to Barkin, the therapeutic action of eugenol on the pulp is cytotoxic and three reaction types may be observed which are:

- Direct tissue damage
- Contact dermatitis
- True allergic reaction

5.3. Preventive measures

1) Avoid tissue contact and follow the manufacturer’s instructions when eugenol-containing ZOE cement is used.
2) Use other safer eugenol-free temporary restorative cement
3) Refer the patient suspected of having an allergy to dental materials for allergy tests prior to dental treatment.

6. Allergy to metals

In Pediatric dentistry nickel and chromium are the most important constituent in preformed metal crowns, space maintainers, brackets, fillings, endodontic instruments, and orthodontic appliances which have an irreplaceable place. So, we must aware of its allergic consequences on the child.
Most of the time, allergic reactions to metals are mainly type-IV reactions.[20]
Nickel sensitivity has been reported in children treated with old generation SSCs with high (up to 72%) nickel content. Based on these findings, the new generation of SSC contains only 9%– 12% nickel. [21]
In association with pediatric dentistry, Ni ions are released by stainless crowns, space maintainers, and orthodontic appliances in the course of time in patients’ saliva. This has been seen to rise after toothbrush abrasion and an increase in the oral pH.[22]

6.1. Clinical features of nickel allergy [22]

6.1.1. Intraoral

1) Stomatitis from mild to severe erythema
2) Papula-perioral rash, lichen planus
3) Loss of taste or metallic taste
4) Burning sensation
5) Soreness at the sides of the tongue
6) Angular cheilitis
7) Severe gingivitis in the absence of plaque

6.1.2. Extraoral

1) Generalized urticarial
2) Widespread eczema
3) Flare-up of allergic dermatitis

4) Exacerbation of preexisting eczema

6.2. Chromate

Chromium differs from nickel, in that it is not antigenic in metal form, but usually only in the hexavalent salt form as chromate. Minute quantities of chromium salts can, however, sensitize. Chromium compounds.[23]

6.3. Treatment

Alternatives to Nickel-Titanium Wires (TSME) were proposed by C. Maspero et al in 2018.
If a diagnosis of nickel hypersensitivity is established, the nickel-titanium arch-wire should be removed and replaced.
Alternatives include:[24]

1) Twist flex stainless steel
2) Fiber-reinforced composite arch-wires
3) Wires such as TMA, pure titanium, and goldplated wires may also be used safely.
4) Altered nickel-titanium arch-wires also exist and include plastic/resin coated nickel-titanium archwires.
5) Ion-implanted nickel-titanium archwires have their surface bombarded with nitrogen ions, which form an amorphous surface layer, conferring corrosion resistance and displacing nickel atoms, and decreasing the risk of an allergic response.

6.3.1. Symptomatic treatments [25]

Steroids: Topical steroids are very useful and represent the first-line treatment.
Calcineurin inhibitors
Psoralen plus UV-A.
Disulfiram
Binding agents and barrier creams:

- Ethylene diamine tetra-acetic acid (EDTA 15%)
- 5-chloro-7-iodoquinolin-8-ol (clioquinol).

However, it has been shown that some patients might benefit from a nickel-free or a low-nickel diet, and must be prescribed according to Vein's guidelines.

6.4. Nickel hyposensitization [25]

Although "nickel vaccination" using oral hyposensitizing treatment is commercially accessible in some countries its potency is still to be definitively proven. Alitretinoin (9-cis retinoic acid): a promising new option in the treatment of chronic, severe, and refractory hand dermatitis acting as an anti-inflammatory and immunomodulator.

7. Drug allergy

Drug allergy is one type of unpredictable ADR (adverse drug reaction) that encompasses a spectrum of immunologically-mediated hypersensitivity reactions with varying mechanisms and clinical presentations. [26]
A considerable proportion of children develop rashes, urticaria, angioedema, and respiratory symptoms while sick, frequently while taking antibiotics. [27] Thus many children are diagnosed with 'suspected antibiotic allergy'. This is understandable since 51 (36.7%) of the anaphylactic deaths in the UK over a 6-year period were due to medication. Sixteen of these deaths resulted from antibiotics, including a 5-year-old child.[28]

7.1. Risk factors for drug allergy: (Fig. 3) [29]

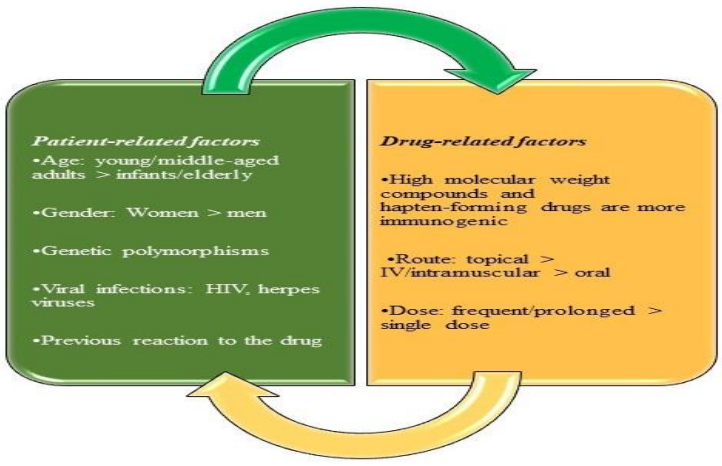

Fig. 3: Risk Factors for Drug Allergy.

Local anesthetics, analgesics, and antibiotics are the most common drug classes used in dental practice, and allergic or pseudo-allergic reactions have been reported for each.

7.2. Signs of drug allergy [30]

7.2.1. Early reactions

1) Extensive pruritus
2) Rhinoconjunctivitis, obstructive respiratory symptoms, nausea, vomiting
3) Pruritus around the mouth, in the palms, and soles
4) Sudden erythema on the skin with conjunctivitis and rhinitis

7.2.2. Delayed reactions

1) Fever, malaise
2) Long-term findings after discontinuation of the drug
3) Lymphadenopathy
4) Pain and burning in the skin
5) Bullous lesions, epidermal separation (Nikolsky sign)
6) Mucosal involvement
7) Edema in the face and diffuse erythematous swelling
8) Confluent lesions in extensive skin areas
9) Eosinophilia (>1.5x109/L)
10) Hepatic involvement

7.3. Diagnosis

1) Drug provocation tests (DPTs)
2) Skin testing in children
3) In vitro and/or ex vivo testing
4) Drug-specific tests
5) The basophil activation test
6) Lymphocyte transformation testing (LTT)
7) Enzyme-linked immune spot (ELISPOT) assays
8) Drug challenge.
9) Drug desensitization.

7.4. Common drug allergies

7.4.1. Local anesthetics

Although the actual incidence of confirmed allergy to local anesthetics is extremely low (,1%), any claim must be given serious attention considering the staggering number of local anesthetic procedures we perform. Cutaneous reactions or airway compromise/obstruction should be regarded as potentially allergic in nature. For these cases, consultation with an allergist is essential. [31]

7.4.1.1. Etiology of allergy to local anesthesia (Fig. 4) [32]

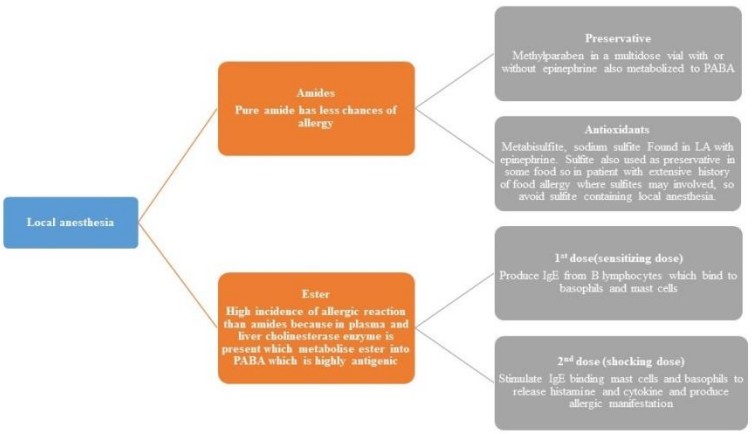

Fig. 4: Etiology of allergy to local anesthesia.

7.4.1.2. Testing of local anesthesia in a dental clinic (Fig. 5) [32]

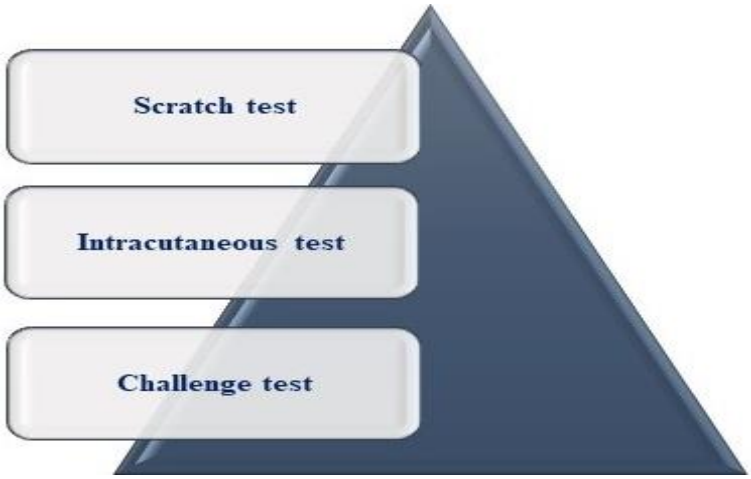

Fig. 5: Testing of Local Anesthesia in Dental Clinic.

I. Scratch test

Least sensitive and less reliable.

II. Intracutaneous test

The primary mode of assessing a patient for local anesthetic allergy.

Most reliable.

Deposit 0.1 ml of test solution into the extensor surface of the patient's forearm that will produce wheal of a few mm in diameter if the patient is allergic. Redness, swelling, and itching should be measured up to 15-20 minutes.

III. Challenge test:

If the patient does not produce an allergic reaction to the intracutaneous test then take the challenge and perform the challenge test. 0.9 ml of local anesthesia that produces no intracutaneous reaction is injected intraorally via supraperiosteal infiltration atruamatically (but without topical anesthesia) above maxillary right or left premolar or anterior teeth.

Observe the injection site, general symptoms like rash/erythema, facial edema, bronchospasm, hypotension, gastrointestinal or neurovascular syndrome, and vital signs for 30 minutes.

This is called an intraoral challenge test and it frequently provokes allergic reactions like fainting, sweating, and palpitations. If there is no allergic manifestation found during the challenge test then we should proceed with intraoral anesthetic block injections.

7.4.1.3. Managing history of local anesthetic allergy [31

Clarify the nature of the reaction

1) Rule out other reactions:
   Syncope: unconsciousness, brief seizures
   Epinephrine: palpitations
   Consider sedation, minimal or no epinephrine
2) Pruritus or rash:
   Non-IgE-mediated;cross-reaction unlikely
   Use alternate agent without vasopressor to avoid preservatives
   May consider allergist referral
3) Urticaria or anaphylactoid:
   Refer to an allergist for lidocaine testing
   Also, provide mepivacaine or prilocaine plain
   Request testing for bisulfites

7.4.2. Nonsteroidal anti-inflammatory drugs

Nausea and dyspepsia are the most common events labeled by patients as being allergic reactions to NSAIDs, but a significant number of patients may describe reactions that appear allergic in nature. True IgE-mediated reactions to aspirin and NSAIDs have been confirmed, but they are rare and are more often a pseudo-allergic mechanism.[33] [34]

For patients giving the details of only a history of rash or pruritus, it is safe to select an alternative NSAID. For those reporting urticaria or respiratory symptoms, it is judicious to avoid all NSAIDs and prescribe acetaminophen, regardless of their underlying respiratory status. It should be mentioned that true IgE-mediated reactions to acetaminophen have also been reported, but there is no relation to reactions involving NSAIDs.[35]

7.4.3. Opioids

Only 1 case of IgE-mediated reaction has been published in the literature, and this claimed cross-reaction among various opioids, including codeine. However, nearly all opioids are capable of producing pseudo allergic reactions by triggering degranulation of mast cells and the direct release of histamine.[32]

7.4.4. Antibiotics

It is preferable to substitute alternate penicillin or cephalosporin for a patient claiming penicillin allergy provided the nature of the reaction was exclusively pruritic (itch) or a maculopapular rash. A history of urticaria (hives) or anaphylactoid symptoms are more persuasive

evidence that the patient's reaction to penicillin was truly IgE mediated, and in this case, there is little recourse but to abstain from prescribing any beta-lactam derivative.[31]

7.4.4.1. Managing history of penicillin allergy. [31]

Clarify the nature of the reaction

1) Hives or Anaphylactoid
   IgE-mediated; cross-reaction possible
   Avoid all Beta Lactum
2) Pruritus or rash
   Non-IgE-mediated; cross-reaction unlikely
   Use alternate penicillin or cephalosporin
3) Dyspepsia, Nausea, Diarrhea
   No issue
   Avoid offending formulation

7.4.5. General anesthetics

Although rare, anaphylaxis may occur in patients treated under general anesthesia. The investigation of severe reactions during general anesthesia is especially challenging given that the patient is often exposed to many co-administered drugs and agents. Reactions during the use of general anesthesia are often due to neuromuscular blocking agents and antibiotics. but have also been related to IV anesthetics (e.g., propofol, thiopentone, etomidate), NSAIDs, chlorhexidine, and latex allergy. [36]

7.5. Prevention of future reactions

The patient should be provided with detailed written information about which drugs to avoid (including over-the-counter medications). Inscribed allergy bracelets/necklaces, such as those provided by MedicAlert®, should also be considered.[29]

8. Rare allergic materials

8.1. Resin material composites

The dental personnel or staff commonly complain of contact dermatitis and asthma caused by methacrylates. HEMA, EGDMA, and TEGDMA are the constituents responsible for occupational contact allergies.[37]
Even though resin-based restorative materials are considered safe, their constituents can leach out and are responsible for allergic contact stomatitis.[38]

8.2. Fissure sealant

Hallstrom U (1993) reported an isolated case in which adverse reactions like asthma and urticaria were reported after fissure sealant placement and the symptoms disappeared after its removal suggesting allergy.[39]

8.3. Mercury associated with amalgam restoration

Delayed hypersensitivity reactions to amalgam restorations are seen as erythematous, pruritic lesions on the oral mucosa and skin of the face and neck. The usual presentation of these reactions is oral lichenoid lesions (OLL). [40]

8.4. Titanium

In Pediatric Dentistry, endodontic hand instruments, rotary instruments, orthodontic brackets, and orthodontic wires contain titanium.
The first case of delayed hypersensitivity reaction to titanium in the form of local granulomatous reaction was described in patients having cardiac pacemakers.[41][42] Titanium allergy has a low prevalence rate of 0.6% and presents with urticaria, eczema, redness of the mucosa.[43][44]

8.5. Alternate substitutes to titanium

Polyether ether ketone (PEEK) which offers mechanical properties and bone-forming capacity similar to titanium is also under investigation.[45]
Allergy to the materials in endodontics such as root canal sealers and obturating materials, Formaldehyde. {Munaco et al., (1978) and Pascon & Spangberg (1990)}, Ledermix paste, Pulpotec reaction and Impression materials were reported.

9. Diagnosis

''LISTEN TO YOUR PATIENTS ……THE PATIENTS WILL GIVE YOU THE DIAGNOSIS'' -Jeffry Okeson
When a patient is suspected of allergy in the dental clinic, a thorough history taking, clinical examination, and confirmatory test should be performed. Prick test and scratch test are used to diagnose immediate hypersensitivity while patch test confirms delayed hypersensitivity.[46]

9.1. Diagnosis of allergy (Table 1) [46]

Table 1: Diagnosis of Allergy

Tests	Indications	Advantages
Skin prick test 	Confirms immediate hypersensitivity. positive predictive value ranging from 95-100%.	1. cost-effective. 2. No lower age limit. 3. More than one allergen can be tested simultaneously 4. Results are immediately available. 5. Minimally invasive. 6. safe. 7. Reliable 8. Convenient 9. Good reproducibility 10. Readily accessible
Intradermal test		Rapid, sensitive and specific, safe and relatively inexpensive per
Patch test. 	Gold standard for diagnosing contact allergy.	
RAST(Radio allergosorbant test). 	particularly useful where SPT is contraindicated	Results of RAST are not affected by prior antihistamine use or use can be performed in patients with widespread skin disease.
Lymphocyte stimulation test.	diagnosis of delayed hypersensitivity reaction.	
The Lymphocyte Transformation Test (LTT)	In-vitro test of metal sensitivity.	
Melisa(memory lymphocyte immuno-stimulation assay test)	To measure the sensitization induced by metals.	

10. Management: (Fig. 6) (Fig.7) [47]

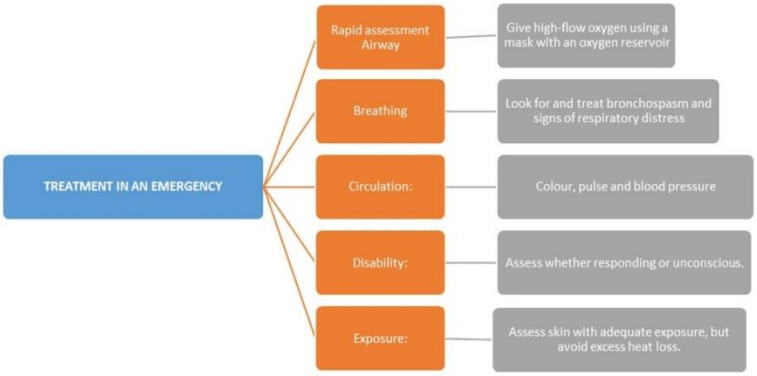

Fig. 6: Treatment of Allergy in an Emergency.

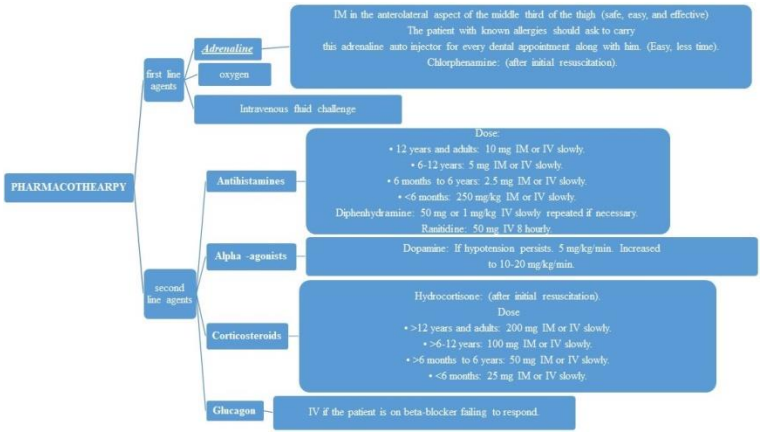

Fig. 7: Pharmacotherapy for Allergic Conditions.

Adrenaline [47]

Adrenaline (epinephrine) intramuscularly (IM) in the anterolateral aspect of the middle third of the thigh (safe, easy, and effective):

- Adult IM dose 0.5 mg IM (=500 µg = 0.5 mL of 1:1000) adrenaline (epinephrine).
- >12 years: 500 µg IM (0.5 mL) that is, the same as the adult dose.

- 6-12 years: 300 μg IM (0.3 mL).
- <6 years: 150 μg IM (0.15 mL).

If the child is small or prepubertal 300 μg (0.3 mL).
IM adrenaline (epinephrine) should be repeated after 5 min if there is no clinical improvement. Patients requiring repeated IM doses may benefit from IV adrenaline (epinephrine). In these circumstances, expert help is required as soon as possible.[48]
Note: IV adrenaline (epinephrine) should only be administered by those having the necessary training and experience such as anesthetists, intensivists, and emergency department physicians.

10.1. Disability management

If the child is conscious: Dentists should place them in a position where they are comfortable and able to breathe easily until the ambulance arrives. If they are feeling dizzy or giddy, they should be laid flat with their legs elevated, if achievable.[46]
If the child is unconscious: Dentists should place them in the recovery position (on their side, supported by one leg and one arm, with the head tilted back and the chin lifted). If the person stops breathing or the heart stops beating, cardiopulmonary resuscitation (CPR) should be performed effectively. [49]

10.2. Monitoring [50]

Maintain the PaO2 as close to normal as possible (approximately 13 kPa or100 mm Hg).

10.3. Further investigation [51]

Mast-cell tryptase as soon as possible after emergency treatment for anaphylaxis.

10.4. In the long-term follow-up [52]

Refer to an allergist to try to identify the allergen to avoid in the future.
Organize autoinjetors (e.g., EpiPen).
Give a written self-management plan, in detail information about anaphylaxis and biphasic reactions, and details of the possible signs and symptoms of a severe allergic reaction.
Motivate the patient to wear a MedicAlert bracelet/necklace advised by the doctor.

11. Allergen immunotherapy

An immune-modulatory method for the treatment of immunoglobulin E (IgE)-mediated allergic diseases to control the symptoms and decrease the sensitivity toward allergen(s) by sequentially introducing an increasing dose of antigen(s) to make a shift of the immunological response from TH2 to TH1.[53]

11.1. Routes of administration of Allergic Immunotherapy [54]

- Sublingual
- Oral
- Intranasal
- Epicutaneous
- Intra lymphatic

11.2. Duration of allergen immunotherapy [55]

Generally administered for 3–5 years; the duration and decision to discontinue it must be individualized.

11.3. Allergen immunotherapy in children

Compliance with the injection regimen or doses may be affected by age and may be problematic, particularly during the adolescent years. It is recommended to start allergen immunotherapy at an early age in children with allergies to improve the natural way of allergic disease.[56]
At present, Allergic immunotherapy is restricted to very few allergens that are not closely related to dental conditions and require further research.

12. Conclusion

We should keep our eyes open and become more vigilant for possible allergic incidence with a child in the dental setting as pediatric dentists hold the privilege of being the first person to diagnose any earliest signs of allergic disorders or any systemic condition, which are manifested more frequently in child's mouth as compared to adults.
If we diagnose allergic conditions at an early age, we can advise the child to wear medical bracelets as well as counsel the parents and inform other health care professionals regarding allergies in the child to avoid future consequences.

13. Impact statement

This article provides an insight into the possibility of allergic reactions to dental materials in the pediatric population, diagnosis of the allergic conditions, their prevention, and treatment options of the possible allergic reactions in the pediatric population in the dental office.

Acknowledgments

I want to thank all my staff members.

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