ALLERGY IN DENTISTRY: MECHANISMS OF DEVELOPMENT AND EFFECTIVE TREATMENT METHODS

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Objectives: This study is conducted to analyse the mechanisms of allergic reaction development in dentistry and the effectiveness of their treatment methods.

Methods: During it, a review of current scientific sources on allergology, immunology, dentistry, pharmacology, and materials science is conducted, mechanisms for the development of allergies of various types are established, the effectiveness of treatment methods is evaluated, and clinical recommendations for allergy therapy in dentistry are formed.

Results: The results show that the development of allergic reactions occurs by two mechanisms. Immediate-type immunoglobulin E-mediated (IgE-mediated) responses are triggered by the release of histamine, serotonin, and other inflammatory mediators through mast cell degranulation due to the binding of the allergen to specific IgE antibodies produced by the immune system in response to its first contact. In dentistry, this type of reaction can be provoked by local anaesthetics, antibiotics, latex, nickel, amalgam, and acrylic resins. Symptoms of immediate allergies range from mild local reactions to life-threatening conditions. Delayed-type allergic reactions are mediated by T-lymphocytes, so in response to contact with the allergen, other cells of the immune system (macrophages, neutrophils) are activated, which secrete their own inflammatory mediators (interferon-gamma, tumour necrosis factor-alpha, etc.). In dentistry, such reactions are usually caused by metals (nickel, cobalt, chromium), cements, gutta-percha, and composite materials.

Conclusions: Understanding the mechanisms of development of allergic reactions helps to differentiate them from pseudo-allergies, the effect of which on inflammatory mediators is conducted without the mediation of the immune system. Structuring information on the mechanisms of development of allergic reactions and methods of their treatment, among which the main ones are pharmacotherapy, immunotherapy, probiotic therapy, and dental approaches, clinical recommendations for the treatment of allergic reactions in dentistry were formed.

Keywords: Mast cells, T-lymphocytes, Anesthetics, Nickel, Latex, Histamine.

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Conflicts of interest:
The authors declare no conflicts of interest.

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L'ALLERGIE EN DENTISTERIE: MÉCANISMES DE DÉVELOPPEMENT ET MÉTHODES DE TRAITEMENT EFFICACES

Objectifs: Cette étude a pour but d'analyser les mécanismes de développement des réactions allergiques en dentisterie et l'efficacité de leurs méthodes de traitement.

Méthodes: Au cours de cette étude, une revue des sources scientifiques actuelles sur l'allergologie, l'immunologie, la dentisterie, la pharmacologie et la science des matériaux est effectuée, les mécanismes de développement des allergies de différents types sont établis, l'efficacité des méthodes de traitement est évaluée et des recommandations cliniques pour le traitement des allergies en dentisterie sont formulées.

Résultats: Les résultats montrent que le développement des réactions allergiques s'effectue selon deux mécanismes. Les réponses médiées par les immunoglobulines E de type immédiat (IgE) sont déclenchées par la libération d'histamine, de sérotonine et d'autres médiateurs inflammatoires par la dégranulation des mastocytes, en raison de la liaison de l'allergène aux anticorps IgE spécifiques produits par le système immunitaire en réponse à son premier contact. En dentisterie, ce type de réaction peut être provoqué par les anesthésiques locaux, les antibiotiques, le latex, le nickel, les amalgames et les résines acryliques. Les symptômes des allergies immédiates vont de réactions locales bénignes à des affections potentiellement mortelles. Les réactions allergiques de type retardé sont médiées par les lymphocytes T. Ainsi, en réponse au contact avec l'allergène, d'autres cellules du système immunitaire (macrophages, neutrophiles) sont activées et sécrètent leurs propres médiateurs inflammatoires (interféron-gamma, facteur de nécrose tumorale alpha, etc.). En dentisterie, ces réactions sont généralement causées par des métaux (nickel, cobalt, chrome), des ciments, de la gutta-percha et des matériaux composites.

Conclusions: La compréhension des mécanismes de développement des réactions allergiques permet de les différencier des pseudo-allergies, dont l'effet sur les médiateurs inflammatoires s'effectue sans la médiation du système immunitaire. En structurant les informations sur les mécanismes de développement des réactions allergiques et les méthodes de leur traitement, dont les principales sont la pharmacothérapie, l'immunothérapie, la thérapie probiotique et les approches dentaires, des recommandations cliniques pour le traitement des réactions allergiques en dentisterie ont été formulées.

Mots-clés: Mastocytes, Lymphocytes T, Anesthésiques, Nickel, Latex, Histamine.

Introduction

The constant development of dentistry has substantially improved the quality of services. The introduction of technologies such as computed tomography, 3D technologies, and the use of lasers allowed increasing the effectiveness of dental treatment and prosthetics, and the revision of requirements for modern dental materials, which were mainly related to ensuring the properties of biocompatibility and hypoallergenic, helped achieve a higher level of safety of procedures. Despite such achievements, the problem of allergic reactions in dentistry has not yet been eliminated due to the influence of many factors, the main of which are individual sensitivity, an increase in the amount of dental materials and the unpredictability of allergic reactions. Depending on the immune profile of a person, an allergy can be caused by any element that is part of the dental material, and the fact that some reactions develop only after a certain time after contact with the allergen makes it difficult to establish causal relationships between the dental material and sensitisation to it in the patient. Therefore, to improve the safety of dental procedures, it is important to analyse the mechanisms of the development of allergic reactions and determine the most effective methods of their treatment.

Oral diseases, encompassing issues associated with dental materials and treatments, are among the most widespread health disorders globally, imposing considerable health and economic burdens while diminishing quality of life [1]. While precise global incidence statistics for dental allergies are few, the extensive utilisation of dental materials and the escalating intricacy of dental operations indicate an augmented exposure to possible allergens.

Oral diseases are persistent, socially influenced ailments that are more prevalent among marginalised populations in low- and middle-income countries, where access to dental care is frequently insufficient [2]. This environment heightens the likelihood of allergic responses stemming from untreated or inadequately managed oral problems and products. Allergic disorders impact over 20-30% of the global population, with medication and dental material allergies representing a specific subgroup of this greater concern [3]. The incidence of allergic disorders, pertinent to dental practice, is increasing worldwide, resulting in considerable morbidity and healthcare expenses.

Dental pain and negative reactions associated with dental materials and procedures represent a considerable public health challenge, with prevalence rates of dental pain varying significantly (e.g., 5% to over 30% in children and adolescents), highlighting a substantial population impacted by dental conditions that may involve allergic elements [2]. The economic ramifications of dental disorders, including treatment expenses and diminished productivity, highlight the necessity of addressing all determinants influencing oral health safety, including allergies to dental materials.

One of the important problems of the study is the lack of a single universal method for diagnosing allergies in dentistry. Analysing the frequency of contact allergies to filling materials, implants, and prosthetics in patients, Forkel et al. [4] used patch testing as a method for detecting hypersensitivity to metals, acrylates, natural substances based on propolis, and other potentially allergenic dental materials. A similar diagnostic method was proposed by Reinhart et al. [5] in a paper on the examination of oral hypersensitivity reactions. The reliability of patch testing not only for patients but also for doctors was confirmed by Warshaw et al. [6] investigated professional contact dermatitis in dental personnel. This method is advisable in case of suspected contact dermatitis but it may not detect other types of allergies in dentistry.

During the assessment of adverse reactions to medications that are most commonly used in dentistry, Ouanounou et al. [7] analysed the frequency of allergic reactions to local anaesthetics, sedatives, analgesics, and antibiotics. Among the main diagnostic methods, they identified anamnesis collection, skin and provocative tests, and laboratory tests to determine specific immunoglobulins E (IgEs). Determining the frequency of titanium allergy caused by dental implants, Poli et al. [8] noted that the primary diagnosis of an allergic reaction to this element was confirmed by immunohistochemical analysis of the biopsy. In the authors' studies, these diagnostic methods were declared reliable but they did not identify how effectively they can differentiate between allergies and pseudo-allergies in dentistry.

Pseudo-allergies also pose a substantial problem for allergy research in dentistry, as they have similar symptoms and can distort the results and make it difficult to identify the true mechanisms of allergic reactions. Stafie and Murariu [9] investigated the safety of drugs for local anaesthesia in dentistry and identified differences between true allergic reactions and pseudoallergy. The analysis showed that although both conditions can cause similar symptoms, their mechanisms of development and approaches to diagnosis are different. In a review paper devoted to the examination of allergic and other adverse reactions to drugs used for anaesthesia, Baldo [10] drew attention to the similarity between true Type I IgE/FcεRI-allergy and pseudoallergic *MRGPRX2*-mediated adverse reactions. The author analysed the current discussions of scientists and doctors regarding procedures for identifying *MRGPRX2* agonists and identified the importance of differential diagnosis for

distinguishing the mechanisms of allergic and pseudoallergic reactions to anaesthetics.

In their study, Jiang and Tang [11] noted that allergy to local anaesthetics is quite rare and accounts for less than 1% of all adverse reactions. Hypersensitivity to anaesthetics in most cases is caused by reactions to preservatives or other excipients, but without an appropriate diagnosis, it can be classified as a true allergic reaction, which in clinical practice can lead to the need to find a replacement for the drug and, accordingly, delays in surgical procedures. Therefore, it is important to differentiate reactions to local anaesthetics using skin and provocative tests (if an immediate reaction is suspected) and patch tests (if a delayed reaction is suspected).

The fact that pseudoallergic reactions in dentistry most often occur during the use of local anaesthetics explains the increased attention to them, but the causes of such reactions can also be other drugs, in particular, antibiotics, nonsteroidal anti-inflammatory drugs, sulfonamides, latex, composite materials, etc., which in the context of differentiation of allergic and pseudoalergic reactions have so far been examined much less.

The purpose of this study was to determine the mechanisms of allergy development to drugs and materials used in dentistry. The objectives were to evaluate the effectiveness of existing therapeutic methods and form clinical recommendations that can be used in clinical practice for the treatment of allergic reactions in dentistry.

Materials and methods

During the study of the mechanisms of development and effective methods of treatment of allergic reactions in dentistry, the analysis of scientific sources on dentistry, allergology, immunology, pharmacology, and materials science was conducted, which included materials on the mechanisms of allergic reactions and the role of the immune system in them, clinical manifestations of allergies, methods of its diagnosis and treatment, pharmacological properties of dental preparations, their effect on the body and possible side effects, the composition and properties of dental materials, as well as the nature of their interaction with biological tissues. Sources for further analysis were selected from publications in the scientomeric databases Pubmed, Google Scholar, Web of Science, Scopus for searching materials science publications. The process of selecting sources for further analysis included creating an initial sample, screening annotations, detailed analysis of the full text, and evaluating the quality of research.

The search for materials to reveal the mechanisms of allergy development in dentistry as an object of the study was conducted according to the keywords: “allergy in dentistry”, “hypersensitivity”, “allergen”, “immune system”, “contact dermatitis”, “immunoglobulins”, “immunological tolerance”, “local anaesthetics”, “lidocaine”, “articaine”, “nickel”, “cobalt”, “chromium”, “composite materials”, “latex”, “allergy to antibiotics”, “nonsteroidal anti-inflammatory drugs”, “immediate allergic reaction”, “delayed allergic reaction”, “anaphylaxis”, “pseudo-allergic reaction”, “provocative tests”, “patch tests”, “immunohistochemistry”.

The search query for evaluating the effectiveness of allergy treatment methods in dentistry was formed according to the keywords: “treatment of allergies to dental materials”, “methods of allergy treatment in dentistry”, “indicators of the effectiveness of allergy treatment”, “immunotherapy”, “drug treatment”. Keywords: “safety of dental procedures”, “prevention of allergic reactions to dental materials”, “New Dental Materials”, “biocompatibility”, “hypoallergenic”, “allergy tests”, “personalised medicine”, “forecasting of allergic reactions”, “acrylic resins”, “cements”, “alternative methods of allergy prevention/treatment in dentistry”, “interdisciplinary approach to allergy treatment” were used to search for materials that are relevant to the task of analysing promising areas of allergy prevention and treatment in dentistry.

The search was conducted in English and Polish. Based on the results of screening by title and annotation, publications that did not correspond to the research subject were excluded. A methodical approach to searching was created to guarantee thorough coverage of pertinent literature. Several databases, including PubMed, Scopus, and Web of Science, were searched using a mix of keywords, including “dental materials”, “allergy”, “biocompatibility”, “new materials”, and “biomaterials in dentistry”. To guarantee that the most recent developments in dental material science were included, the search was restricted to research released between 2019 and 2025. The following standards for inclusion were used: research with human subjects; research that assessed allergic reactions or evaluated the biocompatibility of dental materials; and research that was published in peer-reviewed publications. Studies that only addressed in vitro testing, animal models, or publications written in languages other than English were disqualified. The most recent and pertinent research on the topic is guaranteed to be included in the review thanks to this methodical search strategy. The exclusion criteria were: review articles, no control group and inclusion/exclusion criteria for clinical trials, and the use of a high-bias methodology for clinical and theoretical studies. Among the publications that met the inclusion criteria, preference was given to clinical studies that meet ethical

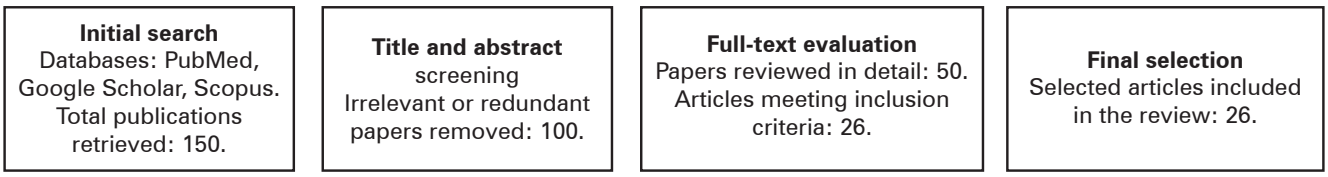

Figure 1. Article selection process for narrative review on allergies in dentistry

standards (have the approval of the ethics committee), and when choosing theoretical works, attention was paid to the citation rate of the article. A flowchart illustrating the article selection process is shown below (Figure 1). A comprehensive search of PubMed, Google Scholar, and Scopus yielded a total of 150 publications. After reviewing titles and abstracts, 100 were removed due to irrelevance and redundancy. A comprehensive evaluation of 50 papers led to the selection of 26 research articles that satisfied the established inclusion criteria.

Standard instruments were used to evaluate each included study's risk of bias. Potential biases in selection, performance, detection, and reporting were assessed for randomised, controlled trials using the Cochrane Risk of Bias Tool. The Newcastle-Ottawa Scale, which considers selection, comparability, and outcome assessment, was used to evaluate the quality of cohort and case-control studies. The risk of bias in each study was categorised as high, moderate, or low, and the possible influence of bias on the findings was examined. Studies with a high risk of bias were identified, and the results were interpreted with caution.

Each study was given a level of evidence depending on its design to make clear the strength of the evidence from the included studies. Randomised controlled trials (RCTs), the gold standard in clinical research, are referred to as Level 1. Cohort and follow-up studies, which offer useful longitudinal data, are included in Level 2. Case-control studies, which are advantageous in determining risk variables and associations, are referred to as level 3 studies. Cross-sectional studies that provide information on the prevalence of conditions or exposures are classified as Level 4. Lastly, Level 5 comprises expert opinions and case reports, which offer little proof but are useful for uncommon or unusual illnesses. Table 1 lists the degree of evidence for each study, and the additional materials provide specifics on the classification process.

Based on the results of examining the selected materials, the main characteristics were analysed to form an understanding of the fundamental differences in the mechanisms of development of allergic and pseudo-allergic reactions in dentistry, and a comparative analysis of allergy treatment methods in dentistry was conducted to form clinical recommendations for improving the safety of dental procedures. This narrative review of current literature does not include original research or direct engagement with human or animal subjects. Therefore, ethical approval was unnecessary. No financial support was obtained for the compilation of this review.

Results

Mechanisms of Allergic Reactions to Dental Materials

Allergy in dentistry is not a rare phenomenon that occurs as a pathological reaction of the immune system to contact with certain materials and drugs used in dental practice. The mechanisms of development of allergic reactions depend on biological intermediaries that determine the rate of their development. They are divided into immediate-type IgE-mediated reactions and delayed-type cell-mediated reactions. Immediate allergic reactions are rapid, intense reactions of the immune system to contact with an allergen. They occur within minutes or hours of contact and can manifest with a variety of symptoms, ranging from mild to life-threatening [12]. Table 1 presents a thorough summary of chosen studies regarding allergic reactions and hypersensitivity in dentistry and medical settings, outlining their design, populations, interventions, outcomes, risk of bias, and levels of evidence.

Table 1. PRISMA table

Source	Study design	Population	Sample size	Inteventions	Outcomes	Risk of bias	Level of evidence
[13]	Experimental	Patients with allergic responses to IgE/IgA	N/A	IgA vs IgE mast cell and basophil activation	IgA can block IgE-mediated allergic activation	Moderate	4
[14]	Case-control	Dental patients with potential allergy cofactors	362	Allergic cofactors in dentistry	Identification of cofactors contributing to dental allergies	Low	3

[15]	Survey	Dental patients in Albania	543	Antibiotics, allergies, resistance	Prevalence and patterns of antibiotics and allergy awareness	Moderate	4
[16]	Cross-sectional	Dental patients receiving prophylaxis	N/A	Antibiotics used in dentistry	Serious antibiotic-related adverse effects following unnecessary dental prophylaxis and their clinical consequences.	Moderate	4
[17]	Cohort	Patients undergoing joint prosthetics	9,256	Latex exposure in prosthetic surgery	Latex allergy increases infection risk	Moderate	2
[18]	Case report	Healthcare workers, latex anaphylaxis	1	Latex in healthcare workers	Latex anaphylaxis in healthcare workers, focusing on occupational risks and management strategies.	Moderate	5
[19]	Cross-sectional	Schoolchildren	2,000	Nickel exposure	Trends and comorbidities in nickel allergy	Low	4
[20]	Clinical	Patients with posterior restorations	278	Amalgam vs composite fillings	Reasons for replacement of restorations	Moderate	3
[21]	Cohort study	Patients with delayed-type hypersensitivity	N/A	Delayed-type drug hypersensitivity	Immune dysregulation and its association with increased incidence of delayed-type drug hypersensitivity reactions.	Moderate	2
[22]	Cross-sectional	Restorative dental material allergy patients	N/A	Restorative dental materials	Probiotics as a strategy for the prevention and treatment of allergies, including their clinical efficacy.	Moderate	4
[23]	Case-control	Asthma and periodontitis patients	1,482	Asthma, medications, and periodontal status	Asthma linked with increased periodontitis risk	Moderate	3
[24]	Follow-up study	Patients with metal implants	N/A	Titanium/metal exposure tested by MELISA	Prevalence of hypersensitivity to metals	Moderate	2
[25]	Case study	Dental patients in institutional setting	N/A	Allergy and hypersensitivity in dental setting	Prevalence and management of allergic reactions	Moderate	5

[26]	Cohort study	Children with local anesthetic allergy	100	Local anesthetics in children	Diagnosis and management of local anesthetic allergies in children, focusing on real-life data and clinical practice.	Moderate	2
[27]	Observational study	Emergency department misdiagnosis	50	Misdiagnosed pseudo-allergic reactions	Misdiagnosis of hypersensitivity reactions in emergency departments, especially regarding pseudo-allergic responses.	Moderate	5
[28]	Survey	General population	5,000	Histamine intolerance measured via DAO levels	DAO levels reflect histamine intolerance	Moderate	4
[29]	Retrospective	Sickle cell patients	412	Antibiotic exposure	Antibiotic allergy prevalence	Moderate	2
[30]	Cohort	Anaphylaxis patients	1,230	Adrenaline administration	Impact of adrenaline on anaphylaxis outcomes	Low	2
[31]	Randomized clinical trial	Peanut allergy patients	201	Oral immunotherapy with antihistamines	Efficacy and safety of peanut immunotherapy	Low	1
[32]	Cross-sectional	General dentists	234	Corticosteroid prescription knowledge in dentists	General dentists' knowledge and practices regarding corticosteroid prescriptions and their impact on patient care.	Moderate	4
[33]	Meta-analysis	Sinus augmentation patients	50	Corticosteroid use in sinus augmentation	Use of corticosteroids in lateral sinus augmentation surgery, evaluating their effectiveness and potential risks.	Low	1
[34]	Experimental	Animal model with mast cell-mediated arrhythmia	N/A	Mast cell stabilizer treatment	Reduced ventricular arrhythmia via mast cell pathway	Moderate	3
[35]	Experimental	Allergic patients	N/A	IgE monoclonal antibody production	IgE antibody specificity and activity	Moderate	3
[36]	Randomized controlled trial	Patients with acute allergic rhinitis	120	Use of probiotic Alkalihalobacillus clausii	Reduction in allergic rhinitis symptoms	Low	1

[37]	Case series	Patients with adverse reactions to dental biomaterials	109	Dental biomaterial exposure	Types and management of biomaterial-related allergies	Moderate	3
[38]	Prospective cohort	Critically ill patients with orotracheal intubation	792	Orotracheal device-related pressure injury	Incidence and predictors of mucosal injury	Low	2

Source: compiled by the author based on [13-38].

At the first contact with an allergen, the immune system produces specific IgE antibodies that bind to the surface of mast cells and basophils – immune system cells containing granules with inflammatory mediators. Fixed on the surface of these cells, IgE, upon repeated contact with the same allergen, binds to it, provoking degranulation of mast cells and the release of a large number of inflammatory mediators – histamine, serotonin, heparin, etc., which cause vasodilation, increased vascular wall permeability, and contraction of the smooth muscles of the bronchi and intestines [13]. The external manifestation of this release is the main symptoms of allergies, including:

- skin manifestations (itching, redness, urticaria);
- respiratory problems (coughing, sneezing, bronchospasm, nasal congestion);
- gastrointestinal disorders (nausea, vomiting, diarrhoea);
- systemic reactions (angioedema, anaphylactic shock).

In dentistry, the symptoms of immediate allergic reactions can vary depending on the type and amount of allergen, the route of its penetration, and individual sensitivity. Most often allergens in dentistry are anaesthetics, in particular, lidocaine and articaine, antibiotics, latex, nickel in dental instruments, acrylic resins for dentures and amalgam for filling, and the more allergen enters the body, the more pronounced the symptoms will be. Allergen penetration in dentistry is conducted through local contact, by inhalation and through the blood. When the allergen comes into contact directly with the skin or mucous membranes, local reactions most often occur – redness, itching, swelling; if the allergen is inhaled, common allergic reactions are sneezing, itching in the nose, runny nose, cough, difficulty breathing, bronchospasm, redness of the eyes, lacrimation, itching of the eyelids; if the allergen enters the blood, systemic allergic reactions may develop, the most difficult of which is anaphylaxis [14, 15].

Allergic reactions to anaesthetics (lidocaine, articaine) can occur through local reactions – swelling, redness, itching at the injection site, and systemic reactions – angioedema, bronchospasm, decreased blood pressure, anaphylactic shock. Symptoms of allergic reactions to antibiotics used during dental procedures (penicillin, cephalosporin) range from skin reactions (rash, pruritus, urticaria) and gastrointestinal disorders (nausea, vomiting, diarrhoea) to the most complex systemic reaction-anaphylactic shock [16]. Latex allergy occurs in approximately 1-8% of people, and among medical professionals – in 10-17% [17]. Despite the fact that this allergen comes into contact only with the skin, in addition to local reactions, it can provoke breathing problems – nasal congestion, sneezing, coughing, difficulty breathing, bronchospasm, and the most severe systemic reaction – anaphylactic shock [18]. Immediate allergic reactions to nickel usually occur in local reactions since the most frequent contact with nickel occurs through the skin, but rarely systemic manifestations can develop, in particular, asthma and eczema. Symptomatic manifestations of allergy to acrylic resins are also in most cases realised through skin reactions but sometimes they can also cause systemic (asthma, anaphylaxis), especially in people with an atopic predisposition [19]. Symptoms of allergic reactions to amalgam are manifested through local reactions – rash, itching, redness at the site of contact with the seal, neurological symptoms, in particular, tremors and headache, may rarely occur [20]. Reactions to each of these allergens can vary substantially depending on a person's individual sensitivity.

Delayed-type allergic reactions in dentistry are less common than immediate-type reactions but can cause substantial discomfort and complication of treatment. They develop more slowly, usually within a few days of contact with the allergen, and are associated with a cellular immune response, namely activation of T lymphocytes. At the first contact with the allergen, the antigen is presented to T-lymphocytes as antigen-presenting cells (macrophages, dendritic cells). Sensitisation to the allergen develops during the recognition of antigens by T-cell receptors. One part of T-lymphocytes activated in response to antigens is converted to effector T-helpers of Type I (Th1), which secrete cytokines that stimulate the inflammatory response, and the other – to memory cells that fix this antigen. Upon repeated contact with the same allergen, sensitised T-helpers of Type I

quickly recognise the antigen and activate other cells of the immune system (macrophages, neutrophils, etc.) that release inflammatory mediators, in particular, interferon-gamma, tumour necrosis factor-alpha, leading to the development of an inflammatory reaction at the site of contact with the allergen. Locally, this is manifested by redness, swelling, itching, and other symptoms [21-39].

The most common materials that cause delayed reactions are metals that are part of prostheses and orthodontic structures, in particular, nickel, cobalt, and chromium; composite materials, including Monomer methacrylate, fillers other than mineral ones, polymerisation initiators, pigments used to stabilise the colour of the composite, acrylic resins used as binders; cements for fixing prostheses and crowns; gutta-percha for filling root canals [22]. In addition to the main symptoms of contact dermatitis as the most common type of delayed allergic reactions, these reactions can cause symptoms of eczema (redness of the oral mucosa), swelling of the gums, lips, and cheeks, ulcers on the mucous membrane and pain at the site of contact with the allergen. At the level of systemic reactions, they can provoke allergic rhinitis, exacerbation of asthma or the development of bronchospasm, enlarged lymph nodes, and symptoms of general weakness – fatigue and increased body temperature [23]. Delayed-type allergic reactions cannot directly cause anaphylaxis since the mechanism of their development is fundamentally different from each other.

Despite the different mechanisms of development, both local and delayed types of allergic reactions affect the safety of dental procedures and require additional efforts to avoid risks. Immediate allergic reactions are more dangerous because of the risk of anaphylactic shock. The rapid development of symptoms after contact with the allergen indicates the likely allergic nature of the disease but to make an accurate diagnosis and exclude other causes, it is necessary to conduct additional examinations, especially considering the variety of allergic manifestations and the possibility of developing pseudo-allergic reactions. Delayed allergic reactions are safer than immediate reactions but the duration of their development makes it difficult to establish an initial diagnosis and requires more detailed allergological studies to identify the allergen.

Understanding the mechanisms of allergy development in dentistry is important for the differential diagnosis of allergic and pseudoallergic reactions. Pseudoallergic reactions, although they have similar symptoms to allergic ones, develop by a different mechanism. Unlike allergies, which are associated with the immune system and the production of specific antibodies, pseudoallergic reactions have a direct toxic effect of the substance on the body's cells [24]. There are several main mechanisms by which pseudoallergic reactions develop – through the direct release of inflammatory mediators, through exposure to other body systems, and through impaired histamine metabolism.

Certain substances such as dental components (nickel, cobalt, chromium), latex, local anaesthetics, composite components, cements, and disinfectants can directly affect mast cells and basophils, causing them to release histamine and other inflammatory mediators. These mediators, in turn, cause the characteristic symptoms of an allergic reaction – redness, itching, swelling [40].

Some substances used in dentistry (composite materials, cements, disinfectants) can directly activate the components of the complementary system, which leads to a cascade of reactions that contribute to the release of inflammatory mediators and tissue damage. The same substances can stimulate the formation of kinins, which leads to swelling, redness, and pain. The complementary and kinin systems interact closely with other systems, so their activation can provoke the development of complex reactions in the body [25-41].

Pseudoallergia in dentistry most often develop due to the direct release of inflammatory mediators and the effect on the complementary system, and less often – a violation of histamine metabolism since it is usually provoked by substances that are part of food products, such as cheese, smoked products, red wine, etc. However, this reaction can be caused by some components of local anaesthetics (esters, amides), filling materials (composite materials and amalgams), and orthodontic structures (nickel, cobalt, chromium, latex), which stimulate mast cells, provoking their degranulation and release of histamine [26]. There are many key aspects that help distinguish between allergies and pseudo-allergic reactions and choose the appropriate treatment (Table 2).

Analysis of the main aspects of allergic and pseudo-allergic reactions (Table 2) shows that both conditions have the same symptoms, but differ to a greater or lesser extent in other characteristics. It is worth adding that angioedema and anaphylaxis in pseudo-allergic reactions are less common and less intense than in allergies. These severe systemic reactions have a common mechanism of development although they are implemented in different ways (allergic reactions – immunological, pseudoallergic – nonimmunological), in both cases the symptoms occur due to the massive release of inflammatory mediators (histamine, serotonin), which cause similar symptoms, including tissue oedema, smooth muscle spasm, and increased vascular permeability. The similarity of the mechanisms of development of systemic reactions complicates

Table 2. Characteristics for differentiating allergic and pseudoallergic reactions

Characteristics	Allergic reactions	Pseudoallergic reactions
Mechanism	Immunological	Nonimmunological (direct toxic effect)
Presence of an IgE antibody	Present	Absent
Trigger	Specific allergen (protein, chemical)	Various substances, often medicines, food products
Development time	There may be a delay (sensitisation) but often a quick response	Usually, quick response after contact with the trigger
Specificity	High specificity to a specific allergen	Low specificity, can occur on various substances
The role of genetics	A substantial role of genetic predisposition	Less pronounced role of genetics
Immune mediators	Histamine, leukotrienes, cytokines	Histamine, serotonin, bradykinin
Diagnostics	Skin tests, specific IgE, elimination diets, provocative tests	Medical history, elimination diets, laboratory tests (general blood test, biochemical parameters)
Complement role	Can play a role	Can play a role much less frequently
Involvement of effector cells	Mast cells, basophils, and eosinophils are involved	Various cells are involved, in particular, neutrophils
Repeatability of the reaction	Repeated contact with an allergen	Usually unpredictable
Symptoms	Skin manifestations: urticaria, itching, redness, peeling. Respiratory symptoms: nasal congestion, sneezing, runny nose, red eyes, itchy eyes, lacrimation, bronchospasm. Gastrointestinal symptoms: nausea, vomiting, diarrhoea, abdominal pain. Common symptoms: headache, weakness, dizziness, fever. Systemic reactions: Quique oedema, anaphylactic shock.	Skin manifestations: urticaria, itching, redness, peeling. Respiratory symptoms: nasal congestion, sneezing, runny nose, red eyes, itchy eyes, lacrimation, bronchospasm. Gastrointestinal symptoms: nausea, vomiting, diarrhoea, abdominal pain. Common symptoms: headache, weakness, dizziness, fever. Systemic reactions: Quique oedema, anaphylactic shock.

Source: compiled by the author based on [27-29].

the differential diagnosis of allergy and pseudo-allergic reaction but simplifies the provision of emergency care since in both cases, regardless of the causes of the reaction, life-threatening symptoms are primarily eliminated by the introduction of epinephrine [30].

Clinical Management of Allergic Reactions

By understanding the mechanisms of allergy development in dentistry, it is possible to analyse the effectiveness of existing methods of treatment. Notably, the most effective way to avoid the consequences of allergic reactions is to eliminate the allergen – eliminating or minimising contact with substances that cause an allergic reaction. However, it can only be used if the doctor is informed about the patient's sensitisation to a particular allergen. In other cases, pharmacological methods, immunotherapy, probiotic therapy, and dental approaches are used to treat allergic reactions.

Pharmacological drugs used to treat allergic reactions in dentistry are divided into three main groups – antihistamines, corticosteroids, and immunomodulators. Antihistamines are the main treatment for allergic reactions. They block histamine receptors, reducing the inflammatory response. The main advantages of this group are rapid effect, relative safety, and a wide spectrum of action, and their disadvantages are associated with the characteristic side effects of antihistamines, especially the first generation) – drowsiness, impaired concentration, dry mouth [31]. Among the drugs in this group, cetirizine, loratadine, desloratadine, and fexofenadine are most often used.

Corticosteroids are powerful anti-inflammatory drugs that suppress the immune system by stabilising the mast cell membrane, which leads to a decrease in the release of histamine and other inflammatory mediators, inhibition

of proliferation and inflammatory cell activity [32]. Their advantage is high efficiency due to the rapid and powerful anti-inflammatory effect, and the disadvantage is a low level of safety due to the possibility of serious side effects with prolonged use (osteoporosis, diabetes, increased blood pressure, immunosuppression) [33]. Depending on the type, corticosteroids can be used in the form of local (creams, gels, ointments, rinses) and systemic medications (tablets, injectable solutions). In dentistry, topical corticosteroids are usually used to treat allergic reactions of the oral mucosa, among them: triamcinolone in the form of ointment and gel, has anti-inflammatory and anti-allergic effects; hydrocortisone in the form of ointment, cream and gel; fluticasone is used in the form of an inhaled spray, but can also be used locally as prescribed by a doctor; mometasone is usually used to treat allergic rhinitis, but can also be used locally in dentistry.

In addition to corticosteroids, there are other immunomodulators that can be used to treat allergies in dentistry. Mast cell membrane stabilisers reduce the release of histamine and other inflammatory mediators. They have relatively few side effects compared to corticosteroids and are well tolerated by patients, but the therapeutic effect develops more slowly than with antihistamines, so they are more often used to prevent allergic reactions [34]. Examples of such drugs are sodium cromoglycate (Kromosol, Allergodil) and nedocromil (Tilade).

Inhibitors of leukotrienes, powerful inflammatory mediators involved in the development of allergic reactions, block the receptors of these mediators, reducing inflammation and bronchospasm. They are most often used in the treatment of allergic rhinitis and asthma, but they can be effective in eliminating respiratory allergic reactions in dentistry. Possible adverse reactions include headache, nausea, and diarrhoea [42]. Leukotriene inhibitors include Montelukast (Singular), zafirlukast (Accolat).

The principle of action of monoclonal antibodies is to block the action of molecules involved in allergic reactions, reducing inflammation [35]. This principle provides them with high efficiency in the treatment of severe allergic reactions, including in dentistry, however, given that the technology of monoclonal antibodies is relatively new, it has a high cost and side effects, the most difficult of which is the development of infections. In the pharmaceutical market, such drugs are represented by omalizumab (Xolair) and dupilumab (Dupixent).

Immunotherapy is one of the most effective methods of treating allergies, especially if other methods do not give the desired result since it is aimed at changing the body's immune response to the allergen, that is, it solves the primary problem of sensitisation. Its principle is that the patient is gradually injected with increasing doses of the allergen, achieving "habituation" and reducing sensitivity to it [43]. Immunotherapy can provide long-term remission of allergy symptoms, reduce the risk of severe allergic reactions, in particular, anaphylactic shock, and in some cases, ensure a complete recovery. The disadvantages of the method include the duration of treatment – the course of immunotherapy is from 3 to 5 years, the risk of allergic reactions during the procedure, and the high cost of therapy. For immunotherapy, special allergen extracts are used, which can be administered sublingually, subcutaneously, or intranasally. Immunotherapy is usually used to treat allergic rhinitis, asthma, and atopical dermatitis, but it can also be effective for allergic reactions to dental materials or latex, which is relevant for both patients and medical personnel.

The effect of probiotics on the intensity of an allergic reaction is realised in several ways: through competition with pathogenic microorganisms for receptors on the cell surface, which prevents their attachment and reproduction; through the production of biologically active substances that have anti-inflammatory and immunomodulatory properties; through stimulation of the production of immunoglobulins that neutralise allergens [36]. Such probiotic capabilities in dentistry are used for allergic stomatitis and allergic reactions to local anaesthetics and latex. The dosage form of probiotics allows them to be used for local application in the oral cavity, in the form of chewing gums, pastes, and gels, and for systemic use – in the form of capsules and tablets. The advantages of probiotic therapy are the minimum number of side effects, naturalness since probiotics are natural components of the human microbiome and a complex effect that extends not only to the fight against allergy symptoms but also to strengthening the overall immune system. The limitations of this method of treatment are the difference in intensity depending on the strain of bacteria and individual characteristics of the body. Currently, research on the effectiveness of the therapeutic effect of probiotics in allergies continues, so it is advisable for doctors to consider them as an additional tool for strengthening the immune system, which cannot yet replace traditional methods of treatment.

Ceramics based on zirconia have transformed prosthodontics and implantology because of their exceptional mechanical qualities, cosmetic appeal, and biocompatibility. Zirconia greatly lowers the risk of allergic reactions, including dermatitis and other metal-related sensitivities, because, in contrast to metals, it does not discharge ions into the surrounding tissues. It is being utilised more and more in crowns, bridges, and dental implants, particularly for people who could be sensitive to metals

like cobalt and nickel. Compared to conventional titanium implants, zirconia implants are far more successful and have a reduced rate of problems in patients with metal allergies, according to studies like those conducted by Mohseni et al. [44] Furthermore, zirconia's long-term success and compatibility with human tissue have been emphasised by clinical research investigating its usage in prosthetic dentistry.

Another promising material that has gained popularity in dental applications is polyetheretherketone (PEEK), which has a low allergenic profile and high biocompatibility. PEEK is an excellent option for dental implants, crowns, and prostheses in sensitive individuals since it is a high-performance polymer that is less likely to result in negative responses than metal- or acrylic-based materials. Studies like Ouldyerou et al. have demonstrated that PEEK is a great substitute for titanium and other metals in dental implants, with positive outcomes in terms of mechanical strength and osseointegration. Patients with metal sensitivity have found this material very helpful, as it provides an allergy-free alternative without sacrificing strength or durability.

Bioactive substances called resin-modified glass ionomer cements (RMGICs) release fluoride, which encourages remineralisation and guards against secondary caries. Compared to conventional resin-based cements, these materials are thought to have a decreased propensity for allergies, which makes them perfect for allergy-sensitive and paediatric populations. RMGICs have demonstrated encouraging outcomes in lowering allergy reactions, especially in children who might be more susceptible to material sensitivities, according to Singh et al. In the treatment of early childhood caries, where biocompatibility is essential, these materials are also helpful.

Concerns over the use of bisphenol-A (BPA), a recognised endocrine disruptor present in certain conventional composite resins, are addressed by BPA-free composite resins. Because they lower the dangers of hormone disruption and are thought to be safer for susceptible groups, these materials are becoming more and more popular in paediatric dentistry and among patients who are allergic. Studies have shown that BPA-free composites do not have the same endocrine-disrupting effects as their BPA-containing equivalents. One such study is that conducted by Šimková et al. Additionally, clinical testing has demonstrated that these materials eliminate the possibility of BPA-related problems while providing strength and aesthetics that are comparable to standard composites.

One of the key aspects of treating allergy patients is the right choice of materials for dental procedures. Modern dentistry offers a wide range of hypoallergenic materials that minimise the risk of allergic reactions, including: titanium and its alloys as an alternative to nickel, chromium, and cobalt; biocompatible ceramic materials as an alternative to metals for the manufacture of crowns, bridges and implants; modern composite materials for filling and manufacturing dental structures; special hypoallergenic plastics for the manufacture of temporary prostheses and other structures [37-48]. In addition to the choice of materials, modification of dental procedures plays an important role, which minimises contact of the oral mucosa with potential allergens and reduces the risk of allergic reactions. Modern methods of treatment allow performing dental procedures with minimal tissue injury, which contributes to faster healing and reduces the risk of developing inflammatory processes [49]. The use of cofferdam allows isolating the treated tooth from saliva and other contaminants, reducing the risk of allergic reactions to dental materials. Compliance with the rules of asepsis and antiseptics helps prevent the development of infectious complications that can increase allergic reactions [38, 50].

By structuring the information obtained about the mechanisms of development of allergic reactions in dentistry and the peculiarities of their treatment methods, it is possible to form clinical recommendations for the treatment of allergies to dental materials, preparations and latex (Table 3).

The proposed algorithm can be used by medical personnel in clinical practice to improve the level of safety of dental procedures and a basis for creating a new theoretical model of allergy treatment in dentistry, which will include step-by-step instructions for determining the type of allergy, and identifying the allergen, detailed treatment regimens for different types of allergies, criteria for evaluating the effectiveness of treatment, predicting possible complications, and developing strategies for their prevention.

Using this algorithm in clinical practice, it is worth considering it as basic recommendations that can be applied, accounting for the characteristics of each patient – individual sensitivity, the presence of concomitant diseases, age, physiological, and immunological features, etc. This will allow choosing the most optimal treatment method and avoiding the risks of developing life-threatening reactions.

Discussion

An allergy as an unpredictable reaction can be quite dangerous, especially if it is not considered during treatment. Allergic symptoms range from mild discomfort to life-threatening conditions, increasing the risk of even the safest dental procedures that use a variety of materials and medications that may be a potential allergen for a particular patient. The practice of allergy testing in dentistry exists but is not

Table 3. Basic clinical algorithm for allergy treatment in dentistry

Allergen type	Reaction type	Pharmacological methods	Non-pharmacological methods	Dental approaches	Prognosis and considerations
Metals (nickel, cobalt, chromium)	Contact dermatitis, atopic dermatitis	Local corticosteroids, antihistamines, immunosuppressants (e.g., cyclosporine for severe cases)	Immunotherapy (limited use), allergen elimination, probiotic therapy (adjunct)	Use hypoallergenic alloys; modify prostheses to avoid direct contact	Chronic dermatitis and eczema can develop with prolonged exposure; early allergen avoidance improves outcomes. Patch testing is gold standard for diagnosis. Systemic contact dermatitis may occur from dietary exposure.
Latex	Anaphylactic reaction, contact dermatitis	Epinephrine (for anaphylaxis), antihistamines, corticosteroids	Immunotherapy (rare), allergen elimination	Replace latex gloves with nitrile or vinyl gloves	Anaphylactic shock is life-threatening; strict latex avoidance is critical. Chronic dermatitis possible with repeated exposure. Early intervention reduces severity.
Dental materials (composites, cements, acrylic resins)	Contact dermatitis, atopic dermatitis	Local corticosteroids, antihistamines	Immunotherapy (in select cases), allergen elimination, probiotic therapy (adjunct)	Select hypoallergenic materials; avoid known allergens	Chronic dermatitis and eczema possible; patch testing and patient history guide material selection
Local anaesthetics (lidocaine, articaine, benzocaine)	Anaphylactic reaction, contact dermatitis	Epinephrine, antihistamines, corticosteroids	Immunotherapy (rare), probiotic therapy (adjunct)	Use alternative anaesthetics; premedication protocols recommended by AAE	Anaphylactic shock risk necessitates emergency preparedness. Premedication and alternative agents reduce reactions
Disinfectants (chlorhexidine, alcohols)	Contact dermatitis, atopic dermatitis	Local corticosteroids, antihistamines	Allergen elimination	Use alternative disinfectants	Chronic dermatitis and eczema possible; patch testing can identify allergens. Alternatives reduce sensitization
Polymers (acrylics, biopolymers)	Contact dermatitis, atopic dermatitis	Local corticosteroids, antihistamines	Immunotherapy (in some cases), allergen elimination	Select hypoallergenic polymers	Chronic dermatitis and eczema possible; hypoallergenic polymers reduce risk

Notes: Prognosis refers to the assessment of the possible consequences of allergies and their impact on human health in the absence of effective treatment.

Source: compiled by the author based on [51, 52].

routine due to the relatively high cost of procedures and the inexpediency of their implementation for patients who have not previously been diagnosed with allergic reactions. Allergy tests are usually performed before complex and long-term treatment, such as implantation or restoration, if there is a history of allergies, or if an allergic reaction is suspected during previous dental procedures. Such diagnostic measures can substantially reduce the risk of developing allergies in patients but do not completely eliminate it. This study proposed clinical guidelines for the treatment of allergies that most often occur during dental procedures to control allergic reactions that could not be avoided.

The problem of allergy occurrence is common for doctors of all medical specialities, which provide for various physical manipulations and the use of pharmacological drugs, but allergists and immunologists are more practically prepared for such reactions in patients [53-55]. In similar cases, specialists in other fields of medicine, in particular, dentistry, may feel less confident, especially when an acute systemic allergic reaction occurs. This standpoint was confirmed by Smereka et al. [56], having assessed the readiness and attitude of dentists to emergency medical care in Poland based on a survey of 419 doctors. According to the results of their study, 55.13% of the survey participants did not feel competent in the treatment of anaphylactic shock. This result is quite high, as it shows that more than half of the doctors surveyed may not be able to cope with its elimination in the event of a life-threatening reaction in a patient. After analysing these indicators, the authors recommended improving pre-graduate and postgraduate training of medical personnel in emergency medical care and increasing the availability of equipment for its provision in dental offices. Agreeing with the recommendations of the authors, it is also worth emphasising the importance of developing and implementing clear and understandable algorithms for the treatment of allergic reactions, the use of which will help to increase the level of confidence of doctors and increase the safety of dental procedures.

Additionally, the level of safety can be increased by reviewing the mandatory allergy tests before conducting treatment measures, at least for sensitivity to those allergens that can cause anaphylactic shock [57]. An example of such an allergen is lidocaine, which, due to its high efficiency and speed of action, is the most common of local anaesthetics, so it is widely used in dentistry [58]. If the recommended doses are followed, lidocaine has low toxicity, which makes it safe to use, but in rare cases, it can cause an anaphylactic reaction. Zhixiang et al. [59], examining the patterns of lidocaine-induced anaphylactic shock, analysed the scientific literature until 2019 and identified 191 cases of this reaction. Notably, only 29.8% of people who developed anaphylaxis had a history of allergies. The mortality rate was 14.1% and correlated with the time of onset of the attack and the method of anaesthesia. These results show that the majority of patients were not informed about the presence of sensitisation to anaesthetics or other medications. This fact can serve as an additional argument in favour of introducing allergy testing before performing procedures using local anaesthesia, even for those patients who have not reported allergic reactions in the past [60].

Given the frequency of interaction of dentists with lidocaine as a potential allergen, it can be considered that they are at risk of developing allergic reactions to this drug. Janas-Nase and Osica [61] analysed the incidence of lidocaine allergy in dentists by evaluating a group of 100 doctors who experienced anaphylaxis-like adverse reactions after local anaesthesia. According to the results of tests, lidocaine allergy was detected in 17% of the study participants, 13% were diagnosed with Type I hypersensitivity, 4% were diagnosed with delayed-type allergy (IgE-independent), and no anaphylactic shock reactions were recorded in this group. These data indicate that allergic reactions to lidocaine are quite common among dentists, but given that they receive a substantially lower concentration of the drug during work than patients, which is also due to the allergen entering the body, the risk of anaphylaxis is slightly lower. It can be agreed with the recommendations of researchers regarding the importance of testing dentists for sensitisation to the most common potential allergens that they come into contact with during their professional activities.

In general, allergies are among the most common occupational diseases of dentists. Japundžić and Lugović-Mihić [62] investigated the frequency of skin reactions to latex in dentists and students. After analysing a survey of 444 participants, 200 of whom underwent skin spot testing, the researchers determined that 56.1% of respondents complained of skin damage, 37% reported lesions on the hands and fingers in the form of erythema, and 29% reported periodic dry skin. Of the 200 allergy samples, 7% of the participants tested positive. This percentage distribution between survey and test results may indicate that the skin manifestations reported by the study participants were mainly related to the duration of use of medical gloves, resulting in discomfort and skin damage. The authors' thesis on the importance of conducting allergy tests can be agreed with since they allow confirming or refuting suspicions of allergies and determining the best methods of therapy, depending on the true causes of skin reactions.

The main directions in the treatment of allergic reactions

are personalised treatment and a comprehensive interdisciplinary approach [63]. Both areas have high prospects, as they allow considering the individual characteristics of each patient, identifying and assessing risks, and minimising or completely eliminating the symptoms and causes of allergies. Depending on the severity and manifestations of an allergic reaction, an allergist-immunologist, dermatologist, otolaryngologist, gastroenterologist, pulmonologist, and cardiologist may be involved in its treatment [64-66]. At the research level, it is very important to involve engineers and developers whose activities are aimed at finding new and modifying existing materials to improve the characteristics of biocompatibility and hypoallergenic [67].

Adachi et al. [68] presented the most extensive plan for implementing an interdisciplinary approach, publishing a strategic plan to combat allergies until 2030. This plan is based on the Basic Law of Japan on measures against allergic diseases and provides for the implementation of the main tasks, which include providing preventive treatment, and an interdisciplinary and international approach to the search for new therapeutic methods. The main drivers of implementation of this plan in the life of researchers are: allergists, dentists, veterinarians and representatives of other medical specialities; scientists who conduct clinical research with the support of pharmaceutical companies and medical devices; manufacturers of food products, and medical and household appliances; patients, their immediate environment, and the general public [69, 70]. Notably, such a plan has not yet been presented by any of the countries. Its implementation is quite a complex and time-consuming process, but successful implementation will fully justify the resources spent since it will have a substantial impact on improving the level of individual and public health. Agreeing with the plan of Japanese authors, it is worth adding that its theoretical construction is quite universal and can be used by other countries, considering amendments formed on the basis of their own regional characteristics, as well as scientific, technical, and economic capabilities. Part of such planning can be the construction of an extended algorithm for the diagnosis and treatment of allergies in dentistry using the analysis of the mechanisms of development of allergic reactions and evaluation of the effectiveness of existing methods of their treatment conducted in this study.

Conclusions

Modern dentistry uses many materials and pharmaceuticals that may contain potential allergens. Depending on the biological mediators, there are two types of mechanisms for the development of allergic reactions – immediate-type reactions (IgE-mediated) and delayed-type reactions (cell-mediated). Immediate reactions develop within a few minutes or hours and provoke symptoms of varying intensity, including life-threatening conditions. The mechanism of development of reactions of this type is the release of a large number of inflammatory mediators (histamine, serotonin, etc.), which occurs due to the degranulation of mast cells, triggered by the binding of the allergen to specific IgE antibodies that were produced by the immune system in response to the first contact with it. Allergens that cause immediate reactions in dentistry include anaesthetics (lidocaine, articaine), antibiotics, latex, nickel, amalgam, and acrylic resins.

Delayed-type allergic reactions develop within a few days after contact with the allergen. This delay, in comparison with immediate reactions, is explained by the fact that the allergic reaction is mediated by T-lymphocytes, some of which, after recognising the allergen, turn into effector T-helpers of Type I, which secrete cytokines to stimulate the inflammatory response, and the other part – to cells that "remember" this antigen. In response to repeated contact, T-helpers activate macrophages, neutrophils, and other cells of the immune system, which in turn secrete other inflammatory mediators – interferon-gamma, tumour necrosis factor-alpha, etc. Delayed reactions in dentistry are provoked by metals in prostheses or orthodontic structures (nickel, cobalt, chromium), composite materials (methacrylic, fillers, pigments, acrylic resins, etc.), cements, gutta-percha.

The main difference between true allergies and pseudo-allergies in dentistry is the mechanism of their development – unlike allergic reactions, pseudo-allergies release inflammatory mediators, affecting mast cells with their own toxic action without the mediation of the immune system.

The main allergy treatments used in dentistry are pharmacotherapy, immunotherapy, probiotic therapy, and dental approaches. Considering the mechanisms of development of allergic reactions, the effectiveness and limitations of treatment methods, in this study, clinical recommendations for the treatment of allergic reactions were formed, which can be used in the clinical practice of dentists.

One of the main directions for continuing research in this area may be to build a theoretical treatment model that will contain clear instructions for the diagnosis and treatment of various types of allergies in dentistry. The limitations of the study were the lack of an opportunity to consider all allergens that cause allergies in dentistry due to the large amount of materials used in it.

References

1. Peres MA, Macpherson LMD, Weyant RJ, Daly B, Venturelli R, Mathur MR, Listl S, Celeste R. K, Guarnizo-Herreño CC, Kearns C, Benzian H, Allison P, Watt RG. Oral diseases: A global public health challenge. Lancet. 2019;394(10194):249–260.
2. Delgado-Pérez VJ, Patiño-Marín N, Rueda-Ibarra V, Márquez-Rodríguez S, Casanova-Rosado AJ, Casanova-Rosado JF, Acuña-González GR, López-Gómez SA, Medina-Solís CE, Maupomé G. Epidemiological and oral public health aspects of dental pain: A narrative review. Cureus. 2024;16(12):e74908.
3. Shin YH, Hwang J, Kwon R, Lee SW, Kim MS, GBD 2019 Allergic Disorders Collaborators, Shin JI, Yon DK. Global, regional, and national burden of allergic disorders and their risk factors in 204 countries and territories, from 1990 to 2019: A systematic analysis for the Global Burden of Disease Study 2019. Allergy. 2023;78:2232–2254.
4. Forkel S, Schubert S, Corvin L, Heine G, Lang CC, Oppel E, et al. Contact allergies to dental materials in patients. Br J Dermatol. 2024;190(6):895–903.
5. Reinhart JP, Stoopler ET, Crawford GH. Oral hypersensitivity reactions. Dermatol Clin. 2020;38(4):467–476.
6. Warshaw EM, Ruggiero JL, Atwater AR, DeKoven JG, Zug KA, Reeder MJ, et al. Occupational contact dermatitis in dental personnel: A retrospective analysis of the North American Contact Dermatitis Group Data, 2001 to 2018. Dermatitis. 2022;33(1):80–90.
7. Ouanounou A, Ng K, Chaban P. Adverse drug reactions in dentistry. Int Dent J. 2020;70(2):79–84.
8. Poli PP, de Miranda FV, Polo TOB, Santiago Júnior JF, Lima Neto TJ, Rios BR, et al. Titanium allergy caused by dental implants: A systematic literature review and case report. Materials. 2021;14(18):5239.
9. Stafie CS, Murariu AM. Local dental anesthesia: Patients at risk for anaphylaxis. Roman J Oral Rehab. 2020;12(4):190–192.
10. Baldo BA. Allergic and other adverse reactions to drugs used in anesthesia and surgery. Anesthesiol Perioper Sci. 2023;1(2):16.
11. Jiang S, Tang M. Allergy to local anesthetics is a rarity: Review of diagnostics and strategies for clinical management. Clin Rev Allergy Immunol. 2023;64(2):193–205.
12. Baldo BA, Pham NH. Classification and descriptions of allergic reactions to drugs. In Drug Allergy: Clin Asp, Diagn, Mechan, Struct-Activ Relationships. (pp. 17-57) 2021. Cham: Springer.
13. El Ansari YS, Kanagaratham C, Burton OT, Santos JV, Hollister BA, Lewis OL, Renz H, Oettgen HC. Allergen-specific IgA antibodies block IgE-mediated activation of mast cells and basophils. Front Immunol. 2022;13:881655.
14. Corvin L, Freitag-Wolf S, Dörfer C, Heine G. Allergies in dentistry and potential cofactors: a case-control study. Quintessence Int. 2025;56(2):162–170.
15. Zeza B, Kraja N, Disha V, Cenameri E, Bardhoshi E. Self-reported antibiotics usage, allergies and resistance of Albanian patients from a dental perspective: A preliminary questionnaire-based survey. Antibiotics. 2024; 13(11):1057.
16. Gross AE, Suda K, Zhou J, Calip GS, Rowan SA, Hershow RC, et al. Serious antibiotic-related adverse effects following unnecessary dental prophylaxis in the United States. Infect Control Hosp Epidemiol. 2021;42(1):110–112.
17. Sherman WF, Ross BJ, Ofa SA, Dowd TC, Lee OC. Latex allergy as an independent risk factor for prosthetic joint infection. Orthopedics. 2022;45(4):244-250.
18. Ngamchokwathana C, Chaiear N. Latex anaphylaxis in healthcare worker and the occupational health management perspective: A case report. SAGE Open Med Case Rep. 2023;11.
19. Hedman L, Lindberg M, Stenberg B, Rönmark E, af Klinteberg M. Self-reported nickel allergy among schoolchildren: Trends in prevalence, risk factors, and atopic comorbidity. Acta Derm Venereol. 2025;105:adv42425.
20. Al-Asmar AA, Ha Sabrah A, Abd-Raheam IM, Ismail NH, Oweis YG. Clinical evaluation of reasons for replacement of amalgam vs composite posterior restorations. Saudi Dent J. 2023;35(3):275-281.
21. Naisbitt DJ, Olsson-Brown A, Gibson A, Meng X, Ogese MO, Tailor A, et al. Immune dysregulation increases the incidence of delayed-type drug hypersensitivity reactions. Allergy. 2020;75(4):781–797.
22. Alharbi EA, Najar AA, Daghriri FA, Ali AM. Biocompatible issues related to restorative dental material-II (Adverse reactions). J Adv Med Dent Sci Res. 2024;12(3):12–20.
23. Saleh MHA, Decker AM, Kalani K, Hoang K, Mandil O, Gathalia P, Ray B, Lugogo N, Wang HL. Association between asthma and periodontitis: A case – Control analysis of risk factors, related medications, and allergic responses. J Periodont Res. 2025;60:44-54.

24. Vrbova R, Podzimek S, Himmlova L, Roubickova A, Janovska M, Janatova T, Bartos M, Vinsu A. Titanium and other metal hypersensitivity diagnosed by MELISA® test: Follow-up study. BioMed Res Int. 2021:5512091.

25. Sagana M, Kumar S. Incidence and management of allergy and hypersensitivity reactions in a dental institution. Adv Pract Nurs. 2021;6:10. Available from

26. Caliskan N, Yildirim G, Bologur H, Gungor H, Karaca Sahin M, Erbay F, et al. Local anesthetics allergy in children: Evaluation of diagnostic tests with Real-Life data. Pediatr Allergy Immunol. 2024;35(2):e14097.

27. Eraky AM, Wright A, McDonald D. Pseudo-allergies in the emergency department: A common misdiagnosis of hypersensitivity type 1 allergic reaction. Cureus. 2023;15(10):1–12.

28. Van Odijk J, Weisheit A, Arvidsson M, Miron N, Nwaru B, Ekerljung L. The use of DAO as a marker for histamine intolerance: Measurements and determinants in a large random population-based survey. Nutrients. 2023;15(13):2887.

29. Wong, K.H. and Soffer, G.K. Characteristics and prevalence of antibiotic allergies in patients with sickle cell disease: A single-center retrospective study. Am J Hematol. 2022;97:E247–E249.

30. Gudichsen JH, Bækdal EA, Mikkelsen S, Lassen AT, Jessen FB, Bindslev-Jensen C, Mortz CG. Prehospital and in-hospital treatment with adrenaline and related prognosis in anaphylaxis patients. Int Arch Allergy Immunol. 2024;185(7):678–687.

31. Chu DK, Freitag T, Marrin A, Walker TD, Avilla E, Freitag A, Spill P, Foster GA, Thabane L, Jordana M, Waserman S. Peanut oral immunotherapy with or without H1 and H2 antihistamine premedication for peanut allergy (PISCES): A placebo-controlled randomized clinical trial. J Allergy Clin Immunol Pract. 2022;10(9):2386–2394.

32. Basirat M, Kia SJ, Dadvar Z. General dentists' knowledge and practice about corticosteroid prescription. Polish Ann Med. 2019;26(2):114–119.

33. Mordini L, Patianna GP, Di Domenico GL, Natto ZS, Valente NA. The use of corticosteroids in the lateral sinus augmentation surgical procedure: A systematic review and meta-analysis. Cli Impl Dent Rel Res. 2022;24(6):776–791.

34. Wang Y, Liu Z, Zhou W, Wang J, Li R, Peng C, Jiao L, Zhang S, Liu Z, Yu Z, Sun J, Deng Q, Duan S, Tan W, Wang Y, Song L, Guo F, Zhou Z, Wang Y, Zhou L, Jiang H, Yu L. Mast cell stabilizer, an anti-allergic drug, reduces ventricular arrhythmia risk via modulation of neuroimmune interaction. Basic Res Cardiol. 2024;119:75–79.

35. Smith BRE, Reid Black K, Bermingham M, Agah S, Glesner J, Versteeg SA, van Ree R, Pena-Amelunxen G, Aglas L, Smith SA, Pomés A, Chapman MD. Unique allergen-specific human IgE monoclonal antibodies derived from patients with allergic disease. Front Allergy. 2023;4:1270326.

36. Rathi A, Khaire RA, Rathi VL. A prospective, interventional, randomized, double-blinded, placebo-controlled, monocentric clinical study to evaluate the efficacy and safety of *Alkalihalobacillus clausii* 088AE in resolution of acute allergic rhinitis symptoms. Glob Adv Health Med. 2025;14.

37. Björkman L. Adverse reactions to dental biomaterials: Experiences from a specialty clinic. Dent Mater. 2024;40(3):563–572.

38. Li Q, Shi X, Lu X, Wang L, Zhu Y, Chen B, Sun H, Lan M. Incidence of, and factors associated with, oral mucous membrane medical device-related pressure injury in critically ill patients with orotracheal intubation: a prospective cohort study. BMJ Open. 2025;15(6):e098114.

39. De Castro RD. Drug hypersensitivity associated with dental treatments. Pesqui Bras Odontopediatria Clín Integr. 2024;24.

40. Di Gioacchino M, Di Giampaolo L, Mangifesta R, Gangemi S, Petrarca C. Exposure to nanoparticles and occupational allergy. Curr Opin Allergy Clin Immunol. 2022;22(2):55–63.

41. Tanwar N, Prakash C, Chaudhary K, Tewari S, Bhagavatheeswaran S. Titanium allergy in dentistry: A new allergen in rapidly evolving implant dentistry. Contemp Clin Dent. 2021;12(3):317–320.

42. Rhyou HI, Nam YH, Park HS. Emerging biomarkers beyond leukotrienes for the management of nonsteroidal anti-inflammatory drug (NSAID)-exacerbated respiratory disease. Allergy Asthma Immunol Res. 2022;14(2):153-167.

43. Zemelka-Wiacek M, Agache I, Akdis CA, Akdis M, Casale TB, Dramburg S, Jahnz-Różyk K, Kosowska A, Matricardi PM, Pfaar O, Shamji MH, Jutel M. Hot topics in allergen immunotherapy, 2023: Current status and future perspective. Allergy. 2024;79:823–842.

44. Mohseni P, Soufi A, Chrcanovic BR. Clinical outcomes of zirconia implants: A systematic review and meta-analysis. Clin Oral Investig. 2023;28(1):15.

45. Ouldyerou A, Merdji A, Aminallah L, Roy S, Mehboob H, Özcan M. Biomechanical performance of Ti-PEEK dental implants in bone: An in-silico analysis. J Mech Behav Biomed Mater. 2022;134:105422.
46. Singh S, Kulkarni G, Kumar RSM, Jain R, Lokhande AM, Sitlaney TK, Ansari MHF, Agarwal NS. Comparative evaluation of the biological response of conventional and resin modified glass ionomer cement on human cells: A systematic review. Restor Dent Endod. 2024;49(4):e41.
47. Šimková M, Tichý A, Dušková M, Bradna P. Dental composites – A low-dose source of bisphenol A? Physiol. Res. 2020;69(Suppl. 2):S295–S304.
48. Logvynenko I, Dakhno L, Bursova V. Effectiveness of topical application with dexamethasone during sagittal split osteotomy of the mandible in minimising clinical symptoms of postoperative neurosensory disorders. BMC Surg. 2025;25(1):76.
49. Logvynenko I, Bursova V. Inferior alveolar nerve injury after sagittal split osteotomy of the mandible: A literature review. Chinese J Plast Reconstr Surg. 2024;6(4):219–227.
50. Missori P, Marruzzo D, Paolini S, Seferi A, Fricia M, Chiara M, et al. Autologous Skull Bone Flap Sterilization after Decompressive Craniectomy: An Update. World Neurosurg. 2016;90:478–483.
51. Tramontana M, Hansel K, Bianchi L, Sensini C, Malatesta N, Stingeni L. Advancing the understanding of allergic contact dermatitis: From pathophysiology to novel therapeutic approaches. Front. Med. 2023;10:1184289.
52. AAE Position Statement: AAE Guidance on the Use of Systemic Antibiotics in Endodontics. J Endod. 2017;43(9):1409–1413.
53. Bogoyavlenskiy A, Zaitseva I, Alexyuk P, Alexyuk M, Omirtaeva E, Manakbayeva A, et al. Naturally Occurring Isorhamnetin Glycosides as Potential Agents Against Influenza Viruses: Antiviral and Molecular Docking Studies. ACS Omega 2023;8(50):48499–48514.
54. Bogoyavlenskiy A, Alexyuk M, Alexyuk P, Berezin V, Almalki FA, Ben Hadda T, et al. Computer Analysis of the Inhibition of ACE2 by Flavonoids and Identification of Their Potential Antiviral Pharmacophore Site. Mol. 2023;28(9):3766.
55. Nabiyev E, Baizakov A, Kashikova K, Askerov R, Argynbayev Z, Bissaliyev B. A New Approach to Arthroscopic Stitching of the Knee Joint Meniscus: A Mathematical Justification. Med J Islam Repub Iran 2023;37(1):108.
56. Smereka J, Aluchna M, Aluchna A, Szarpak Ł. Preparedness and attitudes towards medical emergencies in the dental office among Polish dentists. Int Dent J. 2019;69(4):321–328.
57. Karłowicz K, Lewandowski K, Tulewicz-Marti E, Maciejewska K, Tworek A, Stępień-Wrochna B, et al. SARS-CoV-2 vaccination in inflammatory bowel disease (IBD) patients – does treatment for IBD negatively affect SARS-CoV-2 antibodies? A single-centre, prospective study. Przegl Gastroenterol. 2024;19(2):198–205.
58. Dovramadjiev T, Pavlova D, Filchev R, Dimova R, Dimov D, Kavaldzhieva K, et al. Technological and Human Approach in Complete Restoration of the Dental Teeth Jaws with Biocompatible Materials. Lect Notes Networks Syst. 2023;645 LNNS:497–506.
59. Zhu Z, Yang J, Dai Y. Literature analysis of 191 cases of anaphylactic shock induced by lidocaine. Chin J Pharmacovigilance. 2022;19(2):210–212.
60. Kimatova K, Yermukhanova L, Talarska D, Dworacka M, Sultanova G, Sarsenbayeva G, et al. Needs of older adults in Kazakhstan: analysis and psychometric properties of the localized version of the EASYCare standard 2010 instrument. Front Pub Health 2025;13:1487827.
61. Janas-Naze A, Osica P. The incidence of lidocaine allergy in dentists: an evaluation of 100 general dental practitioners. Int J Occupat Med Environ Health 2019;32(3):333–339.
62. Japundžić I, Lugović-Mihić L. Skin reactions to latex in dental professionals – First Croatian data. Int J Occup Saf Ergon. 2019;25(3):423–428.
63. Yermukhanova LS, Urazaeva S, Artukbaeva M, Azhenova K, Almakhanova M, Zhaubassova A, et al. Determination of the air pollution index of atmospheric air in Aktobe. Annals Tropic Med Pub Health 2017;10(3):664–666.
64. Arapbaevna KZ, Ardak A, Abzhanovna AG, Bahitkerevna DA, Uringalievna BA, Izbasarovna KE, et al. Modern diagnostic approaches for early detection of antiphospholipid syndrome. Archiv Venezol Farmacol Terapeut. 2021;40(2):178–186.
65. Dyba M, Berezenko V, Zabara D, Bezpala A, Donskoi B. Monocyte subpopulations in children with autoimmune liver disease. Pathol, Res Pract. 2024;263:155622.
66. Matyushin N, Ermakov D, Vasileva I, Vakolyuk R, Spaska A. Investigating kidney function changes in young adults with COVID-19: Serum creatinine level, glomerular filtration rate, and biochemical profile analysis. Electron J Gen Med. 2023;20(6):em547.
67. Ilderbayev OZ, Zharmakhanova GM, Okassova AK, Nursafina AZ, Ilderbayeva GO. Comparison of the performance of lipoperoxidation-antioxidant

protection system in rats at different periods under immobilization stress effects. Med J Islam Repub Iran 2021;35(1): 1–6.

68. Adachi T, Kainuma K, Asano K, Amagai M, Arai H, Ishii KJ, et al. Strategic Outlook toward 2030: Japan's research for allergy and immunology-Secondary publication. Allergol Int. 2020;69(4):561–570.
69. Ilderbayeva G, Utegenova A, Ilderbayev O, Sembaeva Z, Askarova G. Assessment of the Combined Effects of Heavy Metal Cobalt and Sublethal Radiation on the Immune System. Biomed Biotech Res J. 2024;8(4):455–463.
70. Ilderbayeva G, Rakhyzhanova S, Utegenova A, Salkhozhayeva G, Ilderbayev O. Combined Effect of Gamma Radiation and Heavy Metals on Some Living Organisms. Biol Trace Elem Res. 2024;203(3):1764-1775.