EURASIAN HEALTH JOURNAL

Volume 18, No. 1. P. 145-156
Journal homepage: https://health-ksma.com/en
ISSN 1694-8882 / e-ISSN 1694-8890

UDC 612.017.3: 669: 616.31: 616.31-07
DOI: 10.54890/1694-8882-2026-1-145

Received: 11.09.2025; Revised: 24.12.2025;
Accepted: 27.02.2026; Published: 31.03.2026

Delayed-type hypersensitivity to metals in dentistry: Modern approaches to diagnostics (literature review)

Sofya Khostelidi*
Doctor of Medical Sciences, Professor
North-Western State Medical University named after I.I. Mechnikov
195067, 41 Kirochnaya Str., Saint Petersburg, Russian Federation
https://orcid.org/0000-0001-5794-5396

Marina Elicheva
Postgraduate Student
North-Western State Medical University named after I.I. Mechnikov
195067, 41 Kirochnaya Str., Saint Petersburg, Russian Federation
https://orcid.org/0009-0004-2901-3013

Ekaterina Burygina
PhD in Medical Sciences, Associate Professor
North-Western State Medical University named after I.I. Mechnikov
195067, 41 Kirochnaya Str., Saint Petersburg, Russian Federation
https://orcid.org/0000-0002-9307-4927

Arailym Abilbayeva
PhD, Associate Professor
Kazakh National Medical University named after S.D. Asfendiyarov
050012, Tole bi Str., 94, Almaty, Republic of Kazakhstan
https://orcid.org/0000-0001-5081-5492

Alexey Silin
Doctor of Medical Sciences, Professor
North-Western State Medical University named after I.I. Mechnikov
195067, 41 Kirochnaya Str., Saint Petersburg, Russian Federation
https://orcid.org/0000-0002-3533-5615

Abstract. Delayed-type metal hypersensitivity, according to the current classification, is classified as subtype IVa. With the introduction of new dental devices, the number of patients with intolerance to metal alloys has increased. The aim of this study was to identify the pathogenesis and clinical manifestations, the main risk factors for the development of delayed-type hypersensitivity to metal structural components, and optimal diagnostic methods in patients in dental practice. A search was conducted on PubMed and e-library (as of February 2026) using the following keywords: adverse effects of dental alloys, skin patch testing, contact allergy to metals, dental materials, allergic reactions, lichenoid reaction. Forty-seven scholarly sources were analysed using bibliographic search, source selection and screening, comparative analysis, and data synthesis. Various diagnostic methods are used to identify these hypersensitivity reactions. A literature review showed that patch testing is the most informative diagnostic method for detecting hypersensitivity reactions to metals used in the fabrication of dental restorations and denture components. They allow for the identification and confirmation of the involvement of a specific causative factor in the development of clinical symptoms in a patient. Delayed-type hypersensitivity is most common to metals such as nickel, cobalt, and chromium. A similar mechanism of hypersensitivity to nickel is recorded in 17% of women and 3% of men, while hypersensitivity to cobalt and chromium is reported in 1-3% of both sexes. An increase in delayed-type hypersensitivity to other metals, such as aluminum, beryllium, copper, gold, iridium, mercury, palladium, platinum, rhodium, and titanium, has also been observed. Patients with immune-mediated pathologies are at high risk for developing delayed-type metal hypersensitivity

Keywords: side effects of dental alloys; skin patch tests; contact allergy to metals; dental materials; allergic reactions; lichenoid reaction

Khostelidi S, Elicheva M, Burygina E, Abilbayeva A, Silin A. Delayed-type hypersensitivity to metals in dentistry: Modern approaches to diagnostics (literature review). Eurasian Health J. 2025;18(1):145-56. DOI: 10.54890/1694-8882-2026-1-145

*Corresponding author (sofianic@mail.ru)

Introduction

Metal implants are widely used in modern dentistry, but they are not biologically inert and can provoke allergic reactions in susceptible patients. Delayed-type hypersensitivity (DTH) to metals is an immune-mediated response involving T lymphocytes that react to specific metal allergens in dental materials and implants. The most common metals associated with DTH include nickel, palladium, titanium, cobalt, and mercury. Allergic reactions to dental alloys may present as localised skin lesions, oral ulcerations, or, rarely, systemic symptoms. Hypersensitivity to metals can significantly reduce a patient's quality of life and result in economic losses. Despite the growing prevalence of this issue, diagnosing DTH to metals remains challenging in dental practice. Key questions persist regarding risk factors, prevention strategies, optimal diagnostic methods, and their standardisation and accessibility. This narrative review examines the pathogenesis and clinical manifestations of delayed-type hypersensitivity to metal dental structures, as well as the optimal diagnostic methods for dental practice.

Research conducted between 2020 and 2026 has significantly advanced the understanding of hypersensitivity reactions to dental prosthetic materials. A. Swalsky *et al*. [1] demonstrated that titanium-based structures can modulate the production of cellular immune mediators responsible for type I and IV hypersensitivity, thereby accelerating corrosion, promoting osteolysis, and increasing the risk of implant failure. Their findings indicated that titanium particles affect various tissues, triggering inflammatory manifestations. The study also explored zirconium dioxide as a potential alternative implant material and underscored the critical need to identify the expected type of immune response to metals for selecting a material that minimises adverse effects. Challenging the historical perception of titanium as inert, P.P. Poli *et al*. [2] reported in 2021 that hypersensitivity reactions to titanium can indeed occur and contribute to implant failure. They concluded that although such reactions are rare, they should not be underestimated and require early recognition and diagnosis to mitigate the risk of complications.

Earlier research established the efficacy of diagnostic methods and characterised hypersensitivity profiles. C. Olms *et al*. [3] confirmed patch testing as an effective diagnostic tool, detecting hypersensitivity reactions in dental patients with the following frequency: nickel (29%), cobalt (23%), palladium (13%), mercury/amalgam (11%), gold (6%), and titanium (3%). F. Di Spirito *et al*. [4] provided a comprehensive analysis of oral, perioral, and systemic hypersensitivity reactions in patients with orthodontic appliances, detailing their epidemiology, macroscopic and microscopic features, metal allergy testing, clinical consequences, and treatment strategies. The authors concluded that fixed orthodontic appliances pose a higher risk of oral hypersensitivity reactions than removable ones due to prolonged mucosal contact, confirmed nickel as a prevalent allergen, and affirmed that diagnostic tests like patch testing are indispensable for managing such reactions. They emphasised that early identification and elimination of the allergen, combined with effective pharmacological and non-pharmacological treatment, can lead to complete symptom resolution and relapse prevention. Addressing a different causative mechanism, N. Chepelova *et al*. [5] systematically compared the damaging effects of galvanism using an in vitro mucosal model based on the HaCaT keratinocyte cell line. Their study highlighted factors key to adverse effects from dental alloys and urged clinicians to pay greater attention to preventive measures that minimise the risk of galvanic coupling and electrical current exposure. The data on potential differences between common alloys presented in this study serve as a valuable reference for treatment planning and material selection.

More recent investigations have refined the clinical and demographic profiles of sensitisation. In a 2024 study, S. Forkel *et al*. [6] analysed sensitisation patterns in patients with suspected contact allergy to dental materials. The cohort was predominantly female (81.2%) and aged ≥40 years (92.8%). Among women with confirmed allergic contact stomatitis (n = 444), the highest sensitisation rates were to metals – nickel (28.6%), palladium (21.4%), and amalgam (10.9%) – followed by (meth) acrylates (4.8%), propolis (6.8%), and Peruvian balsam (11.4%). Allergic contact stomatitis was diagnosed in a smaller number of men (n = 68), among whom amalgam showed the highest sensitisation rate (13.6%). The authors reinforced the necessity of skin allergy testing to reduce the risk of hypersensitivity. In a parallel study assessing the frequency and clinical significance of contact allergy in patients with intraoral and perioral symptoms, M. Al-Gawahiri *et al*. [7] found that 285 patients (79.2%) had a positive patch test reaction to at least one allergen. Sodium tetrachloropalladate was the most common sensitiser (27.2%), followed by nickel sulfate (23.3%). Clinical significance, defined as a patch test reaction relevant to the patient's (peri)oral complaints, was established in 32.7% of patients. The authors concluded that testing with a dental patch test series is crucial for patients presenting with such symptoms. Despite significant research progress, key questions remain regarding optimal diagnostic methods, novel risk factors for allergic reactions, and the development of comprehensive prevention guidelines for dental practice. This review aimed to synthesise the literature on the pathogenesis and clinical manifestations of delayed-type hypersensitivity to metal dental structures and to identify the most effective diagnostic methods for application in clinical dental practice.

Materials and Methods

The methodological framework of this study is grounded in the principles of systemic analysis, synthesis, and the critical appraisal of contemporary scientific literature indexed in major international and national scientometric databases, specifically Scopus, MEDLINE/PubMed, Web of Science, and the e-library registry. To ensure the highest degree of relevance and scientific rigor, a comprehensive search for primary publications was conducted through February 2026. The search strategy employed an expanded set of keywords, including terms such as "hypersensitivity", "intolerance reaction", "delayed-type hypersensitivity (DTH)", "orthodontic materials", "dental crowns", "prosthetic metal structures", "implants", "adverse effects of dental alloys", "skin patch tests", "corrosion of metals", and "contact allergy to metals".

The initial search phase identified a total of 890 sources related to metal hypersensitivity and diagnostic challenges in prosthetic dentistry. To ensure data integrity and eliminate redundancy, a multi-stage deduplication procedure was implemented. This involved an initial automated screening using the specialised bibliographic management software EndNote, which was subsequently followed by a meticulous manual cross-verification by two independent researchers. During this rigorous process, 157 duplicates were identified and removed, resulting in a refined dataset of 733 unique records for preliminary analysis.

The subsequent selection process was governed by predefined and stringent inclusion and exclusion criteria designed to minimise the risk of selection bias and ensure the validity of the findings. The exclusion criteria specifically targeted clinical case reports due to their limited generalisability, preprints, gray literature, and conference proceedings that had not undergone formal external peer review. Primary emphasis was placed on high-quality full-text analytical reviews, systematic reviews, and original longitudinal clinical studies published in high-impact journals. Following an initial screening of titles and abstracts, 530 records were evaluated, of which 483 were excluded for failing to meet the thematic or methodological standards of the study. Consequently, 47 full-text publications were admitted for comprehensive qualitative and quantitative review.

A complex array of analytical methods was applied during the evaluation of the selected material. The method of theoretical systematisation was utilised to categorise dental alloys based on their chemical composition and electrochemical properties. Comparative analysis was employed to evaluate the diagnostic sensitivity and specificity of various clinical protocols, such as patch testing, the lymphocyte transformation test (LTT), and the Memory Lymphocyte Immunostimulation Assay (MELISA). Furthermore, descriptive analysis was applied to structure epidemiological data, including patient demographics, gender distribution, allergic history, and common comorbidities. The quality of the included studies was appraised based on the level of evidence, study design, and statistical reliability. The final stage involved the synthesis of pathogenetic models of type IV hypersensitivity reactions, enabling the integration of clinical signs with advanced diagnostic outcomes to formulate evidence-based recommendations for the management of patients in prosthetic dentistry.

Epidemiology and risk factors of metal hypersensitivity

Over the past 20 years, the prevalence of dental metal structures in patients has increased. For example, in the United States, the percentage of patients with at least one dental implant rose from 0.7% to 5.7% between 2000 and 2016. Experts estimate that by 2026, the proportion of people with dental implants could reach 23%. Similarly, the use of fixed orthodontic appliances is expected to grow [4,8]. With the introduction of new dental materials, the number of patients intolerant to metal alloys has increased [3,6,7]. The incidence of these reactions is 1 case per 700-2600 dental procedures in clinical practice [9]. The high-risk group includes patients with immune-mediated diseases, as well as a history of metal hypersensitivity [10-11]. J.P. Thyssen & T. Menné [10] reviewed changes in the epidemiology of dental materials in Europe and the USA. They noted that nickel use is regulated in Europe, resulting in a recent decline in nickel hypersensitivity cases. E. Valentine-Thon & H.W. Schiwara [12] studied the MELISA diagnostic method and confirmed that nickel remains the most common cause of hypersensitivity. They also identified hypersensitivity to titanium (42%), cadmium (18%), gold (17%), palladium (13%), lead (11%), and beryllium (9%), findings supported by G. Forte *et al*. [11]. Subsequent research examined immunological responses involving both innate immune cells and adaptive immune responses with T cells [13-14].

Metals such as cobalt, chromium, molybdenum, titanium, and their alloys are widely used in modern implantology, prosthetics, and orthodontics. Materials used in dentistry differ in their physical, chemical, and mechanical properties. All are biocompatible and suitable for creating prosthetic structures, as well as safe for use on patients. Metals are used in the manufacture of artificial crowns and bridges, prefabricated posts and cast inserts removable partial dentures and dental implants, as well as fixed orthodontic appliances. In their study, M. Arakelyan *et al*. [8] reviewed the potential side effects of metal orthodontic appliances, identified risk factors that worsen these effects, and provided recommendations for diagnosis, treatment, and prevention. They concluded that side effects from dental alloys remain a significant concern due to the widespread use of metal appliances in dentistry. Understanding the mechanisms and risk factors behind these side effects is

essential for developing effective treatment plans and patient recommendations. Metals represent an important class of substances that cause hypersensitivity. These materials are widely distributed in the environment, typically found in soil, food, and water. Metals are used in industrial production and are present in consumer products. Examples include jewellery, cosmetics, paints, leather, prosthetics and implants, household goods, dyes, personal adornments, and pharmaceuticals. The industrialisation and modern lifestyles throughout the 20th century have led to increased exposure to these metals, which, in turn, has increased the risk of developing delayed-type metal hypersensitivity.

Delayed-type metal hypersensitivity is primarily caused by prolonged or repeated skin exposure to consumer items such as jewellery, mobile phones, clothing fasteners (such as zippers, buckles, and hooks), textiles, and leather goods treated with metals. In Europe, North America, and Scandinavia, a significant share of metal-induced dermal toxicity results from occupational exposure in the metallurgy and construction industries [9]. In Europe, the prevalence of allergic contact dermatitis to nickel, chromium, and cobalt was approximately 20%, 4%, and 7%, respectively (data from the European Surveillance System for Contact Allergies, ESSCA) [15].

According to J.M. Baló-Banga *et al*. [16], outbreaks of SARS-CoV-2 infection have led to significant changes in the health status and herd immunity of populations within countries or even small geographic regions. This study retrospectively assessed allergy testing to dental prosthetic materials using an in vivo type IV cellular immune assay – skin tests. The study found a significant increase in positive reactions to chromium, gold thiosulfate, nickel sulfate, and palladium chloride, rising from 8% to 39%. Based on the study's results, the researchers concluded that a significant increase in cellular hypersensitivity and polysensitivity to dental materials, particularly metals, was observed during the COVID-19 pandemic. The authors attribute the rise in metal hypersensitivity to humoral changes following SARS-CoV-2 infection, including a "bradykinin storm" in severe cases. Vaccinations and the increase in post-COVID syndrome cases have also significantly affected the population's immune system. There are no data on the prevalence of contact allergies to metals in Russia.

According to research by B.L. Schwartz *et al*. [17], women suffer from nickel- and cobalt-associated allergic contact dermatitis more often than men due to piercings and jewelry, while chromium-associated allergic contact dermatitis predominantly affects men due to occupational activities in the construction and metallurgy industries. Recently, an increase in allergic contact dermatitis to other metals has been observed, including aluminum, beryllium, copper, gold, iridium, mercury, palladium, platinum, rhodium, and titanium [1,2,17]. Patients with concomitant allergic diseases (bronchial asthma, eczema, allergic rhinitis) have an increased risk of allergic reactions to metal dental structures. Also, important risk factors include a history of previous reactions to dental prosthetic materials and occupational factors for medical personnel (long-term exposure to metals) [17-18]. Current epidemiological data show a steady increase in metal hypersensitivity among dental patients. Key triggers include denture material, especially base alloys; duration of use; allergy history; and existing somatic conditions.

Pathogenesis of delayed-type hypersensitivity to metals

The pathogenesis of metal hypersensitivity can be associated with different types of reactions according to the Gell and Coombs classification, but the most common is type IV, which manifests as chronic inflammation with lymphoid infiltration. According to the updated classification of the European Academy of Allergy and Immunology (EAACI) [18], this type of reaction, associated with the dominant participation of T-cytotoxic lymphocytes, is classified as subtype IVa (EAACI-2023 nomenclature). Clinically, delayed-type reactions manifest as contact dermatitis, eczema, or lichenoid reactions in the oral cavity at sites of contact with the oral mucosa. M.Z. Lisiecka *et al*. [19] report that the installation of metal dental structures leads to continuous exposure of the body to metal. The pathogenetic mechanisms of hypersensitivity are supported by oxidative processes in the oral cavity, followed by the release of metal ions into tissues. The released ions, which are haptens by nature, can form complexes with endogenous proteins, thereby activating the immune system, inducing a local inflammatory response, and even damaging bone structures. Possible implant loosening due to aseptic osteolysis should be considered. It is linked to a local inflammatory response to wear and corrosion products on the implant's mating surfaces. The immune response to implant particles primarily involves local activation of macrophages. Soluble and insoluble particles from cobalt-chromium-molybdenum alloys can activate monocytes and macrophages, leading to the secretion of proinflammatory cytokines such as IL-1beta, TNF-alpha, IL-6, and IL-8. This occurs through increased NF-κB transcription factor expression and activation of the inflammasome in human macrophages. Local and systemic inflammation not only reduces osteoblast function but also increases osteoclast activity [20-21]. Ions can be detected in the tissues surrounding the crown or implant, as well as in the lymph nodes.

Oral mucosal biopsies from patients with suspected hypersensitivity to metal implants reveal perivascular lymphocytic infiltrates characteristic of DTH. These reactions are typically dominated by Th1 cells, but eosinophils are also observed, indicating the involvement of Th2 cells. Osteolysis, metal ion release, and implant loosening are interrelated processes. Metal ions stimulate

chemokine secretion, thereby attracting osteoclast precursors and leading to osteolytic lesions and implant destabilisation [22]. The pathogenesis of metal allergy involves sensitisation and an effector phase, each of which requires activation of both innate and adaptive immunity. Sensitisation begins with the first contact of the oral mucosa with an allergen, which can be captured by Langerhans cells. The irritant action of chemical agents creates an inflammatory environment, leading to the maturation of dendritic cells and their migration to the lymph nodes, where they present antigenic epitopes to T cells. Activated T cells differentiate into effector cells and resident memory cells. The authors note that nickel-specific T-cell clones may cross-react with palladium. This cross-reactivity in CD4+ T-cells occurs less frequently with cobalt. F. Riedel *et al*. [20] emphasise that understanding these responses is important when selecting implant materials. This may also affect regulations on metal content in consumer products.

That activation of the innate immune system plays a key role in the development of metal hypersensitivity. Two main mechanisms have been identified: 1) functional mimicry of pathogen-associated molecular patterns (PAMPs), leading to the activation of innate immune receptors via haptens [20]; 2) the reaction of haptens with extracellular matrix components, which triggers the release of damage-associated molecular patterns, which activate innate immune receptors [23]. Nickel and cobalt are examples of functional mimicry of PAMPs, as they interact with histidine residues of Toll-like receptor 4 (TLR4), leading to its dimerisation and activation of proinflammatory signaling pathways such as IKK2/NF-κB. This induces the production of key proinflammatory cytokines such as TNFα and interleukin-8. A similar mechanism is likely to apply to palladium, although the precise details of its interaction with TLR4 require further study [24]. In addition, patients with clinical manifestations of metal hypersensitivity exhibit changes in mucosal immunity, with a significant decrease in the levels of secretory and serum IgA and lysozyme in saliva [25].

The adaptive immune response induced by metals is primarily mediated by CD8+ T cells, which produce interferon-γ and play a key role in the development of contact hypersensitivity [18]. CD4+ T cells are capable of performing a regulatory function by suppressing the immune response through the secretion of IL-4, IL-5, and IL-10 [20]. However, depending on the type of metal, other T cell subtypes, such as Th1, Th17, Th22, and Th9, may also predominate. For example, nickel causes strong activation of the innate immune system and the induction of a Th1/Th17/Th22 response, whereas cobalt and chromium preferentially stimulate Th17 [26]. When a sensitised individual is re-exposed to an allergen or cross-reactive substance, memory T cells initiate a rapid and aggressive secondary immune response, resulting in an inflammatory reaction at the site of allergen contact. In a sensitised organism, dendritic cells, macrophages, Langerhans cells, or keratinocytes capture haptens and present them to effector T cells and resident memory T cells formed during the sensitisation phase. T cell infiltration into tissue begins approximately 24 hours after contact with the allergen (delayed hypersensitivity) and is triggered by chemokines and alarmins released by epithelial and other cells. Regulatory T cells are also involved in the allergic reaction to metals, but their role is poorly understood. Metal ions can accumulate in the lysosomes of macrophages, which can also lead to type IV hypersensitivity reactions [20].

C. Lohmann *et al*. [27] study demonstration – there are two main types of tissue responses to the released ions: non-specific granulomatous responses mediated by macrophages and lymphocytic responses dominated by cytokine-releasing T-lymphocytes. Tissue responses are described according to the predominant cellular response as either a macrophage-dominant type or a lymphocyte-dominant type describing a T-lymphocyte response. Various inflammatory mediators may be involved: cytokines (IL-1, IL-2, IL-4, IL-5, IL-6, IL-10, IL-13, IL-17 and IFN-γ), chemokines (MIP-1α and MIP-1β) and growth factors (GM-CSF and FDGF). An exception is nickel, which is considered the main cause of contact dermatitis. It is capable of activating T-lymphocytes by interacting with molecules of the major histocompatibility complex and the T-cell receptor.

Also noteworthy are pseudoallergic reactions that develop without the involvement of immunological mechanisms, directly under the action of the drug or its metabolites, which cause the direct release of inflammatory mediators such as histamine, bradykinin, and leukotrienes. The clinical manifestations of pseudoallergic reactions are comparable to IgE-mediated reactions, but there is no sensitisation of the body to the corresponding allergen. M. Zemelka-Wiącek [28] outlined current methods for assessing metal exposure, diagnostics, mechanisms, biomarkers, and the clinical effects of metal implants. C.T. Rodrigues Neves *et al*. [29] investigated whether titanium salts irritate or sensitise a reconstructed human skin model with Langerhans cells. In this model, exposure to a titanium salt induced Langerhans cell migration from the epidermis. This process was linked to CCL5 and increased IL-10 mRNA levels, with no changes in IL-1β or CCR7. The researchers concluded that titanium implants may induce inflammation and cytotoxicity through local irritation and corrosion, rather than metal hypersensitivity. These findings indicate that symptoms associated with titanium implants are likely due to localised inflammation from irritants, rather than an allergic reaction to titanium.

The corresponding immune response may develop in the form of local conditions, such as a lichenoid reaction,

or may exacerbate autoimmune diseases affecting the joints, skin, and salivary glands. Metal ions entering the gastrointestinal tract with saliva can also potentially accumulate in various tissues and organs. However, the systemic toxicity of dental alloys is questionable, as the daily intake of metal ions from dental structures is well below the toxicity threshold [30]. In addition to immune reactions, some metals can have toxic or irritant effects, thereby initiating inflammatory reactions [15]. Another important issue is galvanic current, which can occur when dissimilar metals are present in the oral cavity, with saliva serving as the electrolyte. Chronic electrical trauma to the oral mucosa is a risk factor for various mucosal lesions, including malignant lesions such as leukoplakia and oral lichen planus [5,8]. Galvanic corrosion of metal structures leads to persistent, long-term sensitisation and increases the risk of hypersensitivity. In addition to non-precious alloys such as nickel, chromium, and cobalt, noble alloys are also used in the fabrication of indirect restorations, including inlays, onlays, and posts. When noble and non-precious metals are used together, electrochemical reactions can occur, leading to the release of metal ions. This release significantly increases the concentration of allergens and exacerbates allergic reactions in sensitised patients, which requires further research and consideration in dental practice [25,28]. However, in the oral cavity, it is difficult to identify the leading mechanism of pathogenesis, since a synergistic effect of several factors can be observed.

Main clinical manifestations

Metal hypersensitivity reactions can manifest as localised inflammatory symptoms, lichenoid reactions (white spots resembling lichen planus), metallic pigmentation, and oral mucosal erosion [31]. Patients with metal hypersensitivity also experience contact allergic dermatitis when exposed to metal-containing substances, such as those found in cosmetics or jewelry. Delayed bone healing, instability, and implant rejection are also observed [17]. Clinical delayed-type hypersensitivity reactions may manifest as localised contact dermatitis at the site of antigen contact with the skin or as systemic contact dermatitis, in which the antigen spreads throughout the body via the bloodstream in sensitised individuals, causing lesions in distant skin areas. The main clinical manifestations of metal hypersensitivity include contact dermatitis and mucositis localised at the site of contact with the metal, as well as eczema-like reactions and palmoplantar pustulosis occurring at distant sites [32].

The main clinical manifestations of metal hypersensitivity are divided into local and systemic. The most common local symptoms are the following: A burning sensation in the mouth, without any visible damage to the oral mucosa. According to M. Arakelyan *et al*. [8] a burning sensation was observed in 17% to 33% of patients with metal restorations in the oral cavity. It should be noted that burning mouth syndrome can occur in patients with vitamin deficiency, hormonal changes associated with menopause, local oral infections, xerostomia, denture-related lesions, allergies, and systemic diseases, including diabetes. Oral lichen planus and lichenoid reaction, which manifest as multiple white papules merging into a characteristic Wickham's network. These conditions occur with a frequency of 12% to 78% among patients with metal structures in the oral cavity. These reactions are precancerous lesions. Pigmentation of the oral mucosa, which appears as a dark spot on the mucous membrane next to the metal structure (more often in contact with amalgam and silver-containing alloys). Leukoplakia is characterised by the appearance of areas of increased keratinisation on the mucous membrane. The prevalence of leukoplakia ranges from 0.5% to 3.4% and is most common in people over 50 years of age. The incidence of malignant transformation ranges from 0.1% to 17%. Erosive and ulcerative lesions, which mainly manifest as recurrent aphthous stomatitis.

In a large Japanese study by M. Kitagawa *et al*. [33] 44% of patients with suspected metal allergy had positive patch tests, and over 42% experienced clinical symptoms such as stomatitis, gingivitis, and pustulosis of the palms and soles. Nonspecific symptoms such as burning in the mouth, metallic taste, and dry mouth may also be associated with hypersensitivity. Systemic symptoms include muscle and joint pain, memory problems, ear/throat/nose complaints, and fatigue. Implant removal often results in improvement, although conservative treatments are also effective in some cases.

In their study, Y. Hiroyasu *et al*. [34] described a clinical case of gradual improvement in a patient with allergic contact dermatitis, which began after the removal of allergenic metal structures from the oral cavity. The authors also noted that previous studies conducted by dermatologists have shown that approximately 80% of patients who had dentures containing allergenic metals removed experienced significant improvement after removal. A.R. Alqahtani *et al*. [35] report a clinical case where a patient developed acute pain, eczema, mild soft tissue swelling, and a severe burning sensation in the mouth and face within four days after titanium dental implant surgery. The patient had a history of allergic contact dermatitis to metal earrings. Given the pronounced clinical manifestations and a history of metal allergy, the dental implant was removed. Immediately after implant removal, a decrease in swelling and burning sensation was noted, and full recovery occurred within three weeks. M. Zigante *et al*. [32] demonstration – the prevalence of allergic sensitisation to nickel and titanium was 16%. Symptoms associated with hypersensitivity included hypogeusia, hyposmia, swelling of the tongue or face, and lacrimation. Metal

ions released from dental alloys accumulate in the oral mucosa, causing pigmentation or chronic inflammatory reactions. In patients with allergies, metal ions can cause type IV hypersensitivity to metals, which primarily affects the perioral skin and oral mucosa. Metal hypersensitivity to metals can also exacerbate autoimmune diseases affecting the joints, skin, and salivary glands (Fig. 1) [8].

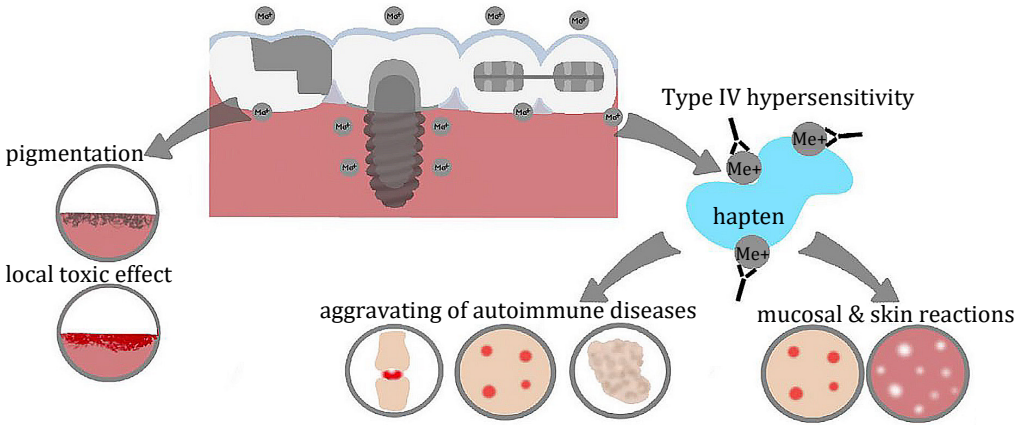

Figure 1. Local and systemic effects of dental alloys
Source: created by the authors based on [8]

Clinical manifestations of metal hypersensitivity vary widely, from localised oral symptoms such as cheilitis, glossalgia, lichenoid reactions, and recurrent aphthous stomatitis to systemic dermatoses like eczema and urticaria, as well as neurological disorders. This variability often complicates timely diagnosis. Effective management requires a thorough review of the patient's medical history, allergy test results, and changes in symptoms after metal replacement. Close collaboration among dentists, allergists, and dermatologists is essential.

Current diagnostic methods for metal alloy hypersensitivity in dentistry and orthopedics

Patch testing remains the gold standard for diagnosing delayed-type hypersensitivity. Most international core series include nickel, chromium, and cobalt, but many medically significant metals are excluded from routine testing. As metallurgy and biotechnology advance, these metals are increasingly used in medical devices such as artificial joints, dental implants, vascular stents, clips, and pacemakers. Routine testing does not cover these metals because some are not yet commercially available as patch test preparations [36]. Access to this method is currently limited in the Russian Federation. Patch testing involves applying an allergen solution on a porous support, such as gauze, sponge, or gel, to defatted skin on the forearm or back in varying concentrations, following International Contact Dermatitis Research Group (ICDRG) guidelines.

Results are recorded after 24, 48, and 72 hours. Ready-made test systems are available in the form of panels from manufacturers in various countries: International Contact Dermatitis Group, European Standard and Dental Material Series, Chemotechnic Dental Screening Series, TRUE Standard Series, German Contact Dermatitis Series, Stomatitis and Dental Hygienist Series, and Dental Screening Series. Most panels contain solutions of gold, palladium, zinc, cobalt, chromium, nickel, and iron salts in concentrations of approximately 100 g/100 ml or mol/L [26]. Nickel salts are included in standard contact allergy diagnostic kits. The patch tests are applied to the skin and evaluated after 48 to 72 hours by comparison with a control group. Patients with positive patch tests for metals found in MC alloys are considered to be at high risk for developing Contact-Type Dermatitis (CTD) in the oral mucosa, which can affect the integrity of the entire dental structure. If a positive patch test is confirmed after denture installation, the denture must be removed.

Preparation for the patch test is as follows. The patient's back skin must be free of rashes to avoid false-positive test results. It is not recommended to use hormonal ointments and leukotriene receptor inhibitors for 5 days before the test. Strenuous physical activity, baths, and saunas should be avoided for 2 days before the test. The examination can only be performed during a period of dermatitis remission, preferably 1 month after an exacerbation. It is also important to note that some patients who have been taking glucocorticosteroids at doses of more than 20 mg per day for a long time or who are undergoing chemotherapy may show a reduced or absent response to causative agents during the patch test. Patch test procedure: a chemical compound in a non-toxic concentration is applied to a hypoallergenic patch, which is placed on the skin of the back in the interscapular region or on the skin of the forearms. The patch with the test samples is applied to dry, clean skin that has been treated with an antiseptic. The outline

of the test areas should be marked with a fluorescent pen or marker. If severe itching or burning of the skin occurs, the test samples must be removed immediately.

The initial evaluation of patch test results is performed 24-48 hours after removal of the test samples, at 30-minute intervals. If necessary, an additional evaluation of the results is performed 72-120 hours after the tests were applied. Re-evaluation makes it possible to determine a delayed response to allergens and rule out an irritant reaction, as some irritant reactions that are positive after 24-48 hours disappear after 96 hours upon re-evaluation [37]. The patch test results are assessed according to the scale recommended by the ICDRG [38]: "-"- negative reaction; "+" – weakly positive reaction (erythema, infiltration, papules); "++" – positive reaction (erythema, infiltration, papules, single vesicles); "+++" – strongly positive reaction (multiple vesicles, bullous reaction); "+-" – questionable reaction (homogeneous erythema, absence of infiltration and vesicles); "IR" – local contact irritation (scattered punctate areas of erythema, no infiltration); "NT" – not tested. It is also possible to evaluate the results of the patch test using a scoring system [39]: 1 score – weakly positive reaction (erythema, itching); 2 scores – moderately positive reaction (erythema, edema); 3 scores – strongly positive reaction (vesiculation beyond the point of contact with the allergen is added to the above manifestations); 4 scores – a very strong positive reaction (general clinical manifestations are added to the above symptoms).

Contraindications to patch testing include exacerbation of dermatitis and its widespread nature, as well as the use of calcineurin inhibitors on the area where the patch test is to be applied for 5-7 days before the examination. The use of systemic antihistamines is also not recommended for 5-7 days before patch testing. A. Can *et al*. [40] studied the diagnostic role and the impact of patch test results on the outcome of dental procedures. The study included 382 adult patients with oral or systemic signs or symptoms caused by the dental prosthetic materials used. The most frequent positive reaction detected during the patch test was caused by metals, among which nickel (29.1%) was the main cause. Clinical improvement after removal of the dental restoration was observed in 82% of patients who had a positive patch test result, while among patients with negative patch test results, this figure was 54% ($p < 0.001$). The authors also note that the presence of a patient's self-reported metal allergy is an important factor in predicting the development of hypersensitivity to metal dental structures. In addition, the patch test results may be useful when performing dental procedures in real life.

For patch testing, ready-made samples of the planned metal alloys for each patient can be used. Samples should be processed to prevent mechanical damage to the skin and should be flat discs 2 mm thick and at least 1.5 cm in diameter. During the first visit, a metal alloy sample is applied to the back of the forearm with a bandage. During the second visit, 48 hours later, the sample is removed, and the local skin reaction is assessed after 20 minutes. If the patient experiences a sharp burning or itching sensation in the area where the sample was applied, it should be removed, and the test results will be assessed sooner. The skin reaction is assessed visually using a special scale recommended by the ICDRG (International Contact Dermatitis Research Group). Contraindications to the test include exacerbation of the underlying disease and periods of acute infectious diseases [37-38]. Skin tests can yield both false-negative results in cases of decreased skin and body reactivity and false-positive results in cases of increased reactivity. Therefore, skin test results should be interpreted only in conjunction with the patient's medical history, clinical status, and oral mucosal testing [38-39].

Oral mucosal tests are also used to diagnose contact reactions to metals. These tests are highly sensitive, but their implementation requires great caution, as they are associated with a high risk of complications [31]. Preparation for oral mucosal testing is the same as for skin testing. One option for testing oral mucosa is the intraoral epimucosal allergy test (IEAT). Before inserting the metal alloy sample into the oral cavity, the mucous membrane and microvasculature (MVA) of the inner cheek are assessed. The MVA of the buccal mucosa is examined with the patient's head supported by a headrest. The microscope tube is inserted perpendicular to the mucosal area being examined. The metal alloy sample is then inserted into the oral cavity and secured to the previously examined area using an intraoral allergy tester. This device, which contains jaws, is distinguished by the jaws being made of plastic and shaped like a U-shaped clamp. One cantilevered end terminates in a ring-shaped projection, and the other in a supporting plate. The ring-shaped projection is equipped with a removable sleeve for securing a cotton swab with the allergen within the said ring-shaped projection (RU Patent No. 2146490). The test results are evaluated after 2 hours. The metal alloy sample is removed from the oral cavity, followed by a repeat examination, evaluation of the oral mucosa, and the microcirculation function in the area of contact with the metal alloy sample. Microcirculation is assessed using the LDF method with a LAKK-02 laser blood flow analyser (LAZMA Scientific and Production Enterprise, Moscow). The results are compared with the initial values obtained before the test. When conducting a VEAT with microcirculation function assessment, only two possible interpretations are possible: positive and negative [25]. Any changes in the microcirculation function, such as structural and functional alterations in microvessels, changes in blood flow, or turbidity of the capillaroscopic background, are considered a positive

reaction to the test material. The absence of qualitative and quantitative changes in microcirculation upon sample administration indicates a negative test result.

Attempts have also been made to diagnose contact reactions to metals using various laboratory diagnostic methods, such as the lymphocyte transformation test (LTT), the leukocyte migration inhibition test (LMIT), the basophil activation test (BAT), the memory lymphocyte immunostimulatory assay (MELISA)®, and the determination of specific IgE antibodies. The lymphocyte transformation test (LTT) is based on the activation and proliferation of memory T cells following co-incubation of patient peripheral mononuclear cells (PMBC) with a putative specific antigen in vitro. The sensitivity of the LTT ranges from 58% to 89% for mild to moderate allergic reactions and from 25% to 75% for severe bullous reactions. The corresponding specificity ranges from 93% to 100% for mild to moderate allergic reactions and from 63% to 100% for severe bullous reactions [41]. Thus, T. Boutefnouchet *et al*. [42] determined the prevalence of metal hypersensitivity by conducting a lymphocyte transformation test to evaluate reactions to potential components of orthopedic implants. This study included 220 patients. According to the study results, among patients who had no previous clinical manifestations of metal allergy, true hypersensitivity to at least one metal was observed in 3.1% of cases.

MELISA is an optimised, standardised version of the lymphocyte transformation test (LTT) [43]. This test is based on the in vitro assessment of peripheral blood lymphocyte proliferation after incubation with metal ions. According to the results of the study by R. Vrbova *et al*. [44], for each metal tested, hypersensitivity to that metal was reduced or eliminated after therapeutic interventions based on the results and recommendations of the original MELISA® test [39]. The leukocyte migration inhibition test (LMIT), or migration inhibition factor (MIF), is based on isolating leukocytes from the patient's blood and adding solutions containing the drugs or metal salts being tested [29]. If leukocytes do not migrate from the area of contact with the allergen, the test result is considered positive, and vice versa. The specificity of the LMIT for drugs is 76.9%, and the sensitivity is 95.2% [45]. The basophil activation test (BAT) is a laboratory assay that quantitatively measures the increase in basophil surface marker expression following allergen stimulation using flow cytometry. The sensitivity and specificity of this diagnostic method are higher than those of measuring specific IgE in patients' serum. In addition to identifying sensitisation in patients at a specific point in time, the BAT can be a useful tool for monitoring dynamic changes in hypersensitivity, including during immunomodulatory therapy [46].

Another laboratory method is the determination of specific IgE antibodies. Various methods are used to quantify allergen-specific antibodies, including enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and the radioallergosorbent test (RAST). The detection of specific IgE antibodies to allergens in the blood serum is a sign of an allergic reaction. Thus, these methods only detect the state of sensitisation. The incidence of specific IgE antibodies in hypersensitivity to prosthetic materials is no more than 15-20% of cases [23,47]. In summary, diagnosing reactions to metal alloys has progressed from basic visual skin assessments to precise analyses of cellular metabolism and microcirculation. Skin tests remain the gold standard for initial screening, while LDF method and cellular technologies (LTT, MELISA®, BAT) provide more detailed differential diagnosis. An effective diagnostic approach should combine clinical presentation, intraoral testing, and laboratory verification to reduce diagnostic errors and support successful orthopedic treatment.

Conclusions

A systematic analysis of current data demonstrates an expanding sensitisation profile in contemporary dental practice. In addition to the predominant roles of nickel, cobalt, and chromium, there is a statistically significant increase in hypersensitivity reactions to titanium, aluminum, and precious metal alloys, including palladium and gold. The pathogenesis of these conditions involves complex cell-mediated delayed-type hypersensitivity mechanisms classified as subtype IVa according to the updated EAACI nomenclature, which are most pronounced in patients with a history of multifactorial sensitisation and concomitant autoimmune disorders. The role of innate immunity, in particular TLR4 activation by nickel and cobalt via functional mimicry of pathogen-associated molecular patterns, represents a critical and underappreciated dimension of the pathogenetic cascade that warrants further investigation. Galvanic corrosion of dissimilar metal structures in the oral cavity further potentiates allergen release and contributes to persistent sensitisation, a factor that must be accounted for in both material selection and treatment planning.

Clinical manifestations of metal hypersensitivity lack pathognomonic features and frequently resemble other oral mucosal lesions, such as lichenoid reactions and burning mouth syndrome. This similarity renders diagnosis based solely on visual examination unreliable and underscores the importance of integrating clinical history with objective testing. Comparative evaluation of diagnostic protocols confirms that skin patch testing remains the gold standard and the most informative method for identifying the etiological factor. In complex clinical cases or when systemic sensitisation is suspected, the integration of modern immunological assays such as the lymphocyte transformation test and the memory lymphocyte immunostimulation assay is warranted, as these methods provide a more precise

characterisation of individual immune reactivity. These findings underscore the necessity of implementing a standardised diagnostic algorithm, including mandatory preoperative screening of high-risk groups, particularly patients with immune-mediated pathologies and a documented history of metal intolerance, as a fundamental measure to ensure the safety of dental treatment and to minimise the risk of postoperative complications and prosthetic material rejection. The absence of epidemiological data on metal contact allergy prevalence in Russia and certain other regions further highlights the need for multicenter prospective studies to inform national clinical guidelines.

Acknowledgements

None.

Funding

None.

Conflict of Interest

None.

References

[1] Swalsky A, Noumbissi SS, Wiedemann TG. The systemic and local interactions related to titanium implant corrosion and hypersensitivity reactions: A narrative review of the literature. Int J Implant Dent. 2024;10(1):58. DOI: 10.1186/s40729-024-00578-3

[2] Poli PP, de Miranda FV, Polo TOB, Santiago Júnior JF, Neto TJL, Rios BR, et al. Titanium allergy caused by dental implants: A systematic literature review and case report. Materials. 2021;14(18):5239. DOI: 10.3390/ma14185239

[3] Olms C, Yahiaoui-Doktor M, Remmerbach TW. Contact allergies to dental materials. Swiss Dent J. 2019;129(7-8):571–9. DOI: 10.61872/sdj-2019-07-08-555

[4] Di Spirito F, Amato A, Di Palo MP, Ferraro R, Cannatà D, Galdi M, et al. Oral and extra-oral manifestations of hypersensitivity reactions in orthodontics: A comprehensive review. J Funct Biomater. 2024;15(7):175. DOI: 10.3390/jfb15070175

[5] Chepelova N, Antoshin A, Voloshin S, Usanova A, Efremov Y, Makeeva M, et al. Oral galvanism side effects: Comparing alloy ions and galvanic current effects on the mucosa-like model. J Funct Biomater. 2023;14(12):564. DOI: 10.3390/jfb14120564

[6] Forkel S, Schubert S, Corvin L, Heine G, Lang CCV, Oppel E, et al. Contact allergies to dental materials in patients. Br J Dermatol. 2024;190(6):895–903. DOI: 10.1093/bjd/ljad525

[7] Al-Gawahiri M, Rustemeyer T, Franken SM, van Zuuren EJ, Ipenburg NA. Frequency and clinical relevance of contact allergy in dental patients. Contact Dermatitis. 2024;90(1):66–73. DOI: 10.1111/cod.14440

[8] Arakelyan M, Spagnuolo G, Iaculli F, Dikopova, N, Antoshin, A, Timashev, P, et al. Minimization of adverse effects associated with dental alloys. Materials. 2022;15(21):7476. DOI: 10.3390/ma15217476

[9] Basko-Plluska JL, Thyssen JP, Schalock PC. Cutaneous and systemic hypersensitivity reactions to metallic implants. Dermatitis. 2011;22(2):65–79. DOI: 10.2310/6620.2011.10055

[10] Thyssen JP, Menné T. Metal allergy – a review on exposures, penetration, genetics, prevalence, and clinical implications. Chem Res Toxicol. 2009;23(2):309–18. DOI: 10.1021/tx9002726

[11] Forte G, Petrucci F, Bocca B. Metal allergens of growing significance: Epidemiology, immunotoxicology, strategies for testing and prevention. Inflamm Allergy Drug Targets. 2008;7(3):145–62. DOI: 10.2174/187152808785748146

[12] Valentine-Thon E, Schiwara HW. Validity of MELISA for metal sensitivity testing. J Lab Med. 2004;28(6):525–33. DOI: 10.1515/LabMed.2004.070

[13] Schmidt M, Goebeler M. Immunology of metal allergies. J Dtsch Dermatol Ges. 2015;13(7):653–9. DOI: 10.1111/ddg.12673

[14] Gupta R, Phan D, Schwarzkopf R. Total knee arthroplasty failure induced by metal hypersensitivity. Am J Case Rep. 2015; 16:542–7. DOI: 10.12659/ajcr.893609

[15] The ESSCA Writing Group. The European surveillance system of contact allergies (ESSCA): Results of patch testing the standard series, 2004. J Eur Acad of Dermatol Venereol. 2008;22(2):174–81. DOI: 10.1111/j.1468-3083.2007.02359.x

[16] Baló-Banga JM, Szoboszlai I, Vajda A. Epicutaneous tests with dental materials before and during COVID-19 pandemic in the Central Hungary region. Orv Hetil. 2024;165(51):2015–25. DOI: 10.1556/650.2024.33187

[17] Schwartz BL, Pithadia DJ, Chen JK. Hypersensitivity to implanted metal devices. Curr Derm Rep. 2023;12:8–22. DOI: 10.1007/s13671-023-00381-0

[18] Jutel M, Agache I, Zemelka-Wiacek M, Akdis M, Chivato T, de Giacco S, et al. Nomenclature of allergic diseases and hypersensitivity reactions: Adapted to modern needs: An EAACI position paper. Allergy. 2023;78(11):2851–74. DOI: 10.1111/all.15889

[19] Lisiecka MZ. Allergic reactions in dental practice: Classification of medicines, mechanisms of action, and clinical manifestations. Clin Rev Allergy Immunol. 2025;68(1):17. DOI: 10.1007/s12016-025-09032-7

[20] Riedel F, Aparicio-Soto M, Curato C, Thierse HJ, Siewert K, Luch A. Immunological mechanisms of metal allergies and the nickel-specific TCR-pMHC interface. Int J Environ Res Public Health. 2021;18(20):10867. DOI: 10.3390/ijerph182010867

[21] Athanasou NA. The pathobiology and pathology of aseptic implant failure. Bone Joint Res. 2016;5(5):162–8. DOI: 10.1302/2046-3758.55.BJR-2016-0086

[22] Kassapidou M, Stenport VF, Johansson CB, Östberg AK, Hammarström JP, Hjalmarsson L. Inflammatory response to cobalt-chromium alloys fabricated with different techniques. J Oral Maxillofac Res. 2021;12(4):e3. DOI: 10.5037/jomr.2021.12403
[23] Podzimek S, Himmlova L, Janatova T, Bjørklund G, Vrbova R, Janovska M, et al. Metal hypersensitivity and pro-inflammatory cytokine production in patients with failed orthopedic implants: A case-control study. Clin Immunol. 2022;245:109152. DOI: 10.1016/j.clim.2022.109152
[24] Oblak A, Pohar J, Jerala R. MD-2 determinants of nickel and cobalt-mediated activation of human TLR4. PLoS One. 2015; 10(3):e0120583. DOI: 10.1371/journal.pone.0120583
[25] Podzimek S, Tomka M, Bartova J, Prochazkova, J. Immune markers in oral discomfort patients before and after elimination of oral galvanism. Neuro Endocrinol Lett. 2013;34(8):802–8. DOI: 10.3389/conf.fimmu.2013.02.00977
[26] Saito M, Arakaki R, Yamada A, Tsunematsu T, Kudo Y, Ishimaru N. Molecular mechanisms of nickel allergy. Int J Mol Sci. 2016;17(2):202. DOI: 10.3390/ijms17020202
[27] Lohmann CH, Hameister R, Singh G. Allergies in orthopaedic and trauma surgery. Orthop Traumatol Surg Res. 2017; 103(1):75–81. DOI: 10.1016/j.otsr.2016.06.021
[28] Zemelka-Wiącek M. Metal allergy: State-of-the-art mechanisms, biomarkers, hypersensitivity to implants. J Clin Med. 2022; 11(23):6971. DOI: 10.3390/jcm11236971
[29] Rodrigues Neves CT, Spiekstra SW, de Graaf NPJ, Rustemeyer T, Feilzer AJ, Kleverlaan CJ, et al. Titanium salts tested in reconstructed human skin with integrated MUTZ-3-derived Langerhans cells show an irritant rather than a sensitizing potential. Contact Dermatitis. 2020;83(5):337–46. DOI: 10.1111/cod.13666
[30] Mikhailova ES. Algorithms for diagnosis of intolerance to dental construction materials. Med Alliance. 2019;7(4):93–105. DOI: 10.36422/23076348-2019-7-4-93-105
[31] Zhou X, Wu Y, Zhu Z, Lu C, Zhang C, Zeng L. Mucosal immune response in biology, disease prevention and treatment. Sig Transduct Target Ther. 2025;10(7):24–34. DOI: 10.1038/s41392-024-02043-4
[32] Zigante M, Rincic Mlinaric M, Kastelan M, Perkovic V, Trinajstic Z, Palj S. Symptoms of titanium and nickel allergic sensitization in orthodontic treatment. Prog Orthod. 2020;21(1):17. DOI: 10.1186/s40510-020-00318-4
[33] Kitagawa M, Murakami S, Akashi Y, Oka H, Shintani T, Ogawa I, et al. Current status of dental metal allergy in Japan. J Prosthodont Res. 2019;63(3):309–12. DOI: 10.1016/j.jpor.2019.01.003
[34] Hiroyasu Y, Kenji I, Yuko M, Ryo F, Daisuke A. metal-free prosthodontic treatment of periungual allergic contact dermatitis: A case report. Cureus. 2025;17(5):e83598. DOI: 10.7759/cureus.83598
[35] Alqahtani AR, Gufran K, Silva F, Rocha MG, Chang J. A clinical case report of a potential acute allergic reaction with titanium dental implant. Case Rep Dent. 2021;2021(1):5592934. DOI: 10.1155/2021/5592934
[36] Spiewak R. Assessment for metal allergy: Patch testing. In: Chen JK, Thyssen JP, editors. Metal allergy. Cham: Springer; 2018. 107–24. DOI: 10.1007/978-3-319-58503-1_11
[37] Johansen JD, Aalto-Korte K, Agner T, Andersen KE, Bircher A, Bruze M, et al. European society of contact dermatitis guideline for diagnostic patch testing – recommendations on best practice. Contact Dermatitis. 2015;73(4):195–221. DOI: 10.1111/cod.12432
[38] Hervella-Garcés M, García-Gavín J, Silvestre-Salvador JF. Update of the Spanish standard patch test series by the Spanish contact dermatitis and skin allergy research group (GEIDAC) for 2016. Actas Dermosifiliogr. 2016;107(7):559–66. DOI: 10.1016/j.ad.2016.04.009
[39] Fonacier L, Bernstein DI, Pacheco K, Holness DL, Blessing-Moore J, Khan D, et al. Contact dermatitis: A practice parameter-update 2015. J Allergy Clin Immunol Pract. 2015;3(3):1–39. DOI: 10.1016/j.jaip.2015.02.009
[40] Can A, Karabacak DE, Yalcin BK, Demir S, Buyukozturk S, Colakoglu B, et al. How important is patch testing with dental materials in real-life clinical practice? Allergy Asthma Proc. 2023;44(2):136–44. DOI: 10.2500/aap.2023.44.220074
[41] Sachs B, Fatangare A, Sickmann A, Glässner A. Lymphocyte transformation test: History and current approaches. J Immunol Methods. 2021;493:013136. DOI: 10.1016/j.jim.2021.113036
[42] Boutefnouchet T, Vallières F, Delisle J, Benderdour M, Fernandes JC. Lymphocyte transformation test reveals low prevalence of true metal hypersensitivity among pre-operative total knee arthroplasty patients. Knee Surg Sports Traumatol Arthrosc. 2022;30(12):4123–33. DOI: 10.1007/s00167-022-06951-2
[43] Vijayaraghavan V, Sabane AV, Tejas K. Hypersensitivity to titanium: A less explored area of research. J Indian Prosthodont Soc. 2012;12(4):201–7. DOI: 10.1007/s13191-012-0139-4
[44] Vrbova R, Podzimek S, Himmlova L, Roubickova A, Janovska M, Janatova T, et al. Titanium and other metal hypersensitivity diagnosed by MELISA® test: Follow-up study. Biomed Res Int. 2021;2021(1):5512091. DOI: 10.1155/2021/5512091
[45] Blinova TV, Lapin SV. Laboratory diagnostics of allergic and a number of other immunopathological conditions in dentistry. Clin Lab Consilium. 2012;1(41):11–20.
[46] Santos AF, Alpan O, Hoffmann HJ. Basophil activation test: Mechanisms and considerations for use in clinical trials and clinical practice. Allergy. 2021;76(8):2420–32. DOI: 10.22541/au.159493194.42634850
[47] Kapruk IYu. The application of vaseline-lanolin basis for diagnosing allergy to nickel. Vestnik VGMU. 2015;14(4):50–6.

Гиперчувствительность замедленного типа к металлам в стоматологии: современные подходы к диагностике (обзор литературы)

Софья Хостелиди
Доктор медицинских наук, профессор
Северо-Западный государственный медицинский университет имени И.И. Мечникова
195067, ул. Кирочная, 41, г. Санкт-Петербург, Российская Федерация
https://orcid.org/0000-0001-5794-5396
Марина Еличева
Аспирант
Северо-Западный государственный медицинский университет имени И.И. Мечникова
195067, ул. Кирочная, 41, г. Санкт-Петербург, Российская Федерация
https://orcid.org/0009-0004-2901-3013
Екатерина Бурыгина
Кандидат медицинских наук, доцент
Северо-Западный государственный медицинский университет имени И.И. Мечникова
195067, ул. Кирочная, 41, г. Санкт-Петербург, Российская Федерация
https://orcid.org/0000-0002-9307-4927
Арайлым Абильбаева
PhD, доцент
Казахский национальный медицинский университет имени С.Д. Асфендиярова
050012, ул. Толе би, 94, г. Алматы, Республика Казахстан
https://orcid.org/0000-0001-5081-5492
Алексей Силин
Доктор медицинских наук, профессор
Северо-Западный государственный медицинский университет имени И.И. Мечникова
195067, ул. Кирочная, 41, Санкт-Петербург, Российская Федерация
https://orcid.org/0000-0002-3533-5615

Аннотация. Гиперчувствительность замедленного типа к металлам в соответствии с современной классификацией относят к IVa подтипу. С внедрением новых стоматологических конструкций отмечается увеличение числа пациентов с непереносимостью металлических сплавов. Целью исследования было определить особенности патогенеза и клинических проявлений, основные факторы риска развития гиперчувствительности замедленного типа к металлическим конструкционным элементам и оптимальные методы ее диагностики у пациентов в стоматологической практике. Поиск информации проводился на платформах PubMed и e-library (по состоянию на февраль 2026 г.) по следующим ключевым словам: побочные эффекты стоматологических сплавов, кожные патч-тесты, контактная аллергия на металлы, стоматологические материалы, аллергические реакции, лихеноидная реакция. В рамках работы было проанализировано 47 научных источников. В исследовании применялись методы библиографического поиска, отбора и скрининга источников, сравнительного анализа, систематизации и обобщения научных данных. Для выявления этих реакций гиперчувствительности применяются различные методы диагностики. Обзор литературы показал, что патч-тесты являются наиболее информативным диагностическим методом выявления реакций гиперчувствительности на металлы, используемые при изготовлении стоматологических реставраций и компонентов зубных протезов. Они позволяют идентифицировать и подтвердить участие конкретного причинного фактора в развитии клинических симптомов у пациента. Выявлено, что наиболее часто гиперчувствительность замедленного типа встречается к таким металлам, как никель, кобальт и хром. Аналогичный механизм гиперчувствительности к никелю зарегистрировано у 17% женщин и 3% мужчин, к кобальту и хрому – у 1-3% представителей обоих полов. Отмечено также увеличение гиперчувствительности замедленного типа к другим металлам, таким как алюминий, бериллий, медь, золото, иридий, ртуть, палладий, платина, родий, титан. Группу высокого риска по развитию гиперчувствительности замедленного типа к металлам составляют пациенты с иммуноопосредованной патологией

Ключевые слова: побочные эффекты стоматологических сплавов; кожные патч-тесты; контактная аллергия на металлы; стоматологические материалы; аллергические реакции; лихеноидная реакция