

Occupational allergens in dentistry

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Purpose of review

Dental professionals and their physicians frequently do not recognize, accurately diagnose or appropriately manage occupational allergies. Dental allergen identification, diagnostics and practical avoidance strategies are summarized in this review.

Recent findings

Methacrylates, natural rubber latex proteins, rubber glove allergens, and glutaraldehyde are the predominant allergens in dentistry. Reactions range from cell-mediated contact allergy to urticaria and occupational asthma.

Summary

Despite recent advances in allergen characterization and increased awareness of selected allergens, treatment of occupational allergies can be improved. Better information and improved cooperation between dental workers and their clinicians is needed.

Keywords

methacrylates, latex, rubber, disinfectants, metals, respiratory, dermatitis

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Abbreviations

FDA US Food and Drug Administration
NRL natural rubber latex

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Introduction

Occupational skin disease and respiratory hypersensitivity are increasingly common in dental professionals, probably reflecting increased allergy recognition and worker exposure. Recent advances have been made in characterizing the more prevalent allergens, such as methacrylates, natural rubber latex (NRL) proteins, rubber glove chemicals and disinfectants. This improved understanding has clearly enhanced the success of occupational allergy management, particularly for type I NRL allergies. New and existing research on the immunological pathogenesis of occupational allergies may still yield better diagnostic, treatment and management strategies. This review surveys recent changes in dental allergen prevalence, diagnostics and management, integrating this evidence with clinical paradigms for patient care and the dental practice environment.

Important dental allergens

Dental workers are exposed to a plethora of allergens including (1) methacrylates in bonding agents and resins; (2) NRL proteins in latex gloves; (3) accelerators and antidegradants in natural and synthetic rubber gloves; and (4) glutaraldehyde in disinfectants. The various metals in restorations and dental appliances, as well as miscellaneous antimicrobials and preservatives, can also be relevant allergens in dentistry [1–3]. While most allergic reactions to these substances are consistent with classic type I or type IV symptoms, IgE-independent occupational asthma and protein-based contact urticaria have also been reported [3,4].

Methacrylates

Occupational type IV contact allergy to methacrylate monomers in dental bonding agents, fillings and restorative materials are now common in dentistry [3,5]. These allergens include methyl methacrylate, 2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate, ethylene glycol dimethacrylate, and triethylene glycol dimethacrylate, many of which cross react [5].

Dental worker allergies to methacrylates may be increasing: recent prevalence estimates range from 1.3 to 14% [1,6]. Although contact dermatitis is the predominant allergic reaction, respiratory symptoms and conjunctivitis in dental personnel have also been reported [3,7–9]. For example, over 60% of occupational asthma and more than 20% of occupational rhinitis studied in Finnish dental personnel were purportedly associated with methacrylates, based on challenge testing [3]. Similarly, bone cements containing metha-

crylates are the source of asthma-like symptoms in some medical personnel [10,11]. Additional studies of controlled respiratory challenge testing and improved measurement of airborne methacrylate vapor and dust are needed to better understand reported occupational asthma due to these compounds [12,13].

Uncured, methacrylate monomers are potent allergens that dental workers handle directly. Studies confirm that methacrylates permeate medical gloves within minutes [14•,15,16]. Rates vary by glove material, chemical structure and solvent; some neoprene and nitrile gloves may show some chemical resistance in controlled studies [14•,16]. But in practical terms, all medical gloves are rapidly permeated by methyl methacrylate and hydroxyethyl methacrylate monomers, due to their concentration (usually 5–30%) and solvent base (ethanol or acetone).

Proteins in natural rubber latex gloves

At least 13 botanical proteins (Hev b 1–13) have been characterized as potential sources of type I allergic reactions to latex gloves [17•]. Bound by cornstarch powder during glove manufacture, allergenic NRL proteins can subsequently be aerosolized through the handling, donning and removal of powdered latex gloves [18]. As in hospitals, dental facilities using powdered latex gloves with high allergen levels can generate NRL allergen levels in room air up to 400 ng per cubic meter, well above current symptom elicitation thresholds [19]. Residual bacterial endotoxins may also be carried by glove powder, potentiating allergic reactions and sensitization rates [20•].

The prevalence of type I NRL allergy may be declining with increased recognition and changes in NRL product manufacturing. Symptoms of type I NRL allergy were reported in only 1.8% of Finnish dental nurses [1]. Type I NRL allergy was diagnosed in only 3% of Canadian dental students, compared with 10% in 1995 [21]. During the last 8 years, type I NRL allergy in US dentists decreased to less than 4% [22].

Symptoms of IgE-mediated type I NRL allergy range from rhinoconjunctivitis and respiratory problems to contact urticaria and pruritic rashes. However, health care workers have also experienced protein-based contact dermatitis to NRL [4]. Recent work suggests that the NRL allergen Hev b 6.01 (prohevein) may contain an important T-cell immunogen for cell-mediated symptoms [23•,24,25•].

Antidegradants and vulcanizing accelerators in rubber products

Numerous chemicals are added to natural and synthetic rubbers during manufacturing. Of these, thiurams,

carbamates and mercaptobenzothiazoles are the most relevant rubber glove allergens [26]. Leached from gloves by sweat, these chemicals can elicit localized type IV allergy symptoms. Glove-based allergic contact dermatitis is often identified in dental workers, and now may be as common as type I NRL allergy [2,22].

Compounding, vulcanization and manufacturing processes are similar for natural rubber and synthetic rubbers (e.g. nitrile, neoprene, butyl rubber, butadiene methyl methacrylate and polyisoprene). These materials contain the same allergenic accelerator and antioxidant chemicals. Elevated residual levels of mercaptobenzothiazoles and thiurams are less frequently detected in medical gloves [26,27]. The common use of carbamates in vulcanized rubbers may still provoke reactions in some sensitized dental workers, as carbamates and thiurams cross react and interconvert [27,28].

Glutaraldehyde

Although the 2003 Centers for Disease Control and Prevention dental infection control guidelines recommend against cold sterilants, glutaraldehyde is still commonly used in dentistry [29]. A potent allergen at concentrations below those used in disinfecting dental instruments, glutaraldehyde frequently provokes type IV delayed reactions, and occasionally respiratory symptoms and rhinitis [30•,31•,32]. Respiratory symptoms are more often reported in medical personnel [33–35]. New evidence suggests that glutaraldehyde may elicit both IgE- and T-cell mediated immunological responses, related in part to exposure level [36•]. As with other low molecular weight chemicals, the immunological pathogenesis of these airway reactions is not yet clear and further investigation is required.

Ravis *et al.* [30•] reported that 79% of studied dental workers had been exposed to glutaraldehyde; 11% were sensitized with a type IV allergy. Of these, none had received adequate chemical safety training. Unfortunately, dental workers frequently report using glutaraldehyde without adequate ventilation, containment or personal protective equipment.

Other dental allergens

Antimicrobials such as thimerosal and chloramine T continue to be recognized dental contact allergens [3,37]. Bisphenol F compounds may be emerging dental allergens that cross react with bisphenol A [38]. Recent work has also shown that metals in fillings, restoratives and dental appliances can be released during dental work and *in vivo*, potentially exposing patients and practitioners to gold, nickel, palladium, and mercury (amalgam) [39,40,41•,42]. Exposure risk may be greater in dentistry, as dentists preferentially select metal restorations for their enhanced durability [43].

Diagnostics

Recently investigated by Warshaw [44••], allergists, dermatologists, and occupational physicians are more likely to be experienced in relevant diagnostic procedures. Not surprisingly, clinician training, experience and interest in occupational allergies are associated with a greater degree of diagnostic success.

Recently, the importance of accurate symptom assessments has received greater attention. The low positive predictive value of self-reported symptoms is well known [45]. Moreover, self-reported glove intolerance correlates poorly with a diagnosis of type I NRL allergy [31•]. In contrast, the predictive value of self-reported rhinoconjunctivitis or asthma for type I NRL allergy is still underestimated.

Patch testing for type IV allergies

Increasingly, the validity and reproducibility of patch test results have been shown to vary with clinician technique and experience [46•,47]. Moreover, the test's positive predictive value ultimately hinges on accurately evaluating worker history and symptoms [46•]. Using single time points and too few allergens, dermatologists and allergists can miss clinically relevant allergies [44••,48•]. For example, Saripalli *et al.* [48•] reported that only 28% of patients with clinically relevant reactions were fully evaluated with 23 allergens (T.R.U.E. or thin-layer rapid use epicutaneous test panels); 25% of patients reacted to other allergens, and would have been missed if the clinician was limited to testing with standard trays. Additional allergens are warranted for patch testing, particularly for those with occupational allergies. As with other allergens, however, US Food and Drug Administration (FDA) regulations make product development a costly and time-consuming venture.

Studies by Farrell and Warshaw have characterized patch test practices by both allergists and dermatologists in the United States [44••,49,50]. They revealed that 53% of allergists and 83% of dermatologists performed patch testing; roughly half use two readings and nearly three-quarters use the T.R.U.E. test system of 23 allergens [49]. European dermatologists are also likely to use this system [44••]. Overall, the use of the 23-allergen T.R.U.E. tests is explained in part by convenience, standardization and lack of time or support personnel. It is interesting to note that 60% of dermatologists with additional training, interest and experience in contact dermatitis did not use the T.R.U.E. test, and most tested with more than 23 allergens [44••]. As noted above, clinician training and experience is critical.

There can be caveats to the interpretability of test results for some dental allergens. For example, thiuram

and carbamate test accuracy can vary with test system (e.g. Finn chamber versus T.R.U.E. test); physicians must interpret these results carefully [48•,51]. In addition, methacrylate cross reactivity, impurities and incomplete identification by manufacturers limits the ability to diagnose specific allergies, and selectively prevent allergen exposure [52]. Currently, positive test results generally require strict avoidance of all bonding agents and resins.

Type I (immediate) allergy to natural rubber latex

Although serologic testing for NRL-specific IgE antibodies is convenient and widely used, its lower sensitivity implies a greater false negative rate (approximately 25%) [53]. Therefore, skin prick testing is still preferred for its higher predictive value [53,54]. Sources of NRL test allergen in Europe and Canada include nonammoniated NRL reagents (e.g. Stallergenes, Antony, France; and ALK-Abello, Lofarma). When these standardized reagents are available, skin prick tests are considered safe and effective.

Unfortunately, in the United States, physicians generally prepare extracts of NRL gloves due to the lack of an FDA-approved test material. In fact, most dermatologists (87.5%) and allergists (74%) in the United States use solutions prepared from gloves [55,56]. Unfortunately, because NRL gloves are no longer reliable sources of NRL allergens, this technique can be problematic. Until more reliable test sources become available, US clinicians should confirm equivocal results with combined serologic and skin prick testing, or multiple serologic tests using different methods (e.g. Pharmacia CAP, Uppsala, Sweden; and Diagnostic Products Corporation AlaSTAT, Los Angeles, California) [53]. Future test materials may include purified recombinant NRL allergens or their related monoclonal antibodies [57].

It is also important to note that two confounding but rare instances have been reported for type I NRL allergy: IgE-mediated reactions to cornstarch and cell-mediated reactions to NRL proteins [4,58,59]. Testing for the latter again requires the use of an unavailable standardized allergen. Neither NRL medical gloves nor crude NRL is a controlled and standardized allergen source. Therefore, testing with these materials should be interpreted with caution.

Occupational asthma

Evaluating the source of asthma or asthma-like symptoms in the occupational environment is difficult. Airborne allergen concentrations can vary by product, chemical, room ventilation, temperature, humidity and other factors. As with other diagnostic methods, controlled testing coupled with a detailed exposure and health history is invaluable.

As reviewed recently, occupational asthma is best diagnosed by inhalation challenge tests with suspected allergens [60•]. An alternative approach is to demonstrate reduced lung function (i.e. peak expiratory flow) in symptomatic workers at work. New techniques involving measurement of exhaled nitric oxide and characterization of induced sputum have yet to be fully validated in the clinical setting.

With respect to NRL protein allergens, respiratory challenge testing should only be performed under tightly controlled conditions, due to frequent adverse reactions [53]. As with skin prick testing, the lack of a standardized NRL allergen source limits the use of this diagnostic technique. Because NRL glove protein and allergen content has decreased over the last several years, it is now difficult to find gloves that provide sufficiently high NRL allergen content to be dependably diagnostic. Moreover, test method and endpoint criteria can be highly subjective, and patient reactions are difficult to blind appropriately.

Management of occupational allergies

Increasingly, clinicians recognize that patient education and diligence are critical for successful allergy management. Dental workers often believe that a few new gloves, products, creams, or other ‘quick fixes’ will solve their allergy problems. Compliance is often poor. One study noted that less than 10% of dentists with a type I NRL allergy fully complied with a latex avoidance program [61]. Success improves when written and oral instruction is provided detailing product choices, alternatives, and mitigating allergen exposure [62]. Follow-up visits, handouts, practical training and targeted information may all be required for workers to learn to avoid allergens and manage their allergy [31•,63••].

Dental workers reportedly can suffer with occupational dermatitis, urticaria or asthma for up to 40 years [31•,64,65]. Even after obtaining a diagnosis, allergen exposure continues due to worker habits, poor understanding, inability to find an alternative product or procedure, and poor manufacturer identification of allergens in dental products [31•,63••]. Considerable effort by both physician and patient may be required to retrain workers to avoid exposure [31•,66]. Unfortunately, as the duration of exposure and symptoms increases, the likelihood of a successful diagnosis, intervention and resolution diminishes [63••,66,67].

Managing occupational type I natural latex rubber allergies

First, workers with type I NRL allergy must wear nonlatex gloves made of nitrile, neoprene, butadiene, synthetic polyisoprene, polyvinyl chloride, polyurethane

or styrene-based copolymers, or some blend thereof. Utility gloves can be made of Viton, Silvershield/4H, nitrile, neoprene, or butadiene polymeric blends. Continued NRL exposure by wearing latex gloves usually means persistent symptoms. One study reported that one-quarter of dentists with urticaria from type I NRL allergy continued to wear NRL gloves, and all were symptomatic as a result [65].

The NRL allergen content in latex gloves is not reliably or consistently low; FDA guidelines and ASTM standards for medical gloves only recommend low levels of extractable NRL allergens [68]. Therefore, it is not surprising that higher levels are still reported [69•]. Unfortunately, NRL allergens have been detected in nitrile gloves, possibly due to contamination during manufacture [69•,70].

Second, coworkers and dental practices must eliminate or minimize the use of powdered latex gloves to reduce environmental NRL allergen loads. Powdered latex gloves still have appreciable levels of NRL allergens [69•]. Multiple studies have demonstrated that replacing these gloves with synthetic rubber or powder-free latex gloves markedly reduces airborne and surface levels of NRL allergens [71].

Finally, some studies suggest that rigorous cleaning may be required to remove existing environmental sources of NRL allergens. Dust particles with NRL can contaminate work surfaces, which then can be resuspended with dental worker activity [72]. Significant contamination has been reported in infrequently cleaned areas, carpets and upholstery in dental offices [73]. More importantly, cleaning these areas resulted in reduced symptoms in NRL allergic personnel.

Managing occupational type IV allergies

As with type I allergies, avoidance is key. Dental workers with a type IV allergy to thiurams or carbamates should select gloves made of polyvinyl chloride (PVC or vinyl), polyurethane (polyisocyanates), or styrene-based copolymers, none of which is vulcanized. These are unlikely to contain similar or cross-reacting chemicals.

Dental workers with type IV contact allergy to methacrylates must avoid contact with dental bonding agents. Unfortunately, permeation-resistant glove materials (e.g. Silvershield/4H) do not have sufficient flexibility for the intricate work involving methacrylates. Developing ‘no-touch’ techniques and selecting products that prevent contact are essential due to the potency and cross-reactivity of these allergens. Female dental workers with methacrylate allergies should also avoid wearing artificial nails, which can contain cross-reacting methacrylates [5,31•].

Managing occupational asthma

Early detection and diagnosis is critical for successful treatment of occupational asthma from dental allergens. Although less studied in dentistry, occupational asthma management is still based on strict avoidance. But as the duration and exposure level increases, chronic obstructive respiratory disease is increasingly likely. Workers may not experience symptom remission with allergen avoidance, possibly due to residual airway hypersensitivity [74]. In health care workers with NRL protein-induced occupational asthma, synthetic glove use was not sufficient for symptom resolution; 16% felt compelled to change or leave their jobs [65,75,76]. Similar mixed outcomes have been reported for dental workers with IgE-independent occupational asthma from methacrylates and disinfectants [3].

Conclusion

Although obvious advances have been made in characterizing dental allergens and understanding potential exposure, improved diagnostic and management techniques are still needed. Not all dermatologists or allergists perform needed testing; corticosteroid therapy is all too often the only treatment. Clinicians must be trained and experienced. Standardized, expedient and relevant diagnostics must be developed, implemented and emphasized in clinical practice.

Occupational asthma and chronic obstructive lung disease have high quality of life and economic costs. Because interventions are not always successful, increases in allergy-related occupational respiratory disease are troubling. Greater research is needed into the risk factors and immunology of occupational asthma, as well as improved methods of detection, treatment and prevention.

Once diagnosed, dental professionals must manage occupational allergies effectively. However, many are poorly informed about occupational allergies and the ramifications of skin disease. Therefore, new approaches must be found to educate dental workers about occupational allergens and solicit a strong commitment to eliminating allergen exposure. Ultimately, the best solution – prevention – must receive greater attention from both medical and dental professionals alike.

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