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INTEGRATED STUDY MASTER'S FINAL THESIS

An Overview on Contact Allergy to Acrylates

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Santrauka

Akrilatų ir metakrilatų monomerai plačiai naudojami nagų kosmetikoje, odontologijoje ir medicinos prietaisuose ir yra gerai dokumentuoti kaip stiprūs alerginį kontaktinį dermatitą sukeliantys etiologiniai veiksniai, veikiantys per IV tipo padidėjusio jautrumo mechanizmą. Šios naratyvinės apžvalgos tikslas – apibendrinti naujausią mokslinę informaciją apie akrilatų sukelto alerginio kontaktinio dermatito imunopatogenezę, klinikinius pasireiškimus, diagnostikos metodus, epidemiologiją ir gydymą, ypač akcentuojant profesines, vartotojų ir medicinos prietaisų aspektus. Straipsniai, paskelbti 2000–2024 m. laikotarpiu, buvo ieškoti keturiose duomenų bazėse, teikiant pirmenybę duomenims, gautiems iš daugiacentrių tyrimų. Dabartinė literatūra rodo sensibilizacijos profilio kaitą – nuo klasikinių profesinių aplinkų, kuriose sensibilizacija dažniausiai pasireiškė tarp odontologijos specialistų ir nagų technologų, prie vartotojų grupių, naudojančių namų sąlygomis skirtus gelio nagų rinkinius, ir asmenų, nešiojančių nuolatinio gliukozės stebėjimo sistemos prietaisus. 2-hidroksietilo metakrilatas (HEMA) yra nustatomas kaip dažniausias sensibilizuojantis akrilatas ir geriausias atrankinis preparatas, kurio teigiamų rezultatų dažnis viršija 90 % tarp sensibilizuotų asmenų, tuo tarpu izobornil akrilatas (IBOA), neturintis struktūrinio ryšio su metakrilatais, reikalauja atskiro ištyrimo ir yra pagrindinis alergenas, sukeliantis su prietaisais susijusį alerginį kontaktinį dermatitą. Diagnostikai svarbu naudoti tinkamus alergenus lopo mėginiams , visą akrilatų seriją su privalomu vertinimu 7-ąją dieną. Tinkamas akrilatų galutinių produktų kietinimas, tinkamos asmeninės apsaugos priemonės ir geresnis epidemiologinis įsijautrinimo cheminėms medžiagoms stebėjimas po jų patekimo į rinką yra esminės prevencinės priemonės.

ABSTRACT

Acrylate and methacrylate monomers have wide applications in nail cosmetics, dentistry, and medical devices and are well documented as strong etiological agents of allergic contact dermatitis mediated by a type IV hypersensitivity mechanism. The purpose of this narrative review was to compile the latest scientific information concerning the immunopathogenesis, clinical manifestations, diagnostic modalities, epidemiology, and treatment of acrylate-induced allergic contact dermatitis, especially focusing on occupational, consumer, and medical device aspects. Four databases were searched for articles published between 2000 and 2024, with preference for data obtained from multi-center surveillance patch test networks. The current literature suggests a transition of sensitization profile from classical occupational settings

where sensitization mostly occurred among dental professionals and nail technicians to consumer groups using home gel nail kits and people wearing continuous glucose monitoring system devices. 2-hydroxyethyl methacrylate (HEMA) is found to be the most common sensitizing agent and best screening marker with a positivity rate above 90% among sensitized subjects, while isobornyl acrylate (IBOA), having no structural relation to methacrylates, requires individual testing and represents the main allergen causing device-related allergic contact dermatitis. All epidemiologic data are available only for clinic-based patch test samples, and all prevalence numbers can be considered minimum estimates. It is important to use a proper patch test, including the entire acrylate series with mandatory reading at Day 7. Proper curing of acrylic substances, adequate personal protective equipment, and better allergen monitoring after marketing are crucial for preventive measures.

KEYWORDS: Acrylates; Allergic contact dermatitis; 2-hydroxy methacrylate; triethylene glycol dimethacrylate; methyl methacrylate; Patch testing; Occupational dermatitis; Nail technicians; dental materials; Skin sensitization; Consumer exposure; prevention and management

INTRODUCTION

1.1 BACKGROUND AND CONTEXT

Acrylates and methacrylates are artificial molecules commonly used in various occupations, cosmetic, and medical fields, such as dental resins, UV-cured nail cosmetics, skin adhesives, and continuous glucose monitors. Despite their wide range of uses, the partially polymerized acrylate monomers are strong sensitizers to the skin, as they penetrate the stratum corneum and create hapten-protein complexes that lead to type IV hypersensitivity mediated by T cells, leading to allergic contact dermatitis (ACD). The resulting inflammatory disease is marked by pruritus, erythema, cracking, and, in severe cases, nail deformities, making it a substantial health problem that has been overlooked by both workers and consumers. In recent years, the incidence rate of ACD cases associated with acrylates has increased significantly, partly due to the increasing use of UV-cured gel nail cosmetics and the development of acrylates in wearable medical devices. Due to their diverse sources and lack of mention in the ingredient list of products, acrylate-induced allergic contact dermatitis can easily be missed in diagnosis. The current review highlights the prevalence, pathophysiology, clinical features, diagnosis, and treatment of acrylate-induced allergic contact dermatitis for a clinically relevant summary of existing research.

1.2 PROBLEM STATEMENT

Despite the common usage of acrylates in occupational settings and consumer products, contact sensitivity to acrylates constitutes an under-recognized health problem. Exposure to acrylates may occur within different occupational and consumer environments, as described in Section 3.4. One of the biggest barriers to diagnosing acrylate-induced dermatitis is the fact that these ingredients are often unlisted on product labeling, thus preventing the diagnosis made by the physician and reducing the patients' ability to avoid sensitization. This is due to the fact that the disease manifests itself through hand dermatitis or periungual and facial eruptions, which are not always immediately recognized as being connected to acrylate exposure. Regulatory practices have proven to be ineffective in avoiding sensitization.

1.3 RESEARCH OBJECTIVES

Objectives to be Achieved Through Literature Review:

1. Understanding the chemistry of acrylate monomers that cause allergic reactions in individuals, along with their mechanisms of exposure through occupational and consumer activities, including dermal, inhalation, and mucosal exposure.

2. Examination of the immune mechanisms responsible for the sensitization due to acrylates, the clinical manifestations arising from it, diagnostic tools available for such reactions, with special attention to patch tests and the epidemiology of acrylate-induced allergic contact dermatitis among occupations and consumers.

3. Evaluating the scientific knowledge available regarding prevention and treatment strategies for allergic contact dermatitis caused by acrylates, with particular emphasis on occupational aspects and consumer products.

1.4 SCOPE AND LIMITATIONS

This review covers acrylate-induced allergy contact dermatitis with regard to eight key clinical factors: sources of exposure, pathogenesis of disease, signs and symptoms, methods of diagnosis, prevalence, occupational and consumer hazards, preventive strategies, and treatment. Acrylates in general, including systemic toxicity, carcinogenicity, and other diseases caused by acrylates, are not covered in this paper. There are two major sources of limitations in the current review paper.

Firstly, this paper focuses on clinic-based literature as the majority of papers used are based on data obtained from patch-test clinics. As pointed out in Section 6.1, the frequency of sensitizations reported in this paper should be considered minimal due to several reasons, such as heterogeneity of testing methodology (panels of allergens, concentrations, and reading periods), as well as the difficulty of exposure assessment because acrylates are often unlabelled in commercial goods. The second set of limitations relates to the nature of this paper. Due to the absence of a systematic design of the review, there was no need to conduct a risk-of-bias analysis of all papers. Therefore, the conclusions drawn in this paper reflect the author's own understanding and analysis of the papers chosen. Only articles in English have been used in this paper, which probably excludes relevant information about acrylates' impact on skin available in other countries.

1.5 METHODS

The present literature review is narrative. Narrative review was determined to be the most appropriate methodology due to the multi-dimensional nature of acrylate-induced allergic contact dermatitis, including different aspects related to immunopathology, occupational medicine, cosmetology, and safety of medical devices, each having its own body of literature, study types, and endpoints. The diversity of study types, exposure contexts, and outcome definitions prevented pooling the available evidence into a systematic review and meta-

analysis, which would have been inappropriate and ineffective. The current narrative review aimed to provide a comprehensive and clinically oriented review of the literature on sources of acrylate exposure, pathophysiology, clinical manifestations, diagnosis, epidemiology, prevention, and management of acrylate-induced allergic contact dermatitis. Despite non-registration of a PRISMA protocol, the procedures of literature search, article selection, and synthesis were undertaken systematically and transparently, as described below.

Four electronic databases were searched: PubMed/MEDLINE, EMBASE, Google Scholar, and Cochrane Library. The inclusion period was extended to publications from January 2000 to December 2024, thus encompassing both contemporary research and landmark publications that influenced the field's clinical and immunological paradigms. A few publications before this period were included when they provided historically significant information, such as original descriptions of acrylate-induced allergic contact dermatitis in nail technicians and dentists. Controlled vocabulary was combined with free-text keyword searching using the Boolean logic operators AND/OR. Search strategies were developed separately for seven clinical aspects investigated in this review. The scope of the literature review included the following seven domains: (1) chemistry and sources of exposure, (2) mechanisms of sensitisation, (3) clinical presentation, (4) diagnostic methods (5) epidemiology, (6) occupational exposure, and (7) prevention and management. Key search terms used were: acrylate, methacrylate, acrylic acid esters, allergic contact dermatitis, contact allergy, skin sensitisation, nail technicians, dental personnel, dental materials, occupational dermatitis, isobornyl acrylate, glucose sensors, insulin pump, medical device, patch test, HEMA, HPMA, EGDMA, baseline series, type IV hypersensitivity, Langerhans cell, topical corticosteroid, and skin protection. The search strings included: (acrylate OR methacrylate) AND ("nail technician" OR "dental personnel" OR "occupational dermatitis"); or (acrylate OR "isobornyl acrylate") AND ("glucose sensor" OR "insulin pump" OR "medical device"); or (acrylate OR HEMA OR HPMA) AND ("patch test" OR "baseline series" OR "contact allergy diagnosis"). Reference lists of all included reviews and key articles were examined by hand search to identify further articles missed during database searches.

Screening of records included a two-step process. In step one, titles and abstracts of all retrieved literature were reviewed according to inclusion and exclusion criteria. Relevant literature covered human subjects or human data, written in English language, discussing exposure to acrylates and/or methacrylates, sensitisation to acrylates/methacrylates, or

allergic contact dermatitis associated with acrylates/methacrylates. It had to address at least one of the seven review domains. Studies eligible for inclusion in the literature review included clinical studies, patch test series, occupational cohort studies, case series, case reports, and narrative/systematic reviews with clinically relevant or epidemiological content. Studies using animal models or in vitro methods were not included if their results could not be applied to human dermatitis patients. Studies dealing only with non-acrylate polymers, conference abstracts presenting no data, and papers not available in English were automatically excluded. Step two involved the retrieval of the complete literature to check if they still fulfilled the inclusion criteria. If the records did not provide any clinically relevant information or their reporting quality was poor enough to preclude proper interpretation, they were eliminated from consideration. Database searches provided hundreds of records relevant to one or more of the seven review domains. Elimination of duplicates at the title stage left about 200–250 records for full-text evaluation. About 76 references are cited in this thesis. Since this paper is a narrative review, the application of a standardized quality assessment tool was not undertaken for all the literature sources included in the paper. However, the quality and robustness of the evidence used to support each claim were taken into account while performing the synthesis process, and this aspect is reflected in the wording of the paper. A hierarchy of evidence was used for selecting the evidence that will be included in the paper. The highest importance was attached to data from large multicenter patch testing studies and epidemiologic surveillance from existing networks, such as the EECDRG, ESSCA, and NACDG, since they provided population-level data on acrylate sensitization. Peer-reviewed systematic and narrative reviews published in relevant dermatology and occupational medicine journals were used to provide clinical context. Peer-reviewed primary sources, including cohort studies, case series, and case reports, were used to support clinical claims. These sources were preferred for the sections where multicentre data were unavailable, e.g., the growing body of research on sensitization related to medical devices. Official guidelines and position statements issued by relevant professional organizations, such as the ESCD, were used to ground diagnostic and treatment recommendations. Sources of grey literature, patient information documents, and other non-peer-reviewed online sources were explicitly excluded as sources of primary evidence for clinical or mechanistic claims. When two papers provided divergent results, both sides of the argument were presented and analysed, and possible explanations for the inconsistency were outlined. For instance, in the debate between cross-reactivity vs. co-sensitization between methacrylates, both sides of the discussion were highlighted and analysed.

All relevant data from each included source were extracted in a narrative fashion. For epidemiological studies, the following data were extracted if provided: study design, population and setting, timeframe, sample size, allergens used, patch test positivity rates, and clinical relevance of reactions. Clinical studies and case series yielded data about the exposure context, clinical manifestations, patch testing outcomes, and patient outcomes. Reviews and guidelines were analysed for their scope, main conclusions, and level of evidence used. The analysis was done thematically, focusing on the seven clinical issues presented above. No statistical pooling was conducted, and the results were synthesized narratively.

OVERVIEW OF ACRYLATES

2.1 CHEMICAL STRUCTURE AND PROPERTIES

The acrylates and methacrylates are ester derivatives of acrylic acid and methacrylic acid, respectively. The common structural feature found in acrylates and methacrylates is a vinyl group, i.e., a carbon-carbon double bond conjugated with carbonyl. It is the reason for both the practical applications and the capacity to cause allergic sensitisation. In this context, the clinically relevant acrylates and methacrylates are represented by low molecular weight monomers that are applied in nail cosmetics, dentistry, and medical devices adhesives. These include 2-hydroxyethyl methacrylate (HEMA), 2-hydroxypropyl methacrylate (HPMA), ethylene glycol dimethacrylate (EGDMA), methyl methacrylate (MMA), triethylene glycol dimethacrylate (TEGDMA), bisphenol A glycidyl methacrylate (bis-GMA), isobornyl acrylate (IBOA), and ethyl cyanoacrylate. They should be distinguished from various high molecular weight polymers based on acrylates and methacrylates, such as polyacrylamide, polyacrylonitirile, and sodium polyacrylate (1).

Electrophilicity, molecular weight, and lipophilicity are among the key characteristics of an acrylate monomer that influence its potential allergenicity. The electrophilic nature facilitates the ability of a free monomer to enter a covalent bond with an amino acid residue of skin protein, creating a hapten-protein complex which triggers type IV hypersensitivity. Methacrylate monomers carry a methyl group on the alpha carbon and have lesser electrophilic activity than acrylates, but they do retain their sensitising properties nonetheless. Interestingly, both HEMA and HPMA have been classified as two of the most frequent allergens found in patch test series despite being methacrylates. The second determining factor is the molecular weight of a monomer; only compounds of low molecular mass (less

than 500 Da) are able to penetrate healthy stratum corneum in amounts required for sensitisation. Both HEMA (130 Da) and MMA (100 Da) are highly penetrating, while bis-GMA (512 Da) is a much slower penetrator (1,2).

The sensitisation risk posed by acrylate products does not depend on the polymer per se but rather on the presence of residual uncured monomer. A fully polymerised acrylate resin, in which the vinyl bonds have been incorporated as part of the polymeric chain, is clinically inert in the overwhelming majority of patients. Residual monomers will always be present where polymerisation is incomplete. In terms of UV and LED polymerised gel nail materials, the extent of conversion will depend on factors such as the power output of the light source, exposure duration, depth of the material layer, and the amount of photoinitiator contained therein. Incomplete curing will lead to higher levels of residual HEMA, HPMA, and EGDMA at the nail plate surface and around the proximal portion of the nails. For dental composite materials, the clinical conversion of monomer units is estimated to be anywhere between 55% and 75%. This implies that a large portion of TEGDMA, bis-GMA, and HEMA molecules will fail to react and thus will leak out into saliva and pulp tissue. Sensitisation risk is thus not inherent to the product but is an exposure modifiable by intervention (1–3).

There is plenty of evidence for clinical relevance of cross-reactivity among methacrylates. Patch tests positive for one methacrylate monomer often react to similar structurally-related substances irrespective of any previous direct exposure to them. The hypothesis of the mechanism of cross-reactivity states that after sensitization to a specific methacrylate hapten, hapten-specific T cells identify the structurally similar hapten-protein complex formed by structurally-related methacrylate monomers because of their similar ester-vinyl chemical structure. Practically, HEMA, HPMA, EGDMA, and TEGDMA share considerable cross-reactivity among themselves. Polysensitization to two or more methacrylate monomers is common in most patch-tested subjects (4). It is still debated whether it represents true cross-reaction or co-sensitization due to concomitant occupational exposure to different methyl methacrylate combinations. However, the management implications are identical regardless (1,5). One important exception among methacrylate monomers is the isobornyl acrylate (IBOA). It is an acrylate ester containing a terpenoid alcohol part and having nothing to do with hydroxyalkyl methacrylates regarding its chemical structure, which means that it is not cross-reactive with methacrylates. The individuals sensitized to IBOA through the use of continuous glucose monitor will not respond positively to methacrylate screening (6).

Another substance used for eyelashes and nails adhesions – ethyl cyanoacrylate – is also not related to the (meth)acrylate family and shows little cross-reactivity with it (5).

Some of the chemical characteristics of acrylate monomers affect both the conduct of patch tests and their interpretation. One is the volatility of low-molecular-weight compounds – HEMA, ethyl acrylate – and the risk of progressively diminishing the concentration of the allergen due to its evaporation from test preparations (7,8). For this reason, it is advised that patch test chambers be filled right before applying them on the skin; the preparations should also be kept refrigerated. There is always a risk that the preparation becomes diluted to a concentration insufficient to induce a reaction, leading to a false-negative test result. Another aspect of the volatility of these compounds is their instability, resulting in an unstable allergen concentration in commercial preparations used across laboratories. This could lead to differences in positivity rates observed between studies. Additionally, because of the evaporation of allergen during the test procedure, delayed reading is advisable as the positive reaction might only develop in 5-7 days (9). Finally, as there is no cross-reactivity between IBOA and other methacrylates, patients allergic to device materials will be undetected unless a separate test with IBOA is performed. This is important for people with diabetes using glucose monitoring devices (6). Table 1 demonstrates acrylates' functional diversity by showing how monomer-specific structural motifs, such as carboxylate groups in polyacrylic acid and nitrile groups in polyacrylonitrile, determine their physicochemical properties.

Acrylate Monomer	Chemical structure (simplified)	Key properties
Polyacrylic Acid	$[–CH_2–CH(COOH)–]_n$	Superabsorbent, pH-sensitive viscosity
Methyl Methacrylate (MMA)	$CH_2=C(CH_3)COOCH_3$	High transparency, UV resistance
Polyacrylamide	$[–CH_2–CH(CONH_2)–]_n$	Water-soluble, forms hydrogels
TEGDMA	$(CH_2=C(CH_3)COOCH_2CH_2O)_2CH_2$	Flexible, high cross-linking efficiency
Polyacrylonitrile (PAN)	$[–CH_2–CH(CN)–]_n$	Thermal stability, UV resistance, wool-like fibers
Ethyl Acrylate	$CH_2=CHCOOCH_2CH_3$	Pungent odor, highly reactive
2-Ethylhexyl Acrylate	$CH_2=CHCOOCH_2CH(C_2H_5)C_4H_9$	Low density, hydrophobic
HEMA	$CH_2=C(CH_3)COOCH_2CH_2OH$	Hydrophilic-hydrophobic balance, viscous liquid
Sodium Polyacrylate	$[–CH_2–CH(COONa)–]_n$	Superabsorbent (1000x water weight), granular powder
Bisphenol A-Glycidyl Methacrylate (Bis-GMA)	Complex epoxy-methacrylate structure	Epoxy resin precursor, poor water solubility

Table 1: Key acrylate monomers, their simplified chemical structures, and characteristic properties. Data highlight the relationship between molecular features (e.g., functional groups, polymer backbones). Abbreviations: TEGDMA – triethylene glycol dimethacrylates

2.2 USE OF ACRYLATES

Acrylates were synthesized for the first time in the mid-nineteenth century, namely, acrylic acid was synthesized in 1843, while methacrylic acid was synthesized in 1865. Acrylate polymerization occurred for the first time in 1877 by German chemists Fittig and Paul, and industrial production of polymethacrylate from methyl methacrylate began in 1928 (10,11). Clinical importance of acrylates in dentistry was identified in 1930 as heat and pressure-moldable polymethacrylate moldings were invented; intraoral polymerization of dental resins via ultraviolet light or chemical polymerization occurred in 1940 and remains fundamental in contemporary dental composite material development (11). MMA was the major component in nail products until the year 1974 when the FDA prohibited its use because of sensitization problems, which made ethyl methacrylate the major nail monomer (12).

Currently, the most clinically relevant acrylates are those that have direct contact with human skin or mucosa. UV and LED gel nail products available on the consumer market from 2010 became the most common cause of acrylate sensitization today (13). Dentistry is associated with composite resins, bonding agents, denture base materials, and orthodontic adhesives; medicine includes acrylates in the form of bone cement for orthopedic and neurosurgical procedures, tissue adhesives like 2-octyl cyanoacrylate, wound dressings, adhesives for electrodes in electrocardiogram, adhesive components in continuous glucose monitors and

insulin pumps (14). Contact lenses made of polymethacrylate have been used since 1936, while intraocular lenses and orthopedic implants involve use of methacrylate-silicon copolymers (15). This variety of acrylate-containing products implies involvement of many specialties in patient care related to the risk of sensitization. Awareness of different acrylate sources in clinical practice is essential for early recognition of the condition.

2.3 EXPOSURE ROUTES

Acrylates enter the body of a human through multiple routes. Depending on the exposure type and duration, they can pose a potential health risk.

1. Mucosal exposure: In the past, acrylates were primarily encountered in manufacturing sectors such as printing, painting, coating, dentistry, and metallurgy. Sources that were most common included coating, floor waxes, leather treatments, paper products, and textiles. One example of an occupational allergic contact dermatitis is among the dental workers, where there is a considerable increase in the number of reported cases in the 1990s. Those dental professionals exposed to composites, bonding agents, and prosthetics have long been considered one of the most significant risk groups. The unique allergenic profile and clinical presentation of such a group are further explored in Section 3.4 (2).

2. Dermal contact: In recent decades, a shift in sensitization from dentistry to the beauty industry has steered a widespread use of acrylates in artificial nails, hair extensions, and eyelash adhesives. 1956 marks the first case of nail-related acrylate allergy reported. Today, approved nail techniques such as gel polish and acrylic nails use a base product that requires UV or LED curing (16). Introduction of the so-called permanent nail polish, which contains photo-bonded acrylates, increased the sensitization to acrylates that appeared on the market around the year 2010. According to an investigation carried out by the European Environmental Contact Dermatitis Research Group (EECDRG) in multicenter clinics across Europe on patients referred for patch testing with positive results for acrylates, 67% were attributed to exposure to nail cosmetics, being the single largest exposure category in this particular group of clinic patients. Occupational and consumer exposure accounted for 56% and 43%, respectively. The epidemiological significance of this occupational exposure pattern is discussed in Section 4.2 (17). Allergic contact dermatitis related to insulin pumps has been reported since the mid-1980s, when it was related to components of infusion, including nickel needles, acrylate adhesives, and methyl methacrylate in cannulas. New cases

have emerged around 2018, when acrylate compound isobornyl acrylate was recognized as an important allergen in Omnipod insulin pump (6).

3. Inhalation: Although this route of exposure to volatile acrylates is not as commonly discussed as dermal exposure, the topic is included in the review as an underappreciated route of sensitization, especially in a setting where ventilation is poor. The unreacted acrylate may be volatilized from resins, dental/cosmetic products, and adhesive products to a concentration that induces respiratory irritation. Although the most common manifestations of acrylate allergy are cutaneous, respiratory symptoms such as wheezing, cough, and even asthma exacerbation have also been reported in acrylate-exposed workers via this route in the use and handling of acrylate materials. For example, a study in the dental industry reported respiratory hypersensitivity reactions in workers exposed to volatile acrylates in a setting where ventilation is poor, such as when mixing/curing resin composites (2). Moreover, reviews on acrylate exposure have expressed concern that even at a low level, the exposure to acrylate vapors induces respiratory irritation and may exacerbate existing respiratory disease, although this is much lower than the level of exposure via the dermal route (18). Figure 1 illustrates how acrylates appear in numerous cosmetic products as well as industrial and healthcare materials, highlighting the diversity of exposure routes (19).

Home and consumer products	Medical products	Industrial goods
Super glues	Adhesive tapes	Adhesives
Nail cosmetics	Wound dressings	Coatings
Eyelash glues	Liquid tissue adhesives	Sealants
Hair extension glues	Bone cements	Paints
Disposable diapers	Dental fillings, adhesives, and prostheses	Lacquers
Sanitary and incontinence pads	Electrocardiogram electrodes	Paper products
In-ear headphones	Intraocular contact lenses	Printing inks
	Diabetes devices (eg, insulin pumps, glucose monitors)	Floor polishes
	Hearing aids	

Figure 1: Acrylate-containing products across cosmetic, industrial, and healthcare settings, illustrating the diversity of exposure routes. Source: Tackling Acrylate Allergy: The Sticky Truth, Cutis 2022

CONTACT ALLERGY TO ACRYLATES

3.1 MECHANISM OF ALLERGIC CONTACT DERMATITIS

In discussing the mechanism of contact allergy that occurs because of acrylate exposure, it becomes imperative to first explain the difference between the two types of contact dermatitis. Irritant contact dermatitis is a non-specific response that releases mediators of inflammation mainly from epidermal cells due to direct chemical damage to the skin. On the other hand, allergic contact dermatitis is an immunologically mediated hypersensitivity

reaction (type IV) caused by exposure to a specific exogenous hapten (20). A hapten is a small chemical molecule that cannot start an allergic reaction by itself, but is capable of interacting with the body's own proteins in such a manner that they change their shape (spatial conformation), which makes them recognizable as a foreign allergen by the immune system (21). Most haptens are electrophilic compounds that like to form covalent bonds with nucleophilic residues on skin proteins, creating antigenic epitopes. Allergenic potential of a hapten is set by several factors, the speed and strength of its binding with proteins, ability to penetrate the skin, its electrophilic properties, hydrophobicity, and overall bioavailability (22). Allergic contact dermatitis requires two phases: The sensitization phase and an elicitation phase for the recruitment and activation of specific T cells at the site of hapten sensitization with skin (23).

3.1.1 SENSITIZATION PHASE

Phase I – Sensitization: When haptens interact with the skin, they immediately interact with keratinocytes, dermal dendritic cells, and Langerhans cells. Langerhans cells release interleukin-1β, interleukin-18, tumor necrosis factor alpha, and granulocyte macrophage colony-stimulating factor. In exchange, they activate Langerhans cells and dermal dendritic cells and induce their migration to the draining lymph node, where they mature and present hapten (contact allergen) – antigen to naïve T cells, causing haptenation (22). This is called the sensitization phase, also referred to as the afferent phase of allergy contact dermatitis. The sensitization step lasts 8-15 days in humans (23). Haptenation also triggers the release of 'danger signals' also called damage–associated molecular patterns, such as hyaluronic acid, extracellular matrix ligands for toll-like receptors (fibronectin, prostaglandin E2, reactive oxygen species, heparin sulfate, tenascin, B defensins, and fibrinogen). These signals intensify the immune response by activating immune cells through the innate receptors like toll-like receptors (TLRs) and nucleotide-binding oligomerization domain (NOD) like receptors (NLRs). One key pathway is pyrin domain containing 3, which is specific for the NLR family in keratinocytes, leading to the release of more cytokines and furthermore promoting dendritic cell maturation. Once matured, the antigen–presenting cells present the processed hapten protein complex to CD8+ or CD4+ T cells. This reaction results in the formation of hapten – specific memory T cells, which are critical for recognizing the allergen upon future exposure. Other immune cells, such as mast cells, release signals that help dendritic cells activate and migrate. Natural killer cells directly start an immune response, especially when adaptive immunity is absent. The sensitization phase 'primes' the immune

system. It builds a memory of the hapten by activating various immune cells, so that in the future, when an exposure happens, the body can react faster and stronger, leading to symptoms seen in allergic contact dermatitis (24).

3.1.2 ELICITATION PHASE

Phase II – the elicitation, effector, or efferent phase represents the second phase of allergic contact dermatitis. Re-exposure of the sensitized individual to the same hapten/antigen results in the activation of innate cells. This causes the recruitment of previously formed antigen-specific memory T cells. Typically, within 24 hours of allergen re-exposure, it is the tissue resident memory T cells that drive the rapid contact hypersensitivity reaction. T cells produce local interferon-gamma, IL-17, IL-22, IL-4, IL-13, and TNF-alpha that trigger cytotoxic CD8+ effector T cells and innate immune cells, resulting in type IV hypersensitivity reaction (24). Other hapten-specific effector CD4+ T cells (including helper T cells and regulatory T

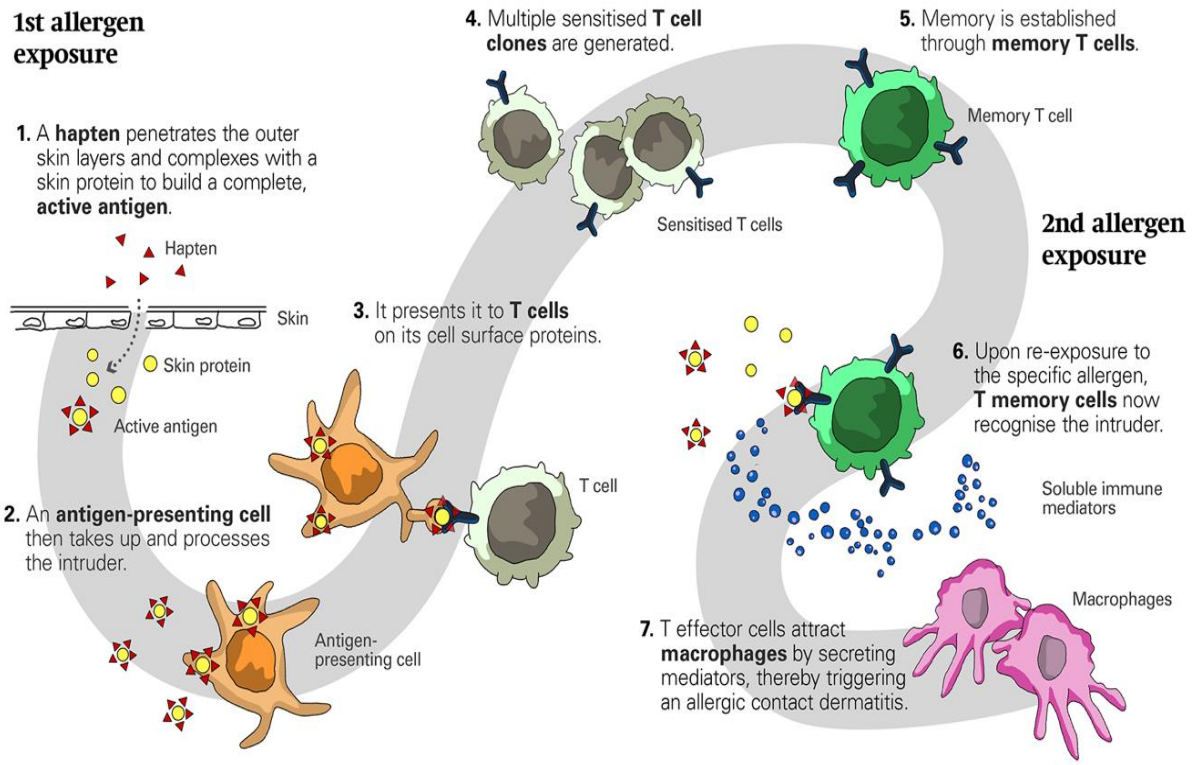

Figure 2: Mechanism of acrylate-induced allergic contact dermatitis, illustrating key events in the sensitisation and elicitation phases including Langerhans cell migration, hapten–protein complex formation, and T-cell activation. Source: Rustemeyer T, Curr Treat Options Allergy 2022

cells) are also key players. CD4+ T cells contribute to the migration of inflammatory cells from the blood to local tissue, apoptosis of keratinocytes, and activation and regulation of other inflammatory cells (25). Pathogenicity of antigen-specific T cells in allergic contact

dermatitis is a key factor, but it was previously believed that innate cells played a secondary role, which depicted a backup role in mediating tissue damage in the elicitation phase. Recent studies demonstrate that innate immune cells are, in fact, critical moderators of the efferent phase of allergy contact dermatitis (24). Innate immune cells that are involved in the allergic contact dermatitis are Langerhans cells and dermal dendritic cells, which are mainly involved in the sensitization phase, but macrophages, mast cells, innate lymphoid cells, neutrophils, basophils, and eosinophils are mainly seen in the elicitation phase (25). Figure 2 provides a visual summary of the principal immunological events in both the sensitization and elicitation phases of acrylate-induced allergic contact dermatitis (21). Each of these immunological processes is characterized by particular mediators. The identities of these immune mediators

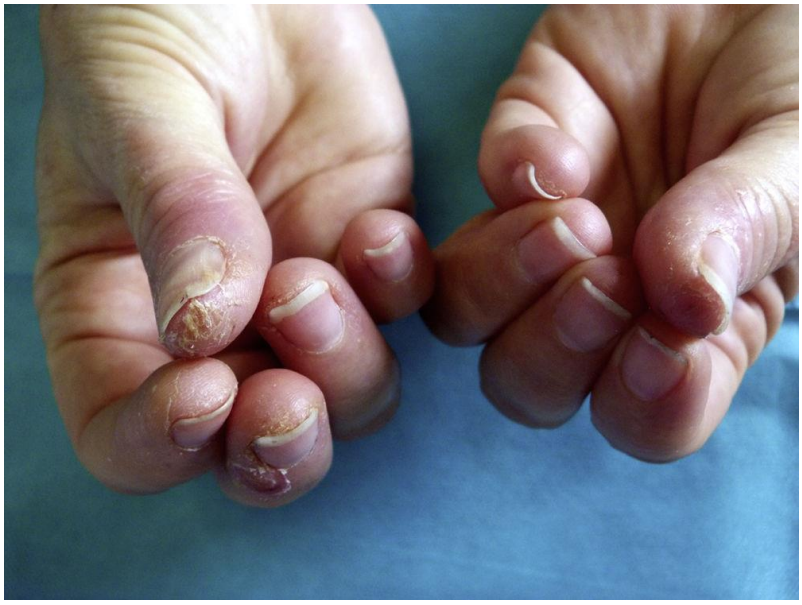

Figure 3: Beauticians commonly show dry fissured pulpitis lesions on their fingertips affecting both hands while presenting more intense symptoms on the dominant hand. Source: Gatica-Ortega et al., Actas Dermosifiliogr 2018

are discussed further for the individual processes of sensitization and elicitation in **APPENDIX A. Key Immune mediators (summary)** , serving as a supplementary guide to the detailed explanation of the mechanisms provided in this chapter.

3.2 CLINICAL PRESENTATION

Allergies to acrylates classically show up as rashes on the face or eyelids, nail damage, skin irritation around the nails, and hand eczema (often with cracked fingertips) (5). Clinical manifestations commonly involve the fingertips and periungual skin among beauticians and nail technicians (Figure 3). In the acute phase, when symptoms first appear, the lesions are

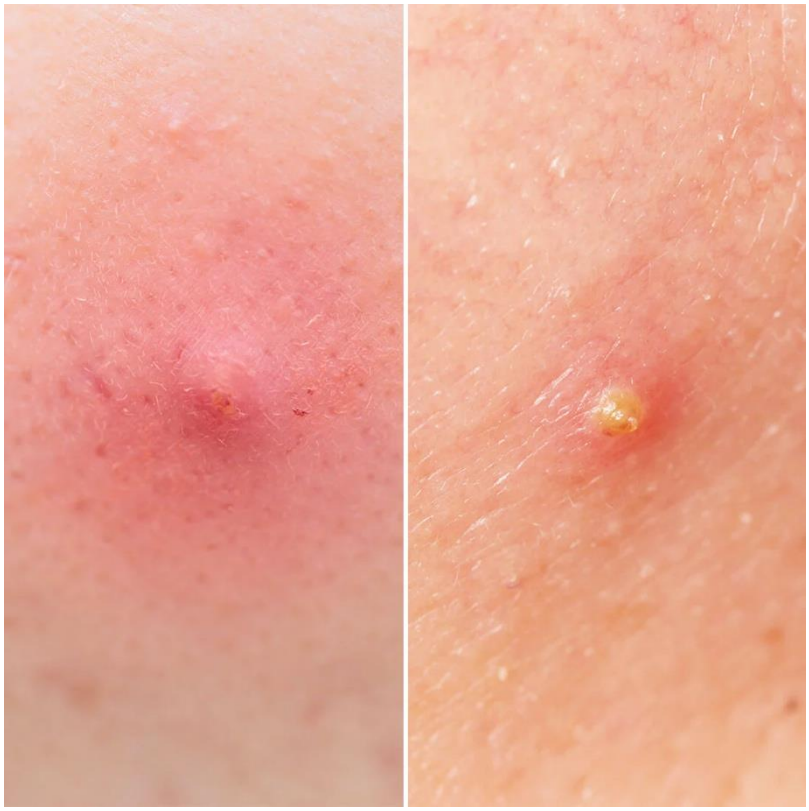

Figure 4: Inflammatory papules and pustules representing morphological features of allergic contact dermatitis. Source: Litchman G et al., StatPearls 2025

exudative and pruritic, but later they progress to a dry, fissured chronic pulpitis with subungual hyperkeratosis, along with pain as the major symptom in that area (16). With the contact of allergen/hapten to the skin, there is this reaction, most often on the hands and face, but it can appear anywhere. In some cases, white patches (leukoderma) may grow on the fingertips, and rashes may show on the face or neck (2,26). Changes in the nail that resemble psoriasis (due to onycholysis and severe subungual hyperkeratosis) can also happen; they characterize a nail lift and thickening under the nails. However, not all skin problems in these areas are allergic, irritant reactions, or conditions like 'acne mechanica' which manifest as inflammatory papules and pustules caused by mechanical pressure should also be considered (27). Figure 4 shows the clinical appearance of papules and pustules, which represent typical morphological characteristics of allergic contact dermatitis caused by acrylates (20). Breathing problems such as asthma can be triggered by acrylates and methacrylates. Among dental personnel, different frequencies of allergies to certain acrylate haptens were observed. Dental workers exhibit a pattern of lesions, where the lesions are localized on the fingertips and sometimes extend to the face due to inhalation of airborne particles. The allergens responsible for this are outlined in Section 3.3. Eczema of the hand and fingertips was noted as a typical clinical indication of allergies to methacrylate in these dental professionals; there

is a possibility for generalized dermatitis as well (5). Acrylates can also cause allergic contact stomatitis, especially if dental materials are not fully polymerized. Symptoms include burning, numbness, or pain in the mouth, inflamed gums, taste alterations, and ulcers (2,5). Allergic contact dermatitis (ACD) caused by acrylates in products such as artificial nail products is often overlooked, as the bridge between manicure products and nail problems is not always obvious. A significant clue in diagnosing is when all nails are affected, and there are no signs of typical nail psoriasis (example salmon patches), meaning nail biopsies are usually unnecessary then. The epidemiological data of EECDRG presented in Section 4.2 provide additional support for the idea that nail cosmetics represent the primary source of acrylate sensitization both in occupational and consumer settings, especially since occupational cases tend to develop quickly after the initial exposure. Most affected individuals had not only one acrylate type but multiple, where the most frequent allergens were 2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate, and ethyl cyanoacrylate. In relation to cosmetology, cutaneous manifestations can become more widespread and persistent since there is repeated occupational exposure. In the context of occupational acrylate exposure, sensitisation can extend beyond the skin to affect the nasal passages and eyes. There is evidence linking methacrylate exposure at work to reduced lung function and airway inflammation. The irritant effect of acrylates causes nasal and respiratory symptoms like conjunctivitis, asthma, and rhinitis. A popular cosmetic procedure involving eyelash extension can cause acrylate-related reactions. The glue used for applying these artificial lashes often contains cyanoacrylates, which can cause blepharitis in clients and hand eczema in workers. Symptoms like conjunctivitis and rhinitis may appear early in the application process due to eosinophil activation in tear glands and nasal tissue (5). A case was reported in which a beautician developed eye and nasal symptoms after using acrylate-based eyelash glue (containing ethyl-2-cyanoacrylate, alkoxy-2-cyanoacrylate, and poly (methyl methacrylate) for two years. Symptoms resolved with stopping the use of the adhesive (2). Redness, swelling, itching, and pain around the nail bed and cuticles, and in some cases, blisters filled with clear fluid may develop; these symptoms generally emerge within a few hours to a couple of days after exposure to the allergen. It may spread to other parts of the body through direct contact with the allergen or by touching the affected area and later the non-affected area (5). In beauticians, lesions on the finger pads of the dominant hand are more commonly seen, often on the first finger. This pattern reflects the stereotypical practice of removing excess polish with the fingers, particularly the index finger, rather than using a tool. Additional affected areas include the dorsum of the nondominant hand, where polish is wiped

off, the forearms, which are also included from resting on a contaminated table, and thighs/abdomen (from spillage). Patients also sometimes present with mild paresthesia, which they describe as a tingling sensation and decreased sensitivity in the fingers (16). Considering dermatologic differential diagnoses, those of acrylate-induced ACD prove numerous and diagnostically challenging. For instance, periungual eczema as well as onycholysis might mimic psoriasis of the nails; however, the lack of salmon patches, pitting, and other signs of psoriasis anywhere on the body, as well as a generalized nature of the disorder and presence of the relevant exposure, make it more likely to be acrylate-related as opposed to psoriasis. Moreover, palmar and digital dermatitis may mimic pompholyx eczema or irritant contact dermatitis provoked by wet work. As far as oral manifestations, the condition should not be confused with aphthous stomatitis, oral lichen planus, and true oral allergy syndrome, which is provoked by food rather than acrylates. Finally, the clinician must get the exposure history of the patient and use an appropriate set of allergens for patch testing rather than limiting to the basic series of patches.

3.3 DIAGNOSIS

Diagnosis of acrylate-induced allergic contact dermatitis (ACD) primarily depends on detailed clinical evaluation (history and physical examinations). The morphology and location of dermatitis are often the best indicators of the causative agent. Patch testing is the gold standard for confirmation of acrylate-induced allergic contact dermatitis (28). Figure 5 shows a positive patch test (5). In beauticians, it is often sufficient with the strong clinical presentations, as they often associate symptom onset with exposure to nail products, especially permanent nail polish. However, confirmation is best attained via patch testing with a panel of acrylates, including 2-hydroxyethyl methacrylate (HEMA), hydroxypropyl methacrylate (HPMA), and ethylene glycol dimethacrylate (EGDMA), which account for most of the reactions and are commonly found in artificial nail systems. Acrylates are volatile and, at room temperature, degrade, so it is crucial that patch tests are prepared once they have been applied. This also helps to discard the first extrusion from the syringe to avoid underdosing. Since acrylate substances are prone to evaporation, they may sometimes result

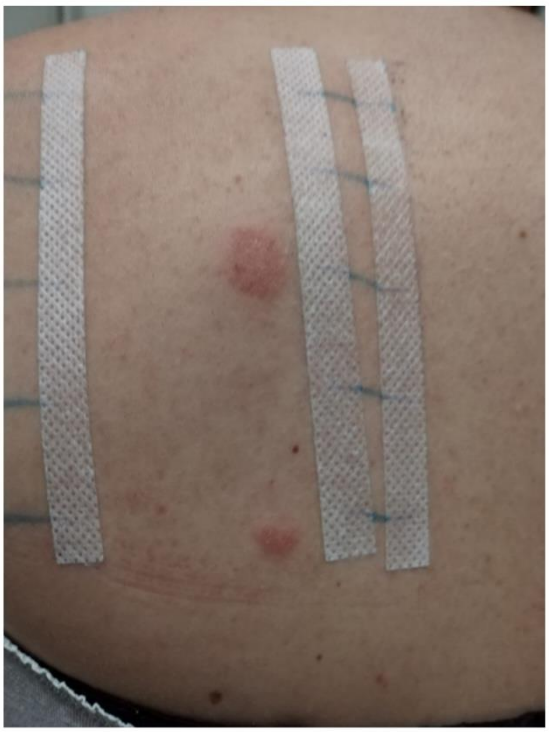

Figure 5: Positive patch test for contact allergens/standard testing procedure. Source: Lugović-Mihić L et al., Cosmetics 2024

in false negatives when they are placed in chambers too early or stored improperly. Strong positive reactions (2+ or 3+) are often yielded by patch testing. Sometimes they present with so-called angry back syndrome (positive patch test reaction which becomes hyper-reactive to

other patch test challenges) or acquired leukoderma. Testing with the actual products is discouraged due to risks of active sensitization and toxicity. Importantly, when testing acrylates, a delayed reading is necessary (16,29). A multicenter study by Forkel et al. demonstrated that without a day 7 reading, an average of 11.7% of acrylate sensitizations would have been missed (9). In comparison to professionals, consumers, particularly those using home kits, may not connect symptoms like periungual eczema or facial dermatitis with nail products. Clinicians should evaluate sequential patterns and exposure risks from occupations or cosmetics (16). Acrylate allergy can be polyvalent, meaning many patients can react to multiple monomers due to cross-reactivity or co-exposure in various formulations. Multiple studies demonstrate that HEMA and HPMA are reliable screening markers, with positivity rates over 90% and 64.1%, respectively, of allergic individuals. This has swiftly led to recent proposals to include them in the European baseline series (2). Acrylates are not included in the standard TRUE (thin-layer Rapid Use Epicutaneous) test series but are included in the North American Comprehensive series and the American Contact Dermatitis Society Core Allergen series. This allows dermatologists to conduct an expanded series of allergens, ensuring accurate diagnosis of acrylate-related ACD, particularly in the workplace, where exposure can lead to disability if not addressed (1,18,28). Regional variations are seen in the baseline series, reflecting variations in exposure, medications, and cultures. Although the European Baseline Series (EBS) is the first reference standard worldwide, many countries within the European Union have their own standardized series (30). Isobornyl acrylate, being a monomer, does not cross-react with other acrylates and must be tested separately, as misdiagnosis may occur if not tested individually. A thorough history and physical, including lesion conformation and distribution on the body, is required for accurate diagnosis. Fungal infections, bacterial superinfections, or even scabies should also be ruled out as a differential diagnosis. For this, various tests like a potassium hydroxide prep, culture, or even dermoscopy can be employed. Patch tests are also of prime importance, especially when avoidance of the causative agent does not yield any results. The diagnosis of acrylate allergy-induced allergic contact dermatitis is mainly based on history-taking and physical examination, and patch testing is considered the definitive method of verification. Patch testing is said to provide a sensitivity rate of 70–80%, with serum testing or skin-prick testing being inferior. Serum testing or skin-prick testing is not recommended since acrylate allergy involves type IV hypersensitivity (1,31). For diagnosing dental acrylic allergy, history taking and physical examination are of prime importance. A detailed examination of the oral cavity should also be conducted. There is even a chance that the patient may present with a similar

manifestation of oral allergy syndrome. Oral allergy syndrome, however, is usually associated with food allergies, not with materials like acrylic. Misdiagnosis may be avoided by patch testing. Finally, to confirm the diagnosis, removal of the acrylic prosthetic, as well as any changes in the manifestation of the symptoms, can even be indicated by a dentist (5). From a practical point of view, the diagnostic algorithm varies depending on clinical practice. In cases of dermatologic and allergic problems, a focus is placed on conducting the patch test employing the extended acrylate series, which involves HEMA, HPMA, EGDMA, MMA, TEGDMA, bis-GMA, IBOA, and ethyl cyanoacrylate substances, read after two or four days and then after seven days; IBOA has to be tested separately and is usually not involved in routine patch test procedures. If the patient consults a dentist about recurring problems, such as soreness, gingival inflammation, or dermatitis around the mouth area following a tooth restoration procedure, he or she needs to take the patch test with the dental material set in addition to the acrylates set. In cases where the patch test is inconclusive, the removal of the offending prosthetic or restoration, along with symptom improvement, constitutes confirmatory diagnostic data. In the fields of diabetology and endocrinology, one needs to remember that any patient wearing a continuous glucose monitoring sensor or insulin pump suffering from geometrical patterned eczematous lesions located in the vicinity of the device needs IBOA patch test and referral to a dermatologist proficient in medical device allergy, and, in case of positive results, device replacement or barrier film usage may be considered pending results. Occupational medicine calls for proving the connection between workplace exposure to allergens and the occurrence of symptoms and their improvement during breaks away from work; such information, combined with a patch test, proves occupational allergic contact dermatitis.

3.4 RISK FACTORS

Acrylate allergy, a type IV hypersensitivity reaction, is now recognized as a major factor in causing allergic contact dermatitis (ACD). The risk factors are seen in not only the "occupational" domain but also in the "environment" and "individual susceptibility" domains. Occupational exposure is considered to be the main source of acrylate sensitivity. Dental and medical practitioners, including dental technicians, dentists, and orthopedic surgeons, are considered to be highly susceptible to this allergy because of their repeated exposure to acrylate monomers in composite resin, dentures, bone cement, and adhesives. The major sensitizing agents among dental workers include low molecular weight methacrylate monomers, particularly those used in uncured composite and bonding materials (as detailed

in Section 3.3) (2,5,32). Industrial workers in printer manufacturing, construction workers, and textile industries are also highly susceptible because they are exposed to paints, inks, and coatings containing acrylate monomers in their work processes. Nail artists, manicurists, and eyelash stylists are also highly susceptible because they are exposed to acrylate-containing nail polish, dip powder, and eyelash adhesives (2,16,32). With the rise of self-home beauty treatments, non-occupational risks are also seen in this case. Artificial nail enhancement, including gel manicure and acrylic nail treatments, contains acrylate monomers. This exposure to allergenic monomers is worsened by the curing of the improver due to insufficient ultraviolet lamp strength or hasty application techniques (18,33). Eyelash extensions with a high base content of cyanoacrylate adhesive can cause rhinoconjunctivitis. Because of the high cross-reactivity of acrylates. For example, sensitization to acrylates from nail care can cross-react with dental or medical adhesives (18,32,33). Medical device utilization is an example. Diabetes care, for instance, utilizes a continuous glucose monitoring system or an insulin pump with an adhesive rich in acrylates. Isobornyl acrylate (IBOA) is a critical allergen component in these devices; in a study involving case studies of device-related allergies, IBOA was a common allergen associated with the majority of confirmed cases of continuous glucose monitors and insulin pumps. Surgical procedures include bone cement, wound dressings, or surgical adhesives like Dermabond. These can cause localized or systemic reactions, especially for healthcare workers who come into contact with these materials (5,6,32). Some biological or behavioral risk factors can also increase the risk of acrylate allergy. These include eczema or psoriasis with a disrupted skin barrier for acrylates to penetrate the body. Individuals with a history of allergies to formaldehyde or latex also become hyperreactive to acrylates. Another possible way of sensitisation involves low-dose exposures to low-risk products like cured polymer preparations that still contain residual levels of monomers. Even acrylate vapors during nail curing and processes possess no different risks to systemic sensitization if ventilation in the facility is inadequate (26,33,34). Table 2 is an overview of some important acrylate and methacrylate monomers with their sources of exposure, patient groups exposed, clinical manifestations, and their relevance in patch testing.

Monomer	Common Sources	Typical patients	Clinical pattern	Patch Test Marker
HEMA	Gel nails, dental bonding	Nail techs dentists	Periungual eczema	Screening allergen
HPMA	Nail systems	Nail techs	Hand eczema	Often co-positive
EGDMA	Dental resins, nails	Dental staff	Hand dermatitis	Extended series
MMA	Dental labs	Technicians	Hand/airborne	Volatile -false negatives
IBOA	CGM devices	Diabetic patients	Geometric plaques	Device series

Table 2: Overview of selected acrylate and methacrylate monomers, their common exposure sources, typical clinical presentations, and diagnostic relevance in patch testing. Abbreviations: HEMA – 2 hydroxyethyl methacrylate; HPMA – 2 hydroxypropyl methacrylate; EGDMA – ethylene glycol dimethacrylate; MMA – methylmethacrylate; IBOA – Isobornyl acrylate.

EPIDEMIOLOGY OF ACRYLATE ALLERGIES

4.1 HIGH RISK POPULATION

As detailed in Section 3.4, the risk group at the highest risk of acrylate sensitivity is made up

Figure 6: A- Nail technician applying gel polish without gloves. B - Industrial worker in a printing/fiberglass factory without a mask. C - Dental workers handling acrylate based composites.

of those whose occupations or recurrent exposures to the monomers in their natural state result in sensitization; these groups include nail technicians, dental professionals, print

industry workers, fiberglass manufacturers, and those who use at-home gel nail sets. People with skin barrier disruption due to atopic dermatitis are at increased risk independently of their occupations. The following sections provide statistical evidence supporting the magnitude of sensitization within the aforementioned populations and the trend towards shifting sensitization risks from occupational to consumer-based environments (2,34). Other people more likely to suffer from an acrylate allergy include those with pre-existing skin conditions like allergic eczema, as their skin is more likely to allow the penetration of acrylate compounds, thus increasing their risk of suffering from an allergic reaction. In addition, people with a history of allergic reactions to various substances are more likely to suffer from an acrylate allergy, as their immune system is more likely to be highly sensitive to substances, thus increasing their risk of having an allergic reaction to acrylate (5). Figure 6 illustrates the principal occupational and consumer groups at elevated risk of acrylate sensitization, together with the exposure contexts associated with each group (35–37).

4.2 PREVALENCE

All quantitative data mentioned in this part are taken from populations that underwent patch test in dermatology clinics due to the suspicion of ACD (and, thus, do not necessarily indicate the level of sensitization in the general population or even among those people occupationally exposed to acrylates). In addition, no prevalence study in a representative sample of the population could establish the prevalence of acrylate sensitization due to the lack of community-based cross-sectional surveys with confirmatory patch tests performed. As such, the presented figures can be considered minimum estimates of the problem. Therefore, in a retrospective cohort of 156 nail technicians and consumers who received patch tests due to suspected ACD, 116 subjects (74.4%) were found to be sensitized to one or several (meth)acrylates (all females), 138 (88.5%) experienced occupational exposure to acrylates, and 18 (11.5%) were consumers. The higher sensitivity is accounted for by the referred nature of the cohort; however, such figures could hardly be considered an indicator of the number of nail technicians sensitized in the general population. Moreover, in the same cohort, the proportion of cases in which (meth)acrylates were established to be the allergen increased from 55% (16 out of 29 cases) in 2009-2013 to 97% (100 out of 127 cases) in 2014-2018 (the increase is attributed to the growing popularity of UV gel nail products). Ethylene glycol dimethacrylate (EGDMA) turned out to be the most common sensitizer in patch-positive cases (in 113 subjects, 72.4%, and in 97.4% of all cases of (meth)acrylate positivity) (38).

In the study by EECDRG, carried out in several European dermatology clinics and including a total of 988 acrylate-positive cases, 67% were attributable to nail cosmetics, including 56% occupational and 43% consumer exposure. Of occupationally exposed persons in this population, 65% became sensitized within the first year after the beginning of their employment (this figure, again, does not indicate how many workers become sensitized in total but applies only to those who already have clinical ACD); the reason for this is explained by the rapidity of sensitization after the first contact with uncured monomers. The majority of patients with positive patch test results were polysensitive to two or several (meth)acrylate monomers. Most patients suffered from polysensitisation due to sensitivity to at least two acrylate monomers, which is consistent with the cross-sensitivity phenomena outlined in Section 3.3 (5,17).

4.3 OUTBREAKS OF ACRYLATE ALLERGIES

The most systematic data on trends in sensitization can be obtained based on surveillance data collected using patch test networks established previously. Nevertheless, it is important to remember that all presented figures refer to positivity rates among consecutively patch-tested dermatology patients, i.e., a specific selected referral population, rather than the prevalence of acrylate sensitization in the general population. Thus, according to the report of the EECDRG published in 2018, the positivity rate in patch tests for acrylates amounted to 1.1% (n = 18,228) among consecutively patch-tested patients attending specialist centers in Europe between 2013 and 2015. In addition, a later multicenter surveillance study conducted in Europe (2019–2020) registered HEMA positivity in 2.3% of 7,675 tested individuals, being even higher in Spain (3.7% of 1,884 patch-tested patients). According to the report of the NACDG, the rate of HEMA sensitivity increased significantly in comparison with 2009–2018 years and amounted to 3.2% (n = 4,111) among consecutively patch-tested patients in 2019–2020, showing a clear upward trend of sensitivity among patients attending patch test clinics, while the data cannot be used for drawing conclusions about trends in the general population.

Occupational patch test data can also contribute to the understanding of current trends in acrylate sensitization. According to the NACDG retrospective analysis, patients referred for patch testing due to suspected occupational contact dermatitis (2001–2016) showed a high prevalence of HEMA sensitization, amounting to 3.4% (83/2,461), ranking fifth place by the number of occupationally relevant reactions (73.5%, 83/113). These statistics were obtained

among patients referred to the investigation of occupational ACDs; thus, the presented figures cannot be extrapolated to the general occupational population and are not considered reliable for assessing sensitization prevalence in it. Also, NACDG analysis of patch-tested dental workers (2001–2018) showed that nearly one out of five cases of occupational ACD among those referred for patch testing was related to sensitization to acrylates. According to a Portuguese retrospective analysis covering a period of seven years, patch testing of patients referred for suspected acrylate ACD revealed that 68% of these cases originated from the workplace, while 80% of them involved nail technicians. Also, a study conducted in Sweden involving 28 nail technicians who attended patch testing showed that 57% tested positive to at least one acrylate monomer, yet these results cannot be generalized to the entire population of nail technicians since the study involved a limited sample size and referred patients (18). As a completely different data source, one can consider the analysis performed by Axler and Lipner (2024) based on social media queries on TikTok, where the researchers analyzed posts labeled with the hashtag #gelallergy. This dataset is substantially different from patch test surveillance data because the reports involve unvetted and nonclinical accounts of suspected reactions; thus, it is subject to strong selection and reporting bias, and the prevalence estimates cannot be drawn on its basis. Out of 366 videos analyzed, only 214 met inclusion criteria; specifically, 112 videos described suspected ACD associated with gel nail polishes and 86 educational videos on the matter, of which 11 were created by certified dermatologists. As regards reactions, 94 videos mentioned at-home gel kit products and 4 nail polishes applied professionally in salons. Analysis of the separate clinical case series of 35 patients with suspected nail-related allergy revealed that 28 patients had patch test-confirmed acrylate sensitization, of which 71% belonged to licensed salon technicians and 29% used home-made kits. Finally, there were also 33 videos describing exposure to non-nail products, such as dental materials, medical implants, insulin pumps, and adhesives (39).

PREVENTION AND MANAGEMENT

5.1 OCCUPATIONAL SAFETY MEASURES

Health professionals should be aware that skin reactions in the workplace can be due to acrylates or their monomers and that applying preventive measures can avoid contact dermatitis. It is advised that personal protective equipment, such as gloves, masks, goggles, and disposable smocks, be worn, and contactless administration methods be used whenever possible in order to reduce skin contact with potentially allergenic agents. Nitrile rubber gloves offer good resistance to methacrylate (MA) penetration capabilities and are more

effective than latex gloves for shorter exposure (15-20 minutes), as shown in patch tests. Recommended replacement after 30 minutes of use of these gloves should be considered. In the beauty industry, where handling of methacrylate-containing gel nail polish, 4H (ethylene vinyl/alcohol polyethylene) finger covers can be used under standard gloves if 4H gloves are not preferred. Double gloving with nitrile gloves provides some protection for no longer than 60 minutes. 4H gloves provide true protection but result in a loss of dexterity. The fingertall technique involves removing the fingers from a 4H glove, inserting them on the fingers, and applying a more flexible glove on top to hold them in place (19) (see **Error! Reference source not found.**) - (40). It is important to constantly take protective precautions to avoid occupational sensitization since, if this condition does develop, it will make changing one's career inevitable. Ensuring that new workers receive adequate personal protection during training is also important. The number of dental patients with acrylate allergies has declined in recent years, likely due to increased awareness of acrylate sensitization risks (2,5). Career counseling is important for individuals who develop allergies to acrylates, as it can impact job eligibility (17). There is a documented case of a manicurist who was unaware of the risks, switched to dental nursing after developing an acrylate allergy, only to suffer a recurrence due to continued exposure to substances like HEMA, HPMA, and EGDMA. To improve occupational safety, it is important to optimize acrylate polymerization conditions such as temperature, pressure, and catalysts, adding cross-linking agents, stabilizers like UV absorbers and antioxidants, and removing impurities can improve product performance and reduce sensitization risks. Nanoparticles may enhance stability and mechanical properties while managing molecular weight distribution, and using controlled radical polymerization can refine the final product (26). Occupational exposure limits (OELs) for acrylate monomers differ by jurisdiction and regulatory authority. They are usually provided as 8-hour time-weighted averages, sometimes accompanied by short-term exposure limits. For methyl methacrylate (MMA), the OSHA allowed exposure limit (PEL) is 100ppm, 8-hour time weighted average, while the American Conference of Governmental Industrial Hygienists (ACGIH) has a threshold limit value (TLV) of 50 ppm, 8-hour time weighted average with a short-term exposure limit of 100 ppm (41). For ethyl acrylate, the OSHA PEL is 25 ppm, 8-hour time-weighted average; on the other hand, the ACGIH TLV is more stringent at 5 ppm, 8-hour time-weighted average, having a short-term exposure limit of 15 ppm (42). The U.S Environmental Protection Agency has derived a chronic inhalation reference concentration (RfC) for MMA of 0.7 mg/m^3. This value, unlike occupational exposure limits, is a risk assessment tool. It can be an appropriate tool for the use of continuous lifetime exposure of

the general population and not for use as an occupational exposure standard (43). Substitutes for acrylates with similar performance but reduced toxicity include epoxy resins, polyurethanes, silicone polymers, vinyl ester resins, styrene acrylic copolymers, and polyester resins. These alternatives can be used across industries such as coating, adhesives, and medical devices. Additives can also reduce the irritant potential of acrylates. Photo initiators help ensure complete curing, which in turn reduces residual monomers. Stabilizers and inhibitors block early polymerization, and plasticizers work to minimize cracking and brittleness. The combination of antioxidants and biocompatible modifications using polyethylene glycol (PEG) helps to reduce skin irritation risks. A beneficial approach to reducing sensitization involves using higher-purity monomers in formulations that contain less monomer. Using cementless joint replacements or non-acrylate dental materials should be considered for individuals allergic to acrylates; clinicians must be trained to offer suitable

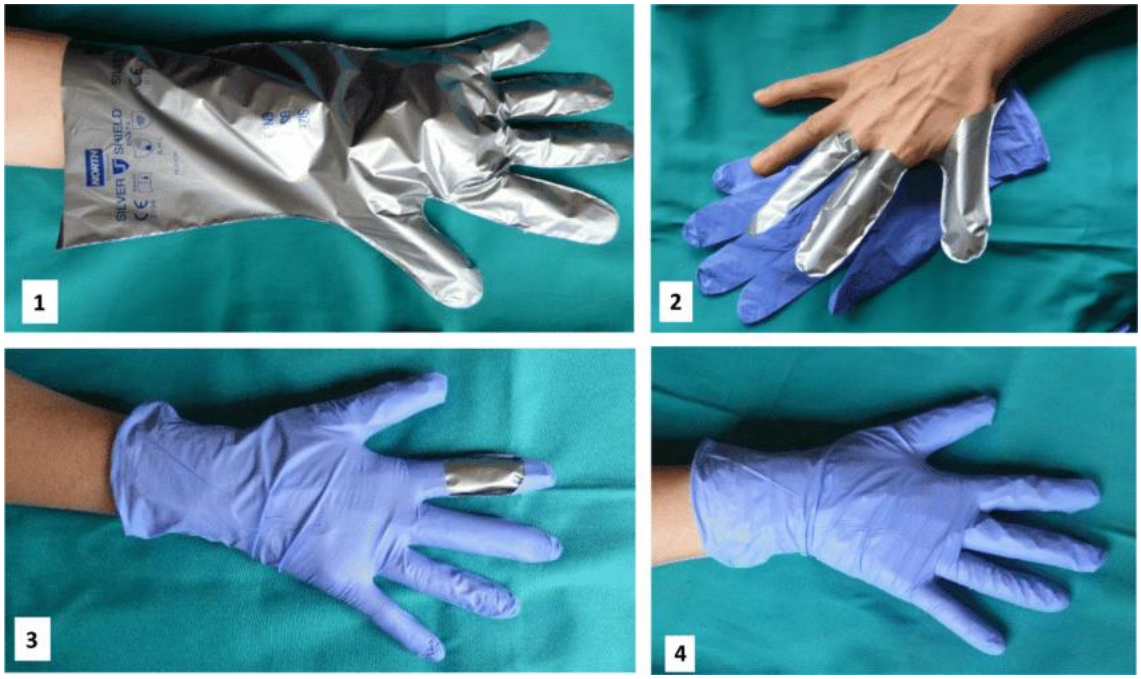

Figure 7:The picture demonstrates the preparation and application of shield 4H (Honeywell safety products EMEA), gloves fingerstalls together with instructions on how to secure them by wearing a nitrile glove over them.

alternatives in medical procedures (5). With respect to occupational medicine, a confirmed diagnosis of occupational allergic contact dermatitis due to exposure to acrylates has far-reaching implications beyond the initial event. In Europe and many national regulatory guidelines, occupational ACD is a reportable condition, and doctors have an obligation to support the reporting procedure. A sensitized employee who continues to work in high-risk occupations, such as nail technicians or dental nurses, will experience recurrent disease with a risk of worsening because sensitization levels do not decline. Occupational counselling

should determine whether it is feasible to remain in the occupation with increased protection or seek alternative employment through occupational retraining programs. A previous case study involving a nail technician with acrylate ACD who was retrained as a dental nurse and then developed sensitization to the acrylates she encountered during her new occupation highlights the importance of considering cross-sensitization issues in acrylate-containing industries when planning occupational change. Reporting occupational diseases to health authorities helps contribute to surveillance reports that may lead to further regulatory action; this has been seen in the past, as in the FDA's decision in 1974 to prohibit the use of methyl methacrylate in nail products (44).

5.2 CONSUMER AWARENESS

Medical adhesives and devices contribute a significant source of acrylate exposure, with growing evidence featuring their role in allergic contact dermatitis (ACD). A review by Spencer et al. warned that wound dressing is becoming a new source of sensitization, a concern that has been confirmed in the literature. 15 out of 16 (94%) tested medical adhesives have found acrylates, as shown in one study that included all seven labelled as hypoallergenic, which still contained acrylates and/or abietic acid. Several case reports have documented ACD caused by acrylate-containing adhesives in electrocardiogram electrodes. Physicians monitoring patients with diabetes should also be aware of acrylates present in glucose monitors and insulin pumps. This involves the adhesives or substances that leach from within the devices to contact the skin of the individual. Isobornyl acrylate has gained particular attention in this context, earning the title of 2020 Allergen of the Year due to its central role in diabetes device-related allergic contact dermatitis. Postoperative ACD triggers are increasingly recognized in cyanoacrylate-based tissue adhesives such as 2-octyl cyanoacrylate. While postoperative data are limited, studies suggest that 2% to 14% of patients may experience skin reactions after its use. Sensitization repeatedly occurs after initial exposure, with symptoms sometimes emerging up to a month later, which sometimes can complicate diagnosis by mirroring infection or other causes. One orthopedic case involved a woman with a known allergy to acrylic nails who experienced joint issues after knee arthroplasty with acrylic bone cement; her symptoms resolved after switching to a cementless implant. Clinicians should remain alert to the global diversity of acrylate-containing products as a source of unexpected sensitisation. Occupational allergic contact dermatitis has been reported from isobornyl acrylate in ultraviolet-cured phone screen protectors, and several cases have been brought about involving acrylates in headphones, as

well as one linked to a wearable fitness tracker (19). As seen in Figure 8, materials degrade when exposed to sweat or moisture, which releases allergens like methyl methacrylate into direct contact with the skin surface (6).

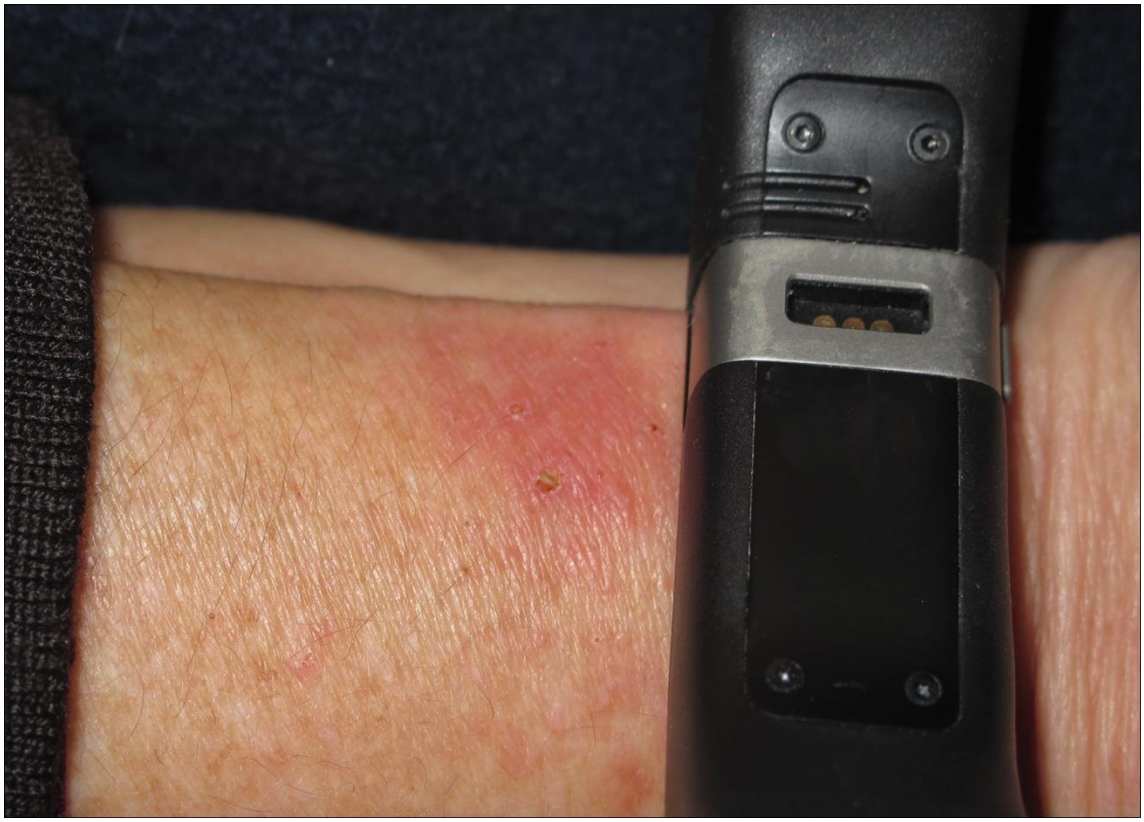

Figure 8: Localized geometric eczematous dermatitis at one site on the left wrist in close contact to wearable device. Source: de Groot A et al., Contact Dermatitis 2025

Considering alternatives is an option for regular nail polish instead of UV-cured gel polishes to minimize exposure to harmful acrylates. Seeking professional services, rather than doing it at home, can ensure proper application and curing, reducing the risk of skin contact and incomplete curing. Being vigilant with product labels, carefully reading the ingredient lists, and being cautious of products lacking clear labelling, especially those purchased from non-EU online platforms. Monitoring for allergic reactions such as skin irritation or nail changes after using gel polish, one should discontinue immediately and consult a healthcare professional. Inform relevant authorities and manufacturers about any adverse reactions to help improve product safety standards and regulations (45). Sensitization has occurred following a single contact in susceptible patients. The omnipresence of acrylates in consumer products, including nail cosmetics, hair products, hand sanitizers, adhesives, and inks, makes avoidance impossible, even for those who would like to try, presenting a barrier to avoidance that is difficult to overcome by education alone (26). For healthcare providers managing diabetic patients who are on CGM technology or insulin pumps, knowledge about acrylate-

induced dermatitis in relation to these medical devices has significant clinical implications. The hallmark clinical presentation of a sharply defined and geometrically shaped eczematous plaque in correspondence with the device's shape should be an indicator of contact allergy rather than an infectious process, pressure ulcer, or irritant dermatitis. Failure to make this distinction could result in the incorrect treatment of the condition, as well as premature discontinuation of using the medical device. In practice, the main issues to determine would be if there is an exact mapping of the rash with the device; if it recurs at every application of the device; and if the resolution of the problem occurs upon discontinuation of the medical device. In such instances, IBOA testing should be undertaken before any attempt to replace the current device due to its varying allergen composition, and even if a new model has been considered "IBOA-free" (6).

5.3 TREATMENT OPTIONS

The primary approach involves the removal or avoidance of the offending agent. Allergic contact dermatitis patients and those exposed to workplace or environmental hazards should wear protective gloves and clothing (46). Effective skin care routines serve as a primary approach to treating contact dermatitis and hand eczema. The main objective should be to repair the skin barrier since this action helps to lower the inflammation and relieve itching. The application of basic skin care practices reduces the dependence on topical corticosteroids. Research indicates that regular application of skin care products can aid in the healing process of both irritant and allergic contact dermatitis without requiring any additional treatments. The treatment plan for eczema requires the selection of skin care products appropriate to its current stage. In the acute phase of the skin, the skin is characterized as moist or weeping, and hydrophilic preparations such as gels, lotions, or creams are most appropriate. Whereas for chronic stages, where the skin is dry and thickened, water in oil-based formulation, like ointments, is typically more effective (47). When skin becomes sore and inflamed, medical professionals often prescribe topical corticosteroids to quickly alleviate the inflammation (47). Topical glucocorticoids serve as a standard treatment for hand eczema and other forms of contact dermatitis because of their ability to suppress inflammation, inhibit immune responses, and control cell proliferation. Choosing the right glucocorticoid requires finding a balance between its ability to treat conditions effectively and its potential to cause side effects such as skin thinning and visible blood vessel formation. Therapeutic index (TIX) is used as a scale where a range of 1 indicates a poor benefit-to-risk balance, and 3 indicates a good balance. Glucocorticoids belong to group 2 and are generally

preferred due to their more favorable safety and efficacy profiles. In cases of acute or severe contact dermatitis, short-term use of stronger glucocorticoids with a lower therapeutic index (TIX) may be necessary to quickly control inflammation. For chronic dermatitis involving thickened or hardened skin, high-potency glucocorticoids may be indicated due to their deeper skin penetration and antiproliferative effects. In sensitive areas such as the face, skin folds, and anogenital regions, weaker glucocorticoids are recommended. Different formulations, such as lotions, creams, and ointments, exist as topical glucocorticoids, and the choice should depend on the severity and appearance of the skin condition, as with basic skin care therapy. Patients with severe and extensive flare-ups may require short-term systemic glucocorticoid therapy such as prednisolone. Prednisolone should be administered at 0.5-1mg per kilogram of body weight daily for a maximum of two weeks with gradual dose reduction when dealing with severe or widespread flare-ups (47).

The steroid-free topical calcineurin inhibitors tacrolimus ointment and pimecrolimus cream use an action mechanism different from corticosteroids. These two creams provide skin-selective treatments that target key factors involved in the pathogenesis of contact dermatitis (48). They represent an alternative to topical glucocorticoid therapy. Their advantage is their safety in long – term use due to the lack of skin atrophy risk and the lack of disturbance in restoration of the skin barrier.

The Janus kinase (JAK) inhibitors target signaling pathways linked with Th2, Th22, Th1, and Th17 reactions, resulting in targeted immunosuppressive, anti-inflammatory, and antiproliferative actions. The small size of these inhibitors allows them to penetrate the skin, making their use both topical and systemic feasible. The topical application of JAK inhibitors is a promising treatment modality for inflammatory skin diseases, including contact dermatitis, although studies related specifically to ACD caused by acrylates are still lacking.

Systemic alitretinoin (9-cis-retinoic acid) has proven to be effective in randomized controlled trials and is FDA-approved for use in patients with severe chronic hand eczema that is unresponsive to conventional topical medications. Alitretinoin is considered suitable for intermittent long-term therapy of hand eczema (47).

Systemic steroids, these medications can be given orally or injected, and may be needed if the rash is severe, associated with swelling, or if the rash covers much of the body. When prescribed for a short period of time, they lead to rapid improvement and are usually considered low risk. In challenging cases, medical professionals may consider oral medications such as cyclosporine, methotrexate, azathioprine, and mycophenolate mofetil (47).

Healthcare professionals sometimes use systemic immunosuppressants such as ciclosporin, azathioprine, and methotrexate off-label for contact dermatitis without established evidence of their effectiveness (not well established). Ciclosporin may be considered for chronic, treatment-resistant hand eczema, particularly when first- and second-line therapies fail. Azathioprine has also shown some benefits in aerogenic contact dermatitis and chronic hand eczema. Phototherapy should be avoided during this treatment due to increased skin carcinogenicity. Methotrexate has been used in cases of refractory hand eczema (47). Phototherapy is used for children and adults with moderate to severe eczema where conventional treatment with emollients and topical steroids does not respond well. Phototherapy is not used if the person has UV-sensitive dermatitis or a photoallergic disorder. Phototherapy uses ultraviolet light to reduce skin inflammation by lowering the number of T cell lymphocytes involved in the immune response. This treatment should be administered two to three times weekly for 12 to 16 weeks, while each session progressively extends from brief intervals (seconds) up to 15 minutes. Three main types of phototherapy methods include narrowband UVB, broadband UVB, and PUVA (UVA combined with a light-sensitizing drug called psoralen). Narrowband UVB has become the phototherapy used most frequently because it has an ideal ratio between effectiveness and safety. At present, the use of broadband UVB therapy has been replaced by narrowband UVB treatment, while PUVA therapy is used only when a patient is resistant to the former (49).

Antiseptic therapy, such as topical antiseptics, is used in cases of superinfected contact dermatitis or in cases of potential colonization with pathogenic microbial germs as the contact dermatitis triggering factor. Therapeutic settings may include the use of potassium permanganate solution and triclosan along with chlorhexidine, polyhexanide, octenidine, and clioquinol as alternative treatment (47). Although antihistamines may provide symptomatic relief from pruritus, topical corticosteroids remain the preferred first-line treatment for the inflammatory component of allergic contact dermatitis, given their superior anti-inflammatory efficacy. The medical team may prescribe topical antibiotics or ointment when

open fissures demonstrate secondary bacterial infection (50). Table 3 demonstrates the sequential treatment method for acrylate allergies.

5.4 FUTURE DIRECTIONS

Ongoing research is essential to develop acrylate alternatives with reduced allergenic potential. Advancements in photo initiator technology have improved curing efficiency,

Stage	Treatment options	Notes
Prevention	Avoid acrylate products, protective clothing	Occupational safety key; 65% develop ACD within 1 year
Basic Care	Emollients, barrier-repair moisturizers	Reduces steroid dependence; essential for both irritant & allergic types
Topical Therapies	Corticosteroids (Group 2 preferred), Tacrolimus, Pimecrolimus	Match vehicle to skin phase (e.g. creams vs ointments); TIX 2 = good balance
Systemic Therapy	Prednisolone (short term), Methotrexate, Cyclosporine, Alitretinoin	For severe or widespread ACD; immunosuppressants used off-label
Phototherapy	NB-UVB (preferred), BB-UVB, PUVA	Used when topical/systemic options fail; avoid in photoallergic conditions
Adjunct Therapies	Antiseptics (e.g. chlorhexidine), Antihistamines, Topical antibiotics	For infection, secondary symptoms, or itch relief
Immunotherapy	Sublingual immunotherapy	For patients who can't avoid acrylate exposure

Table 3: Shows the treatment stages for acrylate allergies starting from preventive measures to higher - level treatment options. Abbreviations: ACD – Allergic Contact Dermatitis; TIX – Therapeutic Index; NB-UVB – Narrowband Ultraviolet B; BB-UVB – Broadband Ultraviolet B; PUVA – Psoralen and ultraviolet A;

reduced residual monomer content, and therefore allergenic potential (5). Some of the future directions in the prevention and management of acrylate allergy include more pre-marketing tests, post-marketing surveillance, as well as more reforms in regulations and harmonization. One of the strategies that is being implemented in primary prevention involves proper risk management of sensitizing compounds. This includes allowing proper risk management before products are brought to the market. Some of the regulations that have been put in place include the REACH (Registration, Evaluation, Authorization and restriction of chemicals) regulation of the EU, which includes non-animal tests for assessing sensitizing potential. The Organization for Economic Co-operation and Development developed an Adverse Outcome Pathway for skin sensitization in 2012. This paved the way for a new generation of validated in vitro tests, including the Direct Peptide Reactivity Assay (DPRA), ARE-Nrf2 Luciferase test, and Human Cell Line Activation Test (H-Clat). All these organizations focus on specific biological key events in the allergic response mechanism. However, these tests are only

capable of simulating isolated key events and do not cover factors such as metabolic activation and skin penetration. To overcome these challenges, innovative test systems such as reconstructed human epidermis (RHE) systems and co-culture systems, such as the HaCaT/THP1 CoCulture Activation Test (COCAT), are being developed to simulate complex cell interactions in the body during the allergic response. To improve the predictive power and risk stratification of these tests, integrated approaches to testing and assessment (IATA) and integrated test strategies (ITS) are also being evaluated. Though there is a significant improvement in pre-market risk assessment, allergic contact dermatitis (ACD) caused by acrylates is seen in post-marketing surveillance due to false negative test results or unseen potential allergens.

A key function of post-marketing surveillance and detection of fresh allergens often begins with high-quality case reports, which should be promoted and propagated on a wider scale to create awareness among clinicians and regulatory bodies. Follow-up studies, including the inclusion of the suspect allergen in patch test series, may help to establish the initial findings and prompt regulatory action. Periodic analysis of patch test data is critical in assessing the real-world prevalence of sensitization and ensuring any updates in risk management are addressed appropriately. While differences in regulatory systems worldwide do pose a question, it is also true that political and economic differences may not allow uniform global standards to be set; however, this could be mitigated through international cooperation and the sharing of safety data. This review suggests that any successful strategy for preventing acrylate sensitization requires a holistic approach, including better premarket testing, post-market surveillance, regulation of products, and global collaboration in the exchange of information about safety (51).

6. DISCUSSIONS

The key takeaway of this review, that acrylate allergy has transitioned from an occupational health risk to a consumer health risk/medical device health risk, is echoed by other reviews. In a 2024 review, acrylate skin allergy was similarly described as an increasingly common problem that is poorly appreciated as a result of new routes of exposure, primarily focusing on nail products and wearables as a result (5). The takeaway of this review is similar to that of others, specifically focusing on the risk of sensitisation among women and children as a result of super glue, nail adhesives, and diabetic pumps, while advocating for more regulatory action to be taken (10). The value of this particular review is that it links the findings from different studies together, showing that while the source of acrylate allergy may vary from a

dental surgery to a nail salon to a FreeStyle Libre glucose sensor, the immunopathway is the same. However, there are significant areas of divergence between the present review and past literature. A 13-year review of the data on the incidence of contact allergy to acrylates and methacrylates identified the occupational route of exposure as the main cause of sensitization and dental personnel and nail technicians as the main risk groups (52). Though the present review does not disagree with the past literature, the more recent evidence that has been synthesized in the present review, including the NACDG (2019–2020), the Spanish multicenter study that identified 3.7% positivity to HEMA, and the TikTok study by Axler and Lipner (2024), suggests that the proportion of the consumer population that has become sensitized to acrylates and methacrylates has increased considerably since the last dataset collected (39). The consumer population deserves the same or greater attention as the occupational population. An analysis of the data collected by the German Information Network of Departments of Dermatology (2004–2013) identified that the consumer population was increasingly contributing to the population of acrylate-sensitized patients, but was still a minority (53).

The path that is apparent from the most recent studies suggests that this has continued to be the case. A particular area of tension within the literature is whether the sensitisation patterns reported within users of nail cosmetic products and dental personnel are indicative of a similar immunological response or should be viewed as distinct clinical entities. The EECDRG reported that 67% of acrylate-related ACDs were related to the use of nail cosmetics, 43% of which were from consumers and 56% from workers, while dental-related sensitisation was present at a lower but constant rate (17). A 5-year Portuguese study reported that 93.4% of a 230-patient population demonstrated cross-reactivity between 2-HEMA, 2-HPMA, and EGDMA (4). These data could be interpreted as indicative of a single class response, thus reinforcing the advice to avoid acrylates from all sources. However, the observation that isobornyl acrylate has emerged as a dominant allergen within continuous glucose monitors from a range of case series across Europe is more difficult to reconcile with this theory (54,55). Cross-reactivity of IBOA is limited to the methacrylates that are dominant in nail and dental screens, indicating that device-related sensitisation could be a partially separate immunopathway. The clinical importance of this distinction is obvious: a patient sensitised by IBOA will not be picked up by a standard screening series for methacrylates, and the clinical presentation of geometric-shaped device-related eczema is unlikely to prompt

a doctor to consider it. The question of whether we are dealing with separate or merely related sensitisation pathways remains to be answered by further studies.

Another interesting result that deserves critical evaluation is that, in all studies, including those from EECDRG, there was a preponderance of sensitisation in nail cosmetics clients compared with professional manicurists (5,17). This result is somewhat unexpected, since occupational exposure tends to have a higher rate of sensitisation due to sheer volume. There are several potential explanations, including the possibility that professional users have developed more consistent preventive habits or that they might be more likely to use more extensive curing methods that prevent monomer residue. Another possibility is that there might be an ascertainment bias, in that clients who have developed ACD might be more likely to seek medical advice and undergo patch testing than those who have developed dermatitis due to general occupational exposures, and therefore appear in patch test statistics at a higher rate. It is not clear from the methodological approach taken in these studies, all of which were retrospective in nature and involved patch test clinic attendees, how these results might be interpreted.

6.1 Limitations of Literature

The limitations of the individual studies are, taken collectively, also the limitations of the evidence base upon which clinical practice in this area currently rests. The most significant of these is the almost universal reliance upon patch test clinic populations as the source of epidemiological data. Because of the specialist nature of the procedure, the variable reimbursement, and the chain of clinical events leading up to it, which in turn reflects existing levels of awareness, the populations from whom data are gathered are, in fact, not representative of all populations of sensitised individuals. The figures for sensitisation that are generally reported, such as the 1.1% figure for acrylate in 18,228 patients from the EECDRG data set for 2013–2015, or the 2.3% figure for HEMA from the multicenter European study for 2019–2020, are, in fact, minimum estimates rather than population-level prevalence figures; population-level prevalence data are lacking, and the prevalence of acrylate allergy in the population remains incompletely characterised. Another aspect is the diagnostic heterogeneity between studies. There is no standard for the selection of allergens to be used in the acrylate patch test, the test concentrations, or the number of readings. A comprehensive two-part review by De Groot and Rustemeyer in 2023-2024 on HEMA identified 11.7% of the sensitisations identified by Forkel et al. would have been missed if late readings were not performed, thus showing the direct impact on the figures (9,33,56). The volatility of acrylate allergens in test

preparations also contributes to the variability in test results. This is where the same allergen in the same test solution may produce different test results based on the conditions and application time (7,8). These are serious issues and, in effect, a patient who is clinically sensitised may be given a false negative result, and the figures may not be comparable. The standard test solution concentrations, 0.1%, 2%, and 10%, for different compound classes, are accepted and agreed upon but have not been verified. Another related issue is that of polyvalent positive patch test results, where several simultaneous positive reactions to the (meth)acrylate series are frequently found, as was the case in all of the studies reviewed, where co-positivity was found in over 93%. However, the literature has been unable to determine whether such findings are due to immunological cross-reactivity, co-sensitisation from simultaneous exposure to a mixture of mixed monomers found in many commercial products, or a combination of both, as suggested by the co-sensitisation hypothesis (4). The suggestion that the carboxyethyl group is responsible for cross-reactivity between acrylates is speculative and based upon a study of 23 patients (44). In a clinical context, it is important to establish whether the polysensitization pattern is a result of immunologic cross-reactivity or co-sensitization secondary to exposure to multiple compounds, as co-sensitization would imply that a patient could be exposed to chemically unrelated acrylate compounds, whereas avoidance of all of the members of the acrylate family is necessary if cross-reactivity is assumed. The practical advice that is given is that all of the acrylate family should be avoided, and while this suggestion is clinically sound, it is based on a speculative hypothesis rather than on immunologic evidence. The issue of transparency in the labelling of products is a structural limitation in research and clinical management. Surveys and analyses on products have shown a lack of disclosure of the presence of (meth)acrylates and non-compliance with EU regulations on labelling in nail cosmetics products (45,57). This is a limitation in exposure assessment in epidemiological research, where researchers cannot identify the patient's exposure based on the information on the labels, and in clinical management, the information on the labels is inadequate. A patient who is advised to avoid products based on ingredients may still experience flare-ups from products identified as acrylate-free but containing other, unlabeled acrylates. This is not a failure in regulation but a failure in research, creating uncertainty in the entire chain of evidence. Lastly, it is important to note that the scope of this article itself is a limitation. The fact that it is a narrative article without a specific selection criterion or a risk of bias assessment means that it cannot claim to represent all evidence equally. The fact that only non-English articles are excluded means that only European and North American data are represented. The fact that nail technology and acrylate exposure are a global phenomenon means that a

systematic underrepresentation of the true diversity of acrylate allergy presentations and allergens could be a problem.

6.2 Sensitization Patterns Across Exposure Settings and Key Controversies

If the patterns of sensitization described across nail cosmetics, dental materials, and medical devices are examined as a whole, a picture emerges that is both clinically instructive and immunologically contentious. The different settings are not simply different populations exposed to different allergens; rather, different allergens are exposed through different routes to different populations, yet are related by common pathophysiological mechanisms of haptenation and T-cell hypersensitivity.

In nail cosmetic products, the most frequently identified sensitisers from cohort studies in Europe and North America are low-molecular-weight methacrylates, with HEMA, HPMA, and EGDMA being the most frequently identified, with HEMA being the most frequently identified of all, as reported in all studies (4,17,51). Sensitivity development was fast, with 65% of the occupational cases happening within the first year of exposure (refer to Section 4.2). This is important clinically because it refutes the common misconception that sensitivity only arises after prolonged cumulative exposure. Rather, it reveals that the risk associated with even short-term intense exposure to uncured monomers cannot be ignored, and hence, screening for pre-exposure sensitivity is necessary. ACD from methacrylate sensitisation increased from 55% of cases from 2009–2013 to 97% of cases from 2014–2018 in the Greek registry, indicating a real epidemiological shift rather than improved awareness of the problem (17,38). This increase coincides temporally with the development and expansion of UV-cured gel nail products, supporting a cause-and-effect relationship between new product formats and increased rates of sensitisation. Incomplete curing due to insufficient UV lamp power or hurried curing processes is a modifiable factor in the exposure process that has been consistently highlighted in the literature as an increased risk factor, yet not addressed in current consumer product regulations.

The allergen profile in dental settings shares some overlap with nail cosmetics, in that HEMA is relevant in both, but differs in that increased concentration exposures of MMA are relevant in dental technicians, and bis-GMA and TEGDMA from composite resin materials. Finnish data on occupational dermatology and NACDG occupational data records from 2001 to 2018 show that acrylate ACD in dental personnel tends to involve fingertips and hands, with some cases showing airborne allergen-induced facial skin in addition to hand dermatitis (58). The

fingertip distribution in dental personnel reflects direct ‘dexterous’ handling and mirrors the distribution in nail cosmetologists who use their dominant index finger to remove excess polish from clients' nails (16). The similarity of the exposure mechanisms in these professional groups may have clinical value inasmuch as it implies that the morphology of the lesions may help in the clinical suspicion of acrylate exposure even without identification of the allergens. On the other hand, unusual findings in dental professionals, including the involvement of lateral surfaces of the fingers in over 90%, remain poorly understood and should not be used as a means of diagnosing acrylate allergy (59).

The glucose sensor context presents a new model of sensitization. While the main allergen in this context, IBOA, is not a monomer used during a medical procedure or a series of procedures, it is an adhesive used continuously. The first description of the FreeStyle Libre-associated IBOA allergy was reported in 2017. Subsequent studies have shown IBOA to be the most common allergen in glucose sensors of various brands, with others showing that device reformulation intended to eliminate IBOA sometimes results in the problem being shifted to another acrylate (54,55,60). A subsequent Spanish case series has further muddied the waters by identifying relevant reactions to non-IBOA acrylates in glucose sensor users, which suggests that the single allergen approach to device reformulation may be an oversimplification (61). A comprehensive review of glucose sensor and insulin pump-associated contact dermatitis in 2025 reinforces the evidence and emphasizes the difficulties in adequate patch testing for device-associated allergy due to the lack of availability of IBOA in standard test series and the need for a specific medical device test series (6). This leaves us with the suspicion that patients suffering from device-associated ACD will be undertreated in centres without access to device test series, and the true extent of undiagnosed patients is unknown. The cross-reactivity debate is the most contentious area of the entire acrylate allergy literature and is an area where it is recommended to be clear about the state of the art. De Groot and Rustemeyer’s review of HEMA in 2024 Part 2 of the literature addressed the specific topic of cross- and co-sensitization and concluded that while HEMA frequently co-sensitizes with HPMA, EGDMA, and TEGDMA on patch testing, the mechanisms of co-sensitization have yet to be established (33).

The implication of the 93.4% co-positivity as evidence of class-wide cross-reactivity could also be due to the simultaneous exposure to multiple monomers in the same nail or dental products (62). The implication of true immunological cross-reactivity is that exposure to any acrylate that will trigger the sensitised T cell clone will trigger an immune reaction. This is true regardless of whether the individual was previously exposed to that specific compound. Co-

sensitisation due to exposure to mixed monomers implies that reactions will be confined to the compounds of the original sensitising material. The advice that is currently given to sensitised patients—namely, that they should avoid all (meth)acrylates—is the appropriate advice in the face of uncertainty. However, it is uncertainty that has significant implications in the real world. To clarify the situation, well-controlled exposure experiments to characterise individual allergens have not been conducted. The gap between the evidence base and existing oversight mechanisms is an area that requires comment. The FDA ban of MMA in nail acrylics in 1974 is evidence that specific action by regulators against individual sensitising acrylate monomers is possible (44). However, the broader group of (meth)acrylate monomers that replaced MMA is still widely used worldwide with minimal pre-market testing for sensitisation potential and no requirement for labelling in many countries. The EU's REACH regulation and OECD's Adverse Outcome Pathway are significant advances in the regulation of chemical safety, but Uter et al. (2020) point out that surveillance of contact allergens after marketing is lacking, with significant gaps in the ability of regulators and clinicians to detect emerging safety signals, where high-quality case reports are the main source of information and surveillance by device/product is lacking (51). The social media data from Axler and Lipner's study, where TikTok videos discussing ACD from gel nail application reached large audiences without verified clinical information, highlights the scale of public health impact and the failure of public health communication (39). These are not trivial issues, and they represent the failure of an evidence base that has defined the public health issue but has not developed the necessary regulatory and public health infrastructure to address it.

7. CONCLUSION

Acrylate derivatives have diverse applications in dentistry, cosmetics, industrial production, and medicine. At the same time, their growing popularity increases cases of allergic contact dermatitis, making them one of the top five causes of sensitization. It is notable that sensitivity to acrylates can emerge quickly and after minimal exposure to uncured products. Furthermore, once acquired, it does not seem to remit with time.

Differential diagnosis of allergic reactions to acrylates is based on the detailed exposure history, clinical assessment, and patch testing with an extended acrylate series. Readings should be extended to day 7 to minimize the number of false negatives caused by the volatile nature of some of the allergens in the panel. 2-Hydroxyethyl methacrylate (HEMA) and 2-hydroxypropyl methacrylate (HPMA) are the most efficient screening substances in nail cosmetics and dentistry, respectively, while isobornyl acrylate (IBOA) requires testing

separately because of its structural divergence from other allergens and frequent sensitizations among CGM device users. Cross-sensitivities to multiple methacrylate monomers are found in the majority of patch-positive cases, and the immunological mechanism underlying this pattern has not yet been established. Nonetheless, wide-scale avoidance of acrylates is recommended for both types of sensitivities. Inability of patients to identify acrylates on labels of products leads to high rates of sensitization in populations using medical adhesives and continuous glucose monitors. Furthermore, post-marketing surveillance of emerging allergens is insufficient at present, creating a need for improved regulatory practices in these spheres and beyond. Avoidance is challenging with modern consumer products and requires additional strategies, including the choice of formulations posing lower risks, thorough curing of products and application of protective equipment. In addition, there is room for future research aimed at development of less allergenic alternatives to conventional acrylates and standardized testing panels. All in all, these findings indicate that acrylate allergy constitutes a developing medical problem, complicated by shifting exposure patterns, difficulties in diagnosis, and ineffective regulatory practices.

8. CLINICAL PRACTICE IMPLICATIONS

Acrylate allergy should be a prime consideration for patients with chronic dermatitis, especially if the affected areas include the hands, face, eyelids, and mouth. Acrylates are also used in adhesives, cosmetics, and medical devices, and without proper and consistent labeling, a review of the patient's and the individual's product use history is pertinent, as it is a thorough and relevant occupational history. In order to ensure that allergens such as 2-Hydroxyethyl methacrylate (2-HEMA), hydroxypropyl methacrylate (HPMA), ethylene glycol dimethacrylate (EGDMA), ethyl cyanoacrylate, and isobornyl acrylate are not missed, the extended acrylates series rather than the routine panels is recommended for the patch test. Patch testing substances need to be made fresh and applied immediately after their retrieval from the freezer because acrylates tend to vaporize due to their high volatility. Evaporation of these chemicals will cause failure of allergens' penetration into the skin, hence causing false-negative results, especially if the patch testing chambers are filled up prematurely. Apart from the technical reasons above, acrylates also have a tendency to cause delayed hypersensitivity reactions, which could take up to five to seven days before any allergic response could be seen. Testing only at days two and four will result in missing out on many reactions, which means a seventh-day test is needed.

Treatment for acrylate allergy involves allergen avoidance. In case of sensitization, the patient is advised to avoid consumer products without appropriate labelling such as do-it-yourself (DIY) gel nail kits, since they lack appropriate regulation in many areas for the amount of acrylates used, along with medical adhesives and devices which could have acrylate monomers. The need for full ultraviolet (UV) curing should always be emphasized because partially polymerized materials will have relatively higher amounts of acrylate monomers, hence increasing sensitization risk. Considering the cross-reactivity reported among the various acrylate and methacrylate monomers, individuals who have developed sensitization would normally need to stay away from all these chemicals rather than seeking a low residual monomer content product among these cross-reactive chemicals. Considering that there is a lot of cross-reactivity, it will mean that a patient who has been sensitized to HEMA will end up developing a reaction to similar molecules like HPMA and EGDMA at first contact, making it difficult to implement any avoidance strategy in such cases. Thus, advice needs to focus on avoiding all acrylate products, such as nail products, dental products, and adhesives, as well as identifying acrylate products in their work environment and at home. The use of nitrile gloves, in association with 4H laminate gloves, ventilation, and curing methods, is a preventive measure. The patient also needs to be educated about the risk of sensitization, and this is a clinically important part of the prevention of the disease. The mainstay of the treatment of acrylate allergy consists of the management of the symptoms. The first line of treatment is the use of topical corticosteroids. Alternatives to topical corticosteroids are topical calcineurin inhibitors and systemic alitretinoin, which are used for chronic cases and those affecting the hands. In order to provide support for long-term management strategies and make the necessary changes in the work environment, it is suggested that cases of occupational contact be reported, and there be collaboration between dermatologists and occupational health professionals.

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APPENDIX A

KEY IMMUNE MEDIATORS (SUMMARY)

Langerhans cells are important epidermal dendritic cells that play a pivotal role in initiating and maintaining allergic contact dermatitis. These cells are found above the basal layer of the epidermis, where they capture antigens via pattern recognition receptors and subsequently present these antigens via MHC and CD1a molecules. The activation of these cells by haptens and TLRs triggers their immune responses through CD4+ and CD8+ cell interactions. They maintain immune tolerance by triggering a state of anergy or generating regulatory T cells when specific conditions exist. (25,63–65).

Skin dendritic cells feature Langerhans cells within the epidermis together with multiple dermal dendritic cells, including an important one, conventional dendritic cells (cDC1 and cDC2). The function of cDC1s includes imitating Th1 responses, while cDC2s serve to stimulate Th2 and Th17 inflammatory reactions. Plasmacytoid dendritic cells create type I interferons during skin inflammation, and monocyte-derived dendritic cells boost immune responses by presenting antigens and secreting cytokines (25).

Inducible skin-associated lymphoid tissue (iSALT) develops around postcapillary venules hours following hapten contact. The structure contains macrophages along with dermal dendritic cells and T cells. Macrophages become active through keratinocyte-produced IL-1 alpha, which leads to the recruitment of dendritic cells. Limited direct human evidence exists, but dendritic cell T cell clusters show local antigen presentation during allergic contact dermatitis (25,66).

Macrophages exist as M1 and M2 types. CD14 and CD16 monocytes differentiate into proinflammatory M1 macrophages, which express HLA-DR, CD80, and CD86 and produce interferon 1,6,12 and tumor necrosis factor alpha. Th2 skewed anti-inflammatory M2 express CD163 and CD206 which include M2a triggered by IL4/IL13, while M2b produce IL10. M2c is involved in apoptotic cell clearance, and M2d is associated with tumors (25,67–69).

Mast cells originate from CD34 hematopoietic precursors and release cytokines, chemokines, and histamine near blood vessels and epithelial surfaces. Research on mouse models revealed that mast cell-deficient strains experience decreased inflammation, which highlights their proinflammatory function during allergic contact dermatitis. Mast cells also release IL10, IL-

1, and IL-36, which stimulate T cell proliferation, which in turn drives Th1/Th17 response and contributes to chronic skin inflammation (70).

Neutrophils are the first immune cells to reach inflammatory skin lesions, which respond to chemokines such as CXCL1, CXCL2, and CXCL10. PAR2 signaling triggers CXCL1 secretion, leading to CXCR2-mediated recruitment. CXCL10 and CXCR3 signaling contribute to pruritus, while TNF-alpha facilitates infiltration. Regulatory T cells prevent neutrophil migration, and NRF2 controls late-stage accumulation and clearance by M2b macrophages. Neutrophil extracellular traps and neutrophil-derived myeloperoxidase increase IL-1 beta production and vascular permeability, identifying neutrophils as therapeutic targets (24,25,71–74).

Eosinophils accumulate in the damaged tissues, and allergic contact dermatitis increases eosinophil cationic protein levels. Serum eosinophilic cationic protein (ECP) levels are associated with formaldehyde sensitization and asthma-like reactions (25,75).

Basophils mediate TH2-related itching and allergic contact dermatitis through interleukins, TSLP and FceRI activation and are associated with Th2 polarization (25,76).

Regulatory mechanism: the regulatory T cells (Tregs) function throughout the sensitization and elicitation stages of allergic contact dermatitis (ACD) and manage to decrease the inflammatory reaction, which used to be attributed only to allergen removal. The Treg family blocks the effector T cell activity and leukocyte infiltration through IL-10 or CD39 pathways, playing an important role in resolving allergic contact dermatitis (ACD)(21).