

Acrylate and methacrylate contact allergy and allergic contact disease: a 13-year review

Ashley Spencer, Paul Gazzani and Donna A. Thompson

Birmingham Skin Centre, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, B18 7QH, UK

doi:10.1111/cod.12647

Summary

Background. (Meth)acrylates are important causes of contact allergy and allergic contact disease, such as dermatitis and stomatitis, with new and emerging sources resulting in changing clinical presentations.

Objectives. To identify the (meth)acrylates that most commonly cause allergic contact disease, highlight their usefulness for screening, and examine their relationship with occupational and clinical data.

Methods. A retrospective review of results from patch tests performed between July 2002 and September 2015, in one tertiary Cutaneous Allergy Unit, was performed

Results. A series of 28 (meth)acrylates was applied to 475 patients. Results were positive in 52 cases, with occupational sources being identified in 24. Industrial exposures and acrylic nails were responsible for 13 and 10 cases, respectively, with wound dressings being implicated in 7. We found that four individual (meth)acrylates (2-hydroxyethyl acrylate, 2-hydroxypropyl methacrylate, bisphenol A glycerolate dimethacrylate, and ethyl acrylate), if used as a screening tool, could have identified 47 (90.4%) of our positive cases.

Conclusions. Our 13-year experience indicates a changing landscape of (meth)acrylate contact allergy and allergic contact disease, with an observed shift in exposures away from manufacturing and towards acrylic nail sources. Wound dressings are highlighted as emerging sources of sensitization. Larger studies are required to establish the sensitivity and specificity of the four (meth)acrylates proposed for potential screening.

Key words: acrylates; allergic contact dermatitis; allergic contact disease; artificial nails; contact allergy; dressings; methacrylates; occupational; screening.

Acrylates and methacrylates [hereafter referred to as (meth)acrylates] are monomers that contain an acryl group derived from acrylic and methacrylic acid, respectively (1, 2). They are unstable potent allergens, and polymerize either spontaneously or as a result of

ultraviolet (UV) light application (3) to form inert substances (4). (Meth)acrylates can be found in a variety of commonly used products, such as adhesives, plastics, textiles, and acrylic nails. They have become increasingly recognized as causes of allergic contact dermatitis, with occupational exposure being reported to play an important role in 40–67.6% of cases (3, 5). Much of the early work focused on dental personnel, with the prevalence of (meth)acrylate sensitivity estimated to be 3.0% among these individuals (6), and reports that they represented up to 45.2% of occupational cases (7). In recent years, however, the more widespread use of artificial nails has resulted in an increased frequency of cases

Correspondence: Dr Ashley Spencer, Birmingham Skin Centre, Sandwell and West Birmingham Hospitals NHS Trust, City Hospital, Dudley Road, B18 7QH Birmingham, UK. Tel: +44121 507 4708. E-mail: ashleyspencer@nhs.net

Conflicts of interest: The authors declare no conflict of interests.
Funding: This work has not received funding.

Accepted for publication 30 May 2016

of (meth)acrylate sensitivity among beauticians and artificial nail users (3–5, 8). Other occupational groups associated with (meth)acrylate contact allergy and allergic contact disease include workers in the fibreglass and printing industries, and those working with paints (3).

The objectives of this study were to analyse cases of allergic contact disease caused by (meth)acrylates, with respect to demographics, clinical presentation, and occupational and other sources of exposure. We also aimed to identify the (meth)acrylates that are most prevalent in contact allergy and allergic contact disease, to highlight patterns of allergens that frequently occur together, and to assess individual allergens and combinations of allergens for potential use as a screening tool.

Materials and Methods

We conducted a retrospective review of results from a subset of patients with suspected contact allergy to (meth)acrylates and allergic contact disease caused by (meth)acrylates who were patch tested at one Cutaneous Allergy Unit over a 13-year period (July 2002 to September 2015). The subset of individuals was identified from a patch test database of 6502 patients held at this unit, with 475 (7.3%) patients having been tested with an extended series of 28 (meth)acrylates (Chemotechnique Diagnostics, Vellinge, Sweden) (Table 1), following potential exposure suspected from their clinical history. No additional (meth)acrylates or cyanoacrylates were tested during this period, although patients were tested with other series and with their own products as clinically indicated; these included diluted glues and other adhesives, and fragments of wound dressings. The case records of patients with positive results were reviewed, and data on sex, age, occupation, clinical presentation, the presence of atopy, the source of (meth)acrylate allergy and patch test results were collected. Manufacturers of products provided by the patients that yielded positive patch test reactions were asked to provide information on individual product ingredients, and samples of these for further patch testing.

IQ Ultra™ Test chambers (64 mm²; capacity 32 µl) (Chemotechnique Diagnostics) were filled with (meth)acrylate preparation, and transferred immediately to the skin on the patient's back or on the most appropriate site elsewhere. These remained under occlusion until the first reading on day (D) 2, and a subsequent reading was performed on D4. Reactions were scored as irritant, negative (–), doubtful (?), weak (+), strong (++), and extreme (+++), according to the guidelines of the ICDRG (9). Only +, ++ or +++ reactions were considered to be positive.

Table 1. Reactivity to all 28 of the (meth)acrylates in our series, with concentrations (in pet.) used for patch testing

(Meth)acrylate	Concentration (%)	Number (%) of positive reactions (52 patients tested)
2-Hydroxyethyl acrylate	0.10	32 (61.5)
2-Hydroxypropyl methacrylate	2.00	29 (55.8)
2-Hydroxyethyl methacrylate	2.00	29 (55.8)
Ethylene glycol dimethacrylate	2.00	28 (53.8)
Ethyl acrylate	0.10	25 (48.1)
Hydroxypropyl acrylate	0.10	24 (46.2)
Triethylene glycol dimethacrylate	2.00	17 (32.7)
Di(ethylene glycol) diacrylate	0.10	15 (28.8)
Methyl methacrylate	2.00	15 (28.8)
Triethylene glycol diacrylate	0.10	12 (23.1)
1,4-Butanediol diacrylate	0.10	12 (23.1)
1,6-Hexanediol diacrylate	0.10	11 (21.2)
1,4-Butanediol dimethacrylate	2.00	10 (19.2)
Butyl acrylate	0.10	10 (19.2)
Bisphenol A glycerolate dimethacrylate	2.00	9 (17.3)
Butyl methacrylate	2.00	8 (15.4)
Epoxy acrylate	0.50	6 (11.5)
Urethane dimethacrylate	2.00	6 (11.5)
2,2-bis[4-(2-Methacryl-oxyethoxy)phenyl]-propane	2.00	4 (7.7)
2-Ethylhexyl acrylate	0.10	3 (5.8)
Pentaerythritol triacrylate	0.10	3 (5.8)
Trimethylolpropane triacrylate	0.10	3 (5.8)
Tri(propylene glycol) diacrylate	0.10	3 (5.8)
Urethane diacrylate (aliphatic)	0.10	3 (5.8)
Urethane diacrylate (aromatic)	0.05	3 (5.8)
Bisphenol A dimethacrylate	2.00	2 (3.8)
Ethyl methacrylate	2.00	2 (3.8)
Oligotriacrylate	0.10	2 (3.8)

Results

Of 475 patients tested with the (meth)acrylate series, 52 (10.9%) had at least one positive reaction. Full results of the patch tests were available for all patients; additional information on demographics, clinical presentation and source of exposure was available for a total of 47 patients. The ages of patients with (meth)acrylate contact allergy and allergic contact disease ranged between 15 and 82 years, with a mean of 43.3 years and mode of 42 years. Thirty-two of 47 patients (68.1%) were female. Seventeen of 47 patients (36.2%) had a past history of atopy (Table 2). Interestingly, atopy was reported in only 1 of 21 patients patch tested up to 2008, and in 16 of 26 patients tested after this time.

Occupational sources of (meth)acrylate exposure were identified in 24 of 47 patients (51.1%), with 13 (27.7%)

Table 2. Clinical details of patients with contact allergy secondary to (meth)acrylates, including year of patch test, age, and sex

Year	Age (years)	Sex	Site of contact allergy	Atopy	Occupation	Occupational?	Exposure to (meth)acrylate
2002	45	M	Hands	No	Gangway manufacture	Yes	Loctite®
2002	42	F	Hands	No	Production assembly	Yes	Glues on assembly line
2002	37	F	Hands	No	Car mechanic	Yes	Hylogrip® 2000
2003	31	M	Hands	No	Car assembly	Yes	Loctite® 243
2003	18	F	Hands	Yes (E)	Beauty technician	Yes	Acrylic nails
2003	58	M	Hands	No	Production assembly	Yes	Loctite® 601
2003	27	M	Hands	No	Industrial flooring	Yes	Flooring adhesives
2004	37	F	Hands, periorbital	No	Beauty technician	Yes	Acrylic nails
2004	62	M	Hands	No	Concentric pump engineer (cars)	Yes	Hylomar® 68344
2006	55	M	Hands, face	No	Car manufacture	Yes	Laquer containing acrylate
2006	44	M	Hands	No	Car manufacture	Yes	Loctite®
2006	63	M	Hands	No	Aeroplane manufacture	Yes	Loctite®
2006	42	M	Face	No	Car manufacture	Yes	Paints
2006	41	F	Hands	No	Beauty technician	Yes	Acrylic nails
2007	45	M	Hands	No	Machine assembly	Yes	Loctite®
2007	42	F	Mouth	No	Nil	No	Dental work
2007	35	F	Hands	No	Beauty technician	Yes	Acrylic nails
2008	54	F	Hands, periorbital	No	Sales manager	No	Acrylic nails
2008	22	F	Hands	No	Beauty technician	Yes	Acrylic nails
2008	31	F	Hands, abdomen	No	Research with acrylates	Yes	DEGDA
2008	66	F	Face	No	Retired (housing renovation)	No	Acrylic nails
2011	47	F	Hands, feet	Yes (A)	Retired (secretary)	No	Acrylic nails
2011	24	F	Hands	Yes (E)	Beauty technician	Yes	Acrylic nails
2012	42	F	Hands	Yes (A)	Social worker	No	Acrylic nails
2012	50	F	Mouth, facial	No	Housing manager	No	Dental work
2012	56	F	Lower legs	No	Retired (nurse)	No	Mepilex® Border dressing
2012	21	F	Hands	Yes (E/R)	Beauty technician	Yes	Acrylic nails
2012	68	F	Legs	Yes (E)	Retired (research)	No	Mepilex® Border dressing, Cavilon™ barrier film, Micropore™ surgical tape
2012	51	F	Hands, feet	No	Secretary	No	Acrylic nails
2012	51	F	Hands, feet	Yes (A/E)	Business manager	No	Dressings
2013	15	F	Hands	Yes (E)	School student	No	Acrylic nails, hairspray containing acrylates
2013	18	F	Hands, feet	Yes (A)	Beauty technician	Yes	Acrylic nails
2013	65	M	Hands	Yes (R)	Electronic engineer	No	Perspex®
2013	56	F	Hands	Yes (R)	Cashier	No	Acrylic nails Pedometer
2013	52	M	Hands	No	Production assembly	Yes	Loctite® 121078
2013	17	F	Hands, face	No	College student	No	Acrylic nails
2014	82	F	Legs	No	Retired (domestic)	No	Dressings
2014	42	F	Hands	Yes (A/R)	Beauty technician	Yes	Acrylic nails
2014	35	F	Hands	No	Carer	No	Acrylic nails
2014	43	F	Face, chest	Yes (E)	Solicitor	No	Acrylic nails
2014	68	M	Legs	No	Retired (finance)	No	Dressings
2014	75	M	Face, feet	Yes (E/A/R)	Retired (surveyor)	No	Mepilex® Border dressing
2014	62	M	Legs	No	Long-term unemployment secondary to illness	No	DryMax® Extra and Mepilex® Border dressings
2015	32	F	Hands	No	Customer service	No	Acrylic nails
2015	22	F	Hands	Yes (E/R)	Beauty technician	Yes	Acrylic nails
2015	15	F	Mouth	Yes (A)	School student	No	Braces adhesive
2015	27	F	Chest, neck	Yes (R)	Nil	No	Acrylic nails

F, female; M, male; A, asthma; E, eczema; R, rhinitis (allergic); DEGDA, di(ethylene glycol) diacrylate.

working in the manufacturing industry and 10 (21.3%) working with acrylic nails. Of those with industrial exposure, 1 patient installed industrial floors and the remaining 12 worked in assembly, 6 of these specifically within car manufacturing. The most common sources of industrial exposure to (meth)acrylates were anaerobic thread sealants, notably Loctite® (Henkel, Düsseldorf, Germany) (n = 7), Hylomar® (Hylomar, Wigan, UK) (n = 1), and Hylogrip® (Hylomar) (n = 1) (Table 2). Those who developed (meth)acrylate allergic contact dermatitis as a result of employment in industry were older (mean age 46.4 years) and more likely to be male (11/13; 84.6%).

Contact with acrylic nails or nail products was the most common source of (meth)acrylate allergic contact dermatitis overall (n = 22; 46.8%); 12 cases were seen in consumers of nail products who did not have relevant occupations. These patients were younger (mean age 36.8 years), and all were female. Acrylic nails were observed as the cause of (meth)acrylate allergic contact dermatitis more frequently after 2008, when 18 of the 22 cases were identified by patch testing; in contrast, 12 of 13 of those with manufacturing industrial exposure were seen before 2008.

Since 2012, there have been 7 cases in whom wound dressings and other wound care products have been implicated as the source of (meth)acrylate contact dermatitis. Mepilex® Border (Mölnlycke Health Care Laboratory, Gothenburg, Sweden) (n = 4) was most commonly noted; another dressing was DryMax® Extra (Aspen Medical Europe, Redditch, UK) (n = 1). One patient was additionally sensitive to other acrylate-containing products that are commonly used in wound care: Cavilon™ No Sting Barrier Film (3M™, Bracknell, UK), a liquid barrier film, and Micropore™ Surgical Tape (3M™), a hypoallergenic surgical tape.

Analysis of the body sites involved in clinical manifestations among the 47 cases showed hand dermatitis to be the most frequent clinical presentation (34/47; 72.3%), with over half of these cases occurring as a result of acrylate nail contact (n = 19). Twelve cases of hand dermatitis were secondary to industrial exposure. Lower limb dermatitis accounted for 10 cases (21.3%) of (meth)acrylate contact allergic disease, 7 of which were secondary to the use of dressings, and 3 to the use of acrylic nails. Allergic contact stomatitis was seen in 3 patients, as a result of dental procedures. Interestingly, 2 patients had isolated facial dermatitis: 1 of these patients had become sensitized by using acrylic nails, and the other by the use of paints in car manufacture. One patient with (meth)acrylate sensitivity secondary to the use of acrylic nails developed dermatitis limited to the neck and chest (Table 2).

The frequencies of positive reactions to the (meth)acrylate series are shown in Table 1. The number of positive reactions per patient ranged from 1 to 16, with a mean of 6.3. Correlation between the most commonly positive allergens was also analysed (Table 3).

Although no single (meth)acrylate would have been a suitable screening allergen on its own, 90.4% of our patients would have been identified by screening with a combination of 2-hydroxyethyl acrylate, 2-hydroxypropyl methacrylate (2-HPMA), bisphenol A glycerolate dimethacrylate (bis-GMA), and ethyl acrylate (n = 47; 90.4%). 2-Hydroxyethyl acrylate was included in this combination because it was the most commonly positive allergen (n = 32). Among the 20 patients who did not react positively to this allergen, 2-HPMA was the most commonly positive allergen (n = 7), and thus the next (meth)acrylate to be included. Of those who did not react positively to either allergen (n = 13), bis-GMA was the most commonly positive allergen (n = 5); when this was excluded, ethyl acrylate was the most frequently positive (meth)acrylate (n = 3). The 5 patients who would not have been identified with this combination of (meth)acrylates were sensitive to different (meth)acrylate monomers with no duplication; these were triethylene glycol dimethacrylate, 1,6-hexanediol diacrylate, trimethylpropane triacrylate, pentaerythritol triacrylate, urethane diacrylate (aromatic), oligotriacrylate, and epoxy acrylate. Subgroup analysis for the most common (meth)acrylates according to source of exposure showed no significant association (Table 4).

Discussion

Our results have reinforced previous work showing (meth)acrylates to be important causes of contact allergy and allergic contact disease, most commonly allergic contact dermatitis. The mean age and range of age for our patients were consistent with previous reports (3, 5, 7, 10, 11), but we found a lower frequency of females than recently reported; 68.1% of our patients were female, as compared with the 97.3% reported by Ramos *et al.* in 2014. Occupational sources of exposure were identified in 51.1% of our patients, which is within the range previously reported (40.9–67.6%) (3, 5, 7).

The recently published literature on (meth)acrylate sensitivity has been dominated by artificial nail allergy. In 2014, a Portuguese group reviewed 37 cases of (meth)acrylate allergic contact dermatitis, and found 28 (75.7%) to be secondary to the use of acrylic nails (3). This year, a group from Leeds reported nails to be the culprit in 46 (85.2%) of 54 patients (12). These are higher frequencies than in our study, but it is important to note

Table 3. Cross-reactivity between the six most commonly positive (meth)acrylates, including the kappa coefficient (which measures concordance between variables)

(Meth)acrylate n (positive)	2-Hydroxyethyl acrylate 32	2-HPMA 29	2-HEMA 29	EGDMA 28	Ethyl acrylate 25	Hydroxypropyl acrylate 24
2-Hydroxyethyl acrylate	–	22 (k = 0.328)	23 (k = 0.407)	22 (k = 0.373)	19 (k = 0.276)	23 (k = 0.622)
2-HPMA	–	–	26 (k = 0.766)	26 (k = 0.806)	22 (k = 0.617)	21 (k = 0.581)
2-HEMA	–	–	–	26 (k = 0.806)	15 (k = 0.081)	20 (k = 0.504)
EGDMA	–	–	–	–	16 (k = 0.195)	22 (k = 0.694)
Ethyl acrylate	–	–	–	–	–	15 (k = 0.267)

k, kappa coefficient; EGDMA, ethylene glycol dimethacrylate; 2-HEMA, 2-hydroxyethyl methacrylate; 2-HPMA, 2-hydroxypropyl methacrylate.

Table 4. Sensitivity as screening allergens of the most commonly positive (meth)acrylates, overall and among specific exposure groups

(Meth)acrylate	Sensitivity as a screening allergen				
	Overall, n (%)	Nail workers/consumers, n (%)	Industry (manufacture), n (%)	Dressings (n)	Dental prostheses (n)
2-Hydroxyethyl acrylate	32/52 (61.5)	13/22 (59.1)	7/13 (53.8)	3/7	2/3
2-HPMA	29/52 (55.8)	13/22 (59.1)	8/13 (61.5)	2/7	1/3
2-HEMA	29/52 (55.8)	13/22 (59.1)	8/13 (61.5)	2/7	1/3
EGDMA	28/52 (53.8)	12/22 (54.5)	7/13 (53.8)	3/7	1/3
Ethyl acrylate	25/52 (48.1)	12/22 (54.5)	2/13 (15.3)	3/7	2/3
Hydroxypropyl acrylate	24/52 (46.2)	10/22 (45.4)	6/13 (46.2)	3/7	0/3

EGDMA, ethylene glycol dimethacrylate; 2-HEMA, 2-hydroxyethyl methacrylate; 2-HPMA, 2-hydroxypropyl methacrylate.

that our data collection commenced earlier. An analysis of nail artists and consumers from the German Information Network of Departments of Dermatology database patch tested for (meth)acrylate contact allergy was published in January 2015; the most commonly positive (meth)acrylate allergens among those with acrylic nail contact, in order of frequency, were hydroxyethyl acrylate, 2-hydroxyethyl methacrylate (2-HEMA), 2-HPMA, and ethylene glycol dimethacrylate (EGDMA) (4). This was consistent with our results overall, and also within the subgroup analysis of patients with acrylic nail exposure.

Over a quarter of patients in our study were exposed to (meth)acrylates in industry, which is a much higher prevalence than has been previously estimated; Ramos *et al.* reported that only 2 of 37 (5.4%) of their patients had industrial exposure to (meth)acrylates (3). The data in Ramos *et al.* were collected from 2006, which was around the time when a shift towards artificial nails as the most prevalent source of (meth)acrylate contact allergy was found in our study. Our findings may also be explained by the higher levels of employment in industry, particularly car manufacturing, in our region.

Anaerobic thread sealants containing (meth)acrylates were the most common sources of industrial exposure among our patients. These are based on esters of (meth)acrylates, and are stable liquids in the presence of oxygen at room temperature. The exclusion of air between

a screw and a socket, particularly in the presence of transition metal ions such as iron and copper, results in the rapid formation of free radicals. The free radicals react with any remaining oxygen to cause polymerization and thus solidification (13). Case reports of anaerobic sealants as causes of allergic contact dermatitis were published in the 1980s (14–16), with Sood *et al.* reporting 5 such cases in a series of 56 patients with (meth)acrylate allergic contact disease in 2003 (10). Since then, the role of anaerobic sealants in (meth)acrylate allergic contact dermatitis has received little attention, although our data show cases up to 2013.

Nail technicians and consumers and also workers in manufacturing industry are at particularly increased risk of developing (meth)acrylate contact sensitization, as they are directly exposed to (meth)acrylate monomers before they are polymerized. Protective measures against acrylate allergy are difficult to apply; although the commonly used gloves do offer some protection, (meth)acrylates can permeate these with prolonged exposure. The breakthrough time varies greatly, according to the type of acrylate, solvent, and glove (17, 18). Gloves that are resistant to (meth)acrylates, such as 4H® (Honeywell Safety Products, Smithfield, Rhode Island, USA), impair the manual dexterity required for work with nails (3) and intricate manufacturing work. Therefore, it is important to employ preventive

measures from the onset of work. Those working with (meth)acrylates should be educated regarding the best choice of glove and the breakthrough time for the particular (meth)acrylate(s) that they are using, the need to change gloves regularly, and the correct method of removal of gloves to prevent skin contamination. Work surfaces and other objects within the work environment should be kept clear of (meth)acrylates (3). Polymerization of monomeric nail products often occurs with the aid of a UV light-emitting diode or UV compact fluorescent light nail-drying lamp system. In order to minimize contact with (meth)acrylate monomers, it is important for UV lamps to be checked and bulbs to be changed regularly, and for the recommended curing time to be adhered to. Two of our patients with hand dermatitis secondary to the use of acrylic nails had concomitant facial dermatitis; this may have resulted from direct transfer of acrylates from the hands to the face; or, alternatively, airborne exposure could have been possible, in which case the use of protective masks would be helpful.

Dressings and wound care products have been identified as newly emerging sources of (meth)acrylate contact allergy and allergic contact dermatitis. Mepilex® Border is a self-adherent absorbent silicone dressing that is used on exuding wounds. It contains a silicone contact layer, an absorbent foam-containing central layer, and an outer polyurethane film (19). Direct communication with the manufacturers has confirmed that the acrylate component of the Mepilex® Border dressing is within the adhesive portion, which contains mainly butyl acrylate. Of the 4 patients who were sensitive to the Mepilex® Border dressing, 2 had positive reactions to butyl acrylate. DryMax® Extra is a highly absorbent dressing that contains sodium polyacrylate superabsorbent particles (20); sodium polyacrylate was not included in our series. Although polymerized acrylates are relatively inert, factors such as local inflammation, reduced skin barrier function and occlusive bandages may enhance their allergenic properties. A French group recently patch tested 354 patients with chronic leg ulcers, and found 0.6% of the patients to be sensitive to EGDMA and 1.4% to be sensitive to the Mepilex® dressing (21). In our study, 28 (54%) patients overall and 3 (42.9%) of those with allergic contact dermatitis secondary to the use of acrylate-containing dressings reacted positively to EGDMA. The manufacturers have indicated to us that the Mepilex® dressing without the border does not contain any (meth)acrylates. Micropore™ Surgical Tape contains isooctyl acrylate (22), which is not included in our series, and the chemical identity and composition of the terpolymer contained in Cavilon™ No Sting Barrier Film has been withheld as a trade secret (23).

Two other unusual sources of (meth)acrylate exposure were poly(methyl methacrylate) (acrylic Perspex®), which is a solid transparent material that is often used in place of glass, and a plastic pedometer containing polyacrylates. These are interesting observations given that it is the monomeric form in which acrylates are potent sensitizers. It is known that acrylate polymers can contain a small amount of residual monomer, and the theoretical risk of allergic contact dermatitis as a result of this has previously been considered in the literature (24).

Previous studies have yielded similar results in terms of the most prevalent allergens (3, 4, 7, 9, 10, 25). The significant correlation between EGDMA and both 2-HPMA and 2-HEMA is interesting. In 1995, Koppula et al. hypothesized that marked cross-reactivity exists between EGDMA, 2-HPMA, and 2-HEMA, because of a shared carboxy ethyl side group (26). Subsequent clinical and animal studies found a significant correlation between 2-HPMA and 2-HEMA, but not EGDMA (3, 25, 27). In 2015, Uter and Geier found a high degree of cross-reactivity for all three (meth)acrylates in a group of females with (meth)acrylate allergic contact disease secondary to the use of artificial nails (4), and our study has shown similar findings in a general patient population. The correlation between hydroxypropyl acrylate and each of EGDMA and 2-hydroxyethyl acrylate is a new observation, with a potential underlying mechanism being unclear. It would be advisable for a patient who is sensitized to one of the above to also avoid the associated (meth)acrylates, to minimize the risk of reactions; however, as a general rule, we would recommend avoidance of all (meth)acrylates in sensitized patients, given that products often contain multiple different (meth)acrylates.

Many studies have investigated the suitability of particular (meth)acrylates as screening allergens. Alto-Korte et al. (25) reported that screening with EGDMA, di(ethylene glycol) diacrylate, 2-HPMA and pentaerythritol triacrylate would have identified 93% of their 66 patients who reacted positively to at least one of a screening series of 36 (meth)acrylates. This combination would have identified 34 (65.4%) of our patients. Goon et al. found that screening with 2-HEMA, triethylene glycol diacrylate (TREGDA) and EGDMA would have resulted in 97.3% of their 38 patients being identified, although patients were tested with a total of five (meth)acrylates (11). This combination would have identified 32 (61.5%) of our patients. In 2014, Ramos et al. suggested 2-HEMA as a screening allergen, with 80.6% of their 37 patients reacting positively (3). If patients did not react positively, they recommended progression to a broader range of allergens, particularly 2-HPMA, TREGDA, ethyl acrylate, EGDMA, and 2-hydroxyethyl

acrylate. Screening our study population with 2-HEMA and with this suggested combination of allergens would have identified 29 (55.8%) and 43 (82.7%) of our patients, respectively. A key difficulty in making comparisons with these studies is that different groups have not used identical (meth)acrylate series. These and our own suggested combination of four (meth)acrylates, namely 2-hydroxyethyl acrylate, 2-HPMA, bis-GMA, and ethyl acrylate, would require further testing with larger studies before recommendations could be made. Establishing a single combination of (meth)acrylates for screening may be difficult, in view of the changing landscape of most prevalent sources of allergic contact disease and geographical variation in certain exposures, for example industry. The (meth)acrylates included may have to be reviewed at intervals and tailored to specific regions.

Our study has some limitations. Although we had a full set of patch test data for all 52 of our patients, data on clinical correlates (age, sex, atopy, source of exposure, and occupation) were available for only 47 cases. Additionally, we did not perform any readings after D4. Swedish studies have shown that readings up to D7 can identify some delayed positive reactions to (meth)acrylates (28–30). Our series did not include cyanoacrylates, which are cyanide derivatives of acrylates that readily polymerize and are found in quick-setting adhesives. Ethyl cyanoacrylate is used in some artificial nail glues, and does not appear to cross-react with other (meth)acrylates (31). Octyl cyanoacrylate is a component of Dermabond™, a topical adhesive that is used for

skin closure and has become increasingly recognized as a cause of allergic contact disease (32–35). Addition of both of these cyanoacrylates to our series could potentially identify a wider range of patients, and enable further exploration of surgical adhesives as causes of allergic contact disease.

In conclusion, over recent years there has been a shift towards acrylic nail exposure as the most common source of (meth)acrylate contact sensitization and cause of allergic contact dermatitis. It is important to not overlook industrial sources of exposure, particularly in regions where there is a high level of industrial employment or in individuals who have come into contact with anaerobic sealants. Dressings containing (meth)acrylates appear to be significant new and emerging sources of sensitization and allergic contact dermatitis, and we therefore encourage clinicians to consider patch testing with (meth)acrylates in patients with leg dermatitis or in instances where dermatitis is localized to dressing sites. We suggest a combination of four (meth)acrylates that would have identified >90% of our patients, but larger studies are required to inform more concrete recommendations on these as screening allergens.

Acknowledgement

The authors would like to thank Dr Iain Foulds, consultant dermatologist at Birmingham Skin Centre 1983–2008, and Susan Wright, patch test technician at Birmingham Skin Centre.

References

- van der Voort E A, van Neer F J, Neumann H A. Acrylate-induced nail contact allergy. *Int J Dermatol* 2014; **53**: e390–e392.
- Sasseville D. Acrylates in contact dermatitis. *Dermatitis* 2012; **23**: 6–16.
- Ramos L, Cabral R, Gonalo M. Allergic contact dermatitis caused by acrylates and methacrylates – a 7-year study. *Contact Dermatitis* 2014; **71**: 102–107.
- Uter W, Geier J. Contact allergy to acrylates and methacrylates in consumers and nail artists – data of the Information Network of Departments of Dermatology, 2004–2013. *Contact Dermatitis* 2015; **72**: 224–228.
- Drucker A M, Pratt M D. Acrylate contact allergy: patient characteristics and evaluation of screening allergens. *Dermatitis* 2011; **22**: 98–101.
- Ohlson C G, Svensson L, Mossberg B, Hk M. Prevalence of contact dermatitis among dental personnel in a Swedish rural county. *Swed Dent J* 2001; **25**: 13–20.
- Geukens S, Goossens A. Occupational contact allergy to (meth)acrylates. *Contact Dermatitis* 2001; **44**: 153–159.
- Roche E, Cuadra J, Alegre V. Sensitization to acrylates by artificial acrylic nails: review of 15 cases. *Actas Dermosifiliogr* 2008; **99**: 788–794.
- Wilkinson D S, Fregert S, Magnusson B et al. Terminology of contact dermatitis. *Acta Derm* 1970; **50**: 287–292.
- Sood A, Taylor J S. Acrylic reactions: a review of 56 cases. *Contact Dermatitis* 2003; **48**: 346–347.
- Goon A T, Bruze M, Zimerson E et al. Screening for acrylate/methacrylate allergy in the baseline series: our experience in Sweden and Singapore. *Contact Dermatitis* 2008; **59**: 307–313.
- Montgomery R, Stocks S J, Wilkinson S M. Contact allergy resulting from the use of acrylate nails is increasing in both users and those who are occupationally exposed. *Contact Dermatitis* 2016; **74**: 120–122.
- Ranchoff R E, Taylor J S. Contact dermatitis to anaerobic sealants. *J Am Acad Dermatol* 1985; **13**: 1015–1020.
- Dempsey K J. Hypersensitivity to Sta-Lok and Loctite anaerobic sealants. *J Am Acad Dermatol* 1982; **7**: 779–784.
- Mathias C G, Maibach H I. Allergic contact dermatitis from anaerobic acrylic sealants. *Arch Dermatol* 1984; **120**: 1202–1205.
- Cond -Salazar L, Guimaraens D, Romero L V. Occupational allergic contact dermatitis from anaerobic acrylic sealant. *Contact Dermatitis* 1988; **18**: 129–132.
- Munksgaard E C. Permeability of protective gloves by HEMA and TEGDMA in the presence of solvents. *Acta Odontol Scand* 2000; **58**: 57–62.

- 18 Andreasson H, Boman A, Johnsson S et al. On permeability of methyl methacrylate, 2-hydroxyethyl methacrylate and triethyleneglycol dimethacrylate through protective gloves in dentistry. *Eur J Oral Sci* 2003; **111**: 529–535.
- 19 Mölnlycke Health Care. Mepilex® Border – product sheet, 2014. Available at: <http://www.molnlycke.co.uk/advanced-wound-care-products/foam-dressings/mepilex-border> (last accessed 05 March 2016).
- 20 Panca M, Cutting K, Guest J F. Clinical and cost effectiveness of absorbent dressings in the treatment of highly exuding VLU's. *J Wound Care* 2013; **22**: 109–110, 112–118..
- 21 Valois A, Waton J, Avenel-Audran M et al. Contact sensitization to modern dressings: a multicentre study on 354 patients with chronic leg ulcers. *Contact Dermatitis* 2015; **72**: 90–96.
- 22 Zheng Y, Choi M J, Zhai H, Maibach H I. Stratum corneum tape-stripping method. In: *Dermatotoxicology*, 8th edition, Wilhelm K P, Zhai H, Maibach H I (eds): Boca Raton, FL, Informa Healthcare, 2013: p. 348–359.
- 23 3M. Cavilon™ No Sting Barrier Film – safety data sheet, 2014. Available at: <http://www.safety.vanderbilt.edu/msds/products/cavilon-no-sting-barrier-film.pdf> (last accessed 09 May 2016).
- 24 Pemberton M A, Lohmann B S. Risk assessment of residual monomer migrating from acrylic polymers and causing allergic contact dermatitis during normal handling and use. *Regul Toxicol Pharmacol* 2014; **69**: 467–475.
- 25 Aalto-Korte K, Henriks-Eckerman M L, Kuuliala O, Jolanki R. Occupational methacrylate and acrylate allergy – cross-reactions and possible screening allergens. *Contact Dermatitis* 2010; **63**: 301–312.
- 26 Koppula S V, Fellman J H, Storrs F J. Screening allergens for acrylate dermatitis associated with artificial nails. *Am J Contact Dermat* 1995; **6**: 78–85.
- 27 Rustemeyer T, de Groot J, von Blomberg B M et al. Cross-reactivity patterns of contact-sensitizing methacrylates. *Toxicol Appl Pharmacol* 1998; **148**: 83–90.
- 28 Goon A T, Bruze M, Zimerson E et al. Contact allergy to acrylates/methacrylates in the acrylate and nail acrylics series in southern Sweden: simultaneous positive patch test reaction patterns and possible screening allergens. *Contact Dermatitis* 2007; **57**: 21–22.
- 29 Goon A T, Isaksson M, Zimerson E et al. Contact allergy to (meth)acrylates in the dental series in southern Sweden: simultaneous positive patch test reaction patterns and possible screening allergens. *Contact Dermatitis* 2006; **55**: 219–226.
- 30 Isaksson M, Lindberg M, Sundberg K et al. The development and course of patch-test reactions to 2-hydroxyethyl methacrylate and ethyleneglycol dimethacrylate. *Contact Dermatitis* 2005; **53**: 292–297.
- 31 Kanerva L. Ethylcyanoacrylate does not cross-react with methacrylates and acrylates. *Am J Contact Dermatitis* 1997; **8**: 54–55.
- 32 Durando D, Porubsky C, Winter S et al. Allergic contact dermatitis to Dermabond (2-octyl cyanoacrylate) after total knee arthroplasty. *Dermatitis* 2014; **25**: 99–100.
- 33 McDonald B S, Buckley D A. Severe dermatitis from Dermabond® surgical glue. *Br J Dermatol* 2014; **170**: 739–741.
- 34 Sachse M M, Junghans T, Rose C, Wagner G. Allergic contact dermatitis caused by topical 2-octyl-cyanoacrylate. *Contact Dermatitis* 2013; **68**: 317–319.
- 35 El-Dars L D, Chaudhury W, Hughes T M, Stone N M. Allergic contact dermatitis to Dermabond after orthopaedic joint replacement. *Contact Dermatitis* 2010; **62**: 315–317.