

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

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In a recent study we showed that all our dental personnel/patients were detected with 2-hydroxyethyl methacrylate (2-HEMA) and 2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane (bis-GMA). We studied 90 patients tested to the acrylate and nail acrylics series at our department over a 10 year period to see whether screening allergens could be found. Patch testing with an acrylate and nail acrylics series was performed. Among the 10 acrylate/methacrylate-allergic occupational dermatitis patients tested to the acrylate series, the most common allergens were triethyleneglycol diacrylate (TREGDA, 8), diethyleneglycol diacrylate (5), and 1,4-butanediol diacrylate (BUDA, 5). All 10 of these patients would have been picked up by a short screening series combining TREGDA, 2-hydroxypropyl methacrylate (2-HPMA), and BUDA or 1,6-hexanediol diacrylate (HDDA). Among the 14 acrylate/methacrylate-allergic nail patients, the most common allergens were ethylene glycol dimethacrylate (EGDMA, 11), 2-HEMA, (9), and triethyleneglycol dimethacrylate (9). Screening for 3 allergens i.e. 2-HEMA plus EGDMA plus TREGDA, would have detected all 14 nail patients. A short screening series combining 2-HEMA, EGDMA, TREGDA, 2-HPMA, bis-GMA, and BUDA or HDDA would have picked up all our past study patients (dental, industrial, and nail) with suspected allergy to acrylate/methacrylate allergens.

Key words: acrylates; allergic contact dermatitis; industrial; nail technicians; patch test; screening.
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Background

In Malmö, we have been patch testing dermatitis patients with suspected contact allergy to acrylates with an acrylate series since the 1980s. This pertains to cases with occupational exposure to acrylates, with the exception of dental personnel, on whom a separate dental series would have been used (1). A special nail acrylics series to patch test patients with suspected contact allergy to nail cosmetics of the acrylate/methacrylate type has been used since 1998. This series originally contained 7 methacrylates, but in 2003 we removed 2 allergens and added another 9 acrylates/methacrylates. The series now contains 14 acrylates/methacrylates, 12 of which are also in the acrylate series (Table 1), with 2 additional allergens i.e. tetrahydrofurfuryl methacrylate (THFMA) and ethyl cyanoacrylate (ECA). Often these nail patients have been patch tested to both the nail acrylics and the acrylate

series. In the present study, we aim to describe our nail patients and our acrylate patients patch tested to the 2 aforementioned acrylate series, and which acrylate/methacrylate allergens detected their acrylate/methacrylate contact allergy.

Patients and Methods

This is a 10 year retrospective study of patients patch tested to the acrylate series and nail acrylics series in the Department of Occupational and Environmental Dermatology, Malmö University Hospital, Sweden, from 1 January 1995 to 31 December 2004.

Patch testing

The allergens were applied onto small (Ø8 mm) Finn Chambers[®] (Epitest Ltd Oy, Tuusula,

Table 1. Acrylate/methacrylate allergens used in 90 patients tested to the acrylate series and/or the nail acrylics series in Malmö from 1 January 1995 to 31 December 2004

Test substance	Abbreviation	Concentration (% pet)
Ethyl acrylate*†	1-EA	0.1
Butyl acrylate*†	BA	0.1
2-Ethylhexyl acrylate*	2-EHA	0.1
2-Hydroxyethyl acrylate*†	2-HEA	0.1
2-Hydroxypropyl acrylate*	2-HPA	0.1
Methyl methacrylate*†	MMA	2.0
Ethyl methacrylate*†‡	EMA	2.0
n-Butyl methacrylate*†‡	BMA	2.0
2-Hydroxyethyl methacrylate*†	2-HEMA	2.0
2-Hydroxypropyl methacrylate*†	2-HPMA	2.0
Ethylene glycol dimethacrylate*†‡	EGDMA	2.0
Triethyleneglycol dimethacrylate*†‡	TREGDMA	2.0
1,4-Butanediol dimethacrylate*	BUDMA	2.0
Urethane dimethacrylate*	UEDMA	2.0
2,2-Bis[4-(2-methacryloxyethoxy)phenyl]propane*	Bis-EMA	1.0
Diethyleneglycol diacrylate*	DEGDA	0.1
Tripropyleneglycol diacrylate*	TPGDA	0.1
Trimethylolpropane triacrylate*†	TMPTA	0.1
Pentaerythritol triacrylate*	PETA	0.1
Oligotriacrylate 480*	OTA480	0.1
Epoxy acrylate*	EpoxyA	0.5
Urethane diacrylate (aliphatic)*	al-UDA	0.1
Urethane diacrylate (aromatic)*	ar-UDA	0.05
Triethyleneglycol diacrylate*†	TREGDA	0.1
n,n-Methylene bisacrylamide*	MbAcryl	1.0
2,2-Bis[4-(methacryloxy)phenyl]propane*	Bis-MA	2.0
2,2-Bis[4-(2-hydroxy-3-methacryloxy-propoxy)phenyl]propane*	Bis-GMA	2.0
1,4-Butanediol diacrylate*	BUDA	0.1
1,6-Hexanediol diacrylate*†	HDDA	0.1
Ethyl cyanoacrylate†	ECA	10.0
Tetrahydrofurfuryl methacrylate†‡	THFMA	2.0
Methacrylic acid‡	MA	1.0
Propylmethacrylate§	PMA	2.0

*Former (1 January 1994 to 29 September 1999) and current acrylate series (from 30 September 1999).

†Current nail acrylics series (from 16 April 2003).

‡Former nail acrylics series (28 July 1998 to 15 April 2003).

§Former (1 January 1994 to 29 September 1999) acrylate series only.

Finland) on Scanpor[®] (Norgesplaster A/S, Venesla, Norway). The tests were applied to the upper part of the back and left for 48 h. Tests were read on day 3 (D3) or D4 and D7 by a dermatologist, and the reactions were scored according to ICDRG criteria.

Supplier of allergens

Chemotechnique Diagnostics (Vellinge, Sweden) supplied the sensitizers for both series. The acrylate/methacrylate allergens are listed in Table 1 with concentrations and vehicle used.

Patients

We retrospectively studied the records of 90 patients (mean age 41.5 years, range 19–64). There were 52 women (mean age 39.8 years, range 19–63) and 38 men (mean age 43.8 years, range 22–64). These were patients with dermatitis suspected to be caused by acrylates/methacrylates, who had

been tested to the acrylate and/or the nail acrylics series during the study period. We excluded patients who had been seen for suspected allergies to dental acrylates who had been tested to either of our dental series (1), as well as patients involved in screening studies in various acrylate/methacrylate-using industries, where the populations included subjects with no clinical evidence of dermatitis (2).

We have subdivided the patients into 2 groups:

The group working with acrylates/methacrylates professionally constituted 53 (58.9%) patients (mean age 42.1 years, range 20–64), all of whom had been patch tested to the acrylate series. This group had 15 women (mean age 37.9 years, range 20–61) and 38 men (mean age 43.8 years, range 22–64). This group includes workers who had been working in printing with ultraviolet (UV)-curing paints, the manufacture of acrylate-based binders for paints, glass repair, mechanical shop work, and the varnishing of doorsteps.

The nail patients were those with dermatitis suspected to be from nail acrylics. These included 13 nail technicians, who had been occupationally exposed, and 24 customers. These patients had been tested with the nail acrylics series, the acrylate series, or both. This group comprised 37 (41.1%) patients. All were women (mean age 40.6 years, range 19–63)

Results

There were 24 patients (mean age 42.3 years, range 20–64) with positive patch tests to acrylate/methacrylate allergens: 10 (mean age 43.9 years, range 20–64) in the acrylate group and 14 (mean age 41.1 years, range 26–56) in the nail group. In the acrylate group there were 8 men (mean age 48.0 years, range 28–64) and 2 women (aged 20 and 35 years), while all in the nail group were women.

The most common sensitizers overall among the 24 allergic individuals were triethyleneglycol diacrylate (TREGDA, 16), ethylene glycol dimethacrylate (EGDMA, 11), triethyleneglycol dimethacrylate (TREGDMA, 10), and 1,6-hexanediol diacrylate (HDDA, 10). The patch test results of our acrylate/methacrylate-allergic patients are shown in Table 2. 5 screening allergens would be needed to pick up all positive patients. These are TREGDA, 2-hydroxyethyl methacrylate (2-HEMA), 2-hydroxypropyl methacrylate (2-HPMA), EGDMA, and HDDA or 1,4-butanediol diacrylate (BUDA).

Acrylate series

10 dermatitis patients reacted to one or more of the acrylates/methacrylates in the acrylate series. The most common allergens were TREGDA (8), diethyleneglycol diacrylate (DEGDA, 5), and BUDA (5).

All 10 patients would have been picked up by screening with 3 allergens: TREGDA, 2-HPMA, and BUDA or HDDA. Of the 10 working with acrylates professionally, 4 had been working in printing with UV-curing paints, 3 had been working in the manufacture of acrylate-based binders for paints (1 in the manufacture of UV-curing printing inks and 2 in the manufacture of paints), whereas 1 each had jobs in glass repair, mechanical shop work, and the varnishing of doorsteps.

In all 10 patients, the indication for patch testing had been work-related eczema. In 9/10 of these cases the acrylate allergy had been concluded to be of present relevance, while 1 was of

Table 2. Patients with positive reactions to acrylates/methacrylates in the acrylate and nail acrylics series* in Malmö from 1 January 1995 to 31 December 2004, with abbreviations as in Table 1. All patch test readings are shown as first reading (D3/D4)/second reading (D7)

Patient no.	Group	Sex	Age	2-EA	BA	2-HEA	2-HPA	MMA	EMA	2-HEMA	2-HPMA	EGDMA	TREGDMA	BUDMA	DEGDA	TPGDA	TMPTA	PETA	OTA480	EpoxyA	al-UDA	ar-UDA	TREGDA	BUDA	HDDA	THFMA
1	A	F	20	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
2	A	F	35	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
3	A	M	28	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
4	A	M	42	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
5	A	M	46	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
6	A	M	47	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
7	A	M	48	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
8	A	M	53	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
9	A	M	56	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
10	A	M	64	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
11	N	F	26	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
12	N	F	28	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
13	N	F	31	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
14	N	F	33	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
15	N	F	36	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
16	N	F	39	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
17	N	F	41	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
18	N	F	42	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
19	N	F	44	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
20	N	F	44	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
21	N	F	50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
22	N	F	51	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
23	N	F	54	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN
24	N	F	56	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	LN

A, occupational acrylate allergy group; F, female; M, male; N, nail acrylic allergy group; nr, not read; NT, not tested. There were no positive reactions to 2-EHA, BMA, UEDMA, bis-EMA, MbAcryl, bis-MA, bis-GMA, ECA, MA, and PMA.

unknown relevance. If only one reading had been made (on D3 but not also on D7), we would have missed 5/35 (14%) of all positive reactions i.e. 1/7 (14%) TREGDA-positive, 2/6 (33%) BUDA-positive, 1/5 (20%) DEGDA-positive, and 1/4 (25%) HDDA-positive acrylate reactions.

Nail acrylics series

Among the 14 patients who reacted, the most common allergens were EGDMA (11), 2-HEMA (9), and TREGDMA (9). Of 8 allergic to 2-HEA (2-hydroxyethyl acrylate), 7 reacted to 2-HEMA. Of eight 2-HPMA-positive patients, 7 reacted to EGDMA and 7 to 2-HEMA. Of the 11 who had reacted to EGDMA, 8 (73%) had simultaneous positive reactions to 2-HEMA and 9 (82%) to TREGDMA. Of the nine 2-HEMA-positive patients, 8 (89%) also reacted to EGDMA. 6/10 TREGDA-positive patients also reacted to 2-HEMA.

13/14 (93%) patients were picked up with the pair combination TREGDA plus EGDMA. 13/14 (93%) patients were picked up with the pair combination 2-HEA plus EGDMA. By combining 3 acrylates/methacrylates i.e. 2-HEMA plus EGDMA plus TREGDA, all 14 patients would have been detected.

Nail technicians (8/13 or 62%) had a higher proportion of positive reactions compared with nail customers (6/24 or 25%). Of the allergic patients, all 8 nail technicians presented with hand eczema, compared with 4 of 6 customers. The remaining 2 nail customers presented with eczema of the nail folds (Fig. 1). 13/14 (93%) of the allergic patients had a clinically relevant contact allergy while 1 patient, an acrylic nail customer with hand eczema who had simultaneous reactions with nickel and cobalt, had uncertain relevance.

If only one reading had been made (on D3 but not also on D7), we would have missed 6/86 (7%) of all positive reactions i.e. 1/8 (13%) 2-HEA-positive, 1/1 (100%) 2-HPA (2-hydroxypropyl acrylate)-positive, 1/9 (11%) 2-HEMA-positive, 1/3 (33%) BUDMA (1,4-butanediol dimethacrylate)-positive, 1/6 (17%) HDDA-positive, and 1/3 (33%) THFMA-positive reactions. For EGDMA, TREGDA, or TREGDMA there would have been no missed patients with only one reading on D3.

8/14 had been patch tested to their own nail preparations, of whom 6 (75%) had positive results. 3/3 who had been tested to acrylic gels had positive reactions, 2/2 who had been tested to acrylic nail filings had reacted, 1/2 who had been tested to acrylic liquids containing mono-

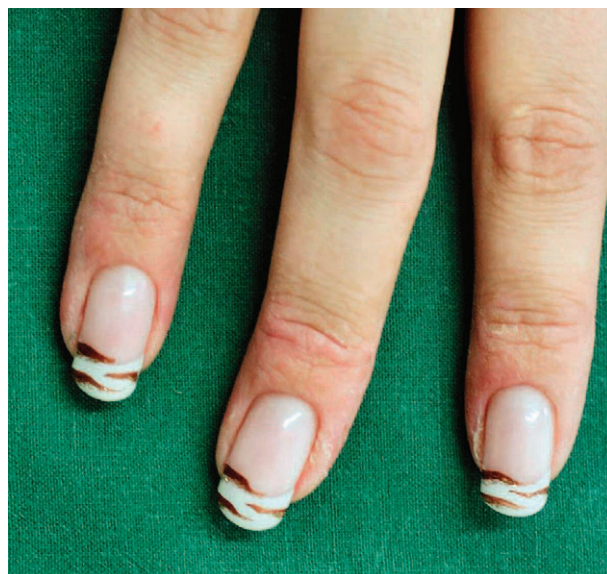


Fig. 1. Nail fold eczema in a nail technician hypersensitive to several nail acrylics.

mers had a positive reaction while 1 who had been tested to an ultrasonic acetone extract of her finished acrylic nail had a negative patch test.

Discussion

Industrial and nail acrylate allergies have been reported, with numerous case reports and new studies being published regularly in recent years (2–9).

We have recently presented our patch test data on contact allergy to acrylates/methacrylates in dental patients and dental personnel (1). Unlike the population of dental personnel and dental patients, where 1–2 markers of contact allergy to acrylates/methacrylates (i.e. 2-HEMA with or without 2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane (bis-GMA) could have picked up 100% of the allergic tested population, the same could not be said for our patients tested to the acrylate series and the nail acrylics, where 3 markers but in different combinations, would be required to detect all the allergic patients. If we were to combine both the nail acrylics and acrylate series into one comprehensive acrylate series (by adding THFMA and ECA to the current acrylate series), 5 markers (TREGDA, 2-HEMA, 2-HPMA, EGDMA, and HDDA or BUDA) would have detected all allergic patients.

In our previous article (1), we had noted that all patients who reacted to EGDMA also reacted to 2-HEMA. In the present study, there were 8 subjects with simultaneous reactions to 2-HEMA and EGDMA of nine 2-HEMA-positive (89%) and 11 EGDMA-positive (73%) patients. Furthermore,

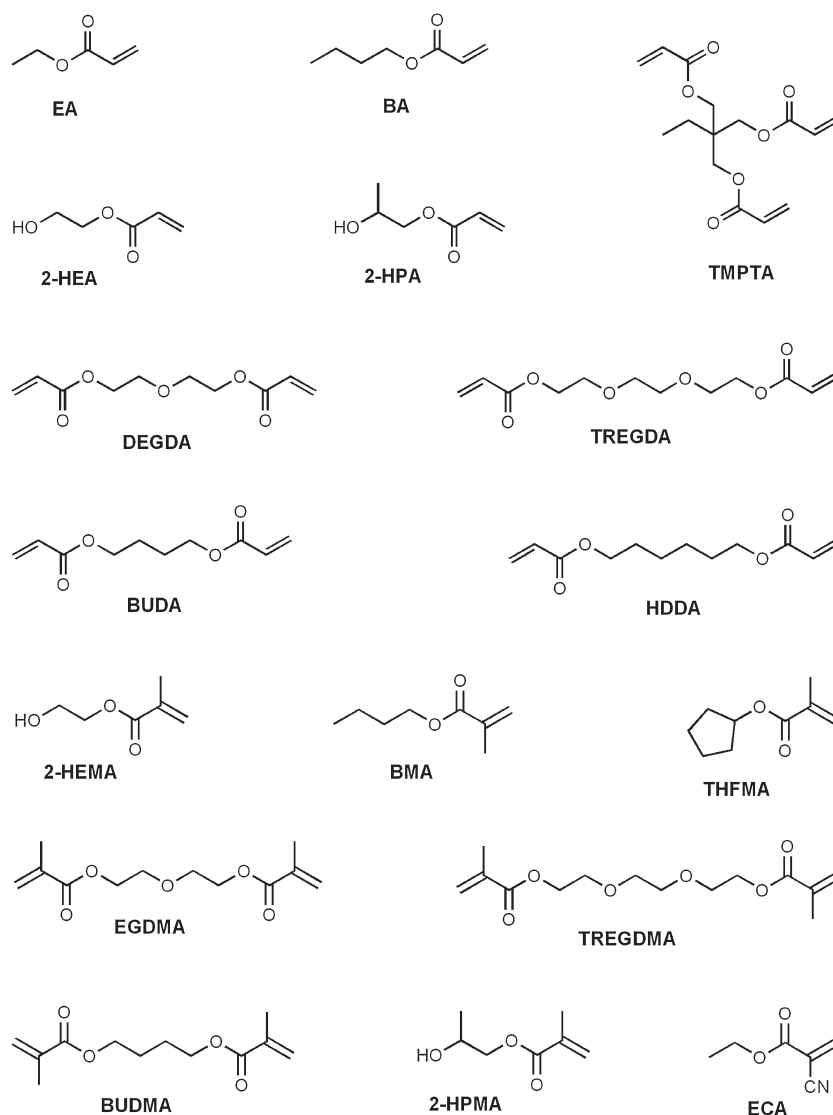


Fig. 2. The chemical structures of those acrylates/methacrylates discussed in the text. BA, butyl acrylate; BMA, n-butyl methacrylate; BUDA, 1,4-butanediol diacrylate; BUDMA, 1,4-butanediol dimethacrylate; DEGDA, diethyleneglycol diacrylate; EA, ethyl acrylate; ECA, ethyl cyanoacrylate; EGDMA, ethylene glycol dimethacrylate; HDDA, 1,6-hexanediol diacrylate; 2-HEA, 2-hydroxyethyl acrylate; 2-HEMA, 2-hydroxyethyl methacrylate; 2-HPA, 2-hydroxypropyl acrylate; 2-HPMA, 2-hydroxypropyl methacrylate; THFMA, tetrahydrofurfuryl methacrylate; TMPTA, trimethylolpropane triacrylate; TREGDA, triethyleneglycol diacrylate; and TREGDMA, triethyleneglycol dimethacrylate.

we also noted in the aforementioned study that in every subject with simultaneous positive patch tests to 2-HEMA and EGDMA, the strength of the positive reaction to 2-HEMA was either greater than or equal to the strength of the positive reaction to EGDMA. The same has been seen in the present study, where 4/9 (44%) of the simultaneous reactors showed stronger reactions to 2-HEMA and 5/9 (56%) the same reactivity.

In the present study, we also saw that all DEGDA-positive acrylate workers had worked in printing with UV-curing paints or in the manufacture of UV-curing acrylate-based inks or paints. All 5 of the DEGDA-positive acrylate

workers also reacted to TREGDA, while another 3 acrylate workers were allergic to TREGDA but not DEGDA. Of these 3 workers, 1 had been manufacturing UV-curing paint, 1 had been working in a mechanical workshop and 1 in the varnishing of doorsteps. Furthermore, we also noted that in every subject among the acrylate workers with simultaneous positive patch tests to DEGDA and TREGDA, the strength of the positive reaction to DEGDA was either greater than or equal to the strength of the positive reaction to TREGDA. When looking at the nail patients, all 4 DEGDA-positive patients simultaneously reacted to TREGDA, and in all but 1, the strength of the

positive reaction to DEGDA was either greater than or equal to the strength of the positive reaction to TREGDA.

In data on allergic reactions to acrylates/methacrylates over a 10 year period (October 1994 to September 2004) comprising 405 patients from the Finnish Institute of Occupational Health, Helsinki, Finland (2), the most common causes of allergic reactions were 2-HPMA (18.2%), followed by 2-HEMA (7.6%) and EGDMA (6.9%). From their data it was not possible to determine which acrylates would have detected all their allergic patients.

In a study from Belgium on screening for contact allergy to artificial nails (3), based on 27 patients in contact with artificial nails, the authors had found that 2-HEMA and ECA were the only 2 allergens needed to diagnose contact allergy to acrylic-containing nail cosmetics in all but one of their patients.

In the aforementioned Belgian study, all 3 TREGDMA-positive patients had also reacted to EGDMA. This is similar to what we have found in our nail patients. We had 9 TREGDMA-positive patients, all of whom had reacted to EGDMA. However, only 9/11 of our EGDMA-positive patients had reacted to TREGDMA. Based on their findings, the authors of the Belgian article recommended deletion of 5 allergens from the Chemotechnique Diagnostics artificial nail series—TREGDMA, butyl methacrylate, butyl acrylate, HDDA, and trimethylolpropane triacrylate. Our data support their findings with the exception of HDDA, with which we had 6 nail patients with positive patch test reactions. Contact allergy to ECA is rare—1/7 had a positive patch test in the Belgian study while 0/7 reacted to this allergen in our study. However, after completion of this study, we subsequently had one patient with a positive reaction to ECA only (4). This patient had used preformed acrylate nails which she glued to the nail plate. The glue contained ECA. Because occasional nail patients are seen with ECA allergy

only, this substance should also be included in a nail-screening series.

All 3 of our detected screening markers for nail acrylic allergy, 2-HEMA, EGDMA, and TREGDA, are found in the nail acrylate-screening series, containing 10 allergens, proposed by the Belgian study. Also in that study, the authors had recommended substituting 2-HPMA for 2-HPA. However, our results contradict theirs, as we had 8 positives to 2-HPMA but only 1 to 2-HPA. Furthermore, the subject who had been 2-HPA positive in our study had also reacted to 2-HPMA with a stronger reaction.

In another study from the USA on acrylic allergy in 56 cases (5), the most common sensitizers from acrylic nails in 25 women were 2-HPMA, 2-HEMA, and EGDMA. This is similar to our findings.

Koppula et al. (6) had earlier suggested 5 screening acrylates for nail acrylate allergy based on data from 11 patients. These were ethyl acrylate, 2-HEA, EGDMA, ECA, and TREGDA. Of these, we had also found in our retrospective study that EGDMA and TREGDA were screening markers for acrylate allergy in nail patients and also ECA in the single case (4). However, Koppula et al. had selected 2-HEA over 2-HEMA as their screening allergen, although in their study there was no significant difference in the number of positive reactions in the 9 patients who had been patch tested to both 2-HEA and 2-HEMA.

The chemical structures of the acrylates/methacrylates mentioned in the text of this article are shown in Fig. 2.

Table 3 summarizes the recommended screening allergens for the various subpopulations of our patients with suspected allergy to acrylate/methacrylate allergens. Combining the recommended screening allergens of both our current and previous (1) studies, a screening series of 7 allergens would have picked up all our past patients (dental, industrial, and nail) with suspected allergy to acrylate/methacrylate allergens. The allergens are

Table 3. Recommended screening allergens in 4 subpopulations and in a combined population with suspected allergy to acrylate/methacrylate allergens

Subpopulation	Recommended screening allergens
Industrial acrylate workers	TREGDA + 2-HPMA + (BUDA or HDDA)
Nail technicians and customers	2-HEMA + EGDMA + TREGDA
Dental personnel	2-HEMA only
Dental patients	2-HEMA + bis-GMA
Our total population of acrylate/methacrylate-allergic patients	TREGDA + 2-HPMA + (BUDA or HDDA) + 2-HEMA + EGDMA + bis-GMA + ECA

Bis-GMA, 2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane; BUDA, 1,4-butanediol diacrylate; ECA, ethyl cyanoacrylate; EGDMA, ethylene glycol dimethacrylate; HDDA, 1,6-hexanediol diacrylate; 2-HEMA, 2-hydroxyethyl methacrylate; HPMA, 2-hydroxypropyl methacrylate; TREGDA, triethyleneglycol diacrylate.

2-HEMA, TREGDA, 2-HPMA, bis-GMA, BUDA or HDDA, EGDMA, and ECA.

Furthermore, the importance of a D7 reading should also be highlighted. If only one reading had been made (on D3 but not also on D7), we would have missed 25% TREGDA-positive, 40% BUDA-positive, and 50% 2-HEMA-positive reactions in the occupational acrylate allergy group as well as 11% 2-HEMA-positive reactions in our nail patients.

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