

Occupational methacrylate and acrylate allergy – cross-reactions and possible screening allergens

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Background: Acrylic resin monomers, especially acrylates and methacrylates, are important occupational allergens.

Aims: To analyse patterns of concomitant patch test reactions to acrylic monomers in relation to exposure, and to suggest possible screening allergens.

Patients/methods: We reviewed the patch test files for the years 1994–2009 at the Finnish Institute of Occupational Health for allergic reactions to acrylic monomers, and analysed the clinical records of sensitized patients.

Results: In a group of 66 patients allergic to an acrylic monomer, the most commonly positive allergens were three methacrylates, namely ethyleneglycol dimethacrylate (EGDMA), 2-hydroxyethyl methacrylate (2-HEMA) and 2-hydroxypropyl methacrylate (2-HPMA), and an acrylate, namely diethyleneglycol diacrylate (DEGDA). The patterns of concomitant reactions imply that exposure to methacrylates may induce cross-reactivity to acrylates, whereas exposure to acrylates usually does not lead to cross-allergy to methacrylates. Screening for triethyleneglycol diacrylate (TREGDA) in the baseline series was found to be useful, as 3 of 8 patients with diagnosed occupational acrylate allergy might have been missed without the screening.

Conclusions: A short screening series of four allergens, EGDMA, DEGDA, 2-HPMA and pentaerythritol triacrylate (PETA), would have screened 93% of our 66 patients; each of the remaining 5 patients reacted to different acrylic monomer(s).

Key words: DEGDA; MBAA; methyl acrylate; PETA; printing work; TREGDA; urethane-acrylic-based filler; UV-cured paints. © John Wiley & Sons A/S, 2010.

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Contact allergy to acrylic resin monomers (acrylates, methacrylates, cyanoacrylates and acrylamides) is most often induced by dental products, artificial nails, and glues (1–7). These products usually contain methacrylates, and patients commonly have allergic reactions to 2-hydroxyethyl methacrylate (2-HEMA), ethyleneglycol dimethacrylate (EGDMA) or 2-hydroxypropyl methacrylate (2-HPMA). 2-HEMA has been recommended as a screen for methacrylate allergy resulting from dental products and artificial nails (7, 8). There are also products that contain mainly acrylates, for

example, UV-cured printing inks and lacquers (9), paints and varnishes (10), and glues (11–13).

Screening for acrylic monomer allergy is a topic of current interest. In Sweden and Singapore, 2-HEMA, methyl methacrylate (MMA), EGDMA, triethyleneglycol diacrylate (TREGDA) and 2-hydroxypropyl acrylate were included in the baseline series, and 1.4% of the tested individuals were positive to some of the allergens (14). At the Finnish Institute of Occupational Health (FIOH), TREGDA has been included in the baseline series since 1991. We have recently described separately

32 (meth)acrylate-allergic patients in dental professions (15), 10 (meth)acrylate glue-derived cases (4) and 24 patients with allergic reactions to epoxy acrylates (16). Besides reporting the results of the TREGDA screening, we analysed together all of our patients with contact allergy to acrylic monomers for frequencies of allergic reactions to individual acrylic monomers and the patterns of concomitant reactions to find possible screening allergens. We also describe in detail patients with occupational contact allergy to acrylates.

Patients and Methods

This was a retrospective study based on clinical investigations of patients suspected of having occupational contact dermatitis. We used Finn

Chambers® (Epitest, Tuusula, Finland), and read the tests two or three times, depending on the day of application (D2, D3 and D4; D2, D3 and D6; or D2 and D5). The patch test methods at the FIOH have previously been described more thoroughly (15). TREGDA (0.1% petrolatum; Chemotechnique Diagnostics, Vellinge, Sweden) has been included in our baseline series since 1991. The composition of the (meth)acrylate series has varied over the years. The individual test substances are given in Table 1.

The patch test records from September 1994 to March 2009 were reviewed for allergic reactions to all acrylic monomers, including those not included in our (meth)acrylate series. We included all patients who were tested with the (meth)acrylate series and had at least one allergic reaction (+/++/+++ +) to some acrylic monomer. We analysed their clinical

Table 1. The number of allergic reactions (+/++/+++ +) in a group of 66 patients with contact allergy to acrylic monomers and tested with the (meth)acrylate series

Acrylic monomer	Abbreviation	No. of patients reacting positively, <i>N</i> (%)	No. of tested patients in the group
Ethyleneglycol dimethacrylate 2%	EGDMA	43 (65)	66
2-Hydroxyethyl methacrylate 1%	2-HEMA	42 (64)	66
2-Hydroxypropyl methacrylate 2%	2-HPMA	42 (64)	66
Diethyleneglycol diacrylate 0.1%	DEGDA	23 (35)	66
Triethyleneglycol diacrylate 0.1%	TREGDA	19 (31)	62
Ethyl acrylate 0.1%	EA	18 (27)	66
Ethyl methacrylate 2%	EMA	18 (27)	66
Methyl methacrylate 2%	MMA	18 (27)	66
Triethyleneglycol dimethacrylate 2%	TREGDMA	15 (23)	66
Tetrahydrofurfuryl methacrylate 2%	THFMA	14 (21)	66
1,4-Butanediol diacrylate 0.1%	BUDA	11 (17)	64
Pentaerythritol triacrylate 0.1%	PETA	11 (17)	64
Tripropyleneglycol diacrylate 0.1%	TPGDA	10 (16)	64
1,4-Butanediol dimethacrylate 2%	BUDMA	9 (14)	65
1,6-Hexanediol diacrylate 0.1%	HDDA	9 (14)	64
Urethane diacrylate, aromatic 0.05%	ar-UDA	7 (11)	64
Dipropyleneglycol diacrylate 0.1%	DPGDA	7 (18)	38
Epoxy diacrylate (epoxy acrylate) 0.5%	bis-GA	7 (11)	66
Trimethylolpropane triacrylate 0.1%	TMPTA	7 (11)	64
Phenoxyethyl acrylate 0.1%	PEA	6 (11)	56
Butyl acrylate 0.1%	BA	6 (10)	60
Glycidyl methacrylate 0.1%	GMA	6 (11)	53
Ethoxylated methacrylate of bisphenol A 2%	EBADMA	5 (14)	37
Urethane dimethacrylate 2%	UDMA	5 (8)	66
Ethoxyethyl acrylate 0.1%	EEA	5 (10)	51
Oligotriacrylate 480 0.1%	OTA480	4 (6)	64
<i>N</i> -butyl methacrylate 2%	BMA	3 (5)	66
2,2-bis[4-(Methacryl-oxyethoxy)phenyl] propane 1%	bis-EMA	3 (5)	66
2,2-bis[4-(2-Hydroxy-3-methacryl-oxypropoxy)phenyl] propane 2%	bis-GMA	3 (5)	66
Urethane diacrylate, aliphatic 0.1%	al-UDA	2 (3)	64
<i>N,N</i> -dimethylaminoethyl methacrylate 0.2%	DMAEMA	2 (7)	27
<i>N,N</i> -methylenebisacrylamide 1%	MBAA	1 (2)	64
Ethyl cyanoacrylate 10%	ECA	1 (2)	64
2,2-bis[4-(Methacryloxy)phenyl] propane 2%	bis-MA	0 (0)	44
2-Ethylhexyl acrylate 0.1%	2-EHA	0 (0)	60
Isobornyl acrylate 0.1%	IBA	0 (0)	49

The result of patch tests in a local hospital was used when the respective allergen was not tested at the FIOH because of known contact allergy.

records for occupation, symptoms, material safety data sheets, results of the chemical analyses of patients' own products, patch test reactions to their own acrylate products, and their diagnosis. When acrylic monomer was not tested in the (meth)acrylate series at the FIOH, because of a previously diagnosed allergy, we included the patch test results from local hospitals in the analyses. For chemical analyses, the product samples were dissolved in acetone, and monomethacrylates and dimethacrylates were analysed by gas chromatography with a mass selective detector at the FIOH (Turku), as previously described (17). Unknown compounds were identified as acrylates if the main ions in their mass spectra had masses of 55, 99 and/or 113, all of which typical of diacrylates and triacrylates.

Patients screened by TREGDA

Between September 1994 and March 2009, a total of 2988 patients were screened with TREGDA in our baseline series; 26 (0.87%) of them had an allergic reaction and 4 a doubtful reaction (0.13%) (Table 2). Twelve of them were not tested with the (meth)acrylate series and were not included in the study group, but they are presented in Table 2.

Patients in the study group

During the same time period, 541 patients were tested with the (meth)acrylate series, and 75 of them had at least one allergic reaction in the series. Ten of these 75 patients had reactions to diglycidylether of bisphenol A epoxy resin in the baseline series and to epoxy (meth)acrylates, but not to aliphatic acrylates. They had not been occupationally exposed to epoxy (meth)acrylates or aliphatic acrylates, so their reactions to epoxy (meth)acrylates represented cross-allergy to epoxy compounds (16). They were excluded from the present study group. These epoxy (meth)acrylates were 2,2-bis[4-(2-hydroxy-3-methacryl-oxypropoxy)phenyl] propane (bis-GMA), epoxy diacrylate (epoxy acrylate) (bis-GA), 2,2-bis[4-(methacryl-oxyethoxy)phenyl] propane (bis-EMA), and glycidyl methacrylate. In addition to the remaining 65 patients, one patient had an allergic reaction to methyl acrylate, an allergen not included in the (meth)acrylate series. Thus, the present study group consists of 66 patients with contact allergy to some acrylic monomer, and they represent 2.1% of all patients investigated during the study period. One patient with non-occupational allergy to ethyl cyanoacrylate (ECA) from a nail glue and another with acrylamide allergy caused by exposure in polyacrylamide gel electrophoresis work (18) were not included, because they had not been tested with the (meth)acrylate series.

Results

The numbers of allergic reactions to individual acrylic monomers in the group of 66 patients are shown in Table 1. Of the 66 patients, 57 were occupational cases, in which the source of sensitization was considered to be highly probably at work. Of the remaining 9 cases, 1 resulted from using artificial nails, 1 was a dental patient, and 7 had an unknown source of sensitization (details not presented). Forty-eight of the occupational cases were mainly exposed to methacrylates. They were: 34 dental workers (9 dentists, 15 dental nurses and 10 dental technicians), 12 glue-derived cases and 2 artificial nail-derived cases. Most of the patients exposed to methacrylates have been presented in our previous reports (4, 15, 16). Nine of the patients were exposed mainly to acrylates (1 laboratory worker, 1 door frame worker, 3 paint factory workers and 4 printers). Their details are given in Table 3, and the first two are also described in detail as case reports below. The numbers of allergic reactions to individual allergens are presented in Table 4 separately for the methacrylate-exposed and acrylate-exposed groups (only the 13 most commonly positive allergens).

Case Reports

Patient no. 1. A 56-year-old laboratory worker (patient no. 1 in Table 3) had been employed in the same chemical company for 35 years. For the last 9 years, she had been involved in polymeric chemistry. In 2007, she developed finger dermatitis while handling methyl acrylate (CAS 96-33-3). The dermatitis healed when she did not handle the chemical, but a more extensive hand and wrist dermatitis appeared in spring 2008, when she again handled the same chemical. She then stopped working with methyl acrylate; the dermatitis healed and did not recur. On patch testing at the FIOH in autumn 2008, she reacted to methyl acrylate diluted in pet.: 2% ++, 0.64% ++, 0.2% ++, 0.064% +, 0.02% ?+ and 0.0064% negative. The baseline series and the (meth)acrylate series gave totally negative results. Of 9 control patients, 1 acrylate-allergic patient reacted to 0.1% methyl acrylate (++), but the other 8 were negative.

Patient no. 2. A 42-year-old female worker with a history of metal intolerance had been employed since 2001 in a plant manufacturing door frames. Her task was to remove pine resin from wooden frames and fill the holes with two-component fillers. In 2003, she developed dermatitis, first on her fingers and later on the forearms and face. In 2005, on patch testing she had allergic reactions to a large number of test substances, including bisphenol A and F-type epoxy resins (both ++), several

Table 2. Results of the screening with triethylene glycol diacrylate (TREGDA) in the baseline series: allergic and doubtful reactions to TREGDA and to other acrylic monomers, patients' occupation, exposure data and (meth)acrylate-related diagnosis

Patient no.	Reaction to TREGDA	Allergic reactions to other acrylic monomers	Occupation	Exposure to acrylic compounds/relevance	(Meth)acrylate-related diagnosis
I (Meth)acrylate series was tested on the same day as the baseline series (reaction to TREGDA in the baseline series did not influence the decision to test all acrylic monomers)					
1	+++	Several methacrylates and acrylates positive	Machinist-assembler	Anaerobic sealants	OACD from methacrylates
2	+++	Several methacrylates and acrylates positive	Plumber	Anaerobic sealants	OACD from methacrylates
3	+++	Several acrylates positive (Table 3, patient no. 2)	Door frame worker	Two-component filler	OACD from acrylates
4	+++	Several acrylates and methacrylates positive	Operator of stone-crushing mill	Not found; chemical analysis negative	CA to (meth)acrylates
5	++	DEGDA ++	Dental nurse	Dental composite resins	OACD from acrylates
6	++	Methacrylates and acrylates positive (Table 3, patient no. 5)	Paint laboratory worker	Raw materials for UV lacquers	OACD from (meth)acrylates
7	++	Several acrylates positive (Table 3, patient no. 4)	Paint factory worker	Raw materials for UV lacquers	OACD from acrylates
8	++	Several acrylates and methacrylates positive	Packer	Not found; self-adhesive label analysed negative	CA to (meth)acrylates
9	+	2-HEMA +, EGDMA +, TREGDMA ++, bis-GMA +	Assembler	Anaerobic sealants	OACD from methacrylates
10	+	Several methacrylates and acrylates positive	Sewing machine mechanic	Anaerobic sealants	OACD from methacrylates
11	+	Several methacrylates and acrylates positive	Assembler	Anaerobic sealants	OACD from methacrylates
12	+	Several acrylates positive, EBADMA +	Dental nurse	Dental composite resins	OACD from acrylates
II (Meth)acrylate series was tested later because of the reaction to TREGDA in the baseline series					
13	++	Several acrylates positive	Gardener	Present exposure not found. Past: acrylate hardeners	CA to acrylates
14	++	Several acrylates positive	Electronic assembler	Not found	CA to acrylates
15	I +, II ++	Several acrylates (Table 3, patient no. 4)	Printer	UV overprint varnish	OACD from acrylates
16	+	Acrylates positive (Table 3, patient no. 9)	Construction worker; ex-printer	Past: UV printing lacquer	OCA to acrylates
17	+	Several acrylates positive, EGDMA ++	Carpenter	Analyses of acrylate board: 0.03% EA (patient had sawed it), no other present exposure	OCA to (meth)acrylates; the source was not clear
18	I ?+, II –	DEGDA +, BUDA ?+ (Table 3, patient no. 3)	Paint factory worker	UV lacquer	OACD from acrylates
III (Meth)acrylate series was not tested in spite of the TREGDA reaction					
19	++	NT (previously known allergy to acrylic monomers)	Hairdresser	Artificial nails	OACD from (meth)acrylates
20	+++	NT	Needle worker	Not found; fabrics analysed negative	CA to TREGDA
21	++	NT (MMA –, BUDMA – in plastics and glue series)	Cook	Dental composite resins? Previous mouth problems	CA to TREGDA
22	++	NT	Vegetable grower	Not found	CA to TREGDA
23	++	NT	Kitchen worker	Not found	CA to TREGDA
24	++	NT	Assembler	Not found	CA to TREGDA
25	+	NT	Cleaner	Not found	CA to TREGDA
26	+	NT	Cleaner	Not found	CA to TREGDA
27	+	NT	Plywood worker	Not found	CA to TREGDA
28	?+	NT	Assembler	Not found	Possible CA to TREGDA
29	?+	NT	Painter	Not found	Possible CA to TREGDA
30	?+	NT	Forest worker	Loctite® glues at home	Possible CA to TREGDA

CA, contact allergy; OACD, occupational allergic contact dermatitis; OCA, occupational contact allergy; –, negative result; NT, not tested; I, first test session; II, second test session; for test substance abbreviations, see Table 1).

Table 3. Occupational cases who were mainly exposed to acrylates or *N,N*-methylenebisacrylamide (MBAA); their occupations, patch test reactions to acrylic monomers, and exposure to acrylic monomers

Test substance	Patient no.								
	1	2	3	4	5	6	7	8	9
	Laboratory worker	Door frame worker	Paint factory worker (19)	Paint factory worker	Paint laboratory worker	Printer [patient 3 in (16); patient 2 in (20)]	Printer	Advertisement (silk print) worker [patient 2 in (16)]	Construction worker, ex-printer [patient 10 in (16)]
MMA	—	—	—	—	—	—	—	—	—
EMA	—	—	—	—	—	—	—	—	—
BMA	—	—	—	—	—	—	—	—	—
2-HEMA	—	—	—	—	—	—	—	—	—
2-HPMA	—	—	—	—	+	—	—	—	—
EGDMA	—	—	—	—	+	—	—	—	—
TREGDMA	—	?+	—	—	+	—	—	—	—
BUDMA	—	—	—	—	—	?+	—	—	—
UDMA	—	—	—	—	—	—	—	—	—
THFMA	—	—	—	—	?+	—	—	—	—
DMAEMA	—	—	NT	NT	—	NT	NT	—	NT
EA	—	—	—	?+	—	?+	—	—	—
BA	NT	—	—	—	+	—	—	—	—
2-EHA	NT	—	—	—	— ^c	—	—	—	—
EEA	—	+	NT	—	++	NT	—	—	—
PEA	—	+	NT	—	?+	++	—	—	—
IBA	NT	—	NT	—	—	—	—	—	—
BUDA	—	?+	?+	+++	+++	—	—	—	+
HDDA	—	—	—	+++	+++ ^c	—	—	—	—
DEGDA	—	+++ ^a	+	+++	+++ ^c	++	—	+	+
DPGDA	—	+	NT ^{a,b}	+++ ^b	+++ ^{a,b}	NT	—	—	NT
TPGDA	—	+ ^a	—	?+ ^b	+++ ^{a,b}	+++ ^b	—	—	—
TREGDA	—	+++ ^a	I ?+, II—	++	++	I +, II ++	—	—	+
TMPTA	—	?+	—	—	+++ ^{a,c}	—	—	—	—
PETA	—	—	—	?+	++	—	—	—	?+

Table 3. Continued

Patient no.									
	1	2	3	4	5	6	7	8	9
Test substance	Laboratory worker	Door frame worker	Paint factory worker (19)	Paint factory worker	Paint laboratory worker	Printer [patient 3 in (16); patient 2 in (20)]	Printer	Advertisement (silk print) worker [patient 2 in (16)]	Construction worker, ex-printer [patient 10 in (16)]
OTA480	—	—	—	—	++ ^c	—	—	— ^a	—
AI-UDA	—	—	—	—	—	—	—	—	—
ar-UDA	—	—	—	—	?+ ^c	—	—	—	—
MBAA	—	—	—	—	—	—	+ ^a	—	—
ECA	—	—	—	—	—	—	—	—	—
bis-EMA	—	—	—	—	—	—	—	—	—
bis-MA	—	NT	—	—	NT	—	—	NT	—
bis-GMA	NT	—	—	—	—	—	—	—	—
EBADMA	—	?+	NT	—	—	NT	NT	—	NT
GMA	—	—	NT	—	—	NT	—	—	++
bis-GA	—	—	—	— ^b	—	++ ^b	—	+ ^d	—
Own product (composition of the product or other data on exposure)	Methyl acrylate 0.64% pet. + +, 0.064% +	Two-component filler, component A, 1% pet. + + + (results of chemical analyses in Table 4)	UV lacquer 0.2% + +, 0.1% +, 0.05% ?+ (MSDS: DPGDA 50%; analysis: DPGDA 43%)	UV lacquer: raw material A 2% pet. + +, 0.67% — (TPGDA and bis-GA ^b); raw material B 0.2% pet. + +, 0.1% — (DPGDA 45% ^b)	UV lacquer: raw material A 0.5% pet. + + (25% TPGDA ^a); raw material B 0.2% pet. + (34% DPGDA ^a); raw material C 0.5% pet. + (84% oligotriacrylates ^a)	UV overprint varnish 2% pet. + + +, 0.2% + + (bis-GA 30–60%, TPGDA 20–50% ^b)	Printing board as is + + +, 5% pet. + +, 2% ?+ (MSDS: 40–50% acrylamide derivatives; analysis: MBAA 0.1%)	UV overprint primer 10% pet. + +, 1% + (13.5% bis-GA ^d ; 0.24% ethylene glycol-based acrylates ^a)	NT (the patient had used a UV lacquer containing 25% polyglycol diacrylate in his past printing work ^b)
Epoxy resin	—	++ ^a	—	—	— ^b	—	—	—	+

MSDS, material safety data sheet; NT, not tested; I, first test session; II, second test session; for test substance abbreviations, see Table 1.

^aChemical analysis; ^bMSDS; ^cinformation from employer; ^dinformation from manufacturer.

Table 4. The numbers of allergic reactions in various subgroups of the 13 most important acrylic monomers

Acrylic monomer	Patients mainly exposed to methacrylates (dental workers, a dental patient, cases related to glue and artificial nails) <i>N</i> = 50	Patients mainly exposed to acrylates (see Table 3) <i>N</i> = 9	Patients with uncertain exposure to acrylic monomers <i>N</i> = 7	All <i>N</i> = 66
EGDMA	39	1	3	43
2-HPMA	40	1	1	42
2-HEMA	40	0	2	42
DEGDA	11	7	5	23
TREGDA	9	5	5	19
EMA	18	0	0	18
MMA	18	0	0	18
EA	13	1	4	18
TREGDMA	14	1	0	15
THFMA	14	0	0	14
BUDA	4	3	4	11
PETA	3	1	7	11
TPGDA	3	3	4	10

For abbreviations, see Table 1.

acrylates (patient no. 2 in Table 3), component A of a urethane-acrylic-based filler for timber (in pet., 10% +++, 3.2% +++, 1% ++), but not to isocyanates or component B of the filler. Component A was analysed for aliphatic acrylates and epoxy monomers, and both acrylates and epoxy resins were found (the results of the chemical analyses are given in Table 5). Acrylate contact allergy was not necessarily the prime reason for her condition; the urethane-acrylic-based two-component filler had probably sensitized her not only to acrylates, but also to epoxy resins.

Screening contact allergy to acrylates with TREGDA in the baseline series

The patch test reactions to TREGDA and to other acrylic monomers, occupations, exposure data and

Table 5. The results of chemical analysis of component A of a urethane-acrylic-based filler for timber used by patient no. 2

Compound	Analysed concentration in the product (%)
DEGDA	0.02
TREGDA	0.02
TPGDA	0.38
TMPTA	0.30
Ethylene propylene-based acrylates ^a	0.21
Ethylene glycol-based acrylates ^b	3.6
Propylene glycol-based acrylates ^b	0.12
Other acrylate-based compounds ^b	14.4
Glycidyl ether of bisphenol F epoxy resin	4.4
Glycidyl ether of bisphenol A epoxy resin	0.04

For test substance abbreviations, see Table 1.

Only aliphatic acrylates and epoxy monomers were analysed.

^aChromatographic elution between DEGDA (MW 214) and TMPTA (MW 296).

^bChromatographic elution after TMPTA but before the glycidylethers (MW 340).

(meth)acrylate-related diagnoses of the 30 patients reviewed are given in Table 2. In 6 patients, the allergic reactions to TREGDA led to further testing with the (meth)acrylate series. In 4 of them, the acrylate allergy was diagnosed as being of occupational origin, and in 2 of them acrylate allergy was the main cause of the present dermatitis (patients no. 15 and no. 18 in Table 2). In 12 patients, further testing with the (meth)acrylate series was not performed because the allergy was diagnosed previously (1 patient), or no present occupational exposure to acrylics was found (11 patients). In the latter group, none of the 11 patients had been tested with TREGDA prior to the investigations at the FIOH, and only 2 of them had been tested with some other (meth)acrylates. During the study period, 5 TREGDA-negative patients were found to react to other acrylates: 1 silk printer and 1 dental nurse were positive for diethyleneglycol diacrylate (DEGDA), 2 patients with unidentified exposure reacted to pentaerythritol triacrylate (PETA) and patient no. 1 was allergic only to methyl acrylate. We are not aware of any active sensitization to TREGDA having occurred in the baseline series.

Hypothetical screening with different acrylic monomers in the group of 66 (meth)acrylate-allergic patients

In the group of 66 patients tested with the (meth)acrylate series and found to be allergic to some acrylic monomers, the most common positive allergen was EGDMA (43 patients; Table 6). In the second step, among the remaining 23 EGDMA-negative patients, the most commonly positive allergen was DEGDA (10 patients; Table 6). In the third step of this hypothetical screening, 2-HPMA was the most commonly positive allergen, giving

Table 6. Hypothetical screening of contact allergy to acrylic monomers in the study group of 66 (meth)acrylate-allergic patients

	Dentists, dental nurses and a dental patient	Dental technicians	Glue- related	Artificial nail-related	Occupational cases mainly exposed to acrylates	Uncertain exposure	All	Sum of the patients screened after each step
<i>N</i>	25	10	12	3	9	7	66	—
I EGDMA		6	11	2	1	3	43 (65.2%)	43 (65.2%)
Patients screened	20							
Remaining patients	5	4	1	1	8	4	23	—
II DEGDA		0	0	0	6	2	10 (15.2%)	53 (80.3%)
Patients screened	2							
Remaining patients	3	4	1	1	2	2	13	—
III 2-HPMA		2	1	1	0	0	5 (7.6%)	58 (87.9%)
Patients screened	1							
Remaining patients	2	2	0	0	2	2	8	—
IV PETA		0	—	—	0	2	3 (4.5%)	61 (92.4%)
Patients screened	1							
Remaining patients	1	2	—	—	2	0	5 (7.5%)	—
Allergens needed for further screening	bis-GMA/bis- EMA/bis-GA	2-HEMA EA/EMA	—	—	MBAA Methyl acrylate	—	—	—

For test substance abbreviations, see Table 1.

Table 7. Number of (cross)-reactions to 2-hydroxyethyl methacrylate and 2-hydroxypropyl methacrylate in the 66 (meth)acrylate-allergic patients of the study group

		2-Hydroxyethyl methacrylate		
		+ / + / + / + / +	? +	Negative
2-Hydroxypropyl methacrylate	+ / + / + / + / +	38	3	2
	? +	1	2	0
	Negative	2	0	18

allergic reactions in 5 patients, and in the fourth step PETA was the best screen, giving 3 allergic reactions. For each step, the commonest allergen was chosen. Five (7.5%) patients would not have been screened with these four allergens, and each of them was positive to different acrylic monomers (Table 6).

The difference between 2-HEMA and 2-HPMA was only marginal. In Table 7, we present the (cross)-reactions to 2-HEMA and 2-HPMA in the group of 66 (meth)acrylate-allergic patients.

Discussion

In reports on the frequencies of allergic reactions to different acrylic monomers, the results may depend greatly on the characteristics of the study groups, that is, the occupations of the patients and the composition of the products to which they have been exposed. In the present material, dental products were the most common sources of sensitization (53%), in line with several other studies (2, 5, 7). Glues were the second most common sources of sensitization (18%), and their proportion has also been quite high in some other previous large patient groups (3, 5). The number of artificial nail-derived cases was small (4.5%) in comparison to other recent studies (1, 3). Printing work and UV-cured paints and lacquers are well-known sources of sensitization, but their share has been variable in previous reports. Acrylate allergy in laboratory work has been reported previously (2), but we have not found any reports of sensitization from products similar to the two-component urethane-acrylate-based filler used in the manufacture of window frames (patient no. 2).

The most commonly found positive acrylic monomers in this group of 66 patients were EGDMA, 2-HEMA and 2-HPMA, which elicited allergic reactions in almost equal proportions (64–65%) of the patients. Animal studies have shown strong cross-reactivity between these three methacrylates (21). The top three allergens were exactly the same in a study from the USA (3), as well as in a UK study, when absolute numbers of allergic patients were counted (5). These three allergens were also among the most important

ones in Sweden (1). In Belgium, 2-HEMA and EGDMA were the top two allergens, but 2-HPMA was not tested (2). These three allergens were important in patients exposed to dental products, glues and artificial nails, products that usually contain methacrylates and often also epoxyacrylates, but seldom acrylates (4, 15). These methacrylate-exposed patients constituted the great majority of our cases, and in addition to reacting to 2-HEMA, EGDMA and 2-HPMA, they reacted to methacrylates – ethyl methacrylate (EMA), MMA, triethyleneglycol dimethacrylate and tetrahydrofurfuryl methacrylate (THFMA) – more often than to acrylates (Table 4).

In Table 3, we have collected cases exposed to acrylates and *N,N*-methylenebisacrylamide (MBAA). In this group, there were several patients whose contact allergy to acrylics was limited to the chemical to which they were exposed: those exposed to methyl acrylate (patient no. 1), to MBAA (patient no. 7) and to DEGDA and bis-GA (patient no. 8). Only one of the acrylate-allergic patients (patient no. 5) had allergic reactions to methacrylates, but this particular patient had been exposed to methacrylates as well. In the study group, there were also 4 patients with unidentified exposure who reacted to acrylates but not to any methacrylates. According to our clinical investigations, the patients in dental professions and the glue-derived cases were almost exclusively exposed to methacrylates or epoxy acrylates, but not to acrylates [chemical analysis showed a low concentration of ethyl acrylate (EA) in a dental composite resin used by one dentist] (4, 15, 16). Thus, our results imply that exposure to methacrylates might induce cross-reactivity to acrylates, whereas exposure to acrylates usually does not lead to cross-sensitization to methacrylates. Similar cross-reactivity rules concerning monoacrylates and monomethacrylates have been presented (22). Our acrylate-allergic patients were mainly exposed and sensitized to diacrylates [tripropylene glycol diacrylate (TPGDA), dipropylene glycol diacrylate (DPGDA), DEGDA, and TREGDA], and not to monoacrylates to the same extent (Table 3). When clinical patients are analysed, it is difficult to draw firm conclusions regarding cross-allergy, because concomitant exposure to several acrylic monomers is always an alternative explanation. Also, the purity of the test materials is a problem; for example, Chemotechnique's aromatic urethane diacrylate (ar-UDA) test substance contains PETA. Consequently, all 7 ar-UDA-positive patients reacted to PETA, and 4 other PETA-positive patients had doubtful reactions to ar-UDA. This strong association could have resulted from the presence of PETA in the test substance of ar-UDA. PETA gave

positive reactions in all 7 patients whose exposure to acrylates remained uncertain (Table 4).

Koppula et al. presented a complex hypothesis on cross-reactions between acrylic monomers sharing a common 'carboxy ethyl side group' (23). In our subjects, THFMA and ECA did not fit this hypothesis. Reactions to ECA were almost absent, although this allergen should have shown cross-reactivity with the commonly positive compounds EGDMA, 2-HEMA and 2-HPMA (ECA, EGDMA, 2-HEMA and 2-HPMA all share the 'carboxy ethyl side group'). THFMA was among the most commonly positive methacrylates in patients exposed and sensitized to EGDMA, 2-HEMA and 2-HPMA. However, we were not able to show any specific exposure to THFMA, leaving cross-allergy as the most probable explanation for the concomitant reactions. THFMA does not have the 'carboxy ethyl side group', and thus, according to Koppula's hypothesis, should not cross-react with EGDMA, 2-HEMA and 2-HPMA.

TREGDA screening

By screening all of our patients with TREGDA in the baseline series, we tried to find contact allergy to acrylates, whose occurrence in the workplace is not always as obvious as that of methacrylates in dental products, glues or artificial nails. Of our patients, 0.9% had allergic reactions to TREGDA. All of our patients had suspicion of occupational skin disease, so it is not surprising that the frequency was higher than among general dermatological patients in Sweden and Singapore [0.7% and 0.5%, respectively (14)]. During the study period, the screening showed cases with occupational contact allergy to acrylates; 3 of 8 cases would probably have been missed without the screening. Without the screening, we would have missed UV-cured lacquers in printing work and in the manufacture of paints. TREGDA, however, does not screen all patients with acrylate contact allergy. DEGDA reactions were more common among our subjects; it might thus be a better screen for acrylate allergy than TREGDA. All 6 TREGDA-allergic cases who were later tested with the (meth)acrylate series reacted to DEGDA.

It must be emphasized that we do not recommend TREGDA (or DEGDA) screening for general dermatology patients, because our results derive from a special clinic of occupational dermatology with highly selected patients. The screening yielded many allergic reactions to TREGDA without clear clinical relevance (group III in Table 2). Active sensitization resulting from previous testing was not a probable cause, because none of the patients had been tested with TREGDA prior to the investigations at the FIOH.

Hypothetical screening of acrylic monomers in the group of 66 patients allergic to acrylic monomers

Goon et al. (1) recommended a short screening series that would have screened all patients with contact allergy to acrylates or methacrylates: TREGDA, 2-HPMA, 1,4-butanediol diacrylate (BUDA)/1,6-hexanediol diacrylate (HDDA), 2-HEMA, EGDMA, bis-GMA and ECA. A corresponding screening series based on the present study group would consist of: EGDMA, DEGDA, 2-HPMA, PETA, 2-HEMA, EA/EMA, bis-GMA/bis-EMA/bis-GA, methyl acrylate and MBAA. The series of Goon et al. (1) would have screened 58 (87.9%) of our 66 patients. The common allergens in the two lists are 2-HEMA, 2-HPMA, EGDMA and bis-GMA. Among the patients from Sweden and Singapore, there was 1 who reacted to BUDA and HDDA, but not to other acrylates. We did not have such a patient, but correspondingly, among our patients, 2 patients reacted to PETA but not to DEGDA or TREGDA. On comparison of the two screening lists and the patients studied for them, the allergens BUDA/HDDA and PETA were found to appear haphazardly in the lists. ECA and MBAA are even more rarely positive allergens than PETA or BUDA/HDDA. They need to be tested separately, because the patients usually do not have reactions to the other allergens in the (meth)acrylate series. The same is true for specific sensitization to epoxy acrylates, although cross-reactions to epoxy acrylates do occur in about 20% of patients allergic to epoxy resin (16, 24). The two groups of patients differed more as regards TREGDA and DEGDA: in our group, DEGDA was more commonly positive than TREGDA, whereas in the Swedish–Singaporean group, the order was reversed. DEGDA was especially important in patients working with UV-curing printing inks or in the manufacture of UV-curing lacquers, but we also found patients reacting to DEGDA and TREGDA among dental personnel, who were not tested with the two diacrylates in the study of Goon et al. (7). In our group, specific exposure to DEGDA was shown in 3 patients, whereas exposure to TREGDA was found in only 1 patient (Table 3). In line with the Swedish–Singaporean study, a study from the UK also reported reactions to TREGDA to be more common than those to DEGDA (5). In Sweden, a late reading on day 7 has been found to be important when patch testing (meth)acrylates (1, 7, 25). In our patients, day 7 readings were performed only occasionally.

The present study is based on selected patients, and our list of allergens should not be taken as a recommendation to screen general dermatological patients or to form a new (meth)acrylate series for aimed testing.

Conclusions

In a group of 66 patients allergic to some acrylic monomer, the most commonly positive allergens were the methacrylates EGDMA, 2-HEMA and 2-HPMA, and the acrylates DEGDA and TREGDA. The three methacrylates were positive in most patients exposed to dental products, glues or artificial nails, and DEGDA was an important allergen in patients exposed to acrylates in printing work and in the manufacture of UV-cured paints. The patterns of concomitant reactions imply that methacrylates might induce cross-reactivity to acrylates, whereas acrylates do not usually induce sensitization to methacrylates. TREGDA was positive in 0.9% of the 2988 patients tested with the baseline series. This screening was found to be very useful, as 3 of 8 patients with diagnosed occupational acrylate allergy would probably have been missed without it. Testing with four allergens, namely EGDMA, DEGDA, 2-HPMA and PETA, would have screened 92.5% of the patients, but screening the remaining 5 patients would have required at least five additional allergens: 2-HEMA, EA/EMA, bis-GMA/bis-EMA/bis-GA, methyl acrylate and MBAA. We do not, however, recommend any screening of (meth)acrylates among general dermatology patients, or claim that the above-mentioned allergens would be the best test substances for aimed testing. Recommendations should be based on larger patient groups.

References

- Teik-Jin Goon A, Bruze M, Zimerson E, Goh C L, Isaksson M. 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: 21–27.
- Geukens S, Goossens A. Occupational contact allergy to (meth)acrylates. *Contact Dermatitis* 2001; 44: 153–159.
- Sood A, Taylor J S. Acrylic reactions: a review of 56 cases. *Contact Dermatitis* 2003; 48: 346–347.
- Aalto-Korte K, Alanko K, Kuuliala O, Jolanki R. Occupational methacrylate and acrylate allergy from glues. *Contact Dermatitis* 2008; 58: 340–346.
- Tucker S C, Beck M H. A 15-year study of patch testing to (meth)acrylates. *Contact Dermatitis* 1999; 40: 278–279.
- Guerra L, Vincenzi C, Peluso A M, Tosti A. Prevalence and sources of occupational contact sensitization to acrylates in Italy. *Contact Dermatitis* 1993; 28: 101–103.
- Goon A T, Isaksson M, Zimerson E, Goh C L, Bruze M. 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.
- Constandt L, Hecke E V, Naeyaert J M, Goossens A. Screening for contact allergy to artificial nails. *Contact Dermatitis* 2005; 52: 73–77.
- Emmett E A. Contact dermatitis from polyfunctional acrylic monomers. *Contact Dermatitis* 1977; 3: 245–248.
- Conde-Salazar L, Vargas I, Tevar E, Barchino L, Heras F. Sensitization to acrylates in varnishes. *Contact Dermatitis* 2007; 18: 45–48.
- Fregert S. Allergic contact dermatitis from ethylacrylate in a window sealant. *Contact Dermatitis* 1978; 4: 56.
- Whittington C V. Dermatitis from UV acrylate in adhesive. *Contact Dermatitis* 1981; 7: 203–204.
- Kiec-Swierczynska M, Krecisz B, Swierczynska-Machura D, Zaremba J. An epidemic of occupational contact dermatitis from an acrylic glue. *Contact Dermatitis* 2005; 52: 121–125.
- Goon A T, Bruze M, Zimerson E, Goh C L, Soo-Quee Koh D, Isaksson M. Screening for acrylate/methacrylate allergy in the baseline series: our experience in Sweden and Singapore. *Contact Dermatitis* 2008; 59: 307–313.
- Aalto-Korte K, Alanko K, Kuuliala O, Jolanki R. Methacrylate and acrylate allergy in dental personnel. *Contact Dermatitis* 2007; 57: 324–330.
- Aalto-Korte K, Jungewelter S, Henriks-Eckerman M L, Kuuliala O, Jolanki R. Contact allergy to epoxy (meth)acrylates. *Contact Dermatitis* 2009; 61: 9–21.
- Henriks-Eckerman M L, Suuronen K, Jolanki R, Alanko K. Methacrylates in dental restorative materials. *Contact Dermatitis* 2004; 50: 233–237.
- Aalto-Korte K, Jolanki R, Suuronen K, Estlander T. Biochemist's occupational allergic contact dermatitis from iodoacetamide and acrylamide. *Contact Dermatitis* 2002; 47: 361–362.
- Estlander T, Jolanki R, Kanerva L. Occupational allergic contact dermatitis from UV-cured lacquer containing dipropylene glycol diacrylate. *Contact Dermatitis* 1998; 39: 36.
- Kanerva L, Estlander T, Jolanki R, Alanko K. Occupational allergic contact dermatitis from 2,2-bis[4-(2-hydroxy-3-acryloxypropoxy)phenyl]-propane (epoxy diacrylate) in ultraviolet-cured inks. *Contact Dermatitis* 2000; 43: 56–59.
- Rustemeyer T, de Groot J, von Blomberg B M, Frosch P J, Scheper R J. Cross-reactivity patterns of contact-sensitizing methacrylates. *Toxicol Appl Pharmacol* 1998; 148: 83–90.
- Guin J D, Work W J. Other plastics. In: *Practical Contact Dermatitis, A Handbook for the Practitioner*, Guin J D (ed.): New York, McGraw-Hill, 1995: 433–475.
- 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.
- Lee H N, Pokorny C D, Law S, Pratt M, Sasseville D, Storrs F J. Cross-reactivity among epoxy acrylates and bisphenol F epoxy resins in patients with bisphenol A epoxy resin sensitivity. *Am J Contact Dermat* 2002; 13: 108–115.
- Isaksson M, Lindberg M, Sundberg K, Hallander A, Bruze M. The development and course of patch-test reactions to 2-hydroxyethyl methacrylate and ethyleneglycol dimethacrylate. *Contact Dermatitis* 2005; 53: 292–297.

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