






Allergic contact dermatitis caused by nail acrylates in Europe. An EECDRG study

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Summary

Background. Allergic contact dermatitis (ACD) caused by nail acrylates, also including methacrylates and cyanoacrylates here, is being increasingly reported.

Methods. A retrospective study in 11 European Environmental Contact Dermatitis Research Group (EECDRG) clinics collected information on cases of ACD caused by nail acrylates diagnosed by aimed testing between 2013 and 2015.

Results. Among 18 228 studied patients, 136 had ACD caused by nail acrylates (0.75%; 95%CI: 0.60–0.90), representing 67.3% (95%CI: 60.4–73.7) of ACD cases caused by acrylates. There were 135 females and 1 male, with a mean age \pm standard deviation of 36.7 ± 12.2 years; 59 (43.4%) were exposed as consumers, and 77 (56.6%) were occupationally exposed. Occupational cases were more frequent in southern Europe (83.7%), and were younger (mean age of 33.4 ± 8.9 years); most developed ACD during the first year at work (65.0%), and at least 11.7% had to leave their jobs. Skin lesions involved the hands in 121 patients (88.9%) and the face in 50 (36.8%), with the face being the only affected site in 14 (10.3%). Most patients reacted to two or more acrylates on patch testing, mainly to 2-hydroxyethyl methacrylate (HEMA) (92.5%), 2-hydroxypropyl methacrylate (88.6%), ethylene glycol dimethacrylate (69.2%), and ethyl cyanoacrylate (9.9%).

Conclusions. Nail cosmetics were responsible for the majority of ACD cases caused by acrylates, affecting nail beauticians and consumers, and therefore calling for stricter regulation and preventive measures. As HEMA detects most cases, and isolated facial lesions may be overlooked, inclusion of this allergen in the baseline series may be warranted.

Key words: acrylates; allergic contact dermatitis; cosmetics; hydroxyethyl methacrylate; nail aesthetics; occupational.

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Acrylates, methacrylates, and cyanoacrylates, referred to as acrylates in this article, are small chemicals that polymerize either spontaneously or in the presence of catalysts, such as ultraviolet (UV) light, giving rise to very resistant polymers. They are used in multiple industrial settings (plastics, fibreglass, glues, adhesives, coatings, lacquers, paints, and printing inks), in medicine (dental restoration, oral prostheses, contact and intraocular lenses, bone cement, surgical glues, and wound dressings), and in aesthetics (nail aesthetics and eyelash or hair extensions) (1, 2). Acrylate monomers are potent sensitizing chemicals, and cause allergic contact dermatitis (ACD) mostly in occupational settings (2). Dental workers were mainly affected, but, within the last decade, nail aesthetics has become the main occupation in which workers suffer from acrylate allergy (3–5). ACD caused by nail acrylates is also frequently affecting consumers, with the increase in popularity of this fashion (4–11).

The technique for sculpturing 'acrylic nails' or 'porcelain nails' based on a powder polymer and a liquid monomer that polymerizes in the presence of a catalyst is now rarely used, as it is time-consuming and causes a disagreeable smell during the procedure (12). Today, the main techniques are based either on acrylates that need UV curing (sculptured gel nails and long-lasting acrylate-based nail varnish) or on cyanoacrylate (glued nail tips or dipping nails). Mixed techniques can sometimes be used, namely gluing nail tips and applying long-lasting UV-cured nail varnish (5) (12). Any of these techniques can cause ACD both in the beauticians, who also often complain of respiratory problems (2, 6, 7), and in the consumer, who may also suffer paraesthesia, pain, onycholysis, and long-lasting and severe nail dystrophy (2, 8, 9), sometimes mimicking psoriasis (10).

Many reports have been recently published from European and non-European countries, particularly from the United Kingdom (4, 13), Portugal (3, 11, 14, 15), Spain (5, 16), and Germany (17), suggesting an almost epidemic dimension of ACD caused by nail aesthetics. Also, a safety concern has been raised by the authorities in Denmark and Sweden restricting the use of home kits for nail aesthetics (9). The present analysis was performed with the objectives of evaluating the panorama of ACD caused by nail aesthetics across Europe, and characterizing the clinical manifestations, the main allergens detected by patch testing, the occupational or non-occupational origin of the dermatitis, and the impact on occupation.

Methods

A retrospective study was performed, reviewing all cases of ACD caused by acrylates related to cosmetic nail procedures (artificial gel nails, glued nails, dipping nails,

and acrylate nail varnish) diagnosed during a period of 3 years (2013–2015) in 11 European Environmental Contact Dermatitis Research Group (EECDRG) clinics from nine European countries – Bari (Italy), Barcelona (Spain), Coimbra (Portugal), Copenhagen and Odense (Denmark), Heidelberg (Germany), Helsinki (Finland), Leeds (United Kingdom), Leuven (Belgium), and Malmö (Sweden). All patients had been patch tested with the European baseline series, and, prompted by their history, also with the acrylate series used in the respective centres (Chemotechnique Diagnostics, Vellinge, Sweden; or Trolab Allergens, SmartPractice, Europe, Reinbeck, Germany). Allergens were applied on the back for 48 h with 8-mm Finn Chambers® on Scanpor® tape (Smartpractice, Europe), IQ or IQ-ultra™ patch test chambers (Chemotechnique Diagnostics), or the Al Test® (Euromedical, Calolziocorte, Italy). Readings and relevance were assessed according to the ESCD guidelines for diagnostic patch testing (18). Only + or stronger patch test reactions were considered to be allergic reactions.

The following data were retrieved from the files of patients with positive reactions to acrylates with relevance for nail aesthetics: age and sex, history of atopy, anatomical site and characteristics of cutaneous and nail lesions, type of exposure to nail acrylates (occupational versus non-occupational), and haptens leading to positive reactions on patch testing. In occupational cases, the time spent at work before the development of cutaneous lesions and the subsequent outcome at work were documented. Data were statistically analysed with spss software (Version 21.0; IBM, Armonk, NY, USA). The *t*-test for independent samples was used to compare quantitative variables (e.g. age) between groups (e.g. occupational versus non-occupational exposure). Fisher's exact test and the χ^2 test with the Yates correction, two-sided, were used to compare nominal variables between different groups. *p*-Values of < 0.05 were considered to be significant. The confidence intervals (CIs) for proportions were set at 95%.

Results

During the 3 years of the study, a total of 18 228 patients were patch tested in the 11 clinics involved in the study: 6084 males (33.4%) and 12 144 females (66.6%), 57.7% of whom were aged > 40 years. The distribution of MOAHLEA factors is shown in Table 1. Positive reactions to acrylates observed during aimed testing occurred in 202 patients (1.11%). Among these, ACD caused by nail acrylates was diagnosed in 136 patients, representing 0.75% of all patch tested patients (95%CI: 0.60–0.90), with percentages varying from 0.07% in Bari to 4.01% in

Table 1. Total number of patch tested patients per year and their MOAHLFA distribution in 11 European clinics, along with positive reactions to/allergic contact dermatitis (ACD) caused by all acrylates and nail acrylates during aimed testing

	2013	2014	2015	2013–2015	%
Total tested	5603	6156	6469	18 228	
Male	1869	2150	2065	6084	33.4
Occupational	904	964	967	2835	15.5
Atopy	1430	1661	1801	4892	26.8
Hand eczema	1753	1988	1909	5650	30.9
Leg dermatitis	429	597	540	1566	8.6
Face dermatitis	1392	1578	1627	4597	25.2
Age > 40 years	3255	3744	3517	10 516	57.7
No. (%) of cases of ACD caused by acrylates	59 (1.05)	78 (1.27)	65 (1.00)	202 (1.11)	
No. (%) of cases of ACD caused by nail acrylates	39 (0.69)	53 (0.86)	44 (0.68)	136 (0.75)	

Table 2. Total number of patch tested patients in each centre, the number and percentage of patients reacting to nail acrylates, and the numbers and percentages of those representing occupational cases and those occupational cases who had concomitant exposure to nail acrylates as consumers

Centre	Patch tested patients (n)	Nail acrylate cases		Occupational cases		Occupational cases with consumer exposure	
		n	%	n	%	n	%
Barcelona	1258	3	0.24	3	100	2	66.7
Bari	2731	2	0.07	2	100	0	
Coimbra	948	38	4.01	31	78.8	18	58.1
Copenhagen (Gentofte)	3113	18	0.58	6	33.3	4	66.7
Copenhagen (Bispebjerg)	1600	2	0.13	0	0	0	
Heidelberg	306	2	0.65	1	50.0	1	100
Helsinki	374	1	0.27	1	100	1	100
Leeds	2383	40	1.68	18	45.0	6	33.3
Leuven	1601	12	0.87	7	58.3	4	57.1
Malmö	2263	11	0.49	6	54.5	1	16.7
Odense	1651	7	0.42	2	28.6	2	100
Total	18 228	136	0.75	77	56.6	39	50.6

Coimbra, and between 0.68% and 0.86% in the 3 years of the study (Table 2). Nail acrylates were responsible for 9.1–100% (mean 67.3%, 95%CI: 60.4–73.7) of all ACD cases caused by acrylates (Table 3), with the lowest percentages being observed in the departments devoted to occupational dermatology, namely Helsinki and Heidelberg.

ACD caused by nail acrylates occurred in 135 females and 1 male, with a mean age \pm standard deviation of 36.7 ± 12.2 years (range 16–79 years). Altogether, 50 had personal atopy (36.8%), 31 had allergic rhinitis (22.8%), 23 had present or past atopic dermatitis (16.9%), and 20 had asthma (14.7%). Atopy was more frequent among nail acrylate cases than in the whole population tested (36.8% versus 26.8%; $p=0.011$). Fifty-nine patients (43.4%) were exposed to nail acrylates only as consumers, aged 17–79 years (mean 40.9 ± 14.4 years). Exposure in an occupational setting occurred in 77 cases (56.6%), namely 76 females and

1 male, aged 16–59 years (mean 33.4 ± 8.9 years). Occupational cases were significantly younger than consumer cases ($p < 0.001$). Occupational causation was observed in 83.7% of the cases from southern Europe (Portugal, Spain, and Italy), and in 43.5% of the cases from the other European countries (36/43 versus 40/92; $p < 0.001$, Fisher's exact test). At least 39 of the 77 occupational cases (50.6%, 95%CI: 39.5–61.8) also reported exposure to nail acrylates as consumers, varying between 100% in the few cases from Odense, Helsinki and Heidelberg to none in Bari (Table 2).

Occupational cases occurred mostly in nail beauticians, 32 of them working only part-time in this job, often in association with hairdressing. One hairdresser developed symptoms only by sharing the salon with a nail beautician. The only male patient was a complementary therapist applying nail acrylates to clients. Cutaneous lesions developed during the training period in 3 patients, and within the first year of work in 26 (65.0%) of the

Table 3. Total number of allergic contact dermatitis (ACD) cases caused by acrylates among the patch tested patients in 11 departments, and the number and percentage of cases related to nail aesthetics

Centre	Patch tested patients (n)	Total number of ACD cases caused by acrylates	Number of ACD cases caused by nail acrylates	Percentage of nail cases among cases of acrylate allergy
Barcelona	1258	3	3	100
Bari	2731	4	2	50.0
Coimbra	948	45	38	84.4
Copenhagen (Gentofte)	3113	22	18	81.8
Copenhagen (Bispebjerg)	1600	4	2	50.0
Heidelberg	306	9	2	22.2
Helsinki	374	11	1	9.1
Leeds	2383	46	40	86.9
Leuven	1601	22	12	54.5
Malmö	2263	27	11	40.7
Odense	1651	9	7	77.8
Total	18 228	202	136	67.3

40 cases for which this information was available. In 6 cases there was concomitant or previous occupational exposure to dental acrylates, with symptoms also developing in relation to occupational or non-occupational nail aesthetic procedures. Consumers performed the technique in nail salons, at home, or among friends, and alternated between sculptured gel nails, glued nails, and long-lasting gel nail varnishes. No information was collected on the number of sessions before the development of skin lesions, or on the precise technique used by each of these individuals.

Skin lesions developed mostly on the fingers, hands, and/or wrists ($n = 121$; 88.9%). Pulpitis with fissures, observed in 84 patients (61.7%), was the main presentation in nail beauticians. Concomitant or isolated acute or subacute eczema was observed on the distal parts of the fingers (78 patients, 57.3%), in 1 case with bullae, on the palms ($n = 15$; 11.0%), or on the wrists/forearms ($n = 13$; 9.6%). The face was involved in 50 patients (36.8%), affecting particularly the eyelids (8 cases), lips (4 cases), or cheeks (3 cases). Twenty-six of the 50 cases with facial lesions occurred in an occupational setting. The neck was involved in association with the face in 16 patients (11.8%). Lesions were localized exclusively on the face/neck area in 14 patients (10.3%). In 1 case, lesions were localized on the trunk. Three technicians reported respiratory symptoms during work with nail acrylates. Subungual hyperkeratosis and long-lasting onycholysis or nail dystrophy were also reported, but this aspect was not specifically investigated.

The acrylate series tested varied in the different clinics, but mostly included 2-hydroxyethyl methacrylate (HEMA), 2-hydroxypropyl methacrylate (HPMA), ethylene glycol dimethacrylate (EGDMA), triethylene glycol

Table 4. Main allergens tested, with the number of patients tested, and number and percentage of positive reactions

Allergens	Patch tested patients (n)	Positive reactions	
		n	%
2-Hydroxyethyl methacrylate 2%	135	124	91.9
Hydroxypropyl methacrylate 2%	119	99	83.2
Ethylene glycol dimethacrylate 2%	117	81	69.2
Triethylene glycol dimethacrylate 2%	98	31	31.6
Methyl methacrylate 2%	114	30	26.3
Ethyl cyanoacrylate 10%	111	11*	9.9

All allergens in pet.

*Eight of the 11 cases reacting to ethyl cyanoacrylate were observed among UK consumers; isolated reactions were observed in 2 cases.

dimethacrylate (TEGDMA), methyl methacrylate (MMA), and ethyl cyanoacrylate (Table 4). Positive reactions were observed mainly to HEMA (91.9%), HPMA (83.2%), EGDMA (69.2%), TEGDMA (31.6%), MMA (26.3%), and ethyl cyanoacrylate (9.9%) (Table 4), with a similar distribution being seen among occupational and non-occupational cases. Positive reactions were also observed to 2-hydroxyethyl acrylate (17 cases), ethyl acrylate (16 cases), tetraethyleneglycol dimethacrylate (13 cases), urethane dimethacrylate (10 cases), butyl acrylate and triethyleneglycol diacrylate (9 cases each), and 1,4-butanediol diacrylate (4 cases).

Most patients reacted to two or more acrylates, often with ++ or +++ reactions (Table 5). A single reaction was observed in 17 patients – to HEMA in 5 cases, to HPMA, ethyl cyanoacrylate, butyl methacrylate and ethylacrylate in 2 cases each, and to ethyl methacrylate, butyl acrylate, triethylene glycol dimethacrylate and

tetraethyleneglycol dimethacrylate in 1 case each. None of the patients reacted exclusively to EGDMA or MMA, and 7 patients reacted to acrylates outside the main group of allergens tested in most centres.

HEMA and/or many other acrylates were present in the gels used for nail sculpting procedures and for long-lasting gel nail lacquers from many different brands, mostly depending on the country of origin. Although there was no information on the precise technique used by each patient, the use of dipping nails or nail tips glued to the nail plate with an ethyl cyanoacrylate glue was frequently reported among UK consumers in association with long-lasting nail gel varnishes, and, in this subgroup of patients, reactions to ethyl cyanoacrylate were particularly frequent (8 of 40 cases, 20.0%). Two of the other 3 patients who reacted to ethyl cyanoacrylate reported concomitant occupational exposure to glues used for eyelash extensions. Apart from acrylates, 56 patients (41.2%) reacted to allergens from the baseline series, mainly to nickel sulfate ($n = 33$; 24.3%), methylisothiazolinone and/or methylchloroisothiazolinone/methylisothiazolinone ($n = 14$; 10.3%), fragrance mix I and/or II ($n = 12$; 8.8%), *p*-phenylenediamine ($n = 8$; 5.8%), thiuram mix, or other rubber additives ($n = 4$; 2.9%).

Among 77 beauticians diagnosed with occupational ACD, information on the outcome was available in 46 cases: 9 (11.7%) had to abandon the job, 34 (44.2%) kept working with skin lesions, and only 3 (3.9%) managed to keep working without skin lesions, 1 of them using two pairs of gloves. Customers improved on removal of the artificial nails/acrylate nail varnish, but some reported long-lasting nail dystrophy or onycholysis.

Discussion

The fact that nail aesthetics were responsible for 67.3% of positive patch test reactions to acrylates confirms that the problem of ACD caused by these chemicals is shifting from industry or dental technicians to those working in nails aesthetics in most countries, as previously reported (3). ACD caused by nail-related acrylates has long been known to exist (8, 19, 20), but its frequency seems to be increasing in many countries, almost as a trend with epidemic dimensions (5), as indicated by a recent report of 230 cases collected from Portugal over a period of 5 years (15). In the present study, 0.75% of all tested patients and 1.1% of females had ACD caused by nail acrylates. The percentage of patients diagnosed did not increase during the 3 years of the study, suggesting a possible plateau of incident cases.

ACD caused by nail acrylates occurred in all European countries, although the frequency of cases varied in

the different centres, being < 0.1% in Bari, Italy, between 0.2% and 0.8% in most countries, and, according to the frequency of previously reported cases (3–7, 9), 1.7% in Leeds, United Kingdom and 4% in Coimbra, Portugal. However, the actual nail acrylate contact allergy frequencies in consecutively tested dermatitis patients at the various clinics are not known, as the figures presented here represent results from aimed testing. Moreover, these clinics may not be fully representative of their country.

ACD caused by nail acrylates is mostly a problem for young females (13), but all age groups can be affected. In this study, the age ranged from 16 to 79 years, with a mean age of 33.6 years, in contrast to most of the patch tested population being aged > 40 years (57.7%). In fact, young females all over Europe adopted this fashion, which involves repeated exposure to acrylates. In some cases, home kits that were introduced around 2010 were used (9). More than half of the cases were related to occupational exposure. For comparison, in large studies this proportion ranged from 25%, as in Israel in 2007, to 31% more recently in the United Kingdom (4), to 75.6% in Portugal in 2017 (15), and to > 90% in Spain, both in 2008 and in 2017 (5, 16). Interestingly, an occupational origin was significantly more frequent in southern Europe (Portugal, Spain, and Italy) than in the other European countries (83.7% versus 43.5%). Approximately half of the beauticians were also consumers, in terms of using nail aesthetics on themselves, which is a lower proportion than in other series (15), although underreporting of personal use of nail acrylates might have occurred.

Cumulative exposure as consumers, with the nail beauticians performing the technique on themselves, potentially with more acrylate spill-over during application, may increase sensitization risk. Moreover, many of these beauticians have other jobs, namely hairdressing, which may cause hand dermatitis and also favour further sensitization to acrylates. As previously reported, ACD mainly affects young workers, with some cases already beginning during apprenticeship or during the first year of work, emphasizing the high sensitizing potency of these acrylates (1), and certainly also the inadequate information on sensitization risk and adequate preventive measures (17). Atopic dermatitis and atopy, which were more frequent among nail acrylate cases, as in other studies (5), may be another possible individual susceptibility factor.

ACD caused by nail acrylates can have a significant impact on the ability to work, with many workers having to leave their jobs, sometimes choosing new jobs in which acrylate exposure is highly predictable (dental assistants or dental prosthesis manufacture). Most workers prefer to continue with their profession even when they have mild dermatitis. Correct procedures to prevent acrylate

Table 5. Main allergens tested, with the total number of patients tested with each allergen, and the numbers of positive, negative and concomitant reactions

Allergens	HEMA			HPMA			EGDMA			TEGDMA			MMA			
	Positive	Negative	NT	Positive	Negative	NT	Positive	Negative	NT	Positive	Negative	NT	Positive	Negative	NT	
Total tested/reactivity																
HEMA total tested	135															
HEMA-positive	124	124	0													
HEMA-negative	11	0	11													
HEMA NT	1	0	0	1												
HPMA total tested	119															
HPMA-positive	99	97	2	0												
HPMA-negative	20	11	9	0												
HPMA NT	17	16	0	1												
EGDMA total tested	117															
EGDMA-positive	81	81	0	0	68	3	10									
EGDMA-negative	36	27	9	0	23	9	4									
EGDMA NT	19	16	2	1	8	8	3									
TEGDMA total tested	98															
TEGDMA-positive	31	30	1	0	26	1	4	23	5	3						
TEGDMA-negative	67	57	10	0	56	7	4	28	27	12						
TEGDMA NT	38	37	0	1	17	12	9	30	4	4						
MMA total tested	114															
MMA-positive	30	29	1	0	22	4	4	24	3	3	13	16	1			
MMA-negative	84	80	4	0	61	15	8	41	29	14	14	41	29			
MMA NT	22	15	6	1	16	4	5	16	4	2	4	10	8			
ECA total tested	111															
ECA-positive	11	9	2	0	8	3	0	9	1	1	3	7	1	5	4	2
ECA-negative	100	97	2	1	87	7	6	66	19	15	26	55	19	20	64	16
ECA NT	25	18	7	0	4	10	11	6	16	3	2	5	18	5	16	4

ECA, ethyl cyanoacrylate; EGDMA, ethylene glycol dimethacrylate; HEMA, 2-hydroxyethyl methacrylate; HPMA, 2-hydroxypropyl methacrylate; MMA, methyl methacrylate; NT, not tested; TEGDMA, triethylene glycol dimethacrylate.

spill-over and direct contact with contaminated objects or working surfaces, and frequent glove replacement, possibly with additional cotton or 4H fingertips, allowed patients to continue working with improvement in their lesions, as has often been reported (5). Acrylates penetrate gloves easily, but regular change of gloves after each client may reduce the number of molecules reaching the skin and keep them below the threshold to induce ACD. Testing with nail acrylates by applying them for limited periods of time over fragments of gloves that act as protective membranes between the acrylate and the skin could prevent skin reaction in an acrylate allergic patient (21).

In the present study, 87.5% of the patients had two or more positive reactions to acrylates, mostly associated with HEMA and/or HPMA. These can be explained either by concomitant sensitization or by cross-sensitization, although this does not include cyanoacrylates. Reactions to ethyl cyanoacrylate in 9 of the 11 patients in this study, mostly from the United Kingdom, can probably be explained by the frequent associations of different nail aesthetic techniques (cyanoacrylate-based glued nails together with long-lasting UV-cured nail varnish). This association was also frequent in other reports from United

Kingdom (8, 16), although less frequent in other studies (3, 5, 15).

Alone, HEMA and HPMA were able to detect 91.9% and 83.2%, respectively, of ACD cases caused by nail acrylates, but were not suitable for detecting allergy to ethyl cyanoacrylate. Therefore, in agreement with previous work and to prevent multiple intense patch test reactions when testing patients with suspected acrylate allergy, we recommend patch testing first with HEMA and ethyl cyanoacrylate, and then with an extended series if these two allergens give negative results.

As is often reported, skin lesions were localized both on areas coming into direct contact with the acrylates (fingers, hands, or wrists), and on ectopic or air-exposed areas (eyelids, face, and neck). This can occur by allergen transport by contaminated tools or hands, but acrylate evaporation can also explain these skin lesions, as well as respiratory complaints reported in a few occupational cases (5). Nail acrylates as the cause of ACD exclusively of the face and neck, observed in 14 patients in this study, may be overlooked if acrylates are not included in a cosmetic series or in the baseline series. As > 1% of females are diagnosed with nail acrylate allergy with

aimed testing, and an additional 30% react to other acrylates, such a percentage of positive patch test reactions to acrylates, their frequent relevance and occasional atypical cases with ectopic localization may support the introduction of HEMA into the European baseline series (22, 23).

Conclusions

This retrospective study on a large series of ACD cases caused by nail acrylates diagnosed all over Europe shows this is a relevant and frequent problem. It affects both consumers and nail beauticians, with significant consequences for the workers: most keep working with dermatitis, but others abandon their jobs and have

to expect limitations in other occupations. Moreover, although the evidence is inconclusive (24), some consumers and workers with ACD caused by acrylates may suffer adverse reactions when they are further exposed to medical procedures involving the use of acrylates (dental restoration, dental prostheses, bone cement, hearing-aids, surgical glues, or insulin pumps) (2).

Therefore, in order to prevent sensitization, authorities that regulate cosmetic products should propose more strict regulations on the use of these highly sensitizing chemicals for aesthetic purposes. In addition, consumers and, particularly, workers during their apprenticeship should be correctly informed about the risk of sensitization to acrylates and the most adequate preventive measures.

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