

Occupational Asthma From Epoxy Compounds



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What is already known about this topic? The respiratory-sensitizing potential of epoxy compounds is largely unknown.

What does this article add to our knowledge? We describe 15 cases of occupational asthma from epoxy resin systems and 3 from triglycidyl isocyanurate.

How does this study impact current management guidelines? Epoxy compounds can cause sensitizer-induced occupational asthma.

BACKGROUND: Two-component epoxy resin systems (ERSs) composed of epoxy resin and polyamine hardeners are extensively used in industrial and construction coating. Triglycidyl isocyanurate (TGIC) is another type of epoxy derivative, mostly encountered in polyester powder paints. Epoxy compounds are well-known skin sensitizers, but their respiratory-sensitizing potential is largely unknown. **OBJECTIVE:** To report patients examined for occupational asthma (OA) from epoxy compounds. **METHODS:** We retrospectively reviewed patient files of cases tested with a placebo-controlled specific inhalation challenge (SIC) according to their workplace exposure—either by mixing epoxy resin and the polyamine hardener of a 2-component paint or by dusting or heating TGIC-containing powder paint. The data were collected from the Finnish Institute of Occupational Health, Helsinki, Finland, and at Fundación Jiménez Díaz Hospital, Madrid, Spain, during 1997 to 2018. We also measured airborne polyamine and solvent vapors at the workplace and during SIC with ERSs. **RESULTS:** Altogether 113 patients with work-related asthma symptoms underwent SIC with ERSs. Fifteen cases (13%) had positive SIC reactions confirming OA; in 12 cases reactions were late-type, in 1 case early, and in 2 cases combined. The median duration of exposure for patients with OA was 10 years; 2 of them (13%) had a diagnosis of allergic contact dermatitis from

ERS compounds. In addition, 3 cases had a positive SIC reaction to TGIC. The airborne polyamine levels measured were low. **CONCLUSION:** ERSs and TGIC can cause sensitizer-induced OA in some exposed workers. Respiratory exposure to ERSs is difficult to demonstrate using air measurements. © 2019 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2019;7:191-8)

Key words: Sensitizer; Hardener; Coating; Painter; Chemical; Polyamine; Triglycidyl isocyanurate; CAS 25068-38-6; CAS 9003-36-5; CAS 2451-62-9

INTRODUCTION

Epoxy resin systems (ERSs) are used extensively at workplaces in, for example, industrial and construction coatings, adhesives, plastic composites, and modern sewage pipe relining materials. They most often appear as 2-component systems, in which the resin is mixed with a hardener at the workplace, resulting in relatively fast polymerization and the formation of hard epoxy plastic. Triglycidyl isocyanurate (TGIC) is a trifunctional epoxy compound used as a hardener in thermosetting polyester powder paints. Figure 1 shows some common epoxy and polyamine structures.

Several chemicals are known to cause occupational asthma (OA) via immunological, mainly IgE-independent, mechanisms.¹ Specific inhalation challenge (SIC) is the most definitive method to identify these respiratory-sensitizing agents.² Although population-based questionnaire studies have shown an increased asthma risk among workers exposed to ERSs,³ their respiratory sensitization capacity is largely unknown. An exception is phthalic anhydride derivatives, which are used as hardeners in special, heat-cured epoxy products; these are well known to cause IgE-mediated sensitization and OA.⁴ OA from ERS components, epoxy resins, and polyamine hardeners has been reported only in solitary case reports.⁵⁻¹⁰ Similarly, only a few cases of OA from TGIC have been published.¹¹⁻¹⁴ Neither TGIC nor epoxy resins nor polyamine hardeners are classified as respiratory sensitizers within the European Union.¹⁵

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Abbreviations used

ERS-epoxy resin system
 FENO-fractional exhaled nitric oxide
 FIOH-Finnish Institute of Occupational Health
 FJD-Fundación Jiménez Díaz Hospital
 HSA-human serum albumin
 ICS-inhaled corticosteroid
 OA-occupational asthma
 SIC-specific inhalation challenge
 SPT-skin prick test
 TGIC-triglycidyl isocyanurate
 WEA-work-exacerbated asthma

Monomeric, liquid-state components of ERSs are highly reactive and sensitizing to the skin, and ERSs are indeed among the most common causes of occupational allergic contact dermatitis in industrialized countries.¹⁶ Besides epoxy resin itself, the polyamine hardeners¹⁷ and reactive diluents in ERSs¹⁸ may sensitize the skin. Although most epoxy resin components are poorly volatile, contact dermatitis on open skin areas such as the face and neck is seen relatively often among patients with epoxy dermatitis,¹⁶ which is suggestive of airborne exposure. Contact dermatitis from TGIC has also been reported.^{19,20}

We report a series of cases of work-related asthma symptoms among workers who were exposed to ERSs and TGIC at the workplace and tested with a placebo-controlled SIC with the relevant workplace agent at the Finnish Institute of Occupational Health (FIOH), Helsinki, Finland, during 1997 to 2018 and at Fundación Jiménez Díaz Hospital (FJD), Madrid, Spain, during 2009 to 2018. Positive reactions confirmed OA, and cases with negative reactions were considered work-exacerbated asthma (WEA).

METHODS**Study population**

The FIOH is the only unit in Finland that performs SICs on patients with suspected OA to epoxy compounds. The cases are referred to the FIOH for confirmation of the diagnosis from all over Finland (population about 5.5 million). In the Allergy Occupational Unit at FJD, patients are referred from all over Spain (population 44 million; another center can also perform these tests). We retrospectively reviewed cases in which the patient had undergone SIC with epoxy resin, polyamine hardener, and TGIC at the FIOH during 1997 to 2018 and at FJD during 2009 to 2018; SIC with ERSs had not been performed at FJD before 2009, because no cases with suspicion of ERSs were referred to the clinic. We collected information on age, sex, smoking, exposure to ERSs and TGIC, work and clinical history, as well as clinical investigations.

Patients who underwent SIC and were exposed to epoxy compounds at the workplace were diagnosed with asthma and had WEA symptoms. Cases with positive SIC reactions were considered OA and those with negative reactions were considered WEA. The cases of negative SIC reactions to ERSs or TGIC and positive SIC reactions to other workplace agents were excluded.

The study was approved by the FIOH (TTL/2/2016). According to the local legislations and ethical committees, no approval was needed because no patient intervention was involved at the FIOH or FJD.

SICs and skin prick tests

At the FIOH, the work-mimicking placebo-controlled SICs were performed in a 6-m³ chamber with a control test (with butyl acetate solvent or 1-component, solvent-based paint) on the first day, followed by ERS tests on the following days, each challenge having a 24-hour follow-up. The ERS tests were performed by mixing 100 to 200 mL of the epoxy resin used in the patient's work with a suitable amount of polyamine according to the mixing ratio at work, and stirring the mixture at 2-minute intervals. The duration of the control test was 15 to 30 minutes, and the first ERS test lasted 30 minutes. The repeated ERS test lasted 45 minutes. TGIC-containing powder paint (mixed with lactose or as is) was dusted for 30 minutes. A control challenge with dusting lactose powder was performed on the previous day. Challenge tests performed at FJD followed a similar methodology to those at the FIOH, although the chamber was 7 m³ and solvent-based paint and lactose (for TGIC) were used for the control test. The total duration of the repeated test was 120 minutes.

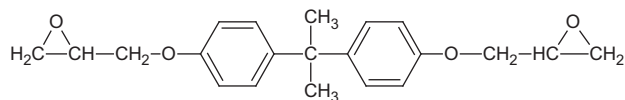
Bronchial reaction was monitored using FEV₁ and fractional exhaled nitric oxide (FENO) before and 24 hours after each challenge, and a histamine/methacholine challenge the day before placebo challenge and approximately 24 hours after the challenge with epoxy compounds. A positive test result was defined as a sustained fall in FEV₁ of 15% or more from prechallenge value, when fluctuations of FEV₁ were less than 10% on a control day.² The reaction was considered early if a significant fall in FEV₁ was detected within 1 hour of the challenge, and late if detected after 1 hour. A combined reaction included both the early and late phases. A 2-fold reduction in the provocative dose/concentration in the histamine/methacholine challenge was considered significant. A 10-ppb increase in FENO from a baseline level of below 50 ppb and a 20% increase from above 50 ppb were considered significant.²¹ Significant changes in FENO and hyperresponsiveness were supportive, but not sufficient alone for a positive SIC result.

Skin prick tests (SPT) with human serum albumin (HSA)-conjugated diglycidyl ether of bisphenol A epoxy resin were performed at the FIOH as described earlier,²² and prick-prick tests with epoxy components were performed at FJD.

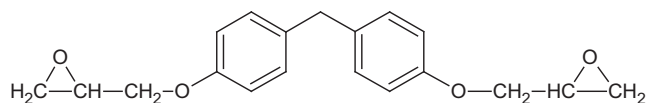
Measurement of polyamines and solvent vapors in the air

We measured airborne polyamines and solvents in the floor-coating process in a Finnish paper factory on 2 subsequent days, as well as in the challenge chamber at the FIOH, to map the level of exposure in epoxy work and to validate the SIC. In the workplace measurements, a construction painter mixed epoxy floor paint with polyamine hardener and spread the mixture on an area of about 50 m² in several repeated phases over 3 to 4 hours. In the SICs, 100 mL of an epoxy floor paint and 30 to 40 mL of its polyamine hardener were mixed together and stirred at 2-minute intervals over 30 minutes. The amount and delivery method were identical to those used in the patient examinations.

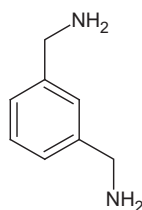
Amines were collected from the breathing zone on impregnated filters (0.52 N H₂SO₄) at a flow rate of 2 L/min and over a collection time of 120 to 180 minutes in the floor-coating process and 30 minutes in the validation SICs. The filters were extracted with methanol and analyzed using liquid chromatography and mass spectrometry, as previously described.²³ Solvent vapors were collected (1) on active charcoal tubes (SKC 226-01 [SKC, Inc., Covington, GA]; flow rate, 0.1-0.2 L/min) and (2) at the workplace also on 3M 3500 dosimeters (3M Company, London, Ontario,



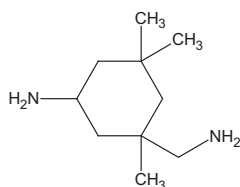
Diglycidyl ether of bisphenol A (DGEBA, the main monomer of epoxy resin), CAS 1675-54-3 (monomer) or 25068-38-6 (resin)



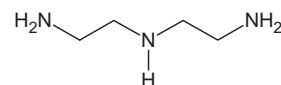
Diglycidyl ether of bisphenol F (DGEBF, the main monomer of DGEBF-epoxy resin), CAS 28064-14-4 (monomer) or 9003-36-5 (resin)



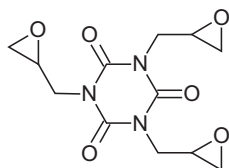
m-Xylylene diamine (m-XDA), CAS 1477-55-0



Isophoronediamine (IPDA), CAS 2855-13-2



Diethylenetriamine (DETA), CAS 111-40-0



Triglycidylisocyanurate (TGIC), CAS 2451-62-9

FIGURE 1. Some common epoxy resin and polyamine structures, their names, and CAS numbers. CAS, Chemical Abstracts Service.

Canada), desorbed with dimethylformamide and analyzed by gas chromatography, as previously described.^{24,25} The collection times were similar to those for the amines. Analyses were performed at the FIOH, in its FINAS-accredited testing laboratory (T013, EN ISO/IEC 17025).

Statistical analysis

We used SPSS version 24.0 (IBM Corporation, Armonk, NY; 2016) for data analysis. We expressed continuous variables as medians and categorical values as percentages. We analyzed the differences between the groups using the Mann-Whitney *U* test or the chi-square test. A *P* value of less than .05 was considered statistically significant.

RESULTS

SIC with ERSs was performed on 113 patients: 99 patients (9 positive and 90 negative results) at the FIOH and 14 patients (6 positive and 8 negative results) at FJD (Figure 2). The proportion of positive SIC reactions was 13% in the whole population; at the FIOH it was 8% and at FJD 43%. Most of the patients were middle-aged men, most commonly working as industrial painters (Table 1). The median duration of

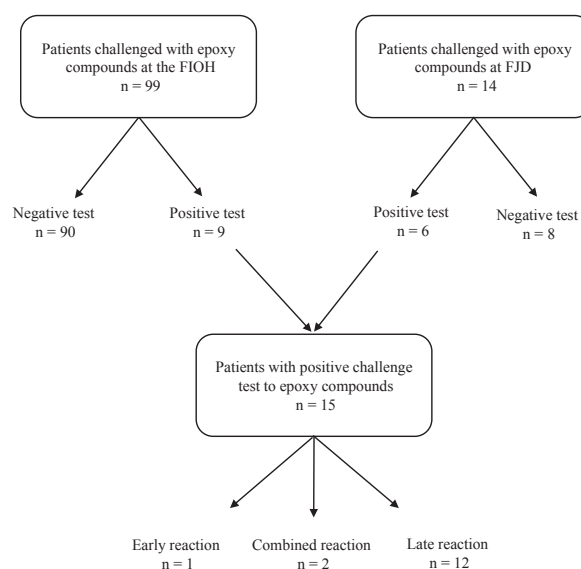


FIGURE 2. Study flowchart. FIOH, Finnish Institute of Occupational Health; FJD, Fundación Jimenez Diaz Hospital.

TABLE I. Characteristics of patients examined using SIC with ERSs

Characteristic	Total (N = 113)	Positive SIC (OA) (n = 15)	Negative SIC (WEA) (n = 98)	P value
Sex, male, n (%)	101 (89)	15 (100)	86 (88)	.152
Age (y), median (Q ₁ -Q ₃)	38 (31-50)	40 (33-53)	38 (31-49)	.632
Current smoking, n (%)	28 (25)	3 (20)	25 (26)	.645
Atopy,* n (%)	42 (37)	7 (47)	35 (36)	.414
Type of work				.824
Industrial painter	40 (35)	7 (47)	33 (34)	
Construction coater	15 (13)	2 (13)	13 (13)	
Production worker (plastics etc)	24 (21)	3 (20)	21 (21)	
Plumber/sewage pipe reliner	8 (7)	1 (7)	7 (7)	
Assembler/mechanic	10 (9)	0 (0)	10 (10)	
Other	16 (14)	2 (13)	14 (14)	
Duration of exposure (y), median (Q ₁ -Q ₃)	9 (4-19)	10 (6-17)	9 (3-19)	.548
Duration of asthma symptoms (y), median (Q ₁ -Q ₃)	1.9 (1.0-4.0)	1.3 (0.6-3.0)	2.0 (1.0-4.1)	.303
Work-related rhinitis symptoms, n (%)	60 (53)	6 (40)	54 (55)	.275
Contact dermatitis from ERSs,† n (%)	25 (22)	2 (13)	23 (24)	.378

*At least 1 positive reaction in SPTs or specific IgE to common environmental aeroallergens.

†Confirmed with patch test.

exposure was 9 years and of asthma symptoms 1.9 years. Of the workers, 53% experienced work-related rhinitis symptoms and 22% were diagnosed with allergic contact dermatitis from ERSs. SPTs to HSA-conjugated epoxy resin were performed in 93 cases in the FIOH. One case with negative SIC test result had a positive SPT reaction. At FJD only 1 SPT was performed; this case with negative SIC test result had contact urticaria and a positive SPT result to epoxy. When we compared patients with positive and negative SIC results, we found no significant differences in sex, age, atopy, type of work, duration of exposure or symptoms, existence of work-related rhinitis symptoms, or allergic contact dermatitis from ERSs (Table I).

Altogether 15 patients had a positive SIC reaction to ERSs, confirming OA (Table II). The most common occupations were metal painting and windmill factory production work. The median duration of exposure was 10 years, and of symptoms 1.3 years (Table I). Three (20%) cases were current smokers and 7 (47%) were atopic. Twelve patients had used inhaled corticosteroids (ICSs) before SIC. Their medication was adjusted before SIC according to asthma control. At the FIOH, ICSs were withheld 1 to 14 days before SIC in 7 cases and continued during SIC in 1 case. At FJD, ICSs were withheld 3 days before challenge in all cases but 1. Two of the cases were diagnosed with contact dermatitis from epoxy resin (Table II). The type of SIC reaction was late in 12 (75%) cases, combined in 2 (12%) cases, and early in 1 (12%) case. A significant increase in hyperresponsiveness was detected in 2 of the 7 (29%) patients with hyperresponsiveness follow-up during SIC. Similarly, a significant increase in FENO was seen in 2 of the 7 (29%) patients. One patient (case 15) had a positive SIC reaction to both ERSs and toluene diisocyanate.

The cases of 3 patients with positive SIC reactions to TGIC are presented in Table III. They were all painters who used powder paint. The duration of exposure to TGIC was 1 to 9 years. They were not atopic, and 2 of them had work-related rhinitis. Peak expiratory flow monitoring at work and off work was compatible with OA in 2 cases. Both early and late SIC reaction types were detected.

The results of the air measurements during coating work at the workplace and SIC to ERSs are presented in Table IV. The level of airborne amines was very low, mostly below the limit of detection in both the workplace measurements and validation SICs. The concentration of airborne solvents was high at the workplace. In the SICs, the airborne solvents were comparable with typical industrial work with solvent-based products. The most common solvent with the highest concentration in all measurements was xylene. The identified amines and solvents were in concordance with the safety data sheets of the respective products.

DISCUSSION

We report 15 cases of OA from ERSs confirmed with positive SIC, as well as 98 WEA cases who were exposed to ERSs at work but had negative SIC results. The median duration of exposure to ERSs was 10 years before OA diagnosis, and the SIC reaction was late-type in most cases. Concomitant contact dermatitis from ERS compounds was detected in 13% of the OA cases and 24% of the WEA cases with negative SIC reactions. We also present 3 OA cases from TGIC. The levels of airborne polyamines were very low in both the workplace measurements and the SIC.

At the FIOH, many SICs with ERSs (99 patients) have been performed in recent decades. A small proportion of positive reactions (8%) may indicate that the sensitizing potential of these compounds is low. At FJD, 43% of the patients have shown a positive SIC reaction, but the total number of cases is smaller (14 cases). No cases with suspicion of ERS-related OA were referred to the unit before 2009, suggesting that the number of suspected cases has increased in recent years in Spain. The difference between the proportions of positive reactions in these units is most likely due to different indications for SIC and different referral practices. At FJD, the pretest probability of OA was higher than it was at the FIOH, when the SIC was considered indicated. Two percent of all SIC-positive OA cases (including SICs with both low- and high-molecular-weight agents) were caused by epoxy compounds at the FIOH (2006-2015) and 6% at FJD (2009-2015). OA most commonly develops within the first years of exposure to occupational

TABLE II. Cases of OA from ERSs confirmed with positive SIC

Patient no.	Job	Smoking	Atopy*	Duration of exposure (y)	Duration of symptoms (y)	Work-related rhinitis	Contact dermatitis from ERSs†	PEF monitoring at work and off work compatible for OA	Obstruction in spirometry	Hyperresponsiveness	FENO	Type of SIC reaction	Increase in hyperresponsiveness in SIC	FENO change during SIC
1	Spray painter in metal industry	—	—	12	1.4	—	—	+	—	—	11	Combined	NA	NA
2	Spray painter in metal industry	+	+	12	4.0	+	—	+	—	+	NA	Late	NA	NA
3	Foreman painting metal parts	—	—	30	4.2	—	+ Epoxy resin	NA	—	+	15	Late	NA	NA
4	Sales rep and technical support in floor coatings	—	—	19	14.0	+	—	Suggestive	+	—	12	Combined	NA	NA
5	Spray painter in metal industry	—	—	17	0.8	+	—	NA	—	—	54	Late	NA	NA
6	Spray painter in metal industry	—	—	29	1.0	+	—	NA	—	+	39	Late	NA	NA
7	Painter in metal industry	+	—	9	1.3	+	—	NA	—	—	NA	Late	NA	NA
8	Painter in metal industry	+	+	4	2.5	+	—	+	+	+	NA	Late	NA	NA
9	Sewage pipe renovator	—	—	4	0.8	—	+ Epoxy resin	Suggestive	—	+	17	Late	+ 10.8-fold	+9
10	Car repair worker	—	+	6	0.4	—	—	NA	—	+	70	Late	—	+17
11	Construction worker	—	—	10	3	—	—	NA	—	—	14	Late	—	+9
12	Windmill factory worker	—	+	8	0.2	—	—	NA	—	+	33	Late	+ 4.5-fold	−7
13	Windmill factory worker	—	+	5	0.6	—	—	NA	—	+	122	Late	—	+20
14	Construction worker	—	+	10	3	—	—	NA	—	—	33	Early	—	+12
15	Windmill factory worker	—	+	8	0.5	—	—	Suggestive	—	+	25	Late‡	—	−11

Note. Cases 1-9 were examined at the FIOH and cases 10-15 at FJD.

NA, Not available; PEF, peak expiratory flow.

*At least 1 positive reaction in SPTs or specific IgE to common environmental aeroallergens.

†Confirmed with patch test.

‡Also, positive SIC reaction to toluene diisocyanate.

TABLE III. Cases of OA from TGIC confirmed with positive SIC

Patient no.	Job	Smoking	Atopy*	Duration of exposure (y)	Duration of symptoms (y)	Work-related rhinitis	Contact dermatitis to TGIC		PEF monitoring at work and off work compatible for OA		Obstruction in spirometry	Hyperresponsiveness	F _{ENO}	Type of SIC reaction	Increase in hyperresponsiveness in SIC	F _{ENO} change during SIC
16	Powder paint shop worker	—	—	9	3	+	—	—	—	—	—	—	26	Late	—	—
17	Powder painter	+	—	7	2	+	—	—	+	—	—	+	NA	Prolonged early	NA	NA
18	Spray painter in metal industry	—	—	1	0.3	—	—	—	+	—	—	+	15	Early	—	+3

Note. Cases 16 and 17 were examined at the FIOH and case 18 at FJD.

NA, Not available; PEF, peak expiratory flow.

* At least 1 positive reaction in SPTs or specific IgE to common environmental aeroallergens.

agents.²⁶ Median duration of exposure to ERSs before OA diagnosis was 10 years. Duration of exposure was similar among patients with OA from isocyanates (median, 10 years; Q₁-Q₃, 5-25 years; $P = .745$) diagnosed in the FIOH and FJD (2006-2015). Cases diagnosed with OA from persulfates during the same time period had slightly longer median duration of exposure, but the difference was not statistically significant (median, 17 years; Q₁-Q₃, 11-25 years; $P = .056$).

In this study, 40% of the patients with OA and 55% of the patients with WEA reported work-related rhinitis symptoms. The proportion was slightly lower than that formerly reported for OA (73%) and work-related asthma (78%) due to chemicals,²⁷ but similar to that for isocyanate OA cases (49%; $P = .532$) and persulfate OA cases (60%; $P = .241$) diagnosed at the FIOH and FJD (2006-2015). We found contact dermatitis from ERS components in 13% of the OA cases and in 24% of the WEA cases. To our knowledge, only case studies have formerly reported concomitant OA and contact dermatitis from epoxy compounds and other chemicals.^{8,28,29} The relatively high proportion of contact dermatitis in our material may reflect substantial dermal exposure to ERSs in this group. Recent data support the claim that skin exposure may contribute to the development of OA.³⁰⁻³² Considering the low airborne levels of ERS components, dermal exposure may play a role in the development of ERS-related OA.

Most of the SIC reactions to ERS components in earlier reports have been late^{5-7,9,10} Similarly, all but 1 of our cases had a late or combined SIC reaction. In our experience, patients report delayed asthma symptoms (12-24 hours) after ERS exposure at the workplace. Hannu et al⁸ reported a case with an immediate SIC reaction and IgE-mediated allergy to epoxy resin, verified by both serum IgE and an SPT. We found 2 SPT-positive cases (2% of tested), both with negative SICs to ERSs. Positive SPTs to ERSs seem to be rare. The FIOH's recent data on 1268 SPTs to the HSA conjugate of epoxy resin showed only 19 (1.5%) positive reactions.²²

The resin part of 2-component ERSs typically contains 20% to 75% of epoxy resin based on the monomer diglycidyl ether of bisphenol A epoxy resin, but some products also contain epoxy resin based on diglycidyl ether of bisphenol F (Figure 1). In addition, some special products contain "reactive diluents," which have related epoxy structures; these have a lower molecular weight and are added to decrease the viscosity of the resin. The hardener part usually contains polyamines such as isophoronediamine, m-xylylenediamine, or diethylenetriamine. Almost all industrial coatings also contain organic solvents, or are diluted with solvents during use. By definition, they are not reactive, but may smell strongly.

Previous case reports have described OA verified by a positive SIC reaction to ERS components: to epoxy resin⁷⁻⁹ and polyamine hardeners containing isophoronediamine and other amines.^{5,6,10} In our material, the SIC method was to mix epoxy resin and polyamine hardener, both of which contain several constituents. We were unable to identify 1 single agent causing the positive reactions; thus, the causal agent may be epoxy resin, polyamine hardener, or any other compound that evaporated during mixing. None of these compounds is classified as a respiratory sensitizer in the European Union, and subsequently, the package labels or safety data sheets of the patients' products did not give information on the respective respiratory hazard. It would be informative to test the epoxy resin and the polyamine hardener, or even specific ingredients, separately in the patients

TABLE IV. Concentration of airborne amines and solvents at coating workplace and in 2 validation SICs

Measurement	Process and amount of ERS used	Sampling time (min)	Number of samples	Air concentration of polyamines/total solvents
Workplace measurement	Mixing and spreading of epoxy floor coating, total volume about 100 L	Polyamines: 120	4	m-XDA: 4/4 samples <LOD* IPDA: 3/4 of the samples <LOD* and 1/4 sample 0.01 µg/m ³
		Solvents: 120-210	8 (4 + 4)	TVOC/active charcoal (N = 4): 15-131 mg/m ³ 3M dosimeter (N = 4): 169-278 mg/m ³
Validation SIC 1	Mixing 100 mL of epoxy paint and 40 mL of hardener	Polyamines: 30	1	TETA: <LOD†
Validation SIC 2	Mixing 100 mL of epoxy paint and 30 mL of hardener	Solvents: 30	1	TVOC/active charcoal: 20.7 mg/m ³
		Polyamines: 30	1	EDA: 0.21 mg/m ³
		Solvents: 30	1	TVOC/active charcoal: 6 mg/m ³

Note. Epoxy resin in the air was not measured because its concentration was expected to be below the LOD.

EDA, Ethylenediamine; IPDA, isophoronediamine; LOD, limit of detection; m-XDA, m-xylylenediamine; TETA, triethylenetetramine; TVOC, total volatile organic compounds (mainly organic solvents from paints).

*LOD was 0.02-0.04 µg/m³, depending on sample.

†LOD was 80 µg/m³.

with a positive reaction to mixed SIC. However, SIC with separate components may miss the generation of possible allergic reactions to products and heat.

Most of the reactive starting materials in ERSs are poorly volatile. However, the heat generated during the mixing of the components, as well as the organic solvents in ERSs, might enhance the evaporation of some of the nonvolatile components. We measured airborne amines and solvents at a large workplace during floor painting as well as in the SIC chamber at the FIOH. Epoxy resin was not measured in the air, because its concentration was expected to be below the limit of detection. The levels of amines were extremely low in both. Solvent fumes were abundant, especially at the workplace. The workplace measurement represented extreme solvent exposure rather than typical exposure in epoxy processes, whereas the validation SICs more likely represented solvent exposure in average epoxy coating work. Our results suggest that asthma, similarly to airborne contact dermatitis, may occur with minimal exposure to epoxy compounds. It is unlikely that these diseases are caused because of irritancy at such low exposure levels. Despite the low level of amines, our patients often report a strong smell of polyamine hardeners at the workplace and in the SIC, meaning that at least some polyamine molecules reach the airways. In addition, the low, nonirritant level of exposure and the delayed reactions in the SIC suggest that the reactions were due to sensitization rather than to irritation. Low air levels of ERS components may cause false-negative findings in SIC,² and we cannot reliably exclude OA in patients with WEA with negative SIC results.

TGIC is a crystalline, nonvolatile cross-linking agent (Figure 1) often present in polyester powder coatings of less than 1% to 10%. It is, in principle, trapped inside the paint particles, but part of the substance may be released into the respiratory tract when TGIC-containing powder is inhaled, or through fumes generated during the curing of these paints at elevated temperatures. To our knowledge, 9 cases of OA to TGIC have been previously reported, 8 of which were confirmed with SIC.¹¹⁻¹⁴ As in our 3 cases, both early and late reaction types have been detected in former studies. IgE-mediated sensitization was not evident in these cases. TGIC has several harmful effects and is classified as, for example, a skin

sensitizer and toxic via inhalation, but not as a respiratory sensitizer, in the European Union.¹⁵

CONCLUSIONS

Epoxy compounds can cause sensitizer-induced OA in some exposed workers, although air concentrations appear to be low. Late-type asthma reactions may hamper the recognition of this disease. The specific causative chemical compounds and the background mechanisms remain unknown. Two-component ERSs are currently used in large quantities in various applications, and new applications such as pipe relining resins and 3D-printing materials have arisen in recent years. Because of their superior technical qualities and excellent durability and workability, it is unlikely that epoxy resins will be replaced by other plastics in the near future. Preventive work, including informing the workers of the sensitization risks, as well as advice on technical measures and skin and respiratory protection, is necessary.

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