

Contact vitiligo following a strong patch test reaction to triglycidyl-*p*-aminophenol in an aircraft industry worker: case report and review of the literature

U. JAPPE¹, J. GEIER² AND B. M. HAUSEN³

¹Department of Dermatology and Venereology, University of Heidelberg, Heidelberg, ²Information Network of Departments of Dermatology, IVDK, University of Goettingen, Goettingen, and ³Dermatology Centre, Elbekliniken Buxtehude, Germany

Epoxy resin systems (ERSs) are a frequent cause of occupational allergic contact dermatitis. A 50-year-old patient developed eczematous skin lesions on the back of his hands, lower arms and eye lids, 2 months after he had started working in aircraft construction. Patch tests showed positive reactions at day 3 to nickel sulfate, epoxy resin based on diglycidyl ether of bisphenol F (DGEBF) and 1,4-butanediol diglycidyl ether (1,4-BDDGE). The chemical triglycidyl-*p*-aminophenol (TGPAP) applied at 1% and 0.1% induced the strongest (+++ positive) reaction. About 4 months after the patch test with TGPAP, the patient presented with 2 circular depigmented spots in the former TGPAP-patch test areas. Dermatohistopathology confirmed the diagnosis of contact vitiligo.

Key words: aircraft industry; contact vitiligo; delayed-type hypersensitivity reaction; epoxy resin; TGPAP preimpregnated epoxy products; triglycidyl-*p*-aminophenol. © Blackwell Munksgaard, 2005.

Accepted for publication 10 May 2005

Epoxy resin systems (ERSs) are a frequent cause of occupational allergic contact dermatitis. Sensitization occurs not only to the resins, but also to hardeners and reactive diluents. However, there are few reports on occupational allergic contact dermatitis due to so-called trifunctional epoxy resins in aircraft workers, uncommon sensitizers which, according to a lack of cross-reactivity, may remain undetected even by expanded epoxy system patch test series (1–3). The following case report underlines that the significance of this particular group of substances is probably underestimated in occupational dermatology.

Case Report

A 50-year-old patient presented with eczematous skin lesions on the back of his hands, lower arms and eye lids. Being a trained tailor but unable to find a job in his profession, he had started working with a temporary work-company dealing with aircraft construction. The patient was an operator of liquefaction and lamination

machines. While filling the machines, he handled uncured epoxy resins. After the lamination process, he stored and packed the products, and cleaned them and the machines using acetone. According to the company, he had contact with Araldit MY 0510[®] (triglycidyl-*p*-aminophenol TGPAP) (Huntsman; vantico, Wehr, Baden, Germany), Araldit PY 306 US[®] (bisphenol F-epoxy resin) (vantico), acetone (Shell Chemicals, Europe BV, Rotterdam, Netherlands), NMP[®] (N-methylpyrrolidone) (BASF), KM177 micro-nized polymer[®] (proprietary resin) (Cytec Industries, West Paterson, NJ, USA), Aradur 976-1[®] (4,4-diaminodiphenylsulfone) (vantico). About 2 months after having started in his new field of activity, he developed erythematous itching skin lesions on the back of his hands, the extensor sides of his lower arms and his eye lids. There was no history of atopic diseases.

He was admitted to our allergy department in order to evaluate as to whether the symptoms were due to an irritant or allergic contact dermatitis and associated with his work. Detailed

history showed exposure to epoxy resins, although direct skin contact was denied. As preventive measures gloves made from rubber and rubber latex were used.

Patch tests were performed and read according to international guidelines (4), refined by the German Contact Dermatitis Research Group (DKG) (5). Patch test exposure time was 48 hr, the tape used was Finn Chambers on Scanpor® (Hermal, Germany).

Because the manufacture of aircraft combines traditional mechanical techniques with chemical techniques, the patient was patch tested with the DKG standard series, rubber series, preservatives, a mechanical workers series, plastics and glues series, and an extended epoxy resins series including 16 study substances of the EPOX 2002 project (6) (Table 1). Positive test reactions at day 3 (D3) were observed to nickel sulfate, epoxy resin based on diglycidyl ether of bisphenol F (DGEBA) and 1,4-butanediol diglycidyl ether (1,4-BDDGE). All other tests remained negative. A DGEBA resin was present at the workplace (Araldit PY 306 US®), rendering this test reaction clinically relevant. In contrast, the relevance of the test reaction to

1,4-BDDGE could not be ascertained, because none of the products used contained 1,4-BDDGE. To our knowledge, no cross-reactions of 1,4-BDDGE with DGEBA or the subsequently tested TGPAP have been described.

In a second patch test session, Aradur 976-1® (4,4-Diaminodiphenylsulfone) and Araldit MY 0510® (TGPAP) were tested at 1% and 0.1% in petrolatum. At D2 and D3, a threefold positive reaction was seen to both concentrations of Araldit MY 0510® but none to Aradur 976-1®. Because acetone and NMP® are skin irritants, and 'KM 177 micro-nized polymer®' is not very well defined, these substances were excluded from the patch test.

Araldit MY 0510® (TGPAP) at 1% and 0.1% was additionally tested in 8 healthy and 7 atopic individuals. Whereas the 1% concentration occasionally induced an irritant reaction, the 0.1% concentration remained negative in all 15 controls.

About 4 month after the patch test with TGPAP, the patient presented with two circular depigmented spots in the former TGPAP-patch test areas (Fig. 1). Dermatohistopathology confirmed the diagnosis of contact vitiligo (Fig. 2).

Table 1. Patch test results of a 50-year-old aircraft industrial worker exposed to epoxy resin systems

Substance	Test reaction at D3		
Resins			
Epoxy resin based on DGEBA (DGEBA-R)	1.00	%pet.	Negative
Epoxy resin based on DGEBA (DGEBA-R)	0.25	%pet.	+
Cycloaliphatic epoxy resin	0.50	%pet.	Negative
Hardeners			
m-Xylene diamine (MXDA)	0.10	%pet.	Negative
Isophorone diamine (IPDA)	0.50	%pet.	Negative
4,4'-Diaminodiphenyl methane (4,4'-DDM)	0.50	%pet.	Negative
Triethylene tetramine	0.50	%pet.	Negative
Methenamine (Hexamethylene tetramine)	1.00	%pet.	Negative
N-Aminoethyl piperazine	0.25	%pet.	Negative
Diethylene triamine	0.50	%pet.	Negative
Dipropylene triamine (DPTA)	0.25	%pet.	Negative
Trimethylhexane-1,6-diamine (mixture of isomers)	0.25	%pet.	Negative
2,4,6-Tris (dimethyl aminomethyl)phenol	0.25	%pet.	Negative
Aminoethylethanolamine	0.25	%pet.	Negative
1,2-Diaminocyclohexane (mixture of isomers)	0.25	%pet.	Negative
Ethylenediamine-di-HCl	1.00	%pet.	Negative
4,4'-Methylene bis (cyclohexylamine)	0.25	%pet.	Negative
Triethyleneglycol diamine	0.25	%pet.	Negative
Reactive diluents			
1,6-Hexanediol diglycidyl ether (1,6-HDDGE)	0.25	%pet.	Negative
1,4-Butanediol diglycidyl ether (1,4-BDDGE)	0.25	%pet.	+
p-tert-Butylphenyl glycidyl ether (PTBPGE)	0.25	%pet.	Negative
Phenyl glycidyl ether (PGE)	0.25	%pet.	Negative
Cresyl glycidyl ether (CGE)	0.25	%pet.	Negative
Butyl glycidyl ether	0.25	%pet.	Negative
Trimethylolpropane triglycidyl ether	0.25	%pet.	Negative
C12/C14 Alkylglycidyl ether	0.25	%pet.	Negative
Versatic acid glycidyl ester	0.25	%pet.	Negative
Resin from the patient's workplace			
Triglycidyl-p-aminophenol (TGPAP)	0.10	%pet.	++
TGPAP	1.00	%pet.	+++

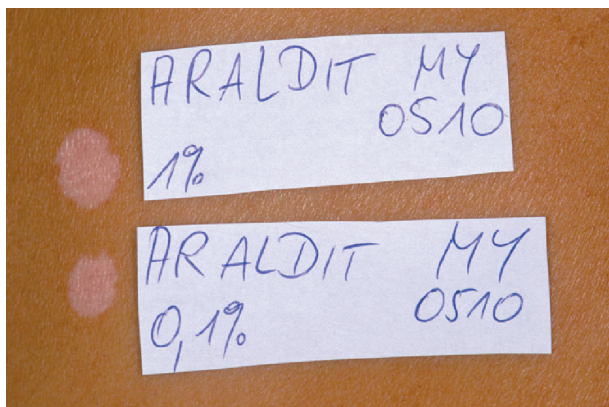


Fig. 1. Depigmented well-demarcated patches in the location of the former threefold positive patch test reactions to Araldit MY 0510 (Huntsman; vantico) (TGPAP) 1% and 0.1%.

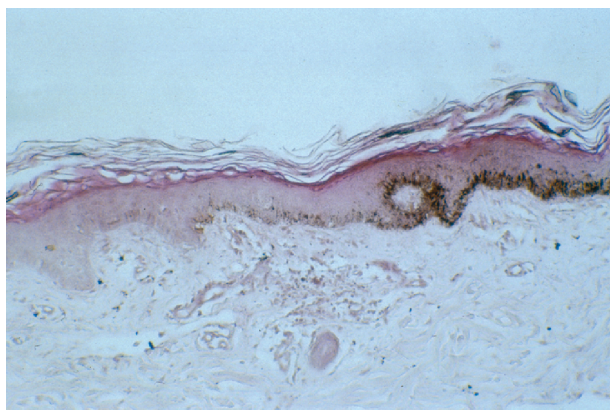


Fig. 2. Histopathology: A silver nitrate stain shows the absence of melanin pigment in basal layer keratinocytes, changes typical of vitiligo, whereas in unaffected skin melanin pigment is detected (magnification: $\times 4.5$).

Discussion

ERS, which are widely used in many trades and industrial fields nowadays, contain several well-known or potential allergens. However, only a fraction of these substances is currently available for routine patch testing. The multi-centre study EPOX 2002 has improved the diagnostics in so far as further frequently used ERS components have been studied (6). However, the development of industrial EPSs is very dynamic confronting allergologists with new and sensitizing substances. Very little has been reported on the sensitizing potential of trifunctional epoxy resins like TGPAP which are used in pre-impregnated epoxy products in the aircraft industry (1–3). The allergenic potential of TGPAP is underlined by the development of an airborne contact dermatitis in an aircraft industrial worker, which has only once been published (1). As in our patient, the eye lids were affected as well, it is possible that he was about to develop an airborne contact

dermatitis to TGPAP. It cannot be excluded that TGPAP-associated occupational allergic contact dermatitis occurs more frequently than assumed, but remains undetected because products from the patients' workplace are not tested. This observation is in accordance with previous publications on polyfunctional ERS. In this context, it is particularly important that TGPAP does not cross-react with the standard epoxy resin DGEBA (2, 3), the patients therefore being negative for the latter and their skin reactions being misinterpreted as irritant instead of allergic contact dermatitis. As additionally pointed out previously (2, 3), actually important ERS are often not investigated, particularly when they are solid, due to a lack of awareness concerning their sensitizing potential. Whereas skin protection is used while working with liquid ERS, epoxy sheets are according to the authors often thought to be nonsensitizing and thus handled with bare hands. However, solid, i.e. cured, epoxy resins still may contain residual sensitizing monomers or oligomers.

Contact dermatitis and subsequent depigmentation has previously been reported for several substances in different settings either occupational or following private use of potentially sensitizing agents. These are mainly hydroquinone, the monomethyl ether as well as the monobenzyl ether of hydroquinone, p-toluene diamine, monobenzene, phenol/catechol derivatives such as p-tert amylphenole, p-tert butyldinitrophenole, p-tert butylphenol, p-tert butyl-catechin, diphenylcyclopropanon, p-phenylenediamine in hair dyes or henna tattoos, azo dyes, aldehydes, ERS, metals and dental acrylics (7). The following pathomechanisms have been hypothesized: photoleukomelanoderma due to pigment blockade, reduction of melanin synthesis, selective destruction of melanocytes resulting from a toxic tissue reaction as well as Koebner-induced vitiligo. The fact that no melanocytes were present in the depigmented area confirmed the diagnosis of exogenous leukoderma following contact dermatitis (contact vitiligo) and not post-inflammatory hypopigmentation. Although the pathogenesis of leukoderma following contact dermatitis has not been understood so far, there is evidence that the prognosis is better than for idiopathic vitiligo (8).

Depigmentation after allergic contact dermatitis due to ERS has already been described (8, 9). However, to our knowledge, this is the first report of contact vitiligo following a positive patch test reaction to TGPAP, suggesting a strong sensitizing potential and pointing to a rare adverse event of patch testing in general.

References

1. Kanerva L, Jolanki R, Estlander T, Henriks-Eckerman M L, Tuomi M L, Tarvainen K. Airborne occupational allergic contact dermatitis from triglycidyl-p-aminophenol and tetraglycidyl-4,4-methylene dianiline in preimpregnated epoxy products in the aircraft industry. *Dermatology* 2000; 201: 29–33.
2. Mathias C G T. Allergic contact dermatitis from a non-bisphenol A epoxy in a graphite fiber reinforced epoxy laminate. *J Occup Med* 1987; 29: 754–755.
3. Bruze M, Edénholm M, Engström K, Svensson G. Occupational dermatoses in a Swedish aircraft plant. *Contact Dermatitis* 1996; 34: 336–340.
4. Wahlberg J E. Patch testing. In: *Textbook of Contact Dermatitis*, Rycroft R J G, Menné T, Frosch P J, Lepoittevin J-P (eds), 3rd edition. Berlin, Springer Verlag, 2001: pp. 435–468.
5. Schnuch A, Aberer W, Agathos M, Brasch J, Frosch P J, Fuchs T H, Richter G. Für die Deutsche Kontaktallergie-Gruppe. Leitlinien der Deutschen Dermatologischen Gesellschaft (DDG) zur Durchführung des Epikutantests mit Kontaktallergenen. *Hautarzt* 2001; 52: 864–866.
6. Geier J, Lessmann H, Hillen U et al. An attempt to improve diagnostics of contact allergy due to epoxy resin systems. First results of the multicentre study EPOX 2002. *Contact Dermatitis* 2004; 51: 263–272.
7. Wattanakrai P, Miyamoto L, Taylor J S. Occupational Pigmentary Disorders. In: *Handbook of occupational Dermatology*, Kanerva L, Elsner P, Wahlberg J E (eds), 2000: 35: 280–294.
8. Kumar A, Freeman S. Leukoderma following occupational allergic contact dermatitis. *Contact Dermatitis* 1999; 41: 94–98.
9. Silvestre J F, Albares M P, Escutia B, Vergara G, Pascual J C, Botella R. Contact vitiligo appearing after allergic contact dermatitis from aromatic reactive diluents in an epoxy resin system. *Contact Dermatitis* 2004; 49: 113–114.

Address:

Uta Jappe, MD, MSc,
 Department of Dermatology and Venereology
 University of Heidelberg
 Voßstrasse 2
 D-69115 Heidelberg
 Germany
 Tel: +49 6221 567011
 Fax: +49 6221 564996
 e-mail: uta_jappe@med.uni-heidelberg.de