

Multicentre patch testing with a resol resin based on phenol and formaldehyde

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Summary

Background. Contact allergy to phenol-formaldehyde resins (PFRs) based on phenol and formaldehyde is not detected by a *p*-tertiary-butylphenol-formaldehyde resin (PTBP-FR) included in most baseline patch test series.

Objectives. To investigate the rate of contact allergy to PFR-2 (a mixture of monomers and dimers from a resol resin based on phenol and formaldehyde) in a Swedish population, and to investigate associated simultaneous allergic reactions.

Methods. Five centres representing the Swedish Contact Dermatitis Research Group included PFR-2 in their patch test baseline series for a period of 1.5 years.

Results. Of 2504 patients tested, 27 (1.1%) reacted to PFR-2. Of those 27 individuals, 2 had a positive reaction to formaldehyde and 2 to PTBP-FR. Simultaneous allergic reactions were noted to colophonium in 6, to *Myroxylon pereirae* in 14, and to fragrance mix I in 15.

Conclusions. The contact allergy frequency in the tested population (1.1%) merits its inclusion in the Swedish baseline series and possibly also in other baseline series. Simultaneous allergic reactions were noted to colophonium, *M. pereirae*, and fragrance mix I.

Key words: baseline series; formaldehyde; phenol-formaldehyde resins; *p*-tertiary-butylphenol-formaldehyde resin; simultaneous contact allergy.

A *p*-tertiary-butylphenol-formaldehyde resin (PTBP-FR) has been included in most baseline patch test series for decades, but this resin does not detect contact allergy to phenol-formaldehyde resins (PFRs) based on phenol and formaldehyde (1–4). Even though there are various resins based on phenol and formaldehyde, PFR-2 (mixture of monomers and dimers from a resol resin based on phenol and formaldehyde) seems to be a good marker for contact

allergy to such resins (1, 3, 5). In the past, it was shown that not only did patch testing with PFR-2 detect patients allergic to the specific resol resin, but simultaneous allergic reactions were also seen to fragrance mix I (FM I), colophonium, and *Myroxylon pereirae* (6). Five centres representing the Swedish Contact Dermatitis Research Group included PFR-2 in their baseline series for a period of 1.5 years to identify the contact allergy rate in the tested population and to investigate possible simultaneous allergic reactions. We also aimed to compare our test results with those of a former study from 1986 (6).

Materials and Methods

Five dermatology clinics (A–E) participated in the study, and a total of 2504 dermatitis patients were tested during

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the time period 1 July 2006 to 31 December 2007. There were 1590 women and 914 men; the mean age was 42.5 years for women (range 5–88 years) and 43.0 years for men (range 12–84 years). The baseline series was purchased from Chemotechnique Diagnostics (Vellinge, Sweden) and supplemented with PFR-2 1.0% w/w in petrolatum from the same supplier in clinics B–D; clinic A already had the test preparation in their baseline series. PFR-2 is a mixture of monomers and dimers from a resol resin based on phenol and formaldehyde (7). The test techniques used were Finn Chambers® (diameter 8 mm) (Epitest Oy, Tuusula, Finland) on Scanpor® tape (Norgesplaster A/S, Vennesla, Norway) in centres A–D, and IQ Ultra® chambers on a high-quality hypoallergenic surgical tape (Chemotechnique Diagnostics) in centre E. The patch testing personnel placed 20 mg of each test preparation into each Finn Chamber (8). In centre A, a micropipette was used when testing liquid test solutions such as formaldehyde (15 µl in each Finn Chamber); the remaining centres let the test solution drop onto the filter paper from the test bottle. Patch tests were removed after 2 days, and read after an additional day or two, according to International Contact Dermatitis Research Group criteria (9). A second reading was performed 7 days after application of patches. A dermatologist read all patch tests in centres A, B, D and E on both days, whereas centre C utilized a specialized nurse for the first reading and a dermatologist for the second one.

Statistical methods

Fisher's exact test for two proportions (two-sided) was used for the statistical analysis, and a *p*-value < 0.05 was regarded as statistically significant.

Results

Of 2504 patients tested, 27 (1.1%) reacted to PFR-2. Of those 27 individuals, 2 had a positive reaction to formaldehyde and 2 to PTBP-FR. Simultaneous allergic reactions were noted to colophonium in 6 patients, to *M. pereirae* in 14, and to FMI in 15 (Table 1). The numbers of allergic patch test reactions to PFR-2, colophonium, *M. pereirae*, PTBP-FR, formaldehyde and FMI in the whole population tested are shown in Table 2.

Comparison of the patch test results for PFR-2 on D3 with those on D7 shows that 25.9% of the allergic reactions would have been missed had a D7 reading not been performed.

Discussion

In this study comprising five centres, the frequency of contact allergy to PFR-2 was 1.1%, a figure that merits

its inclusion in the Swedish baseline series (10). The resol resin PFR-2 has been tested in the baseline series in centre A, Malmö, Sweden for decades, because there has been a manufacturer of resol resins associated with occupational skin diseases in the area (11, 12). Binders based on PFR-2 are also used in the production of adhesives, laminates, impregnation products, surface coatings, and casting sand, and many cases of allergic contact dermatitis have been published (4, 13, 14). The clinical relevance of the allergic reactions to PFR-2 and the other allergens was intentionally not included in the study, and this may at first seem to be a weakness. Identifying the clinical relevance of any sensitizer is not standardized, and it would be necessary to have the capacity to analyse chemically the presence of the 14 separate individual sensitizers identified in PFR-2, a task that very few centres in the world could perform. PFRs are known to be both irritants and potent sensitizers, and contain methylol-substituted monomers and dimers, which are the major sensitizers (1, 7). As stated earlier, the common PTBP-FR does not detect contact allergy to PFRs based on phenol and formaldehyde, and patients allergic to this latter resin will be missed if PFR-2 is not tested. In this study, less than 10% of patients allergic to PTBP-FR had a simultaneous contact allergy to PFR-2 (Table 2).

Furthermore, among those 27 patients allergic to PFR-2, simultaneous reactions to colophonium, *M. pereirae* and FMI in the baseline series were seen in 22.2%, 51.9% and 55.6%, respectively, possibly because of the presence of low molecular weight phenols in these compounds (6). This pattern of simultaneous reactions was already shown by Bruze in the middle of the 1980s (6). Interestingly, 14 of the 27 PFR-2-allergic patients had multiple contact allergies, that is, three or more. One consequence of these simultaneous test reactions is that an unexplained allergic test reaction to *M. pereirae* or FMI could indicate a clinically relevant contact allergy to PFR-2 (15).

Even though formaldehyde is one of the main raw materials in the production of PFRs, only 4.1% of those allergic to formaldehyde reacted to PFR-2; that is, 93% of the patients with contact allergy to PFR-2 did not react to formaldehyde. However, allergic contact dermatitis resulting from PFR-impregnated casting sand has been attributed to formaldehyde (16, 17).

The high frequency of positive reactions to PFR-2 that would have been missed if a D7 reading had not been performed reinforces the importance of a late (D7) reading. This has also been seen in a study from The Netherlands, where 20.0% of positive reactions to a PFR were only seen on the D6/D7 reading (18).

Table 1. Patch test results in 27 patients with a contact allergy to phenol-formaldehyde resin (PFR)-2 and the pattern of simultaneous allergic patch test reactions to *p*-tertiary-butylphenol-formaldehyde resin (PTBP-FR), colophonium, formaldehyde, *Myroxylon pereirae*, and fragrance mix I, respectively

Centre and patient no.	PFR-2 1.0% pet.		PTBP-FR 1.0% pet.		Colophonium 20.0% pet.		Formaldehyde 1.0% aqua		<i>Myroxylon pereirae</i> 25.0% pet.		Fragrance mix I 8.0% pet.	
	D3/D4	D7	D3/D4	D7	D3/D4	D7	D3/D4	D7	D3/D4	D7	D3/D4	D7
A 1	—	+	—	?	—	—	—	—	++	+	++	+
A 2	+++	+++	—	—	?	—	—	—	++	++	+	+
A 3	++	+	—	—	—	—	—	—	—	—	—	—
A 4	++	++	—	—	—	—	—	—	+	—	—	—
A 5	++	++	—	—	—	—	—	—	—	—	—	—
A 6	?	+	—	—	—	—	—	—	?	—	—	—
A 7	+	—	—	—	—	—	—	—	++	+	+++	+++
A 8	++	?	—	—	—	—	—	—	++	+	+	?
A 9	++	++	—	—	—	—	—	—	—	—	—	—
A 10	+	—	—	—	—	—	—	—	—	—	—	—
A 11	—	+	—	—	—	—	—	—	—	—	++	—
A 12	++	++	+	++	?	+	—	—	++	+	+++	+
B 1	++	++	—	—	—	++	—	—	+++	++	+++	++
B 2	+	+	—	—	—	—	—	—	+	+	+	+
C 1	++	+	—	—	—	—	—	—	IR	IR	++	IR
C 2	+	++	—	—	++	++	—	—	++	++	++	+
C 3	—	+	—	—	—	—	—	—	++	+	+	+
C 4	+++	+++	—	—	+	+	—	—	—	—	—	—
D 1	+	—	—	—	—	—	—	—	—	—	—	—
D 2	—	+	—	—	—	—	+	—	+	—	+	—
D 3	—	+	—	—	—	—	—	—	—	—	—	—
D 4	+	+	—	—	—	—	—	—	+	—	+	—
D 5	+	+	—	—	—	—	+	+	+	+	—	—
D 6	+	+	—	—	—	—	—	—	+	+	++	+
D 7	+	—	++	+	++	+	—	—	—	—	—	—
D 8	+	—	—	—	+++	++	—	—	—	—	—	—
E 1	—	+	—	—	—	—	—	—	—	—	+++	+
Total number of allergic reactions/sensitizer independent of reading day	27		2		6		2		14		15	

IR, irritant reaction.

Table 2. Number and percentage of allergic patch test reactions to phenol-formaldehyde resin (PFR)-2, *p*-tertiary-butylphenol-formaldehyde resin (PTBP-FR), colophonium, *Myroxylon pereirae*, formaldehyde and fragrance mix I in each centre and in the whole patch-tested population of 2504 patients

Centre	PFR-2, n (%)	PTBP-FR, n (%)	Colophonium, n (%)	Formaldehyde, n (%)	<i>Myroxylon pereirae</i> , n (%)	Fragrance mix I, n (%)	Total no. of tested patients
A	12 (1.1)	10 (1.0)	39 (3.7)	23 (2.9)	74 (7.0)	81 (7.7)	1051
B	2 (0.8)	3 (1.2)	6 (2.5)	5 (2.1)	15 (6.3)	12 (5.0)	239
C	4 (2.3)	0	6 (3.5)	3 (1.7)	7 (4.0)	6 (3.5)	173
D	8 (1.2)	7 (1.0)	22 (3.2)	13 (1.9)	40 (5.8)	55 (8.0)	685
E	1 (0.3)	3 (0.8)	12 (3.4)	5 (1.4)	21 (5.9)	9 (2.5)	356
Total no. of allergic reactions	27 (1.1)	23 (0.9)	85 (3.4)	49 (2.0)	157 (6.3)	163 (6.5)	2504
Simultaneous allergy to PFR-2 in those patients with other allergies*	Not relevant	2/23 (8.7)	6/85 (7.1)	2/49 (4.1)	14/157 (8.9)	15/163 (9.2)	

*Contact allergy to PTBP-FR, colophonium, formaldehyde, *Myroxylon pereirae*, and fragrance mix I.

During this testing in five centres, no reactions to PFR-2 appearing beyond day 7 were noted; that is, no patch test sensitization was noted.

In conclusion, testing with PFR-2 is needed to detect contact allergy to resol resins based on phenol-formaldehyde. The contact allergy frequency in the tested population (1.1%) merits its inclusion in the Swedish baseline series, and possibly also in other baseline series after appropriate investigations, such as multicentre

patch-testing in a country. Simultaneous allergic reactions were noted to colophonium, *M. pereirae*, and FM I.

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