

Screening allergic reactions to resol resin based on phenol and formaldehyde in a clinic of occupational dermatology

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Summary

Background. Allergic reactions to resol-type phenol formaldehyde resin [phenol formaldehyde resin 2 (PFR2)] are relatively common. It has been suggested that PFR2 should be included in baseline series. However, a recent international study found clinical relevance in only 25% of patients.

Objectives. To report the results of screening with PFR2 over a 5-year period (2012–2016), and to study the clinical relevance of allergic reactions to PFR2 over a 15-year period (2002–2016).

Methods. At the Finnish Institute of Occupational Health, PFR2 was added to the baseline series in 2012. We had previously tested PFR2 in the plastic and glue series. We searched the patch test files for patients with allergic reactions to PFR2, and analysed their patch test results, occupation, exposure, and diagnosis.

Results. During the screening period of 5 years, a total of 10 (1.6%) patients reacted positively to PFR2. Seven of these had occupational allergic contact dermatitis caused by phenol formaldehyde resin (PFR). In 3 patients, we found no exposure to PFR. Over the preceding 10 years, the clinical relevance of 10 additional allergic reactions to PFR2 was similarly high.

Conclusions. In an occupational dermatology clinic, 70% of PFR2 reactions were clinically relevant. Further studies in general dermatology clinics are needed.

Key words: carpenter; chipboard; colophonium; filter paper; foundry; grinding wheel; laminate; monomethylol phenol; phenol formaldehyde resin; plywood worker.

Phenol formaldehyde resins are polymers manufactured from various phenols and formaldehyde. Resol-type phenol formaldehyde resins are manufactured with an excess of formaldehyde under alkaline conditions. They contain monomers and dimers with reactive hydroxymethyl groups, hydroxymethyl phenols, which are the strongest allergens in this group of chemicals (1). Resins

made of different phenols will contain different allergens, and patients should be tested with the specific phenol formaldehyde resin that they are exposed to. However, phenol formaldehyde resin 2 (PFR2) has been shown to be a good marker of contact allergy to various phenol formaldehyde resins (2).

Five centres in Sweden included PFR2 (Chemotechnique, Vellinge, Sweden) in their baseline series, and reported a high frequency (1.1%) of allergic reactions in the patch-tested population. This study did not assess the clinical relevance of the allergic reactions (3). Simultaneous reactions were noted for colophonium, *Myroxylon pereirae*, and fragrance mix I. The ICDRG conducted a similar screening in their baseline series, and reported a similar frequency of allergic reactions, namely, 1.2% (4).

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Simultaneous reactions to *M. pereirae* and fragrance mix I were overrepresented. Clinical relevance was found in 25% of the cases. The authors of this study recommended the inclusion of PFR2 in the ICDRG baseline series, and possibly in other baseline series, after appropriate investigations.

At the Finnish Institute of Occupational Health (FIOH), we included PFR2 (Chemotechnique) in our baseline series in 2012. In this study, we wanted to report the results of this screening over a period of 5 years (2012–2016). We also wanted to study exposure and diagnoses of our PFR2-positive patients, and to expand the retrospective analysis of clinical relevance to a period of 15 years (2002–2016).

Materials and Methods

The FIOH has a clinic of occupational dermatology. All our patients have a suspected occupational skin disease, and they come from all parts of Finland. We ask them to bring samples of the suspected products from the workplace and the products that they use at home. We performed patch tests with Finn Chambers® (Smart Practice, Phoenix, AZ, USA) in accordance with ESCD guidelines (5). We read the tests two or three times: on day (D) 2, D3, and D4, on D2, D3, and D6, or on D2 and D5, depending on the day of application (Monday, Tuesday, or Wednesday). We also asked patients to inform us if they had noticed new reactions after the final reading.

In January 2012, we included 1% PFR2 (pet.; Chemotechnique) in our baseline series. We had previously tested PFR2 in the plastic and glue series. Patients exposed to formaldehyde resins are tested with a special resin series in addition to the plastic and glue series. This special resin series comprises urea, phenol, and melamine formaldehyde resins, which are commonly used in the Finnish woodwork industry. These resins have varied over the years.

After patch testing, exposure to positive allergens is assessed in cooperation with a dermatologist and a chemist. This assessment often includes time-consuming inquiries to the manufacturers if safety data sheets do not provide sufficient information. We decide whether or not a contact allergy is of probable occupational origin. For a diagnosis of occupational allergic contact dermatitis (OACD), we need to identify sufficient exposure to the allergen, and skin symptoms must be related to this exposure. Allergic reactions to work materials may also support the diagnosis of OACD.

We searched the patch test files for patients with allergic reactions to PFR2 and the phenol formaldehyde resins of the resin series. We analysed the data regarding their

occupations, patch test reactions, exposure, and diagnoses.

Results

During the screening period 2012–2016, a total of 635 patients were tested with PFR2 in the baseline series. Ten (1.6%) of these reacted positively to this allergen. Seven (70%) had been diagnosed with OACD caused by phenol formaldehyde resin. All of these 7 patients were tested with the special resin series and the plastic and glue series in the first patch test session. Table 1 shows the details of these patients (patients 1–7). We were unable to identify exposure to phenol formaldehyde resins among the remaining 3 patients. One of them, a cleaner (PFR2 reaction +++), was sensitized to formaldehyde (2% aq. +); the second patient, a boat upholsterer (PFR2 reaction +), was extremely sensitized to colophonium; and the third patient, an assistant nurse (PFR2 reaction +), was strongly sensitized to *p*-tert-butylphenol formaldehyde resin (PTBPFR). The third patient was not tested with the plastic and glue series (or the special resin series) in the first patch test session, and her PFR2 allergy would not have been found without screening in the baseline series. She needed the second patch test session in any case for confirmation of OACD caused by rubber accelerators.

During the period 2002–2011, a total of 10 patients (of 605) reacted positively to PFR2 when it was tested in the plastic and glue series. Six of these had been diagnosed with OACD or occupational contact allergy caused by phenol formaldehyde resins, and their details are shown in Table 2 (patients 8–13). One of the remaining 4 patients had used a glue based on phenol formaldehyde resin in his leisure time (PFR2 reaction ++). The second patient, a worker in a shoe factory (PFR2 reaction +), had probable occupational contact allergy to PTBPFR (++) from shoe glues, but current personal exposure to PTBPFR was not found. The third patient, a nurse (PFR2 reaction ++), had non-occupational contact allergy to PTBPFR (++) and the fourth patient, a laboratory assistant in a concrete production plant (PFR2 reaction ++), was not exposed to phenol formaldehyde resins at work or home. Thus, exposure to phenol formaldehyde resin was identified in 7 of 10 patients in this group.

During the period of 15 years (2002–2016), another 3 patients had occupational contact allergy to phenol formaldehyde resins without a clear allergic reaction to PFR2 (2 patients in 2012–2016, and 1 patient in 2002–2011). They reacted positively to some phenol formaldehyde resins in the special resin series. Two of these were plywood workers, and 1 was a driver who

Table 1. Patients who reacted positively to phenol formaldehyde resin 2 (PFR2) in the baseline series (2012–2016) and who had occupational allergic dermatitis caused by phenol formaldehyde resin (PFR). Description of their occupations, and patch test reactions to PFR-related allergens (also cross reacting substances in the baseline series) and patients' own products

Occupation (task)	1	2	3	4	5	6	7
Patch test results	Furniture production worker (tooling of chipboard)	Plywood worker	Plywood worker	Plywood worker	Plywood worker	Plywood worker	Laminate production worker
PFR2	+++	+	+++	+++	++	+	+
Formaldehyde	–	–	IR*	++	+	–	++
PTBPFR	–	–	–	–	–	–	–
Colophonium	++	–	–	–	–	–	–
<i>Myroxylon pereirae</i> (balsam of Peru)	+++	–	–	–	–	–	–
Fragrance mix I	IR	–	–	+	–	–	–
Monomethylol phenol	+++	–	–	–	–	–	–
Resin series test substances (all 5% pet.)							
Resorcinol-PFR Prefere 4030†	+++	?+	+++	+++	+	?+	?+
PFR Prefere 707916L‡	NT	++	+++	+++	++	++	?+
PFR Phenodur PR 263§	+++	–	+++	+++	+	+	+
PFR Prefere 707530†	+++	NT	NT	NT	NT	NT	NT
Own products	Chipboard dust moistened with water ++ Ultrasonic extract (ethanol) from chipboard dust +++ Ultrasonic extract (acetone) from chipboard I +++ Ultrasonic extract (acetone) from chipboard II +++ Ultrasonic extract (ethanol) from chipboard II + Ultrasonic extract (ethanol) from chipboard dust III +	PFR Prefere 141810† 5% ?+ Chipboard dust ++ Ultrasonic extract (ethanol) from chipboard dust +++ Ultrasonic extract (acetone) from chipboard I +++ Ultrasonic extract (acetone) from chipboard II +++ Ultrasonic extract (ethanol) from chipboard II + Ultrasonic extract (ethanol) from chipboard dust III +	PFR Prefere 141810† 2% + Chipboard dust ++ Ultrasonic extract (ethanol) from chipboard dust +++ Ultrasonic extract (acetone) from chipboard I +++ Ultrasonic extract (acetone) from chipboard II +++ Ultrasonic extract (ethanol) from chipboard II + Ultrasonic extract (ethanol) from chipboard dust III +	PFR Prefere 141021† 5% +++ 1.6% +++ Ultrasonic extract from Phenol Film in acetone +++ ethanol +++ Ultrasonic extract from Imprex Film in acetone +++ ethanol +++	PFR Prefere 1072§ phenol resin 1% ?+ Ultrasonic extract from Phenol Film in acetone +++ ethanol +++ Ultrasonic extract from Imprex Film in acetone +++ ethanol +++	PFR Prefere 1072§ phenol resin 5% – Ultrasonic extract (acetone) from laminate ++	PFR Prefere 707935L† 5% + Ultrasonic extract (acetone) from laminate ++

IR, irritant reaction; ?+, doubtful reaction; NT, not tested; PTBPFR, *p-tert*-butylphenol formaldehyde resin.

Baseline series allergens were purchased from Trolab (Almirall Hermal (Reinbek, Germany) in 2012–2015 and from Chemotechnique (Vellinge, Sweden) in 2016 (applied to patient 3).

*Formaldehyde was tested 1%, and a micropipette was not used.

†Prefere resins, Erkner, Germany.

‡Allnex, Luxembourg.

§Hexion, Puhos, Finland.

Table 2. Patients who reacted positively to phenol formaldehyde resin 2 (PFR2) in the plastic and glue series (2002–2012) and who were exposed to phenol formaldehyde resins (PFRs) at work. Their occupations, PFR-related diagnosis, and patch test reactions to PFR-related allergens (also cross-reacting substances in the baseline series) and patients' own products.

Occupation (task)	Patient no.					
	8	9	10	11	12	13
Worker in production of sanding discs/grinding wheels		Furniture production worker	Foundry worker	Carpenter (tooling of high-pressure laminate in furniture production)	Assembler in the production of filters for machines and vehicles (handling of PFR-impregnated filter papers)	Plywood worker
PFR-related diagnosis	OACD	OCA	OACD	OACD	OACD	OACD
Patch test results						
PFR2	++	++	+	+	++	+
Formaldehyde	–	–	IR	–	–	–
PTBPFR	–	–	+	–	–	–
Colophonium	–	–	+++	–	–	–
<i>Myroxylon pereirae</i> (balsam of Peru)	–	–	+	–	–	–
Fragrance mix I	–	–	++	?+	++	–
Monomethylol phenol (1% pet.)	–	–	–	–	–	–
Resin series test substances (all 5% pet.)						
Resorcinol-PFR Prefere 4030*	++	–	NT	–	NT	NT
PFR Phenodur PR 263†	++	–	–	+	++	–
PFR Prefere 707530*	++	–	NT	+	NT	NT
PFR Fenorex 6260	NT	NT	–	NT	++	++
PFR Pribex 7530	NT	NT	–	NT	++	?+
Patient's own products	PFR Prefere 807841* 5% ++			Floor laminate dust 10% pet. ++ Ultrasonic extract (ethanol) from laminate dust ++	Binzer 1 phenolic resin type 1 5% ++ Filter paper ++	Boy PF 10 phenol resin 10% ++

IR, irritant reaction; OACD, occupational allergic contact dermatitis; OCA, occupational contact allergy; NT, not tested; PTBPFR, *p-tert* butylphenol formaldehyde resin.

Baseline series allergens were from Trolab.

*Prefere resins, Erkner, Germany.

†Allnex, Luxembourg.

transported phenol formaldehyde resins to plywood factories and had to wash the containers of the vehicle regularly. Thus, PFR2 detected 14 (82%) of the 17 cases with relevant contact allergy to phenol formaldehyde resins during the whole period of 15 years.

Discussion

The frequency of allergic reactions to PFR2 during the screening period at the FIOH was higher than that in the two previous multicentre screening studies (3, 4). This is not surprising, as all of our patients are referred for suspected occupational contact allergy. Patients exposed to multiple chemicals (especially resins) are overrepresented at the FIOH in comparison with patients in general dermatology clinics. In contrast to the findings of the ICDRG study, the reactions to PFR2 were also mostly relevant at the FIOH; that is, exposure to phenol formaldehyde resins was found, and patients' symptoms were at least partly caused by this exposure.

In the ICDRG study, 20% of the allergic reactions were not seen on D3 or D4, but first appeared on D7 (4). In the Swedish study, the corresponding figure was 26% (3). Our frequency of allergic reactions might have been considerably higher if we had regularly performed a D7 reading. On the other hand, D7 reactions to PFR2 might represent cross-reactions more often than D3–D4 reactions, and the relatively low concentration of the commercial PFR2, namely 1% (see below), might also lead to D7 reactions. In fact, we prefer Monday tests with readings on D2, D3 and D4 for patients with suspected phenol formaldehyde resin allergy, because we suspect that some patients have the strongest reactions to phenol formaldehyde resins during the weekend (on D4–D5 or D3–D4), and we see only doubtful reactions on Friday and/or Monday.

Simultaneous allergic reactions to *M. pereirae* (balsam of Peru), fragrance mix I and PTBPFR were approximately as common as in the ICDRG study, and simultaneous allergic reactions to colophonium were as common as in the Swedish multicentre study. Simultaneous reactions to formaldehyde were more common than in the two preceding studies, but true overrepresentation was negligible, because the group was small and formaldehyde allergy has been very common in our patient population (6). Only 1 of our 20 PFR2-positive patients reacted to 2-monomethylolphenol (1% pet.; Chemotechnique), which is a known allergen in phenol formaldehyde resins.

Considering these high frequencies of allergic reactions to PFR2, reports of contact allergy to phenol formaldehyde resins are relatively scarce (1). In the present study population, PFR2 allergy was most commonly found

in workers involved in the production of plywood: the number of PFR2-positive plywood workers was 6, and 2 plywood workers were diagnosed by testing with the special resin series. Rademaker reported 2 plywood workers with phenol formaldehyde resin allergy in New Zealand (7). One of our patients worked in a foundry and was exposed to phenol formaldehyde-impregnated casting sand, a source of phenol formaldehyde resin sensitization that has been previously described (8, 9). One of our patients was sensitized while producing grinding wheels composed of abrasive material sealed with a phenol formaldehyde resin glue. Older studies have found the production of abrasive paper and the use of grinding wheels to be sources of sensitization to phenol formaldehyde resin (1). One of our patients handled resin-impregnated filter papers. Phenol formaldehyde resin allergy caused by filters has also been found in previous studies (1). Laminate production workers with phenol formaldehyde resin allergy have been reported in Sweden (10). Our study population included 1 patient working in the lamination of chipboard. Three of our patients were joiners in the production of furniture, and were exposed to phenol formaldehyde resins when tooling chipboard, laminate, or plywood. Two of these reacted positively to dust from laminate or chipboard or ultrasonic extracts made from chipboard. Owen and Beck have reported a case in a patient working in a joinery (9).

Should PFR2 be included in the European baseline series? Our findings are not in opposition to this possibility. The present data confirm that PFR2 is a good marker of contact allergy to phenol formaldehyde resins, as it detected 82% of our cases with relevant allergy. The woodwork industry is important in Finland, and PFR2 screening in Finnish general dermatology clinics might yield more clinically relevant allergic reactions than the ICDRG study (4). At the FIOH, PFR2 screening in the baseline series did not really help us to find patients with a relevant contact allergy. Their exposure to phenol formaldehyde resin was so clear that they would all have been found by testing with the plastic and glue series. In addition, the screening in our practice caused no harm (for example, delays resulting from unnecessary retesting): the only patient who was not tested with the plastic and glue series in the first session and whose allergy would not have been found without PFR2 screening needed a second session for other reasons.

Over the period of 15 years, 3 cases of OACD caused by phenol formaldehyde resin were not detected by PFR2. Thus, testing with patients' own resins is important. Phenol formaldehyde resin can usually be tested in a concentration of 5% pet., but not always: the pH of the test

substance must always be checked, because some of the products are extremely alkaline. Bruze reported two late reactions to PFR2 5% pet. among 564 tested persons (2). We have not seen late reactions to patients' own phenol formaldehyde resins or phenol formaldehyde resins in our special resin series, although we usually test them at 5%. Adjusting the pH in pet.-based test substances is not possible, but lower concentrations (1% or 2%) can

be chosen. Testing with ultrasonic extracts made from various resin-containing materials was also useful for assessing relevance.

In conclusion, PFR2 screening in the baseline series at the FIOH yielded allergic reactions at a frequency of 1.6%, and as many as 70% of these reactions were clinically relevant. This encourages further studies on PFR2 screening in general dermatology clinics.

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