Western University Scholarship@Western

Chemistry Publications

Chemistry Department

4-25-2021

Patch testing with aluminium Finn Chambers could give falsepositive reactions in patients with contact allergy to aluminium

Lisbeth Rosholm Comstedt

Jakob Dahlin

Magnus Bruze

Yolanda S. Hedberg

Mihály Matura

See next page for additional authors

Follow this and additional works at: https://ir.lib.uwo.ca/chempub

Part of the Chemistry Commons

Authors

Lisbeth Rosholm Comstedt, Jakob Dahlin, Magnus Bruze, Yolanda S. Hedberg, Mihály Matura, and Cecilia Svedman

ORIGINAL ARTICLE



Patch testing with aluminium Finn Chambers could give falsepositive reactions in patients with contact allergy to aluminium

Lisbeth Rosholm Comstedt¹ | Jakob Dahlin¹ | Magnus Bruze¹ | Yolanda Hedberg² | Mihály Matura³ | Cecilia Svedman¹

¹Department of Occupational and Environmental Dermatology, Skåne University Hospital, Lund University, Malmö, Sweden

²Department of Chemistry, The University of Western Ontario, London, Ontario, Canada

³Department of Dermatology, Skaraborg Hospital Skövde, Skövde, Sweden

Correspondence

Lisbeth Rosholm Comstedt, Department of Occupational and Environmental Dermatology, Skåne University Hospital, Jan Waldenströmsgata 16, plan 5, S-20502 Malmö, Sweden. Email: lisbeth.rosholm_comstedt@med.lu.se

Abstract

Background: Earlier laboratory studies have shown that sodium tetrachloropalladate, *Myroxylon pereirae*, caine mix II, and palladium chloride trigger the release of aluminium (AI) from Finn Chambers (FC).

Objectives: To investigate whether aluminium realease from FC could influence the diagnostic outcome of patch testing with FC.

Method: A retrospective analysis of patch test results from 2010 to 2019 was performed. A two-sided Fisher's exact test was used to calculate any overrepresentation of contact allergy to Al among patients with positive reactions to sodium tetrachloropalladate, *Myroxylon pereirae*, caine mix II, and palladium chloride.

Results: A total of 5446 patients had been tested with FC during the study period. There was a significant overrepresentation of contact allergy to AI among patients with positive reactions to sodium tetrachloropalladate, *Myroxylon pereirae*, caine mix II, and palladium chloride. Patients with a strong AI allergy had significantly higher amounts of concomitant reactions to sodium tetrachloropalladate, *Myroxylon pereirae*, caine mix II, and palladium chloride compared to patients with weak AI allergy. These results were not seen for patients tested with Finn Chambers AQUA. **Conclusion:** In patients with contact allergy to AI, patch testing with Finn chambers could give false-positive reactions to sodium tetrachloropalladate, *Myroxylon pereirae*, caine mix II, and palladium chloride.

KEYWORDS

aluminium corrosion, caine mix II, contact allergy to aluminium, Finn chambers, *Myroxylon pereirae*, palladium chloride, sodium tetrachloropalladate

1 | INTRODUCTION

Patch testing is an in vivo test considered to be the gold standard in the diagnosis of contact allergy. Patch testing needs to be performed under standardized procedures, and taking into consideration all practical aspects from storage and purity of test substances, through loading and applying the chambers, to reading the results.¹⁻⁷ The

European Society of Contact Dermatitis recommends optimal dosing for Finn chambers (aluminium chambers; SmartPractice, Phoenix, Arizona), Van der Bend chambers (plastic chambers; Van der Bend Medical Supplies, Brielle, Netherlands), and IQ chambers (plastic chambers; Chemotechnique Diagnostics, Vellinge, Sweden), which are the three most commonly used test chamber systems.⁷ Finn chambers (FCs) are made of aluminium (Al), which is normally a passive (non-corroding)

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

 $\ensuremath{\mathbb{C}}$ 2021 The Authors. Contact Dermatitis published by John Wiley & Sons Ltd.

² WILEY-CONTAC

metal. When in contact with air or water it forms a thin surface laver of Al oxide, which makes the metal resistant to corrosion.⁸ As with most passive metals, it might, however, locally corrode under certain conditions, such as in the presence of salts.⁸

The prevalence of contact allergy to Al is low⁹ and patients with contact allergy to AI do not normally react to an empty FC.¹⁰ This suggests that FCs are a safe choice in standard patch testing. A new system, Finn Chamber AQUA (FCA), has been developed, for which the Al chamber is coated with absorbent paper. This test system was developed to resist moisture and remain in place even during exercise and showers.¹¹

New chemical analyses from Hedberg et al. show, however, that various patch test preparations can induce AI release from Finn chambers in vitro due to Al corrosion.¹² In the study, different batches of FC and FCA were investigated with 32 different baseline preparations. These were exposed to artificial sweat containing 5.0 g/L NaCl, 1.0 g/L urea, 1.0 g/L lactic acid, with the pH adjusted to 6.5.¹² It was found that sodium tetrachloropalladate hydrate (Na-Pd) 3% pet. and caine mix II (CM II), 10% pet. released significantly higher amounts of Al compared to an Al Finn Chamber in artificial sweat. Palladium chloride (Pd-Cl) 2% pet. and Myroxolon pereirae (MP) 25% pet. also induced increased Al release in FC, although not statistically significant.¹² The explanation for the AI release is that surface-available chlorides from metal salts can cause localised corrosion (pitting corrosion) to AI metal.^{8,12} Several metal salts used for patch testing contain chloride ions. Acids, especially in the combination with chlorides from sweat, can also cause corrosion to Al metal.¹³ MP contains high amounts of organic acid and CM II contains hydrochloric acid, which is corrosive to Al.¹² The Al -release from FC into artificial sweat was found to be 16-4100-fold higher than the AI release from FCA.

FC with 8 mm inner diameter have been used for the past 40 years, until 2017, as standard chambers when patch testing at the Department of Occupational and Environmental Dermatology, Skåne University Hospital Malmö, Sweden. As a result of a change in work routines in 2018, we currently use FCA as standard chambers.

Contact allergies to nickel and palladium are known to crossreact.¹⁴⁻¹⁶ In an earlier study,¹⁷ we discussed the relevance of contact allergy to palladium when the patient was not allergic to nickel. After discussion on preliminary results on triggered AI release from FC, later published in,¹² we raised the guestion whether positive reactions to Na-Pd and Pd-Cl without concomitant reactions to nickel sulphate hexahydrate (Ni) could be an expression of contact allergy to Al.

The aim of this retrospective study was to investigate whether AI release from FCs could have had any influence on our diagnostic outcomes of patch testing during the years when we used FCs. Our research questions were as follows:

1. Is there an overrepresentation of simultaneous contact allergies to MP, CM II, Na-Pd, and Pd-Cl among patients with Al allergy and, at the same time, no overrepresentation of simultaneous allergies to test preparations with substances known to not trigger AI release in artificial sweat, such as fragrance mix 1 (FM 1), Ni, potassium dichromate (K-Cr), and tixocortol-21-pivalate (TP)?

- 2. Is the number of simultaneous positive reactions to possible combinations of MP, CM II, Na-Pd, and Pd-Cl higher among patients with contact allergy to Al compared with patients not allergic to Al?
- 3. Is there an overrepresentation of patients with palladium allergy without simultaneous nickel allergy as compared to those with both palladium and nickel allergy among patients with contact allergy to Al?
- 4. Do patients with a strong Al allergy have more concomitant reactions to MP, CM II, Na-Pd, and Pd-Cl compared to patients with a weak Al allergy?
- 5. In cases of an overrepresentation of contact allergies to MP, CM II, and palladium among patients with contact allergy to Al, is there also an overrepresentation of these contact allergies when the patients were tested with FCA?

2 METHOD AND MATERIAL

2.1 Method

We conducted a retrospective study of patch test results from 2010-2019 at the Department of Occupational and Environmental Dermatology Skåne University Hospital, Malmö, Sweden. All patch test data and basic characteristics of the patients were filed in our computer system, Ekta. For the data analysis, irritant and doubtful reactions were classified as negative reactions. Positive reactions included +, ++, and +++ reactions.⁷

2.2 **Subjects**

All patients patch tested with FC, the Swedish baseline series, and the extended Malmö baseline series because of suspected contact allergy at the Department of Occupational and Environmental Dermatology, Skåne University Hospital, Malmö, from 01-01-2010 until 31-12-2017 were included. Corresponding patients tested with FCA from 01-01-2018 until 31-12-2019 were also included. One hundred and sixty-nine patients were tested two or more times, but these were counted as one test occasion in this study. In the cases where a patient had developed new contact allergies at a later test occasion, all the positive reactions from the past and the present were counted as one test occasion. Patients who had not been tested with all the substances (MP, CM II, Na-Pd, Pd-Cl, FM 1, Ni, K-Cr, TP) and patients who had not been tested with any of the Al substances (aluminium chloride hexahydrate (Al-Cl) or aluminium lactate (Al-lac)) were excluded from the study.

Patch testing and patch test readings 2.3

Table 1 shows the concentration and suppliers of the selected test substances that were used in our baseline series and our extended

Substance	Supplier	Vehicle	Concentration w/w, %		
Aluminium chloride hexahydrate	MPBio-medicials, Inc. Eschwege, Germany	Pet.	10		
Aluminium lactate	Sigma Aldrich, Steinheim, Germany	Pet.	12		
Myroxolon pereirae	Chemotechnique Diagnostics, Vellinge, Sweden	Pet.	25		
Caine mix II	Chemotechnique	Pet.	10		
Sodium tetrachloro-palladate	Sigma Aldrich	Pet.	3		
Palladium chloride	Chemotechnique	Pet.	2		
Fragrance mix 1	Chemotechnique	Pet.	8		
Potassium dichromate	Chemotechnique	Pet.	0.5		
Nickel sulphate hexahydrate	Chemotechnique	Pet.	5		
Tixocortol-21-pivalate	Chemotechnique	Pet.	0.1		
Finn Chambers and Finn Chambers AQUA	(Epitest Ltd Oy, Tuusula, Finland or Smart-Practice, Phoe (Norgeplaster A/S) Oslo, Norway	nix, Arizona, USA) mo	ounted on Scanpor tape,		

TABLE 1 Suppliers and concentration of patch test material for the selected test substances used at the Department of Occupational and Environmental Dermatology, Skåne University Hospital, Malmö, Sweden, 2010–2019

Note: The applied amount is 20 mg in all these cases and the inner chamber area is 0.5 cm².

baseline series during the study period. The patch test preparations were applied on the upper back of the patients with 20 mg of the test preparation in 8 mm FC or FCA.⁷ All test personnel were trained and their dosing technique was regularly validated during the study period. The patch tests were removed on day (D) 2. Readings were performed twice, on D3 or D4 and D7.

2.4 | Ethics

The study was approved by the Regional Ethical Review Board, Lund Sweden (Dnr 2020/02190). When patients are patch tested they are informed that data may be used for comparisons on a group level and approval is mandatory if the patients' data are stored in the computer system.

2.5 | Definition

Contact allergy to AI was defined as either a positive reaction to AI-CI and/or AI-lac.

Isolated palladium allergy was defined as positive reactions to Na-Pd and/or Pd-Cl without concomitant reactions to Ni, independent of any other contact allergy.

2.6 | Statistical analysis

A two-sided Fisher's exact test was performed using SPSS software, version 26 (IBM, Armonk, NY) and was used to calculate whether the difference in prevalence of MP, CMII, Na-Pd, Pd-Cl, isolated palladium allergy, FM1, Ni, K-Cr, and TP between patients with and without contact allergy to Al was statistically significant. The test was also used to calculate whether there was a statistically significant difference in concomitant reactions in patients with a strong Al allergy (3+/2+) compared to patients with a weak Al allergy (1+).

3 | RESULTS

A total of 5446 consecutive patients were patch tested with FC and the substances AI, MP, CM II, Na-Pd, Pd-Cl, FM 1, Ni, K-Cr, and TP during 2010–2017; 3636 were female (66.8%) and 1810 were male (33.2%); mean age was 44.4 years. Forty-eight (0.9%) patients had contact allergy to AI. Positive patch test reactions to MP, CM II, Na-Pd, and Pd-Cl were all overrepresented in patients with contact allergy to AI, whereas positive patch test reactions to FM 1, Ni, K-Cr, or TP were not. Table 2 shows the prevalence and distribution of contact allergy to the test substances among patients with and without AI allergy.

Table 3 shows the prevalence of concomitant reactions to MP, CM II, Na-Pd, and Pd-Cl and concomitant reactions to FM 1, Ni, K-Cr, and TP in those with and without Al allergy.

Five hundred and twenty-five (9.6%) patients were positive to either Na-Pd or Pd-Cl. Ten of the palladium-allergic patients had contact allergy to Al (patients 4–10 and 24–26, Table 4); 77 (14.7%) patients had an isolated palladium allergy. Contact allergy to Al was significantly overrepresented in those with an isolated palladium allergy compared to patients with concomitant reactions to nickel and palladium (5/10 vs 5/448 P < .001).

Among the 48 patients with positive reactions to Al, 20 patients had 3+ / 2+ reactions to Al and 28 patients had a 1+ reaction (Table 4). Among the 20 patients with a strong allergy (3+/2+), we found 19 reactions to MP and/or CM II, and/or Na-Pd, and/or Pd-CI out of 80 possible reactions. Among the 28 Al-allergic patients with 1 + reactions to Al, we found 11 out of 112 possible reactions to MP and/or CM II, and/or Na-Pd, and/or Pd-CI (19/80 vs 11/112; two-

WILEY_

CONTACT

TABLE 2 Number of concomitant positive patch test reactions to the selected test substances stratified by contact allergy to aluminium

Positive reactions to	Chamber	Number (%)	Aluminium positive (%)	Aluminium negative (%)	P-value
Myroxolon pereirae	Finn Chambers	340/5446 (6.2)	8/48 (16.7)	332/5398 (6.2)	.009
	Finn Chambers AQUA	92/1450 (6.3)	2/11 (18.2)	90/1439 (6.2)	.15
Caine mix II	Finn Chambers	78/5446 (1.4)	4/48 (8.3)	74/5398 (1.4)	.005
	Finn Chambers AQUA	16/1450 (1.1)	0	16/1439 (1.1)	
Sodium tetrachloro-palladat e	Finn Chambers	489/5446 (9.0)	9/48 (18.8)	480/5398 (8.9)	.036
	Finn Chambers AQUA	172/1450 (11.9)	1/11 (9.1)	171/1439 (11.8)	>.99
Palladium chloride	Finn Chambers	382/5446(7.0)	9/48 (18.8)	373/5398 (6.9)	.005
	Finn Chambers AQUA	124/1450 (8.6)	1/11 (9.1)	123/1439 (8.5)	>.99
Isolated palladium ^a	Finn Chambers	77/5446 (1.4)	5/48 (10.4)	72/5398 (1.3)	.001
	Finn Chambers AQUA	38/1450 (2.6)	0	38/1439 (2.6)	
Nickel sulphate hexahydrate	Finn Chambers	924/5446 (17.0)	6/48 (12.5)	918/5398 (17.0)	.56
Fragrance mix 1	Finn Chambers	320/5446 (5.9)	4/48 (8.3)	316/5398 (5.9)	.37
Tixocortol-21-pivalate	Finn Chambers	53/5446 (1.0)	1/48 (2.1)	52/5398 (1.0)	.38
Potassiom dichromate	Finn Chambers	303/5446 (5.6)	4/48 (8.3)	199/5398 (3.7)	.1

Note: Statistically significant differences among the patients with and without aluminium allergy (P < .05) are marked in bold.

^alsolated palladium indicates contact allergy to sodium tetrachloropalladate and or palladium chloride without a simultaneous nickel allergy.

TABLE 3 Number of positive reactions to different combinations of concomitant reactions to the aluminium corrosion triggering test substances and to test substances not triggering aluminium release in artificial sweat

Positive reactions for:	Number (%)	Aluminium positive (%)	Aluminium negative(%)	P-value
MP + CMII	19/5446 (0.3)	3/48 (6.3)	16/5398 (0.3)	<.001
$MP + Na ext{-}Pd$	42/5446 (0.8)	2/48 (4.2)	40/5398 (0.7)	.052
$CMII + Na ext{-Pd}$	15/5446 (0.3)	2/48 (4.2)	13/5398 (0.24)	.007
MP + CMII + Na-Pd + Pd-cl	4/5446 (0.07)	48(2.1)	3/5398 (0.06)	.04
MP + Pd-cl	32/5446 (0.6)	2/48 (4.2)	30/5398 (0.6)	.03
CMII + Pd-cl	11/5446 (0.2)	2/48(4.2)	9/5398 (0.17)	.004
FM1 + K-Cr	27/5446 (0.5)	2/48(4.2)	25/5398 (0.5)	.02
FM1 + Ni	66/5446 (1.2)	1/48(0.2)	65/5398 (1.2)	.44
FM1 + TP	12/5446 (0.2)	0	12/5398 (0.2)	>.99
FM1 + K-Cr + Ni	9/5446 (0.2)	1/0.2	8/5398 (0.15)	.08
K-Cr + Ni	58/5446 (1.1)	1/0.2	57/5398 (1.1)	.40
FM1 + K-Cr + Ni + TP	1/5446 (0.02)	0	1/5398 (0.02)	>.99
FM1 + K-Cr + TP	1/5446 (0.02)	0	1/5398 (0.02)	>.99
FM1 + Ni + TP	2/5446 (0.04)	0	2/5398 (0.04)	>.99
K-Cr+Ni+TP	1/5446 (0.02)	0	1/5398 (0.02)	>.99
K- Cr + TP	2/5446 (0.04)	0	2/5398 (0.04)	>.99
Ni + TP	10/5446 (0.2)	0	10/5398 (0.2)	>.99

Note: The patch test results are stratified by contact allergy to aluminium. Statistically significant differences among the patients with and without aluminium allergy (*P* < .05) are marked in bold.

Abbreviations: CMII, caine mix II; FM1, Fragrance mix 1; K-Cr, potassium dichromate; MPk, Myroxylon pereirae; Na-pd, sodium tetrachloropalladate; Ni, nickel sulphate hexahydrate; Pd-Cl, palladium chloride; TP, tixocortol-21-pivalate.

sided Fisher's exact test, P = .015). These results are illustrated in Figure 1. Figure 2 illustrates that the increased number of concomitant reactions in the group with strong Al allergy was due to an increased number of patients reacting to one or more of the corrosion-triggering substances.

A total of 1450 patients were patch tested with FCA during 2018–2019. Eleven patients were found to have contact allergy to Al (0.8%). Two of these patients had concomitant reactions to MP (18.2%, 2/11 vs 90/1439); (two-sided Fisher's exact test, P = .15). None of the 11 patients had an isolated palladium allergy or concomitant reactions to

Aluminium patch test reaction	Patients number	Myroxylon pereirae	Caine mix II	Na ₂ PdCl ₄	\mathbf{PdCl}_2
3+	1-3	_	-	-	_
	4	-	-	Positive	Positive
	5	Positive	Positive	Positive	Positive
	6	Positive	-	Positive	Positive
2+	7-9	-	-	Positive	Positive
	10	-	-	Positive	-
	11-13	Positive	-	_	-
	14-20	-	-	-	-
	21	Positive	-	_	-
	22-23	Positive	Positive	-	-
1+	24	-	Positive	Positive	Positive
	25	-	-	Positive	Positive
	26	_	-	_	Positive
	27-48	-	-	-	-

Note: The patients grade of allergy to aluminium is shown together with their concomitant reactions to *Myroxylon pereirae*, caine mix II, sodium tetrachloropalladate (Na_2PdCl_4), and palladium chloride ($PdCl_2$).

Abbreviation: -, negative.

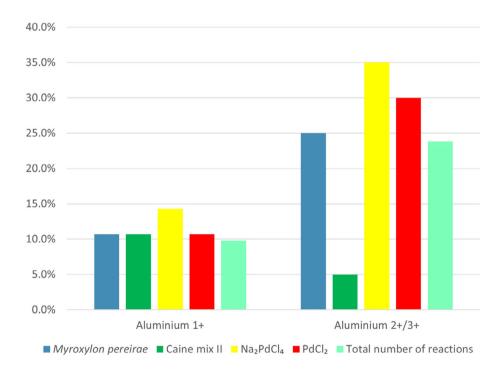


FIGURE 1 Percentage of aluminium (Al)-allergic patients. (28 with 1+ and 20 patients with 2+/3+ reactions) with concomitant reactions to *Myroxylon pereirae*, caine mix II, sodium tetrachloropalladate, and palladium chloride. The number of concomitant reactions was significantly higher among the patients with 2+/3+ Al allergy compared to patients with 1+ Al allergy, (two-sided Fisher's exact test: P = .015). Each column represents the percentage of reactions to the specific test substance out of the number of possible reactions. For example, among the patients with 2+/3+ allergy to Al, there were five reactions to *Myroxylon pereirae* out of 20 possible reactions (25%). The turquoise column represents the total number of reactions out of the total numbers of possible reactions to *Myroxylon pereirae*, caine mix II, sodium tetrachloropalladate, and palladium chloride in each group

CM II. One of the 11 patients (9.1%) with positive reactions to Na-Pd and Pd-Cl had a positive reaction to Ni. The prevalence of Na-Pd and Pd-Cl reactions among patients negative to Al was 11.9% and 8.6%,

respectively. A comparison of the prevalence of Na-Pd and Pd-Cl reactions among patients with and without aluminium allergy was not significant (two-sided Fisher's exact test).

/ILEY_

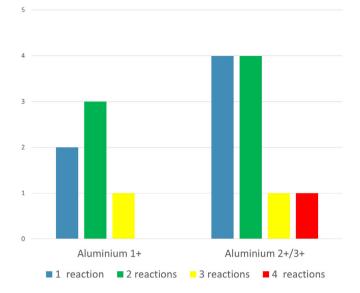


FIGURE 2 The number of patients with concomitant reactions to any of the four substances causing aluminium (Al) release. Twenty-eight patients had a 1+ reaction and 20 patients had 2+/3+ reactions to Al. The figure shows the number of patients with concomitant reactions to one or more of the four test substances in each group. The number of patients with concomitant reactions was higher among patients with 2+/3+ reactions to Al (two-sided Fisher's exact test: P < .001)

4 | DISCUSSION

6

 \perp WILEY_

Because contact allergy to Al is rare, Al-Cl or Al-lac are not included in the European baseline series. The earlier recommended patch test concentration of AI-CI (2.0%) is lower than the elicitation threshold for many Al-allergic patients.¹⁰ Today, the recommended test preparation for tracing Al allergy is Al-Cl, 10% pet.^{10,18,19} In Malmö, we have tested this preparation and a preparation with Al-lac 12% pet. since February 2010 This provides us with unique data on Al-allergic patients and an opportunity to investigate whether the laboratorie results (in artificial sweat) from Hedberg et al. could have any impact on our clinical work. Hedberg et al. found the highest Al release from FC filled with Na-Pd 3% pet.¹² According to Hedberg et al., this Al release would correspond to an AI patch test dose of 0.5% AI-CI which is a low concentration compared to the doses used for patch testing in Malmö. However, some patients will test positively to a dose corresponding to 0.5% AI-CI or lower.^{10,20} It was, hence, not surprising that we found an overrepresentation of Al allergy among patients with positive reactions to Na-Pd, MP, CM II, and Pd-Cl, which all caused high Al release in the previous studies compared to an empty FC (Table 2). These overrepresentations of simultaneous contact allergies to Na-Pd, MP, CM II, and Pd-Cl in Al-allergic patients indicated that one explanation for some of these simultaneous contact allergies was false-positive reactions.

Positive reactions to palladium often follow nickel allergy and have most often been explained as cross-sensitization, because nickel and palladium have similar chemical structures.^{14,17} The palladium reaction is, therefore, often neglected if the patient is also allergic to

nickel. However, if a patient has an isolated palladium reaction, it is often difficult to explain the exposure and clinical relevance, at least in Sweden, where palladium is not used in dental alloys.²¹ In one of our earlier studies,¹⁷ which was performed while we still used FC, we suggested that isolated palladium allergy could be due to contact allergy to Al. The group of palladium-allergic patients, thus, consists of those with and without simultaneous contact allergy to nickel. We found that Al allergy was overrepresented among patients with an isolated palladium allergy (P < .001, Table 2). The results, thus, support our previous hypothesis that a positive reaction to palladium alone, apart from being a true palladium allergy, may actually be a false-positive reaction due to a strong contact allergy to Al when patch testing with FC.

It was apparent that patients with Al allergy tested with FC more often had concomitant reactions to more than one of the four substances (MP, CM II, Na-Pd, and Pd-Cl), compared to Al-negative patients (Table 3). Also, patients with a strong Al allergy hade more concomitant reactions to MP, CM II, Na-Pd and Pd-Cl than patients with a weak Al allergy (Figures 1 and 2).

To ensure that our results were not caused by coincidental allergies, we chose to calculate the prevalence of Al allergy among patients with contact allergies to a group of other test substances that were shown to have a lower or similar Al release than an empty FC, according to Hedberg et al.¹² FM 1 was chosen because it contains common perfume allergens, just as MP. K-Cr and Ni were selected because they are common metal allergens with a high sensitization prevalence among dermatitis patients, similarly to the two palladium salts. TP was chosen because it is closely related to hydrocortisone, a substance found in topical medications such as CM II. No overrepresentation of Al allergy was found among patients with contact allergy to these four substances causing low or no Al-release (Table 2), which supports our hypothesis. When different combinations of contact allergy to FM 1, K-Cr, Ni, and TP were investigated we found an overrepresentation of AI allergy in those with contact allergy to FM 1 and K-Cr but not for any other combinations of contact allergy to the four chosen substances and AI (Table 3).

FC were introduced in 1975 by V Pirilä V, Finland.¹ There are only a few case reports about patients with Al allergy reacting to FC when patch tested.²²⁻²⁵ Testing with only an empty FC is insufficient to detect Al allergy and not recommended for that purpose.^{10,18,19} This is not the first time that patch test substances and their interactions with AI in FC have been investigated. In 1985, Fischer and Maibach investigated the reaction of cobalt and nickel salts with Al in FC in vitro. Even though they found that nickel and cobalt did react with Al on the surface in the chambers, they concluded that pet, which is used routinely as vehicle in patch testing, seems to protect the surface in the chambers from corrosion from these two metal salts.²⁶ This is very much in line with the results from Hedberg et al.¹² investigating Al release from an empty FC exposed to artificial sweat and FC with 32 different baseline preparations. They found that many patch test preparations resulted in a significantly lower release of Al compared with an empty FC,¹² probably due to the protection of pet.; however, test substances with high amounts of chloride (Na-Pd, Pd-Cl) and acid

(MP, CM II) caused corrosion to the Al surface. This corrosion and secondary Al release was not found for FCA.¹² To further support our findings and the results from the laboratory study by Hedberg et al., we investigated the patch test data from 2018–2019, where we have been using FCA. We found approximately the same prevalence of Al allergy, (0.9% during 2010–2017 vs 0.8% during 2018–2019) and the same prevalence of MP allergy (6.2% during 2010–2017 vs 6.3% during 2018–2019). We did not find any statistical overrepresentation of MP allergy among patients with Al allergy when testing with FCA.

Clinically, false-positive reactions to MP, CM II, Na-Pd, and Pd-Cl in Al-allergic patients may have a substantial impact on the diagnostics, management, and prevention of contact dermatitis. One way to avoid false-positive reactions due to Al release from FC is the use of another test chamber, such as FCA, and various plastic chambers such as Van der Bend and IQ chambers. It is not a trivial matter to change the patch test system in a patch test clinic. New guidelines and other routines regarding dosing and taping of the new system will be needed.²⁷ Physicians and clinicians would have to learn the new test systems, their advantages and disadvantages, and possible new false-positive reactions.^{28,29} If FC are used, it is recommended to also test all patients with Al-Cl in the baseline series. Whenever positive reactions are noted to Al-Cl and MP or CM II or Na-Pd or Pd-Cl, additional patch testing with the latter allergens should be performed in a test system that does not release Al.

5 | CONCLUSION

Testing with AI FC may give false-positive reactions to MP, CM II, Na-Pd, and Pd-Cl due to contact allergy to Al and triggered Al corrosion by these substances. Patients with a strong Al allergy could have more false-positive reactions as compared to patients with a weak Al allergy. The use of patch test chambers not releasing Al, for example FCA, or a plastic chamber, such as Van der Bend and IQ chambers, will eliminate the risk of false-positive reactions to MP, CMII, Na-Pd, and Pd-Cl in Al-allergic patients.

DISCLOSURE

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Lisbeth Comstedt: Data curation; formal analysis; investigation; methodology; project administration; software; writing-original draft. Jakob Dahlin: Data curation; investigation; methodology; writing-original draft. Magnus Bruze: Conceptualization; formal analysis; investigation; methodology; supervision; writing-original draft. Mihály Matura: Conceptualization; writing-original draft. Yolanda Hedberg: Conceptualization; software; writing-original draft. Cecilia Svedman: Conceptualization; funding acquisition; investigation; methodology; project administration; supervision; writing-original draft.

DATA AVAILABILITY STATEMENT

Data available on request from the authors

ORCID

Lisbeth Rosholm Comstedt b https://orcid.org/0000-0002-2606-5588

Magnus Bruze b https://orcid.org/0000-0002-2919-3227 Yolanda Hedberg b https://orcid.org/0000-0003-2145-3650

REFERENCES

- 1. Pirila V. Chamber test versus patch test for epicutaneous testing. *Contact Dermatitis*. 1975;1(1):48-52.
- Fischer T, Maibach H. Finn chamber patch test technique. Contact Dermatitis. 1984;11(3):137-140.
- Fischer T, Maibach HI. Improved but not perfect, patch testing. Am J Contact Dermatitis. 1990;1:73-90.
- Fregert S. Manual of Contact Dermatitis. 2nd ed. Copenhagen: Munksgaard; 1981.
- Bruze M, Isaksson M, Gruvberger B, Frick-Engfeldt M. Recommendation of appropriate amounts of petrolatum preparation to be applied at patch testing. *Contact Dermatitis*. 2007;56(5):281-285.
- Svedman C, Isaksson M, Bjork J, Mowitz M, Bruze M. 'Calibration' of our patch test reading technique is necessary. *Contact Dermatitis*. 2012;66(4):180-187.
- Johansen JD, Aalto-Korte K, Agner T, et al. European Society of Contact Dermatitis guideline for diagnostic patch testing - recommendations on best practice. *Contact Dermatitis*. 2015;73(4):195-221.
- Szklarska-Smialowska Z. Pitting corrosion of aluminium. Corros Sci. 1999;41(9):1743-1767.
- Liden C, Bruze M, Thyssen JC. Metals. Contact Dermatitis. 5th ed. Springer; 2011:642-680.
- Siemund I, Zimerson E, Hindsen M, Bruze M. Establishing aluminium contact allergy. *Contact Dermatitis*. 2012;67(3):162-170.
- https://www.smartpractice.com/shop/wa/Sw. Accessed ccP-F-CimS, December 30.
- Hedberg YS, Wei Z, Matura M. Quantification of aluminium release from Finn chambers under different in-vitro test conditions of relevance for patch testing. *Contact Dermatitis*. 2020;83(5):380-386.
- 13. Brett CMA. On the electrochemical behaviour of aluminium in acidic chloride solution. *Corros Sci.* 1993;28(4):279-296.
- Hindsén M, Spiren A, Bruze M. Cross-reactivity between nickel and palladium demonstrated by systemic administration of nickel. *Contact Dermatitis*. 2005;53(1):2-8.
- Wahlberg JE, Boman AS. Cross-reactivity to palladium and nickel studied in the Guinea pig. Acta Derm Venereol. 1992;72(2):95-97.
- Pistoor FH, Kapsenberg ML, Bos JD, Meinardi MM, von Blomberg ME, Scheper RJ. Cross-reactivity of human nickel-reactive T-lymphocyte clones with copper and palladium. *J Invest Dermatol.* 1995;105(1):92-95.
- Rosholm Comstedt L, Dahlin J, Bruze M, et al. Prevalence of contact allergy to metals: nickel, palladium, and cobalt in southern Sweden from 1995-2016. *Contact Dermatitis*. 2020;82(4):218-226.
- Bruze M, Lundh K, Gruvberger B, Hindsen M. Aluminium chloride hexahydrate at 2% is insufficient to trace contact allergy to aluminium. *Contact Dermatitis*. 2008;59(3):183-184.
- Bruze MMM, Netterlid E, Siemund I, Svedman C. Patch testing with aluminium chloride hexahydrate in petrolatum. *Contact Dermatitis*. 2020;83(2):176-177.
- Siemund I, Mowitz M, Zimerson E, Bruze M, Hindsen M. Variation in aluminium patch test reactivity over time. *Contact Dermatitis*. 2017; 77(5):288-296.
- Oädlalegeringar för metallkeramik: basmetallegeringar. Kunskapscenter för Dentalamaterial, Socialstyrelsen; 2007.
- King N, Moffitt D. Allergic contact dermatitis secondary to the use of aluminium Finn chambers(R). *Contact Dermatitis*. 2018;78 (5):365-366.

-WILEY-CONTACT

- 23. Dwyer CM, Kerr RE. Contact allergy to aluminium in 2 brothers. *Contact Dermatitis*. 1993;29(1):36-38.
- 24. Tosti A, Vincenzi C, Peluso AM. Accidental diagnosis of aluminium sensitivity with Finn chambers. *Contact Dermatitis*. 1990;23(1): 48-49.
- Netterlid E, Hindsen M, Bjork J, et al. There is an association between contact allergy to aluminium and persistent subcutaneous nodules in children undergoing hyposensitization therapy. *Contact Dermatitis*. 2009;60(1):41-49.
- Fischer T, Maibach H. Aluminium in Finn chambers reacts with cobalt and nickel salts in patch test materials. *Contact Dermatitis*. 1985;12 (4):200-202.
- Luu H, Mowitz M, Bruze M, Engfeldt M, Isaksson M, Svedman C. A comparative study between the two patch test systems Finn chambers(R) and Finn chambers(R) AQUA. *Contact Dermatitis*. 2020;84(5):290-298.

- Hamnerius N, Mowitz M. Two cases of contact allergic reactions to Finn chamber AQUA test chambers. *Contact Dermatitis*. 2019;81(4):320-322.
- 29. Sanchez-Gilo A, Gomez-de la Fuente E, Vicente-Martin FJ. Allergic contact dermatitis caused by Finn chambers AQUA in two patients. *Contact Dermatitis*. 2019;80(4):246-247.

How to cite this article: Rosholm Comstedt L, Dahlin J, Bruze M, Hedberg Y, Matura M, Svedman C. Patch testing with aluminium Finn Chambers could give false-positive reactions in patients with contact allergy to aluminium. *Contact Dermatitis*. 2021;1–8. <u>https://doi.org/10.1111/cod</u>. 13870