Patch testing with aluminium Finn Chambers could give false-positive reactions in patients with contact allergy to aluminium

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Abstract

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

Objectives: To investigate whether aluminium release 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 Al among patients with positive reactions to sodium tetrachloropalladate, Myroxylon pereirae, caine mix II, and palladium chloride. Patients with a strong Al allergy had significantly higher amounts of concomitant reactions to sodium tetrachloropalladate, Myroxylon pereirae, caine mix II, and palladium chloride compared to patients with weak Al allergy. These results were not seen for patients tested with Finn Chambers AQUA.

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

The prevalence of contact allergy to Al is low and patients with contact allergy to Al do not normally react to an empty FC. 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.

New chemical analyses from Hedberg et al. show, however, that various patch test preparations can induce Al release from Finn chambers in vitro due to Al corrosion. 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. 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. The explanation for the Al release is that surface-available chlorides from metal salts can cause localised corrosion (pitting corrosion) to Al metal. 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. MP contains high amounts of organic acid and CM II contains hydrochloric acid, which is corrosive to Al. The Al release from FC into artificial sweat was found to be 16-4100-fold higher than the Al 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 cross-react. In an earlier study, we discussed the relevance of contact allergy to palladium when the patient was not allergic to nickel. After discussion on preliminary results on triggered Al release from FC, later published in, we raised the question 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 Al release from FC 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 Al 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.

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.

2.3  Patch testing and patch test readings

Table 1 shows the concentration and suppliers of the selected test substances that were used in our baseline series and our extended
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. 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 Al was defined as either a positive reaction to Al-Cl and/or Al-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, CM II, 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 Al, 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 Al. Positive patch test reactions to MP, CM II, Na-Pd, and Pd-Cl were all overrepresented in patients with contact allergy to Al, 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 Al 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-Cl 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-Cl (19/80 vs 11/112; two-
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

### Table 2

| Positive reactions to Chamber | Number (%) | Aluminium positive (%) | Aluminium negative (%) | $P$-value |
|-----------------------------|------------|-------------------------|------------------------|-----------|
| Myroxylon 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 tetrachloropalladate | 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*         | 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      |
| Potassium 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.

| 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-Pd                        | 42/5446 (0.8)           | 2/48 (4.2)             | 40/5398 (0.7) | .052  |
| CMII + Na-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(1.1)              | 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.
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).

**TABLE 4**  Forty-eight patients were positive to aluminium chloride hexahydrate and/or aluminium lactate during 2010–2017

| Aluminium patch test reaction | Patients number | Myroxylon pereirae | Caine mix II | Na₂PdCl₄ | PdCl₂ |
|-------------------------------|----------------|-------------------|-------------|---------|-------|
| 3+                            | 1–3            | –                 | –           | –       | –     |
| 4                             | Positive       | Positive          | Positive    | Positive |
| 5                             | Positive       | –                 | Positive    | Positive |
| 6                             | Positive       | –                 | Positive    | Positive |
| 2+                            | 7–9            | –                 | –           | Positive | Positive |
| 10                            | Positive       | –                 | –           | Positive |
| 11–13                         | Positive       | –                 | –           | –       |
| 14–20                         | Positive       | –                 | –           | –       |
| 21                            | Positive       | –                 | –           | –       |
| 22–23                         | Positive       | Positive          | –           | –       |
| 1+                            | 24             | –                 | Positive    | Positive | Positive |
| 25                            | –              | Positive          | 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 (Na₂PdCl₄), and palladium chloride (PdCl₂).

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 (Na₂PdCl₄), and palladium chloride (PdCl₂). 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 a 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.
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

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 Al-Cl (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 laboratory 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 Al patch test dose of 0.5% Al-Cl, 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% Al-Cl 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 had 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 Al 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 Al (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 Al 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
needed. Physicians and clinicians would have to learn the new test system in a patch test clinic. New guidelines and other chambers, such as Van der Bend and IQ chambers. It is not a trivial matter to change avoidance of false-positive reactions due to Al release from FC is the use of FCA, or a plastic chamber, such as Van der Bend and IQ chambers. It is not a trivial matter to change patch testing with the latter allergens should be performed in a test system that does not release Al.

5  |  CONCLUSION

Testing with Al 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 Rosholm Comstedt: Data curation; formal analysis; investigation; methodology; project administration; software; writing-original draft.

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DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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