

# Patch Testing With Formaldehyde 2.0% (0.60 mg/cm<sup>2</sup>) Detects More Contact Allergy to Formaldehyde Than 1.0%

Marléne Isaksson, MD, PhD,\* Iris Ale, MD, DM,† Klaus E. Andersen, DMSc,‡ Chee-Leok Goh, MD, MRCP (UK), MMed,§ An Goossens, PhD,|| Hemangi Jerajani, MD,¶ Kayoko Matsunaga, MD, PhD,# John McFadden, DM,\*\* and Magnus Bruze, MD, PhD\*

**Background:** The International Contact Dermatitis Research Group increased the patch test concentration of formaldehyde from 1.0% aqueous (aq) to 2.0% aq (in 2011).

**Objective:** This study was designed to investigate the outcome of the decision.

**Methods:** Consecutive dermatitis patients in 8 different clinics were patch tested with formaldehyde 1.0% aq and 2.0% aq. The test solutions were applied with a micropipette to the filter paper discs in the respective chamber.

**Results:** A total of 2778 patients were tested with 1.0% aq and 2766 to 2.0% aq. Sixty-five patients (2.3%, calculated from 2766 tested, to 2.0% aq) had positive patch test reactions interpreted as contact allergy to formaldehyde. This is a rather low frequency. Of these 65, 46 were women (46/1703 [2.7%]) and 19 were men (19/1063 [1.8%]). Thirty-six reacted only to 2.0% aq, 21 patients reacted to both concentrations, and 8 patients reacted only to 1.0% aq. Significantly, more patients reacted to 2.0% aq compared with 1.0% aq ( $P < 0.001$ ). There was no significant sex difference. A total of 0.8% irritant reactions were recorded to formaldehyde 2.0% aq and 0.1% to 1.0% aq.

**Conclusions:** The increased formaldehyde patch test concentration to 2.0% aq revealed more formaldehyde contact allergy.

Formaldehyde, one of the oldest and widely used preservatives, is a common contact allergen and has been included in the baseline series since the 1930s.<sup>1</sup> Based on the patient's history, it is difficult to suspect contact allergy to formaldehyde because it is common in the environment. It is also difficult to completely cure allergic contact dermatitis caused by formaldehyde, because it is almost impossible to totally avoid exposure to formaldehyde-containing products. Danish and Swedish studies in the 1990s showed that formaldehyde or formaldehyde-releasing preservatives are widely used in many

consumer products (cosmetics, household, and industrial products).<sup>2,3</sup> To optimize prevention of allergic contact dermatitis, the establishment of contact allergy to formaldehyde by a thoroughly evaluated patch test technique is important. Formaldehyde has been regarded as a problematic patch test substance with poor reproducibility of allergic reactions.<sup>4</sup> It has been judged to give irritant reactions, which have been interpreted as positive reactions.<sup>5</sup> The recommended patch test concentration has been reduced from 5% aqueous (aq) to 2% aq in the United States in the 1960s<sup>6</sup> and from 4.0% aq to 1.0% aq in several other baseline series and now again increased to 2.0% aq in the European baseline series and in the International Contact Dermatitis Research Group (ICDRG) baseline series.<sup>7</sup> In the Malmö Department, patch testing with formaldehyde 2.0% aq has been used in patients with doubtful reactions to formaldehyde 1.0% aq and when there has been a strong suspicion of contact allergy to formaldehyde. Furthermore, micropipettes are recommended to be used routinely for dosing liquid patch test solutions.<sup>8</sup> Fifteen microliter is the optimal dose for 8-mm Finn Chambers.<sup>9</sup>

The present study investigated in several ICDRG member clinics the outcome of the increased patch test concentration in a series of consecutive dermatitis patients tested with both 1.0% aq to 2.0% aq formaldehyde.

Furthermore, we compared the relationship between contact allergy to formaldehyde and the formaldehyde-releasing preservatives

From the \*Department of Occupational and Environmental Dermatology, Lund University, Skåne University Hospital, Malmö, Sweden; †Allergy Center and Department of Dermatology, University Hospital, Republic University of Uruguay, Montevideo; ‡Department of Dermatology and Allergy Centre, Odense University Hospital, University of Southern Denmark; §Department of Dermatology, National Skin Center, Singapore; ||Contact Allergy Unit, Department of Dermatology, University Hospital K.U. Leuven, Belgium; ¶Department of Dermatology, MGM Medical College, Navi Mumbai, India; #Department of Integrative Medical Science for Allergic Disease, Fujita Health University School of Medicine, Nagoya, Japan; and \*\*St John's Institute of Dermatology, Contact Dermatitis Clinic, St Thomas' Hospital, London, United Kingdom.

Address reprint requests to Marléne Isaksson, MD, PhD, Department of Occupational and Environmental Dermatology, Jan Waldenströms gata 16, SE 205 02, Malmö, Sweden. E-mail: marlene.isaksson@skane.se.

The authors have no funding or conflicts of interest to declare.

DOI: 10.1097/DER.0000000000000510

© 2019 American Contact Dermatitis Society. All Rights Reserved.

**TABLE 1.** The Total Number of Tested Patients in the 8 Centers

| Patch Testing Center | Formaldehyde 1.0% aq |      |      | Formaldehyde 2.0% aq |      |      | Quaternium-15 2.0 pet* |     |      | Imidazolidinyl Urea 2.0% pet* |     |      | Diazolidinyl Urea 2.0% pet |     |      |
|----------------------|----------------------|------|------|----------------------|------|------|------------------------|-----|------|-------------------------------|-----|------|----------------------------|-----|------|
|                      | Total                | M    | F    | Total                | M    | F    | Total                  | M   | F    | Total                         | M   | F    | Total                      | M   | F    |
| A                    | 244                  | 197  | 47   | 244                  | 197  | 47   | NT                     |     |      |                               |     |      |                            |     |      |
| B                    | 470                  | 142  | 328  | 470                  | 142  | 328  | 470                    | 142 | 328  | 242                           | 45  | 197  | 210                        | 32  | 178  |
| C                    | 727                  | 236  | 491  | 723                  | 237  | 486  | 724                    | 237 | 487  | 724                           | 237 | 487  | 724                        | 237 | 487  |
| D                    | 256                  | 84   | 172  | 256                  | 84   | 172  | 256                    | 84  | 172  | 256                           | 84  | 172  | 256                        | 84  | 172  |
| E                    | 43                   | 28   | 15   | 43                   | 28   | 15   | NT                     |     |      |                               |     |      |                            |     |      |
| F                    | 567                  | 181  | 386  | 559                  | 181  | 378  | 567                    | 181 | 386  | 566                           | 181 | 385  | 566                        | 181 | 385  |
| G                    | 302                  | 145  | 157  | 302                  | 145  | 157  | 302                    | 145 | 157  | 302                           | 145 | 157  | 302                        | 145 | 157  |
| H                    | 169                  | 49   | 120  | 169                  | 49   | 120  | 169                    | 49  | 120  | 169                           | 49  | 120  | 169                        | 49  | 120  |
| Total                | 2778                 | 1062 | 1716 | 2766                 | 1063 | 1703 | 2488                   | 838 | 1650 | 2259                          | 741 | 1518 | 2227                       | 728 | 1499 |

\*In centers B and C, Quaternium-15 was tested at 1.0% pet, and in center G, imidazolidinyl urea was tested at 2.0% in aq.

F indicates female, M, male; NT, not tested.

imidazolidinyl urea 2.0% petrolatum (pet), Quaternium-15 2.0% pet, and diazolidinyl urea 2.0% pet.

## MATERIALS AND METHODS

### Study Population

Eight patch testing clinics representing 8 countries participated in the study from January 1, 2014, to December 31, 2014. In these clinics, 2778 consecutively patch-tested dermatitis patients, 1062 males (mean age = 39.1 years, range = 6–86) and 1716 females (mean age = 43.7 years, range = 3–94), took part (Table 1).

### Substances

Formaldehyde 37% aq (wt/wt) was bought from Acros Organics (Pittsburg, PA) and used for preparing the formaldehyde patch test solutions at the Department of Occupational and Environmental Dermatology in Malmö. Formaldehyde 2.0% aq (0.60 mg/cm<sup>2</sup>) and 1.0% aq (0.30 mg/cm<sup>2</sup>) were prepared from the same batch and sent from Malmö to the participating clinics at the following 5 occasions: December 2013, February 2014, April 2014, August 2014, and October 2014. Each center patch tested its own 3 formaldehyde releasers: imidazolidinyl urea 2.0% pet, Quaternium-15 2.0% pet, and diazolidinyl urea 2.0% pet.

In Odense, Denmark, the T.R.U.E. Test system (SmartPractice, Phoenix, AZ) was used to test formaldehyde instead of formaldehyde 1.0% aq supplied by Malmö. Formaldehyde in the T.R.U.E. Test system corresponds to 180 µg/cm<sup>2</sup>. Quaternium-15 (100 µg/cm<sup>2</sup>), imidazolidinyl urea (600 µg/cm<sup>2</sup>), and diazolidinyl urea (550 µg/cm<sup>2</sup>) were also tested within the T.R.U.E. Test system in Odense.

### Patch Testing

The test preparations were provisionally included into the baseline series in all clinics. Patch testing and reading of the patients followed the routines of the participating clinics, using Finn Chambers on Scanpor

tape (Ø 8 mm; SmartPractice), in 7 clinics, whereas 1 clinic used Van der Bend chambers (8 × 8 mm; Brielle, the Netherlands), respectively.

For solutions, a micropipette was to be used to apply the correct dose for the test system of choice (ie, for a Finn Chamber [15 µL, 30 µL/cm<sup>2</sup>]; for a Van der Bend chamber [20 µL, 30 µL/cm<sup>2</sup>]).<sup>8</sup> For the test preparations in pet, 20 mg was applied to Finn Chambers as recommended by the European Society of Contact Dermatitis.<sup>10,11</sup> The test chambers remained on the back for 2 days, and readings were taken following the guidelines of the ICDRG.<sup>12</sup> The common reading day was day 3 (D3) or D4 (reading 1). A late reading, if mandatory in the respective center, was performed 7 to 8 days after application of patches in 2139 patients. In centers B and H, a D7 reading was not mandatory. A dermatologist read all patch tests. A positive reaction on D3 or D4 was registered as a positive reaction in the present study, and the results in this article are based on these readings only, if not otherwise stated. An individual test protocol designed for the study was filled in for each patient with patch test reactions (allergic, doubtful, or irritant) to at least one of the following test preparations: formaldehyde 1.0% aq and 2.0% aq, imidazolidinyl urea 2.0% pet, Quaternium-15 2.0% pet, and diazolidinyl urea 2.0% pet.

It was emphasized that all patch test reactions without an obvious morphology of an allergic or irritant nature must be classified as doubtful. Late reactions beyond D8 were to be reported.

### Statistical Analysis

The McNemar test was used to compare the number of positive reactions to formaldehyde 2.0% aq and 1.0% aq. Fisher exact 2-tailed test was used to compare the contact allergy rate in males and females, as well as the association between formaldehyde and the separate formaldehyde-releasing preservatives. The differences were considered significant when  $P < 0.05$ .

## RESULTS

A summary of patch test reactions to formaldehyde is given in Table 2.

**TABLE 2. The Positive Reactions to All Tested Substances**

| Patch Testing Center | Formaldehyde 1.0% aq |    |    | Formaldehyde 2.0% aq |    |    | Quaternium-15 2.0% pet |   |    | Imidazolidinyl Urea 2.0% pet |   |   | Diazolidinyl Urea 2.0% pet |   |   |
|----------------------|----------------------|----|----|----------------------|----|----|------------------------|---|----|------------------------------|---|---|----------------------------|---|---|
|                      | Total                | M* | F† | Total                | M  | F  | Total                  | M | F  | Total                        | M | F | Total                      | M | F |
| A                    | 1                    | 0  | 1  | 0                    | 0  | 0  | NT‡                    |   |    | NT                           |   |   | NT                         |   |   |
| B                    | 4                    | 0  | 4  | 7                    | 0  | 7  | 9                      | 0 | 9  | 5                            | 0 | 5 | 6                          | 0 | 6 |
| C                    | 13                   | 4  | 9  | 21                   | 9  | 12 | 4                      | 2 | 2  | 4                            | 2 | 2 | 2                          | 2 | 0 |
| D                    | 3                    | 1  | 2  | 6                    | 1  | 5  | 4                      | 1 | 3  | 0                            | 0 | 0 | 0                          | 0 | 0 |
| E                    | 0                    | 0  | 0  | 2                    | 0  | 2  | 0                      | 0 | 0  | 0                            | 0 | 0 | 0                          | 0 | 0 |
| F*                   | 6                    | 1  | 5  | 14                   | 4  | 10 | 5                      | 1 | 4  | 4                            | 2 | 2 | 3                          | 1 | 2 |
| G                    | 0                    | 0  | 0  | 0                    | 0  | 0  | 2                      | 1 | 1  | 0                            | 0 | 0 | 0                          | 0 | 0 |
| H                    | 2                    | 0  | 2  | 7                    | 3  | 4  | 1                      | 0 | 1  | 0                            | 0 | 0 | 0                          | 0 | 0 |
| Total                | 29                   | 6  | 23 | 57                   | 17 | 40 | 25                     | 5 | 20 | 13                           | 4 | 9 | 11                         | 3 | 8 |

\*Center using T.R.U.E. Test system.

†Indicates female, M, male; NT, not tested.

Fifty-seven of the patients reacted positively to formaldehyde 2.0% aq, but 36 of the 57 patients reacted negatively to formaldehyde 1.0% aq, 21 patients reacted to both concentrations, and 8 patients reacted positively to formaldehyde 1.0% aq but negatively to 2.0% aq. Twenty-nine patients reacted to formaldehyde 1.0% aq (Fig. 1). Significantly, more patients reacted to 2.0% aq compared with 1.0% aq ( $P < 0.001$ ). Thus, in all, 65 patients (2.3%, calculated from 2766 tested to 2.0% aq), 46 women (46/1703 [2.7%]) and 19 men (19/1063 [1.8%]), had contact allergy to formaldehyde. The sex difference was not statistically significant ( $P = 0.16$ ). The proportion of women and men, mean age, and range of the groups reacting to 2.0% aq only and to both concentrations were similar.

Among positives to 2.0% aq, 6 patients reacted only on D7, and among positives to 1.0% aq, 8 patients reacted only on D7 (Table 3).

Eighteen patients had doubtful reactions to 2.0% aq, without being positive to 1.0% aq formaldehyde. Fourteen patients had doubtful reactions to 1.0% aq, but 11 of these reacted positively to 2.0% aq. Twenty-one irritant reactions (0.8%) were recorded to 2.0% aq and 3 (0.1%) to 1.0% aq (Table 4).

In all, 49 positive reactions to the tested formaldehyde releasers were found (Table 5). Among the formaldehyde-allergic patients detected by testing 1.0% aq, 14 of 25 patients with contact allergy to Quaternium-15, 4 of 11 patients with contact allergy to diazolidinyl urea, and 3 of 13 cases with contact allergy to imidazolidinyl urea were found. The corresponding numbers of contact allergies found when testing formaldehyde 2.0% aq were 18/25, 7/11, and 6/13, respectively (Table 5). The association between contact allergy to

formaldehyde, independent of patch test concentration used, and the 3 formaldehyde-releasing preservatives was statistically significant ( $P < 0.001$ ) (Table 5).

## DISCUSSION

Patch testing with formaldehyde 2.0% aq at 30  $\mu\text{L}/\text{cm}^2$  detected in consecutive dermatitis patients twice as many formaldehyde-allergic individuals compared with 1.0% aq ( $P < 0.001$ ). This is in accordance with 2 recent studies in which the dose also was carefully monitored.<sup>13,14</sup> The standard concentration in the 1980s was 2.0% aq. When the patch test system at many clinics was changed from the AI-test to the Finn Chamber system, the ICDRG anticipated an increased risk of irritant reactions from formaldehyde 2.0% aq and therefore lowered the recommended patch test concentration to 1.0% aq.<sup>1</sup> Contact allergy to formaldehyde 1.0% aq was found in approximately 2.5% of patients tested with the European baseline series 1991–2000.<sup>15</sup> In 1983–1984, the prevalence value of sensitization to formaldehyde 2.0% aq tested with the Finn Chamber technique in a Swedish study of hand eczema was 1.6%.<sup>16</sup> Formaldehyde allergy is reported to be more common in women than in men and a significant allergen in women with hand eczema.<sup>16</sup> This may be explained by the finding that formaldehyde contact allergy is often associated with the usage of cosmetics and household products.<sup>17,18</sup> We did not find an overrepresentation of women in the present study. Formaldehyde is a ubiquitous allergen that might be difficult to avoid. Product-labeled ingredient lists and available information are often

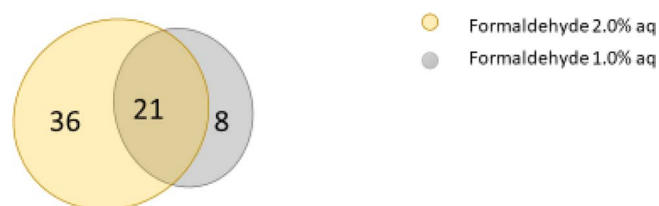


**Figure 1.** The distribution of exclusive and concurrent reactions to formaldehyde 1.0% aq and formaldehyde 2.0% aq.

**TABLE 3. Number of Positive Reactions to Formaldehyde 2.0% and 1.0% by Reading Day and Proportions Among Positives**

| Concentration | D3 or D4 Only | D7 or D8 Only | D3 or D4 and D7 or D8 | Total |
|---------------|---------------|---------------|-----------------------|-------|
| 2.0%          | 25 (41.7%)*   | 6 (10.0%)     | 29 (48.3%)            | 60    |
| 1.0%          | 11 (31.4%)    | 8 (22.9%)     | 16 (45.7%)            | 35    |

\*Four patients were not read on D7; therefore, they are not included in the sum.

**TABLE 4. Patch Test Reactions to 2 Different Concentrations of Formaldehyde (wt/vol%)**

| Formaldehyde<br>(wt%/vol%) | Contact Allergy<br>Reactions |    |    |     |     | Other<br>Reactions |     |     |     | Total<br>Tested |
|----------------------------|------------------------------|----|----|-----|-----|--------------------|-----|-----|-----|-----------------|
|                            | +++*                         | ++ | +  | Tot | %†  | ?‡                 | %†  | IR§ | %†  |                 |
| 2.0                        |                              |    |    |     |     |                    |     |     |     |                 |
| All§                       | 3                            | 22 | 32 | 57  | 2.1 | 18                 | 0.7 | 21  | 0.8 | 2766            |
| Men                        | 1                            | 7  | 9  | 17  | 1.6 |                    |     |     |     | 1063            |
| Women                      | 2                            | 15 | 23 | 40  | 2.3 |                    |     |     |     | 1703            |
| 1.0                        |                              |    |    |     |     |                    |     |     |     |                 |
| All                        | 1                            | 5  | 23 | 29  | 1.0 | 3                  | 0.1 | 3   | 0.1 | 2778            |
| Men                        | 1                            | 2  | 7  | 10  | 0.9 |                    |     |     |     | 1062            |
| Women                      | 0                            | 3  | 16 | 19  | 1.1 |                    |     |     |     | 1716            |

\*The recorded reaction D3/D4.

†Proportion (%) among tested patients.

‡Doubtful reaction without positive reaction to formaldehyde 2.0%.

§Sex is given only for allergic reactions.

||Eight patients reacted to 1.0% without reacting to 2.0%.

||In addition, 11 patients had doubtful reactions to 1.0% but reacted positively to 2.0.

IR indicates irritant reaction.

inadequate to confirm the potential for formaldehyde exposure, and chemical-based spot test kits may have utility for identification of potential formaldehyde exposure from personal care products.<sup>19</sup>

Among all patients tested, irritant reactions to formaldehyde 2.0% aq and 1.0% aq were noted in (21/2766) 0.8% and (3/2778) 0.1% of the patients, respectively (Table 4), in accordance with another study in which 0.4% and 0.1% of the patients, respectively, had irritant reactions.<sup>13</sup> Here, however, most irritant reactions were reported from one clinic, and interlaboratory variation in patch test scoring cannot be excluded.

The low number of irritant reactions to 2.0% aq and 1.0% aq in this study may be related to the usage of micropipettes, which enables exact dosage. According to previous results, there is a large increase of irritant reactions between 2.0% aq (0.60 mg/cm<sup>2</sup>) and 3.0% aq (0.90 mg/cm<sup>2</sup>). There is, thus, a narrow range of concentrations with which formaldehyde can be tested and by which the detection

of contact allergy can be established without either missing contact allergies or causing irritant reactions. Such a narrow range makes an exact test dose per area even more important. A recent study at the department of occupational and environmental dermatology in Malmö<sup>20</sup> showed that with the commonly used drop technique, by which the solution is applied by squeezing the plastic bottle containing the solution, the amount applied might vary between approximately 11 and 44 mg. Because the dose of allergen is dependent of the amount of solution applied, this might well cause varying results with regard to allergic reactions and also more frequent irritant reactions.

Among all patients tested, doubtful reactions to formaldehyde 2.0% aq and 1.0% aq were noted in 18 (0.7%) of 2766 patients and 14 (0.5%) of 2778 patients, respectively (Table 4).

Doubtful reactions are problematic in the diagnostics of contact allergy. These reactions may be the expression of both irritant reactions and weak contact allergies.<sup>21</sup>

Patch testing with any sensitizer can result in a doubtful reaction, but it varies among different allergens.<sup>21</sup> Reactions to formaldehyde belong to patch test reactions that are considered to be difficult to evaluate. In our study, there were relatively more doubtful reactions to 1.0% aq compared with 2.0% aq (14/29 vs 18/57, respectively). However, 11 (79%) of the 14 doubtful reactions to 1.0% aq turned out to be positive when 2.0% aq formaldehyde was tested and were thus confirmed contact allergies (Table 4). This means that the theoretical “price” in the form of doubtful reactions that are *not* contact allergies could be the same regardless of patch test concentration but also that, by testing with 2.0% aq, a considerable proportion of doubtful reactions to 1.0% aq are diagnosed as formaldehyde allergy.

Ten percent (6/60) of our formaldehyde-allergic patients had positive patch tests to 2.0% aq only on D7. This means that the number of contact allergies to formaldehyde 2.0% aq that would have been missed if no reading on D7–D8 had been performed is substantial and shows the importance of a late reading on D7–D8.

At present, all the 3 investigated formaldehyde releasers are included in the international baseline series. Under the assumption that patients found to have contact allergy to formaldehyde are advised to avoid products that contain formaldehyde releasers, our results

**TABLE 5. Positive Reactions to Formaldehyde 2.0% and 1.0% Among Patients With Contact Allergy to Formaldehyde Releasers in 2778 and 2766 Patients, Respectively**

|                        | Total No.<br>Positive<br>Reactions |     | Simultaneous Reactions to Formaldehyde |    |        |      |    |        |
|------------------------|------------------------------------|-----|----------------------------------------|----|--------|------|----|--------|
|                        | n*                                 | %†  | 2.0%                                   |    |        | 1.0% |    |        |
|                        |                                    |     | n‡                                     | %§ | P      | n‡   | %§ | P      |
| Formaldehyde releasers |                                    |     |                                        |    |        |      |    |        |
| Quaternium-15          | 25                                 | 1.0 | 18                                     | 72 | <0.001 | 14   | 56 | <0.001 |
| Diazolidinyl urea      | 11                                 | 0.5 | 7                                      | 64 | <0.001 | 4    | 36 | <0.001 |
| Imidazolidinyl urea    | 13                                 | 0.6 | 6                                      | 46 | <0.001 | 3    | 23 | <0.001 |

\*Total number of positive reactions.

†Proportion (%) of positive reactions among all tested.

‡Number of simultaneous positive reactions to a formaldehyde releaser.

§Proportion (%) of formaldehyde-allergic patients among positives to a formaldehyde releaser.

imply that there are few additional cases found by routinely testing these 3 formaldehyde releasers when formaldehyde 2.0% aq is used. For Quaternium-15, 0.3% are missed, and for imidazolidinyl urea and diazolidinyl urea, 0.3% and 0.2% are missed, respectively. When 1.0% aq formaldehyde is tested, the figures are 0.4%, 0.4%, and 0.3%, respectively. These numbers are too low to qualify the 3 releasers to be included in the baseline series, according to published recommendations.<sup>22</sup>

## CONCLUSIONS

The present study shows that patch testing with formaldehyde 2.0% aq (wt/vol) while using a micropipette detects twice as many reacting individuals compared with 1.0% aq. Furthermore, this dose does not give a high frequency of irritant reactions when micropipettes are used. The decision by the ICDRG to increase the patch test concentration of formaldehyde from 1.0% aq to 2.0% aq in 2011 was soundly based. With regard to Quaternium-15, imidazolidinyl urea, and diazolidinyl, their presence in the baseline series seems to be superfluous.

## REFERENCES

1. Trattner A, Johansen JD, Menne T. Formaldehyde concentration in diagnostic patch testing: comparison of 1% with 2%. *Contact Dermatitis* 1998;38:9–13.
2. Flyvholm MA, Hall BM, Agner T, et al. Threshold for occluded formaldehyde patch test in formaldehyde-sensitive patients. Relationship to repeated open application test with a product containing formaldehyde releaser. *Contact Dermatitis* 1997;36:26–33.
3. Gruvberger B, Bruze M, Tammela M. Preservatives in moisturizers on the Swedish market. *Acta Derm Venereol* 1998;78:52–56.
4. Brasch J, Geier J, Henseler T. Evaluation of patch test results by use of the reaction index. An analysis of data recorded by the Information Network of Departments of Dermatology (IVDK). *Contact Dermatitis* 1995;33:375–380.
5. Andersen KE, White IR, Goossens A. Allergens from the standard series. In: Frosch PJMT, Lepoittevin JP, eds. *Contact Dermatitis*. Berlin, Germany: Springer Verlag; 2006:473–475.
6. Epstein E, Maibach HI. Formaldehyde allergy. Incidence and patch test problems. *Arch Dermatol* 1966;94:186–190.
7. Alikhan A, Cheng LS, Ale I, et al. Revised minimal baseline series of the International Contact Dermatitis Research Group: evidence-based approach. *Dermatitis* 2011;22:121–122.
8. Bruze M. Contact sensitizers in resins based on phenol and formaldehyde. *Acta Derm Venereol Suppl (Stockh)* 1985;119:1–83.
9. Isaksson M, Gruvberger B, Frick-Engfeldt M, et al. Which test chambers should be used for acetone, ethanol, and water solutions when patch testing? *Contact Dermatitis* 2007;57:134–136.
10. Bruze M, Isaksson M, Gruvberger B, et al. Recommendation of appropriate amounts of petrolatum preparation to be applied at patch testing. *Contact Dermatitis* 2007;56:281–285.
11. 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;73:195–221.
12. Wilkinson DS, Fregert S, Magnusson B, et al. Terminology of contact dermatitis. *Acta Derm Venereol* 1970;50:287–292.
13. Hauksson I, Pontén A, Gruvberger B, et al. Routine diagnostic patch-testing with formaldehyde 2.0% (0.6 mg/cm<sup>2</sup>) may be an advantage compared to 1.0%. *Acta Derm Venereol* 2010;90:480–484.
14. Isaksson M, Bråred-Christensson J, Engfeldt M, et al. Patch testing with formaldehyde 2.0% in parallel with 1.0% by the Swedish contact dermatitis research group. *Acta Derm Venereol* 2014;94:408–410.
15. Wilkinson JD, Shaw S, Andersen KE, et al. Monitoring levels of preservative sensitivity in Europe. A 10-year overview (1991–2000). *Contact Dermatitis* 2002;46:207–210.
16. Meding B, Swanbeck G. Occupational hand eczema in an industrial city. *Contact Dermatitis* 1990;22:13–23.
17. Cronin E. Formaldehyde is a significant allergen in women with hand eczema. *Contact Dermatitis* 1991;25:276–282.
18. Flyvholm MA, Menné T. Allergic contact dermatitis from formaldehyde. A case study focussing on sources of formaldehyde exposure. *Contact Dermatitis* 1992;27:27–36.
19. Ham JE, Siegel PD, Maibach H. Undeclared formaldehyde levels in patient consumer products: formaldehyde test kit utility. *Cutan Ocul Toxicol* 2019; 38:112–117.
20. Frick-Engfeldt M, Gruvberger B, Isaksson M, et al. Comparison of three different techniques for application of water solutions to Finn Chambers®. *Contact Dermatitis* 2010;63:284–288.
21. Pontén A, Goossens A, Bruze M. Recommendation to include formaldehyde 2.0% aqua in the European baseline patch test series. *Contact Dermatitis* 2013;69:372–374.
22. Bruze M, Condé-Salazar L, Goossens A, et al. Thoughts on sensitizers in a standard patch test series. The European Society of Contact Dermatitis. *Contact Dermatitis* 1999;41:241–250.