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## Patch testing results in adult patients with dermatitis during the coronavirus disease 2019 pandemic



Allergic contact dermatitis (ACD) represents a delayed hypersensitivity reaction to a contact allergen with variable presentations, including erythema, vesiculation, or lichenification, depending on the allergen, exposure, and chronicity. Patch testing (PT) is the reference standard for identifying contact allergens implicated in ACD. Among the general adult population, ACD has a prevalence of approximately 21%.<sup>1</sup> Positive PT reactions in the evaluation of occupational ACD occur in up to 25% to 36% of health care workers (HCWs).<sup>2</sup> Relevant allergens detected in HCWs include the following: formaldehyde, formaldehyde-releasing preservatives (quaternium-15, 2-bromo-2-nitropropane-1,3-diol), glutaraldehyde, and rubber accelerators (carba mix, thiuram mix).<sup>2</sup> ACD related to personal protective equipment (PPE) is well documented, including during the coronavirus disease 2019 (COVID-19) pandemic. Facial mask ACD attributed to N95 or KN95 respirators or surgical masks may be linked to textile dyes, formaldehydes released in textile processing, rubber accelerators (elastic banding), preservatives and disinfectants (sterilization), or diisocyanates (polyurethane production).<sup>3–6</sup>

We conducted an institutional review board–approved, retrospective chart review of adult patients ( $\geq 18$  years) who underwent PT with the North American Contact Dermatitis panel in our office for the evaluation of suspected ACD from January 2018 to March 2021. Patients were identified by coding query (CPT 95044). Metal PT data were excluded. Time periods were defined as follows: pre–COVID-19 (January 2018–February 2020) and COVID-19 pandemic (July 2020–March 2021). PT was deferred from March 2020 to June 2020. Data gathered included patient demographics, dermatitis history (location, duration, clinical features), atopic dermatitis (AD) history, and PT results. Patients had at least 2 PT readings performed by the same reader, at 48 hours (PT removal) and 72 or 96 hours after application. Readings were graded using the International Contact Dermatitis Research Group system.<sup>7</sup> Reactions of 1+, 2+, or 3+ were considered positive PT readings. Statistical analyses were performed using the  $\chi^2$  or Fisher's exact tests. Results with  $P$  less than .05 were considered statistically significant.

A total of 99 patients (median age: 49 years [interquartile range, 37–59 years], 91% women, 21% HCWs) had suspected ACD evaluated with PT. Clinical characteristics including age and sex, HCW occupation history, and AD history were comparable among the pre–COVID-19 ( $n = 65$ ) and COVID-19 pandemic ( $n = 34$ ) groups, respectively: (median age: 50 vs 47 years; female sex: 89% vs 94%; HCW: 22% vs 21%; AD history: 11% vs 20%). The dermatitis pattern was documented on the face (59%), extremities (28%), trunk (19%), and generalized (17%). The dermatitis location, duration, and documented descriptions were comparable between the groups.

The rates of positive PT reaction to any allergen were 54% in the pre–COVID-19 group and 88% in the COVID-19 pandemic group ( $P <$

.001). Among all dermatitis cases, positive PT reactions to fragrance mix-I (FM) and glutaraldehyde were detected at significantly higher rates in the COVID-19 pandemic cohort compared with the pre–COVID-19 group (32% vs 9%;  $P = .004$ , and 18% vs 3%;  $P = .01$ ), respectively. Table 1 illustrates the PT results among all dermatitis cases. There were no differences in positive PT allergens in HCWs ( $n = 21$ ) in the pre–COVID-19 and COVID-19 pandemic groups. Some patients had positive PT reactions with personal products (COVID-19 pandemic:  $n = 5$ , pre–COVID-19:  $n = 2$ ). One product in each group contained FM components and other fragrances, but none contained glutaraldehyde.

Facial dermatitis occurred in 54% ( $n = 35$ ) of patients in the pre–COVID-19 group and 68% ( $n = 23$ ) in the COVID-19 pandemic group. The COVID-19 pandemic group consisted of more patients with AD history (22% vs 3%;  $P = .03$ ); otherwise, clinical characteristics and dermatitis features were comparable. Among patients with facial dermatitis, positive PT reaction to FM was detected at a significantly higher rate in the COVID-19 pandemic group (39% vs 11%;  $P = .02$ ). Other positive PT allergens in patients with facial dermatitis included the following (COVID-19 pandemic vs pre–COVID-19): formaldehyde (22% vs 6%), glutaraldehyde (17% vs 6%), and textile dye mix (13% vs 0%).

To the best of our knowledge, this is the first descriptive study comparing PT results in the evaluation of suspected ACD before and during the COVID-19 pandemic. Our data reveal significantly higher rates of positive PT reaction to FM and glutaraldehyde in the COVID-19 pandemic period. In addition, a significantly higher rate of positive PT reaction to FM in patients with facial dermatitis was noted.

FM represents a common positive PT allergen with an overall prevalence of up to 9.2%, and its components are found in personal care products, cleaning solutions or detergents, hand soaps, and sanitizers.<sup>8</sup> Positive PT reaction to FM was detected at a higher than usual reported rate in the COVID-19 pandemic group. This may be attributed to small sample size or a true increase in FM sensitization in our cohort. One patient in each group also exhibited positive PT reaction to personal products containing fragrances, suggesting high clinical relevance. Increased exposure to fragrance-containing products, including FM components (alpha-amylcinnamaldehyde, cinnamic aldehyde, cinnamic alcohol, eugenol, isoeugenol, geraniol, hydroxycitronellal, oak moss), balsam of Peru, linalool, limonene, or essential oils, for hand hygiene and cleaning of reusable masks could increase susceptibility to developing ACD.

Glutaraldehyde, a disinfecting agent and preservative, is used for sterilizing medical equipment. Thus, HCWs may exhibit higher sensitization rates through occupational exposures. In 1 study, glutaraldehyde had a 3.6% positive PT prevalence among HCWs and non-HCWs.<sup>9</sup> Glutaraldehyde-positive PT reaction was noted

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**Table 1**  
Frequency of Positive Patch Test Allergens

Patch test allergens	Pre-COVID (n = 65)	COVID-pandemic (n = 34)	All patients (n = 99)	P value
Positive patch test (to any allergen)	35 (54)	30 (88)	65 (66)	<.001
Carmine 2.5%	12 (18)	9 (26)	21 (21)	.35
Nickel sulfate hexahydrate	10 (15)	8 (24)	18 (18)	.31
Fragrance mix 1	6 (9)	11 (32)	17 (17)	.004
Disperse blue 106	5 (8)	5 (15)	10 (10)	.30
Textile dye mix	3 (5)	6 (18)	9 (9)	.06
Formaldehyde 2%	3 (5)	6 (18)	9 (9)	.06
Glutaraldehyde	2 (3)	6 (18)	8 (8)	.01
Cobalt (II) chloride hexahydrate	6 (9)	1 (3)	7 (7)	.41
Methylisothiazolinone 0.2%	2 (3)	4 (12)	6 (6)	.17
Propolis	2 (3)	3 (9)	5 (5)	.33
4-Phenylenediamine base	4 (6)	0 (0)	4 (4)	.29
Bacitracin 20%	2 (3)	2 (6)	4 (4)	.60
Cocamidopropyl betaine	2 (3)	2 (6)	4 (4)	.60
Balsam of Peru 25%	2 (3)	2 (6)	4 (4)	.60
Quaternium 15	1 (2)	2 (6)	3 (3)	.27

Abbreviation: COVID-19, coronavirus disease 2019.

among HCWs in the pre-COVID-19 and COVID-19 pandemic groups. Glutaraldehyde and formaldehyde are chemical disinfectants. Glutaraldehyde is used for sterilization during the manufacturing process of some PPE as a safer alternative to formaldehyde, which is a known human carcinogen.<sup>10</sup> Despite regulations on formaldehyde use for sterilization, both glutaraldehyde and formaldehyde have been detected in respirators and surgical masks.<sup>4,6</sup> Increased exposure to these contact allergens may lead to new allergic sensitization and clinical ACD.

The retrospective nature and paucity of documented PPE use in most cases represented study limitations. The small sample size precluded a subanalysis of other location-specific dermatitis. The small number of HCWs in this study may have limited the detection of differences in PT-positive allergens.

In summary, these observational findings suggest that FM and glutaraldehyde could represent relevant contact allergens in patients presenting with suspected ACD after the start of the COVID-19 pandemic. Although mask mandates have eased, certain individuals continue to wear PPE more consistently, including HCWs, immunocompromised patients, and those in certain work environments. These individuals may carry an increased risk of allergic sensitization with cutaneous exposures and, thus, providers should consider fragrance, glutaraldehyde, and other previously noted contact allergens as potential culprits in the evaluation of new-onset dermatitis. Identification of allergens by PT can guide management and patient education in avoidance. Additional investigation and future prevalence data would be useful in confirming these findings.

## Delayed IgE-mediated hypersensitivity to *Arthrospira platensis* (spirulina)

Spirulina is the commercial name of lyophilized *Arthrospira platensis*, a filamentous cyanobacteria (blue-green microalgae) naturally found in tropical and subtropical lakes. It is considered to be one of the richest protein sources of microbial origin.<sup>1</sup> There is a growing interest in

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spirulina from the food, cosmetic, and health industries because of its high protein content (62%–68% dry mass), and the presence of essential amino and fatty acids, minerals, and vitamins.<sup>1–3</sup>

We present a case of a healthy 48-year-old woman with delayed hypersensitivity to spirulina. In January 2022, the patient presented to the emergency department with mild left plantar aspect swelling and acute tongue swelling starting approximately 3 hours and 7 hours,