

Report

Positive concomitant test reactions to allergens in the standard patch test series

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Introduction

Patch testing is the gold standard in the diagnosis of suspected contact allergy.¹ Concomitant test reactions may reflect associations between allergens, which may result either from reaction of the immune system to compounds with similar chemical structure (cross-reaction or cross-sensitization) or the sensitization to allergens that commonly occur together (co-reaction or co-sensitization). Cross-reacting allergens are particularly important when advising patients with true allergies about chemicals to avoid, because they are able to develop an allergic reaction even in the absence of originally causative allergen.

Many of these cross-reactions are assumed, but there are only a few larger studies that substantiate our suppositions which are based on our own observations.^{2,3}

Abstract

Background Patch testing is performed to evaluate suspected allergic contact dermatitis. Common wisdom suggests that various allergens cross-react but only a few larger studies have published confirmations of this. The purpose of our study was to identify significant correlations between positive test reactions in a screening series.

Methods A total of 1235 patients undergoing patch testing to the Hermal standard series at the Massachusetts General Hospital, Contact Dermatitis Clinic between 1990 and 2006 were investigated.

Results Two or more positive reactions were seen in 411 patients (33.3%). Sensitizations to eight pairs of allergens were found to have significant correlation ($P \leq 0.0001$). A strong association was observed for cross reactions between formaldehyde and its releasers quaternium 15 and imidazolidinyl urea and between balsam of Peru and fragrance mix. Moreover, significant co-sensitization was identified for potassium dichromate and colophony. Three significant pairings in our study were associations between fragrances and metals. Our data confirm the previously published cross-reactions in the literature between fragrance components, and formaldehyde and formaldehyde-releasing preservatives. The increased numbers of patients with metal and fragrance sensitization can be considered as a random finding due to independent sensitization.

Conclusion Being aware of cross-reacting allergens is essential to success in resolving allergic dermatitis when counseling patients.

Therefore, this study adds to the allergic cross-reaction knowledge base. The purpose of this study was to identify significant correlations between positive test reactions in a screening series.

Methods

After obtaining approval from the Institutional Review Board, data were collected from charts reviewed for 1235 patients undergoing patch testing to the Hermal standard series at the Massachusetts General Hospital Contact Dermatitis Clinic between 1990 and 2006. Testing and readings were conducted according to international guidelines.^{1,4} "Angry back" reactions were excluded. To evaluate for associations between allergens, the Fisher's exact test was used. Correlations were considered significant at $P \leq 0.0001$.

Table 1 Positive tested allergens of those patients with at least two reactions, $N = 411$

Allergen	n, (%)
Fragrance mix	145 (35.3)
Nickel sulfate	125 (30.4)
Balsam of Peru	122 (29.7)
Cobalt chloride	73 (17.8)
Quaternium 15	65 (15.8)
Formaldehyde	64 (15.6)
Neomycin sulfate	45 (10.9)
Colophony	43 (10.5)
Potassium dichromate	39 (9.5)
N-isopropyl-N-phenyl-4-phenyldiamine	35 (8.5)
Paraben mix	33 (8.0)
4-Phenyldiaminebase	31 (7.5)
Carba mix	28 (6.8)
Balsam of Tolu	27 (6.6)
Phenylmercuric acetate	27 (6.6)
Imidazolidinyl urea	22 (5.4)
Epoxy resin	20 (4.9)
p-tert-Butylphenol formaldehyde resin	18 (4.4)
Benzocaine	17 (4.1)
MCI/MI (3 : 1 in water)	17 (4.1)
Mercapto mix	13 (3.2)
Clioquinol	13 (3.2)
Sodium metabisulfite	12 (2.9)

Percentage positive are given in parenthesis.

Results

Two or more positive reactions were seen in 411 patients (33.3%). The most common allergens in this group are shown in Table 1. The mean age was 46.3 years, and 70.1% were women. As illustrated in Table 2, sensitizations to eight pairs of allergens were found to have significant correlation ($P \leq 0.0001$). Of those, four pairs were cross-reactions, while the remaining four pairs occurred as a result of co- or independent sensitization.

Discussion

Our study revealed a similar number of significant associations of allergens in a standard series, compared with other large studies of concomitant test reactions, as shown in Table 2.

Akin to results from the NACDG,² a strong association was observed for cross-reactions between formaldehyde and its releasers quaternium 15 and imidazolidinyl urea (Table 2). In our study, three of these formaldehyde-related pairings predominated in the list of cross-reacting allergens. Moreover, we observed a significant relationship between fragrance mix and balsam of Peru. (change the order of allergens). Overlap of certain ingredients

Table 2 Significant associated sensitizations from our study compared to findings from a study conducted by the North American Contact Dermatitis Group

MGH, 1990–2006 $N = 1235$ Standard tray	NACDG, ² 1985–1989 $N = 4055$ Standard tray
Fragrance mix/Balsam of Peru	Cinnamic alcohol/Balsam of Peru
Formaldehyde/Quaternium 15	Formaldehyde/Quaternium 15
Formaldehyde/Imidazolidinyl urea	Carba mix/Thiuram mix
Quaternium 15/Imidazolidinyl urea	Cinnamic alcohol/Cinnamic aldehyde
Potassium dichromate/Colophony	Diaminodiphenylmethane/PPD
Fragrance mix/Nickel sulfate	Benzocaine/PPD
Balsam of Peru/Nickel sulfate	Mercapto mix/Mercaptobenzothiazole
Balsam of Peru/Cobalt chloride	

explains their frequent association and can be categorized as cross-reactivity. Significant associations between potassium dichromate and colophony likely represent co-sensitization, which is expected because these agents are found together in leather products⁵ and eye cosmetics.⁶

Three significant pairings in our study were associations between fragrances and metals. These relationships seem rather unlikely and most probably result from independent sensitization because of the individual's habits.

Conclusion

Significant associated sensitizations included fragrances, metals and preservatives. In comparison with earlier studies, cross-sensitizations to preservatives were overrepresented in our study population. Perhaps this reflects a greater influence (usage patterns) of these chemicals today. The co-sensitization of potassium dichromate/colophony may result from co-occurrence in leather products and eye cosmetics. When advising patients with true allergies about avoiding chemicals, physician should always include cross-reacting allergens as those are able to elicit similar reactions.

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