How To Test For Fragrance Allergy

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GOAL

To describe the process of fragrance detection in determining the cause of cosmetic allergic contact dermatitis.

OBJECTIVES

1. To discuss the modifications of fragrance mixtures (FM) used to test for fragrance allergy.
2. To identify which FM components are associated with greater responses.
3. To describe which FM is preferred for routine patch testing.

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Fragrance is the most common cause of cosmetic allergic contact dermatitis. Fragrance allergy detection is best accomplished by testing with the fragrance mixture, balsam of Peru, and either jasmine synthetic or absolute. It would be desirable to have common fragrance allergens listed on cosmetic labels so that patients could avoid the allergens to which they are allergic.

Perfume is the most common cause of allergic contact dermatitis reactions due to cosmetics.[1] Approximately 1% or more of the general population is allergic to fragrance. American manufacturers have labeled cosmetic ingredients for the past 20 years. In 1997, ingredient labeling was also instituted in the EC in Europe. One problem with ingredient labeling is that fragrances are listed as fragrances without further specification. Since fragrance allergy is the most common cause of allergic contact dermatitis due to cosmetics, it would be beneficial to have disclosure on the label of the most common fragrance allergens. Although it is impossible to list all of the ingredients in perfumes, it would be easy to list the fragrance materials that are known to be allergenic. This measure would be of great benefit to both the consumer and the physician.

In the 1960s, the use of balsam of Peru was helpful in detecting fragrance allergy. In the late 1970s, a fragrance mixture consisting of eight different components was introduced and greatly improved the detection of fragrance allergy. The initial fragrance mixture (FM) consisted of eight separate components at a concentration of 2% each, totaling 16% in petrolatum. In the early 1980s, the concentration was reduced to 8% to lessen the false-positive reactions observed with the 16% formulation (Table I). However, reducing the concentration of the ingredients in the FM to half of the original concentrations may have induced more false-negative responses. The addition of sorbitan sesquioleate to the FM to keep the ingredients in solution may also augment its potency for certain components and cause false-positive responses.

Recently, a study based on 14 years of FM use reported a 5.5% positive response rate.[2] Another report cited an 8.3% prevalence in 1072 patients tested recently in Europe with FM.[3] The FM is the number 1 or 2 reacting substance in most reported patch test series. A more extensive series for fragrance testing includes 14 fragrance allergens (Table II).

In 1995, the European Environmental and Contact Dermatitis Research Group reported results from a multicenter study of 48 fragrance materials. The researchers tested 1072 patients for responses to FM and the individual ingredients in FM.[3] Their findings were similar to those of previous studies. Few responses were elicited to the additional fragrance materials evaluated; however, due to the study design, the number of subjects tested with each material was limited to 100 patients or slightly more. Thus, the statistical power of the investigation precluded the formulation of definite con-

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Table I.

Fragrance Mixture in Petrolatum

1. Cinnamic alcohol	1%
2. Cinnamic aldehyde	1%
3. Hydroxycitronellal	1%
4. Isoeugenol	1%
5. Eugenol	1%
6. Oakmoss absolute	1%
7. α-Amylcinnamic alcohol	1%
8. Geraniol	1%

Table II.

Fragrance Screening Series in Petrolatum

1. Cinnamic alcohol	5%
2. Cinnamic aldehyde	1%
3. Hydroxycitronellal	4%
4. Isoeugenol	5%
5. Eugenol	5%
6. Oakmoss absolute	5%
7. α-Amylcinnamic alcohol	5%
8. Geraniol	5%
9. Benzyl salicylate	2%
10. Sandalwood oil	2%
11. Anisyl alcohol	5%
12. Benzyl alcohol	5%
13. Coumarin	5%
14. Musk ambrette (also a photoallergen)	5%

clusions with respect to the allergenicity of the materials. Several of the new fragrance components did produce notable responses; these were lyral and citronellol, which were associated, respectively, with a 2.8% and 1% response prevalence in 106 subjects tested in Barcelona. Lilial [2-methyl-3(4-tert-butyl-phenyl) propionaldehyde], which has been reported to cause allergic contact dermatitis in a single case of a user of underarm deodorant, did not cause a positive response in any of the 106 patients tested.[4]

Table III.

Responses to Fragrance Materials in Japan

Test Substance	No. Tested	% Positive
Essential oils		
• Jasmine oil	183	18.6
• Cananga oil	183	14.2
• Ylang ylang oil	183	13.7
• Sandalwood oil	137	10.2
• Patchouli oil	183	6.0
• Lavender oil	183	3.3
• Bulgarian rose oil	137	2.9
• Geranium oil	183	1.6
Specific chemicals		
• Methoxycitronellal	137	16.7
• Benzyl salicylate	183	15.3
• Geraniol	183	13.7
• Hydroxycitronellal	138	9.4
• Eugenol	183	4.4
• Cinnamic alcohol	183	2.7
Balsam		
• Balsam of Peru (Peruvian balsam)	183	0.5

A group of investigators who evaluated the use of FM and Peruvian balsam as screening test substances to detect fragrance allergy in perfume-sensitive patients found that either of the two test materials yielded a positive response in almost all of this selected sample of patients.[5] While Asian patients were more likely to react to benzyl salicylate, Western patients were more likely to react to isoeugenol and oak moss absolute. The authors found that three other essential oils (sandalwood, narcissus, and ylang ylang) and benzyl salicylate accounted for many of the positive responses that were not detected by FM and Peruvian balsam. The addition of these materials (three of which have been part of the Japanese fragrance screening tray [Table III])[6] as screening-test substances

would be expected to improve the sensitivity of screening materials used to detect fragrance allergy.

Because jasmine is widely used and accounts for a significant number of positive responses,[7] its use as an additional screening test material has recently been investigated by the World Fragrance Research Team (WFRT) as a follow-up to their recent study.[8] The investigators reported that 19 out of the 754 patients tested with a combined jasmine-FM screening test material were positive for perfume allergy. The authors noted that these patients would not have been identified by testing with FM alone. Although testing with jasmine/FM mix and FM simultaneously increased the total number of the allergic patients identified, testing with the jasmine/FM mix would have identified only 63 perfume-sensitive patients, whereas testing with FM would have identified 67. There was concordance of response for both test substances in only 44 instances; thus, adding more ingredients to the FM apparently eliminated some of the positive responses that were evident with FM alone. The latter results demonstrate the difficulty in developing new test substances for patch testing for fragrance allergy.

In the same investigation, the WFRT determined that testing with Peruvian balsam, FM, and either jasmine/FM mix or a mixture of five natural fragrance ingredients increased the number of positive patients to 95. In contrast, choosing one or another of the additional mixes resulted in a failure to identify 5 of the total of 100 fragrance-allergic patients who were identified by testing with all four fragrance test materials. These findings suggest that the addition of jasmine synthetic or a mixture of natural fragrance materials to the present screening panel of 25% Peruvian balsam and 8% FM may help to identify a significant number of patients allergic to fragrance materials.

For routine patch testing, the use of the 8% FM, 25% balsam of Peru, and either jasmine synthetic or absolute 10% in petrolatum is recommended. In addition, testing with the actual cosmetics used by the patient is essential.

In conclusion, it would be very helpful if the common fragrance allergens were listed on cosmetic labels. Patients could thus avoid the substances to which they are allergic.

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The Faculty Disclosure Policy of the College of Medicine requires that faculty participating in a CME activity disclose to the audience any relationship with a pharmaceutical or equipment company that might pose a potential, apparent, or real conflict of interest with regard to their contribution to the program.
Dr. Larsen reports no conflict of interest.