

# Allergic Contact and Photoallergic Contact Dermatitis to Plant and Pesticide Allergens

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**Background:** The panel of patch test allergens used for the evaluation of patients with suspected photoallergy typically does not include plant and pesticide allergens. The prevalence of allergic contact dermatitis and photoallergic contact dermatitis to plant and pesticide allergens was determined for this subgroup of patients.

**Observation:** Positive reactions were detected in 12 of 26 patients who were tested with our photoallergen series: 5 with allergic contact dermatitis, 5 with photoallergic contact dermatitis, and 2 with both. Four of the 12 patients had positive patch and photo-patch test reactions to plant allergens, pesticide allergens, or both. The positive patch test reactions were to the plants *Taraxa-*

*cum officinale* (dandelion) and *Tanacetum vulgare* (tansy) and to the pesticides folpet and captafol. Positive photo-patch test reactions were to the pesticides folpet and captan. The histories of the patients suggested that 2 or 3 of the 4 patients had clinically relevant reactions. In the other 8 patients, positive reactions to the patch and photo-patch tests included fragrances, sunscreens, and antibacterial agents.

**Conclusion:** Plant and pesticide allergens should be included in the patch and photo-patch test series used for the evaluation of patients with suspected photoallergy.

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**T**HE DERMATOLOGIC manifestations of the photosensitivity disorders, including photoallergic contact dermatitis (PACD), occur on exposed areas of the body. In addition, allergic contact dermatitis (ACD) to airborne substances also is found on non-covered sites. Clinically, the distinction between airborne ACD and PACD may be difficult. Plant and pesticide allergens are known to cause airborne ACD and PACD; however, these allergens are not used routinely in patch and photo-patch testing. The purpose of this prospective study was to determine the value of including plant and pesticide allergens in patch and photo-patch testing of photosensitive patients.

Of the additional PACD reactions, 3 were to sunscreens, with 2 to *p*-aminobenzoic acid and 1 to butylmethoxydibenzoylmethane; 6 were to fragrances, with 3 to musk ambrette, 2 to 6-methylcoumarin, and 1 to sandalwood oil; and 3 to antibacterial agents, with 1 to sulfanilamide, 1 to bithionol, and 1 to fenitrothion. The remainder of the reactions were to therapeutic agents, with 1 to diphenhydramine, 1 to chlorpromazine, and 1 to promethazine.

## REACTIONS TO PLANTS AND PESTICIDES

Patient 1 was a 59-year-old woman with skin type VI and a 10-year history of a recurrent, erythematous, edematous, pruritic, papular eruption on her face. Medications consisted of conjugated estrogen and methoxyprogesterone acetate. Although she denied photosensitivity, the dermatitis became worse during the summer. Previous patch testing showed a positive patch test reaction to balsam of Peru. With the use of fragrance-free products, the condition improved for approximately 1 year, from August 1993 to June 1994. Subsequently, she experienced a flare-up that began while she was on vacation in Nevada; the flare-up persisted throughout the summer and continued throughout the year.

Phototests showed a normal MED-A of 45 J/cm<sup>2</sup> and a normal MED-B of 108 mJ/cm<sup>2</sup>. Patch and photo-patch tests showed a reac-

## RESULTS

### OVERALL REACTIONS

Of 26 patients, 12 had positive reactions: 5 with ACD, 5 with PACD, and 2 with both ACD and PACD (Table 2). Four of the 12 patients had positive reactions to plant allergens, pesticide allergens, or both. The ACD reactions were to the plants *Taraxacum officinale* (dandelion) and *Tanacetum vulgare* (tansy) and to the pesticides folpet and captafol. The PACD reactions were to the pesticides folpet and captan. Of the additional ACD reactions, 2 were to oxybenzone, 1 was to homosalate, and 1 was to fen-

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## PATIENTS AND METHODS

### PATIENTS

Between March 1994 and August 1996, phototests, patch tests, and photo-patch tests were performed on 26 consecutive patients who were examined because of a suspected photodermatitis or airborne ACD. For example, patients with polymorphous light eruption were not included in the study.

### LIGHT SOURCES FOR PHOTOTESTS AND PHOTO-PATCH TESTS

The UV-A source was Ho-UV-A bulbs (National Biologic Corp, Twinsburg, Ohio), and the UV-B source was FS40 bulbs (National Biologic Corp). A slide projector (Eastman Kodak Company, Rochester, NY) with a quartz halogen 82 V projector lamp and a water filter served as the visible light source.<sup>1</sup>

### METHODS AND EVALUATION OF PHOTOTESTS, PATCH TESTS, AND PHOTO-PATCH TESTS

Phototests were performed to UV-B, UV-A, and visible light. To obtain the minimal erythema dose (MED) determinations for UV-B and UV-A, a template with a series of 1.5 × 1.5-cm openings with removable flaps was placed on uninvolved skin. The template openings were exposed to incremental increases of UV-B or UV-A. The MED is defined as the lowest dose of UV radiation that produces perceptible erythema covering the entire irradiated area. The normal MED ranges used for UV-B were dependent on skin type. The following reference ranges in mJ/cm were used: for skin type I (always burn, never tan), 20 to 30; II (usually burn, tan less than average), 25 to 35; III (sometimes burn, tan less than average), 30 to 50; IV (rarely burn, tan more than average), 45 to 60; V (brown-skinned persons), 60 to 100; and VI (dark-

skinned persons), 100 to 200. For UV-A, an MED greater than 20 J/cm<sup>2</sup> was considered normal, regardless of the skin type. Any response to visible light radiation was considered abnormal.<sup>2</sup> For visible light tests, the projector lamp was positioned 15 cm from the upper inner arm, and exposure times of 15, 30, 45, and 60 minutes were used.

Patch and photo-patch tests were performed as recommended in the guidelines of the North American Contact Dermatitis Group.<sup>3</sup> On day 1, duplicate sets of photoallergens were applied to the back and then covered by opaque tape. On day 2, the MED responses to UV-A (MED-A) and UV-B (MED-B) were quantified, the sites exposed to visible light were evaluated, and 1 set of photo-patch tests was exposed to UV-A (10 J/cm<sup>2</sup> or 50% of the MED-A).<sup>1</sup> The patches on the nonirradiated site were kept covered for an additional 24 hours and were removed for the initial evaluation at 48 hours. The exception was 6-methylcoumarin, which was irradiated 30 to 60 minutes after application.<sup>4</sup>

At 48 and 96 hours, the irradiated and nonirradiated patch test sites were evaluated. By using a scoring system recommended by the North American Contact Dermatitis Group, the responses were graded as follows: 1+, erythema, infiltration, possibly papules; 2+, edema and vesicles; and 3+, bullae and ulcers.<sup>3</sup> Equally positive reactions on the patch and photo-patch test sites or on the patch test site alone were interpreted as ACD. If a positive reaction was greater on the photo-patch test site than on the patch test site, ACD and PACD were present. A negative patch test reaction and a positive photo-patch test reaction were interpreted as PACD.<sup>5</sup> The photoallergens used were the New York University Skin and Cancer Photoallergen Series (**Table 1**) that were obtained from Chemotechnique (Rexdale, Ontario) and Trolab (Hudson, Quebec).

A diagnosis of chronic actinic dermatitis (CAD) was made in the patients with an eczematous photosensitivity eruption with low MED-A, MED-B, and/or visible light responses, whether or not concomitant contact or photocontact sensitivity to airborne or other allergen was present.<sup>6</sup>

tion to *T officinale* of 2+ at the nonirradiated site and 1+ at the irradiated site. When additional historical information was requested, the patient stated that she drinks dandelion tea prepared from loose leaves. After avoiding the tea, the eruption cleared. A subsequent challenge, which involved drinking a cup of dandelion tea, was followed by a recurrence of the eruption 12 hours after exposure. This reaction to *T officinale* was considered the cause of airborne ACD during the summer, and the habit of drinking dandelion tea allowed the reaction to persist during the winter months.

Patient 2 was a 45-year-old woman with skin type II and a pruritic generalized dermatitis that spared her face, occurred 3 to 4 hours after sun exposure, and persisted for 3 or 4 days. The eruption also developed after sun exposure through window glass. She denied the use of any oral medications. Phototests showed a normal MED-A of 15 J/cm<sup>2</sup> and a normal MED-B of 72 mJ/cm<sup>2</sup>. Patch and photo-patch tests showed 1+ reactions to *T officinale*, captafol, and fenticlor on the covered and irradiated sites. She also had 1+ reactions to captan and folpet on the irradiated sites only. These reactions were clinically relevant since she had recently sprayed her property with fungicides and pesticides. The diagnoses of ACD and PACD were made.

Patient 3 was a 68-year-old man with skin type VI and a 2-month history of blisters on his hands and a pruritic eruption on his arms and legs, trunk, and scalp. He was not taking any oral medications. The physical examination revealed lichenified plaques with scale on the dorsa of both hands, the occipital scalp, the posterior neck, the arms and legs, and the trunk.

Phototests showed a low MED-A and a low MED-B of 3 J/cm<sup>2</sup> and 24 mJ/cm<sup>2</sup>, respectively. Patch and photo-patch tests showed a 1+ reaction on the covered and irradiated sites to *T vulgare*. Based on these results, the patient had CAD with an ACD.

Patient 4 was a 56-year-old woman with skin type VI and a 6-month history of burning and itching of the skin that occurred after exposure to direct sunlight, exposure through windows, and exposure to fluorescent lamps. Medications included hydroxyzine hydrochloride, acetaminophen, and ibuprofen. The physical examination revealed lichenified plaques on the face and dorsa of the hands and mild erythema on the posterior neck. There was sparing of the nasolabial folds and cheeks inferior to the eyelids.

Phototests showed a low MED-A of 2 J/cm<sup>2</sup> and a low MED-B of 6 mJ/cm<sup>2</sup>. Patch and photo-patch tests

showed 2+ reactions to folpet on the covered and irradiated sites. A diagnosis of CAD with ACD was made.

## COMMENT

In 12 of 26 patients with a history suggestive of photodermatitis, PACD was present in 5, ACD in 5, and PACD and ACD in 2. The present study was relatively unique because both plant and pesticide allergens and their relationship to airborne dermatitis were studied. Patch and photo-patch tests yielded positive reactions in 46% (12/26); 27% (7/26) were PACD and 27% (7/26) were ACD. An earlier study from our institution by Fotiades et al<sup>4</sup> noted that 8% of patients with suspected photosensitivity had PACD. The rate of positive patch and photo-patch tests in the present series is also greater than that previously reported by DeLeo et al,<sup>5</sup> who found a 20% overall positive response rate and a diagnosis of PACD in 11% in a sample of 187 subjects. An earlier study from the Mayo Clinic noted positive photo-patch test reactions in 38% (27/70); 31% (22/70) were ACD and 20% (14/70) were PACD.<sup>7</sup> Although the number of patients in the present study is fewer than that in earlier studies, which are described for comparison, the use of percentages is a useful way to compare data. Perhaps this will serve as the basis for future larger studies, which will allow a more appropriate comparison of the proportion of positive reactions. The increased percentage of positive responses, 46% in the present study, can be attributed at least in part to the inclusion of plant and pesticide allergens in our photoallergen series. In addition, the patch and photo-patch tests were performed only on patients with suspected photoallergy and not on all photosensitive patients.

Lisi et al<sup>8</sup> studied irritant contact dermatitis and ACD in 652 patients in Italy, and pesticides accounted for approximately 19% of the clinical lesions that were observed in 125 patients with ACD. The positive reactions to pesticides were mainly due to captan, captafol, and folpet. The results of the present study, in which positive pesticide reactions occurred exclusively to these substances, were consistent with this observation. Patient 2 in the present study is, to our knowledge, the first reported case of PACD to folpet. Despite their frequent use in suburban and rural areas, pesticides have been notably absent from many studies of airborne contact dermatitis and PACD.

The present study showed positive reactions to plant and pesticide allergens in patients with CAD. An association has been noted between CAD and airborne allergy to *Compositae* plants.<sup>9,10</sup> Patient 3 in this study had CAD and an ACD reaction to a *Compositae* plant, *T vulgare* but a negative reaction to a sesquiterpene-lactone mix. Screening with the sesquiterpene-lactone and *Compositae* mixes may not be sufficient to thoroughly evaluate airborne allergy to plants.<sup>11,12</sup> Patient 4 had CAD and ACD to folpet. The inclusion of plant and pesticide allergens in photo-patch testing may reveal previously unrecognized associations with CAD.<sup>11</sup>

The findings of an earlier study<sup>13</sup> of allergy to *Compositae* plants were similar to findings in the present study. Contact allergy to *Compositae* plants was found to be an important factor in patients with summer exacerbation of dermatitis, even without photosensitivity. One pa-

**Table 1. New York University Skin and Cancer Unit Photoallergen Series\***

| Allergen   | Concentration, %<br>in Diluent |
|--|--------------------------------|
| <b>Antigens</b>  |                                |
| <i>p</i> -Aminobenzoic acid (PABA)                             | 5.00 alcohol                   |
| Bithionol (2,2'-thiobis[4,6-dichlorophenol])                   | 1.00 pet                       |
| Chlorhexidine diacetate  | 0.50 water                     |
| Chlorpromazine   | 0.10 pet                       |
| Cinoxate   | 1.00 pet                       |
| Dichlorophen   | 1.00 pet                       |
| Diphenhydramine  | 1.00 pet                       |
| Fenticlor (2,2'-thiobis[4-chlorophenol])                       | 1.00 pet                       |
| Hexachlorophene  | 1.00 pet                       |
| 1-(4-Isopropylphenyl)-3-phenyl-1,3-propanedione (Eusolex 8020) | 2.00 pet                       |
| Menthyl anthranilate   | 5.00 pet                       |
| 3-(4-Methylbenzyliden)-camphor (Eusolex 6300)                  | 2.00 pet                       |
| 6-Methylcoumarin   | 1.00 pet                       |
| Musk ambrette  | 1.00 alcohol                   |
| Musk ambrette  | 1.00 pet                       |
| Octyl dimethyl PABA  | 5.00 alcohol                   |
| Octyl methoxycinnamate   | 7.50 pet                       |
| Oxybenzone (BZP-3)   | 3.00 pet                       |
| Petrolatum control   | 100.00 pet                     |
| Promethazine   | 1.00 pet                       |
| Sandalwood oil   | 2.00 pet                       |
| Sulfanilamide  | 1.00 pet                       |
| Sulisobenzene (BZP-4)  | 10.00 pet                      |
| Thiourea (thiocarbamide)                                       | 0.10 pet                       |
| Tribromosalicylanilide   | 1.00 pet                       |
| Trichlorocarbanilide   | 1.00 pet                       |
| Triclosan  | 2.00 pet                       |
| <b>Plants and plant derivatives</b>                            |                                |
| <i>Achillea millefolium</i>                                    | 1.00 pet                       |
| Alantolactone  | 0.10 pet                       |
| <i>Arnica montana</i>  | 0.50 pet                       |
| <i>Chamomilla romana</i>                                       | 1.00 pet                       |
| <i>Chrysanthemum cinerariaefolium</i>                          | 1.00 pet                       |
| Diallyldisulfide   | 1.00 pet                       |
| Lichen acid mix  | 0.30 pet                       |
| $\alpha$ -Methylene- $\gamma$ -butyrolactone                   | 0.01 pet                       |
| Propolis   | 10.00 pet                      |
| Sesquiterpene lactone mix                                      | 0.10 pet                       |
| <i>Tanacetum vulgare</i>                                       | 1.00 pet                       |
| <i>Taraxacum officinale</i>                                    | 2.50 pet                       |
| <b>Pesticides</b>  |                                |
| Benomyl  | 0.10 pet                       |
| Captan   | 0.10 pet                       |
| Captafol   | 0.10 pet                       |
| Folpet   | 0.10 pet                       |
| Maneb  | 1.00 pet                       |
| Pyrethrum  | 2.00 pet                       |
| Zineb  | 1.00 pet                       |
| Ziram  | 1.00 pet                       |

\*pet indicates petrolatum; BZP, benzophenone.

tient had a flare-up of dermatitis after drinking tea made from *Achillea millefolium* (yarrow).<sup>13</sup>

The phototoxic effects of *Compositae* plants and the difficulty in interpreting presumed positive photo-patch test results in patients with persistent photosensitivity have been described. False-positive patch and photo-patch test results have been known to occur if testing is performed on hyperreactive skin.<sup>14</sup> A report<sup>15</sup> on photo-patch testing noted that in patients with CAD, many of the positive results could

**Table 2. Reactions to the New York University Skin and Cancer Unit Photoallergen Series\***

| Patient No./<br>Sex/Age, y                | Skin<br>Type | Positive Test Results†                     |   | MED-A,<br>J/cm <sup>2</sup> | MED-B,<br>mJ/cm <sup>2</sup> | Diagnosis |
|---|--------------|--|---|-----------------------------|------------------------------|-----------|
|   |              | Patch                                      | Photo-Patch   |                             |                              |           |
| <b>Reactions to Plants and Pesticides</b> |              |  |   |                             |                              |           |
| 1/F/59                                    | VI           | <i>Taraxacum officinale</i><br>(dandelion) | <i>T officinale</i>   | 45                          | 108                          | ACD       |
| 2/F/45                                    | II           | Captafol, dandelion fenticlor              | Captafol, dandelion fenticlor, folpet, captan   | 15                          | 72                           | ACD, PACD |
| 3/M/68                                    | VI           | <i>Tanacetum vulgare</i> (tansy)           | <i>T vulgare</i>  | 3                           | 24                           | ACD, CAD  |
| 4/F/56                                    | VI           | Folpet                                     | Folpet  | 2                           | 6                            | ACD, CAD  |
| <b>Additional Positive Reactions</b>      |              |  |   |                             |                              |           |
| 5/M/46                                    | III          | ...  | PABA, 6-methylcoumarin  | 45                          | 108                          | PACD      |
| 6/M/77                                    | VI           | Oxybenzone                                 | Oxybenzone  | 12                          | 36                           | ACD, CAD  |
| 7/F/27                                    | I            | ...  | PABA, promethazine, chlorpromazine, fenticlor,<br>butylmethoxydibenzoylmethane, sulfanilamide | 12                          | 72                           | PACD      |
| 8/M/72                                    | II           | Oxybenzone                                 | Oxybenzone, diphenhydramine   | 18                          | 96                           | ACD‡      |
| 9/M/63                                    | IV           | ...  | Bithionol, musk ambrette  | 3                           | 36                           | PACD, CAD |
| 10/F/58                                   | III          | Homosalate                                 | 6-Methylcoumarin  | 18                          | 108                          | ACD, PACD |
| 11/M/67                                   | II           | ...  | Sandalwood oil, musk ambrette   | 12                          | 96                           | PACD, CAD |
| 12/M/64                                   | II           | ...  | Musk ambrette   | 18                          | 48                           | PACD      |

\*MED-A indicates minimal erythema dose to UV-A light; MED-B, MED to UV-B light; ACD, allergic contact dermatitis; CAD, chronic actinic dermatitis; PABA, p-aminobenzoic acid; PACD, photoallergic contact dermatitis; and ellipses, no positive results were found. For definitions of skin types, see the "Methods and Evaluation of Phototests, Patch Tests, and Photo-Patch Tests" subsection of the "Patients and Methods" section.

†For patients 5 to 12, reactions were not to plants or pesticides.

‡Diagnosis of PACD was not definite.

have been phototoxic reactions of uncertain relevance. Nevertheless, clinically relevant reactions in this subgroup of patients have been noted.

One patient with UV-A photosensitivity took a potentially photoactivating medication (patient 4 was taking ibuprofen), the tests were not performed on hyper-reactive skin, and none of our patients was diagnosed with a PACD to *Compositae* plants. Patients 1 and 2 had ACD reactions to *T officinale*, and patient 3 had an ACD reaction to *T vulgare*. The only diagnosis of PACD to a plant or pesticide was in patient 2 who had I+ reactions to folpet and captan on the irradiated sites only. These 2 reactions of patient 2 and the 3 reactions to the plants did not represent aggravation of a positive contact control by irradiation. Regarding the additional cases of PACD in patients with and without CAD, we have not observed phototoxic reactions during photo-patch testing, but physicians should be aware of their existence and their potential to confound the interpretation of results.

The clinical differentiation of PACD and airborne ACD has rested primarily on the clinical distribution pattern with the findings of sparing of photoprotected areas of the face and neck. This clinical differentiation may be difficult as demonstrated in an illustrative case reported by Davies and Kersey,<sup>16</sup> in which a groundsman who experienced an eczematous eruption in a photodistribution on his face, neck, and forearms was found to have an ACD to *A millefolium*. Besides outdoor exposure, the increasingly common practice of patients using herbal remedies, which contain plant products, offers an additional method of exposure to plant products. Of the patients in the present study with positive reactions, 33% (4/12) would not have been given the correct diagnosis if plant and pesticide allergens had been omitted. In the routine evaluation of photosensitive patients with suspected photoallergy, airborne allergens, such as plants and pesticides, should be included.

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