

# True Photoallergy to Sunscreens Is Rare Despite Popular Belief

Tatyana Shaw, Brenda Simpson, Brittney Wilson, Holly Oostman, David Rainey, and Frances Storrs

**Background:** Rising use of sunscreen products has led to increased reporting of adverse reactions to sunscreens.

**Objective:** To investigate possible photoallergic reactions in patients who identified themselves as "being allergic" to sunscreens.

**Methods:** Patients filled out questionnaires about types of sunscreens they used and timing of their "allergic" reactions. Next, they consented to be photopatch-tested with active sunscreen ingredients, including the new sunscreen Anthelios SX (containing Mexoryl SX) and the new ultraviolet filters Tinosorb M and Tinosorb S. Standard allergen patch testing was also done.

**Results:** Twenty-seven patients self-reported "sunscreen allergy." Photopatch testing is difficult for patients; hence, only 11 agreed to proceed with the testing. Eight patients had negative patch testing results. One patient reacted to benzophenone-2. Another had a prior reaction to titanium dioxide and titanium oxalate but did not react to the silicone-coated titanium in our study. Yet another patient had relevant photopatch reactions to benzophenone-3 and ethylhexyl dimethyl para-aminobenzoic acid (PABA). None reacted to the Tinosorbs or Anthelios SX. Few positive reactions to the standard allergens were not relevant.

**Conclusion:** Although small, this study parallels prior studies in concluding that true delayed type IV hypersensitivity (allergic contact dermatitis and photoallergy) to sunscreens is more infrequent than patients tend to believe.

INCREASED PUBLIC AWARENESS of the harmful effects of ultraviolet (UV) light exposure has greatly increased the use of sunscreen products in developed countries.<sup>1</sup> Sunscreen and sunblock chemicals may be found in a diverse variety of skin care and cosmetic products. As a result of increased exposure, reports of adverse effects to sunscreen products have increased.<sup>2,3</sup> Up to 19% of patients report experiencing an adverse event due to sunscreen-containing products.<sup>4</sup> Adverse effects from sunscreen products may include urticaria, allergic and irritant contact dermatitis, and phototoxic and photoallergic reactions.<sup>2</sup> Numerous nomenclatures exist for active sunscreen ingredients. In most countries, the International Nomenclature Cosmetic Ingredient (INCI) names are used. In the United States, there are standardized Food and Drug Administration (FDA) names for

sunscreen chemicals. Sunscreen manufacturers are not required to list ingredients by their FDA-standardized names; thus, synonyms are commonly used for various active sunscreen chemicals. This article will refer to sunscreen chemicals by their INCI names; synonyms are provided in Table 1.

Sunscreen products contain active chemicals as well as inactive ingredients, any of which may be problematic (Table 2<sup>1,3-62</sup>). Past studies revealed that inactive ingredients (such as fragrance, preservatives, formaldehyde releasers, antimicrobial agents, and lanolin) were among the most common culprits in allergic and photoallergic reactions caused by cosmetic products including sunscreens.<sup>4,31,36,52,60</sup> Since the late 1980s, however, the active chemical sunscreen ingredients have been implicated as increasingly important causes of allergic and (particularly) photoallergic contact dermatitis.<sup>3,42,60</sup>

The most commonly reported allergen among the active sunscreen chemicals in the 1960s was para-aminobenzoic acid (PABA), whose sensitizing potential created enough concern to prompt its virtual disappearance from the US sunscreen market.<sup>2</sup> In recent years, most sunscreen products have been advertised as "PABA free."<sup>63</sup> In the United Kingdom, however, PABA continued to be marketed until 2007 and is still advertised for sale through the Internet.<sup>8</sup> The next most commonly reported allergenic sunscreen chemical was a derivative of PABA, ethylhexyl

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**Table 1.** Sunscreen Active Ingredients on Sunscreen Patch Test Tray

| <i>INCI Name, Concentration, and Vehicle</i> | <i>Synonyms</i>                                 | <i>Chemical Name</i>                                                               | <i>Trade Names</i>          | <i>Manufacturer</i>                          |
|----------------------------------------------|-------------------------------------------------|------------------------------------------------------------------------------------|-----------------------------|----------------------------------------------|
| Ethylhexyl methoxy-cinnamate 7.5% pet        | Octyl methoxycinnamate; octinoxate              | 2-Ethylhexyl 4-methoxycinnamate                                                    | Parsol MCX<br>Eusolex 2292  | Chemotechnique Diagnostics, Tygelsjo, Sweden |
| Benzophenone-4 10% pet                       | Sulisobenzone                                   | 2-Hydroxy-4-methoxybenzophenone-5-sulfonic acid                                    | Uvinul MS-40                | Chemotechnique Diagnostics, Tygelsjo, Sweden |
| Benzophenone-3 10% pet                       | Oxybenzone                                      | 2-Hydroxy-4-methoxybenzophenone                                                    | Eusolex 4360                | Chemotechnique Diagnostics, Tygelsjo, Sweden |
| PABA 10% pet                                 | para-Aminobenzoic acid                          | 4-Aminobenzoic acid                                                                | —                           | Chemotechnique Diagnostics, Tygelsjo, Sweden |
| Ethylhexyl salicylate 5% pet                 | Octyl salicylate 2-Ethylhexyl 2-hydroxybenzoate | Benzoic acid, 2-hydroxy-, 2-ethylhexyl ester<br>Salicylic acid, 2-ethylhexyl ester | —                           | Chemotechnique Diagnostics, Tygelsjo, Sweden |
| Methyl anthranilate 5% pet                   | Meradimate                                      | —                                                                                  | —                           | Chemotechnique Diagnostics, Tygelsjo, Sweden |
| Benzophenone-10 10% pet                      | Mexenone                                        | 2-Hydroxy-4-methoxy-4'-methyl-benzophenone                                         | —                           | Chemotechnique Diagnostics, Tygelsjo, Sweden |
| Ethylhexyl dimethyl PABA 10% pet             | Padimate O<br>Octyl dimethyl PABA               | 2-Ethylhexyl-p-dimethyl aminobenzoate                                              | Escalol 507<br>Eusolex 6007 | Chemotechnique Diagnostics, Tygelsjo, Sweden |
| Phenylbenzimidazole sulfonic acid 10% pet    | Ensulizole                                      | 2-Phenylbenzimidazole-5-sulfonic acid                                              | Eusolex 232                 | Chemotechnique Diagnostics, Tygelsjo, Sweden |
| Homosalate 5% pet                            | —                                               | Benzoic acid, 2-hydroxy-, 3,3,5-trimethylcyclohexyl ester                          | Eusolex HMS                 | Chemotechnique Diagnostics, Tygelsjo, Sweden |
| Butyl methoxydibenzoylmethane 5% pet         | Avobenzone<br>Dibenzoylmethane                  | 1-(4-tert-butylphenyl)-3-(4-methoxyphenyl)1,3-propandione                          | Parsol 1789<br>Eusolex 9020 | Chemotechnique Diagnostics, Tygelsjo, Sweden |
| Octocrylene 1% pet                           | Octocrylene                                     | 2-Propenoic acid, 2-cyano-3,3-diphenyl-, 2-ethylhexyl ester                        | Eusolex OCR                 | Chemotechnique Diagnostics, Tygelsjo, Sweden |
| Benzophenone-2 1% pet                        | —                                               | 2,2',4,4'-tetrahydroxybenzophenone                                                 | —                           | AllergEAZE, Calgary, Alberta, Canada         |
| Ethylhexyl dimethyl PABA 5% in ethyl alcohol | Padimate O<br>Octyl dimethyl PABA               | 2-Ethylhexyl-p-dimethyl aminobenzoate                                              | Escalol 507<br>Eusolex 6007 | Chemotechnique Diagnostics, Vellinge, Sweden |
| PABA 5% in ethyl alcohol                     | para-Aminobenzoic acid                          | 4-Aminobenzoic acid                                                                | —                           | Chemotechnique Diagnostics, Vellinge, Sweden |
| Isoamyl p-methoxycinnamate 10% pet           | Amiloxate; octyl methoxycinnamate               | Isopentyl p-methoxycinnamate                                                       | Neo Heliopan E1000          | Chemotechnique Diagnostics, Vellinge, Sweden |
| 4-Methylbenzylidene camphor 10% pet          | Enzacamene                                      | 3,4-Methylbenzylidene camphor                                                      | Eusolex 6300                | Hermal Trolab, Hudson, Quebec, Canada        |
| Zinc oxide 10% pet                           | —                                               | —                                                                                  | Z-Cote                      | BASF Corporation, Florham Park, NJ           |
| Iron oxide 2% pet                            | —                                               | —                                                                                  | —                           | Color Techniques, South Plainfield, NJ       |
| Dihydroxyacetone 10% aqueous                 | —                                               | —                                                                                  | —                           | EMD Chemicals Inc., Hawthorne, NY            |
| Titanium (IV) oxide 0.1% pet                 | —                                               | —                                                                                  | —                           | Aldrich Chemical Co., Milwaukee, WI          |

Table 1. Continued

| INCI Name, Concentration, and Vehicle                       | Synonyms                                         | Chemical Name                                                                                                            | Trade Names | Manufacturer                                             |
|-------------------------------------------------------------|--------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|-------------|----------------------------------------------------------|
| Titanium dioxide (silicone coated) 1% pet                   | —                                                | —                                                                                                                        | —           | Mineral and Pigment Solutions Inc., South Plainfield, NJ |
| TEA-salicylate 5% pet                                       | Trolamine salicylate; triethanolamine salicylate | 2-[bis(2-hydroxyethyl)amino]ethanol; 2-hydroxybenzoic acid                                                               | —           | AllergEAZE, Calgary, Alberta, Canada                     |
| Titanium oxalate 1% pet                                     | —                                                | —                                                                                                                        | —           | Chemotechnique Diagnostics, Tygelsjö, Sweden             |
| Terephthalylidene dicamphor sulfonic acid (sunscreen as is) | Anthelios SX with Mexoryl SX                     | (Ecamsule)                                                                                                               | —           | L'Oréal, Clark, NJ                                       |
| Drometrizole trisiloxane 10% pet                            | Mexoryl XL                                       | Phenol, 2-(2H-benzotriazol-2-yl)-4-methyl-6-[2-methyl-3-[1,3,3,3-tetramethyl-1-[(trimethylsilyl)oxy]disiloxanyl]-propyl] | Silatrizole | Chemotechnique Diagnostics, Vellinge, Sweden             |
| Methylene-bis-benzotriazolyl tetramethylbutylphenol 2% pet  | Bisotrizole                                      | —                                                                                                                        | Tinosorb M  | Ciba Specialty Chemicals Co., Tarrytown, NY              |
| bis-Ethylhexyloxyphenol methoxy-phenyl triazine 2% pet      | Bemotrizinol<br>Tinosorb S                       | —                                                                                                                        | Tinosorb S  | Ciba Specialty Chemicals Co., Tarrytown, NY              |

INCI = International Nomenclature Cosmetic Ingredient; PABA = para-aminobenzoic acid; pet = in petrolatum.

dimethyl PABA, for which there were comparatively fewer reports of sensitization or photocontact sensitization.<sup>64</sup> By the late 1980s, the most commonly reported allergens among the active sunscreen ingredients were the benzophenones; specifically, benzophenone-3 remains the leading cause of allergic and photoallergic reactions to active sunscreen chemicals.<sup>2,63</sup> The pattern of allergy to chemicals evolves with time; thus, a study of allergic contact dermatitis from both new and traditional sunscreens is timely and relevant.

Active sunscreen chemicals are cited in the literature as the most common photoallergens; however, the true incidence of photoallergic contact dermatitis reactions to sunscreens in the general population remains unknown.<sup>3,28,32,33,42,65</sup> The most common active chemical agents that induce a photoallergic response are benzophenone-3, benzophenone-4, ethylhexyl dimethyl PABA, and the dibenzoylmethanes.<sup>21</sup> As new sunscreen chemicals enter the market, new incidents of allergic contact dermatitis from these agents are reported, and more are expected. The newest sunscreen chemical on the US market is terephthalylidene dicamphor sulfonic acid (Mexoryl SX, L'Oréal, Clark, NJ), which is an ingredient

in Anthelios SX (L'Oréal). The product versions of drometrizole trisiloxane (Mexoryl XL, L'Oréal), methylene-bis-benzotriazolyl tetramethylbutylphenol (Tinosorb M, Ciba Specialty Chemicals Co., Tarrytown, NY), and bis-ethylhexyloxyphenol methoxy-phenyl triazine (Tinosorb S, Ciba Specialty Chemicals Co.) are not yet approved by the FDA but have been used for many years in Europe and more recently in Canada. A case of allergic contact dermatitis from methylene-bis-benzotriazolyl tetramethylbutylphenol (Tinosorb M) already has been reported in Spain.<sup>11</sup> Furthermore, an Italian multicenter study of 1,082 patients with histories and clinical features suggestive of photoallergic contact dermatitis noted five positive photopatch-test reactions to Anthelios XL (L'Oréal).<sup>10</sup> Those reactions were attributed to the active sunscreen chemical Mexoryl XL. Only two of five patients were retested with pure Mexoryl XL, and their reactions were confirmed as photoallergic reactions.

The objective of this study was to profile the allergic and photoallergic reactions to traditional and newer sunscreen chemicals in a series of patients who reported a subjective adverse reaction to at least one sunscreen product. We hypothesized that patients who identify

**Table 2.** Studies of Allergic Reactions to Sunscreen Ingredients

| <i>Year</i> | <i>Study Design</i>      | <i>n</i> | <i>Inclusion Criteria</i>                           | <i>Results</i>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <i>Author</i>       | <i>Ref</i> |
|-------------|--------------------------|----------|-----------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|------------|
| 2009        | Retrospective            | 83       | Suspect systemic photosensitivity                   | PPT: benzophenone-3 (3 rxns), benzophenone-4 (3 rxns), promethazine (7 rxns), chlorpromazine (2 rxns), NSAIDs (20 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Cardoso J et al     | 5          |
| 2009        | Double-blind, randomized | 94       | Healthy volunteers                                  | Irritant rxns: 2% benzophenone-4 (1 rxn), 5% benzophenone-4 (4 rxns), 10% benzophenone-4 (6 rxns), 2% methylene-bis-benzotriazolyl tetramethylbutylphenol (2 rxns), 5% methylene-bis-benzotriazolyl tetramethylbutylphenol (6 rxns), 10% methylene-bis-benzotriazolyl tetramethylbutylphenol (1 rxn)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Kerr A et al        | 6          |
| 2009        | Prospective              | 18       | “Cinnamon sensitive”                                | No positive PT or PPT rxns to cinnamate UV filters (ethylhexyl methoxycinnamate or isoamyl-p-methoxycinnamate); but cinnamon and/or cinnamon-related fragrances PT (7 rxns) PPT (34 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Pentinga S et al    | 1          |
| 2009        | Retrospective            | 182      | Suspected photo-dermatoses and/or sunscreen allergy | PT: benzophenone-4 (6 rxns), benzophenone-3 (3 rxns), PABA (3 rxns), ethylhexyl methoxycinnamate (3 rxns), hexachlorophene (3 rxns), chlorhexidine (1 rxn), ethylhexyl dimethyl PABA (3 rxns), triclosan (2 rxns), ethylhexyl salicylate (3 rxns), homosalate (1 rxn), triclocarban (1 rxn), thiourea (1 rxn); ppt: benzophenone-4 (8 rxns), benzophenone-3 (5 rxns), PABA (6 rxns), ethylhexyl methoxycinnamate (3 rxns), hexachlorophene (3 rxns), chlorhexidine (3 rxns), ethylhexyl dimethyl PABA (4 rxns), 4-methylbenzylidene camphor (3 rxns), butyl methoxydibenzoylmethane (2 rxns), triclosan (4 rxns), ethylhexyl salicylate (3 rxns), methyl anthranilate (2 rxns), phenylbenzimidazole sulfonic acid (1 rxn), homosalate (1 rxn), triclocarban (1 rxn)                                                                                                                                                                                           | Scalf L et al       | 7          |
| 2009        | Case report              | 1        | —                                                   | PPT: PABA 10% pet                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Waters A et al.     | 8          |
| 2008        | Case report              | 1        | —                                                   | PPT: butyl methoxydibenzoylmethane, ethylhexyl methoxycinnamate, isoamyl-p-methoxycinnamate, phenoxyethanol, fragrance mix                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Collaris E, Frank J | 9          |
| 2008        | Retrospective            | 1,082    | History or clinical features of PACD                | PT: ketoprofen (13 rxns), ibuprofen (1 rxn), octocrylene (9 rxns), benzophenone-10 (7 rxns), benzophenone-3 (6 rxns), butyl methoxydibenzoylmethane (4 rxns), piroxicam (3 rxns), fentichlor (3 rxns), promethazine (3 rxns), fragrance mix I (3 rxns), trichlorocarbanilide (3 rxns), dichlorophene (3 rxns), ethylhexyl methoxycinnamate (2 rxns), isoamyl-p-methoxycinnamate (1 rxn), benzophenone-4 (1 rxn), bithionol (1 rxn), chlorhexidine digluconate (1 rxn), musk mix (1 rxn), ethylhexyl triazone (1 rxn), sesquiterpene lactone mix (1 rxn), thiourea (1 rxn); PPT: arylpropionic derivatives (102 rxns): ketoprofen (97 rxns), ibuprofen (4 rxns), ibuprofen (1 rxn), octocrylene (14 rxns), piroxicam (10 rxns), fentichlor (10 rxns), ethylhexyl methoxycinnamate (10 rxns), benzophenone-10 (9 rxns), benzophenone-3 (9 rxns), butyl methoxydibenzoylmethane (5 rxns), fragrance mix I (5 rxns), drometizole trisiloxane (5 rxns), isoamyl-p- | Pigatto P et al     | 10         |

Table 2. Continued

| Year | Study Design  | n     | Inclusion Criteria                               | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Author                    | Ref |
|------|---------------|-------|--------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|-----|
|      |               |       |                                                  | methoxycinnamate (3 rxns), promethazine (3 rxns), benzophenone-4 (2 rxns), bithionol (2 rxns), chlorhexidine digluconate (2 rxns), PABA (2 rxns), trichlorocarbanilide (1 rxn), dichlorophene (1 rxn), musk mix (1 rxn), tribromosalicylanilide (1 rxn), polyethylene glycol-25 PABA (1 rxn), ethylhexyl triazone (1 rxn), 4-methylbenzylidene camphor (1 rxn), ethylhexyl dimethyl PABA (1 rxn), triclosan (1 rxn), 6-methylcoumarin (1 rxn), etofenamate (1 rxn)                                                                                                                                                                                                                                                                   |                           |     |
| 2007 | Case report   | 1     | —                                                | PT: methylene bis-benzotriazolyl tetramethylbutylphenol (Tinosorb M)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Gonzalez-Perez R et al    | 11  |
| 2007 | Case report   | 1     | —                                                | PT: ethylhexyl salicylate (2-ethylhexyl salicylate) in 10% white paraffin, Olay Total Effects at 48 and 96 hr                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Singh M, Beck M           | 12  |
| 2006 | Case report   | 1     | —                                                | PT: decyl glucoside allergy in methylene-bis-benzotriazolyl tetramethylbutylphenol (Tinosorb M)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Andersen K, Goossens A    | 13  |
| 2006 | Prospective   | 1,155 | Photosensitivity, sunscreen rxn, photodermatoses | PT: SPF 60 commercial sunscreen product (26 rxns), butyl methoxydibenzoylmethane (10 rxns), benzophenone-3 (9 rxns), benzophenone-4 10% (9 rxns), ethylhexyl dimethyl PABA (7 rxns), 4-methylbenzylidene camphor (6 rxns), ethylhexyl methoxycinnamate (5 rxns), isoamyl-p-methoxycinnamate (4 rxns), ethylhexyl triazone (3 rxns), PABA (3 rxns), benzophenone-4 (2 rxns), own products (33 were commercial sunscreens) (45 rxns); PPT: benzophenone-3 (27 rxns), butyl methoxydibenzoylmethane (22 rxns), SPF 60 sunscreen (14 rxns), isoamyl-p-methoxycinnamate (14 rxns), octyl methoxycinnamate (8 rxns), benzophenone-4 (2 rxns), ethylhexyl triazone (2 rxns), PABA (1 rxn), own commercial sunscreens and products (26 rxns) | Bryden A et al            | 14  |
| 2006 | Retrospective | 35    | Topical ketoprofen rxn                           | PT: ketoprofen (2 rxns); PPT: ketoprofen (35 rxns), fenofibrate (9 rxns), benzophenone-3 (6 rxns), benzophenone-10 (6 rxns), benzophenone-4 (0 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Hindsen M et al           | 15  |
| 2006 | Case report   | 1     | —                                                | PPT: benzophenone-3 PT: amide anesthetic (lignocaine and prilocaine)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Langan S, Collins P       | 16  |
| 2006 | Prospective   | 82    | Clinical diagnosis of PACD                       | PT: dichromate (10 rxns), ethylhexyl dimethyl PABA (1 rxn), cetyl alcohol (1 rxn), 4-methylbenzylidene camphor (1 rxn); PPT: benzophenone-3 (22 rxns), ethylhexyl methoxycinnamate (8 rxns), benzophenone-4 (2 rxns), benzophenone-10 (2 rxns), benzophenone-3 (2 rxns), phenylbenzimidazole sulfonic acid (1 rxn), 4-methylbenzylidene camphor (1 rxn), ethylhexyl dimethyl PABA (1 rxn), 6-methylcoumarin (1 rxn)                                                                                                                                                                                                                                                                                                                  | Rodriguez E et al         | 17  |
| 2006 | Case report   | 1     | —                                                | PT: ethylhexyl salicylate                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Shaw D                    | 18  |
| 2005 | Case report   | 1     | —                                                | PT: benzophenone-3, cetyl alcohol; PPT: benzophenone-3, benzophenone-10                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Kiec-Swierczynska M et al | 19  |

Table 2. Continued

| Year       | Study Design             | n      | Inclusion Criteria         | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Author                       | Ref    |
|------------|--------------------------|--------|----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|--------|
| 2005       | Case report              | 2      | —                          | PT: octocrylene (2 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Madan V, Beck M              | 20     |
| 2004       | Prospective              | 250    | Suspected PACD             | PT: butyl methoxydibenzoylmethane; PPT: benzophenone-3, benzophenone-4, musk ambrette, PABA, ethylhexyl dimethyl PABA, antibacterial agents                                                                                                                                                                                                                                                                                                                                                                                                                                                            | DeLeo V                      | 21     |
| 2003, 2004 | NACDG patch-test results | 10,713 | Suspected ACD              | 1998–2002 prevalence of PT rxns to benzophenone = 0.6% (59% relevance); 2003–2004 prevalence of PT rxns to benzophenone = 0.5% (70.3% relevance); 1998–2002 prevalence of PT rxns to cinnamic aldehyde = 3.6% (not specific to chemical sunscreens but also to fragrances and flavoring), and 2003–2004 was 2.3%                                                                                                                                                                                                                                                                                       | Pratt M et al, Marks J et al | 22, 23 |
| 2003       | Case report              | 2      | —                          | PPT: octocrylene (2 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Carrotte-Lefebvre I et al    | 24     |
| 2003       | Case report              | 2      | —                          | PT: benzophenone-3 (1 rxn); PPT: benzophenone-3 (2 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Nedorost S                   | 25     |
| 2002       | Case report              | 1      | —                          | PPT: isoamyl-p-methoxycinnamate, benzophenone-3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Cook N, Freeman S            | 26     |
| 2002       | Retrospective            | 172    | Suspected photosensitivity | PT: perfume mix (25 rxns), benzophenone-10 (3 rxns), isopropyl dibenzoylmethane (2 rxns), ethylhexyl methoxycinnamate (2 rxns), butyl methoxydibenzoylmethane (1 rxn), benzophenone-3 (1 rxn), ethylhexyl dimethyl PABA (1 rxn), 4-methylbenzylidene camphor (1 rxn); PPT: perfume mix (11 rxns), butyl methoxydibenzoylmethane (5 rxns), isopropyl dibenzoylmethane (4 rxns), ethylhexyl methoxycinnamate (3 rxns), PABA (3 rxns), benzophenone-3 (3 rxns), benzophenone (2 rxns), 4-methylbenzylidene camphor (1 rxn); combined PT and PPT: perfume mix (4 rxns), isopropyl dibenzoylmethane (1 rxn) | Crouch R et al               | 27     |
| 2002       | Retrospective            | 81     | Known photosensitivity     | PPT: UV filters (28 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Lee P, Freeman S             | 28     |
| 2000       | Retrospective            | 2,390  | Known photosensitivity     | Decreasing order, Test period 1 (1985–1990): PT: balsam of Peru, Compositae mix, colophony, wood tar, UV filters; PPT: tiaprofenic acid, fenticlor, carprofen, isopropyl-dibenzoylmethane, benzophenone-3<br>Test period 2 (1991–1997): PT: balsam of Peru, Compositae mix, chlorophene, UV filters; PPT: fenticlor, carprofen, chlorpromazine, benzophenone-3, isopropyl dibenzoylmethane                                                                                                                                                                                                             | Neumann N et al              | 29     |
| 2002       | Case report              | 1      | —                          | PPT: ethylhexyl triazone (1 rxn), butyl methoxydibenzoylmethane (1 rxn)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Sommer S et al               | 30     |
| 2001       | Retrospective            | 19     | Known photosensitivity     | PT: sunscreen base (fragrance, diazolidinylurea, imidazolidinylurea) (6 rxns), benzophenone-3 (2 rxns), butyl methoxydibenzoylmethane (1 rxn); PPT: benzophenone-3 (9 rxns), butyl methoxy-dibenzoylmethane (8 rxns), methoxycinnamate (3 rxns), benzophenone (1 rxn), PABA (0 rxns)                                                                                                                                                                                                                                                                                                                   | Cook N, Freeman S            | 31     |

Table 2. Continued

| Year | Study Design  | n     | Inclusion Criteria                  | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Author           | Ref |
|------|---------------|-------|-------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|-----|
| 2001 | Retrospective | 2,715 | Presumed photosensitivity disorders | PT: benzophenone-10 (13 rxns), benzophenone-3 (8 rxns), isopropyl dibenzoylmethane (4 rxns), PABA (7 rxns), ethylhexyl dimethyl PABA (3 rxns), butyl methoxydibenzoylmethane (3 rxns), isoamyl-p-methoxycinnamate (3 rxns), ethyl methoxycinnamate 2 rxns), ethylhexyl methoxycinnamate (4 rxns), amyl dimethyl PABA (4 rxns); PPT: benzophenone-3 (14 rxns), benzophenone-10 (9 rxns), isopropyl dibenzoylmethane (6 rxns), PABA (5 rxns), ethylhexyl dimethyl PABA (5 rxns), butyl methoxydibenzoylmethane (4 rxns), isoamyl-p-methoxycinnamate (2 rxns), ethyl methoxycinnamate (2 rxns), ethylhexyl methoxycinnamate (2 rxns), amyl dimethyl PABA (2 rxns), phenylbenzimidazole sulfonic acid (1 rxn), drugs (16 rxns), musk ambrette (11 rxns), antiseptic trichlorocarbanilide (1 rxn) | Darvay A et al   | 32  |
| 2000 | Prospective   | 167   | Suspected photosensitivity          | PPT: butyl methoxydibenzoylmethane (8 rxns), benzophenone-3 (5 rxns), ethylhexyl methoxycinnamate (5 rxns), ethylhexyl dimethyl PABA (1 rxn), musk ambrette (1 rxn)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Bell H, Rhodes L | 33  |
| 1999 | Retrospective | 475   | ACD from cosmetic ingredients       | PT/PPT: benzophenone-3 (14 rxns), isopropyl dibenzoylmethane (7 rxns), isobutyl PABA (4 rxns), PABA (2 rxns), ethylhexyl methoxycinnamate (2 rxns), butyl methyl dibenzoylmethane (2 rxns), phenyl salicylate (2 rxns), ethylhexyl dimethyl PABA (2 rxns), phenylbenzimidazole sulfonic acid (1 rxn), benzyl salicylate (1 rxn), ethyl methoxycinnamate (1 rxn), cinoxate (1 rxn)                                                                                                                                                                                                                                                                                                                                                                                                            | Goossens A et al | 34  |
| 1999 | Prospective   | 370   | Suspected photodermatitis           | PT: benzophenone-3 (27 rxns), isopropyl dibenzoylmethane (14 rxns); PPT: ethylhexyl methoxycinnamate (2 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Journe F et al   | 35  |
| 1998 | Retrospective | 61    | Suspected sunscreen allergy         | PT: ethylhexyl methoxycinnamate (1 rxn), benzophenone-3 (1 rxn), fragrance/balsam of Peru (8 rxns); PPT: benzophenone-10 (1 rxn), ethylhexyl methoxycinnamate (1 rxn), benzophenone-3 (1 rxn), ethylhexyl dimethyl PABA (1 rxn), cinnamate (1 rxn)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Ang P et al      | 36  |
| 1998 | Retrospective | 335   | Suspected photosensitivity          | PT: isopropyl dibenzoylmethane (4 rxns), benzophenone-3 (1 rxn, 1 urticarial rxn), PABA (1 rxn); PPT: benzophenone-3 (15 rxns), isopropyl dibenzoylmethane (8 rxns), butyl methoxydibenzoylmethane (6 rxns), ethylhexyl methoxycinnamate (3 rxns), PABA (2 rxns), phenylbenzimidazole sulfonic acid (2 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Berne B, Ros A   | 37  |
| 1998 | Prospective   | 12    | Photodistributed eruption           | PT/PPT: ketoprofen and tiaprofenic acid (12 rxns), fenofibrate (8 rxns), benzophenone-3 (3 rxns), unsubstituted benzophenone (11 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Le Coz C et al   | 38  |
| 1998 | Case report   | 1     | —                                   | PPT: 4-methylbenzylidene camphor, ethylhexyl methoxycinnamate, benzophenone-3, butyl methoxydibenzoylmethane                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Schmidt T, et al | 39  |

Table 2. Continued

| Year | Study Design  | n   | Inclusion Criteria               | Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Author                 | Ref |
|------|---------------|-----|----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|-----|
| 1998 | Case report   | 1   | —                                | PPT: benzophenone-3 (2% pet); erythema-multiforme-like eruption following PACD to benzophenone-3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Zhang X et al          | 40  |
| 1997 | Case report   | 1   | —                                | PT: ethylhexyl dimethyl PABA, ethylhexyl methoxycinnamate, fragrance, balsam of Peru; PPT: ethylhexyl methoxycinnamate; contact sensitization to fragrance, balsam of Peru, and ethylhexyl methoxycinnamate was associated with the photosensitization to Parsol                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Ricci C et al          | 41  |
| 1997 | Prospective   | 402 | Suspected photosensitivity       | PT: fragrance (178 rxns), methylbenzylidene camphor (32 rxns), isopropyl dibenzoylmethane (30 rxns), preservatives (24 rxns), butyl methoxydibenzoylmethane (15rxns), preservative (11 rxns), isoamyl-p-methoxycinnamate (4 rxns), benzophenone-3 (3 rxns), ethylhexyl methoxycinnamate (3 rxns), PABA (2 rxns), emollient-lanolin alcohol (2 rxns), phenylbenzimidazole sulfonic acid (1 rxn), ethylhexyl dimethyl PABA (1 rxn); PPT: isopropyl dibenzoylmethane(32 rxns), fragrance (14 rxns), butyl methoxydibenzoylmethane (13 rxn), isoamyl-p-methoxycinnamate (10 rxns), benzophenone-3 (9 rxn), phenylbenzimidazole sulfonic acid (7 rxns), methylbenzylidene camphor (5 rxns), octyl methoxycinnamate (4 rxns), PABA (2 rxns), ethylhexyl dimethyl PABA (2 rxns) | Schauder S, Ippen H    | 42  |
| 1996 | Case report   | 1   | —                                | PT: 4-methylbenzylidene camphor (1 rxn), isopropyl dibenzoylmethane (1 rxn); PPT: isopropyl dibenzoylmethane (1 rxn)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Marguery M et al       | 43  |
| 1995 | Retrospective | 203 | Referred for photosensitivity    | PT: fragrance (47%), UV filters (39%), antimicrobial agents (7%); PPT: UV filters (57%), fragrance (18%), antimicrobial agents (13%); PT: amyl dimethyl PABA (2 rxns), ethylhexyl dimethyl PABA (2 rxns); PPT: amyl dimethyl PABA (5 rxns), ethylhexyl dimethyl PABA (4 rxns), PABA (3 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Fotiades J et al       | 44  |
| 1995 | Case report   | 1   | —                                | PPT: ethylhexyl methoxycinnamate                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Kimura K, Katoh T      | 45  |
| 1995 | Case report,  | 1   | —                                | PPT: butyl methoxydibenzoylmethane (8 rxns), benzophenone-3 (5 rxns), ethylhexyl methoxycinnamate (5 rxns), ethylhexyl dimethyl PABA (1 rxn), musk ambrette (1 rxn)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Parry E et al          | 46  |
| 1995 | Case report   | 3   | —                                | PPT: benzophenone-3 (3 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Silva R et al.         | 47  |
| 1994 | Prospective   | 283 | Suspected photodermatoses        | PPT: benzophenone-3 (35 rxns), PABA derivatives (17 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Szczurko C et al       | 48  |
| 1994 | Prospective   | 108 | Suspected photodermatoses        | PT/PPT: benzophenone-3 (4 rxns), isopropyl dibenzoylmethane (3 rxns), PABA (1 rxn), ethylhexyl methoxycinnamate (1 rxn)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Trevisi P et al        | 49  |
| 1993 | Retrospective | 214 | 99 photodermatoses, 115 controls | PT: benzophenone-10 (6 rxns), benzophenone-3 (2 rxns), ethylhexyl dimethyl PABA (4 rxns), PABA (2 rxns), isopropyl dibenzoylmethane (2 rxns), butyl methoxydibenzoylmethane (1 rxn), cinnamic ester (5 rxns), ethylhexyl dimethyl methoxycinnamate (1 rxn), 4-methylbenzylidene camphor (2 rxns)                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Bilsland D, Ferguson J | 50  |

Table 2. Continued

| Year | Study Design                | n     | Inclusion Criteria                    | Results                                                                                                                                                                                                                                                                                                                                                                                      | Author                    | Ref |
|------|-----------------------------|-------|---------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|-----|
| 1993 | Case report                 | 1     |                                       | PPT: benzophenone-3                                                                                                                                                                                                                                                                                                                                                                          | Collins P,<br>Ferguson J  | 51  |
| 1993 | Double-blind,<br>controlled | 603   | Randomized<br>population              | PT: none of the people tested were allergic to the sunscreen active ingredients, parabens (2 rxns), methylparabens (1 rxn), propylparabens (1 rxn), PVP/eicosene copolymer (1 rxn), fragrance (1 rxn); PPT: sunscreen formulation (2 rxns), placebo (1 rxn), no rxns to the two active ingredients in the sunscreen formulation (ethylhexyl methoxycinnamate, butyl methoxydibenzoylmethane) | Foley P et al             | 4   |
| 1992 | Retrospective               | 187   | Suspected<br>photosensitivity         | PT: fragrance (3 rxns), antibacterial (2 rxns), PABA (2 rxns), benzophenone-3 (1 rxn), butyl methoxydibenzoylmethane (1 rxn), formalin (1 rxn); PPT: antibacterial (11 rxns), promethazine (5 rxns), Benzophenone-3 (5 rxns), PABA (4 rxns), fragrance (4 rxns), formalin (3 rxns), pentyl dimethyl PABA (1 rxn), chlorpromazine (1 rxn)                                                     | DeLeo V et al             | 3   |
| 1991 | Prospective                 | 27    | Complaint of<br>sunscreen side effect | PT: benzophenone-3 (1 rxn); PPT: benzophenone-3 (2 rxns); RAST: menthyl anthranilate (2 rxns), butyl methoxydibenzoylmethane (2 rxns), 4-methylbenzylidene camphor (2 rxns), homosalate (1 rxn), ethylhexyl methoxycinnamate (1 rxn), benzophenone-3 (1 rxn)                                                                                                                                 | Fischer T,<br>Bergström K | 52  |
| 1989 | Case report                 | 4     | —                                     | PPT: benzophenone-3 (4 rxns)                                                                                                                                                                                                                                                                                                                                                                 | Knobler E et al           | 53  |
| 1988 | Prospective                 | 70    | Suspected<br>photodermatoses          | PT: 22 patients (31%); PPT: 27 patients (38.5%) 14 were relevant PPT rxns; PT/PTT: most frequently chlorpromazine (13 rxns), musk ambrette (9 rxns), promethazine (8 rxns)                                                                                                                                                                                                                   | Menz J et al              | 54  |
| 1988 | Retrospective               | 1,993 | Suspected<br>photodermatoses          | Most frequent causes: PT: perfume mix, balsam of Peru, lichen mixture; PPT: musk ambrette, PABA                                                                                                                                                                                                                                                                                              | Thune P et al             | 55  |
| 1987 | Case report                 | 10    | —                                     | PT: isopropyl dibenzoylmethane (9 rxns), 4-methylbenzylidene camphor (5 rxns)                                                                                                                                                                                                                                                                                                                | de Groot A et al          | 56  |
| 1987 | Case report                 | 1     | —                                     | PT: butyl methoxydibenzoylmethane                                                                                                                                                                                                                                                                                                                                                            | de Groot A,<br>Weyland J  | 57  |
| 1987 | Retrospective               | 280   | PT/PTT to sunscreen<br>products       | PT: benzophenone-10 (6 rxns), isopropyl dibenzoylmethane (5 rxns), ethylhexyl dimethyl PABA (2 rxns), butyl methoxydibenzoylmethane (1 rxn), amyl dimethyl PABA (1 rxn), ethoxy ethyl-p-methoxy cinnamate (1 rxn); PPT: isopropyl dibenzoylmethane (1 rxn), butyl methoxydibenzoylmethane (1 rxn), PABA (1 rxn), ethylhexyl methoxycinnamate (1 rxn)                                         | English J et al           | 58  |
| 1985 | Retrospective               | 713   | Known cosmetic<br>ACD                 | PT: ethylhexyl dimethyl PABA (5 rxns), glyceryl PABA (5 rxns), PABA (3 rxns), amyl dimethyl PABA (2 rxns), benzophenone-4 (2 rxns), benzophenone-8 (1 rxn), benzophenone unspecified (1 rxn), UV absorber unspecified (1 rxn)                                                                                                                                                                | Adams R,<br>Maibach H     | 59  |
| 1983 | Retrospective               | 745   | Suspected<br>photodermatoses          | PT: balsam of Peru (30 rxns), PABA (23 rxns), lichen mix (21 rxns), perfumes (10 rxns); PPT: promethazine (24 rxns), chlorpromazine (22 rxns), musk ambrette (19 rxns), PABA (19 rxns), fenticlor (12 rxns)                                                                                                                                                                                  | Wennersten G et al        | 60  |

Table 2. Continued

| Year | Study Design | n | Inclusion Criteria | Results                                                             | Author               | Ref |
|------|--------------|---|--------------------|---------------------------------------------------------------------|----------------------|-----|
| 1978 | Case report  | 1 | —                  | PPT: 5% PABA alcohol base (1 rxn), 5% PABA petrolatum base (0 rxns) | Mathias C et al      | 61  |
| 1978 | Case report  | 2 | —                  | PPT: homomenthyl salicylate (2 rxns)                                | Rietschel M, Lewis C | 62  |

ACD = allergic contact dermatitis; *n* = number of subjects; NSAIDs = nonsteroidal antiinflammatory drugs; PABA = para-aminobenzoic acid; PACD = photoallergic contact dermatitis; pet = in petrolatum; PPT = positive photopatch-test reaction; PT = positive patch-test reaction; PVP = polyvinyl pyrrolidone; Ref = reference; rxn = reaction; SPF = sun protection factor.

themselves as “allergic to sunscreens” may not have relevant photoallergy or allergic contact dermatitis.

## Methods

This study, approved by the institutional review board, was conducted in a specialty contact dermatitis clinic between July 2007 and January 2009 and was funded by a grant from the American Contact Dermatitis Society. The objective of the study was to investigate whether patients who identify themselves as allergic to sunscreens have relevant allergic or photoallergic contact dermatitis from sunscreens, based on patch testing and photopatch testing results.

Patients (18 years of age or older) who identified themselves as “allergic” or as “having a reaction” to sunscreens were recruited from Oregon Health & Science University, Portland Veterans Affairs Medical Center, and community dermatology clinics. As patients contacted the

clinic, the patch testing and photopatch testing were discussed with them. Testing involved at least 4 days of participation from patients; patients spent some of the time in a rather confined warm box that administered UV light. The majority of patients interested in participating could not commit several hours to such a time- and labor-intensive study. Of 27 patients who contacted the clinic initially, only 11 agreed to complete the testing involved. Although there was a \$50 (US) compensation for completion of the testing, the participants found it difficult to undergo 4 days of rigorous testing, and many struggled to fulfill the study requirements.

All patients who participated in the study filled out a questionnaire (shown in Figure 1) detailing their reactions to sunscreens, the onset and duration of their reactions, their family history, and their history of atopy.

All 11 patients were patch-tested with the 65 allergens on the North American standard tray, 36 allergens on our supplemental tray, a 28-allergen sunscreen tray (see Table

| Questionnaire                                                                                     |
|---------------------------------------------------------------------------------------------------|
| <b>Please describe the worst reaction that you have had after using sunscreens.</b>               |
| <b>How long after you applied the sunscreen did the rash start?</b>                               |
| <b>How long did the rash last?</b>                                                                |
| <b>How often does this reaction occur when using sunscreens?</b>                                  |
| <b>Does this reaction occur when the sunscreen is applied but no sunlight contacts your skin?</b> |
| <b>What brand/type of sunscreens gives you trouble?</b>                                           |
| <b>Do you know of any topical substances you are allergic to?</b>                                 |
| <b>Does anyone in your family have this problem?</b>                                              |
| <b>Do you have a history of eczema, asthma, or hay fever?</b>                                     |

Figure 1. Questionnaire

1), and any relevant personal sunscreens. The North American standard tray allergens were those listed in the 2005–2006 patch-test results reported by the North American Contact Dermatitis Group and were obtained from Chemotechnique Diagnostics (Malmö, Sweden).<sup>66</sup> The allergens on the supplemental tray were obtained from various sources and were designed to test for regional causes of allergic contact dermatitis.

The manufacturers of the sunscreen chemicals are listed in Table 1. Because we were unable to obtain the individual sunscreen ingredient Mexoryl SX, we tested with an entire product, Anthelios SX, which the manufacturer generously provided. Tinosorb S and Tinosorb M are not approved for use in the United States; however, they have been used in Europe and were recently approved for use in Canada. Owing to the geographic proximity of Oregon to Canada, our patients could have obtained sunscreens in Canada although no patients specifically reported having done so.

Patch testing was done with a standardized technique with 8 mm Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster Alpharma A/S, Vennesla, Norway) by dispensing approximately 3 mm segments of allergen on each chamber.<sup>66</sup> To dispense a liquid allergen, the filter paper was wetted with the allergen, evaporated partially, and then applied to the patient's back.

Initially, patients were photopatch-tested to determine their minimal erythema dose (MED) for both UVB and UVA spectra according to the protocol described by Dr. Vincent De Leo.<sup>67</sup> Both UVB and UVA were tested to determine if any of the patients had reduced MED values that could point to an internal photosensitivity. Only UVA was used for the photopatch testing. That same day (day 1), the sunscreen allergens were placed into Finn Chambers and applied directly to normal uninvolved skin of the back in duplicates for patch and photopatch testing. At 24 hours (day 2), the photopatches were removed, and patients were assessed for any skin reactions. On the same day, reading was done to determine the patient's MED. As none of the patients had abnormal UVA MEDs, one set of photopatches was irradiated with UVA (10 J/cm<sup>2</sup>). Immediately after UVA exposure, the photopatch tests were read to determine immediate-type hypersensitivity reactions; the patch areas were then covered with opaque tape material. The next reading was at a further 24 hours (day 3), and the final reading was at 5 to 7 days. The patients were instructed not to get their backs wet for the duration of the patch testing and photopatch testing and through the day of the final reading.

The North American standard tray allergens and the supplemental tray allergens were also placed on day 1 of testing. Those patches were removed and read 48 hours later (day 3), and the final reading was done on day 5 or day 7.

Five patients reported immediate reactions to sunscreens on the questionnaire shown in Figure 1. In addition to being patch- and photopatch-tested as described above, three of these five patients were also tested for contact urticaria from common contact urticaria-inducing substances (resorcinol 1% in petrolatum [pet], cinnamic aldehyde 1% pet, benzoic acid 5% pet, sorbic acid 2% pet, sodium benzoate 5% pet, and white 100% petrolatum), sterile water (as a negative control), histamine (as a positive control), and the patients' personal sunscreens. The allergens were applied to the 8 mm Finn Chambers and taped to the volar forearms with Scanpor tape. These patches were initially read 30 minutes after occlusion. If the test sites were negative, then the patients underwent 8 mm scratch-testing with sterile disposable needles (ALK-Abello, Horsholm, Denmark) to re-apply the contact allergenic substances for another 30 minutes.

## Results

During the study period, 27 patients contacted the clinic about the study, all stating they had an allergy to sunscreens. After the study testing was detailed to these patients, only 11 agreed to proceed. All 11 patients (10 women and 1 man, with an average age of 51 years) were patch- and photopatch-tested according to the methods described above. Questionnaire results appear in Table 3. All patients reported "an allergy to sunscreen" or "a reaction to sunscreen," which they described as "itchy red bumps and burning." Most reported worsening with sun exposure, and 9 of the 11 patients had some history of atopy. Five patients (patients 1, 4, 6, 8, and 10) reported an immediate onset of the skin rash and a quick resolution within 1 day. The other six patients reported that the onset of the rash was 1 to 2 days after the use of sunscreen and that the reaction lasted up to 1 week. In this study, all 11 patients had immediate readings done after photopatch testing to look for immediate-type hypersensitivity reactions. Three patients (patients 1, 6, and 10) had additional testing for contact urticaria as described above (see "Methods"). Although there are previous reports of immediate-type hypersensitivity to benzophenone-3, the result of the reading immediately following UVA exposure was negative for all patients we tested; hence, none of them had contact urticaria from the sunscreen allergens tested.<sup>37,68</sup>

**Table 3.** Questionnaire Results: Onset of Rash is in Relationship to Sunscreen Use

| <i>Patient</i> | <i>Onset of Rash</i> | <i>Duration of Rash</i> | <i>History of Atopy</i>                           |
|----------------|----------------------|-------------------------|---------------------------------------------------|
| 1              | Minutes              | Hours                   | Hay fever; sister with sunscreen reaction         |
| 2              | 1–2 days             | 3–5 days                | Asthma, hay fever                                 |
| 3              | 1 day                | 1–3 days                | None                                              |
| 4              | 5–6 hours            | 12 hours                | Hay fever; offspring with sunscreen reaction      |
| 5              | 1 day                | 4–5 days                | Hay fever                                         |
| 6              | Immediately          | 1–2 days                | Hay fever, eczema; mother with sunscreen reaction |
| 7              | Hours                | 1 week                  | None                                              |
| 8              | Minutes to 1 day     | 1 day                   | Hay fever, eczema                                 |
| 9              | 1 day                | 4–5 days                | Asthma, psoriasis                                 |
| 10             | 30 minutes           | 1–2 days                | Eczema, asthma, hay fever                         |
| 11             | 1 day                | 1 week                  | Hay fever                                         |

The results of patch testing and photopatch testing appear in Table 4. Patient 6 had a delayed-type hypersensitivity photopatch-test reaction to benzophenone-2. Overall, benzophenone-2 is a rare contact allergen that has been reported to be problematic in perfume preparations.<sup>69</sup> It is not a common sunscreen ingredient; hence, it is difficult to interpret the relevance of this reaction. Patient 5 had a history of delayed-type hypersensitivity reactions to titanium dioxide and titanium oxalate on prior patch testing, but when the patient was tested with silicone-coated titanium dioxide in this study, a reaction was not produced. Yet another patient had relevant positive photopatch-test reactions to benzophenone-3 and ethylhexyl dimethyl PABA; this patient had a

history of using sunscreen products with those ingredients. None of the 11 patients reacted to bis-ethylhexyloxyphenol methoxyphenyl-triazine (Tinosorb S), methylene-bis-benzotriazolyl tetramethylbutylphenol (Tinosorb M), or Anthelios SX. There were some positive reactions to the standard allergens such as nickel, gold, and balsam of Peru, but none were relevant to sunscreens (see Table 4).

## Discussion

True allergic reactions to active UV filters are overestimated, as evidenced by our present study. The 11 participants in our study considered themselves to be “sunscreen allergic” and described “itchy red bumps” or

**Table 4.** Patch- and Photopatch-Test Reactions

| <i>Patient</i> | <i>Standard North American Tray + Supplemental Tray</i>                      | <i>Sunscreen Tray and Personal Sunscreens</i>                                             |
|----------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| 1              | None                                                                         | None                                                                                      |
| 2              | Gold, cinnamic aldehyde, fragrance mix I (all PT, D7)                        | Benzophenone-3 (PPT, D7), ethylhexyl dimethyl PABA 5% (PT, D2) and 10% (PT and PPT, D3)   |
| 3              | None                                                                         | None                                                                                      |
| 4              | None                                                                         | None                                                                                      |
| 5              | Balsam of Peru (PT, D2), nickel (PT, D2, D7), cobalt (PT, D7), gold (PT, D7) | Titanium dioxide, titanium oxalate (both PT, D2 and D7 on prior testing but not retested) |
| 6              | None                                                                         | Benzophenone-2 (PPT, D7)                                                                  |
| 7              | Disperse Blue, gold (both PT, D7)                                            | None                                                                                      |
| 8              | Gold, nickel (both PT, D7)                                                   | None                                                                                      |
| 9              | Balsam of Peru (PT, D2), nickel (PT, D2, D7), thimerosal (PT, D7)            | None                                                                                      |
| 10             | None                                                                         | Iron oxide—irritant (PT and PPT, D7)                                                      |
| 11             | None                                                                         | None                                                                                      |

D = day; PABA = para-aminobenzoic acid; PPT = positive photopatch-test reaction; PT = positive patch-test reaction.

“burning” or both after applying a variety of sunscreens. However, the reactions that patients described following the use of the sunscreens were not reproduced during the study. It is possible that the reactions our patients experienced were multifactorial, variations of polymorphous light eruption,<sup>70</sup> or maybe irritant reactions to a combination of products, sweating, and sun exposure.

Our study showed that delayed-type hypersensitivity allergic contact dermatitis and photoallergic contact dermatitis from sunscreens are more infrequent than patients tend to believe. Such a negative study result can provide reassurance when patients are counseled on the use of sunscreens. We saw no reactions to the newer sunscreens (Tinosorb S, Tinosorb M, and Anthelios SX) at this time, which may be explained by the minimal exposure of the population to the sunscreens at large. Experience will tell their allergenic potential.

It is interesting that patient 2 reacted to cinnamic aldehyde but not to any of the cinnamate UV filters in this study. This is consistent with a study published this year that showed that allergy to cinnamic aldehyde does not translate into an allergy to cinnamate UV filters.<sup>1</sup>

The main limitation to this study was the small number of subjects. Of the initial 27 individuals who reported having a sunscreen allergy, only 11 decided to participate in the study. This suggests that studies based on patch testing and photopatch testing may be so labor intensive as to deter the recruitment of participants and the retention of existing ones. Another major limitation was the inability to test with Mexoryl SX alone.

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