

Article type : Letter to the Editor

Photopatch Test Results of the North American Contact Dermatitis Group, 1999-2009

DeLeo, Vincent A.;¹ Adler, Brandon L.;¹ Warshaw, Erin M.;² Maibach, Howard I.;³ Belsito, Donald V.;⁴ Fowler, Joseph F. Jr.;⁵ Fransway, Anthony F.;⁶ Marks, James G. Jr.;⁷ Mathias, C.G. Toby;⁸ Pratt, Melanie D.;⁹ Rietschel, Robert L.;¹⁰ Storrs, Frances J.;¹¹ Zug, Kathryn A.;¹² Sasseville, Denis¹³

Author Affiliations:

¹ Department of Dermatology, Keck School of Medicine, University of Southern California, Los Angeles, CA

² Department of Dermatology, University of Minnesota, Minneapolis

³ Department of Dermatology, University of California San Francisco

⁴ Department of Dermatology, Columbia University Irving Medical School, New York, NY

⁵ Division of Dermatology, University of Louisville, KY

⁶ Associates in Dermatology, Fort Myers, FL

⁷ Department of Dermatology, Pennsylvania State University, State College, PA

⁸ Trihealth, Cincinnati, OH

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/phpp.12742](#)

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⁹ Division of Dermatology, University of Ottawa, Ontario, Canada

¹⁰ University of Arizona Department of Veterans Affairs Health Care System, Tucson, AZ

¹¹ Department of Dermatology, Oregon Health Science University, Portland

¹² Department of Dermatology, Dartmouth-Hitchcock Medical Center, Lebanon, NH

¹³ Division of Dermatology, Sunnybrook Health Sciences Centre, University of Toronto, Ontario, Canada

Corresponding Author:

Brandon L. Adler, MD

1441 Eastlake Avenue

Ezralow Tower, Suite 5301

Los Angeles, CA 90033

brandon.adler@med.usc.edu

Tel: (323) 442-0084

Fax: (323) 442-0067

Word Count: 957

Conflict of Interest: B.L.A. has served as an investigator for AbbVie and as a consultant for Skin Research Institute, LLC. E.M.W. has received an investigator-initiated grant from Wen by Chaz Dean and served as a consultant for Wen by Chaz Dean and Noven Pharmaceuticals. D.S. receives royalties from UpToDate (Wolters Kluwer Health). The other authors have no funding or conflicts of interest to declare.

IRB Statement: The study was approved as an exempt study by the Institutional Review Board at St. Luke's Roosevelt Hospital Center.

Photoallergic contact dermatitis (PACD) is an unusual but not rare form of photosensitivity with an etiology similar to that of allergic contact dermatitis (ACD), with the added requirement of concomitant exposure to ultraviolet (UV) light.¹ Photopatch testing (PPT) is a critical tool for diagnosing PACD. There are only a few large studies of photoallergens from North America.²⁻⁴ We present a retrospective analysis of North American Contact Dermatitis Group (NACDG) PPT results from 1999-2009. The study was approved as exempt by the Institutional Review Board at St. Luke's Roosevelt Hospital Center.

The procedure for minimal erythema dose (MED) determination and PPT in the NACDG has been detailed previously.⁵ Briefly, on day 1 irradiations were performed to determine MED to UVB and UVA, and on that day 24 photoallergens (Chemotechnique Diagnostics AB, Malmo, Sweden), often supplemented with a baseline series and patients' own products, were applied to the back in duplicate with a standardized technique using Finn Chambers (Epitest Ltd. Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster Alpha AS, Vennesla, Norway). On day 2 or 3, allergens were removed, and one set was irradiated with UVA 10 J/cm² or, if the UVA MED was less than 10 J/cm², a dose of at least 1 J/cm² less than the MED was used. The other set of allergens acted as the unirradiated control. Two readings of the test sites were performed in each patient, on day 3 or 4 and one of days 5-10. Patch test reactions were graded as +/- (weak/doubtful/macular erythema), + (mild), ++ (strong), or +++ (very strong). Contact allergy was defined as equally positive reactions at the non-irradiated and irradiated sites; photo-contact allergy, as a positive reaction only at the irradiated site; and photoaggravated contact allergy, as both sites being positive but the irradiated site more intensely positive. A reaction was considered clinically relevant if the patient was determined to have had definite, probable, possible, or past contact with the allergen and the timing of the exposure was consistent with development of dermatitis.⁶ Lastly, each patient was assigned up to three final diagnoses, taking into consideration the testing results as well as history, physical findings, and other relevant diagnostic procedures (biopsies, serologies, etc.).

During the 10-year study period, 363 patients were evaluated. Sixty-five percent were women; most were white (77%) with Fitzpatrick skin types I-II (64%) (Table 1). Most patients (66%) were young to middle-aged adults (21-60 years old).

Allergens and test results are in Table 2. Of 8,712 individual tests performed in duplicate, 135 were read as photo-contact allergy, 82 as contact allergy, and 34 as photoaggravated contact allergy. The allergen classes most often producing photo-contact reactions were sunscreens (58%, most commonly oxybenzone, avobenzone, and 2-hydroxy-methoxy methyl benzophenone), followed by antimicrobials (25%, mostly fentichlor), NSAIDs (ketoprofen, 10%), and fragrances (7%, largely musk ambrette). Regarding contact allergy, sunscreens also represented the majority (71%), with fewer antimicrobials and fragrances (each accounting for 11%). Half (50%) of photoaggravated reactions were caused by sunscreens, followed by antimicrobials (41%). The overall clinical relevance was 62%, notably higher for sunscreens (91%) compared to non-sunscreens (17%). Although reactions to the antimicrobial fentichlor were relatively common, none was considered clinically relevant.

There were a total of 475 final diagnoses, most commonly ACD (34%), non-photo-related conditions (31%), and PACD (21%). Various other forms of photosensitivity were diagnosed in nearly 40% of cases, and undefined photosensitivity in 8%.

We present the largest series of photopatch-tested patients from North America during the first decade of the 2000s, highlighting the preeminence of sunscreens, as well as select antimicrobials, NSAIDs, and fragrances, in causing PACD. The prevalence of PACD and responsible photoallergens have varied over the past half-century depending primarily on exposure patterns of the populations studied.¹ During the present study period, publications from North America and Europe routinely reported PACD in approximately 20-40% of patients with suspected photosensitivity,^{2-4,7-10} consistent with our finding of 21%. These rates suggest that PACD is far from rare, although regional variations in photoallergen exposures, referral patterns, and PPT practice limit direct comparisons between them; nor do they permit estimation of the prevalence of PACD in the general population. Nonetheless, it may be supposed that a not inconsequential number of cases goes undiagnosed, owing to the relatively few providers who routinely perform PPT.¹¹

In our series, the most common photoallergens were sunscreens (especially benzophenones) and NSAIDs. In addition to increased routine usage relating to advancing knowledge of photocarcinogenesis and photoaging, sunscreens are widely incorporated in personal care products. Accordingly, our results showcase high rates of clinically relevant reactions to sunscreen agents during PPT. More recently NSAIDs have predominated in European reports, with reactions to octocrylene and benzophenones proposed to represent co- or cross-reactions to the NSAID ketoprofen.⁷ Of note, topical ketoprofen is not available in the United States and Canada. Despite frequent reactions to the antimicrobial fentichlor, like other studies,¹² we found strikingly low clinical relevance. Rates of PACD to the fragrance musk ambrette, one of the most common photoallergens of the 1970s-1980s, declined since its removal from personal care products.^{3,4} These and other considerations have led to alteration of allergen panels in the NACDG and other group studies over time.¹

One limitation of this study is NACDG data are predominantly from a referral-based population and may not represent the general population. Additionally, the practice of PPT suffers from a lack of standardization (including such basic aspects as allergen occlusion time, UVA irradiation dose, and timing of delayed readings), potentially leading to false-negative or false-positive readings.¹¹ While there is a need to work toward a consensus protocol based on high-quality evidence, PPT remains the most useful biological assay to diagnose photoallergy in clinical practice. Future studies should examine temporal and demographic trends in PPT to enhance recognition of emerging photoallergens and patient risk factors.

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Tables

Table 1. Characteristics and final diagnoses of photopatch tested patients (N=363).

Characteristic	Number (%)
Sex	
Male	124 (34.2)
Female	235 (64.7)
Unknown	4 (1.1)
Age, years	
<20	24 (6.6)
21-40	98 (27.0)
41-60	142 (39.1)
>60	88 (24.2)
Unknown	11 (3.0)
Race/ethnicity	
White	278 (76.6)
Black	24 (6.6)
Asian	20 (5.5)
Hispanic	15 (4.1)
Other/unknown	26 (7.2)
Fitzpatrick phototype	
I-II	231 (63.6)
III-IV	79 (21.8)
V-VI	20 (5.5)

Unknown	33 (9.1)
Final diagnosis*	
Allergic contact dermatitis	122 (33.6)
Other (non-photo)	112 (30.9)
Photoallergic contact dermatitis	75 (20.7)
Polymorphous light eruption	72 (19.8)
Photosensitivity undefined	29 (8.0)
Chronic actinic dermatitis	26 (7.2)
Photodrug reaction	13 (3.6)
Connective tissue disease	13 (3.6)
Actinic prurigo	8 (2.2)
Solar urticaria	5 (1.4)

*Up to 3 diagnoses were allowed for each patient.

Table 2. Results of photopatch testing in 363 patients.

Category	Allergen	Concentration and vehicle	Photo-contact allergy, n (%)	Contact allergy, n (%)	Photoaggravated contact allergy, n (%)	Clinical relevance, n (%)
Sunscreen	Oxybenzone (benzophenone-3)	10% in pet	28 (7.7)	19 (5.2)	5 (1.4)	52/52 (100.0)
Antimicrobial	Fentichlor (thiobis-chlorophenol)	1% in pet	26 (7.2)	6 (1.7)	9 (2.5)	0/41 (0.0)
Medication	Ketoprofen	5% in pet	13 (3.6)	5 (1.4)	2 (0.6)	5/20 (25.0)
Sunscreen	Butyl methoxydibenzoylmethane (avobenzone)	5% in pet	11 (3.0)	2 (0.6)	0 (0.0)	12/13 (92.3)

Sunscreen	2-hydroxy-methoxy methyl benzophenone (benzophenone-8)	10% in pet	9 (2.5)	6 (1.7)	3 (0.8)	14/18 (77.8)
Fragrance	Musk ambrette	1% in pet	7 (1.9)	3 (0.8)	1 (0.3)	2/11 (18.2)
Sunscreen	Sulisobenzone (benzophenone-4)	10% in pet	5 (1.4)	12 (3.3)	1 (0.3)	12/18 (66.7)
Sunscreen	Octyl dimethyl PABA (padimate O)	10% in pet	5 (1.4)	8 (2.2)	6 (1.7)	17/19 (89.5)
Sunscreen	Octinoxate (octyl methoxycinnamate)	7.5% in pet	5 (1.4)	4 (1.1)	1 (0.3)	10/10 (100.0)
Sunscreen	Para-aminobenzoic acid (PABA)	10% in pet	5 (1.4)	2 (0.6)	0 (0.0)	7/7 (100.0)
Sunscreen	Homosalate	5% in pet	5 (1.4)	2 (0.6)	0 (0.0)	7/7 (100.0)
Sunscreen	Octisalate	5% in pet	4 (1.1)	1 (0.3)	1 (0.3)	5/6 (83.3)
Antimicrobial	Triclosan	2% in pet	4 (1.1)	1 (0.3)	0 (0.0)	2/5 (40.0)
Antimicrobial	Dichlorophene	1% in pet	3 (0.8)	2 (0.6)	3 (0.8)	2/8 (25.0)
Fragrance	Sandalwood oil	2% in pet	2 (0.6)	2 (0.6)	0 (0.0)	2/4 (50.0)
Sunscreen	Phenylbenzimidazole-5-sulfonic acid (ensulizole)	10% in pet	1 (0.3)	2 (0.6)	0 (0.0)	3/3 (100.0)
Antimicrobial	Bithionol (thiobis-dichlorophenol)	1% in pet	1 (0.3)	0 (0.0)	2 (0.6)	0/3 (0.0)
Other	Thiourea (thiocarbamide)	0.1% in pet	1 (0.3)	0 (0.0)	0 (0.0)	0/1 (0.0)
Fragrance	Lichen acid mix	0.3% in pet	0 (0.0)	4 (1.1)	0 (0.0)	3/4 (75.0)
Plant	Sesquiterpene lactone mix	0.1% in pet	0 (0.0)	1 (0.3)	0 (0.0)	1/1 (100.0)
Sunscreen	Menthyl anthranilate	5% in pet	0 (0.0)	0 (0.0)	0 (0.0)	NA
Antimicrobial	Hexachlorophene	1% in pet	0 (0.0)	0 (0.0)	0 (0.0)	NA
Antimicrobial	Chlorhexidine diacetate	0.5% in water	0 (0.0)	0 (0.0)	0 (0.0)	NA
Antimicrobial	Tribromosalicylanilide	1% in pet	0 (0.0)	0 (0.0)	0 (0.0)	NA
		TOTAL	135 (37.2)	82 (22.6)	34 (9.4)	156/251 (62.2)

pet, petrolatum

NA, not applicable