

Allergic and Photoallergic Contact Dermatitis: A 10-year Experience

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Background: Photoallergic contact dermatitis (PACD) is a hypersensitivity reaction that occurs when a previously photosensitized exogenous agent comes into contact with UV radiation. Currently, there are no studies profiling photoallergic reactions in Canada. Because the photoallergen profile changes over time, it is necessary to continually update our knowledge to ensure proper recognition of allergens and appropriate treatment of patients.

Objective: This study aimed to profile photoallergic reactions in Canada.

Methods: A retrospective chart review of all patients who underwent photopatch testing at Toronto Western Hospital between January 2001 and December 2010 was completed. Photoallergic, allergic, and irritant reactions were recorded for 26 common allergens.

Results: Ninety-nine patients (61.9%) had at least 1 positive reaction to the test allergens. Fifty-four patients (33.8%) had at least 1 photoallergic reaction. All 26 allergens produced at least 1 allergic or photoallergic reaction. The most common relevant photoallergens were benzophenone-3, octyl dimethyl para-aminobenzoic acid (PABA) in 5% alcohol, and butylmethoxy-dibenzoylmethane.

Conclusions: This study is the first to profile photoallergic contact reactions in Canada. It is clear that the culprit photoallergen in PACD can often be identified in a properly selected population. Future surveillance is necessary to continue to characterize PACD trends in Canada and to help better treat and screen this patient population.

PHOTOALLERGIC CONTACT dermatitis (PACD) is a delayed type IV hypersensitivity disorder that occurs when a previously photosensitized agent is exposed to UV radiation again.¹ A PACD has a similar presentation to other forms of allergic contact dermatitis (ACD). Photoallergic contact dermatitis generally affects photodistributed areas and spares the anatomically shadowed portions of the body.² Although a PACD can cause significant distress to patients, the actual incidence of this disorder remains unclear. In particular, the incidence of PACD to sunscreen ingredients has been reported to range anywhere from 1% to 40% in patients with a history of photosensitivity.³ This large variation is thought to result from differences in patient selection, test methodology, test allergen battery, and nonstandardized interpretation of the results.¹ Furthermore, similar to other allergens, the prevalence and frequency of reactions to specific photoallergens is thought to be location and time period dependent.³

A recent prospective multicenter study of 1031 patients provided information on the incidence of PACD and common photoallergens in Europe.⁴ A total of 346 photoallergic reactions occurred in 200 (19.4%) subjects. Photoallergic contact dermatitis was most commonly caused by the topical non-steroidal anti-inflammatory drugs ketoprofen (128 subjects) and etofenamate (59 subjects). Of the organic UV absorbers, octocrylene, benzophenone-3, and butylmethoxydibenzoylmethane most frequently elicited PACD. Allergic contact dermatitis was less commonly observed than PACD, comprising 55 reactions in 47 (4.6%) subjects. The incidence of PACD was much higher than what was found in previous studies.^{5,6} Although to some degree this may relate to patient selection, this is in disagreement with the literature where it appears that PACD is much less common than ACD, at least to sunscreen ingredients.^{7–10}

In a recent North American study, 182 patients were photopatch tested.¹¹ Of these patients, 54 (29.7%) had at least 1 positive photoallergic reaction, and 29 (15.9%) had at least 1 contact allergic reaction. Fentichlor, chlorpromazine, promethazine, and benzophenone-4 produced the most photoallergic reactions. A second North American study similarly showed a PACD incidence of 39.5% with definite relevant photoallergic reactions in 11.2% of tested patients.¹² Of the positive photoallergic reactions, 23.2% were caused by sunscreen ingredients, 23.2% by antimicrobials, 20.3% by topical medications, 13% by fragrances, 11.6% by plant derivatives, and 8.7% by pesticides.

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Although many PACD studies have been undertaken in Europe and North America, there is minimal information on PACD in Canada. Because PACD prevalence changes with different populations and trends in product usage, it is necessary to be aware of new photoallergens.

METHODS

After approval from our institutional ethics review board, a retrospective chart review of all patients presenting to Toronto Western Hospital for photopatch testing between January 2001 and December 2010 was completed. The age, sex, date of testing, positive photoallergic and allergic contact test results, and clinical diagnoses were collected.

Photopatch Tests

Photopatch testing was completed at Toronto Western Hospital using a standardized procedure and trained evaluators. The North American Standard Photopatch Test Tray was used as the test battery. Four categories of allergens were tested: sunscreen ingredients, fragrances, antimicrobials, and commercially available sunscreen products. On day 1, a phototest to UVA and UVB was completed to determine the minimal erythema dose (MED) to UVB, and the response to 5 and 10 J/cm² UVA. Duplicate sets of allergens were applied to the patients' back. At 24 hours, 1 set of allergens were uncovered and exposed to UVA at a dose of 5 J/cm², if there had been no reaction to this dose of UVA 24 hours after exposure. Patients who reacted to 5 J/cm² did not undergo patch testing. The other set of allergens was shielded from the UVA exposure. Twenty-four-hour reactions to the nonirradiated compounds were assessed 15 to 20 minutes later. The following day, the irradiated patches were read 24-hours after irradiation, and the nonirradiated patches were read 48 hours after they had been applied. Patients were advised to contact the clinic if a positive reaction appeared at a later time point.

A reaction was considered positive if there was a well-demarcated area of erythema filling the borders of the allergen patch. Reactions were rated either +/–, 1+, 2+, or 3+, where +/– is faint erythema, not filling the entire exposed area, 1+ is positive (nonvesicular macular erythema), 2+ is strong (erythema and edema), and 3+ is an extreme reaction (spreading, bullous, and ulcerative erythema). Only reactions labeled as a clear 1+ or above were included as positive allergic reactions. +/– reactions were not included in the data evaluation. Reactions were labeled as irritant if a response was produced within 30 minutes of application or 30 minutes of UV exposure. Allergens that produced both contact and photocontact reactions were recorded separately.

RESULTS

Photopatch tests were performed on 160 patients at Toronto Western Hospital between January 2001 and December 2010. Thirty-seven patients were male, 123 were female, and the mean age

was 43.9 years, with a range between 14 and 76 years. The most common reasons for photopatch testing were photodistributed rash after negative lupus and porphyria workup (30 patients); rash, swelling, or pruritus after sun exposure (72 patients); and pruritus or rash after sunscreen application (40 patients).

Allergens

In total, 99 (61.9%) of the 160 patients had at least 1 reaction to the test allergens. Fifty-four patients (33.8%) had at least 1 photoallergic reaction, and 78 patients (48.8%) had at least 1 allergic contact reaction. Nineteen patients (11.9%) had a photoirritant reaction, and 29 patients (18.1%) had both a photoallergic and allergic reaction. All 26 allergens produced at least one allergic or photoallergic reaction (Table 1). The most common relevant photoallergens were benzophenone-3, (12 reactions), octyl dimethyl para-aminobenzoic acid (PABA) in 5% alcohol (5 reactions), and butylmethoxydibenzoylmethane (Parsol [Omdiderm Pharma Canada, Vaudreuil, Canada] 1789; 5 reactions). The most common allergens producing contact allergic reactions were octyl dimethyl PABA in 5% alcohol (24 reactions), sandalwood oil (20 reactions), benzophenone-3 (17 reactions), and triclosan (17 reactions). The main compounds that produced both contact and photocontact allergies in the same patient were octyl dimethyl PABA in 5% alcohol (8 reactions), octyl dimethyl PABA in 5% petrolatum (8 reactions), benzophenone-3 (6 reactions), and 6-methyl coumarine (6 reactions). All categories of tested allergens had similar reaction incidence rates.

Sex and Photoallergens

A total of 123 females and 37 males were photopatch tested during the 10-year period. Of those tested, 17 (45.9%) of the males had a positive PACD reaction, whereas only 37 (30.1%) of the females tested showed a positive PACD to any of the tested allergens.

Minimal Erythema Dose to UVB and Photoallergy

There was no significant difference ($P < 0.05$) in photoallergic reactions in patients with different measured MED to UVB. The incidence of photoallergic reactions was 30.8%, 40.9%, 38.1%, 32.1%, 16.7%, and 15.4% for MEDs of 20, 30, 40, 50, 60, and greater than 60 mJ/cm², respectively.

Sunscreen Ingredients/UV Filters

There were 59 (36.9%) of 160 patients who had at least 1 reaction to any sunscreen ingredient or commercially available product. Twenty-seven patients (45.8%) had a photoallergic reaction, 40 (67.8%) patients had an allergic contact reaction, 16 (27.1%) had both an allergic and photoallergic reaction, and 4 patients (6.8%) had an irritant reaction (Table 2). All sunscreen ingredients tested produced at least 1 photoallergic or allergic contact reaction.

Forty patients presented to the clinic complaining of a "sunscreen allergy" or giving a history suggestive of a sunscreen-related cause. Of these patients, 26 (65%) were found to have positive photoallergic

TABLE 1. Photoallergens and Reaction Incidences

Allergen	PACD Incidence, n (%)	ACD Incidence, n (%)	Irritant Incidence, n (%)	PACD + ACD Incidence, n (%)
Parsol MCX	4 (4.0)	11 (11.1)	0 (0.0)	1 (1.0)
Benzophenone-4	0 (0.0)	3 (3.0)	0 (0.0)	0 (0.0)
Thiourea	0 (0.0)	4 (4.0)	1 (1.0)	1 (1.0)
Dichlorophene	4 (4.0)	16 (16.2)	1 (1.0)	2 (2.0)
Chlorhexidine diacetate	2 (2.0)	13 (13.1)	0 (0.0)	3 (3.0)
Sandalwood oil	2 (2.0)	20 (20.2)	0 (0.0)	3 (3.0)
Chlorpromazine hydrochloride	13 (13.1)	4 (4.0)	1 (1.0)	0 (0.0)
PABA 4-amino benzoic acid in 5% alcohol	2 (2.0)	15 (15.2)	2 (2.0)	4 (4.0)
Petrolatum	1 (1.0)	2 (2.0)	0 (0.0)	0 (0.0)
3,4,5-Tribromosalicylanide	0 (0.0)	4 (4.0)	0 (0.0)	0 (0.0)
Octyldimethyl PABA in 5% alcohol	5 (5.1)	24 (24.2)	2 (2.0)	8 (8.1)
Benzophenone-3	12 (12.1)	17 (17.2)	0 (0.0)	6 (6.1)
Promethazine hydrochloride	13 (13.1)	7 (7.1)	2 (2.0)	0 (0.0)
Octyldimethyl PABA in 5% petrolatum	4 (4.0)	16 (16.2)	1 (1.0)	8 (8.1)
Bithionol	1 (1.0)	4 (4.0)	0 (0.0)	0 (0.0)
PABA 4-amino benzoic acid in 5% petrolatum	2 (2.0)	4 (4.0)	1 (1.0)	1 (1.0)
Fentichlor	8 (8.1)	7 (7.1)	2 (2.0)	0 (0.0)
Octyl salicylate	0 (0.0)	7 (7.1)	1 (1.0)	2 (2.0)
Butylmethoxydibenzoylmethaneparsol 1789	5 (5.1)	12 (12.1)	0 (0.0)	0 (0.0)
Homosalate	2 (2.0)	6 (6.1)	0 (0.0)	1 (1.0)
Methylantranilate	2 (2.0)	3 (3.0)	3 (3.0)	0 (0.0)
6-methyl coumarine	3 (3.0)	13 (13.1)	1 (1.0)	6 (6.0)
4-Methylbenzyliden camphor	0 (0.0)	1 (1.0)	1 (1.0)	1 (1.0)
Octocrylene	0 (0.0)	6 (6.1)	0 (0.0)	1 (1.0)
Triclosan	3 (3.0)	17 (17.2)	0 (0.0)	4 (4.0)
Hexachlorophene	2 (2.0)	10 (10.1)	0 (0.0)	3 (3.0)

and/or allergic reactions to their own sunscreens and/or sunscreen components.

DISCUSSION

This retrospective chart review assessed the incidence of photoallergic and allergic contact reactions to photopatch testing at our center in Toronto, among patients who had been referred for photopatch testing. Overall, the incidence of PACD in this group of patients was higher than expected according to recent published

literature, and photoallergic reactions were less common than allergic contact reactions. These findings disagree with the recent literature.⁴ There are several reasons for the difference in overall incidence of allergic reactions. Because test allergens have not been uniformly standardized at all sites, our relatively higher reaction incidence may be due to a larger or more focused test battery of allergens, allowing us to determine the actual culprit allergen in more people. A more discriminatory selection of the patient population to be tested could skew the results toward an increased incidence as well. Differences in test interpretation by different

TABLE 2. Sunscreens and Reaction Incidences

Sunscreen	PACD Incidence, n (%)	ACD Incidence, n (%)	Irritant Incidence, n (%)	PACD + ACD Incidence, n (%)
Marcelle SPF 25	5 (8.5)	2 (3.4)	0 (0.0)	1 (1.7)
Neutrogena SPF 55	10 (16.9)	16 (27.1)	1 (1.7)	8 (13.6)
Avene SPF 50	6 (10.2)	10 (16.9)	1 (1.7)	0 (0.0)
Anthelios SPF 60	5 (8.5)	22 (37.3)	0 (0.0)	8 (13.6)
Ombrelle Extreme SPF 30	5 (8.5)	16 (27.1)	1 (1.7)	3 (5.1)
Minesol Roc SPF 40	0 (0.0)	5 (8.5)	0 (0.0)	0 (0.0)
Solbar Zinc SPF 30	1 (1.7)	3 (5.1)	0 (0.0)	0 (0.0)
Coppertone SPF 45	2 (3.4)	4 (6.8)	0 (0.0)	1 (1.7)
Spectra SPF 50	2 (3.4)	1 (1.7)	0 (0.0)	0 (0.0)
Patient's own sunscreen	1 (1.7)	6 (10.2)	1 (1.7)	0 (0.0)

assessors may also lead to differences in reported photoallergic or allergic contact reactions. However, this increased incidence could also be a marker of different societal habits and preferences in sunscreen use because the prevalence of photoallergy has not been studied in a Canadian population.

More females were photopatch tested than males, which is a common trend and may reflect an increased use of sunscreen products by women or an increased willingness in women to seek medical attention.⁴ Interestingly, in those patients tested, males had a much larger positive reaction rate than females, which does not concur with previous literature.⁶ It is possible that because males are less likely to visit a physician, those who do present may have more distressing complaints than their female counterparts. Another recent study also showed an increased incidence of positive PACD in males compared with females.⁴

It is interesting to note that every allergen in our test battery produced at least 1 allergic or photoallergic reaction. Allergens that did not produce any photoallergic reactions include benzophenone-4, thiourea, 3,4,5-tribromosalicylanide, octyl salicylate, octocrylene, and 4-methylbenzylidene camphor. Although several recent studies have shown more positive photoallergic reactions to octocrylene,^{4,11} our study did not find any positive photoallergic reactions to this UV filter. After the consensus of methodology for photopatch testing in Europe created by the European Taskforce for Photopatch Testing, there has been a push toward removing the non-UV filters in the test allergen battery because many are now considered of historical relevance only.¹³ Our study found a diverse group of positive photoallergens apart from UV filters, with a lack of an emerging trend. All UV filters, fragrances, antimicrobials, and medications used produced positive reactions.

This study is limited by its retrospective nature. It is, however, the first to investigate photocontact allergy in a Canadian population. Because this is a single-center study with a moderate sample size, it could form a good basis for a larger, multicenter Canadian study. Because of the retrospective nature of this study, information for determining the relevance of positive reactions via the COADEX system, a classification system created for assessing relevance of positive patch test results, was not always available.¹³ Furthermore, the retrospective nature of the data makes it difficult to correct any flaws in the testing design. Specifically, patients were instructed to inform the clinic if there was a reaction greater than 48 hours after testing. Although we would assume that most patients with positive reactions would return to clinic to complete their testing, it is possible

that this underestimates the rate of photoreactions because some patients may not report late positive reactions. A prospective study could have corrected for this by ensuring that all patients had a scheduled clinic visit 5 to 7 days after the testing. Future prospective studies would help to further characterize photoallergy in Canada.

As noted above, in 2004, a group of European contact dermatologists and photobiologists produced a consensus statement regarding the methodology, allergens, and test interpretations for photopatch testing.¹³ These recommendations have allowed for a standardized test procedure throughout Europe that will enable comparison of photoallergen testing across different test centers. A similar initiative in North America would be beneficial.

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