

PHOTOCONTACT DERMATITIS

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Exogenous photochemical sensitivity is a term that is used to describe skin disease caused by the interaction of electromagnetic radiation and an exogenously acquired chemical agent. In all exogenous chemical photosensitivity responses, both chemical and radiation are necessary for the response to be produced. The exposure route can be either systemic or topical, and the mechanism of the response can be either irritant (toxic) or allergic (Table 1). This results in four possible entities: photoirritant contact dermatitis (PICD), photoallergic contact dermatitis (PACD), photoallergy to a systemic agent, and phototoxicity to a systemic agent.

The distinction between the mechanism of action (allergic versus toxic) is a fairly easy one to make on the basis of clinical features in the case of topically applied chemicals. By definition, photopatch testing to a chemical-inducing PACD will reveal positive responses in only sensitized individuals, and negative responses in unsensitized individuals or the population in general. By contrast, all, or at least the vast majority, of the population will develop positive reactions to phototesting to a phototoxic agent (PICD); other differences are outlined in Table 2. They include reaction occurring on first exposure to the chemical agent and light in PICD with a sensitization delay being necessary for PACD. The timing of the response to testing will be delayed in PACD as it is in allergic contact dermatitis. In PICD the timing of the response varies depending on the chemical involved; tars, for instance, induce an immediate positive reaction in skin on exposure to radiation whereas psoralens produce a response in skin 48 to 72 hours after exposure to light.

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Table 1. TYPES OF EXOGENOUS PHOTOCHEMICAL SENSITIVITY

Route of Exposure	Pathophysiology	
	Toxic	Allergic
Topical	Photoirritant contact dermatitis	Photoallergic contact dermatitis
Systemic*	Phototoxicity to a systemic agent	Photoallergy to a systemic agent

*Photosensitivity to a systemic agent or a photodrug reaction.

Clinically and histologically, PACD presents as an eczematous response whereas PICD will result in erythema, edema and bullous lesions clinically, and necrosis of keratinocytes histologically. The dose of both chemical and radiation necessary to induce the response is more critical to the production of PICD as compared with PACD.

The differences between phototoxicity and photoallergy to systemic agents are less clear, and such distinctions are usually based on animal and in vitro studies and not on a clinical basis. When the distinction has been made, almost all photosensitivity to systemic agents has been thought to be toxic in mechanism. In addition, most offending chemicals are therapeutic agents (Table 3). For these reasons it is convenient to refer to all such reactions as photosensitivity to a systemic agent (PSA) or photodrug reactions.

The diagnosis of a photodrug reaction is made primarily by history of ingestion of a photosensitizing agent and the presentation of a skin reaction in a photodistribution. Exposure of uninvolved skin to etiologic radiation while the patient is taking the drug may or may not reproduce the eruption. Similarly, PICD is a diagnosis made by careful history taking to reveal skin exposure to the photoirritant. Photopatch testing in such patients is contraindicated, as a positive response might be

Table 2. DIFFERENCES BETWEEN PHOTOALLERGIC AND PHOTOIRRITANT CHEMICAL REACTION

	Photoallergic	Phototoxic
Incidence	Low	High
Occurrence of first exposure	No	Yes
Onset after UV exposure	24–48 hours	Minutes to days
Radiation	Not crucial	Important
Clinical morphology	Eczematous erythroderma	Erythema and edema, bullous, eczematous, urticarial, papular, pigmentation, lichenoid, pseudoporphyria
Route of Exposure		
Topical	+++	++
Systemic	+	+++

Table 3. SYSTEMIC DRUGS AND CHEMICALS REPORTED TO CAUSE PHOTSENSITIVITY

Anticancer drugs	Antipsychotic drugs <i>Continued</i>
Actinomycin D	Perphenazine
Dacarbazine	Piperacetazine
Doxorubicin hydrochloride	Prochlorperazine
Fluorocytosin	Thioridazine
Fluorouracil	Thiothixene
Hydroxyurea	Tricyclic antidepressants
Methotrexate	Trifluoperazine
Procarbazine	Diuretics
Vinblastine	Acetazolamide
Antidepressants	Amiloride
Amitriptyline	Bendroflumethiazide
Amoxapine	Cyclothiazide
Desipramine	Chlorthiazide
Doxepin	Furosemide
Imipramine	Hydrochlorothiazide
Isocarboxazid	Hydroflumethiazide
Maprotiline	Methyclothiazide
Nortriptyline	Metolazone
Protriptyline	Polythiazide
Trimipramine	Quinethazone
Antihistamines	Trichlormethiazide
Carbinoxamine	Hypoglycemics
Cyproheptadine	Acetohexamide
Diphenhydramine	Chlorpropamide
Antimicrobials	Gilpizide
Ciprofloxacin	Glyburide
Demeclocyclin	Tolazamide
Doxycycline	Tolbutamide
Enoxacin	Nonsteroidal anti-inflammatory drugs
Flerofloxacin	Ketoprofen
Griseofulvin	Carprofen
Methacycline	Naproxen
Minocycline	Phenylbutazone
Nalidixic acid	Piroxicam
Norfloxacin	Sulindac
Oxytetracycline	Other
Sulfadoxine-pyrimethamine	Amiodarone
Sulfamethizole	Captopril
Sulfamethoxazole-trimethoprim	Carbamazepine
Sulfasalazine	Clofibrate
Sulfasoxazole	Cyclamate
Tetracycline hydrochloride	Disopyramide
Antiparasitic drugs	Etretinate
Bithionol	Fenofibrate
Chloroquine	Gold salts
Pyriminium pamoate	Hematoporphyrin
Quinine	Isotretinoin
Antipsychotic drugs	Oral contraceptives
Chlordiazepoxide hydrochloride	Psoralen derivatives
Chlorpromazine	Promethazine
Chlorprothixene	Quinidine sulfate and gluconate
Fluphenazine	Trimeprazine
Haloperidol	Triacetyldiphenolisatin

severe and would be expected to occur in the general population, and thus would not be helpful in making the diagnosis.⁷

Exposure of uninvolved skin to etiologic radiation while the patient is taking the drug may or may not reproduce the eruption. While patch testing is frequently performed in these patients, the results are very difficult to interpret, as most of these agents are phototoxic; therefore, a positive response is nondiscriminating. Investigators have begun to examine the reaction patterns of the response in an attempt to distinguish the allergic response from the toxic or irritant one.²⁸ Similarly, PICD is a diagnosis made by careful history taking to reveal skin exposure to the photoirritant. Photopatch testing is not recommended, as severe reactions may occur and positive reactions would be expected to occur in all individuals regardless of previous exposure and responses; thus, it would not be helpful in making the diagnosis. The most common agents producing PICD are as follows:

Tars

Therapeutics

Pitch, creosote

Furocoumarins

Therapeutic

Fragrance materials*

Plant products that contain psoralen†

Lime

Celery

Parsnip

Fig

Rue

Wild fennel

Parsley

Cow parsnip

Limone

Dyes

Eosin, methylene blue

Disperse blue 35

The reactions occur through topical exposure, and ingestion of these substances does not usually induce a systemic photosensitization. When the reaction is bullous it is easily recognized, and when the reaction presents only as hyperpigmentation, the diagnosis is sometimes more difficult to make (Figs. 1 and 2).

The pathophysiologic mechanism involved in photoallergic contact

*Berloque dermatitis.

†Phytophotodermatitis (not all inclusive).



Figure 1. Photoirritant contact dermatitis to limes.

dermatitis has been extensively studied. These studies routinely revealed that the immunologic process involved in this reaction is analogous to the process occurring in plain allergic contact dermatitis to a nonphotosensitized antigen. The mechanism involved in the production of the photoantigen is less clearly defined. Photoallergic contact dermatitis is believed to be immunologically mediated as a delayed type of hypersensitivity. This prevailing view is based on clinical observation, studies in human volunteers and experimental animals, and an occasional *in vitro* observation.¹⁰

As in all photosensitized processes, the initial event in PACD is the absorption of radiant energy by a chromophore, in this case the photoantigen. The absorbed energy produces a photochemical change in the photoantigen. This results in either production of a stable photoproduct or a short-lived excited state molecule. This photosensitized molecule is then conjugated with a protein carrier to produce a complete antigen. From this point on it is believed that the mechanism involved in induction of sensitivity in PACD is essentially the same as the mechanism involved in induction of allergic contact dermatitis. This includes antigen processing by Langerhans' cells and presentation of the antigen



Figure 2. Photoirritant contact dermatitis to cow parsnip.

to the lymphoreticular system with resultant proliferation of T cells.¹⁰ Elicitation of PACD necessitates re-exposure to both the photoantigen and radiant energy. The evidence linking allergic contact dermatitis and PACD is mostly circumstantial, and originated with initial clinical observations noting the similarity of the gross morphology of the responses and the eruptions. In addition, histologic examination of PACD revealed changes similar to those seen in allergic contact dermatitis, including epidermal changes ranging from spongiosis to acanthosis and an accompanying dense perivascular round-cell infiltrate.^{11, 12} Induction studies in humans with sulfa and salicylanilides also supported a delayed immune mechanism.^{12, 39}

In animal systems, PACD has been induced to various agents.^{16, 34} ultraviolet-A radiation (UVA) alone is now known to be sufficient for induction, which is theoretically sound because the absorption spectra for all of the photoantigens used in these models falls within the UVA range.^{14, 17, 21, 27} These animal experiments documented that PACD was immunologically mediated: the reactions were acquired, the reactions were based on immunologic memory, and the reactions were specific for the inducing antigen.¹⁰

Sensitivity was transferable by use of peritoneal exudate cells²⁶ and

lymph node cells,^{17, 21, 35} but not humoral factors, and that sensitization could be achieved in B-cell-deficient animals; and finally, the T-cell mediation of PACD was most clearly demonstrated by transfer of PACD sensitivity with lymph node cells from sensitized animals, even after pretreatment of the cells, with T-cell-specific antigens and complement. In the same studies it was demonstrated that the identity of the major histocompatibility complex between the donor and the recipient of the immune cells was necessary for successful transfer.^{17, 21, 26, 35}

Langerhans' cells have been shown to be necessary for induction of PACD,^[24,25] and mast cells have been shown to play a role in elicitation of the reaction^[26]. In vitro studies utilizing sensitized cells further support a cell-mediated immunologic mechanism for PACD similar to that of allergic contact dermatitis.¹⁸

One area of controversy in the understanding of the mechanism of PACD is the role of ultraviolet (UV) in the formation of the complete antigen. One view holds that UV absorption transforms the photoantigen into a stable photoproduct that binds to protein. The other view theorizes that UV absorption induces formation of an unstable, excited-state molecule that binds to the carrier. In fact, there is evidence that either of these mechanisms may be operative depending on the specific photoantigen in question.^{4, 33} Finally, oxygen intermediates, produced by the irradiation of the photoantigen, have been shown to be important in the production of the complete antigen in PACD.²⁴

The ability to develop PACD has been shown in animals to be under genetic control.⁴ This control has been shown to be linked to the major histocompatibility complex.³⁸ In addition, a high level of melanin content of the skin of animals used in genetic studies may interfere with the photocoupling of the antigen and the epidermal cell.³⁸

The incidence of photoallergic contact dermatitis in the general population is unknown. The incidence data available are based on positive photopatch test results in groups of patients with presumed photosensitivity referred to tertiary care facilities for diagnostic photopatch testing. In Canada, 6% of such patients phototested were found to have PACD in a study published in 1975.³⁸ In England, 25% of tested patients were found to have positive photopatch tests in each year during the 1970s.⁶ The Scandinavian Multicenter Photopatch Study more recently found 274 positive photopatch tests and 369 positive plain patch tests in 1993 patients tested between 1980 and 1985. Of these, 217 patients (11%) were thought to have clinically relevant positive tests resulting in a diagnosis of PACD.³⁶ In the United States, 70 patients were tested at the Mayo Clinic during the same 5-year period. Of those tested, 38.5% and 31% had positive photopatch test and plain patch tests, respectively. Only 14 patients (20%) tested had clinically relevant photopatch tests.²³ In a study from New York, 187 patients were phototested with positive

photopatch tests, resulting in the diagnosis of PACD in 20 patients (11%).⁸ Taken together it would appear that the incidence of PACD in individuals with a history of a photosensitivity eruption would be approximately 10% to 20%. This rate is considerably lower than for positive tests in groups of patients patch tested because of suspected plain allergic contact dermatitis. This would suggest that the differential diagnosis of the individual with photosensitivity is more confusing and that the clinical picture of PACD is not as well defined as that for allergic contact dermatitis. More careful screening of such patients might result in a higher positive response rate, but would also likely result in failure to correctly diagnose some individuals. A significant number of patients with a history of photosensitivity may have PACD in addition to other light-induced or light-aggravated conditions, like polymorphous light eruption or connective tissue disease. The treatment of such photosensitive individuals almost invariably includes chemical suncreening. Because some of the most common photoantigens inducing PACD are sunscreen chemicals, the optimum management of most, if not all, photosensitive patients includes photopatch testing. Failure to diagnose PACD, especially to a sunscreen agent in a photosensitive patient, could lead to an unnecessarily prolonged clinical course.²²

The PACD response is invariably an eczematous one (Fig. 3). Patients develop acute or subacute eczema with erythema and papules, and occasionally vesicles in sun-exposed and chemically exposed skin. The reaction develops in a delayed manner 1 to 3 days after exposure. The history may be confusing. Not all patients will recognize the relationship between sun exposure and the development of the eruption.



Figure 3. Subacute eczema in a photodistribution caused by photoallergic contact dermatitis to musk ambrette in cologne.

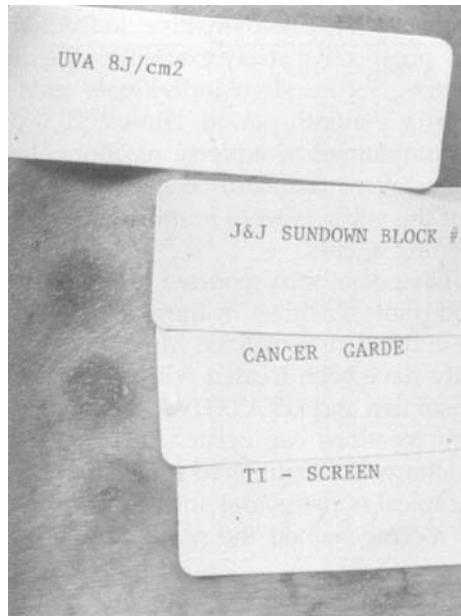


Figure 4. Positive photo-patch tests to three sunscreens in a patient with photoallergic contact dermatitis to oxybenzone.

Agents which induce PACD fall primarily into four major groups of substances: antimicrobials, fragrances, sunscreens, and medicaments. Many antimicrobials were used in bar soaps during the 1960s, and caused a large number of cases of PACD; these were primarily salicylanilides. Two fragrances became prominent photosensitizers during the 1970s and 1980s: musk ambrette in men's colognes and 6-methylcoumarin in sun-tanning lotions. When these agents were recognized as posing a problem, they were removed from personal care products. None of the highly photosensitizing agents are presently utilized in the United States and Western Europe. Most recently, sunscreens have come to the fore as the most common photosensitizers (Fig. 4).^{5, 37} Presently the most common allergens appear to be oxybenzone and isopropyl dibenzoylmethane,^{5, 37} the latter not presently in usage in the United States.

The development of PACD to sunscreens appears to be more likely in patients who are already photosensitive because of some other cause, including idiopathic photosensitivity² and porphyria.¹⁵ This increase in reported reactions to sunscreen agents might suggest that these agents are high-level sensitizers. More likely, photosensitivity to sunscreens is an extremely unlikely occurrence. The seeming increase in PACD is probably more related to the increase in usage of these products by the

general population and by photosensitive individuals. Foley et al,¹³ performed the only prospective study examining the question of toxicity of sunscreen products. Six hundred individuals used either sunscreen or control cream for a 7-month period. Almost 20% of the individuals using the creams complained of adverse reactions. Only 10% of those individuals, however, were found to be allergic to components of the cream, and none of the subjects were found to have allergy or PACD to the active sunscreens agents.

Medicaments have also been reported to induce PACD. Phenergan cream is a common photosensitizer in Europe.³⁶ 8-Methoxypsoralen is a potent phototoxin and a rare sensitizer. Most patients who have developed this sensitivity have been treated with the agent topically.²² Clinicians who utilize psoralen and UVA (PUVA) photochemotherapy should be aware that such reactions can occur. Any systemic photosensitizer may induce photoallergy if encountered topically. In addition, farmorubicin,¹ suprofen,²⁰ topical nonsteroidal anti-inflammatory agents,^{30, 31} and hexamidine³ have recently joined the ranks of new agents reported to cause PACD.

The diagnosis of PACD requires photopatch testing. Once the antigen has been identified, treatment consists of avoidance. Some reactions, including those to oxybenzone, may persist with recurrence on sun exposure even though the antigen is no longer being utilized. If patients avoid sun exposure, the sensitivity will finally resolve.

PHOTOPATCH TESTING TECHNIQUES

Photopatch testing, simply stated, is patch testing with the addition of radiation to induce formation of the photoantigen. The equipment necessary are appropriate light sources, antigens (Table 4), and light-opaque shielding for the period after removal of Finn chambers before readings.

With very few exceptions, the most notable being diphenylhydramine hydrochloride, the radiation responsible for formation of the photoantigen and clinical PACD falls within the UVA spectrum (320–400 nm). The ideal light source should produce UVA radiation in a continuous spectrum (fairly uniform radiation from 320–400 nm) of sufficient irradiance and field size to allow radiation of 20 to 25 antigen sites with a dose of 5 to 10 J/cm² within a reasonable time (~30 minutes). The source should also produce little ultraviolet-B radiation (UVB) or should be equipped with a filter to remove most of such radiation. Three to 5 mm of window glass is adequate filtration to block UVB radiation.

In a recent study, the effect of the spectrum of the light source utilized in photopatch testing on false-negative responses was addressed. Three different sources—a broad-spectrum UVA source, a nar-

Table 4. PHOTOANTIGENS

	Concentration	Vehicle
Octyl methoxycinnamate	7.5%	In petrolatum
Sulsobenzene (BZP-4)	10%	In petrolatum
Cinoxate	1%	In petrolatum
Thiourea (thiocarbamide)	1%	In petrolatum
Diclorophen	1%	In petrolatum
Triclosan	2%	In petrolatum
Hexachlorophene	1%	In petrolatum
Chlorhexidine diacetate	0.5%	In H ₂ O
Sandalwood oil	2%	In petrolatum
Chlorpromazine hydrochloride	0.1%	In petrolatum
Musk ambrette	1%	In petrolatum
Para-aminobenzoic acid	5%	In alcohol
Petrolatum control		
Tribromosalicylanilide	1%	In petrolatum
Octyl dimethyl PABA	5%	In alcohol
Oxybenzone (BZP-3)	3%	In petrolatum
Promethazine	1%	In petrolatum
Octyl dimethyl PABA	5%	In petrolatum
Bithionol (thiobis-dichlorophenol)	1%	In petrolatum
Para-aminobenzoic acid	5%	In petrolatum
Musk ambrette	1%	In alcohol
Fenticlor (thiobis-chlorophenol)	1%	In petrolatum
Octyl salicylate	5%	In petrolatum
Butyl methoxydibenzoylmethane	5%	In petrolatum
Homosalate	5%	In petrolatum
Methyl anthranilate	5%	In petrolatum
6-Methylcoumarin	1%	In alcohol*

*Apply 6-Methylcoumarin 30–60 minutes before irradiation on both sides.

row spectrum UVAI source, and a UVA/UVB source—were utilized for the testing. The broad-spectrum UVA source produced the most sensitive assay with the fewest false-negative responses.³² Table 4 lists the most common of such sources available. A photometer/radiometer matched to the source is also required for proper dosimetry. Such source/radiometer matching is most easily accomplished by purchasing the two units from the same manufacturer. By far the most readily available source in dermatology offices is the unit used for delivery of photochemotherapy (PUVA).

The dose of radiation used in photopatch testing has varied between 1 and 10 J/cm² in most studies. Theoretically, the largest dose which does not alone induce erythema in skin would be most likely to yield production of the photoantigen and a positive test. Because the minimal erythema dose (MED) in the UVA range is between 20 and 60 J/cm², any dose which can be conveniently delivered below this level can be used, and 10 J/cm² has been selected more or less arbitrarily to fulfill these two criteria.

Duguid et al⁹ examined the effect of dose of radiation on the

elicitation of positive responses in patients known to be photoallergic to certain antigens. Although the subject number and photoantigen diversity were relatively small, the study revealed that smaller doses, even as little as 1 J/cm², could be utilized for testing. The authors suggested a dose of 5 J/cm² as their standard. Until a larger number of antigens and patients are tested in similar studies, the 10 J/cm² dose still seems reasonable.

In addition to photopatch testing, it is recommended that the patient being tested also be given graded doses of radiation in the UVB range for determination of the MED. Such testing assists in distinguishing transient and persistent light reactivity. This necessitates a UVB light source:

UVA

- Fluorescent black lights
- Fluorescent PUVA lights
- Mercury halide lamp with filter
- Hot quartz lamp with filter*
- Sunlight with filter

UVB

- Fluorescent sun lamp
- Mercury halide lamp without filter
- Sunlight
- Hot quartz lamp without filter

PROTOCOL FOR PHOTOPATCH TESTING

A recommended protocol for photopatch testing is as follows:

Day 1—Apply irradiation for MEDs (with immediate readings);
apply 2 sets of antigens

Day 2—Read MEDs

Day 2 or 3—Remove antigen patches; irradiate one set of antigens;
recover antigens

Day 4 or 5—Read patch and photopatch tests 48 hours after patch
irradiation

Day 5 or after—Second patch and photopatch reading

This protocol should reliably diagnose PACD, and will also aid in the differential diagnoses of other common types of photosensitivity.

On day one, two sets of photoantigens are applied, one set to either side of the upper back. The antigens are applied in Finn chambers, as

*Discontinuous spectrum—less desirable.

described previously. Graded doses (8–10 doses) of UVB radiation are applied to previously unexposed skin sites (approximately 1 cm² area each) on one buttock. These doses should include the dose of radiation that would normally correspond to the patient's MED. For a patient with skin of light complexion, 10, 20, 30, 40, 50, 60, 70, and 80 mJ/cm² would be appropriate. These doses are dependent, however, on the light source and photometer utilized. UVA at a dose to be utilized for photopatch testing, usually 10 J/cm², is then delivered to a single site on the opposite buttock (~1 cm²).

On day 2 the patient returns and the phototest sites are evaluated for erythema. The MED in the UVB range is determined as the site with minimal perceptible erythema. Whether such a MED is "normal" or "lowered" is determined by experience with the particular light source used. If there is erythema at the UVA site this represents a definite abnormality, and titration with delivery of graded doses of UVA is required to determine the proper UVA photopatch dose. This is done in an analogous fashion to UVB MED testing using doses of 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 J/cm² of UVA with reading on day 3.

Assuming that UVA 10 J/cm² did not elicit a response, the photopatch test continues on day 2. Both sets of antigens are removed, marked, and readings are done at all sites for contact allergy or irritancy. One set of patches (dark control) is covered with light opaque material, and the other set is exposed to UVA 10 J/cm². The irradiated set is then also covered with light opaque material. Gauze pads covered with aluminum foil or black felt are suitable light-opaque material. The patient returns for readings preferably on day 5 (48 hours after irradiation) and at one later time point up to a week after irradiation. Two readings are recommended, and might be scheduled at 48 and 72 hours; 48 and 96 hours; 48 hours; and one week. If scheduling a 48-hour reading is impossible, two readings could be done at 24 and 72 hours or 24 and 96 hours.

If 10 J/cm² of UVA alone produced erythema, then a lower dose must be used for photopatch testing. That dose is determined by reading the MED testing (on day 3) to graded doses of UVA applied on day 2. A dose less than the MED must be used. It is sometimes suggested that a dose of 50% of the MED should be used, but any dose which alone will not produce erythema can be used. Use of too low a dose may result in false-negative photopatch tests. With a lowered MED in the UVA range, the irradiation of patches will be on day 3. The patches are therefore in place for 48 rather than 24 hours. There is no evidence to suggest that major differences occur between these two different testing schedules. As before, two readings should be done.

One antigen, 6-methylcoumarin, is not applied on day 1 with the other antigens. This agent's ability to form a photoantigen disappears

rapidly after application to skin. For this reason, the antigen is *applied on the day of patch irradiation* (usually day 2). It is applied in duplicate, in Finn chambers for a 30-minute period before irradiation.

Reading the photopatch test is done as for a patch test. An area of significant controversy exists, however, in distinguishing photocontact allergy from plain contact allergy. The system used by the North American Contact Dermatitis Group is shown in Table 5.

It is agreed that a positive response in the irradiated site and negative response in the covered site is diagnostic of photoallergy. Likewise, equal positives in both irradiated and covered sites is diagnostic of plain contact allergy. The North American system allows for the diagnosis of both allergy and photoallergy when both sites are positive, but when the irradiated patch is significantly more positive than the covered site. In the system used by the Scandinavian group and the Mayo Clinic group, any reaction in the covered site results in a diagnosis of plain contact allergy.

Occasionally, irradiation appears to inhibit a positive patch test reaction. In such cases, the nonirradiated site will be reactive whereas the irradiated site will be negative. The pathophysiology of such an occurrence is not understood, and neither are its clinical ramifications. Such a response, if clinically relevant, may be significant.

As with plain patch testing, false-positive and false-negative reactions can occur in photopatch testing. One particularly common false-positive or photo-irritant response is to the phenothiazine agents (chlorpromazine and promethazine). Actually, all photoallergens can act as phototoxins under the correct circumstances. Differentiation is sometimes difficult.

In an attempt to differentiate toxic and allergic responses, Neumann and colleagues²⁸ examined the patterns of the responses of the photopatch test readings over time. They divided the responses into four patterns: (1) a crescendo response typical of photoallergy, with a delay in the positive response becoming greater over time; (2) a decrescendo

Table 5. READING THE PHOTOPATCH TEST

Diagnosis	Reading	
	Irradiated Site	Unirradiated Site
No sensitivity	—	—
Photocontact allergy	+	—
Contact allergy	+	+
Photocontact allergy and contact allergy	++	> +

+ = positive; — = negative.

response with immediate positivity reducing over time, typical of photo-irritancy; and (3) two patterns of unknown origin, the plateau pattern and the combined immediate and delayed pattern. Such studies hold promise in assisting in definition of the response to photopatch testing in the clinical setting. Further work, including linking the pattern of the response to clinical relevance in individual patients, is necessary.

Recent reports of the pattern of an immediate response of an urticarial type along with a delayed eczematous response has been associated with true PACD to oxybenzone (personal communication, F. Storrs and 35, 1994). Some antigens will produce an immediate photoirritant response. Erythema is noted at the completion of the irradiation period. This is not clinically relevant and may be disregarded. In addition to the photoallergens in the tray, patients can be tested to their own products, particularly to sunscreens and fragrance-containing cosmetics. Industrial cleansers, as well as personal care cleansers, which may be the source for antibacterial agents, must be diluted appropriately.

CHRONIC ACTINIC DERMATITIS

Persistent Light Reactions

As with plain contact dermatitis, avoidance of contact with the photoallergen in a patient with photoallergic contact dermatitis usually results in clearing of the dermatitis and the photosensitivity. Occasionally, however, the patient will continue to be photosensitive (i.e., he or she will continue to react to light with the development of dermatitis). Such patients were first observed with the antibacterial photoallergens, and were referred to as *persistent light reactors*. In contrast, patients who clear once the photoallergen is removed were called *transient light reactors*.

Occasionally, continued photosensitivity remained localized to the distribution of the original photoallergen exposure; this was called a localized persistent light reaction, and was seen with the antibacterial bithionol. In such patients it was postulated that the sensitivity was related to persistence of allergen at the sites of initial exposure. In these individuals, exposure of previously uninvolved skin to UV-produced normal reactions (normal MED in UVB and UVA ranges). Photopatch testing (UVA and allergen), of course, produced a positive response.

Other patients, however, developed a generalized photosensitivity in the absence of continued antigen exposure. Most notable were patients photoallergic to the antibacterials tetrachlorosalicylanilide (TCSA) and tribromosalicylanilide (TBS), and more recently, to the fragrance musk ambrette. In these individuals, exposure of previously uninvolved



Figure 5. A nurse with eczema of the nose induced by photoallergic contact dermatitis to hydrochlorothiazide and Quinaglute. She was exposed topically to the agents when she opened capsules and crushed tablets of the drugs for her elderly patients.

skin to irradiation without allergen resulted in abnormal reactivity. This resulted in a lowered MED in the UVB range (possibly in the UVA and visible ranges). These responses were different both quantitatively and qualitatively from sunburn or MED erythema. Clinically and histologically the reactions were eczematous. The responses represented reproduction of the clinical eruption without antigen. This type of response

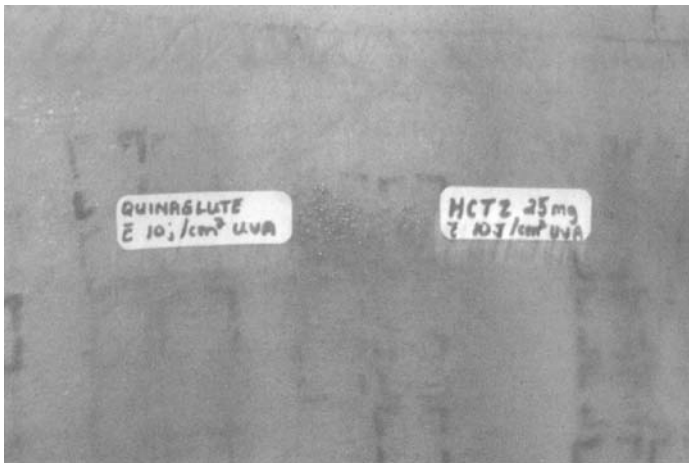


Figure 6. Positive photopatch tests to hydrochlorothiazide and Quinaglute plus UVA in the patient seen in Figure 5.

is more difficult to explain pathophysiologically than the localized persistent light reactions. Not only has skin not previously exposed to light or antigen developed sensitivity, the spectrum has shifted from UVA into the UVB range. It has been suggested that the original photoallergic reaction (UVA + allergen) has resulted in the development of an endogenous photoallergen, probably an altered carrier protein, with absorption and activation in the UVB range. It is interesting to note that only certain of the photoallergens are apparently capable of inducing such sensitivity. This includes a number of the antibacterial halogenated phenols, phenothiazines, and musk ambrette.

Although the severity of photosensitivity in patients with persistent light reaction varies greatly, many patients have been severely debilitated. Such individuals reacted adversely to minimal sun exposure (less than one minute of natural exposure), and were even believed to be reacting to indoor fluorescent lighting. The eczematous eruption became chronic, and spread to involve non-sun-exposed areas, sometimes eventuating in generalized erythroderma. Histology occasionally revealed an atypical infiltrate leading to the misdiagnosis of mycosis fungoides. Such patients were referred to as having *actinic reticuloid*, and most were older males. Patients of similar age and sex with a similar disseminated photosensitive eczematous response have also been reported under the terms *photosensitive eczema*, *eczematous polymorphous light eruption*, and *photosensitivity dermatitis*. The photobiologic criteria for diagnoses of these various conditions is listed in Table 6. All of these patients have in common a persistent eczematous clinical eruption of sun-exposed skin with extension to non-sun-exposed areas, sensitivity to UVB (with possible sensitivity to UVA and visible radiation), and chronic eczematous changes on skin biopsy with or without atypical infiltrate. It has been noted that patients may develop or lose criteria for differentiating these various diagnoses. It has been suggested, therefore,

Table 6. CHRONIC ACTINIC DERMATITIS

	Spectrum of Sensitivity			Photopatch Test	Abnormal Histology
	UVB	UVA	Vis		
Persistent light reaction	+	±	—	+	—
Actinic reticuloid	+	+	±	±	+
Photosensitive eczema	+	—	—	—	—
Photosensitivity dermatitis and actinic reticuloid syndrome	+	±	±	±	±
Eczematous polymorphous light eruption	+	±	—	—	—

that all such patients represent variations of a single process, and that they all be grouped under the diagnosis *chronic actinic dermatitis* (CAD).²⁹ Patients with CAD may or may not have positive photopatch tests. They may also have multiple positive plain patch test to airborne or industrially relevant antigens, like chrysanthemum and dichromates. Photobiologic testing in these individuals will reveal a lowered MED to UVB. The test site will be eczematous clinically and histologically.

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