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Photocontact Dermatitis and Its Clinical Mimics: an Overview for the Allergist

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Abstract

Photo-contact dermatitis (PCD) describes the adverse cutaneous reaction that occurs in some patients as a result of simultaneous exposure to a contactant and to light. PCD can be subdivided into photo-allergic and photo-irritant dermatitis depending on whether the contactant respectively invokes an allergic or irritant reaction. Photo-irritant reactions are commonly caused by plants, psoralens, and medications taken internally, whereas photo-allergic reactions are commonly caused by sunscreens and topical nonsteroidal anti-inflammatory medications. The work-up of photo-contact dermatitis includes a thorough history and physical exam augmented by patch and/or photopatch testing, as the cornerstone of treatment for PCD is identification and avoidance of the irritating or allergenic chemical. Photo-contact dermatitis has the potential to significantly impact quality of life, so an informed approach to diagnosis and management is critical. Clinical mimics of PCD include polymorphic light eruption, solar urticaria, actinic prurigo, hydroa vacciniforme, cutaneous porphyrias, and systemic disorders with photosensitivity such as lupus and dermatomyositis. Herein, we review the clinical presentation, differential diagnosis (including the clinical mimics mentioned above), pathogenic mechanisms, diagnostic testing, and therapeutic considerations for PCD.

Keywords Photo-contact dermatitis · Photo-allergic dermatitis · Photo-irritant dermatitis · Solar urticaria · Photopatch testing

Introduction

Photocontact dermatitis (PCD) is an adverse reaction caused by a chemical that contacts skin and incites an inflammatory response after exposure to ultraviolet (UV) and/or visible light. Recognizing PCD is key to preventing future exacerbations by avoiding the photo-reactive chemical and/or minimizing exposure to relevant light wavelengths. In this review, we will discuss the differential diagnosis of PCD, differentiate between photo-irritant and photo-allergic forms, and describe an approach to management that includes photopatch testing and treatment considerations.

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Differential Diagnoses

The location of the dermatitis is the most common tip-off for suspecting PCD since it corresponds to sites of contact with the photo-reactive chemical and to UV or visible light. A sun-exposed distribution distinguishes PCD from regular contact dermatitis (CD), atopic dermatitis, or other eczematous conditions not directly related to sun exposure.

Photo-distributed sites typically include the face and the extremities, with natural contours and barriers in these sites making particular regions more (or less) prone to affectation. Thus, the periorbital fossae (protected by the eyebrows or eyeglasses), the submental area (shaded by the nose), and the post-auricular area (shielded by the ears) are often spared. By contrast, extensor forearms and anterior legs are usually more involved compared to flexor forearms and posterior legs, respectively.

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On the other hand, a photosensitive eruption like PCD need not involve all sun-exposed areas since contact with a photo-reactive chemical is required for causation. A study of 480 patients with CD and PCD revealed 10% of cases with dermatitis confined to the face [1], consistent with sites of exposure to the photo-reactive chemical. Especially in severe cases, the converse may also occur, in which the dermatitis expands beyond sun-exposed sites. In these circumstances, the initial site of the eruption becomes of utmost diagnostic importance.

The differential diagnosis can be narrowed further by a temporal relationship between sun exposure and the skin eruption, seasonal variation in manifestations, duration of the dermatitis, exposure to potential photo-reactive agents, family medical history, and systemic symptoms.

Table 1 lists several photodermatoses, many of which can mimic PCD clinically [2–6]. Among the immune-mediated disorders, the most common is polymorphic light eruption (PMLE), in which inflammatory papules and plaques typically arise in early spring and subsequently improve through the summer (termed "hardening"). Skin findings tend to recur annually, eventually resolving as the patient ages. PMLE is thought to be a delayed-type hypersensitivity reaction, in which an endogenous photo-antigen becomes immunogenic upon sunlight exposure [2]. It is more commonly seen in women, and although found in individuals of all skin types, has a preponderance for lighter skin (particularly Fitzpatrick type I).

Less likely to be mistaken for PCD are two rare photodermatoses thought to also represent delayed-type hypersensitivity reactions: actinic prurigo, which is associated with conjunctivitis and cheilitis; and hydroa vacciniforme, which has the potential for causing scars.

Unlike the aforementioned dermatoses, solar urticaria (SU) presents as hives, rather than dermatitis. SU shares with photo-irritant CD immediate triggering within minutes of sun exposure, whereas clinical onset of photo-allergic CD and PMLE is delayed by several hours or even days. Because clinical recognition of solar urticaria is especially pertinent to the allergist, this skin eruption is described in further detail in a later section below.

The porphyrias, which are caused by genetic or acquired defects in the heme biosynthesis, can be categorized into two groups differentiated by presence or absence of light-induced skin lesions. The photosensitive (or cutaneous) group includes porphyria cutanea tarda (PCT), erythropoietic protoporphyria, congenital erythropoietic porphyria (Gunther), hepatoerythropoietic porphyria, variegate porphyria, and hereditary coproporphyria. PCT is, by far, the most common porphyria. Its clinical features include blistering, hypertrichosis, milia, and scarring (in addition to dermatitis), and it may be associated with hepatitis C viral infection. Erythropoietic protoporphyria (EPP) is the most common inherited form of porphyria and usually presents in childhood with burning or prickling pain and itching in visible-light exposed skin within as little as a few minutes after exposure, usually without bullae formation [7, 8]. Management of the porphyrias largely relies on genetic counseling and photoprotective measures, although the alpha-melanocyte stimulating hormone, afamelanotide, has shown promise for improving photosensitivity [9–11].

Photosensitive disorders with potential for systemic involvement, such as lupus erythematosus, dermatomyositis, and some porphyrias, are best considered or excluded based on findings elicited from a thorough review of systems [2].

Finally, PCD can co-exist with other dermatologic conditions. For example, a pre-existing eruption can be exacerbated by PCD, when a topical therapeutic agent turns out to be photo-reactive. A study of 89 patients with chronic actinic dermatitis included at least 13 cases that tested positively to various agents on photopatch testing [12].

Table 1 Categorization of photodermatoses [2–6]

Pathogenesis	Example	General info
Immunologically mediated	Polymorphic light eruption	Pruritic papules commonly seen in younger patients, particularly women
	Actinic prurigo	Predominantly in patients of Native American descent; associated with HLADR4
	Solar urticaria	Type I hypersensitivity (IgE mediated); fluid-filled plaques/wheals
	Hydroa Vacciniforme	Pruritic papules in children; likely related to EBV infection
Due to exogenous substance	Photo-irritant	Direct cellular injury caused by exposure to chemical activated by light
	Photo-allergic	Delayed-type IV hypersensitivity caused by exposure to chemical activated by light
Photo-reactive systemic diseases	Systemic lupus erythematosus	Systemic symptoms of lupus include an erythematous, photosensitive rash
	Porphyrias	Abnormalities in heme production; manifests dermatologically as photosensitive blisters
	Xeroderma pigmentosum	Autosomal recessive alteration in DNA repair mechanisms
	Nutritional deficiencies	Pellagra; cheilitis
Other photo-exacerbated conditions	Chronic actinic dermatitis	Pre-existing dermatitis worsened by exposure to sunlight

Solar Urticaria

SU is a rare cutaneous reaction to light characterized by wheal-and-flare formation and/or angioedema within minutes of UV exposure. The earliest descriptions of SU was likely made by Merklen in 1904 [13], followed a year after by Ward, who was first to provoke urticaria by means of controlled sun exposure [14]. It was Duke, who coined the term "solar urticaria" in 1923 to describe this dermatologic condition [15].

SU is classified as a physical type of urticaria, along with aquagenic, pressure, and thermal as other types [16]. SU accounts for less than 1% of all urticaria and approximately 7% of all photodermatoses [5]. A 10-year retrospective study of patients in a tertiary dermatology center in Singapore revealed only 19 cases of SU were diagnosed over an entire decade [17]. Most studies show women to be more often affected than men [17, 18]. All races and skin types can be affected, although a retrospective chart review of 280 patients with photodermatoses in the USA showed a significantly higher proportion in Caucasians than in African-Americans [19]. New-onset SU is most commonly seen in young adults typically between the ages of 20–40 [20, 21], although pediatric SU has been reported [22–26].

Clinical manifestations of SU are analogous to those of other urticarial reactions, with wheals and surrounding erythema as the hallmark manifestation. Unique to SU among urticarias is the sun-exposed distribution of eruptions, particularly on the arms, legs, and "V" of the chest [21]. However, since UVA can penetrate thin clothing, lesions may sometimes appear even on covered areas. Interestingly, more chronically sun-exposed surfaces, such as the face and dorsum of the hands, are relatively spared [27, 28]. As with most types of urticaria, concurrent pruritus is the chief complaint for many patients.

The diagnosis of SU is easily made clinically, especially in patients who present with characteristic wheals on sun-exposed skin sites and which resolve within 24 h of stopping light exposure. As cited previously, emergence of urticaria within minutes of light exposure differentiates SU from PMLE and many other photosensitive disorders. Diagnostic challenges include cases in which the morphology is not exactly urticarial but just macular erythema or even pruritus without visible lesions. Another variant is a "fixed" form of SU in which location and morphology of lesions are constant with each eruption and can be reproduced by phototesting [29]. Rarely, systemic symptoms such as headache and loss of consciousness have occurred in association with SU [30].

Histologically, SU resembles other types of urticaria, in which there is endothelial swelling and a dermal infiltrate of neutrophils and eosinophils around vessels [31].

Despite considerable research, the pathogenesis of SU is incompletely understood. The disorder is thought to be an IgE-mediated, type I hypersensitivity reaction, but differs from other IgE-mediated urticarias by a requirement for light to cause the condition. It is believed to be due to an endogenous chromophore in skin and/or serum of affected patients. Rajka demonstrated passive transfer of SU from an affected patient to an unaffected individual via intradermal injection of serum from the former to the latter [32]. Following exposure to relevant light wavelengths, the inciting chromophore undergoes a molecular change to become an activated photoallergen. Upon re-exposure to light, mobilization of the patient's immune system results in IgE activation and mast cell degranulation, leading to the formation of clinically appreciable urticaria. The role of light-mediated IgE activation in SU has been described for decades, with Leenutaphong et al. in 1989 developing a classification system delineating two types [33]. In some patients, an abnormal chromophore is present that becomes antigenic when exposed to light (Type I), while in others, SU is caused by abnormal circulating IgE antibodies that bind to a normal chromophore (Type II). More than 20 years earlier, Harber et al. suggested classifying SU based on the wavelength of light involved [34]. They proposed categorizing SU into types I–VI, based on their respective action spectra. Harber also described a type of SU associated with protoporphyria, which has since been debunked.

Interestingly, patients develop SU upon exposure to different wavelengths of light that vary from individual to individual [31]. The particular wavelength of light that elicits hives is termed the patient's action spectrum (AS), which can range from UVB (280–320 nm), UVA (320–400 nm), and even parts of the visible light spectrum (400–500 nm) [17, 22]. Phototesting can help delineate a patient's AS, which can then be avoided in her or his management. In contrast to AS, some patients may exhibit an inhibition spectrum (IS) that, instead, prevents photo-allergens from binding mast cells [35, 36]. Identification of an IS, which is typically a longer wavelength than AS, can guide specific phototherapy, has been successfully utilized as a treatment modality for preventing development of SU [35]. An IS is more likely to be present in patients who have a latent period between light exposure and wheal formation. Overlap between AS and IS during phototesting may complicate determination of the precise wavelengths responsible for SU.

Phototesting (PT) has the potential for identifying specific wavelengths of light causing SU, and it can also be used to monitor treatment responses. Magerl et al. recently updated their consensus recommendations for performing PT in patients with SU and other chronic, inducible urticarias [37]. They recommend that patients discontinue antihistamines and glucocorticoids several days prior to testing to reduce the chance of a diminished wheal response. The anti-urticarial effect of these medications can mask positive skin reactions, leading to false negative readings. Discontinuation is only necessary when testing for wheal-and-flare reactions, as antihistamines and glucocorticoids do not affect delayed-type

hypersensitivity. It is also recommended that PT be performed on the buttocks to achieve reproducibility of results. UVA light is tested with increasing intervals from 2.4 to 6.0 J/cm^2, while UVB is tested with increasing intervals from 24 to 60 mJ/cm^2. The minimal urticarial dose (MUD) is then recorded for each. Visible light is tested using a Kodachrome projector.

The cornerstone treatment of SU is avoidance of the offending light wavelengths. Protective clothing, broad-spectrum sunscreen, and minimizing time spent outdoors is recommended for all patients experiencing light sensitivity [21]. If pharmacological treatment is needed, oral H_1-blocking antihistamines are first-line. These medications may provide extremely effective, symptomatic treatment if taken every day (or when sun exposure is anticipated). For prophylaxis, a daily regimen is more effective compared with "as needed" intake. To achieve satisfactory relief from pruritus, higher than standard doses are often required. If symptoms continue to be inadequately controlled despite high doses, or if more definitive treatment is desired, other immunosuppressive drugs may be indicated.

Interestingly, UV radiation can be used to promote immune tolerance and thus reduce photosensitivity. As cited previously, this phenomenon of "hardening" can occur naturally in some patients who demonstrate tolerance to sunlight, as spring becomes summer. Various phototherapy protocols may include UVB, UVA, or visible wavelengths, or UVA in combination with psoralens delivered topically or orally (PUVA) [5, 38, 39]. This process may be conceptualized as a form of desensitization to light.

Other therapies used to treat SU include intravenous immunoglobulin, plasmapheresis, cyclosporine, and afamelanotide [35, 40, 41]. The anti-IgE recombinant monoclonal antibody omalizumab, which was approved by the US FDA for treatment of chronic, idiopathic urticaria in 2014, has also been tried for SU, in which many patients achieve improvement of symptoms or even clinical remission [42, 43].

SU is a chronic condition, and intermittent urticarial eruptions can occur for years and even decades. Spontaneous resolution is possible, however, with studies showing approximately 25% of patients experiencing clinical resolution (defined as at least 2 years without symptoms) within 10 years of diagnosis, and 46% with clinical resolution 15 years after initial manifestations [22, 44].

Mechanisms Causing Photo-Irritant (or Photo-Toxic) vs. Photo-Allergic Dermatitis

PCD can be classified into photo-irritant (or photo-toxic) vs. photo-allergic types, with disparate mechanisms and manifestations. This dichotomy runs parallel with divergence between irritant vs. allergic CD. In both irritant and photo-irritant dermatitis, skin cells are injured directly by free radical production, with inflammation developing after initial exposure to the chemical; sensitization is not required [6]. By contrast, allergic and photo-allergic dermatitis require T cell activation (sensitization) to produce an inflammatory response that develops in a delayed manner (hours to days) [6, 45, 46].

Symptomatology and histology have been touted to distinguish photo-irritant from photo-allergic dermatitis, with the former said to cause burning and blistering, whereas the latter results in pruritus and eczema. The irritant form supposedly gives rise to necrotic keratinocytes, while the allergic type produces epidermal spongiosis and a dermal mononuclear cell infiltrate [6]. In our experience, however, these distinctions are neither consistent nor reliable.

In photo-allergic CD, small chemical haptens penetrate the skin, where they are activated by exposure to sunlight (usually UVA wavelengths). In their activated state, haptens bond covalently with endogenous carrier proteins. The hapten-protein conjugate is taken up by antigen presenting cells, especially epidermal Langerhans cells and dermal dendritic cells that migrate to lymph nodes [47], where the antigenic conjugate is presented to memory T cells that proliferate and trigger a type IV hypersensitivity reaction. Upon re-exposure to the exogenous substance in the presence of light, the T cell-mediated immune response ensues involving multiple cytokines and their receptor signaling pathways.

Why photo-allergens cause inflammation in some patients and not in others is not well understood. One theory asserts that immune tolerance in "normal" individuals is disrupted in affected patients. Consistent with this theory is evidence that photo-allergic patients are prone to suffer from concurrent allergic CD. A study of 35 patients who were photo-allergic to topical ketoprofen showed a majority of these cases to also suffer from allergic CD [48]. Similar concurrence of allergic and photo-allergic dermatitis was reported in reaction to etofenamate in flogoprofen gel [49]. These cases suggest that a generalized predisposition to type IV allergy occurs in particular individuals, with or without the collusion of sunlight.

And yet, for most individuals, sunlight is inherently immunosuppressive (rather than immune-stimulatory), and this property has been exploited in using UV light (phototherapy) to alleviate a variety of inflammatory skin disorders, including psoriasis, cutaneous T cell lymphoma, pruritus, atopic dermatitis, and even CD.

As cited previously, photo-irritant CD results from direct and immediate cellular injury (in contrast to the delayed immune response of photo-allergic CD). Epidermal keratinocytes are our primary defense barrier against environmental injury, and as such these cells are the principal target of photo-irritant reactions [50]. However, the mechanism for causation of photo-toxic reactions to systemically administered drugs is not known, although this type of photo-reactive disease tends to be triggered by UVB (rather than UVA) wavelengths.

Photo-Irritant Chemicals

Photo-irritant dermatitis accounts for the vast majority of PCD (up to 90% of cases) [51], and plants or plant products are the major cause (termed phytophotodermatosis).

Plants containing psoralens are the most common culprit, with the acute phase presenting as blisters and eczema, and the chronic phase as brown hyperpigmentation. Because psoralens are a component of citrus fruits (lemons and limes), figs, celery, fennel, parsley, and parsnip, this form of phytophotodermatosis develops frequently in chefs, bartenders, and other handlers of these foods.

Psoralens are activated by UVA wavelengths (PUVA) and this phenomenon has been used to more effectively treat (photochemotherapy) the same inflammatory skin disease cited previously, either through topical application or oral ingestion of particular psoralen moieties [52].

It should be noted, however, that because psoralens intercalate between nucleic acids, their reactivity following UV exposure can cause DNA mutations, leading to carcinogenicity.

Besides psoralens, many drugs taken systemically can cause photo-irritant dermatitis. These medications include tetracyclines (particularly doxycycline), sulfonamides, fluoroquinolones, amiodaraone [2, 51], and chemotherapeutic agents. A thorough medication history is thus an important component of managing patients with photo-distributed eruptions.

Photo-Allergic Chemicals

The most common causes of photo-allergic dermatitis are sunscreens and topical medications (Table 2). Benzophenone-3 is responsible for close to 90% of sunscreen-induced allergic CD [53–55], but the portion due to photo-allergy has not been well threshed out. Also note that commercial products may incorporate benzophenones and other sunscreen agents for reasons other than to shield human beings from sunlight (e.g., it is present in ink products to prevent photo-degradation and extend shelf life).

Less common causes of sunscreen-induced allergic or photo-allergic dermatitis are para-aminobenzoic acid (PABA) and dibenzoylmethanes [56]; butyl-methoxydibenzoylmethane, salicylates, octocrylene, and cinnamates [56–58] including one in (Parsol MCX) [59], and ensulizole [60]. A study of 23,908 patients with CD to sunscreen indicated that women and younger patients were more affected [61], perhaps due to these groups' greater use of sunscreens.

Among topical medications, the most common causes are nonsteroidal anti-inflammatory drugs (NSAID), with topical ketoprofen as the leading photo-allergen [62], followed by topical etofenamate and piroxicam gel [49, 63]. Individuals allergic to topical piroxicam also tend to be allergic to thimerosal, most likely due to cross-reactivity to a commonly shared thiosalicylate moiety [63]. Note that thimerosal was a commonly used preservative in vaccines, tattoo ink, eye drops, and contact lens solutions. Because of increasing topical use of NSAID, fueled by the notion that this type of administration may be safer compared with oral intake, we may yet witness more cases of allergic and photo-allergic dermatitis to these drugs.

Other photo-allergic drugs include phenothiazines (chlorpromazine and promethazine), sulfanilamides, and quinidine sulfate [57, 64]. Chlorpromazine was the top photo-sensitizer in a retrospective study of photopatch testing of 4957 patients in China [64], with sulfanilamides ranking fourth.

While the term phytophotodermatosis has been used mostly to denote psoralen-induced dermatitis and a photo-irritant mechanism, there are other plant-derived chemicals, such as lavender, musk ambrette, and olaquindox [65–68] that can cause photo-allergic reactions. Many of these botanicals are used increasingly as fragrances and in aromatherapy. Musk ambrette used to be a highly ranked cause of photo-allergic CD, but its prevalence has steadily declined, most likely due to greater awareness of its potential health hazard [12]. Olaquindox is a pig-feed additive used to prevent bacterial enteritis; it is a derivative of the photo-sensitizer, quindoxine, previously used as an antibiotic and growth-promoting agent in pig feed. Also, olaquindox is structurally similar to chlorpromazine [67].

A study in India of 35 patients with photo-reactive dermatitis showed components of *Parthenium hysterophorus* [68] by patch testing to be the most common culprit. A different study in New York City of photopatch tested patients revealed the plant allergens and pesticide ingredients, folpet and captan, to be the top offenders [69].

Overall, it is more common for patients to encounter photosensitizing agents from topical pharmaceuticals or cosmetic products than from occupational exposure [1].

Table 2 Categorization of photo-allergens

Photo-allergen	Examples
Sunscreens	Benzophenones, para-aminobenzoic acid (PABA), salicylates, octocrylene, cinnamates
NSAID	Ketoprofen, piroxicam, etofenamate
Other medications	Chlorpromazine, promethazine, sulfanilamides, quinidine sulfate
Fragrances	lavender, musk ambrette
Other	Olaquindox, thimerosal, plant allergens, pesticides

Photopatch Testing

While patch testing to diagnose allergic CD in the USA is performed by many dermatologists and some allergists, photopatch testing to diagnose PCD is conducted more sparingly, even among well-established medical centers. A survey of photopatch testers [70] revealed that chemicals tested were relatively consistent (components of sunscreens, NSAID, patient's own products), but the wavelengths and doses of UV light used plus the timing of readings varied greatly, highlighting a need for standardizing an approach to photopatch testing to maximize accuracy and consistency of results.

In general, photopatch testing is considered an adjunct to regular patch testing. (For the sake of brevity, we will discuss only the features unique to photopatch testing and not the basic features of regular patch testing.) Allergens are placed on back skin in duplicate (visit day 1). One set of allergens is exposed to UV light 24 h later (visit day 2). Patches are read for the first time after another 24 h (visit day 3), and finally after another 48 h (visit day 5).

Because the overwhelming majority of photo-allergens react to UVA (rather than UVB) wavelengths, a broad-band source of UVA light is required. Because UVB or visible light may be the relevant trigger in rare cases, corresponding light sources may be needed to complete evaluation. To determine the amount of light to be applied, patients should be phototested with varying doses of UVA on visit day 1, and the minimum dose producing erythema determined on visit day 2. Readings on visit days 3 and 5 will identify positive allergens from the set not exposed to UV light, as well as positive photo-reactive allergens (from the set exposed to UV light). Similar to regular patch testing, allergic vs. irritant reactions can be distinguished by the pattern ensuing from visit days 3 to 4, with a crescendo response favoring allergy and a decrescendo reaction favoring irritancy.

In deciding which allergens to test, practitioners should be cognizant of evolving trends in personal care products. For example, benzophenones other than benzophenone-3 are no longer routinely used as UV filters in sunscreen, and may not need to be included in testing [71]. As cited previously, there are worldwide differences in exposure, so this aspect should be incorporated in managing patients.

As is the case for regular patch testing, photopatch testing results much be evaluated in the context of the patient's entire clinical picture to establish relevance. For example, a patient may test positive for a particular substance, but further questioning may indicate it to be irrelevant.

Treatment

The mainstay of treatment for PCD is avoidance of the photoreactive chemical. Avoidance is the safest and most effective way to prevent future eczematous outbreaks, highlighting the importance of patch and photopatch testing as methods of identifying the causative substance(s). When counseling patients about avoidance of their specific allergens, it may be beneficial to utilize a program such as the Contact Allergen Management Program (CAMP) provided by the American Contact Dermatitis Society (ACDS). This site allows providers to input positive allergens and subsequently provides a list of products bereft of these substances, often referred to as a "safe" list, to help patients identify products that they *can* theoretically use. Likewise, patients can themselves utilize apps such as "SkinSAFE", which provide information on product ingredients and recommendations for products that do not contain the patient's particular sensitizing substances. Patients who are allergic to various sunscreen components should be advised to avoid chemical sunscreens and, instead, utilize products with physical UV blockers, such as titanium dioxide and zinc oxide that are not prone to cause CD.

Although avoidance is ideal, many patients may require treatment while attempting to identify the underlying trigger and avoid it. For acute treatment, topical corticosteroids or calcineurin inhibitors are usually very beneficial. In severe cases, systemic steroids may be needed. Chronic severe cases may require steroid-sparing immunosuppressive agents for longer-term management, including mycophenolare mofetil and azathioprine.

Impact on Quality of Life

Although generally a self-limiting condition, PCD can be greatly distressing and uncomfortable for patients. Additionally, if the inciting substance is not identified and continues to be encountered, the condition may fail to improve or even worsen. In such circumstances, PCD can have a significant impact on the lives of those who suffer from it. So far, there is little consensus on the most appropriate way to measure PCD severity and impact on quality of life.

The easiest, cheapest, and most accessible method to rate severity in PCD patients is a visual assessment scale [72]. The physician may evaluate aspects of the dermatitis such as the size of erythematous region and the presence or absence of bullae, scaling, and fissuring to estimate the degree of reaction. However, there is currently no consensus on a recommended visual scale. Similarly, patients may fill out a survey that helps determine the impact PCD has on their quality of life, with questions being aimed at investigating the impact of dermatitis on social and occupational functioning. Currently, the Dermatology Life Quality Index (DLQI) is most often used for this purpose, although most physicians do not distribute quality of life questionnaires to their patients [72].

A more objective (but uncommonly utilized) method for assessing disease severity in PCD is the evaluation of

transepidermal water loss (TEWL). By comparing stratum corneum hydration in affected and non-affected sites, clinicians can evaluate the degree of cutaneous dehydration caused by the hypersensitivity reaction, with more severe dehydration observed in more severe cases. When using this approach, it is important to keep in mind the natural variations in skin thickness throughout different locations of the body [72]. Coupling of colorimetry with laser Doppler flow-meters (LDF) is another method of evaluating disease severity. Colorimetry evaluates the varying degrees of erythema caused by PCD by assessing reabsorbed light reflected from illuminated skin. LDF measures the frequency shift remitted from erythrocytes beneath the skin, and is proportional to the number of red blood cells in the sub-cutaneous microcirculation [72]. With either method, it may be more useful to compare affected and non-affected areas within a single individual than to compare patients to controls, as these measurements can be influenced by age, race, or ambient temperature.

Although these various measurements of reaction severity and impact on quality of life may provide a deeper understanding of PCD patients, they are infrequently used, perhaps in large part due to the fact that most patients are treatable with the avoidance of causative substances and usually recover completely from their cutaneous reactions. Such investigations may be warranted, however, in severe cases where decisions must be made between topical versus systemic steroid treatment, especially in cases where third-party payers or insurance companies may require measures of impact on patient quality of life. Currently, there are no guidelines to direct treatment intensity, and decisions are made by clinical judgment alone. It is possible that these indices of severity, if developed into simpler and more rapid tools for future use, may aid physicians and/or insurers in making such decisions regarding approach to treatment.

Summary and Conclusions

PCD is an adverse cutaneous reaction that occurs in patients exposed simultaneously to a sensitizing exogenous agent and sunlight (or rarely artificial light source). Solar urticaria is an important consideration in the differential diagnosis and must be recognized as a distinct entity from PCD, as outlined in great detail previously in this manuscript. As with any photodermatosis, PCD is recognizable clinically by its presentation in sun-exposed areas of the skin, with relative sparing of non-sun-exposed areas. PCD incorporates both photo-allergic dermatitis and photo-toxic dermatitis, each of which has a unique set of causative substances, pathogenesis, and clinical manifestation. Although the exact incidence of various forms of PCD is unknown, these conditions (and their associated morbidity) can be prevented if recognized clinically and the exogenous culprit is identified. Although PCD has been well-described, a consensus on methods for photopatch testing and systematic reporting of results in the USA are lacking. The development of such guidelines and a registry could greatly improve our understanding of the true incidence, as well as improve the accuracy and consistency of diagnosis. Further research on allergenic and toxic medications, cosmetic products, and environmental agents is critical in order to provide accurate and updated safety information to patients. As new chemicals enter the market and social trends result in different allergen exposures, our approach to PCD dermatitis will likewise continue to evolve.

Compliance with Ethical Standards

Conflicts of Interest Margaret Snyder, B.S.A. declares that she has no conflicts of interest. Jake E. Turrentine, M.D. is the Section Editor of the Self-Assessment Section of *Dermatitis* and serves on the Investment Committee for the American Contact Dermatitis Society. Ponciano D. Cruz, Jr., M.D. is the Editor-in-Chief of *Dermatitis* and is a consultant for Mary Kay Cosmetics, Inc.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Not applicable as there were no individual participants in this review.

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