Chapter 17

Phototoxic and Photoallergic Reactions

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Contents

17.1 Introduction

An exogenous substance may cause photosensitivity by phototoxic or photoallergic mechanisms, or by inducing a dermatosis which is exacerbated by exposure to ultraviolet (UV) radiation (Table 1). Phototoxicity is commoner than photoallergy, and is distinguished from it by the lack of an immunological basis. The characteristics of these two reaction patterns are shown in Table 2. However, it must be recognized that all attempts to classify substances causing these reactions are partly arbitrary; in particular, many agents are capable of producing photosensitivity by multiple and unique mechanisms, with corresponding differences in clinical presentation.

Phototoxicity may be due to systemically administered agents (usually drugs), or contact with substances (most commonly plants). Photoallergy is almost always due to topically applied substances (including sunscreens).

Mechanisms of phototoxicity and photoallergy are discussed in greater detail in Chap. 6. With regard to photoallergy, its predisposing factors and prevalence, individual photoallergens and the investigation of suspected photoallergy are described in the chapter on photopatch testing (Chap. 27).

17.2 Mechanisms of Photosensitization

Molecules that absorb photons are called chromophores. The chemical structure of a chromophore determines the wavelengths of radiation that it absorbs (its "absorption spectrum"). UVB is radiation of wavelength 280–315 nm, UVA is 315–400 nm, and wavelengths above this are visible light. Only a few chromophores, for example eosin, absorb light in the visible spectrum. Most phototoxicity and photoallergy is caused by UVA rather than UVB for several reasons: (1) most photosensitizers absorb UVA more than UVB; (2) there is much more UVA than UVB in sunlight; (3) sunburn occurs with small doses of UVB and so creates an upper limit to the dose of UVB that can be tolerated; and (4) more UVA penetrates to the dermis (particularly relevant to systemically administered photosensitizers). The latter is one reason why *in vitro* absorption spectra may differ from *in vivo* action spectra [1] (the action spectrum is the ability of different wavelengths of radiation to cause an effect).

17.2.1 Mechanisms of Phototoxicity

When a chromophore absorbs a photon, the energy promotes electrons within the molecule into an excited state. These return to the ground state by giving out radiation (for example, fluorescence) or heat, or by causing a chemical reaction. Products of the latter

Table 1. Mechanisms and clinical manifestations of photosensitivity caused by exogenous substances (adapted from Ferguson [18])

Mechanism	Clinical manifestations	Examples of topical agents	Examples of systemic agents
Phototoxicity	Immediate-onset erythema. Prickling, burning, edema or urticaria. May show delayed erythema or hyperpigmentation	Coal tar, anthraquinone-based dyes	Benoxaprofen, amiodarone, chlorpromazine
	Delayed-onset erythema (at 12–24 h; = exaggerated sunburn)		Fluoroquinolones, tetracyclines, thiazides, quinine, amiodarone, chlorpromazine retinoids
	Late-onset erythema (24–120 h), may develop blisters, hyperpigmentation	Psoralens	Psoralens
	Pseudoporphyria		Frusemide, amiodarone, tetracyclines
	Photoonycholysis		Tetracyclines, psoralens
	Telangiectasia		Calcium-channel blockers
Photoallergy	Eczema	Sunscreens, Musk ambrette	Rare/controversial
Induction of photosensitive dermatosis	Lupus erythematosus		Hydralazine
	Lichenoid reaction		Thiazides
	Melasma		Oral contraceptive pill
	Pellagra		Hydantoin

Table 2. Comparison between phototoxic and photoallergic reactions (adapted from [37])

	Phototoxic	Photoallergic
Occurs in all individuals with sufficient dose	Yes	No
Incidence after exposure	High	Low
Required concentration of photosensitizing agent	High	Low
Required dose of ultraviolet	High	Low
Reaction possible after single exposure	Yes	No
Ultraviolet action spectrum	Same as absorption spectrum	Broader than absorption spectrum
Commonest appearance	Erythema	Eczema
Limited to exposed area	Yes	May spread
Flare-up reactions	No	Possible
Cross-reactions	No	Possible

are called photoproducts and the reactions generating them can be divided into three types:

- Type I Transfer of an electron leads to the formation of free radicals. These free radicals react with oxygen thereby generating reactive oxygen species.
- Type II Energy transfer leads directly to the formation of reactive oxygen species.
- Type III Energy transfer leads directly to the formation of stable phototoxic products.

As can be seen from the above, types I and II are dependent on oxygen; they are sometimes called "photodynamic reactions" and the reactive oxygen species they produce cause damage to cells. They are more common than type III reactions. An individual phototoxic substance usually causes phototoxicity by multiple molecular pathways. Systemically administered phototoxic agents tend to cause most damage to endothelial cells and mast cells, and topically applied ones to keratinocytes. The cellular location of damage tends to be inside the cell in the case of lipophilic sensitizers, and hydrophilic ones tend to damage cell membranes (Chap. 6).

17.2.1.1 Examples

Furocoumarins (Psoralens)

These are unusual among photosensitizing substances in several respects: they operate predominantly through a type III mechanism, they target DNA, and some of the processes involved are reasonably well understood. They form complexes between adjacent base pairs in DNA, and then on UVA irradiation a covalent bond is formed between the furocoumarin and a pyrimidine base (particularly thymine) on the DNA. This process is an example of cycloaddition and it yields a monoadduct with a furocoumarin molecule linked to one DNA strand. If there is now further absorption of UVA, a similar reaction can take place with a pyrimidine base on the opposite strand of DNA, a process of bifunctional cycloaddition which results in interstrand cross-linking [2]. The mechanism of erythema production from furocoumarin phototoxicity is not fully clear, but there is a correlation between the ability of a psoralen to cross-link strands of DNA with the production of an erythematous response [3]. 4,6,4´-Trimethylangelicin, a psoralen that forms monoadducts only, is far less phototoxic than 8-methoxypsoralen, which engages in bifunctional cycloaddition [4]. However, the erythema from furocoumarin phototoxicity may also be related to membrane damage caused by photodynamic processes [5].

Dyes

The absorption of visible light and UVA by dyes such as acridine orange causes generation of singlet oxygen which results in tissue damage, particularly to membranes [6].

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

These produce photoproducts which generate free radicals [7, 8].

Amiodarone

After exposure to UV, amiodarone loses iodine (deiodination) and there is aryl radical formation. This aryl radical is able to take hydrogen from chemical donors such as linoleic acid. A dienyl radical is formed, which can then produce a peroxy radical causing lipid peroxidation. This reaction may be the reason for the deposition of lipofuscin in the skin associated with amiodarone phototoxicity [9].

17.2.2 Mechanisms of Photoallergy

A stable photoproduct is generated by a photochemical reaction as described above. In photoallergy, that photoproduct acts as a hapten or a complete antigen to generate a type-IV hypersensitivity reaction. This hypersensitivity is essentially the same as that underlying allergic contact dermatitis; in the sensitization phase Langerhans cells migrate to lymph nodes and present antigens to T-lymphocytes. In the elicitation phase these T-cells meet the antigen in the skin and react to it. The histology and morphology of a photoallergic contact reaction are similar to those of an ordinary allergic contact reaction and, on immunohistological examination, $CD4^+$ lymphocytes are present in the infiltrate [10]. Both the sensitization and elicitation phases of the reaction require the generation of the allergen by ultraviolet radiation.

Many compounds that can cause photoallergy are halogenated aromatic hydrocarbons [11]. One chemical that has been studied is tetrachlorosalicylanilide, which used to be a common photoallergen until it was withdrawn. UV causes it to undergo photochemical dechlorination, generating free radicals that react with albumin; albumin modified in this way may be antigenic [11].

The action spectrum of photoallergy is usually in the UVA range. Exceptions to this, in which both UVA and UVB have been incriminated, include NSAIDS [12] and diphenhydramine hydrochloride [13].

Some agents, for example phenothiazines, are capable of producing both phototoxicity and photoallergy.

17.3 General Features of Photosensitive Eruptions

Phototoxicity and photoallergy due to topically applied substances have a distribution corresponding to the overlap of the application of the substance and UV exposure. Photosensitivity due to systemic administration of a phototoxic substance tends to have a distinctive distribution identical to that of chronic actinic dermatitis. It involves the face (especially the forehead, cheeks, chin, and helices of ears), upper chest, sides and back of the neck, and dorsal aspects of the forearms and hands. The skin proximal to the second and third fingers is more affected than that proximal to the fourth and fifth, and the proximal phalanges are affected but not the middle or distal ones. There may be well-demarcated cut-offs at the edges of clothing, such as on the V-of-the-chest and beyond the sleeves. Shaded areas of exposed skin, such as upper eyelids, behind the ears, under the chin, skin creases and finger-web spaces, are typically spared. This may help distinction from airborne allergic contact dermatitis.

However, this classic distribution is not always obviously present, reasons for which include the penetration of thin loose-weave clothing by UVA, and the spread of photoallergic (but not phototoxic) reactions to include unexposed skin. Asymmetrical exposure to UV (for example, due to car travel) may cause an asymmetrical rash.

When attempting to determine if a patient is photosensitive it is very helpful if the patient has noticed that their condition deteriorates with sun exposure. Patients sensitive to UVA are less likely to observe this than those sensitive to UVB. This is because UVA shows less seasonal variation and penetrates cloud, windows, and thin loose-weaved clothing. Therefore, exacerbations related to discrete episodes of intense sun exposure, which are more easily recognized by patients, do not dominate the clinical picture. Also, the shorter the latent period between exposure and deterioration the easier it is for the patient to make the association.

17.4 Phototoxicity

Some of the systemic and topical agents reported to cause phototoxic reactions are listed in Tables 3 and 4. The incidence of phototoxicity with each drug varies greatly between reports. The commonest types of phototoxicity seen by dermatologists are phototoxicity due to psoralen-UVA (PUVA) therapy and to other orally administered drugs, and phytophototoxic dermatitis.

Phototoxicity will theoretically occur in all individuals exposed to a high enough dose of both the phototoxic substance and UV. However, in practice it frequently seems to be idiosyncratic, for reasons that are not entirely clear. Differences in drug metabolism between individuals (which may be genetic) may predispose some people. Fair-skinned individuals who report high sunburn sensitivity (Fitzpatrick skin-types I and II) may be more susceptible. This is certainly the case with PUVA therapy, and may be due not only to the fact that a lower dose of UV is required to cause erythema in these people, but also to possible differences in the shape of the dose–response curve and duration of erythema.

Investigation of contact phototoxic reactions by photopatch testing is not usually indicated; these reactions are difficult to interpret because all individuals will theoretically react given enough sensitizer and the cutaneous absorption of that sensitizer is difficult to reliably calibrate. Instead, the diagnosis comes from the history and examination. In the case of systemic phototoxic reactions, irradiation with a broad-band source or monochromatic irradiation, on and off the suspected drug, will establish to what degree the minimum phototoxic dose (on the drug, evaluated at an appropriate time interval after UV, which depends on the suspected photosensitizer) is lower than the minimum erythema dose (off the drug).

Phototoxicity usually resolves quickly after ceasing exposure to the photosensitizer. If there are strong reasons not to stop a systemic drug that is causing phototoxicity, changing the time of administration from the morning to the evening may help [14], as may reducing the dose, because phototoxicity is, by its nature, dose-dependent. Amiodarone and its major metabolite can persist in the skin for months after stopping it so that phototoxicity can be prolonged. During the development of new drugs that are chemically related to known photosensitizers, it is essential to test for phototoxicity before they are marketed. A variety of *in vitro* methods exist, and *in vivo* testing is performed which allows the calculation of a "phototoxicity index" [15].

The increased carcinogenic risk in patients who have had many oral PUVA treatments is well recognized, and the possibility exists that other photosensitizing drugs may also promote photocarcinogenesis. It has been shown in mice that fluoroquinolones can do this, but it is probably of no significance for humans who usually take only short courses [16]. The significance is uncertain for patients with cystic fibrosis who take long courses of high-dose fluoroquinolones and have a high incidence of phototoxicity [17].

17.4.1 Clinical Features of Phototoxicity

These vary depending on the photosensitizing agent. The complexity and variability of the processes involved defy the construction of a perfect classification. The following attempt is summarized in Table 1 (adapted from Ferguson [18]).

17.4.1.1 Immediate-onset Erythema

During UVA exposure patients develop a prickling or burning sensation with erythema, which becomes edematous or urticarial if severe. This is similar to the features of erythropoietic protoporphyria. In addition, there may be associated subsequent hyperpigmentation.

Tar

Workers exposed to coal tar, or derivatives such as creosote, may develop tar "smarts." The reaction consists of burning and smarting of the exposed skin and this is often associated with erythema that leads to hyperpigmentation. The phenomenon occurs in the summer months and is related to the degree of UVA exposure. The reactions may be caused by volatile fumes as well as by direct contact.

Amiodarone

Approximately 50% of patients develop an immediate prickling or burning sensation with erythema [19]. This immediate erythema settles but may reemerge 24 h later [20]. It is dose-related. The minimum erythema dose is reduced over the range 335–460 nm. A minority of patients get a slate grey pigmentation due to the deposition of an amiodarone metabolite complex in the skin. Amiodarone and its major metabolite can persist in the skin for months after stopping administration, so that the symptoms of acute phototoxicity can be prolonged for months, and the pigmentation for years.

Chlorpromazine

This can produce immediate erythema and discomfort. In addition, a slate-grey pigmentation may occur, as with amiodarone.

17.4.1.2 Delayed-onset Erythema

This has a time-course similar to that of sunburn (peak erythema at 12–24 h) and if severe may look like "exaggerated sunburn." Tetracyclines, retinoids, thiazides, and quinine may produce this response. Among the tetracyclines, the order of likelihood of provoking phototoxicity is: demeclocycline (syn. demethylchlorotetracycline) >doxycycline>others.

17.4.1.3 Late-onset Erythema

This is caused by psoralens, and is characterized by erythema maximal at 72–96 h after UVA exposure, which may be followed by hyperpigmentation lasting months or even years. If the dose is low and the exposures are repeated only hyperpigmentation develops.

Phytophototoxic Contact Dermatitis

This is caused by topical contact with psoralens from plants, followed by UVA exposure. Many common plants contain psoralens and examples are listed in Table 5. The compounds are lipid soluble and penetrate the epidermis readily, and this is enhanced by high humidity. There are a variety of manifestations possible depending on the manner in which exposure occurs. For example, strimmers (weed whackers) deliver a buckshot of weeds creating irregular, nonlinear red macules ("strimmer dermatitis"). Topical contact with lime juice is a famous culprit. If walking through long weeds, bizarre linear angular red streaks can develop at the site of contact, which may become bullous. This may be confused with "pseudophytophototoxic dermatitis" (caused by an irritant contact dermatitis in response to compounds in, for example, buttercups), and allergic contact dermatitis (for example to poison ivy, common in the USA).

Berloque Dermatitis

This was caused by the inclusion in some perfumes of bergamot oil, which contains "bergapten" (5-methoxypsoralen). The reaction occurred where the perfume had been applied; the term "berloque" refers to the drop-like shape of the patches. It is now rare due to the prohibition of psoralens from cosmetic products; if bergamot oil is used it must be psoralen-free.

17.4.1.4 Pseudoporphyria, Photoonycholysis, and Telangiectasia

Some phototoxic drugs are capable of producing pseudoporphyria, characterized by skin fragility,

blistering and milia formation after minor trauma, features also seen in porphyria cutanea tarda and variegate porphyria. A similar picture may develop in patients with chronic renal failure on dialysis, and in frequent users of sunbeds; the mechanisms of these are not clear. Photoonycholysis occurs via a phototoxic mechanism. Exposed-site telangiectasia is a rare side-effect of calcium channel blockers, usually occurs without a history of acute phototoxicity, and resolves over many months. It is believed the vasculature is the phototoxic target [15].

17.5 Photoallergy

Photoallergy is a type-IV hypersensitivity reaction to an antigen generated by the interaction of sunlight with a topically applied substance. Its predisposing factors and prevalence, individual photoallergens, and the investigation of suspected photoallergy by photopatch testing are described in Chap. 27. Currently, the commonest photoallergens in the western world are sunscreens. Some photoallergens are also contact allergens, and some also cause phototoxic reactions.

17.5.1 Clinical Features of Photoallergy

Photoallergy nearly always manifests as eczema, and has histological features identical to allergic contact dermatitis. It may be acute, subacute or chronic, and a spectrum of reactions is therefore possible including erythema, bullae, and lichenification. There may be spread onto unexposed sites and the eruption can become widespread but the exposed areas tend to remain the most severe. The latent period between exposure and appearance/deterioration of eczema depends on the severity of the reaction, but is usually 2–48 h later.

The differential diagnosis of photoallergic contact dermatitis includes the following.

17.5.1.1 Phototoxicity

Many photoallergens also have phototoxic potential. Clinically, it may be difficult to differentiate between phototoxic and photoallergic contact reactions. Table 2 lists features that may help in the differentiation. Typical phototoxicity has the appearance of sunburn (which may be severe); however, in practice the distinction can be difficult, and repeat episodes of phototoxicity can cause a dermatitis clinically and histologically [15]. The presence of sunburn-type erythema alone probably indicates a toxic reaction, which may be confirmed on histological examination. Many case reports allocating the type of photosensitivity reaction to a particular compound do so on insecure grounds; there has been a tendency to falsely ascribe a photoallergic basis to phototoxic reactions.

Table 3. Systemic agents causing phototoxicity

Antibiotics	Fluoroquinolones
	Nalidixic acid
	Sulphonamides, e.g., sulphamethoxazole
	Tetracyclines, e.g., tetracycline, oxytetracycline, doxycycline, chlortetracycline, demethylchlortetracycline
Anticancer agents	Dacarbazine
	Fluorouracil
	Vinblastine
Cardiovascular agents	Amiodarone
	Frusemide
	Quinidine
	Thiazide diuretics, e.g., chlorothiazide, hydrochlorothiazide, cyclopenthiazide
Psychoactive agents	Phenothiazines, e.g., chlorpromazine, phenothiazine
	Tricyclic antidepressants, e.g., protriptyline, clomipramine, dothiepin, imipramine, maprotiline
Therapeutic agents	Psoralens
	Porphyrins
Miscellaneous	Antimalarials; chloroquine, hydroxychloroquine
	Griseofulvin
	Nonsteroidal anti-inflammatory drugs, e.g., azapropazone, benoxaprofen, piroxicam, tiaprofenic acid
	Quinine
	Retinoids, e.g., acitretin, isotretinoin
	Sulphonylureas

Table 4. Some topical agents causing phototoxicity

Dyes	Eosin, acridine orange, acriflavin
Psoralens	Present in plants (see Table 5), essential oils, used therapeutically
Biocides	Fenticlor Halogenated salicylanilides
Sunscreens	2-Ethoxyethyl-*p*-methoxycinnamate Isoamyl-*p*-*N*,*N*′-dimethylamino-benzoate
Miscellaneous	Balsam of Peru Buclosamide Coal tar and derivatives Cadmium sulfide Chlorpromazine Porphyrins

17.5.1.2 Allergic Contact Dermatitis

It may also be difficult to differentiate between photoallergy and allergic contact dermatitis (ACD). Many photoallergens can also cause ACD. Sunscreens can cause ACD and because they are typically applied at times of sun exposure it is usually clinically impossible to differentiate photoallergy from ACD to sunscreens. A chronic eczema on the exposed areas is usually not due to photosensitivity but is the result of airborne ACD. Airborne ACD characteristically involves the upper eyelids and extends below the chin and behind the ears, but does not always do so.

Table 5. Examples of plants containing psoralens (from [21])

Family name	Source	Common
Moraceae	*Ficus carica*	Fig
Rutaceae	*Citrus aurantifolia*	Sweet lime
	Citrus bergamia	Bergamot orange
	Citrus limon	Lemon
	Ruta graveolens	Rue
Umbelliferae	*Heracleum mantegazzianum*	Giant hogweed
	Pastinaca sativa	Parsnip
	Apium graveolens	Celery
	Daucus carota	Carrot

Causes of airborne ACD include colophony, fragrances, and phosphorus sesquisulfide, but the most common cause worldwide is Compositae *(*Asteraceae*)*. Exposure to Compositae allergens is increased in summer. Patch testing with leaves or flowers of Compositae will not always detect Compositae dermatitis, because of ranges in the amount of the allergens in species and seasonal variation. Occlusive patch tests performed with some commercially available oleoresin extracts have caused false-positive irritant reactions. Open tests with these oleoresins may give false-negative results in Compositae-sensitive subjects. The development of a sesquiterpene lactone mix by Ducombs and Benezra [21] gave reliability in the detection of Compositae sensitivity. This mix consists of a 0.1% dilution of an equal mixture of alantolactone, costunolide, and dehydrocostuslactone. The latter two substances are the more important allergens in the mix. This mixture is not irritating, and active sensitization is rare at this concentration. As an alternative to this mix, 1% costus oil may detect the majority of Compositae-sensitive individuals, but the oil contains a variable amount of allergen and may be sensitizing. A Compositae mix developed by Hausen [22] contains the oleoresins of five Compositae species. Compositae are contact allergens; there is no convincing evidence that Compositae are significant photoallergens [23].

A further source of diagnostic confusion is that ACD can be photoexacerbated, in the same way that, for example, atopic eczema can be in some patients. This has been reported with a number of allergens, for example tosylamide/formaldehyde resin [24], but rather than being specific to particular allergens this may reflect a general tendency among particular individuals. There is experimental evidence for this in mice and humans, which is discussed in Chap. 27 in relation to photoaugmentation of photopatch test reactions.

17.5.1.3 Photodermatoses

Chronic actinic dermatitis (CAD) is discussed below. Polymorphic light eruption (PLE) is rarely, if ever, truly eczematous but may cause diagnostic confusion particularly because approximately 15% of patients report that it is exacerbated by sunscreens [25]. Theoretically this may occur if the sunscreen is more effective at filtering UVB than UVA, and UVA is provoking the eruption and UVB is helping to prevent it by causing immunosuppression. Patients who develop PLE for the first time while using a sunscreen often wrongly believe they are allergic to it.

17.5.2 Prognosis of Photoallergy

The duration of photoallergy after stopping the application of a topical sensitizer is variable, typically between a few days [26] and several weeks [27]. Ketoprofen may persist in the epidermis for at least 17 days [28].

For decades it has been reported that occasionally after withdrawal of a topical photoallergen a tendency to dermatitis from sun exposure can persist for years, and this is termed "persistent light reactivity" (PLR) or, if the duration is shorter, sometimes "recurrent transient light reactions." It has been postulated that the drug results in allergic sensitization to endogenous allergens. There is claimed experimental support for such a mechanism [29], whereby tetrachlorosalicylanilide causes oxidation of histidine with modification of albumin into a weak allergen. Further irradiation with UVB, in the absence of the initial photosensitizer, may produce enough oxidized antigenic protein to elicit a cell-mediated immune response at all skin sites. Many agents have been implicated including musk ambrette, ketoprofen, and halogenated phenols (e.g., fenticlor). However, the existence of PLR as a discrete entity is controversial. Many argue that the evidence for a causative role for topical photoallergens in the generation of a prolonged state of endogenous photosensitivity is weak and prefer to regard such patients as having developed chronic actinic dermatitis (CAD) without preceding topical photoallergy [15, 23]. They challenge the basis on which the diagnosis of contact photoallergy was made, usually believing that the reaction was a phototoxic one, or turn causality in the opposite direction and regard such patients as having CAD which has predisposed to the development of contact photoallergy.

17.5.3 Photoallergy due to Systemically Administered Drugs

Photosensitivity with an eczematous morphology that is claimed to be due to a systemic agent has been reported many times. Substances reported to cause photoallergy in this way include sulphonamides, sulphonylurea derivatives, chlorothiazides, quinine, quinidine, and piroxicam [30]. Some of these reports support the diagnosis with positive photopatch tests but the systemic agents reported to cause photoallergy are generally also known to cause phototoxicity, and therefore photopatch tests in such reports may have been misinterpreted (see Chap. 27). Experimentally, it has been claimed that the intraperitoneal injection of chlorpromazine or sulphanilamide in mice, with UV irradiation to the skin, causes photosensitivity that can be transferred with lymph node cells [31]. In a suspected case, it is possible to dilute the drug, preferably to several concentrations, and photopatch test the patient; other subjects should also be tested in this way to investigate possible phototoxicity. However, metabolites may be the relevant photosensitizers so this procedure might lead to false-negative results. Therefore systemic photochallenge, giving twice the normal dose of the suspected agent with irradiation of the skin before and at intervals after ingestion, has been advocated [32].

17.6 Chronic Actinic Dermatitis (CAD)

Synonyms: photosensitivity dermatitis, actinic reticuloid [33].

This condition will be discussed here because of its photosensitive nature, the high prevalence among sufferers of concomitant allergic contact dermatitis (ACD) to airborne allergens, and the relatively high prevalence of CAD among patients with photoallergy.

CAD is uncommon, typically affects patients over 60 years of age with a male:female ratio of approximately 6:1, affects all races, and is commoner in temperate climes. It sometimes occurs on the background of endogenous nonphotosensitive eczema. Patients frequently have ACD, particularly to Compositae, colophony and fragrances, which may precede the development of CAD. Many patients are keen gardeners who have therefore had considerable exposure to these allergens and sunshine. The occurrence of CAD among atopic eczema patients aged 30–50 years is increasingly being recognized [34]. The pathogenesis is not completely understood but may involve a type-IV hypersensitivity response to a UV-induced autoantigen [35].

It presents as a persistent patchy or confluent eczematous eruption, which is often lichenified and may show very infiltrated pseudo-lymphomatous papules or plaques. It typically has a photosensitive distribution and worsens in summer and after episodes of sun exposure. However, the condition is often perennial and patients are often unaware of the role of sun exposure. Also, the condition may only patchily affect exposed sites, and may progress to covered areas and occasionally erythroderma.

On monochromator phototesting, there are usually abnormal reactions to UVA and UVB wavelengths, and sometimes also to visible light [35, 36]. Testing with broad-band sources provokes the eruption. Patch testing is vital to detect ACD. Histology is not

usually helpful in making the diagnosis, but when examined shows a chronic eczema and, in severe long-standing cases, pseudo-lymphomatous changes.

Treatment comprises avoidance of sun exposure by changes in behavior, use of tight-weave long sleeves/trousers and a hat, and the application of broad-spectrum high-factor sunscreens of low allergenic potential. Patients should be advised how to avoid any relevant allergens. Topical steroids and emollients are useful. If these measures are inadequate, oral immunosuppressive therapy with ciclosporin, azathioprine or mycophenolate mofetil may be required. Prolonged low-dose PUVA or TL-01 treatment is sometimes effective. With avoidance of sunshine and relevant airborne allergens, many patients notice a gradual reduction in their photosensitivity over a few years [36].

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