Photocontact Dermatitis

9

Domenico Bonamonte, Caterina Foti,
Francesca Ambrogio and Gianni Angelini

Photocontact dermatitis is an adverse reaction caused by a chemical substance coming in contact with the skin, that elicits an inflammatory response after exposure to ultraviolet rays (UV) and/or visible light [1–10]. This includes forms of contact irritation and forms of contact allergy.

9.1 Physiopathomechanism

In general, for a photochemical reaction to occur, the radiating energy needs to be absorbed by a molecule (a chromophore). The chromophores present in the skin are both endogenous (DNA, melanin) and exogenous (drugs and other photosensitizing contactants). Each chromophore absorbs a given wavelength (absorption spectrum) determined by the arrangement of its atoms. The range of action of a molecule is governed by the capacity of a given wavelength to provoke a biological response [11]. It is well known that light has been arbitrarily subdivided on the basis of its wavelengths into UVC (200–280 nm), UVB (280–320 nm), UVA (320–400 nm) and visible light (400–800 nm). The wavelengths that provoke the activation of most photocontactants lie in the UVA range. In fact, they penetrate more deeply into the skin than UVB rays, and can interact with drugs and other substances that distribute in the more proximal skin layers. For some substances, such as halogenated salicylanilides, the spectrum of action also extends to the UVB band [12], while the spectrum of action of others, like diphenhydramine, is exclusively in the UVB range [13]. Naturally, visible light, by penetrating down to the subcutaneous tissue, can also photoactivate various substances.

9.1.1 Phototoxic Reactions

It is necessary, for a phototoxic reaction to develop, (a) that the contactant reaches vital cells, (b) that light of an adequate wavelength penetrates the skin and (c) that energy photons be absorbed by the photocontactant [14]. Theoretically, all subjects exposed to sufficient quantities of phototoxic substances and to light of an adequate wavelength can develop a phototoxic dermatitis [15]. In practice, however, such manifestations are not observed in 100% of subjects, due to both host and environmental

D. Bonamonte (✉) · C. Foti · F. Ambrogio
Department of Biomedical Science and Human Oncology, University of Bari "Aldo Moro", Bari, Italy
e-mail: domenico.bonamonte@uniba.it

G. Angelini
Professor of Dermatology, University of Bari "Aldo Moro", Bari, Italy

G. Angelini et al. (eds.), *Clinical Contact Dermatitis*, https://doi.org/10.1007/978-3-030-49332-5_9

factors. The quantity of substance present in the skin is very important, for instance, and in the case of drugs this depends on the administration route, degree of intestinal absorption, and on the distribution and metabolism of the drug itself. Another important factor is the quantity of radiations that reaches the skin, that varies according to the skin pigment, quantity of hairs and thickness of the corneum. Moreover, an increased humidity, temperature and strong winds will also contribute to worsen the skin damage [16].

The transfer of energy from light to a chromophore in the skin causes electron excitation, that in turn triggers the formation of layers of unstable atoms with unpaired electrons or electron triplets. Naturally, therefore, molecules with a particular structure, often with double bonds alternating with single bonds or with aromatic rings, are those prone to trigger photodynamic reactions [17]. Excited molecules can return to the basal state following the emission of light (fluorescence or phosphorescence), release of heat, or transfer of energy to other molecules. This energy release can provoke damage to macromolecules and cellular organules, as well as the formation of inflammation mediators.

The phototoxicity mechanism is a dual one, being both direct (oxygen-independent) and indirect (oxygen-dependent) [1, 18, 19]. In turn, direct phototoxicity ensues in two ways: (a) by direct interaction of an excited chromophore with a target site through a covalent bond (furocoumarins, for example, combine with a pyrimidinic DNA base) [20]; (b) through the formation of a stable phototoxic product, as occurs with chlorpromazine [21, 22]. Indirect or photodynamic phototoxicity can develop in two forms: (c) a type I reaction, in which excited chromophores, in their triplet state, react with oxygen to form highly reactive free radicals that can cause the skin damage; (d) in type II reaction, instead, the activated chromophores transfer energy to oxygen atoms, forming singlet oxygen. The latter has a remarkable power to oxidize and thereby damage cellular components. Unlike type I reactions, in which the chromophore is chemically charged, in the second type the chromophore is not chemically altered.

Most phototoxic substances very likely act through the photodynamic mechanism and cause damage along various routes. The cellular target of photodynamic substances varies: topical products are more likely to damage the keratinocytes, whereas drugs administered orally or parenterally act on the mast cells and dermal endothelial cells. The type of subcellular target depends on the characteristics of the phototoxic substance: hydrophilic substances harm the cell membrane, whereas hydrophobic substances spread in the cell and damage the cytoplasmic or nuclear substances [23].

9.1.2 Photoallergic Reactions

Photoallergic contact dermatitis can be defined as an acquired photoreactivity, depending on a cell-mediated hypersensitivity reaction to photosensitizing contactants. The quantity of substance capable of eliciting a photoallergic reaction is less than that needed to induce a phototoxic reaction and often does not induce the chemical reaction on first exposure. The histology and morphology of a photoallergic contact dermatitis are similar to those of an ordinary allergic contact reaction [24], and on immunohistological examination, lymphocytes of the $CD4^+$ type are present in the infiltrate [25].

Photoallergic reactions are a particular type of cell-mediated hypersensitivity because energy is needed to produce a photoantigen, that then triggers the immune response. It is thought that light converts the photocontactant into an immunologically active product via various mechanisms [26]. After the absorption of luminous energy, some substances, like halogenated salicylanilides, chlorpromazine, bithionol, and paraaminobenzoic acid, reach an unstable, excited state that leads to the formation of free radicals. The latters can combine in complexes

with covalent bonds that have a possible haptenic action. Otherwise, in the presence of albumin, free radicals can form photoadducts with proteins, producing a complete antigen. Alternatively, the photocontactant reaction with UVA rays can give rise to stable photoproducts that act as haptens. Then the haptens bind to protein vectors to form a complete antigen. Moreover, light absorption can provoke further alterations in the hapten-protein complex, forming yet other antigens. Further exposure to light can even cause the formation of the same photoproducts, or similar compounds, from endogeous substances. The latter mechanism could explain the persistent reactivity to light phenomenon [27, 28].

After the complete antigen has formed, the pathogenic mechanism is the same as for ordinary contact allergy [29–32].

9.2 Phototoxic Contact Dermatitis

9.2.1 Etiology

The substances responsible for phototoxic contact dermatitis are reported in Table 9.1.

Furocoumarins. Furocoumarins are tricyclic hydrocarbons with a furan ring condensed to a coumarin ring. They are present in various types of plants belonging to the Umbelliferae, Rutaceae, Moraceae, Leguminosae, and Rosaceae families [24] (see Chap. 16). Among the various furocoumarins isomers (denominated psoralens), only those with a linear structure like psoralen are photoactive; the angular structure, like that of pimpinella and angelicin, annuls or reduces the photoactivity of the compound, interfering with the molecule binding sites (only single function photoadducts are formed). The photoactive action of furocoumarins is due to their ability to absorb photons in order to form photoadducts with the DNA pyrimidinic bases cytosine, uracyl and thymine, above all through the 3' and 4' bonds of the coumarin ring and 4' and 5' bonds of the furan ring. Such a bond is an instance of cycloadduction, in which rich but short-lasting states of energy are formed, and their dissipation is what causes the cellular damage. The phototoxicity of furocoumarins can also be correlated to damage to the cell membrane caused by the production of singlet oxygen, i.e. through a type II photodynamic mechanism [33].

Tar and Pitch. Coal-tar derivatives, such as acridine, anthracene, benzopyrene, phenanthrene, and pyridine, are common photosensitizing substances. Their spectrum of action is between 320 and 430 nm. They provoke phototoxicity by means of an oxygen-dependent mechanism. Phototoxic tar dermatitis is most frequently observed in workers using substances to impermeabilize roofs and in road workers laying asphalt. Wood tars are not generally photosensitizers.

Dyes. The dyes responsible for phototoxic contact dermatitis include methylene blue, fluorescein, eosin, acridine orange, acriflavin, neutral red, anthraquinone, toluidine blue [34, 35]. Through the absorption of visible light and UVA, dyes cause oxidation via a type II photodynamic mechanism and hence cell membrane damage.

Table 9.1 The most common topical phototoxic substances

Furocoumarins
Coal and derivatives (acridine, anthracene, phenanthrene, pyrene)
Dyes (acridine orange, eosin, acriflavin)
Buclosamide
Chlorpromazine
Fenticlor
Halogenated salicylanilides
Essential oils (bergamot, cedar, citron, sandalwood, lavender, lime, neroli)

9.2.2 Clinical Features

Photocontact irritant reactions are actually an exacerbation of the normal skin response to exposure to the sun. The resulting lesions are intensely erythematous, sometimes edematous or erythemato-bullous, and are strictly localized,

Table 9.2 Clinical features of photocontact dermatitis

Features	Phototoxic reaction	Photoallergic reaction
Incidence	High	Low
Dose	Large doses needed	Small doses are enough
Occurrence on first exposure	Yes	No
Onset after UV exposition	Minutes to hours	24–48 hours
Clinical presentation	Sunburn-like eruption: erythema, edema, vesicles, bullae	Eczematous lesions
Sites	Exposed areas with sharp limits	Exposed areas, with possible extension to non exposed areas
Residual hyperpigmentation	Intense and persistent for months	Unusual and modest, lasting few days
Histology	Necrotic keratinocytes, dermal infiltrate of lymphocytes, macrophages, and neutrophils	Spongiotic dermatitis, dermal lymphohistiocytic infiltrate
Cross-reactivity	None	Common
Regression	Quick	Possible persistence/recurrence
Diagnosis	Clinical	Clinical and photopatch tests

the margins being confined to photoexposed skin sites that have come in contact with the causal agent. The patient's subjective symptoms are pain and burning. Hyperpigmentation is a common sequela and can persist for weeks after the resolution of the dermatitis, that generally lasts a few days. Differential diagnosis must be made with photocontact allergic dermatitis and airborne contact dermatitis (Table 9.2) [36].

It should be remembered that window glass, which absorbs UV radiation of wavelengths shorter than 320 nm, will protect subjects from phototoxic reactions linked to an action spectrum below 320 nm, but not from phototoxic contactants with a higher action spectrum, such as tar-derivatives and furocoumarins. Apart from the above classic clinical picture, photocontact irritant reactions can present with particular morphological aspects depending on the etiological agent.

9.2.2.1 Phytophototoxic Contact Dermatitis

Such forms are generally observed in warmer months, due both the greater intensity of the sunrays and to the greater quantity of plant photoactive compounds. The intensity of the response to photoactive agents varies according to various factors, such as the chemical nature and concentration of the substance, the intensity and duration of the exposure to light, and the skin absorption of light, that in turn depends on the thickness of the corneum, and the quantity of melanin and of body hairs.

The clinical pictures, both occupational and non occupational, are prevalently erythemato-vesico-bullous, most often localized on the hands and forearms (Fig. 9.1), or else striped erythemato-edematous lesions scattered over the limbs and trunk. These lesions appear after a latent period of about 10–24 hours, and reach the maximum expression after 1–3 days from the harmful contact. During the autumn, the lesions are only erythematous, featuring little or no exudation.

Other phytophototoxic reactions include *dermatitis bullosa striata pratense* and berloque dermatitis (see Chap. 16). The former is linked to contact with plants containing furocoumarins and occurs if two conditions are present: the skin must be wet, and must be exposed to the sun. The complaint therefore develops more commonly after sunbathing in meadows. The onset of the eruption occurs a few hours after the contact, and features striped erythematous and vesico-bullous lesions in various sites, showing a bizarre distribution. It persists for 8–10 days and leaves hyperchromic sequelae that are slow to heal. The plants implicated vary from one nation to another.

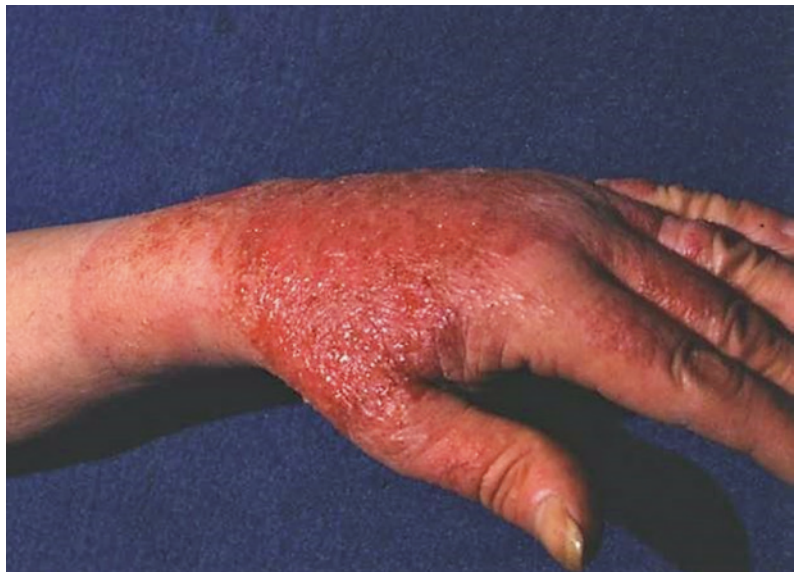

Fig. 9.1 Irritant phytophotocontact dermatitis due to furocoumarins in *Ficus carica*

Berloque dermatitis is characterized by the presence of 'pendant' or 'drop' lesions, and is caused by cosmetics (cologne, other perfumes) with a fragrance base that usually contains bergamot oil. There is certainly an individual susceptibility to this form of dermatitis, even if all the aspects are not entirely clear. The clinical manifestations are hyperchromic and reflect the way the perfume dribbled down the skin. The sites most often affected are the sides of the neck and the arms; the trunk may also be involved. The hyperchromic lesions, that have a more accentuated pigmentation at the margins, have a bizarre distribution and last for months. Diffuse forms are also possible, due to the use of tanning creams with a furocoumarin base. The interval between the application of the perfume and exposure to the sun is not more than 1–2 hours. The residual hyperpigmentation in phytophotocontact reactions is due to an increased melanocytes mitotic activity, increased number of functioning melanocytes and increased production of melanosomes.

Workers exposed to coal tar and its derivatives can present *tar "smarts"*: a reaction consisting of burning and smarting of photoexposed sites, associated with erythema and residual hyperpigmentation. The disorder, that is observed in summer months due to the higher degrees of UVA exposure, can be caused both by volatile fumes and by direct contact.

9.3 Photoallergic Contact Dermatitis

9.3.1 Etiology (Table 9.3)

Antimicrobials. In the 1960s and '70s, the most common photoallergens were the antimicrobials, and foremost among these, halogenated salicylanilides and other halogenated phenols (tetrachlorosalicylanilide, tribromosalicylanilide, dibromosalicylanilide, trichlorocarbanilide, bithionol, hexachlorophene) added to soaps and cosmetics. These substances are no longer used nowadays: halogenated salicylanilides cross-react among themselves and with bithionol and hexachlorophene.

Photosensitizing antimycotics are mainly buclosamide, fentichlor, and bromosalicylchloranilide. Fentichlor cross-reacts with bithionol and hexachlorophene, bromosalicylchloranilide with tribromosalicylanilide, and buclosamide with antidiabetics and diuretic sulfamide-derivatives [37–39].

Sulfanilamide is also a cause of photoallergy. It is currently much less commonly used as a topical agent than in the past. Subjects who have been allergized to sulfanilamide by topical route must be warned never to take sulfamide-derivatives used as drugs for systemic use, like hypoglycemic sulfonamides (chlorpropamide, tolbutamide) and thiazide diuretics (chlorothiazide, hydrochlorothiazide) due to cross-reactivity [40, 41]. The spectrum of action of sulfanilamide is the UVB range.

Furocoumarins. Furocoumarins, that have a prevalently phototoxic activity, can also induce photocontact allergy. Some subjects suffering from phytophoto dermatitis from *Ficus carica*, after patch tests with ethanol extract of fig leaf and with three pure psoralens (5-methoxypsoralen, 8-methoxypsoralen, and 4'-5'-8- trimethylpsoralen) in serial dilutions from 0.1 to 0.0001% and subsequent irradiation with UVA, presented positive reactions to the fig leaf and to 8-methoxypsoralen down to the 0.0001% dilution [24, 42]. Apart from cases of spontaneous photoallergy, cases of photoallergy to furocoumarins after PUVA therapy have been reported in the literature [43–49]. Finally, some authors succeeded in eliciting self-induction of phytophotoallergy after repeated exposure to psoralens and to parts of the *Heracleum laciniatum* plant [50].

Fragrances. Photoallergic contact dermatitis due to fragrances is much more rare than the common contact allergy. Musk ambrette, a synthetic fragrance fixative used in both the food and cosmetic industries, has caused numerous cases of photoallergy. Like the halogenated salicylanilides, musk ambrette has also provoked a persistent reaction to light in several individuals [51, 52]. 6-Methylcoumarin (no longer used in cosmetics), a synthetic organic lactone structurally related to the furocoumarins, induced rare cases of photocontact allergy, together with oak moss, eugenol, and cinnamic aldehyde [53].

Sunscreens. In previous years, in particular in the USA, Scandinavia and Germany, the ingredients in suncreens were among the most common photosensitizing agents [54–56]. Instead, in a multicentric Italian study, the incidence of photoallergy to sun filters was down in fifth place, after topical medicaments, additives of cosmetics, perfumes and antimicrobials [57]. These chemicals can also induce regular contact allergy. Many sunscreen lotions contain two or more active ingredients to provide a broader spectrum of photoprotection. In the past, PABA derivatives were the most common sensitizing sunscreens but nowadays oxybenzone is the most common [54, 58].

Suncreens can be subdivided into two groups, namely chemical filters that absorb ultraviolet rays and reflective screening agents that act as a physical barrier. The former, in turn are distinguished according to their absorption spectrum into UVA filters (benzophenones, dibenzoylmethanes) and UVB filters (PABA derivatives, benzophenones, cinnamates, salicylates). Currently, cinnamates and salicylates are the most widely used, and reports of allergic reactions to these are relatively low. Since the late'90s, several new filters have been developed and to date, only sporadic reports of photocontact allergy and contact sensitivity have been made [9, 59–68]. Such reports are increasing over time, however, because today many cosmetic products, such as moisturizing, anti-wrinkle, and facial creams and other makeup (e.g., lipstick), nail varnish, shampoo and other cleansing products, and hair products, contain sunscreen agents [67]. At present, the main sunscreens responsible for photoallergic contact dermatitis are oxybenzone or benzophenone 3, octocrylene, butymethoxydibenzoyl methane, and cinnamates [63, 64, 66, 68, 69]. Newer filters, such as Mexoryl SX® (terephthalylidene dicamphor sulfonic acid), Tinosorb M® (methylene bis-benzotriazolyl tetramethylbu-

tylphenol or bisoctrizole), and Tinosorb S® (bis-ethylhexyloxyphenol methoxyphenyl triazine), rarely cause photoallergy. This is because they are mostly photostable molecules used in sunscreen mixtures. Moreover, they photostabilize older photo-unstable filters, like dibenzoyl methanes. This is why, despite the growing employment of products containing UV filters, there has been no parallel increase in photoallergic contact dermatitis [4]. Nevertheless, some of them can induce allergic contact dermatitis, in particular Tinosorb M®, owing to the surfactant decyl glucoside, used to solubilize the active molecule of bisoctrizole [70, 71].

Non-steroidal Anti-inflammatory Drugs (NSAIDs). NSAIDs, increasingly used in topical form for the relief of musculo-skeletal pain, can be subdivided into different classes: propionic acid derivatives (ketoprofen, ibuprofen, suprofen, tiaprofenic acid), arylacanoic acid (diclofenac, etofenamate), oxicam (piroxicam), and indomethacin and benzydamine [9]. The arylpropionic derivatives have been reported to be the group responsible for the largest number of allergic and photoallergic contact dermatitis reactions [57, 72–75]. In particular, ketoprofen, and related drugs (piketoprofen, dexketoprofen) or cross-reactive substances are those mainly responsible [66]. Ketoprofen, recently used also in transdermal patches, often induces severe forms of photocontact allergy, that develop immediately after the start of treatment, and can persist or recur after exposure to the sun without any apparent further contact with the drug: this may be explained by the fact that after topical exposure, the drug persists in the skin for more than two weeks [76]. There have also been reports of cases of ectopic, connubial, or "by proxy" contact dermatitis due to contact with other people's skin/hands contaminated by ketoprofen gel or by contact with contaminated objects, such as clothes that retain the drug even after washing [77–81]. Photocontact allergy due to ketoprofen is frequently associated with various photopatch test cross-reactions: with other arylpropionic NSAIDs (tiaprofenic acid, suprofen); benzophenone UV filters, mainly oxybenzone; fentichlor; and systemic hypolipemic fenofibrates that induce systemic photosensitivity. Positive photopatch tests to octocrylene (UV filter) and patch tests to fragrance mix I and to its constituent, cinnamic alcohol, are also associated with photoallergy to ketoprofen [63, 82–89].

Another NSAID that induces allergic and photoallergic contact dermatitis is piroxicam, mostly after previous contact allergy to thimerosal and its moiety thiosalicylic acid, since photoproducts of piroxicam are chemically similar to these allergenic chemicals [63, 90]. Benzydamine, used mainly in mouthwashes or genital soaps, induces photocontact allergy that manifests as cheilitis and dermatitis of the chin or of the hands, respectively [63, 91].

Phenothiazine Derivatives. These are used in some European countries as topical antihistamines (promethazine, isothipendyl chlorhydrate) or muscle relaxants (chlorpromethazine), as also chlorpromazine. The latter is used as a tranquilizer, but can induce photocontact allergy in health staff handling the substance [57, 92–102].

9.3.2 Clinical Features

Photocontact allergy can develop in subjects of all ages. The predominant clinical aspect is eczematous: in the acute phase the lesions are of erythemato-edemato-vesicular, and sometimes bullous type (Figs. 9.2, and 9.3); in the subacute or chronic phases, erythema, desquamation and lichenification are most commonly observed. The sites affected are photoexposed areas (Fig. 9.4), although after repeated injury even covered sites can be involved. In most cases, avoidance of the photoallergen and of substances that cross-react with it induces remission of the dermatitis. However, in some cases photosensitization persists and can lead to chronic photodermatitis (a persistent reaction to light).

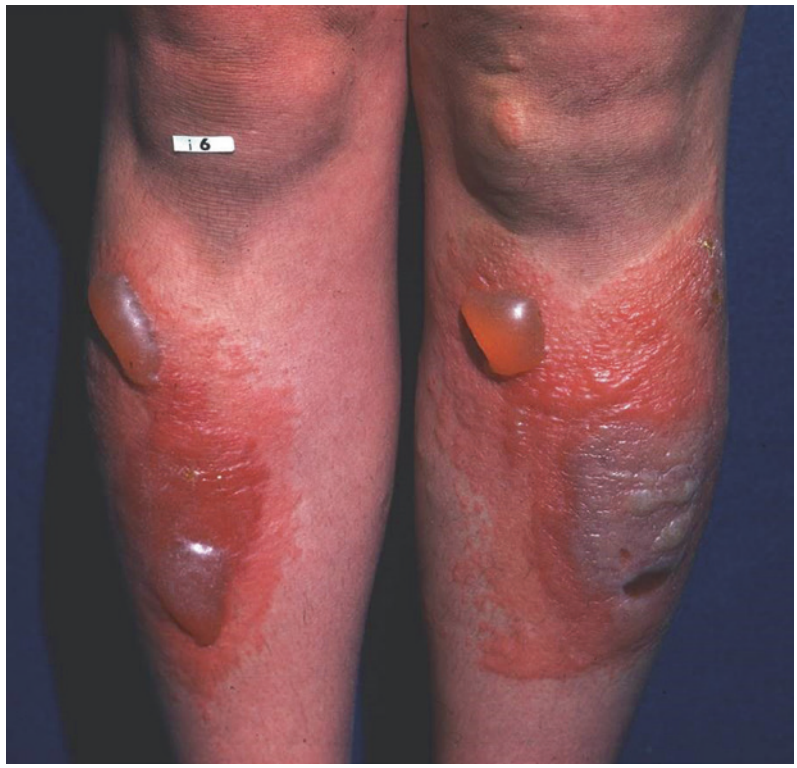

Fig. 9.2 Bullous photoallergic contact dermatitis from topical non-steroidal anti-inflammatory drugs (Reproduced with permission by Angelini and Coll [94])

Since phototoxic and photoallergic reactions can manifest similar clinical characteristics, differential diagnosis can be difficult, especially bearing in mind that many substances can provoke both types of reactions. Table 9.2 lists some differential diagnosis elements.

9.3.2.1 Contact Phytophotoallergy

Contact phytophotosensitization to the furocoumarins contained in plants is not a common observation. Nor is differential diagnosis with phytophototoxic reactions always easy; in our experience, the clinical picture is comparable [24, 42]. Relative clinical differences include any involvement of unexposed sites and a more modest residual pigmentation in cases of allergy. Therefore, it is on the basis of photopatch tests that the pathogenic mechanism needs to be identified.

9.3.2.2 Allergic Photocontact Dermatitis Due to Promethazine and Sulfanilamide

In some cases, photoallergizing substances induce peculiar clinical pictures. Allergic photocontact dermatitis from promethazine features erythematous manifestations in photoexposed sites, that are purplish-violet in color, edematous, with little or no exudation (Figs. 9.5, 9.6, and 9.7), smooth and with minor desquamation [93–95].

Allergic photocontact dermatitis due to sulfamide is recognizable not only by the intensely erythematous lesions in exposed sites but also by large, scattered papulo-vesicular lesions in non exposed sites and erythemato-edemato-vesico-bullous lesions in exposed sites (Figs. 9.8, and 9.9) [93–95].

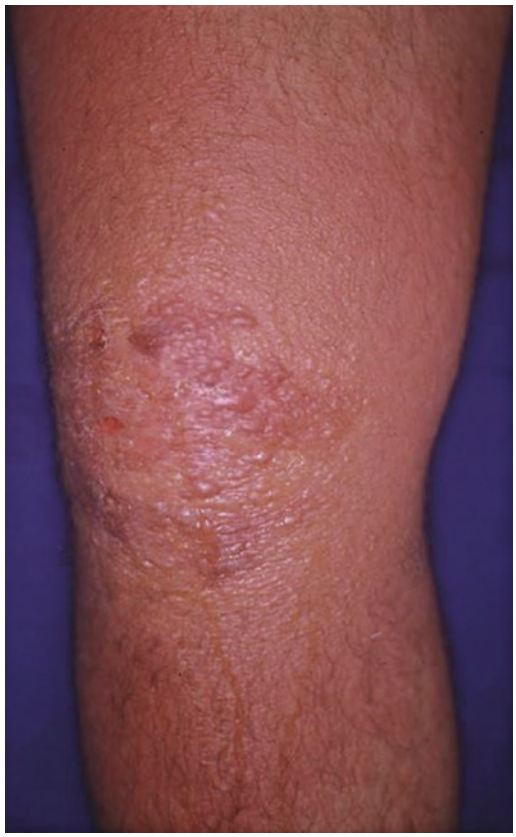

Fig. 9.3 Allergic photocontact dermatitis from topical non-steroidal anti-inflammatory drugs

9.4 Chronic Actinic Dermatitis

This is a contact dermatitis-like reaction, with an immune-mediated basis, to sunlight-induced endogenous cutaneous antigens [103, 104]. Chronic actinic dermatitis, first described 40 years ago by Hawk and Magnus [105], denominates a combination of various different presentations of the same condition, such as persistent light reactivity, actinic reticuloid, photosensitive eczema, photosensitivity dermatitis, and actinic reticuloid syndrome. What these various observations have in common is a chronic photosensitivity, progressively worsening over several years with no tendency to regression. There are three diagnostic criteria of this complaint: (a) a persistent eczematous eruption, associated with papules and plaques infiltrates, affecting sun-exposed skin and sometimes extending to covered sites; (b) histology shows a chronic eczema with or without cutaneous lymphoma-like changes; and (c) phototesting shows a reduction in the minimal erythema dose (MED) to UVA, UVB, and/or the visible light range.

This condition mainly affects men aged 40 to 80 years, women accounting for only 10–22% of cases [106]. In a study of 178 patients, the age distribution was 6% in subjects under the age of 40, 43% in 40–59 year-olds and 51% in those over 60 [107]. All races can be affected but in particular Caucasians [108], and it has also been described in association with allergic contact dermatitis to common or airborne allergens (in particular plant antigens, fragrances, and topical medications), human immunodeficiency virus (HIV) [109], and atopic dermatitis [110].

The pathogenic mechanism is not yet entirely known. It is certainly an acquired disease, in which environmental rather than genetic factors play a role. Chronic actinic dermatitis is likely a contact allergy-like, delayed-type hypersensitivity response to sunlight-induced endogenous cutaneous allergens, probably as a result of an increased immunological reactivity induced by airborne contact dermatitis or else a reduced immune-suppressive capacity of photodamaged skin, or perhaps both factors, especially in subjects with long term hypersensitivity to light and airborne contactants [103]. The presence of $CD8^+$ T-cell infiltrates in damaged skin fosters a delayed-type immune reaction, likely to photo-induced cutaneous autoantigens. These could be due to an altered carrier protein, nuclear material (RNA or DNA), or a native skin antigen (such as histidine) altered by UV radiation [104].

The classic clinical picture of chronic actinic dermatitis is that of a pruriginous

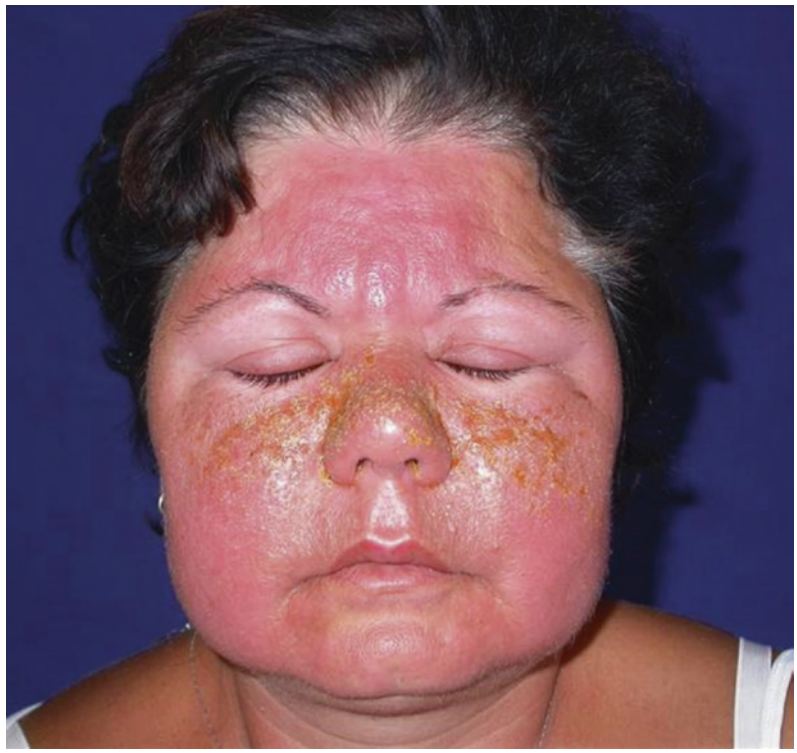

Fig. 9.4 Allergic photocontact dermatitis

dermatitis, with eczematous lesions, often with scaly lichenification and infiltrated plaques, in exposed sites, largely the face, scalp, neck (Figs. 9.10, 9.11, and 9.12), upper chest, dorsal surfaces of the arms and the hands. In general, the margins of the dermatitis are distinct, delineating the covered skin limits, and shadowed areas, like the depths of skin furrows, upper eyelids, scalp under the hair, skin under the chin, and behind the ears, are spared. Over time, non exposed areas may become involved. In rare, severe cases there may also be a tendency to a leonine face [111]. Palmar and plantar eczema are not unusual, and in severe cases generalized erythroderma may develop [111].

Chronic actinic dermatitis can manifest on normal skin but is more often observed in subjects with previous allergic or photoallergic contact dermatitis; occasionally, the onset may be observed after photosensitization due to systemic drugs or after a polymorphous light eruption [112].

In many cases contact allergy to oleoresins of Compositae plants (especially chrysanthemum), phosphorus sesquisulfide, rubber, colophony, fragrances, and sunscreens is also present [111]. Photoallergic contact dermatitis is possible, but more rarely observed.

The disease has a chronic course, and the probability of resolution after 5 years is 10%, after 10 years 20% and after 15 years 50% [113]. Contact allergy, with positive patch tests to 1 or more substances, aggravates the prognosis. In the most serious cases there are also psychological disturbances, and even suicide has been reported [111]. There does not seem to be a

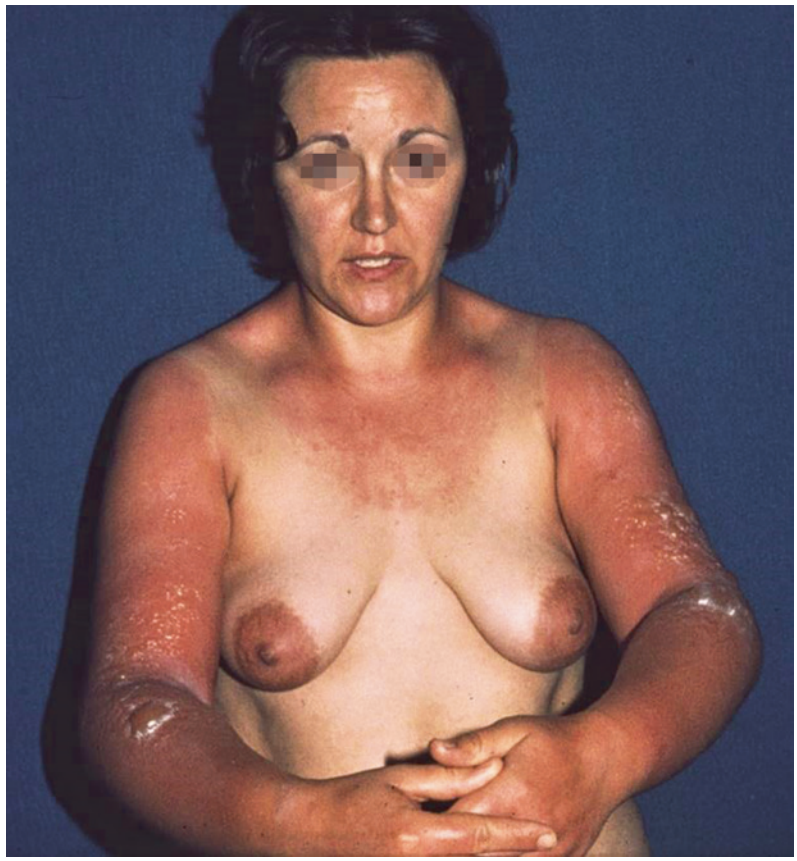

Fig. 9.5 Allergic photocontact dermatitis from promethazine: purplish-violet edematous lesions (Reproduced with permission by Meneghini and Angelini [102])

risk of evolution to lymphomas [114], although this risk could be increased if the disease is treated with immunosuppressants [115].

Histology shows epidermal spongiosis, acanthosis and sometimes hyperplasia, with perivascular lymphocytic infiltrates in the upper dermis. Immunophenotypic markers are helpful to differentiate chronic actinic dermatitis from cutaneous T-cell lymphoma: in the former there is a predomination of CD8+cells, and in the latter of CD4+cells [103].

The diagnosis relies on the clinical history, examination, phototests and patch tests. As regards phototests, a reduction of the MED to UVB is observed in nearly all patients, in many patients to UVA, and only in few cases to visible light. Photopatch tests may be done if there is suspected allergy to sunscreens, but must not be performed in patients in whom a very low dose of UVA, as is usually employed for these tests (below 5 J cm^2), causes an abnormal erythematous response [107]. Differential diagnosis must be made with allergic, photoallergic and airborne contact dermatitis and with photoaggravated skin diseases.

The clinical management involves topical treatments, informing the patient of the need to avoid sunlight and various allergens as much as possible, and in severe cases, phototherapy or systemic immunosuppressive treatment [107, 116].

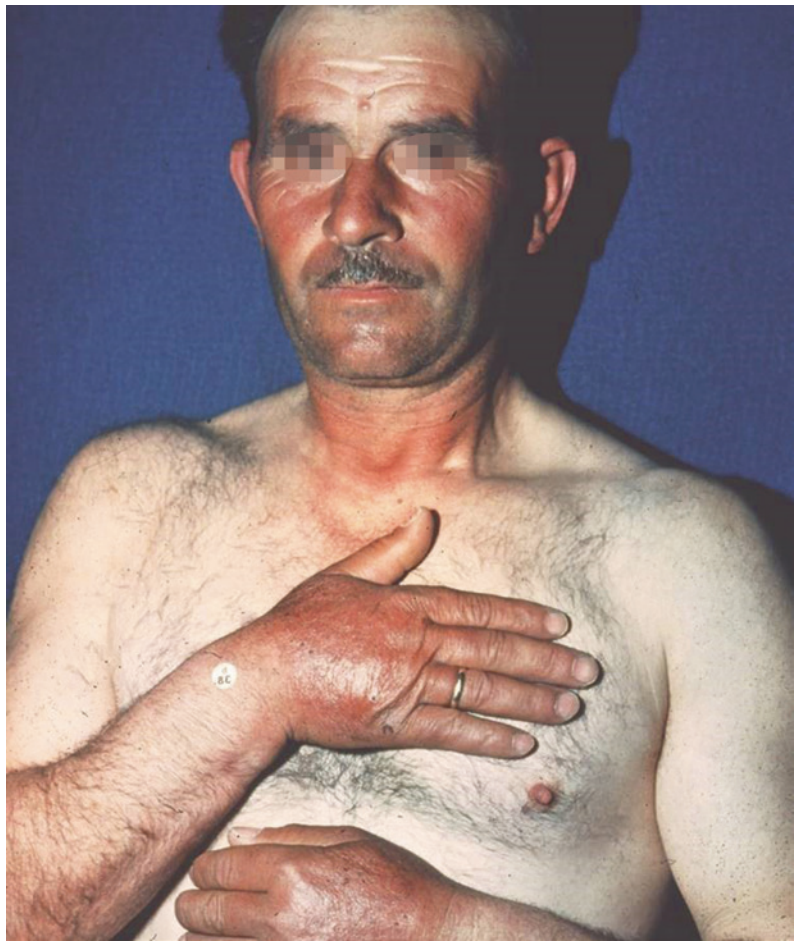

Fig. 9.6 Allergic photocontact dermatitis from promethazine: purplish-violet edematous lesions (Reproduced with permission by Bonamonte and Coll [101])

9.5 Diagnosis and Management

The diagnosis of photocontact dermatitis is based on clinical-morphological criteria and on a history of exposure to photosensitizing agents. For diagnostic-etiopathogenic purposes phototests and photopatch tests are essential [117–119]. The latter must be performed in all patients, including children, with photodermatitis, photoaggravated dermatitis, intolerance to sunscreens, or exposure to NSAIDs [4, 66, 68]. In subjects with chronic actinic dermatitis, polymorphic light eruption, and cutaneous lupus erythematosus, photopatch tests serve to exclude allergies, to UV filters for example. In these cases with a reduced UV sensitivity threshold,

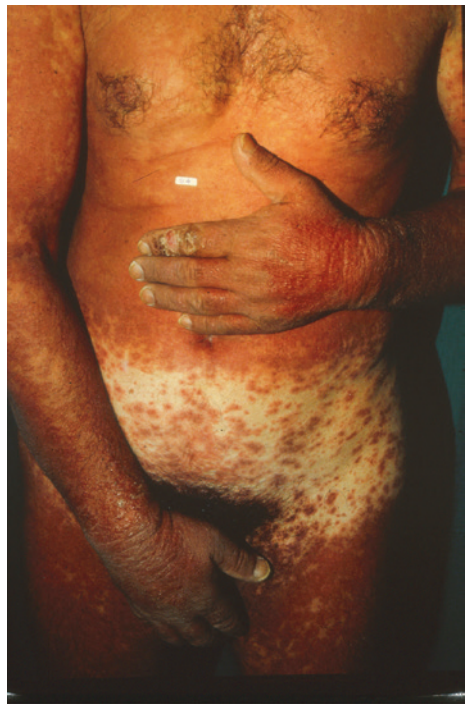

Fig. 9.7 Allergic photocontact dermatitis from promethazine used to treat the hands eczema

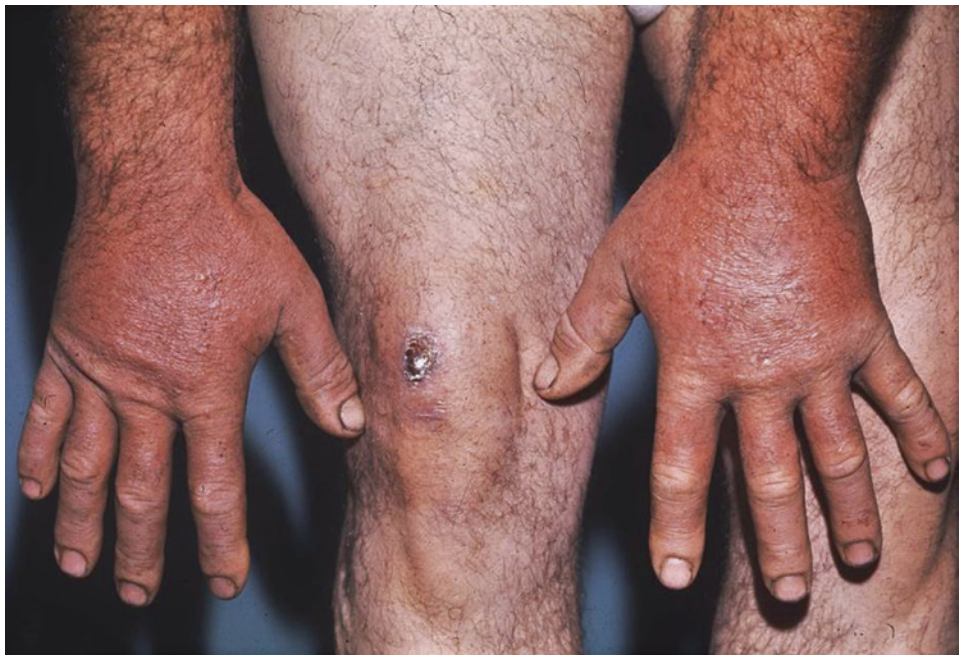

Fig. 9.8 Allergic photocontact dermatitis due to sulfamide used to treat a skin wound

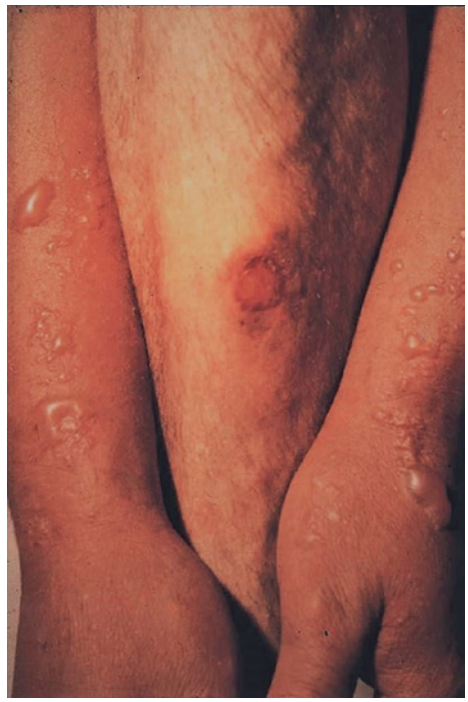

Fig. 9.9 Allergic photocontact dermatitis due to sulfamide used to treat a skin wound (Reproduced with permission by Angelini and Coll [94])

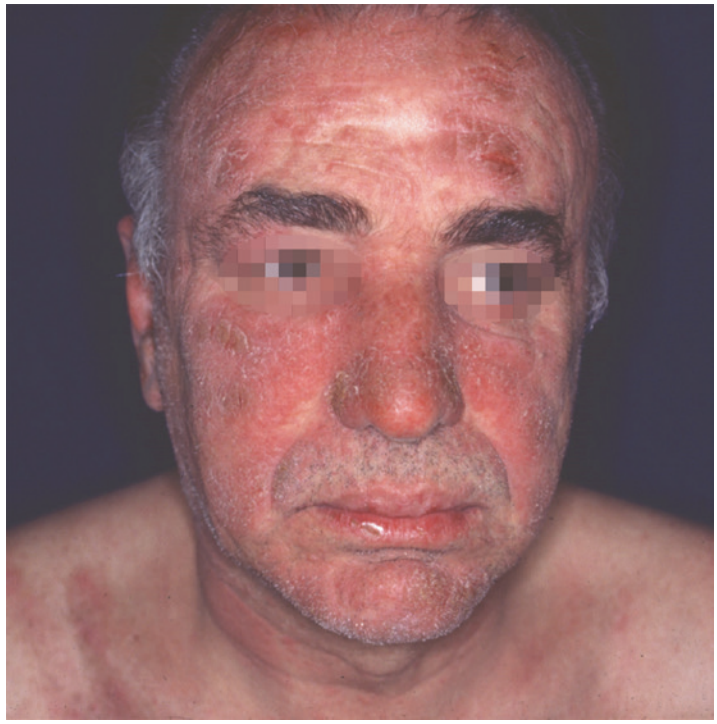

Fig. 9.10 Chronic actinic dermatitis

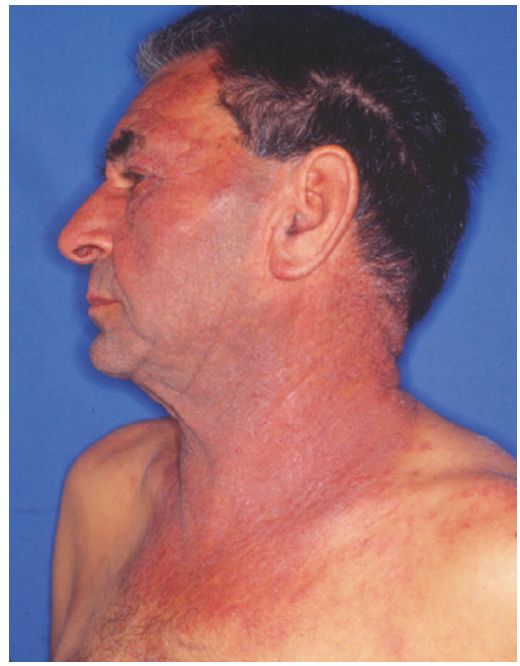

Fig. 9.11 Chronic actinic dermatitis

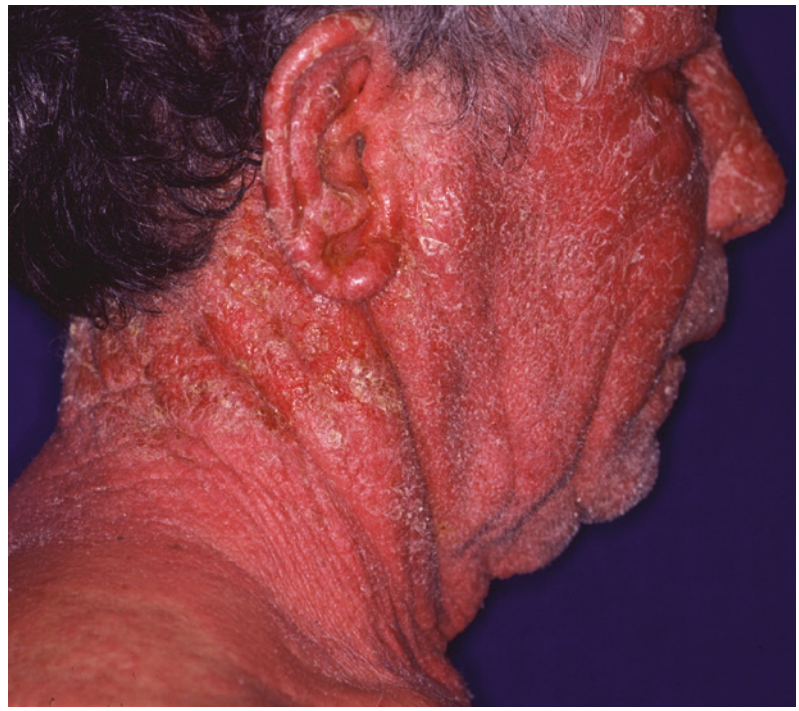

Fig. 9.12 Chronic actinic dermatitis

Table 9.3 Topical photoallergens

Halogenated antimicrobials
Chlorhexidine
Hexachlorophene
Chlorosalicylamide
Buclosamide
Fenticlor (*bis*-(2-hydroxy-5-chlorophenyl) sulphide
4',5-Dibromosalicylanilide
Tetrachlorosalicylanilide
Bithionol (2,2'-thiobis (4,6-dichlorophenol))
Tribromosalicylanilide
Trichlorocarbanilide
Triclosan
Plants
Ficus carica
Compositae
Lichens
Frullania
Furocoumarins
Psoralen
8-Methoxypsoralen
5-Methoxypsoralen
Sunscreens
PABA (*p*-aminobenzoic acid)
Benzophenone-3
Benzophenone-10
Butylmethoxydibenzoylmethane (Parsol 1789)
Dimethoxane
2-Ethoxyethyl-*p*-methoxycinnamate
Glyceril-*p*-aminobenzoate
4- Isopropyldibenzoylmethane (Eusolex 8020)
3-(4-Methylbenzylidene)-camphor (Eusolex 6300)
Octylmethoxycinnamate (Parsol MCX)
Octocrylene (Eusolex OCR)
Fragrances
Musk ambrette
Musk xylol
Methyl coumarin
Oak moss
Eugenol
Cinnamic aldehyde
Non steroidal anti-inflammatory drugs
Ketoprofen
Ibuproxam
Tiaprofenic acid
Surprofen
Piroxicam
Benzidamine
Diclofenac
Colors
Brilliant lake red R
Erythrocin-AL
Lithol red-CA
Permanent orange
Toluidine red
Fenothiazines
Chlorpromazine
Promethazine
Others
Sulphanilamide
Benzocaine
Benzidamine
Chlormercaptodicarboximide
Coal tar derivatives
Dibucaine
Diphenhydramine
Quinine sulphate
Stilbenes
Thiourea
Dimethylthiourea

photopatch tests must be performed together with phototests, in order to plan an adequate UV dosage for the photopatch tests [120].

Apart from treating the dermatitis, patients must avoid exposure to the sun, and are recommended to wear photoprotective clothing/devices since photosensitizing substances can persist in the skin for days. The use of UV filters, being one of the commonest causes of photoallergy, is not advised unless they are just physical filters (titanium dioxide and zinc oxide) that do not induce contact allergy or photoallergy.

Once the allergen implicated has been identified, all the substances that may cross-react with it must also be avoided. This is a major problem if it includes all substances with a benzophenone ring, namely ketoprofen, other arylpropionic derivatives, UV filters (oxybenzone, octocrylene) and oral fenofibrates: particular care must therefore be taken when selecting cosmetics and all products containing UV filters.

Usually, window glass does not protect against phototoxic and photoallergic reactions, since ordinary glass (3 mm thick) only protects against UV rays at less than 320 nm. Patients are advised to wear dark clothing with a weave pattern of the fabric. The sunless tanning agents are not protective despite the fact that they make the skin tone a little darker.

Photocontact dermatitis can be very distressing for patients, especially if the substance implicated is not identified or else is ubiquitous in the environment, in which cases the dermatitis may have a significant impact on their quality of life .

References

1. White IR. Phototoxic and photoallergic reactions. In: Rycroft RJG, Menné T, Frosch PJ, et al editors. Textbook of contact dermatitis. Berlin: Springer-Verlag; 2001. p. 367.
2. Rietschel RL, Fowler JF Jr. Photocontact dermatitis. In: Rietschel RL, Fowler JF Jr, editors. Fisher's contact dermatitis. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 397.
3. Grandolfo M. Fotodermatite da contatto. In: Angelini G, Vena GA, editors. Dermatologia professionale e ambientale, vol. II. Brescia: ISED; 1999. p. 523.

4. Gonçalo M. Photoreactions and testing. In: Johansen JD, Lepoittevin J-P, Thyssen TP, editors. Quick guide to contact dermatitis. Berlin: Springer; 2016. p. 81.
5. DeLeo VA. Photocontact dermatitis. Dermatol Therapy. 2004; 17:279.
6. Snyder M, Turrentine JE, Cruz PD Jr. Photocontact dermatitis and its clinical mimics: an overview for the allergist. Clin Rev Allergy Immunol. 2018. https://doi.org/10.1007/s12016-018-8696-x.
7. Kutlubay Z, Sevim A, Engin B, et al. Photodermatoses, including phototoxic and photoallergic reactions (internal and external). Clin Dermatol. 2014; 32:73.
8. Honary G. Photoallergy. Rev Environ Health. 2014; 29:233.
9. Kerr A, Ferguson J. Photoallergic contact dermatitis. Photodermatol Photoimmunol Photomed. 2010; 26:56.
10. Coffin SL, Turrentine JE, Cruz PD Jr. Photodermatitis for the allergist. Curr Allergy Asthma. 2017; 17:36.
11. Coohill TP. Action spectra again? Photochem Photobiol. 1991; 54:859.
12. Freeman RG, Knox JM. The action spectrum of photocontact dermatitis. Arch Dermatol. 1968; 97:130.
13. Emmet EA. Diphenhydramine photoallergy. Arch Dermatol. 1974; 110:249.
14. Toback AC, Anders JE. Phototoxicity from systemic agents. Clin Dermatol. 1986; 4:223.
15. Emmet EA, Phototoxicity from exogenous agents. Photochem Photobiol. 1979; 30:429.
16. Owens DW, Knox JM. Influence of heat, wind, and humidity on ultraviolet radiation injury. In: Kripke ML, Sass ER, editors. Ultraviolet carcinogenesis. J Natl Cancer Inst Monogr. 1978; 50:161.
17. Harber LC, Baer RL. Pathogenic mechanisms of drug-induced photosensitivity. J Invest Dermatol. 1972; 58:327.
18. Kornhauser A, Wamer W, Giles A. Light-induced dermal toxicity: effects on the cellular and molecular level. In: Marzulli FN, Maibach HI, editors. Dermatotoxicology, Hemisphere, 3rd ed. Washington; 1987. p. 377.
19. Gould JW, Mercurio MG, Elmets CA. Cutaneous photosensitivity diseases induced by exogenous agents. J Am Acad Dermatol. 1995; 33:551.
20. Song PS, Tapley KJ. Photochemistry and photobiology of psoralens. Photochem Photobiol. 1979; 29:1177.
21. Epstein JH. Chlorpromazine photosensitivity: phototoxic and photoallergic reactions. Arch Dermatol. 1986; 98:354.
22. Kochevar IE, Lamola AA. Chlorpromazine and protriptyline phototoxicity: photosensitized oxygen-independent red cell hemolysis. Photochem Photobiol. 1979; 29:791.
23. Spikes JD. Photosensitized reactions in mammals. In: Daynes Ra, Spikes JD, editors. Experimental and clinical photoimmunology. Boca Raton: CRC Press; 1983. p. 69.
24. Bonamonte D, Foti C, Lionetti N, et al. Photoallergic contact dermatitis to 8-methoxypsoralen in *Ficus carica*. Contact Dermatitis. 2010; 62:343.
25. Takashima A, Yamamoto K, Kimura S, et al. Allergic contact and photocontact dermatitis due to psoralens in patients with psoriasis treated with topical PUVA. Br J Dermatol. 1991; 124:37.
26. Elmets CA. Cutaneous phototoxicity. In: Lim HW, Soter NA, editors. Clinical photomedicine. New York: Marcel Dekker; 1993. p. 207.
27. Epling GA, Wells JL, Ung Chan Yoon. Photochemical transformations in salicylanilide photoallergy. Photochem Photobiol. 1988; 47:167.
28. Li ASW, Chignell CF. Spectroscopic studies of cutaneous photo-sensitizing agents. XII. Spin-trapping study of the free radicals generated during the photolysis of photo allergens bithionol and fentichlor. Photochem Photobiol. 1987; 46:445.
29. Bergtresser PR. Immune mechanism in contact allergic dermatitis. Dermatol Clin. 1990; 8:3.
30. Gerberick GF, Ryan CA, Von Barger EC, et al. Examination of tetrachlorsalicylanilide (TCSA) photoallergy using in vitro photohapten-modified Langerhans-cell enriched epidermal cells. J Invest Dermatol. 1991; 97:210.
31. Gerberick GF, Ryan CA, Fletcher ER, et al. Increased number of dendritic cells in draining lymph nodes accompanies the generation of contact photosensitivity. J Invest Dermatol. 1991; 96:355.
32. Tokura Y, Takigawa M. Immunological mechanisms of contact photosensitivity. Eur J Dermatol. 1993; 3:87.
33. Kochevar IE. Mechanisms of drug photosensitization. Photochem Photobiol. 1987; 45:891.
34. Cronin E. Contact dermatitis. Edinburgh: Churchill Livingstone. 1980; 414.
35. Nater JP, De Groot AC. Phototoxic and photoallergic contact dermatitis. In: Nater JP, De Groot AC, editors. Unwanted effects of cosmetics and drugs used in dermatology, 2nd ed. Amsterdam: Elsevier; 1985. p. 109.
36. Angelini G, Vena GA. Airborne contact dermatitis. Clin Dermatol. 1992; 10:123.
37. Burry JN, Hunter GA. Photocontact dermatitis from Jadit. Br J Dermatol. 1970; 82:224.
38. Burry JN. Photoallergies to fentichlor and multifungin. Arch Dermatol. 1967; 95:287.
39. Burry JN. Cross sensitivity between fentichlor and bithionol. Arch Dermatol. 1968; 97:497.
40. Angelini G, Meneghini CL. Oral tests in contact allergy to para-amino compounds. Contact Dermatitis. 1981; 7:311.
41. Harber LC, Lashinsky AM, Baer RL. Photosensitivity due to chlorothiazide and hydroxychlorothiazide. N Engl J Med. 1959; 261:1378.
42. Angelini G, Vena GA, Meneghini CL. Contact dermatitis from *Ficus carica*. In Frosch PJ, Dooms-Goossens A, Lachapelle JM, et al, editors. Current topics in contact dermatitis. Berlin: Springer-Verlag; 1985. p. 163.

43. Fischer T, Alsins J. Treatment of psoriasis with trioxalen baths and dysprosium lamps. Acta Derm Venereol. 1976; 56:383.
44. Fulton JE, Willis I. Photoallergy to methoxalen. Arch Dermatol. 1968; 98:445.
45. Plewing G, Hofmann C, Braun-Falco O. Photoallergic dermatitis from 8-methoxypsoralen. Arch Dermatol Res. 1978; 262:201.
46. Sidi E, Bourgeois-Gavardin A. Mise en point du traitement de vitiligo par l' *Amni majus*. Press Med. 1953; 61:436.
47. Saihan EM. Contact allergy to methoxalen. Br Med J. 1979; 2:20.
48. Weissmann J, Wagner G, Plewing G. Contact allergy to methoxypsoralen. Br J Dermatol. 1980; 102:113.
49. Takashima A, Yamamoto K, Kimura S, et al. Allergic contact and photocontact dermatitis to psoralens in patients with psoriasis treated with topical PUVA. Br J Dermatol. 1980; 124:37.
50. Kavli G, Volden G. Phytophotodermatitis. Photodermatology. 1984; 1:65.
51. Giovinazzo VJ, Harber LC, Bickers DR, et al. Photoallergic contact dermatitis to musk ambrette: histopathologic features of photobiologic reactions observed in a persistent light reactor. Arch Dermatol. 1981; 117:344.
52. Burry JN. Persistent light reaction associated with a sensitivity to musk ambrette. Contact Dermatitis. 1981; 7:46.
53. De Groot AC, Frosh PJ. Adverse reactions to fragrances. A clinical review. Contact Dermatitis. 1997; 36:57.
54. DeLeo VA, Suarez SM, Maso MJ. Photoallergic contact dermatitis. Results of photopatch testing in New York, 1985 to 1990. Arch Dermatol. 1992; 128:1513.
55. Thune P, Jansen C, Wennersten C, et al. The Scandinavian multicenter photopatch study 1980–85: final report. Photodermatol. 1988; 5:261.
56. Schauder S, Ippen H. Contact and photocontact sensitivity to sunscreens. Review of a 15-year experience and of the literature. Contact Dermatitis. 1997; 37:221.
57. Pigatto PD, Legori A, Bigardi AS, et al GIRDCA. Italian multicenter study of allergic contact photodermatitis; epidemiological aspects. Am J Contact Dermatitis. 1996; 7:158.
58. Szczurko C, Dompmartin A, Michel M, et al. Photocontact allergy to oxybenzone: ten years of experience. Photodermatol Photoimmunol Photomed. 1994; 10:144.
59. Sommer S, Wilkinson SM, English JSC, et al. Photoallergic contact dermatitis from the sunscreen octyltriazone. Contact Dermatitis. 2002; 46:304.
60. Large-Asschenfeldt B, Huegel R, Brasch J. Anaphylactic reaction caused by the UVA absorber disodium phenyl dibenzimidazole tetrasulfonate. Acta Derm Venereol. 2005; 85:280.
61. Gonzalez-Pérez R, Trébol I, Garcia-Rio I, et al. Allergic contact dermatitis from methylene-bis-benzotriazolyl tetramethylbutyl-phenol (Tinosorb M). Contact Dermatitis. 2007; 56:121.
62. Hughes TM, Martin JA, Lewis VJ, et al. Allergic contact dermatitis to drometrizole trisiloxane in a sunscreen with concomitant sensitivities to other sunscreens. Contact Dermatitis. 2005; 52:226.
63. Cardoso JC, Canelas MM, Gonçalo M, et al. Photopatch testing with an extended series of photoallergens: a 5-year study. Contact Dermatitis. 2009; 60:325.
64. Bryden AM, Moseley H, Ibbotson SH, et al. Photopatach testing of 1115 patients: results of the U.K. multicenter photopatch study group. Br J Dermatol. 2006; 155:737.
65. Pigatto PD, Guzzi G, Schena D, et al. Photopatch tests: an Italian multicentre study from 2004 to 2006. Contact Dermatitis. 2008; 59:103.
66. EMCPPTS Taskforce, Kerr A, Ferguson J, Haylett A, et al. A European multicentre photopatch test study. Br J Dermatol. 2012; 166:1002.
67. Uter W, Gonçalo M, Yazar K, et al. Coupled exposure to ingredients of cosmetic products, III, Ultraviolet filters. Contact Dermatitis. 2014; 71:162.
68. Haylett A, Chiang YZ, Nie Z, et al. Sunscreen photopatch testing: a series of 157 children. Br J Dermatol. 2014; 171:370.
69. De Groot AC, Roberts DW. Contact and photocontact allergy to octocrylene: a review. Contact Dermatitis. 2014; 70:193.
70. Andersen KE, Goossens A. Decyl glucoside contact allergy from a sunscreen product. Contact Dermatitis. 2006; 54:349.
71. Andrade P, Gonçalo M, Figueiredo A. Allergic contact dermatitis to decyl glucoside in Tinosorb M®. Contact Dermatitis. 2010; 62:119.
72. Pigatto PD, Mozzanica N, Bigardi AS, et al. Topical NSAID allergic contact dermatitis. Italian experience. Contact Dermatitis. 1993; 29:39.
73. De la Cuadra-Oyanguren J, Perez-Ferriols A, Lecha-Correlero M, et al. Results and assessment of photopatch testing in Spain: towards a new standard set of photoallergens. Actas Dermosifilolograficas. 2007; 98:96.
74. Montoro J, Rodriguez M, Diaz M, et al. Photoallergic contact dermatitis due to diclofenac. Contact Dermatitis. 2003; 48:115.
75. Fernanez de Corres L. Photodermatitis from benzydamine. Contact Dermatitis. 1980; 6:285.
76. Guy RH, Kuma H, Nakanishi M. Serious photocontact dermatitis induced by topical ketoprofen depends on the formulation. Eur J Dermatol. 2014; 24:365.
77. Sugiura M, Hayakawa R, Kato Y, et al. 4 Cases of photocontact dermatitis due to ketoprofen. Contact Dermatitis. 2000; 43:16.

78. Hindsen M, Isaksson M, Persson L, et al. Photoallergic contact dermatitis from ketoprofen induced by drug contaminated personal objects. J Am Acad Dermatol. 2004; 50:215.
79. Devleeschouwer V, Roelandts R, Garmyn M, et al. Allergic and photoallergic contact dermatitis from ketoprofen: results of (photo)patch testing and follow-up of 42 patients. Contact Dermatitis. 2008; 58:159.
80. Izu K, Hino R, Isoda H, et al. Photocontact dermatitis to ketoprofen presenting with erythema multiforme. Eur J Dermatol. 2008; 18:710.
81. Béani J. Les photosensibilisations graves. Ann Dermatol Vénéreol. 2009; 136:76.
82. Le Coz CJ, Bottlaender A, Scrivener J-N, et al. Photocontact dermatitis from ketoprofen and tiaprofenic acid: cross-reactivity study in 12 consecutive patients. Contact Dermatitis. 1998; 38:245.
83. Pigatto PD, Bigardi A, Legori A, et al. Cross reactions in patch testing and photopatch testing with ketoprofen, thiaprophenic acid and cinnamic aldehyde. Am J Contact Dermatitis. 1996; 7:220.
84. Girardin P, Vigan M, Humbert P, et al. Cross reactions in patch testing with ketoprofen, fragrance mix and cinnamic derivatives. Contact Dermatitis. 2006; 55:126.
85. Avenel-Audran M, Dutartre H, Goossens A, et al. Octocrylene, an emerging photoallergen. Arch Dermatol. 2010; 146:753.
86. Karlsson I, Vanden Broecke K, Martensson J, et al. Clinical and experimental studies of octocrylene's allergic potency. Contact Dermatitis. 2011; 64:343.
87. Infante Hermando L, Serra-Baldrich E, Dordal T, et al. Photoallergic contact dermatitis caused by benzophenones in magazine inks. Contact Dermatitis. 2013; 69:124.
88. Foti C, Bonamonte D, Conserva A, et al. Allergic and photoallergic contact dermatitis from ketoprofen: evaluation of cross-reactivities by a combination of photopatch testing and computerized conformational analysis. Curr Pharm Des. 2008; 14:2883.
89. Wolverton JE, Soter NA, Cohen DE. Fentichlor photocontact dermatitis: a persistent enigma. Dermatitis. 2013; 24:77.
90. Gonçalo M, Figueiredo A, Tavares P, et al. Photosensitivity to piroxicam: absence of cross-reaction with tenoxicam. Contact Dermatitis. 1992; 27:287.
91. Lasa Elgezua O, Gorrotxategi P, Gardeazabal Gracia J, et al. Photoallergic hand eczema due to benzydamine. Eur J Dermatol. 2004; 14:69.
92. Epstein S. Chlorpromazine photosensitivity: phototoxic and photoallergic reactions. Arch Dermatol. 1968; 98:354.
93. Angelini G. Topical drugs. In: Rycroft RJG, Menné T, Frosch PJ, et al, editors. Textbook of contact dermatitis. Berlin: Springer-Verlag; 1995. p. 477.
94. Angelini G, Vena GA, Grandolfo M, et al. Iatrogenic contact dermatitis and eczematous reactions. Clin Dermatol. 1993; 11: 467.
95. Angelini G, Vena GA, Meneghini CL. Allergic contact dermatitis to some medicaments. Contact Dermatitis. 1985; 12:263.
96. Barbaud A, Collet E, Martin S, et al. Contact sensitization to chlorpromethazine can induce persistent light reaction and cross-photoreactions to other phenothiazines. Contact Dermatitis. 2001; 44:373.
97. Kerr A, Woods J, Ferguson J. Photocontact allergic and phototoxic studies of chlorpromethazine. Photodermatol Photoimmunol Photomed. 2008; 24:11.
98. Birbas N, Sartor V, Bulai Livideanu C, et al. Contact photoallergy to isothipendyl chlorhydrate. Dermatology. 2012; 214:289.
99. Monteagudo-Paz A, Salvador JS, Martinez NL, et al. Pulpitis as clinical presentation of photoallergic contact dermatitis due to chlorpromazine. Allergy. 2011; 66:1503.
100. Monteiro AF, Rato M, Martins C. Drug-induced photosensitivity: photoallergic and phototoxic reactions. Clin Dermatol. 2016. https://doi.org/10.1016/j.clindermatol.2016.05.006.
101. Bonamonte D, Foti C, Romita P, et al. Colors and contact dermatitis. Dermatitis. 2014; 25:155.
102. Meneghini Cl, Angelini G. Le dermatiti da contatto. Lombardo Ed., Roma; 1982.
103. Trakatelli M, Charalampidis S, Novakovic LB, et al. Photodermatoses with onset in the elderly. Br J Dermatol. 2009; 161(Suppl.3):69.
104. Santoro FA, Lim HW. Update on photodermatoses. Semin Cutan Med Surg. 2011; 30:229.
105. Hawk JLM, Magnus IA, Chronic actinic dermatitis: an idiopathic photosensitivity syndrome including actinic reticuloid and photosensitive eczema. Br J Dermatol. 1979; 101(Suppl.17):24.
106. Hawk JLM, Lim HW. Chronic actinic dermatitis. In: Lim HW, Hönigsmann H, Hawk JLM, editors. Photodermatology. New York: Informa Healthcare; 2007. p. 169.
107. Dawe RS, Ferguson J. Diagnosis and treatment of chronic actinic dermatitis. Dermatol Ther. 2003; 16:45.
108. Hawk JLM. Chronic actinic dermatitis. Photodermatol Photoimmunol Photomed. 2004; 20:312.
109. Meola T, Sanchez M, Lim HW, et al. Chronic actinic dermatitis associated with human immunodeficiency virus infection. Br J Dermatol. 1997; 137:431.
110. Russel SC, Dawe RS, Collins P, et al. The photosensitivity dermatitis and actinic reticuloid syndrome (chronic actinic dermatitis) occurring in seven young atopic dermatitis patients. Br J Dermatol. 1998; 138:496.
111. Millard TP, Hawk JLM. Photodermatoses in the elderly. Clin Geriatr Med. 2001; 17:691.
112. Lim HW, Morison WL, Kamide R, et al. Chronic actinic dermatitis: an analysis of 51 patients evaluated in the United States and Japan. Arch Dermatol. 1994; 130:1284.

113. Dawe RS, Crombie IK, Ferguson J. The natural history of chronic actinic dermatitis. Arch Dermatol. 2000; 136:1215.
114. Bilsland D, Crombie IK, Ferguson J. The photosensitivity dermatitis and actinic reticuloid syndrome: no association with lymphoreticular malignancy. Br J Dermatol. 1994; 131:209.
115. Thestrup-Pedersen K, Zachariae C, Kaltoft K, et al. Development of cutaneous pseudolymphoma following cyclosporin therapy of actinic reticuloid. Dermatologica. 1988; 177:376.
116. Ferguson J. Chronic actinic dermatitis. In: Ferguson J, Dover JS, editors. Photodermatology. London: Manson Publishing; 2006. p. 39.
117. Angelini G, Bonamonte D, Cristaudo A, et al. Linee guida SIDAPA su dermatite da contatto. Ann Ital Dermatol Allergol. 2009; 63:43.
118. Gonçalo M, Ferguson J, Bonevalle A, et al. Photopatch testing: recommendations for a European photopatch test baseline series. Contact Dermatitis. 2013; 68:239.
119. Stingeni L, Bianchi L, Hansel K, et al. Italian guidelines in patch testing adapted from the European Society of Contact Dermatitis (ESCD). Giorn Ital Dermatol Venereol. 2019; 154:227.
120. Bruynzeel D, Ferguson J, Andersen K, et al. Photopatch testing: a consensus methodology for Europe. JEADV. 2004; 18:679.