Common causes and management of photosensitivity

A high index of suspicion is needed to diagnose cases of photosensitivity as the temporal relationship of a rash on exposed sites with sunlight exposure is not always obvious.

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Photosensitivity is a common clinical problem in which exposure to relatively small amounts of ultraviolet (UV) and/or visible radiation results in abnormal cutaneous reactions. Classically, a photosensitive eruption occurs on sun-exposed sites, with sparing of shaded areas, and is exacerbated in spring and summer. The severity can range from a mild inconvenience to severe morbidity. Not uncommonly, the temporal relationship with sun exposure can be subtle, and a high index of suspicion is required for diagnosis. Photosensitivity reactions may be debilitating and can result in significant morbidity. It is, therefore, most important to consider photosensitivity in any patient with a rash on exposed sites.

This article discusses the causes, diagnosis and management of photosensitivity and then specific photosensitivity disorders in more detail.

Causes of photosensitivity

Photosensitivity occurs in a diverse group of disorders (Table 1). The acquired idiopathic photodermatoses are endogenous photosensitivity disorders with a probable immunological basis. Endogenous photosensitivity may also be a prominent feature of several metabolic and rare genetic syndromes. Exogenous photosensitivity, via toxic or allergic mechanisms, results from topical or systemic administration of photosensitising agents such as drugs. Several skin diseases, most importantly the connective tissue diseases, may be photoexacerbated even though they are not primarily caused by sunlight.

The wavelengths of light that elicit a photosensitive reaction are referred to as its action spectrum. The UV wavelengths are usually responsible. To some extent, the action spectrum may be specific for a particular photosensitivity disorder – for example, drug eruptions usually have an action spectrum in the UVA band. The usual source of causative radiation is sunlight, although artificial sources include suntanning beds, phototherapy lamps and arc welding.

Photosensitivity mechanisms

The two main mechanisms of photosensitivity postulated are:

- phototoxicity, in which light energy is

IN SUMMARY

- **Photosensitivity is a feature of a wide range of disorders, including the idiopathic photodermatoses, some metabolic disorders and a few rare genetic syndromes. It also occurs after exposure to certain drugs and other exogenous agents.**
- **A photosensitive reaction classically occurs on sun-exposed sites and spares those that are shaded or covered by clothing.**
- **A history of exposure to a photosensitising agent must be explored in all patients with photosensitivity.**
- **Referral to a dermatologist, or a photodermatology centre if available, for light testing and patch testing may be helpful in establishing the diagnosis.**
- **General treatment measures include avoidance of photosensitisers and sun protection.**
- **Specific treatment measures include oral corticosteroids, antihistamines, antimalarials, cyclosporin, azathioprine, thalidomide and light therapy.**

Table 1. Disorders with photosensitivity features

Idiopathic photodermatoses
Polymorphous light eruption
Juvenile spring eruption
Chronic actinic dermatitis
Solar urticaria
Actinic prurigo
Hydroa vacciniforme

Exogenous photosensitivity
Photocontact dermatitis
Drug photosensitivity

Metabolic disorders
Porphyrias
Pellagra

Genetic syndromes
Bloom's syndrome
Cockayne's syndrome
Hartnup disease
Rothmund–Thompson's syndrome
Trichothiodystrophy
Xeroderma pigmentosum

Photoaggravated diseases
Atopic dermatitis
Psoriasis
Seborrhoeic dermatitis
Autoimmune diseases
- bullous pemphigoid
- dermatomyositis
- lupus erythematosus (discoid and systemic)
- pemphigus

Darier's disease
Grover's disease
Infections
- herpes simplex labialis
- HIV

Lichen planus
Rosacea

Table 2. Clinical clues to photosensitivity

Timing
Temporal relationship of rash with sun exposure (can be variable)
Seasonal exacerbation in spring or summer

Exposure
Photosensitising medication
Phototosensitising substances (plants, chemicals)

Distribution
Exposed sites (face, neck, back of hands)
Sparing of covered areas (upper eyelids, under nose, under chin, behind ear lobes)

absorbed by a molecule (chromophore), often from an exogenous source such as a drug, resulting in direct tissue damage via reactive chemical species such as oxygen free-radicals
- photoallergy, in which a molecule of an exogenous substance or a normal body constituent absorbs light energy and undergoes structural and chemical change to become antigenic, resulting in an immune reaction that causes photosensitivity.

Clinical features and diagnosis

The clinical clues to photosensitivity are summarised in Table 2. Photosensitivity may first appear at any age, although genetic conditions usually present in infancy or childhood, while chronic actinic dermatitis (an acquired idiopathic photosensitivity) predominantly affects elderly men.

The distribution and timing of the eruption are important in establishing the diagnosis. A rash predominantly on exposed sites such as the dorsa of the hands, face and neck, with sparing of shaded areas such as the upper eyelids, under the nose, beneath the chin and behind the ear lobes, is strongly suggestive of photosensitivity (Figure 1). However, in severe cases, the rash may involve covered areas and progress to generalised erythema of the skin (erythroderma). An airborne contact dermatitis may affect similar sites but without the areas of sparing.

A temporal relationship between the rash and sun exposure is usually present and exacerbations typically occur in summer or spring. When there is a delay between sun exposure and onset of the rash or if the rash persists all year round there may not be such a relationship.

Exacerbation or appearance of the rash after exposure to the sun through window glass, or despite the use of sunscreens, points to UVA or visible light as the causative wavelengths. Rarely, severely photosensitive patients may react to

artificial domestic lighting.

A history of exposure to photosensitising medications or other substances should be explored in all patients who present with a rash predominantly on exposed sites.

Investigating photosensitivity

If the diagnosis of photosensitivity is obvious (such as in drug photosensitivity), a definite clinical diagnosis can be made without specific investigations. Specific investigations depend on both the clinical features and the suspected diagnosis.

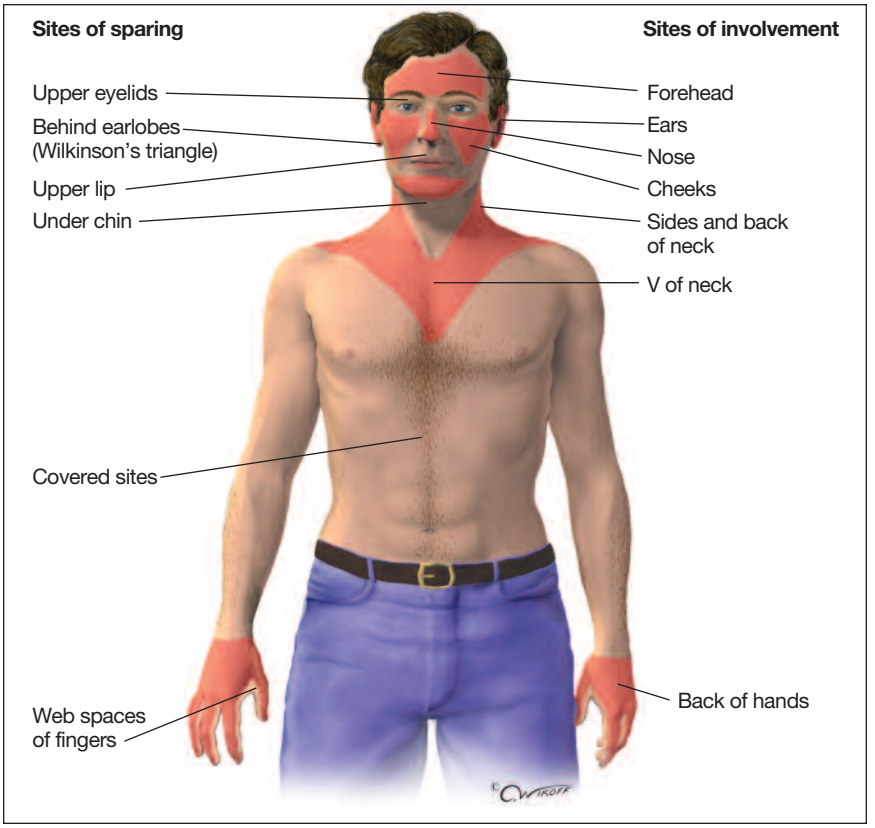
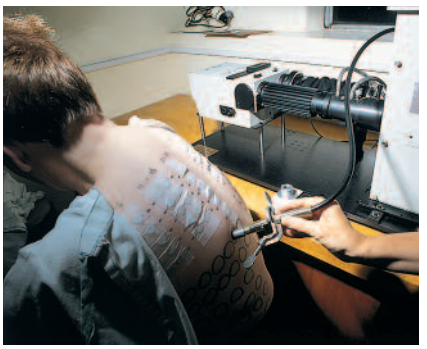
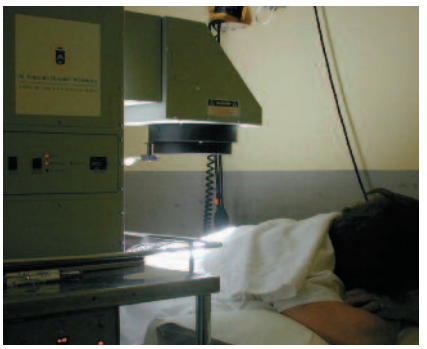


Figure 1. Classical sites of involvement and sparing in photosensitivity.





Figures 2a and b. Investigating photosensitivity. a (left). Light testing using a monochromator. Note also the epicutaneous patch tests for delayed hypersensitivity on the upper back. b (right). Light testing using a solar simulator.

Laboratory tests

Tests that may be clinically indicated include antinuclear, anti-Ro and anti-La antibodies (in suspected lupus erythematosus) and porphyrin studies (in suspected porphyria).

Light testing

Light testing using natural sunlight with timed exposure or artificial UV sources, such as phototherapy tubes, may help confirm photosensitivity, provide diagnostic information and exclude conditions that simulate photosensitivity.

Photodermatology referral centres use specialised equipment to show that the patient develops erythema (a sunburn reaction) at lower doses than normal or that the skin reaction is abnormal (eczematous or urticarial; see Figures 2a and b).

Patch testing

Patch testing to airborne allergens is also useful in confirming or excluding airborne contact dermatitis (which can mimic photosensitivity) and in identifying other chemicals causing allergic contact dermatitis.

Photopatch testing

Exposing patch tests to measured UV radiation can be of use in identifying chemicals causing photocontact dermatitis.

Skin biopsy

Biopsy of the affected skin is generally not helpful in diagnosing photosensitivity, but may be useful in confirming lupus erythematosus or other photoaggravated dermatoses.

Management

Avoiding photosensitisers

If a topical or systemic photosensitising substance is found to be causative, it should be avoided or excluded from the patient's environment.

Sun protection

All photosensitive patients should reduce or avoid sun exposure. Patients should be advised to :

- wear a wide-brimmed hat
- wear protective clothing when outdoors (tight weaves and dark colours are best)
- stay in the shade where possible
- engage in outdoor activities early or late in the day
- use topical sunscreens that contain reflective agents, such as titanium dioxide, and absorptive chemicals, such as cinnamates, benzophenones and Parsol 1789 (avobenzone), which provide protection into the UVA spectrum in addition to UVB protection.

Treatment

If photosensitiser avoidance and the use of sun protection measures are not sufficient, specialist referral will usually be warranted. Various therapies may be prescribed by the dermatologist, such as topical and oral corticosteroids, antimalarials (e.g. hydroxychloroquine [Plaquenil]), immunosuppressives (e.g. azathioprine [Azahexal, Azamun, Imuran, Thioprine] and cyclosporin [Cysporin, Neoral, Sandimmun]), antihistamines and thalidomide.

Paradoxically, the careful use of UV radiation may be therapeutic in conditions such as the idiopathic photodermatoses, with the aim of rendering the skin nonreactive to sunlight ('hardening'). In Australia, phototherapy using narrowband 311 nm UVB wavelengths has now largely superseded the use of psoralen–UVA (PUVA) as it does not involve the use of oral photosensitisers and is believed to be associated with a lower long term risk of skin cancer.

Idiopathic photodermatoses

Polymorphic light eruption

Polymorphic light eruption is the most common idiopathic photodermatosis and affects 5 to 15% of the population. It usually presents in late teens and young adult life, is more common in women, and affects all races and skin types.

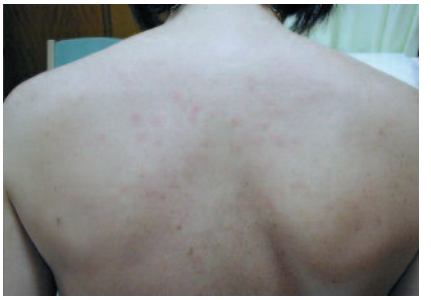


Figure 3. Polymorphous light eruption – a pruritic erythematous papular eruption occurring on the back several hours to days after sun exposure.

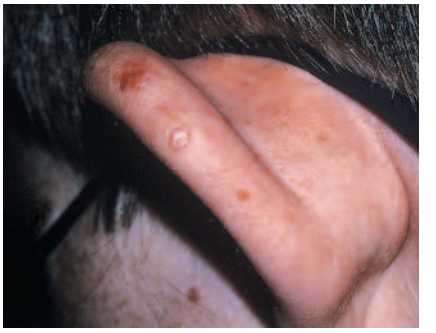


Figure 4. Juvenile spring eruption – pruritic papules and blisters, often transient, on the outer helice of the ear of a young boy.

The diagnosis of polymorphic light eruption is largely based on clinical grounds, particularly on the time course and typical morphology of the eruption. Itchy erythematous papules, vesicles or sometimes nodules appear within hours to days of sun exposure (Figure 3), usually after a prolonged period of reduced sun exposure (such as after winter or on travelling to a sunny environment), and take days to several weeks to resolve. The rash may involve any site, but is more common on the arms, trunk, thighs and the dorsa of the feet. Regularly exposed areas such as the face and hands are often 'hardened' by previous sunlight exposure.

Juvenile spring eruption

Juvenile spring eruption is regarded as a variant of polymorphic light eruption. It typically affects 5- to 12-year-old boys in spring and is characterised by transient itchy papules and blisters on the outer helices of the ears (Figure 4).

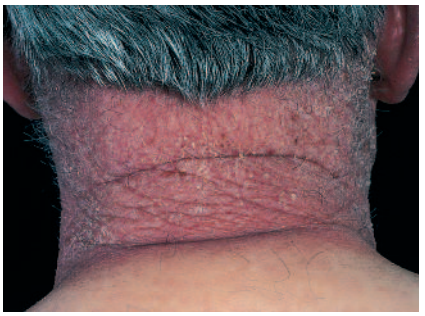
Chronic actinic dermatitis

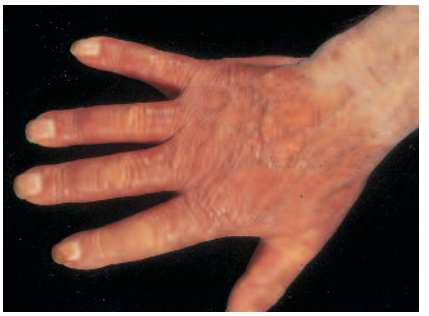
An uncommon photodermatosis, chronic actinic dermatitis typically affects elderly men and outdoor enthusiasts. Clinical features range from an eczematous eruption (early stages) on sun-exposed areas to chronic infiltrated nodules and plaques that may simulate cutaneous lymphoma (Figures 5a and b).

Severe cases can be profoundly debilitating, especially if the eruption persists year round, extends into covered sites or progresses toward erythroderma. The condition is usually chronic, although the photosensitivity component may resolve in some patients, and is believed to be due to a delayed type IV hypersensitivity reaction to an endogenous allergen. Light testing is essential in confirming the diagnosis.

Solar urticaria

Solar urticaria is a rare condition that may arise *de novo* or following exposure to exogenous photosensitisers. It is characterised by itchy urticarial erythematous papules and wheals that develop within minutes of sun exposure and resolve over several hours. In severe cases, systemic signs of histamine release such as dizziness, headache, bronchospasm and syncope may occur. The pathogenesis is unclear but is thought to be IgE-mediated. Light testing is diagnostic if wheal formation is induced within a few minutes of irradiation (Figure 6).





Figures 5a and b. Chronic actinic dermatitis – chronic eczematous changes confined to sun-exposed areas. Note the sharp cut-off of the rash at the collar line and wrists.

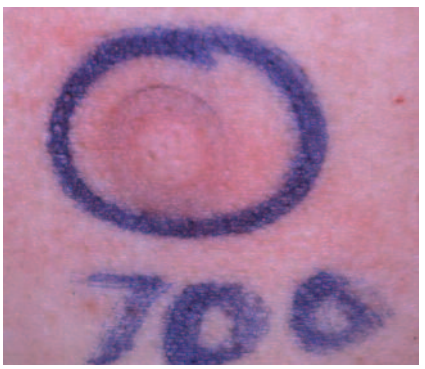
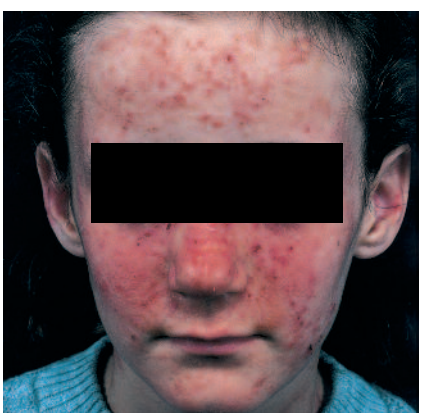


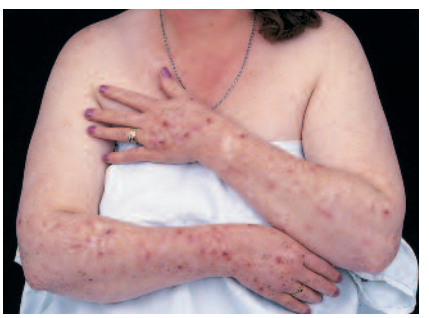
Figure 6. Solar urticaria. An urticarial lesion induced by monochromator light testing using 700 nm (visible) light. The action spectrum is variable and may include UVB, UVA and/or visible light.

Actinic prurigo and hydroa vacciniforme

Actinic prurigo and hydroa vacciniforme are rare photosensitivive conditions. Actinic prurigo may be a variant of polymorphic light eruption but is usually more severe and begins in early childhood. An extremely high correlation of certain genotypes (HLA-DR4 and HLA-DRB1*0407) with actinic prurigo has been established, indicating a genetic predisposition. It is characterised by an itchy, excoriated papular or nodular rash with persistent crusted lesions that develop on the face (typically on the nose and lower lip) and arms (Figures 7a and b). Conjunctivitis and photophobia occur in severe cases. The eruption is typically worse in summer, but not always clearly related to sun exposure.

Hydroa vacciniforme is an extremely rare photosensitive disease that affects children and teenagers. Primarily the face and ears are involved. Painful macules appear on sun-exposed skin and evolve into vesicobullae that crust and heal to leave varicella-like pockmarked scars. The condition usually resolves in the late teenage years.





Figures 7a and b. Actinic prurigo. Pruritic excoriated papules and nodules occurring on (a, left) the face and (b, right) exposed arms.

Exogenous photosensitivity

Photocontact dermatitis

Photocontact dermatitis is the result of skin contact with a photoactive substance, followed by light exposure (usually UVA). It may be phototoxic or, less commonly, photoallergic in nature.

Phototoxic contact dermatitis

Phototoxic contact reactions are often described as exaggerated sunburn but can range from low grade erythema or pigmentation to severe erythema with pain and blistering. They can be caused by a number of chemicals (Table 3). The offending agent is often identified by the history and the sites involved (the reaction is usually localised to the site of contact).

Coal tar derivatives used as topical therapeutic agents in the treatment of psoriasis and sometimes dermatitis are known to cause photosensitivity. Occupational topical exposure to coal tar derivatives may occur, for example, among handlers of roofing materials.

Psoralen-like substances (furocoumarins) occur naturally in certain plants, including fruits such as figs, lemons, limes and bergamot oranges, and vegetables such as celery, parsley and parsnip. Oral ingestion of these plant products is usually insufficient to cause systemic photosensitivity, but topical exposure leading to a phototoxic reaction may occur in certain occupations such as gardeners, salad chefs and bartenders. Therapeutic photosensitisation using topical psoralens occurs in bath and topical PUVA therapies.

Photoallergic contact dermatitis

In photoallergic contact reactions, the eczematous reaction at sites of contact is

usually delayed (typically 48 hours following light exposure), which is consistent with a type IV hypersensitivity reaction. Sunscreens are currently the most usual cause (Table 3). Photopatch testing is indicated and is diagnostic.

Drug photosensitivity

Drugs commonly causing photosensitivity are listed in Table 4; some are discussed further below. The most common mechanism of drug photosensitivity is a phototoxic process, which classically produces an exacerbated sunburn-like rash within minutes to hours after light exposure and peaks several days later (Figure 8a). A chronic eczematous rash develops with continued use of the drug. Clinical features that may occur in drug photosensitivity are listed in Table 5. Light testing may be useful in confirming the diagnosis. Withdrawal of the offending agent typically leads to quick resolution of the eruption, but photosensitivity may be prolonged if the drug has a long elimination time.

Table 3. Agents causing photocontact dermatitis

Phototoxic agents

Coal tar derivatives
Plants containing psoralen-containing substances, e.g. celery, parsnip, fig, lime
Psoralens
Retinoic acid

Photoallergic agents

Sunscreens
- benzophenones
- cinnamates
- PABA derivatives

Antibacterial agents
- halogenated salicylanilides*
- hexachlorophene

Fragrances
- musk ambrette*

*Mainly of historical significance

In contrast, photoallergy due to systemic agents is uncommon. The reactions are mainly eczematous and they are not dose-dependent.

Table 4. Drugs causing photosensitivity reactions

Amiodarone*
Antibiotics
- sulfonamides
- tetracyclines (doxycycline,* minocycline, tetracycline)
- trimethoprim
- quinolones (ciprofloxacin, norfloxacin, ofloxacin)

Antimalarial agents
- chloroquine
- quinine

Antineoplastic agents
- dacarbazine
- fluorouracil
- methotrexate
- vinblastine

Diltiazem
Diuretics
- thiazides*
- frusemide*

Griseofulvin
Hypoglycaemic agents
- sulfonylureas

Lipid lowering agents
- fibric acid derivatives

Nonsteroidal anti-inflammatory drugs
- naproxen
- piroxicam*
- ketoprofen
- ibuprofen

Phenothiazines
- chlorpromazine*
- prochlorperazine*
- promethazine

Psoralens*
Retinoids
- isotretinoin
- acitretin

Tricyclic antidepressants

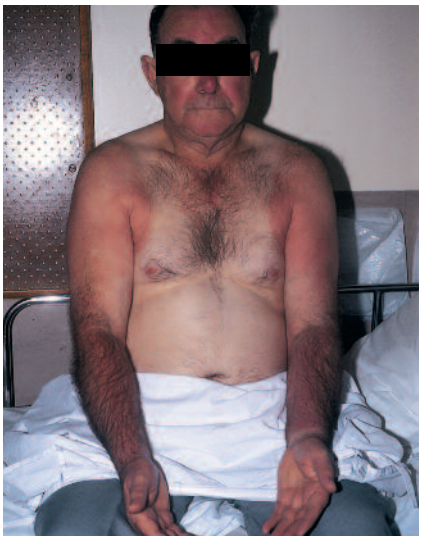
*Commonly reported

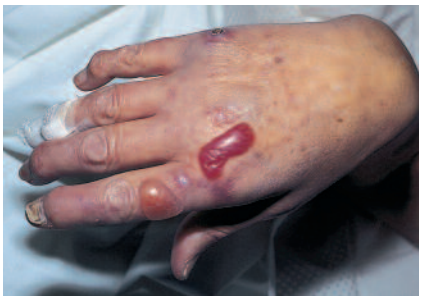
Systemic phototoxic agents

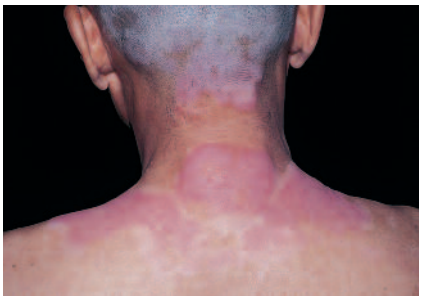
- **Amiodarone.** Amiodarone has been reported to cause an acute phototoxic reaction and a dose-dependent slate-blue pigmentation (particularly on the nose and cheeks). Photosensitivity may persist for 12 months after withdrawal of the drug.
- **Antibiotics.** Antibiotics such as the tetracyclines, sulfonamides and quinolones can produce phototoxic reactions. Tetracyclines may also cause photo-onycholysis, and minocycline not uncommonly causes hyperpigmentation in sun-exposed areas.
- **Antimalarial agents.** The role of chloroquine as a phototoxic agent is controversial. Quinine is a phototoxic agent and has also been reported to produce positive photopatch reactions, lichenoid eruptions and an evolution to chronic actinic dermatitis.
- **Diuretics.** The thiazide diuretics are well-established phototoxic agents and can also result in persistence of photosensitivity for many years. Both thiazides and frusemide have been reported to cause lichenoid eruptions and pseudoporphyria (Figures 8a and b).
- **Antifungal therapy.** Photosensitivity to griseofulvin is well-recognised but is uncommon. Nevertheless, all patients should be warned of this adverse effect.
- **NSAIDS.** NSAIDs, particularly the propionic acid derivatives (ibuprofen, ketoprofen, naproxen) have been reported to

Table 5. Clinical features of drug photosensitivity

Exaggerated sunburn
Dermatitis (acute or chronic)
Pruritus
Urticaria
Lichenoid eruptions
Porphyria-like rash
Hyperpigmentation
Onycholysis







Figures 8a to c. Skin changes in drug photosensitivity can have variable morphology. a (left). Exaggerated sunburn reaction in a patient taking a thiazide diuretic – note the sparing of clothed areas and under the watch. b (centre). Pseudoporphyria in a patient taking frusemide – serous and haemorrhagic blisters on the dorsa of the hands. c. (right) Systemic phototoxic reaction to psoralen – in this case, 8-methoxypsoralen was administered as part of PUVA therapy for vitiligo (note that the reaction is maximal in areas of depigmentation).

cause eczematous, vesicobullous and pseudoporphyria eruptions. Photosensitivity is reported to occur in approximately 2% of patients taking piroxicam.

- **Psoralens.** Phototoxicity caused by psoralens has decreased in prevalence because PUVA therapy has been largely superseded by other forms of phototherapy that do not involve the use of oral photosensitisers (Figure 8c).
- **Retinoids.** Young, active patients on isotretinoin for acne should be warned of photosensitivity and advised to take appropriate photoprotective measures.

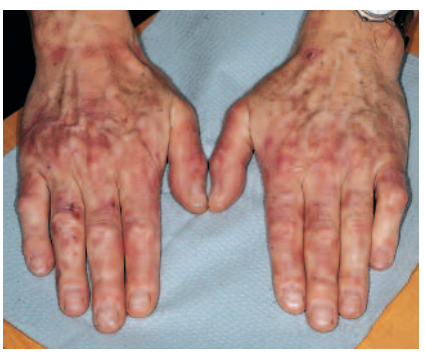


Figure 9. Porphyria cutanea tarda. In this case, skin fragility is manifested by painful erosions, hyperpigmentation and milial cysts on the dorsa of the hands.

Genetic and metabolic disorders

It is beyond the scope of this article to discuss in detail the metabolic and genetic syndromes involving photosensitisation. Three conditions are, however, briefly mentioned below.

Erythropoeitic protoporphyria

Erythropoeitic protoporphyria is a genetically determined condition in which a lack of the enzyme ferrochelatase results in an accumulation of protoporphyrin in red blood cells and plasma. Skin pain or stinging caused by a phototoxic mechanism occurs within minutes of sun exposure, and infants may present with uncontrollable crying after sun exposure. Erythematous patches, oedema and urticarial lesions can develop. Lesions may leave characteristic cribriform scarring on the nose and cheeks. Hepatobiliary disease has been reported in some patients.

Raised protoporphyrin levels in red blood cells and plasma is diagnostic. Unfortunately, there is no effective treatment. Clothing and broad spectrum opaque sunscreens are protective, and carotene may be helpful in some cases.

Porphyria cutanea tarda

Patients with porphyria cutanea tarda do not usually present with acute photosensitivity although exposure to sunlight plays a part. The predominant complaint is skin fragility, which is manifested by blisters containing serous or haemoserous fluid on the backs of hands following minor trauma, resulting in milial cysts, erosions, hyperpigmentation and localised scleroderma (Figure 9).

The abnormality is a functional deficiency of the liver enzyme uroporphyrinogen decarboxylase, and may be hereditary or acquired. Precipitating factors include alcohol, oestrogen, iron and chlorinated hydrocarbons. Diagnosis is established by porphyrin studies (blood, urine and faeces), which also distinguish this condition from other less common porphyrias.

Pellagra

Pellagra is caused by niacin and tryptophan deficiency. It is seen in severe nutritional deficiency, bowel bypass syndrome, carcinoid tumour and isoniazid therapy. The photosensitive dermatitis of pellagra typically resolves to leave a dusky, red-brown skin colour (Figure 10).

Photoaggravated dermatoses

Atopic dermatitis

Patients with atopic dermatitis often find that sunlight is beneficial for their

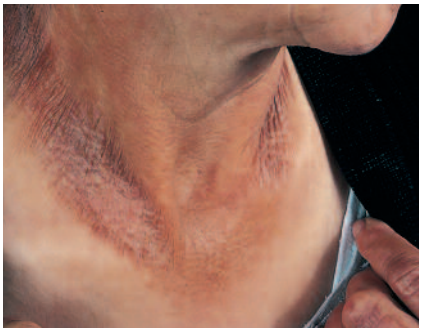


Figure 10. Pellagra. The photosensitive rash on the neck has a typical dusky, red-brown skin colour.

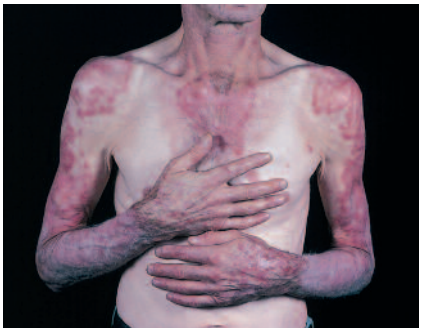


Figure 11. Subacute cutaneous lupus erythematosus. In this case, multiple annular erythematous plaques occurred on the arms and trunk in a photosensitive distribution. Note the relative sparing of areas covered by a singlet.

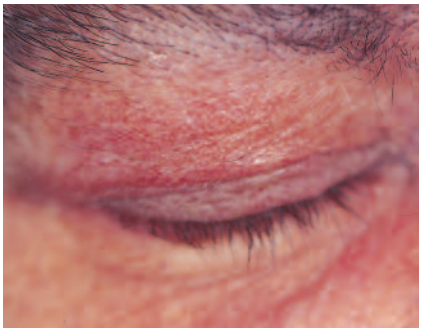


Figure 12. Dermatomyositis. Note the classical heliotrope rash on the upper eyelid.

condition. A few, however, find that their condition worsens after sun exposure or in summer. Truly photosensitive eczema is very uncommon and other potential aggravating factors such as heat and irritant topical preparations should be excluded. The results of light testing are usually normal.

Seborrhoeic dermatitis

Seborrhoeic dermatitis is a common condition that can be either exacerbated or improved by exposure to ultraviolet light. However, low autumn and winter temperatures and central heating causing decreased humidity are also known to exacerbate the condition.

Psoriasis

Paradoxically, sunlight or UV radiation is often beneficial in psoriasis but the disease may sometimes occur mainly on sun-exposed sites, although this does not necessarily indicate photosensitivity. Truly photosensitive psoriasis is uncommon. More common, however, is the appearance of psoriasis in areas of sunburn (Koebner phenomenon).

Lupus erythematosus

Photosensitivity is a common feature of lupus erythematosus, both cutaneous and systemic, particularly when anti-Ro antibodies are present. The skin lesions are polymorphic, predominantly affecting sun-exposed sites, and range from an acute papular eruption to well-defined scaly plaques and occasionally, bullae (Figure 11). A butterfly rash occurs in a photodistribution over the cheeks in systemic lupus erythematosus. Associated symptoms of arthralgia, headaches and fatigue may be present. Sun protection is a vital feature in the overall management.

Other photoaggravated dermatoses

Photoexacerbation of the cutaneous manifestations of dermatomyositis is well-recognised (Figure 12). Photosensitivity has been also been reported in patients with pemphigus.

Summary

Photosensitivity is a common clinical problem that may often be debilitating and can result in significant morbidity. It is, therefore, important to consider photosensitivity in any patient with a rash on exposed sites. The temporal relationship with sunlight exposure is, however, not always obvious and the diagnosis requires a high index of suspicion. Exposure to photosensitisers, especially medication, must be considered in all patients, since withdrawal of the offending agent is likely to be curative. General management includes sun protection measures and avoidance of photosensitisers. Specific treatment modalities include low dose UV radiation and systemic immunosuppressive therapies. MT

Further reading

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