caused by chronic poor hygiene.

**Treatment**

Cutaneous symptoms should be treated appropriately. If necessary, treatment for mental imbalance may be necessary with cooperation from a psychiatrist.

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**Photosensitive diseases**

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1. **Solar dermatitis, Sunburn**

Erythema and blisters are produced by prolonged exposure to sunlight (mainly UVB). Pathologically, sunburn cells (apoptotic epidermal cells), epidermal spongiosis, edema in the dermal blood vessels, inflammatory cellular infiltration, necrosis and subcutaneous blistering are present. Erythema occurs several hours after photoradiation on the exposed site, and it gradually becomes edematous (Fig. 13.14). Solar dermatitis is most severe 12 to 24 hours after irradiation, after which it gradually resolves. Exfoliation and pigmentation occur in several days. Pigmentation is left after healing in some cases. Application of sunscreen is helpful for prevention. Cold compresses and steroid ointments are effective. When blistering is present, the same treatments as those for burns are applied.

---

2. **Photosensitive dermatoses**

**Outline**

- Photosensitive dermatoses are cutaneous diseases that are caused or aggravated by sunlight exposure.
- Both extrinsic factors (e.g., drugs) and intrinsic factors (e.g., inherited diseases, metabolic disorders) may be involved.
- They are caused by direct action of drugs (phototoxic dermatitis) or by immunological mechanism (photoallergic dermatitis).
- Xeroderma pigmentosum is a hereditary photosensitive dermatosis that is induced by intrinsic factors.

**Pathogenesis**

The two main causative factors of photosensitive dermatoses...
are extrinsic chemicals and intrinsic factors (Tables 13.4 and 13.5). This section describes photosensitive dermatoses that are caused by extrinsic factors. Extrinsic photosensitive dermatosis is inflammation of skin caused by the excitation of chromophores by daily exposure to radiation (mainly UVA). Chromophores reach the skin either from outside (skin lotion, perfume, fruit juice, tar) to induce photocontact dermatitis or from within the body (drugs, food). The mechanisms of inflammation are phototoxic

<table>
<thead>
<tr>
<th>Drug Classification</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychoactive</td>
<td>Chlorpromazine, promethazine, diazepam, carbamazepin, imipramine</td>
</tr>
<tr>
<td>Muscle relaxant</td>
<td>Alfloqualone</td>
</tr>
<tr>
<td>Antihistamine</td>
<td>Diphenhydramine, mequitazine</td>
</tr>
<tr>
<td>Antibacterial agent</td>
<td>Nalidixic acid, enoxacin, ofloxacin, ciprofloxacin, lomefloxacin, sparfloxacin, fleroxacin, tosuloxacin, tetracycline, doxycyclin</td>
</tr>
<tr>
<td>Antifungal agent</td>
<td>Griseofulvin, fluycytosine, itraconazole</td>
</tr>
<tr>
<td>Antinflammatory</td>
<td>Ketoprofen, tiaprofenic acid, suprofen, piroxicam, ampiroxicam, actarit, diclofenac, naproxen</td>
</tr>
<tr>
<td>Antihypertensive agent</td>
<td>Hydrochlorothiazide, trichlormethiazide, meticran, clofenamide, tripamide, metolazone, furosemide, tilosol HCl, pindolol, diltilazem HCl, nicardipine HCl, nifedipine, captopril, lisinopril</td>
</tr>
<tr>
<td>Antidiabetic</td>
<td>Tolbutamide, chlorpropamide, glibenclamide, carbutamide, glumidine sodium</td>
</tr>
<tr>
<td>Antipodagric</td>
<td>Benzbromarone</td>
</tr>
<tr>
<td>Antitumor agent</td>
<td>5-FU, tegafur, dacarbazine, flutamide</td>
</tr>
<tr>
<td>Lipid-lowering drug</td>
<td>Simvastatin</td>
</tr>
<tr>
<td>Prostatomegaly therapeutic agent</td>
<td>Tamsulosin</td>
</tr>
<tr>
<td>Photochemistry therapeutic agent</td>
<td>8-Methoxypsoralen, trioxypsoralen, hematoporphyrin derivative</td>
</tr>
<tr>
<td>Vitamin</td>
<td>Eretinate, pyridoxine, VB12</td>
</tr>
<tr>
<td>Antirheumatic</td>
<td>Sodium aurothiomalate, methotrexate</td>
</tr>
</tbody>
</table>


**Table 13.5 Classification of photosensitive dermatosis.**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Cause</th>
<th>Diagnostic name</th>
<th>Described in...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extrinsic photosensitive dermatosis</td>
<td>Drug</td>
<td>Phototoxic dermatitis</td>
<td>Chapter 13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Photoallergic dermatitis</td>
<td>Chapter 13</td>
</tr>
<tr>
<td>Intrinsic photosensitive dermatosis</td>
<td>Accumulation of chromophore in skin</td>
<td>Pellagra</td>
<td>Chapter 17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Porphyria</td>
<td>Chapter 17</td>
</tr>
<tr>
<td></td>
<td>DNA repair defect</td>
<td>Xeroderma pigmentosum (XP)</td>
<td>Chapter 13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cackayne syndrome</td>
<td>Chapter 13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bloom syndrome</td>
<td>Chapter 13</td>
</tr>
<tr>
<td></td>
<td>Decrease of melanin</td>
<td>Albinism</td>
<td>Chapter 16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phenylketonuria</td>
<td>Chapter 17</td>
</tr>
<tr>
<td></td>
<td>Unknown</td>
<td>Hydroa vacciniforme</td>
<td>Chapter 13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Solar urticaria</td>
<td>Chapter 13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polymorphous light eruption</td>
<td>Chapter 13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic actinic dermatitis (CAD)</td>
<td>Chapter 13</td>
</tr>
</tbody>
</table>
the excited substance itself becomes toxic) and photoallergic
(the excited substance becomes an allergen that induces inflam-
mation by immunoreaction) (Fig. 13.15, Table 13.6).

### Table 13.6 Phototoxic reaction and photoallergic reaction.

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Phototoxic reaction</th>
<th>Photoallergic reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>More than one exposure to agent required?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Onset of reaction after exposure to agent and light</td>
<td>hours to 1 day</td>
<td>24-72 hours</td>
</tr>
<tr>
<td>Clinical features</td>
<td>Exaggerated sunburn</td>
<td>Dermatitis</td>
</tr>
<tr>
<td>Distribution</td>
<td>Sun-exposed skin</td>
<td>Sun-exposed skin</td>
</tr>
<tr>
<td>Spread to unexposed areas?</td>
<td>No</td>
<td>Yes (possible)</td>
</tr>
<tr>
<td>Pathologic feature</td>
<td>Necrosis of epidermal cell (sunburn)</td>
<td>Spongiosis, eczema</td>
</tr>
<tr>
<td>Cross reaction caused by similar compounds?</td>
<td>Almost never</td>
<td>Yes (sometimes)</td>
</tr>
<tr>
<td>Amount of agent required for photosensitivity</td>
<td>Large</td>
<td>Small</td>
</tr>
</tbody>
</table>

1) **Phototoxic dermatitis**

- Phototoxic dermatitis may occur in anyone by the combination of a certain dose of drugs and sun exposure.
- It may occur even at the first irradiation (usually by UVA), without any latency.
- The main causative drugs are psoralen, coal tar, thiazide drugs, and tetracycline.

#### Clinical features

Sunburn-like symptoms are mainly seen. That is, erythema and edema are followed by exfoliation and pigmentation. Perfume may cause both allergic contact dermatitis and phototoxic dermatitis (Berloque dermatitis) on the neck, especially the sides.

#### Photocontact dermatitis

The skin comes into direct contact with the causative agent. Subsequent exposure to light of a certain wavelength causes photocontact dermatitis. It is classified by onset mechanism as phototoxic or photoallergic.
Drugs that accumulate in the skin absorb light at a certain wavelength. Exposure to light at that wavelength causes phototoxic dermatitis. Each drug affects a particular site.

Intake of the causative substance should be discontinued. Sunlight is avoided by sunscreen and a hat. The treatments are the same as those for contact dermatitis.

2) Photoallergic dermatitis

Outline

- Photoallergic dermatitis is photosensitive dermatitis that is caused by a type IV allergy reaction, which is induced by sun exposure after topical application or intake of a drug.
- Erythema and blistering are the main symptoms.
- Chlorpromazine, thiazide drugs and oral antidiabetics are the main causative drugs.

Clinical features

Erythema and serous papules occur on the sun-exposed site, progressing to edema blistering, and erosion.

Pathogenesis

Chromophores that somehow attach to the skin react to exposure to light of a certain wavelength (mostly UVA, sometimes visible light) to become allergenic, or they may convert into hapten, connect with biologic proteins and become photoallergenic. After sensitization, the causative substance is re-exposed to light when it reaches the skin surface, where it induces type IV allergic reaction (Fig. 13.15). This reaction does not occur without sensitization; that is, inflammation is not caused by the first exposure, nor does allergic reaction occur in everyone. A person who has been sensitized is prone to light-induced inflammation even from a minute amount of the substance.

Laboratory findings, Diagnosis

Photo-patch test: The test substance is patched as in the usual patch test. The minimal erythema dose (MED) of the patient is also determined. After 24 hours, half of the patch site is exposed to a slightly smaller amount of UV than that of the first MED exposure. The other half is left unexposed. The result is determined 48 hours after exposure (Figs. 13.16 and 13.17).

Photo-drug test: Application of the suspected drug is discontinued for at least 20 days. A normal dose of a test drug is applied for 2 days. The diagnosis is photoallergic dermatitis if an eruption is produced by exposure to light.
Intake of the causative substance and sunlight exposure should be avoided. The treatment is the same as that for contact dermatitis. A photosensitive disease called “persistent light reaction,” which is categorized as a chronic actinic dermatitis (CAD), may remain after discontinuation of the causative substance.

3. Solar urticaria

Definition, Pathogenesis, Clinical features

An allergen is intrinsically produced in skin by exposure to light, against which type I allergy is induced. Several minutes after light exposure (mostly the visible spectrum, but also UVA and UVB in some cases), extremely itchy urticaria occurs; however, it disappears in several hours. Anaphylactic shock may be caused in rare cases.

Diagnosis, Examinations

Solar urticaria is generally diagnosed from the recurring eruptions caused by exposure to sunlight or to artificial light. However, wheals may be produced or aggravated by light shielding in some cases; certain wavelengths in the light are thought to inhibit wheals. In young patients, differential diagnosis from erythropoietic protoporphyria may be necessary.

Treatment

The patient is shielded from the sun, and antihistamines are applied as a symptomatic treatment. PUVA treatment may be performed as a desensitization treatment. Immunosuppressants and plasma exchange have been reported to be effective in severe cases.

4. Chronic actinic dermatitis (CAD)

Clinical features, Pathogenesis

Chronic actinic dermatitis (CAD) most frequently occurs in adult males. An intractable eczematous change whose main symptom is slowly progressing lichenoid plaques occurs on exposed areas of the body and becomes chronic (Figs. 13.18-1 and 13.18-2). In some cases, the lesions progress to erythroderma, leading to cutaneous lymphoma-like subcutaneous nodules, thickening of the skin, or facies leontina. It is hypothesized that intrinsic antigens are produced by light exposure for some reason; however, the details of the onset mechanism are unknown. Photosensitive diseases used to be called “persistent light reaction” “actinic reticuloid” or “photosensitivity dermatitis.” Now these are categorized as forms of CAD.
Eczematous lesions are the main symptom of CAD. As CAD progresses, lymphocytic infiltration and atypical cells are seen in all dermal layers, and Pautrier microabscess-like lesions may occur in the epidermis (actinic reticuloid).

Laboratory findings, Diagnosis, Treatment

The minimal erythema dose (MED) for UVB is greatly reduced. The MED for UVA and visible light is also reduced in some cases. For differential diagnosis, the skin is subjected to repeated UVB exposure and if eczematous lesions appear then the diagnosis is CAD. Topical steroids are helpful. Complete light shielding is essential. Tacrolimus ointment is also useful. Oral steroids and immunosuppressants are effective in severe cases.

5. Polymorphous light eruption

Clinical features

Polymorphous light eruption occurs most commonly in women between the ages of 10 to 30. Itchy erythema and papular eruptions appear at sun-exposed sites. They become chronic and tend to gradually worsen. The condition also worsens in summer and subsides in winter.

Pathogenesis, Diagnosis

Polymorphous light eruption is thought to be an allergic reaction to light. In practice, all photosensitive diseases with unknown causes and without specific symptoms of other photosensitive diseases are considered to be polymorphous light eruption. It requires reconsideration as to whether it is an independent disease.

6. Hydroa vacciniforme

Outline

- Hydroa vacciniforme is a rare intrinsic photosensitive disease seen in infants.
- Blisters with concave centers form at sun-exposed sites on the face and dorsa of the hands.
- Epstein-Barr viruses are involved. The disease resolves naturally at puberty.
- Sun shading is important.

Clinical features, Pathogenesis

Hydroa vacciniforme first appears in infants 2 to 3 years of age and resolves naturally at puberty. It occurs more often in males. Erythema and blisters with concave centers are produced by exposure to sunlight or UVB, and crusts form later on. These
leave atrophic scarring when they heal. They mostly occur in the
face, auriculae, and dorsa of hands (Fig. 13.19). The lesions are
sensitive to light and tend to worsen in summer. When the EB
group A is the severest, and the variant
group is the mildest. In the variant group, UDS is normal; how-
ever, there is failure in DNA modification after synthesis. Group
A and the variant group are the most frequently occurring in
Japan, together accounting for 80% of all XP cases. All groups
are autosomal recessive and occur in 1 person out of 100,000 to
1.5 persons out of 100,000. About 30% of patients with XP are
born from consanguineous marriages. The main genes responsi-
ble for XP have been identified (Chapter 29).

Clinical features
Abnormalities are not found at birth; however, intense and
delayed sunburn in 1- to 2-month-old infants may be recognized
as the onset of XP group A. Extremely intense and persistent
sunburn recurs on sun-exposed sites such as the face and dorsa of
hands and forearms. As sunburn recurs, the skin dries and
coarsens, presenting an unwashed appearance with ephelides-like
pigmented patches, exfoliation, hypopigmented macules and

Diagnosis, Examinations, Treatment
Hydroa vacciniforme is diagnosed by laboratory findings. The
symptoms may resemble those of porphyria; however, the por-
phyria level in hydroa vacciniforme is within the normal range.
Direct sun exposure is avoided. Sunscreen is helpful.

7. Xeroderma pigmentosum (XP)

Outline
- XP occurs in persons with congenital failure in the DNA
  repair process. The cells are easily damaged by UV.
  Sunburn frequently occurs.
- All types are autosomal recessive inherited.
- A malignant tumor may occur as a complication with age.
- Complete shading of light is an effective treatment.

Classification, Pathogenesis
Patients with xeroderma pigmentosum (XP) have a congenital
failure in repairing and eliminating DNA that is damaged by UV
exposure. The failure results in severe photosensitive symptoms.
UV causes a replication fork bypass of a pyrimidine (thymine-
thymine) dimer.

XP is classified by unscheduled DNA synthesis (UDS), a clas-
sification index, into 8 subtypes: groups A to G, and a variant
group (Table 13.7). Group A is the severest, and the variant
group is the mildest. In the variant group, UDS is normal; how-
ever, there is failure in DNA modification after synthesis. Group
A and the variant group are the most frequently occurring in
Japan, together accounting for 80% of all XP cases. All groups
are autosomal recessive and occur in 1 person out of 100,000 to
1.5 persons out of 100,000. About 30% of patients with XP are
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Clinical features
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hands and forearms. As sunburn recurs, the skin dries and
coarsens, presenting an unwashed appearance with ephelides-like
pigmented patches, exfoliation, hypopigmented macules and

Fig. 13.19 Hydroa vacciniforme.

Fig. 13.20 Xeroderma pigmentosum (group
D).
Pigmentation on the face of a woman in her 20s.
The cutaneous symptoms are mild.
telangiectasia (Fig. 13.20). Seborrheic keratosis, small tumors, and ulcers occur in succession at the base of these lesions in childhood. Basal cell carcinoma, squamous cell carcinoma, keratoacanthoma and malignant melanoma occur subsequently.

Eye symptoms such as photophobia, blepharitis, dacryorrhea, and conjunctivitis occur in childhood and progress to ectropion, blindness, and malignant tumor in the terminal stages. Progressive neurological symptoms occur 6 months after birth, leading to articulatory disorder, gait disorder and intellectual impairment. Disturbance in growth, such as dwarfism and spondyloschisis, also occur.

Groups E, F, and G are often overlooked due to their mild symptoms. The carcinogenic period is the third decade of life. Eye symptoms and neurological symptoms are rarely found in these groups. Nevertheless, cutaneous symptoms and neurological symptoms in some cases of groups E, F, and G closely resemble those found in group A (Fig. 13.21). In the variant group, MED is almost normal, but ephelides gradually appears after childhood. Although eye symptoms and neurological symptoms are rarely seen, basal cell carcinoma or squamous cell carcinoma occurs in adulthood.

**Laboratory findings, Diagnosis**

XP diagnosis is confirmed by the MED level, DNA and RNA syntheses after UV exposure, measurement of UDS, and gene test.

**Treatment**

Sunlight should be thoroughly avoided by limiting outings in daytime, wearing clothes that cover the body thoroughly, keeping the hair long, wearing UV-screening eyeglasses, sticking UV-screening film on windows, applying shades to fluorescent lamps, and applying sunscreen. Early detection and treatment of cutaneous malignant tumor are important. Neurological disorders are treated by regular listening-comprehension tests, speech training, and motor ability retention training.

**UDS value**

UDS (unscheduled DNA synthesis), a test for xeroderma pigmentosum (XP), shows the potential degree of recovery from DNA damage under UV exposure, expressed as a percentage compared to normal controls. Cells are scattered in a petri dish and exposed to UV. When cultured in [3H] thymidine solution, damaged DNA is repaired, and the cells absorb [3H] thymidine. The amount of [3H] thymidine is measured by autoradiography for comparison with normal cases; patients with XP have reduced UDS values.