Antimicrobial Photosensitive Reactions

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Photosensitivity reactions are recognized as unwanted adverse effects of an array of commonly administered topical or systemic medications, including nonsteroidal anti-inflammatory agents, antifungals, and antimicrobials. When a drug induces photosensitivity, exogenous molecules in the skin absorb normally harmless doses of visible and UV light, leading to an acute inflammatory response. In phototoxic reactions, the damage to tissues is direct; in photoallergic reactions, it is immunologically mediated. In vitro and in vivo assay systems can assist in predicting or confirming drug photosensitivity. The incidence of photosensitivity reactions may be too low to be detected in clinical studies and may become recognized only in the postmarketing stage of drug development. Some drugs have been withdrawn because of photosensitivity effects that appeared after general release. Photosensitivity reactions have been studied for a number of topical antimicrobials and for the sulfonamides, griseofulvin, the tetracyclines, and the quinolones. Incidence and intensity of drug phototoxicity can vary widely among the different compounds of a given class of antimicrobials. When phototoxic effects are relatively low in incidence, mild, reversible, and clinically manageable, the benefits of an antimicrobial drug may well outweigh the potential for adverse photosensitivity effects.

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antifungals (eg, griseofulvin), and the antimicrobials nalidixic acid, fluoroquinolones, sulfonamides, tetracyclines, and antiprotozoans. Although such reactions rarely involve the morbidity and mortality seen with other adverse effects, including toxic epidermal necrolysis, Stevens-Johnson syndrome, anaphylaxis, or systemic toxicity, they do constitute a common dermatologic and pharmaceutical concern. Not infrequently, the incidence of photosensitivity reactions to antimicrobials is too low to be detected even in very careful analyses of phase 2 and 3 clinical studies. During the postmarketing period, when larger groups of outpatients are exposed to direct sunlight, photosensitivity may be recognized as a major deterrent to use of the drug. This was the case with nalidixic acid, a nonfluorinated quinolone uroantiseptic; an increased incidence of severe bullous photosensitivity reactions was seen following its introduction in 1962.

The members of the tetracycline group have been reported to induce photosensitivity in 25% to 90% of patients receiving demethylchlortetracycline, 20% receiving doxycycline, 7% receiving methacycline, and more rarely for those receiving minocycline. For the fluoroquinolones, a rapidly growing group of new generation potent antibacterial quinolone derivatives, the reported incidence of photosensitivity varies from 1% to 4% for ciprofloxacin to 10% and even 19% for floxacin. No member of these widely used systemic anti-infective agents has been withdrawn for photosensitivity adverse reactions, except tetracycline.

The problem of establishing the therapeutic parameters of a photosensitizing antimicrobial preparation may lead the clinician to completely reject its use, on the one hand, or underestimate its potential drawbacks in a non–life-threatening situation, on the other. The indications for the clinical use of most anti-infective agents should therefore rely on familiarity with the pathogenetic mechanisms, clinical presentations, diagnosis, and means of preventing potential photosensitivity reactions.

BIOPHYSICAL AND BIOCHEMICAL BACKGROUND

Photosensitization is a process in which reactions to normally innocuous radiation are induced in a biological system by the introduction of a specific radiation-absorbing substance, referred to as a photosensitizer. The latter causes another component of the system, a substrate, to be changed by radiation.

Photosensitivity reactions are induced by a delimited range of the electromagnetic spectrum that includes visible light and UV radiation. Ultraviolet (200-400 nm) and visible (400-800 nm) lights, to which the skin is continually exposed, are produced by the sun and artificial sources, such as tanning beds and fluorescent lamps. The UV spectrum is divided into 3 parts with arbitrary limits, ie, UV-A (wavelength 320-400 nm), also called black light; UV-B or “sunburn” radiation (wavelength 290-320 nm), and UV-C (wavelength 200-290 nm). Of these wavelengths, only UV-A and UV-B are involved in photosensitivity reactions, since UV-C is blocked by the ozone layer of the atmosphere. Ultraviolet radiation penetrates the skin to varying degrees before being transmitted or absorbed by molecules acting as substrates or endogenous chromophores. The latter include epidermal keratins, melanin, nucleic acids, hemoglobin, porphyrins, lipoproteins, carotene, and aromatic amino acids, such as tyrosine, tryptophan, and histidine.

Photon absorption leads to an energy transfer, promoting the electronic state of the chromophore molecule to an excited singlet state. Such an excited molecule is short-lived and can undergo several transformations. It may return to its ground state with the emission of heat (and sometimes fluorescence) or cross to a triplet state, in which the molecule is very active chemically and often reacts with other chemicals. Transformation from triplet to ground state allows sufficient time for energy transfer and initiation of biological changes, consisting in damage of several macromolecules, particularly nuclear DNA. A third change involves molecules absorbing a sufficient amount of energy for the formation of free radicals. These are highly reactive and can lead to substantial chemical activity with surrounding tissue damage. Skin reacts to such UV damage with an acute inflammatory response, commonly known as晒伤.

In cases of drug photosensitivity, similar acute inflammatory reactions occur in the skin in the presence of foreign molecules (exogenous chromophores), which absorb normally harmless doses of UV and visible radiation and create an electronically excited state. Absorbed photons from the electromagnetic spectrum are converted into chemical energy used in chemical reactions. These can transform the original chemical into a photoproduct, transfer the energy to a protein molecule, or shed the energy as either light or heat. Clinically, this process can result in erythema, edema, and sometimes blistering, as well as an increase in melanin formation.

For most chemical photosensitizers, the absorption and the action spectra are nearly equal, lying either in the visible or UV range, usually UV-A and UV-B. Visible light–induced photosensitivity occurs with porphyrins, several dyes, and the fluoroquinolones tosufloxacin, sparflloxacin, enoxacin, and clinafloxacin. Photosensitizers, nonsteroidal anti-inflammatory agents, phenothiazines, griseofulvin, sulfonamides, tetracyclines, nalidixic acid, and most fluoroquinolones react primarily with UV-A. A limited number of chemicals, for instance floxacin, depend mainly on UV-B activation. In vitro photosensitivity requiring both UV-A and UV-B have been reported with the quinolones, oxolinic acid, pipemidic acid, rosoxacin, and the newly developed fluoroquinolone sparflloxacin.

MECHANISMS OF PHOTOSENSITIVITY

Although the precise pathogenesis of drug–induced photosensitivity is not completely understood for all of the photosensitizing com-

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Phototoxic reactions result from direct cellular damage produced by the photoproducts, provided enough of the chemical and radiation exposure are present. No immunologic mechanisms are involved in phototoxic reactions, so they can manifest themselves during an initial exposure. Phytophotodermatitis caused by bergamot oil, parsley, celery, dates, and other plants containing the furocoumarins is a classic example of phototoxic reaction (Figure 1). At a molecular level, most phototoxic reactions (eg, in the case of acrilavine, porphyrins, chlorothiazide, tetracyclines, nonsteroidal anti-inflammatory agents, quinolones, and certain dyes, such as methylene blue) develop in the presence of oxygen, in which free radicals resulting from photo-oxidation and peroxidation processes cause injury to cell nuclei, cytoplasm, and cellular membrane components. Phototoxicity reactions to psoralens, although rarely requiring molecular oxygen, are for the most part oxygen independent. In those cases, UV-A-induced covalent binding (formation of cyclobutane dimers) between the chemical and the molecules of DNA occurs. Similar dimers are formed between chlorpromazine and RNA molecules.13,20 The factors that strongly influence the incidence, intensity, and clinical features of phototoxic reactions include (1) the nature, concentration, absorption, and pharmacokinetics of the drug; (2) quantity and spectrum of radiant energy; and (3) factors related to the skin thickness of the stratum corneum, quantity of melanin, temperature, and humidity.

Most phototoxic eruptions clinically resemble exaggerated sunburns and are characterized by rapid onset of a burning sensation, erythema, edema, and sometimes vesiculation (Figure 2). Eruptions develop shortly after exposure to light with intensity increasing in a dose-dependent manner. Persons with light skin (types I and II) seem to be more prone to develop phototoxic reactions, whereas in darker skins melanin offers some degree of protection.

A distinct type of phototoxic eruption consisting of diffuse pigmentation on light-exposed areas is reported in relation to several drugs, including amiodarone, chlorpromazine, minocycline, and quinine. The phototoxic effect of some drugs on nails is a well-known phenomenon referred to as photo-onycholysis. The latter may be the only manifestation of photosensitivity.

Pseudoporphyria, a condition clinically similar to porphyria cutanea tarda but lacking abnormalities in porphyrin metabolism, has been described as a variant of a phototoxic reaction in conjunction with sulfonamides, griseofulvin, nalidixic acid, and the tetracyclines.14

Photoallergy

Photoallergy refers to immunologically mediated photosensitivity reactions, in which immediate (humoral-mediated) hypersensitivity, delayed (cell-mediated) hypersensitivity, or both develop to a photo-activated compound (a drug or chemical) transformed into a hapten or a complete antigen during radiation.20 In contrast to phototoxic reactions, photoallergy is usually elicited by the longer UV-A wavelengths (>315 nm). Phototoxic drug responses develop only in sensitized persons and are not dose dependent, although a sensitized person is likely to get a stronger reaction with a much higher dose.13,21,22 Cell-mediated responses require a latency period for the immunologic memory to develop after the first contact with the photosensitizer; on subsequent exposures the elicitation of response is shorter.1,22

The delayed type of photoallergy is more frequent. The pathogenetic mechanisms of photoallergic reactions are quite similar to those seen in allergic dermatitis, ie, the photoantigen (hapten) is presented by epidermal Langerhans cells to T lymphocytes with all the subsequent features of delayed skin hypersensitivity response of lymphocytic infiltration, release of lymphokines, activation of mast cells, and increased cytokine expression.13

According to the mode of administration of the photosensitizer, photoallergic reactions can be classified as either contact photoallergic dermatitis or photoallergy induced by systemic agents.21 Several factors may influence the incidence, intensity, and some clinical features of photoallergic reactions: quantity and location of the drug on or in the skin; quantity, spectrum, and penetration capabilities of the activating radiation; thickness of the horny layer; degree of melanin pigmentation; and immunologic state of the affected person.20 The last seems to be of great importance, because photosensitivity reactions are found frequently in immunocompromised human immunodeficiency virus–infected patients.23
Clinically, drug-induced photosensitive reactions can appear as solar urticaria or as eczematous or lichenoid dermatitis on predominantly light-exposed areas.\textsuperscript{13,20} The eruption usually disappears spontaneously once the offending photosensitizer has been removed. In rare instances, however, photosensitivity may persist longer and relapse with minimal UV radiation, despite the lack of contact with the photosensitizing substance. This condition, defined as persistent light reaction, is observed in relation to topical photosensitizers and, more rarely, through systemic photosensitization.\textsuperscript{13,20} 

**Diagnosis**

Determining the exact mechanism of a photosensitivity reaction is important because phototoxins can be manipulated and rendered harmless by decreasing the dose or the amount of radiation, whereas photosensitizing reactions do not significantly change with alterations in these parameters.\textsuperscript{22} Unfortunately, several agents confuse the issue by having both phototoxic and photosensitizing properties. These include the phenothiazines, quinolone derivatives, sulfonamides, and thiazide diuretics.\textsuperscript{21,22}

**Drug-Induced Lupus Erythematosus**

More than 70 drugs have been reported as causing symptoms and serologic markers of lupus erythematosus.\textsuperscript{24} Drug-induced lupus resembles a mild form of systemic lupus erythematosus marked by the presence of antinuclear antibodies in the blood; this presence generally resolves on discontinuation of the drug.\textsuperscript{25} Drugs associated with drug-induced lupus have no common chemical makeup or structure and seem to influence immune regulation in different ways.\textsuperscript{16,26} Probably mimicking the spontaneous disease rather than unmasking an underlying diathesis.\textsuperscript{27}

Subacute cutaneous lupus erythematosus is the subtype of lupus erythematosus most frequently associated with photosensitivity. Symptoms of subacute cutaneous lupus erythematosus include widespread symmetric superficial lesions, often of the shoulders, upper part of the chest, back, and neck, which evolve into psoriasiform or annular plaques. There is epidermal separation because of severe injury to the basal keratinocytes.\textsuperscript{20} While numerous drugs can induce lupus erythematosus–type abnormalities, fewer have been reported as associated with subacute cutaneous lupus erythematosus and photosensitivity (Table 1). Those that include hydrochlorothiazide, griseofulvin,\textsuperscript{26} and, more rarely, sulphasalazine.\textsuperscript{29}

The mechanism of photosensitivity reactions in drug-induced lupus is not well understood. It has been suggested that a drug may interact chemically with cell molecules to enhance the immunogenic susceptibility of self antigens and also that these drugs or their metabolites may alter the functioning of immune active cells.\textsuperscript{23} It has been shown in vitro and in vivo that the binding of specific antinuclear antibodies to the surface of keratinocytes is accentuated by exposure to UV light. This same antibody system is highly associated with photosensitive lupus erythematosus syndromes,\textsuperscript{30} suggesting that photoactive drugs may be synergistic with these antibodies in producing the cutaneous lesions of subacute cutaneous lupus erythematosus.\textsuperscript{31}

**METHODS FOR IDENTIFYING PHOTOSENSITIVITY OF DRUGS**

To date, no single method of assaying drug photosensitivity has emerged as the ideal yardstick for establishing photosensitivity. A panel of in vitro and in vivo assay systems has been established for studying photosensitivity reactions, which taken together have proven useful either to predict or to confirm the photosensitizing hazards of a new compound.\textsuperscript{17,32}

In vitro methods used in preliminary screening for photosensitivity include measurement of UV and visible light absorption spectra of the drug; quantification of its ability to photooxidize histidine, to induce photohemolysis, and to inhibit yeast growth and mitogen-induced lymphocytic blast transformation; testing on skin equivalents; mutagenicity testing on different organisms and strains; and ability to bind to a protein carrier, such as serum albumin.\textsuperscript{32} Once the photosensitizing potential has been confirmed through these screening tests, sophisticated in vitro methods may be applied to explore the possible photosensitivity mechanisms and pathways through measurement of triplet excited state production of excited singlet state oxygen,\textsuperscript{22,23} and photodynamic interaction with DNA (DNA strand breaks and conversion of the supercoiled closed circular form of plasmid DNA to the open circular form).\textsuperscript{33} While the photosensitizing action of drugs depends on factors that could not be reproduced in vitro, such as those governing penetration and localization of topical agents in the skin, as well as absorption, metabolism, distribution, and excretion of systemic drugs, several animal models are used to assess a photosensitizer’s potency in vivo. Hairless mouse skin, guinea pig, albino mice, and rat auricular skin and retina are most commonly used for experimentally reproducing human skin response to drugs and UV exposure.\textsuperscript{19,22,35}

Under clinical conditions, the epidemiological data and clinical features are usually conclusive enough

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**Table 1. Drug-Induced Lupus Erythematosus (LE)**

<table>
<thead>
<tr>
<th>Drugs Associated With Reactive LE Serology and/or Clinical Manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydralazine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drugs Associated With LE and Photosensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Griseofulvin</td>
</tr>
</tbody>
</table>

*Data in this table from Harber and Baer,\textsuperscript{16} Cush and Goldings,\textsuperscript{27} Gould et al,\textsuperscript{26} Alarcon-Segovia and Kraus,\textsuperscript{27} Shapiro et al,\textsuperscript{28} Laversuch et al,\textsuperscript{29} and Miyagawa et al.\textsuperscript{31}
for the diagnosis of a photosensitivity drug eruption. Histological findings can be hardly decisive in differentiating phototoxic from photoallergic reactions, but they may be relevant for the diagnosis of lichenoid eruptions, porphyria cutanea tarda, and pseudoporphyria from other (idiopathic) photosensitivity disorders. In porphyria cutanea tarda and pseudoporphyria, the direct immunofluorescence testing reveals a characteristic deposition of IgG at the basement membrane zone and around dermal blood vessels (Figure 3).36

A provisional diagnosis of photoallergic contact is confirmed by the technique of photopatch testing, in which the photosensitizing drug is simultaneously applied at 2 sites, 1 of which is subsequently irradiated. A number of standard photopatch test series exist for screening chemically induced photoallergy.37

**PHOTOSENSITIVITY REACTIONS TO ANTIMICROBIAL DRUGS**

The ability to cause photosensitivity reactions is a common adverse effect of several anti-infective agents and their derivatives. Most of them are cyclic and tricyclic hydrocarbons, frequently containing an alternative double-bond isoprene or naphthyridine nucleus.13 Both phototoxic and photoallergic reactions are reported (Table 2).

**Topical Antimicrobials**

The halogenated salicylanilide derivatives tetrachorosalicylanilide; 3,4′,5-tribromosalicylanilide; 4′,5-dibromosalicylanilide; and the antifungal bromochlorosalicylanilide incorporated as germicides and deodorants in soaps and other toiletries are typical examples of topical photosensitizers. The epidemic incidence of photocontact allergic dermatitis and persistent light eruption they caused in the 1960s rapidly led to their withdrawal from the market in most countries. Other related topical antimicrobials, such as carbamidic derivatives hexachlorophene and 3,4,4′-trichlorocarbanilide (triclocarban), actually used as antiseptics, and antibiotics are phototoxins.17

Cases of phototoxic reactions have been recently described in conjunction with some cosmetic, antiseptic, and spermicidal preparations (eg, hexoméidine) containing the nonionic surfactants nonoxynol 9 and 10.38 Local antiseptics containing sulfanilamide, sulfa-derived drugs, including sulfanilamide antibacterials, hypoglycemics, and diuretics, have been well-known causes of photosensitivity reactions. The action spectrum of sulfonamides lies within the UV-B range and, to a lesser extent, in the UV-A wavelengths.37 Photoallergic and, less frequently, phototoxic reactions are common adverse effects seen among patients treated with sulfafacetamide, sulfadiazine, sulfaguanidine, and sulfapyridine.

A case of phototoxic eruption progressing to Stevens-Johnson syndrome was recently reported after prophylactic ingestion of the antimalarial combination product containing chloroquine and sulfadoxine-pyrimethamine (Fansidar), the latter component being incriminated as the cause of this unusual adverse reaction.

Other sulfonamides, such as sulfamethoxazole and the trimethoprim-sulfamethoxazole combination, although known to induce Stevens-Johnson syndrome and toxic epidermal necrolysis, are relatively safe in regard to photosensitivity. Sulfasalazine (salazopyrin), used in the treatment of rheumatoid arthritis, chronic bowel disease, and other inflammatory diseases, is reported to produce a diffuse hyperpigmentation of the skin in light-exposed areas.42,43

Dapsone (formerly dianimodiphenylsulfone), a sulfone antibac-

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**Table 2. Photoactive Antimicrobials**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Action Spectrum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical antimicrobials†</td>
<td>Unknown</td>
</tr>
<tr>
<td>Chloroquinol</td>
<td>UV-A</td>
</tr>
<tr>
<td>Halogenated salicylanilides‡</td>
<td>UV-A</td>
</tr>
<tr>
<td>Sulfonamides</td>
<td>UV-B</td>
</tr>
<tr>
<td>Olaziquindox</td>
<td>UV-A, UV-B</td>
</tr>
<tr>
<td>Topical antifungals</td>
<td>UV-A</td>
</tr>
<tr>
<td>Jadit</td>
<td>UV-A</td>
</tr>
<tr>
<td>Multifungin</td>
<td>UV-A</td>
</tr>
<tr>
<td>Fentichlor</td>
<td>UV-A</td>
</tr>
<tr>
<td>Antibiotics†</td>
<td>Unknown</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>UV-A</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>UV-A</td>
</tr>
<tr>
<td>Nalidixic acid</td>
<td>UV-A</td>
</tr>
<tr>
<td>Ceftazidine</td>
<td>Unknown</td>
</tr>
<tr>
<td>Griseofulvin</td>
<td>UV-A</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>Unknown</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>Unknown</td>
</tr>
<tr>
<td>Sulfonamides</td>
<td>UV-B</td>
</tr>
</tbody>
</table>

*Data in this table from Gould et al.26†Topical antimicrobials are photoallergens, and antibiotics are phototoxins.‡Halogenated salicylanilides may have UV-B as an action spectrum.

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**Sulfonamide Derivatives**

Since 1939 when Epstein50 first reported photoallergic contact dermatitis following intradermal injection of sulfanilamide, sulfa-derived drugs, including sulfanilamide antibacterials, hypoglycemics, and diuretics, have been well-known causes of photosensitivity reactions. The action spectrum of sulfonamides lies within the UV-B range and, to a lesser extent, in the UV-A wavelengths.37 Photoallergic and, less frequently, phototoxic reactions are common adverse effects seen among patients treated with sulfafacetamide, sulfadiazine, sulfaguanidine, and sulfapyridine.

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material known for years for its antilepromatous action and currently prescribed in the treatment of several noninfectious dermatoses, was identified in the 1980s as causing photosensitivity. Six cases of presumably phototoxic dermatitis were reported from India among patients with leprosy who were treated for 2 to 9 months with dapsone in a standard dosage of 100 mg/d.44

Sulfonamides should be also considered among drugs capable of exacerbating preexisting hepatic porphyrias and inducing sporadic porphyria cutanea tarda. Several cases of drug-induced porphyria cutanea tarda have been reported in association with the sulfonylurea hypoglycemic drugs tolbutamide and chlorpropamide, which are chemically related to sulfonamide compounds.17,45

**Grisofulvin**

For many years, griseofulvin has been persistently listed among the systemic photosensitizing drugs. The precise mechanisms of the various photosensitivity reactions it causes are not completely clarified; however, UV-A radiation is responsible for eliciting griseofulvin photosensitivity.

In animal models, griseofulvin in high doses interferes with porphyrin metabolism to cause phototoxic reactions. In humans, griseofulvin has been shown to inhibit heme synthesis, which results in increased urinary porphyrin excretion and appearance of acute hepatic porphyrias, especially in susceptible individuals.10-18 Griseofulvin is known to exacerbate a preexisting systemic lupus erythematosus or unmask a lupus diathesis. There are also reports of cases of subacute cutaneous lupus erythematosus induction by oral administration of griseofulvin.31

**Tetracyclines**

Tetracycline antibiotics serve as an excellent example of the phototoxic hazards of antibacterial agents. Among them, chlor derivatives are most frequently reported to cause phototoxicity.9,40,50 Chlorotetracycline and doxycycline are more phototoxic than tetracycline, oxytetracycline, methacycline, or minocycline. In one study,31 doxycycline (200 mg/d) was compared with minocycline (200 mg/d), and phototoxic reactions were noted in 11 of 15 subjects and 0 of 17 subjects, respectively. In a double-blind crossover study with doxycycline (100 mg twice daily), lymecycline (600 mg twice daily), and placebo, run-in combination with UV-A radiation in a series of 15 healthy volunteers, doxycycline was found to have greater phototoxic potency than lymecycline (which is available abroad). The phototoxic reaction was dependent on the dose of doxycycline and the UV-A intensity. Bjellerup and Ljunggren32 recommend that therapy with doxycycline be avoided during summertime and in sunny climates. There are differences in the phototoxic potential of tetracycline derivatives in vitro as well.46 In an assay of the UV-A–induced hemolysis of human red blood cells in the presence of 8 commercial tetracyclines, the extent of cells undergoing hemolysis was 85% for doxycycline (50 μg/mL; UV-A, 72 J/cm²), 36% for methacycline (200 μg/mL), and only 18% for tetracycline, oxytetracycline, and chlortetracycline (200 μg/mL). Minocycline did not show hemolytic effect.51

Common clinical manifestations of tetracycline photosensitivity include sunburn, sometimes with blistering, papular eruption, or both.9 Marked residual pigmentation is frequently observed. Photonicohylysis is a common feature with many tetracyclines, occurring 3 to 6 weeks after drug administration on the distal portion of 1 or several nails. In addition, chromonychia with white, yellow, or brown discoloration of nail plates may be observed (Figure 5).
1980s, several fluoroquinolones have been marketed worldwide, including ciprofloxacin, ofloxacin, norfloxacin, pefloxacin, lomefloxacin, temafloxacin, fleroxacin, enoxacin, tosufloxacin, and sparfloxacin. It has become, however, increasingly clear that new fluoroquinolones still exhibit varying degrees of photosensitizing activity. For the most part, they produce photosensitive reactions, although there are a few reports of photoallergy as well. Most of the photoallergic reactions are reported among patients treated with enoxacin and characterized by eczematous clinical and histological features, a prolonged induction period after first administration, and a dose-independent reproducible response. Three cases of photoallergic reactions to lomefloxacin were reported after confirmation by positive results to scarified photopatch tests. A prolonged lichenoid eruption is observed in some patients treated with sparfloxacin, but photoallergy has not been confirmed with this drug. A severe generalized febrile subcorneal pustular eruption has been reported in a patient treated with norfloxacin. Photo-onycholysis is an occasional adverse effect of treatment with fluoroquinolones.

Clinical and epidemiological studies encompassing all fluoroquinolone compounds are not available. But, empirical studies have suggested pefloxacin and fleroxacin as the most potent photosensitizers, while enoxacin, norfloxacin, and ofloxacin are less potent. Comparing the phototoxic histological changes of mouse ear skin occurring following systemic administration of quinolones and UV-A exposure, sparfloxacin given in doses of 50 or 100 mg/kg induced responses similar to those of enoxacin,34 and sparfloxacin has been reported with this drug. A severe generalized febrile subcorneal pustular eruption has been reported in a patient treated with norfloxacin. Photo-onycholysis is an occasional adverse effect of treatment with fluoroquinolones.

Management of Antimicrobial Photosensitivity

Photosensitization of the skin by several groups of antimicrobial agents is a problem that is increasingly attracting attention. It is still anticipated that the ideal antimicrobial drug providing appropriate bacterial coverage in a dose too small to cause photosensitivity will be found among tetracyclines and fluoroquinolones. If the photosensitizing effect of a drug is known before patient exposure, appropriate clinical management might control the incidence of photosensitivity adverse reactions. Avoidance of direct sunlight and sun-tanning facilities, use of protective clothing and appropriate UV-A and UV-B sunscreens, and evening dosing strategy are factors that can minimize the risk of photosensitivity effects of most antimicrobials.

Accepted for publication February 12, 1998.

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