by UV-B. Patients with chronic actinic dermatitis usually manifest a broad spectrum of UV hyperresponsiveness and require meticulous photoprotection, including avoidance of sun exposure, use of high-SPF (>30) sunscreens, and, in severe cases, systemic immunosuppression, such as with azathioprine.

The management of drug photosensitivity involves first and foremost the elimination of exposure to the chemical agents responsible for the reaction and the minimization of sun exposure. The acute symptoms of phototoxicity may be ameliorated by cool moist compresses, topical glucocorticoids, and systemically administered NSAIDs. In severely affected individuals, a rapidly tapered course of systemic glucocorticoids may be useful. Judicious use of analgesics may be necessary.

Photoallergic reactions require a similar management approach. Furthermore, patients with persistent light reaction and chronic actinic dermatitis must be meticulously protected against light exposure. In selected patients to whom chronic systemic high-dose glucocorticoids pose unacceptable risks, it may be necessary to employ an immunosuppressive drug such as azathioprine, cyclophosphamide, cyclosporine, or mycophenolate mofetil.

Porphyria The porphyrias (Chap. 430) are a group of diseases that have in common inherited or acquired derangements in the synthesis of heme. Heme is an iron-chelated tetrapyrrole or porphyrin, and the nonmetal chelated porphyrins are potent photosensitizers that absorb light intensely in both the short (400–410 nm) and the long (580–650 nm) portions of the visible spectrum.

Heme cannot be reutilized and must be synthesized continuously. The two body compartments with the largest capacity for its production are the bone marrow and the liver. Accordingly, the porphyrias originate in one or the other of these organs, with an end result of excessive endogenous production of potent photosensitizing porphyrins. The porphyrins circulate in the bloodstream and diffuse into the skin, where they absorb solar energy, become photoexcited, generate ROS, and evoke cutaneous photosensitivity. The mechanism of porphyrin photosensitization is known to be photodynamic, or oxygen-dependent, and is mediated by ROS such as singlet oxygen and superoxide anions.

Porphyria cutanea tarda is the most common type of porphyria and is associated with decreased activity of the enzyme uroporphyrinogen decarboxylase. There are two basic types of PCT: (1) the sporadic or acquired type, generally seen in individuals ingesting ethanol or receiving estrogens; and (2) the inherited type, in which there is autosomal dominant transmission of deficient enzyme activity. Both forms are associated with increased hepatic iron stores.

In both types of PCT, the predominant feature is chronic photosensitivity characterized by increased fragility of sun-exposed skin, particularly areas subject to repeated trauma such as the dorsa of the hands, the forearms, the face, and the ears. The predominant skin lesions are vesicles and bullae that rupture, producing moist erosions (often with a hemorrhagic base) that heal slowly, with crusting and purplish discoloration of the affected skin. Hypertrichosis, mottled pigmentary change, and scleroderma-like induration are associated features. The diagnosis can be confirmed biochemically by measurement of urinary porphyrin excretion, plasma porphyrin assay, and assay of erythrocyte and/or hepatic uroporphyrinogen decarboxylase. Multiple mutations of the uroporphyrinogen decarboxylase gene have been identified in human populations. Some patients with PCT have associated mutations in the *HFE* gene, which is linked to hemochromatosis; these mutations could contribute to the iron overload seen in PCT, although iron status as measured by serum ferritin, iron levels, and transferrin saturation is no different from that in PCT patients without *HFE* mutations. Prior hepatitis C virus infection appears to be an independent risk factor for PCT.

Treatment of PCT consists of repeated phlebotomies to diminish the excessive hepatic iron stores and/or intermittent low doses of chloroquine and hydroxychloroquine. Long-term remission of the disease can be achieved if the patient eliminates exposure to porphyrinogenic agents and prolonged exposure to sunlight.

Erythropoietic protoporphyria originates in the bone marrow and is due to a decrease in the mitochondrial enzyme ferrochelatase secondary to numerous gene mutations. The major clinical features include acute photosensitivity characterized by subjective burning and stinging of exposed skin that often develops during or just after sun exposure. There may be associated skin swelling and, after repeated episodes, a waxlike scarring.

The diagnosis is confirmed by demonstration of elevated levels of free erythrocyte protoporphyrin. Detection of increased plasma protoporphyrin helps distinguish erythropoietic protoporphyria from lead poisoning and iron-deficiency anemia, in both of which erythrocyte protoporphyrin levels are elevated in the absence of cutaneous photosensitivity and elevated plasma protoporphyrin levels.

Treatment includes reduction of sun exposure and oral administration of the carotenoid β-carotene, which is an effective scavenger of free radicals. This drug increases tolerance to sun exposure in some affected individuals, although it has no effect on deficient ferrochelatase.

An algorithm for managing patients with photosensitivity is presented in Fig. 75-1.

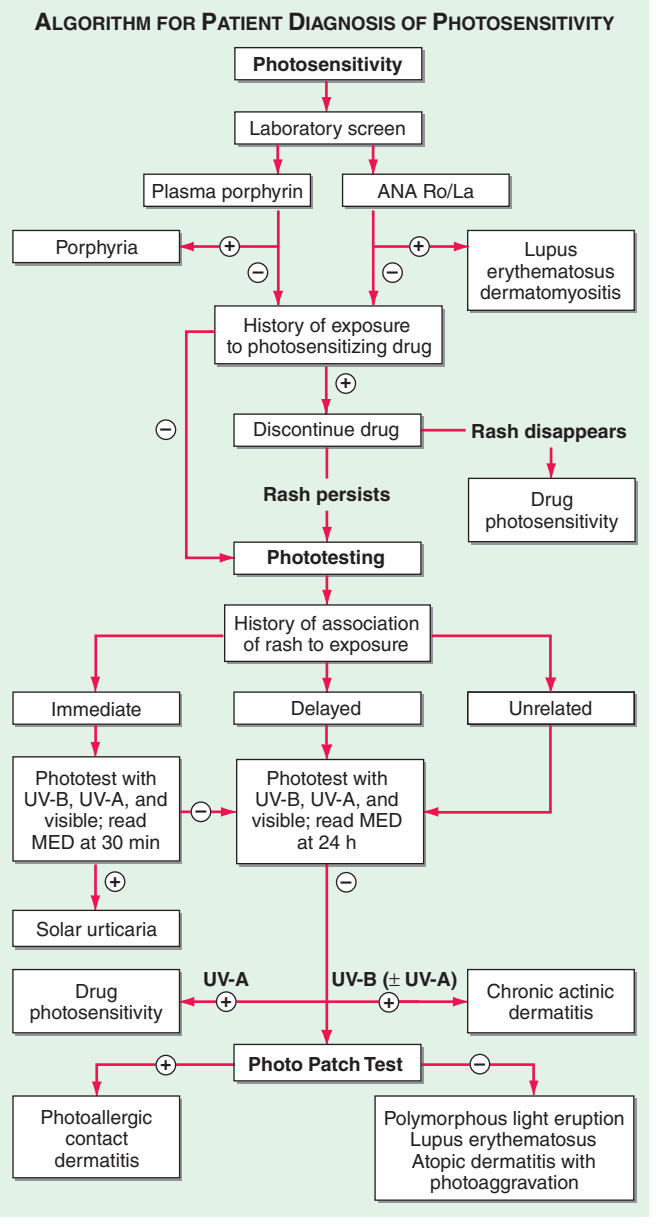

FIGURE 75-1 Algorithm for the diagnosis of a patient with photosensitivity. ANA, antinuclear antibody; MED, minimal erythemal dose; UV-A and UV-B, ultraviolet spectrum segments including wavelengths of 320–400 nm and 290–320 nm, respectively.