PUVA THERAPY: IMMUNOLOGIC AND GENOTOXIC APPROACHES TO RISK EVALUATION

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PUVA (psoralen and near ultraviolet light) is a DNA-damaging, clinically effective treatment. If we have patience, studies of PUVA therapy should give us a rare opportunity to learn much about not only the diseases it treats, but also about diseases it may cause. PUVA is a gamble, a calculated risk.

"Leprosy is not exactly what I have, but what in the Bible is called leprosy (see Leviticus 13, Exodus 4:6, Luke 5:12-13) was probably this thing, which has a twisty Greek name it pains me to write. The form of the disease is as follows: spots, plaques, and avalanches of excess skin, manufactured by the dermis through some trifling but persistent error in its metabolic instructions, expand and slowly migrate across the body like lichen on a tombstone. I am silvery, scaly. Puddles of flakes form wherever I rest my flesh. Each morning, I vacuum my bed. My torture is skin deep: there is no pain, not even itching; we lepers live a long time, and are ironically healthy in other respects. Lusty, though we are loathsome to love. Keen-sighted, though we hate to look upon ourselves. The name of the disease, spiritually speaking, is Humiliation."

John Updike, "From the Journal of a Leper"
Psoriasis is a common chronic dermatologic disease which, when extensive, tests in the extreme the hypothesis that beauty is only skin deep. Its consequences in terms of morbidity are not severe, but, like leprosy, psoriasis can cause social debilitation and profound psychological anguish. It can occur in any part of the skin, but most commonly affects sites of trauma (elbows, knees, lower back, scalp). The primary lesion is a sharply demarcated, erythematous papule, which coalesces with others to form plaques covered with micaceous scale. About 6% of patients with psoriasis also have an associated arthritis.

Tissues affected by psoriasis display parakeratotic hyperkeratosis and acanthosis, and contain Monroe microabscesses, elongated dermal papillae, and engorged dermal capillaries. Accelerated epidermal turnover occurs such that cells multiply, mature, and exfoliate at 7-10 times the normal rate. The stratum granulosum is absent or diminished, and an inflammatory infiltrate invades the subpapillary dermis. The aetiology of common psoriasis is not known; the disease is not contagious, but it is probably a polygenic threshold disease most likely to occur in individuals carrying HL-A13 and HL-A17 (Svejgaard et al., 1974). There is no known cure for psoriasis.

Various treatment modalities have been used to achieve remission in widespread plaque psoriasis. As recently as ten years ago, arsenic trioxide and ionizing radiation were used to treat persistent lesions. Conventional approaches consist of topical applications of agents such as coal tar and dithranol, usually in combination with far ultraviolet light (UVB) irradiation during 2-4 week hospital admissions. Topical steroid preparations are popular, too, and are not unpleasant to the senses, as are the tars. However, steroids can produce unstable disease, and bear attendant risks of adrenocortical suppression after systemic absorption. Treatments using cytotoxic chemicals such as methotrexate are generally very effective but unsafe, at least with respect to their acute toxicity, especially evident in the liver.

In 1974 (Parrish et al., 1974), a new photochemotherapeutic approach to psoriasis employing psoralen and near ultraviolet light (UVA) was introduced. This treatment, known as PUVA, has come into widespread use for generalized psoriasis. It is also being used to treat several other conditions with dermatologic manifestations, including mycosis fungoides, urticaria pigmentosa, and vitiligo (hypopigmentation).

Psoralens are derived from the furocoumarins, which are naturally occurring compounds extractable from Ammi majus, a weed that grows in the Nile valley. The most commonly used derivative