MECHANISM OF TETRACYCLINE PHOTOTOXICITY

To the Editor:

We read with interest the recent paper, "Mechanism of Tetracycline Phototoxicity," by Hasan et al [1]. The authors studied the in vitro photodegradation rate and in vitro phototoxicity of seven types of tetracycline antibiotics and proposed that phototoxicity induced by these agents involves the photosensitization of biologic molecules and the production of photoproducts. These findings complemented those of our previous study with demethylchlortetracycline (DMCT), published in 1983 [2]. We demonstrated that one of the biologic substrates involved in DMCT-induced phototoxicity was the complement system. Our conclusion was reached based on the following: (1) In vitro, irradiation of serum containing DMCT resulted in photoinactivation of the complement system, associated with the generation of chemotactic activity for human polymorphonuclear leukocytes. (2) In guinea pigs, depletion of complement, or induction of leukopenia, suppressed the DMCT phototoxic response, indicating that the complement system, and its products of activation are pivotal for the full manifestation of DMCT-induced phototoxicity in vivo.

In vitro, irradiation of DMCT prior to its addition to the serum abrogated the ability of DMCT to photoinactivate the complement system [2]. We suggested this was due to the photodegradation of the DMCT molecule, as reported previously by Stratigos and Magnus [3]. This photodegradation was confirmed by Hasan et al [1].

While partial understanding of phototoxicity induced by the tetracycline group has been achieved, it is obvious that more studies need to be done to fully elucidate its pathogenesis in humans.

Henry W. Lim, M.D.
Irma Gigli, M.D.
Division of Dermatology
University of California
San Diego, California

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REPLY

We appreciate the interest of Drs. Lim and Gigli in our publication "Mechanism of Tetracycline Phototoxicity" [1]. The two investigations, that of Lim et al [2] and ours, appear to focus on different steps in the mechanism of tetracycline phototoxicity. All photobiologic responses are initiated by absorption of electromagnetic radiation. The subsequent photochemical reactions initiate biochemical processes that result in the expression of a biologic response. Our studies addressed the light absorption process and the formation of radicals and reactive oxygen species. Based on our characterization of visible-absorbing tetracycline photoproducts as photosensitizers, we hypothesized that these photoproducts may be responsible for the extension of the phototoxicity action spectrum beyond the long-wavelength end of the tetracycline absorption spectrum. The findings of Lim et al [2] would suggest that the biologic expression of DMCT-induced phototoxicity requires an intact complement system. However, the involvement of complement in phototoxicity induced by long-wavelength absorbing photoproducts was not tested, since only UVA light was used in the work of Lim et al [2]. We agree with Drs. Lim and Gigli that the mechanisms for phototoxicity induced by the tetracycline group of antibiotics are complex and more investigations are needed.

Tayyaba Hasan, Ph.D.
Irene E. Kochevar, Ph.D.
Daniel J. McAuliffe, B.S.
Department of Dermatology
Harvard Medical School
Massachusetts General Hospital
Boston, Massachusetts

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