CLINICAL EXPERIENCE WITH THE EFFECT OF ORAL 8-METHOXYPSORALEN ON THE PIGMENTARY RESPONSES OF THE SKIN TO SUNLIGHT*

NORMAN B. KANOF, M.D., Med.Sc.D.

8-methoxypsoralen can sometimes induce melanin repigmentation in vitiliginous skin. Since this fact was first formally reported by El Mofty (1) in 1952, many investigators have observed the effect of methoxsalen on the responses of "normal" and diseased skin to sunlight. It was soon reported (2, 3) that topical application of 8-methoxypsoralen prior to sun exposure would increase the pigmentation of "normal" skin. Many of us who were studying this drug and its effects in vitiligo also noted that its oral use seemed to intensify the pigmentary response of normal skin to sun exposure. This action was discussed informally many times before it was reported in the literature in 1955 (4, 5).

Since 1952, I have had the opportunity to observe the effect on the skin's responses to sunlight of methoxsalen administered orally in more than 200 persons. This number includes patients with and without vitiligo, in clinic and private practice.

Methoxsalen was taken in doses of ten or twenty milligrams one to two hours prior to sun exposure once or twice daily. The maximum daily dose of the psoralen was 40 mg. Many patients took this drug for many months without interruption. Because some early reports implied that toxic reactions to methoxsalen might occur, urinalyses, blood counts and liver function tests were performed at regular intervals on many of these persons. We did not observe any evidence of liver damage or any effect on the blood or urine from 8-methoxypsoralen in any of our patients. An occasional patient complained of some gastrointestinal distress, but it was never necessary to discontinue therapy because of this.

The amount of sun exposure which should follow the administration of methoxsalen was difficult to standardize because of the wide range of individual tolerance. The chemical augments all of the skin's responses to sunlight, the unwanted inflammatory ones as well as the sought-after pigmentation. It is necessary to stress the fact that methoxsalen does not allow limitless sun exposure without burning (which many patients assume). Our rule of thumb was to allow initially such sun exposure as the patient knew, from past experience, his skin could tolerate without burning. The length of exposure could then be increased as hyperpigmentation and especially as thickening of the horny layer occurred.

When methoxsalen and sunlight exposure were combined in this manner, distinct intensification of the tanning response beyond that to be expected from a similar exposure to sunlight without preceding 8-methoxypsoralen occurred in about 75 per cent of the patients. Little or no augmentation of tanning occurred in the remaining 25 per cent. Redness and some mild discomfort of the exposed areas did occasionally occur but severe inflammatory effects were not seen unless there was gross overexposure to sunlight before hyperpigmentation had appeared.

SUMMARY

8-methoxypsoralen taken by mouth prior to sun exposure augments the skin responses to sunlight.

By careful attention to the dose of the drug and to the amount of subsequent sun exposure, it is possible, in many persons, greatly to accentuate the skin's pigmentary responses to sunlight with little or no increase in the skin's inflammatory response.

We have seen no toxic effects from the oral administration of methoxsalen in doses up to 40 mg. daily for many months.

Carefully controlled investigative procedures are necessary to determine the safest and most efficient method to use methoxsalen for sun tanning.

* From the Department of Dermatology and Syphilology of the New York University-Post-Graduate Medical School (Dr. Marion B. Sulzberger, Chairman) and the Skin and Cancer Unit of the University Hospital, New York, N. Y.

REFERENCES

1. El Mofty, A. M.: Observations on the use of *Ammi majus* Linn. in vitiligo. Brit. J. Dermat., **65:** 431, 1952.
2. Lerner, A. B., Denton, C. R. and Fitzpatrick, T. B.: Clinical and experimental studies with 8-methoxypsoralen in vitiligo. J. Invest. Dermat., **20:** 299, 1953.
3. Kanof, N. B.: Melanin formation in vitiliginous skin under the influence of external applications of 8-methoxypsoralen. J. Invest. Dermat., **24:** 5, 1955.
4. Lerner, A. B.: Potentiation of suntanning through ingestion of 8-methoxypsoralen. J. Invest. Dermat., **25:** 1, 1955.
5. Fitzpatrick, T. B., Hopkins, C. E., Blickenstaff, D. D. and Swift, S.: Augmented pigmentation and other responses of normal human skin to solar radiation following oral administration of 8-methoxypsoralen. J. Invest. Dermat., **25:** 187, 1955.