Correspondence

Effect of ketoconazole in the hyperandrogenism, insulin resistance and acanthosis nigricans (HAIR-AN) syndrome

To the Editor: We read with interest the article by Van Cutsem et al. (J AM ACAD DERMATOL 1991;25:257-61) regarding the antiinflammatory effects of ketoconazole. In their experimental model, the authors found topical ketoconazole to be highly effective in reducing hyperkeratosis. In a previous experience,[1] oral administration of ketoconazole has proved to be useful in the hyperandrogenism, insulin resistance, and acanthosis nigricans (HAIR-AN) syndrome. We have reported that it improves the acanthosis nigricans in addition to the androgen profile and menstrual pattern.[2]

The beneficial effect of ketoconazole on acanthosis nigricans in this syndrome may be related to (1) a decrease in insulin resistance secondary to the decreased androgen level[3]; (2) a possible antiinflammatory effect through inhibition of the arachidonic acid cascade (Van Cutsem et al.); and (3) a hypothetical direct action of ketoconazole on the somatomedin C/insulin-like growth factor I receptor, stimulation of which by high concentrations of insulin induces keratinocyte replication.[4, 5]

We conclude that oral ketoconazole, apart from its known effects on hyperandrogenism and induction of cyclic menses, may alleviate acanthosis nigricans, at least in the context of the HAIR-AN syndrome.

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REFERENCES

1. Pepper GM, Poretsky L, Gabrilove JL, et al. Ketoconazole reverses hyperandrogenism in a patient with insulin resistance and acanthosis nigricans. J Clin Endocrinol Metab 1987;65:1047-52.
2. Muñoz-Torres M, Vidal Puig A, Tercedor J, et al. Hiperandrogenismo, resistencia a la insulina y acantosis nigricans: respuesta a dosis bajas de ketoconazol. Endocrinologia 1990;37:57-9.
3. Shoupe D, Lobo RA. The influence of androgens on insulin resistance. Fertil Steril 1984;41:385-8.
4. Nickoloff BJ, Misra P, Morhenn VB, et al. Further characterization of the keratinocyte somatomedin-C/insulin-like growth factor I (SM-C/IGF-I) receptor and the biological responsiveness of cultured keratinocytes to SM-C/IGF-I. Dermatologica 1988;177:265-73.
5. Rendon MI, Cruz PD Jr, Sontheimer RD, et al. Acanthosis nigricans: a cutaneous marker of tissue resistance to insulin. J AM ACAD DERMATOL 1989;21:461-9.

Topical mechlorethamine in the treatment of mycosis fungoides

To the Editor: The article by Breneman et al. deals with a subject of great practical importance (J AM ACAD DERMATOL 1991;25:1059-64). However, I would like to call your attention to what is either a serious flaw in the design of the study, or a misprint. The authors state that subjects who used the liquid vehicle were given 50 ml of the study solution, whereas the subjects who used the ointment were told to use "the same amount they normally used," approximately 15 gm. It is difficult to cover the entire body surface with only 15 gm of ointment. Try it sometime. Thirty grams is the bare minimum. No wonder the subjects could manage to cover only about half of their bodies. I hope the authors meant *50*, not *15* gm. If not, I am afraid that their conclusions are erroneous.

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Reply

To the Editor: We thank Dr. Silver for the interest he expressed in our study. When instructing our patients on the use of ointment-based mechlorethamine, we routinely instruct patients to use enough ointment to adequately cover their entire skin surface with a *thin* film of ointment. We discourage application of excessive amounts because of physician and patient concerns regarding the potential for contamination. As Dr. Silver mentions, the patients in the ointment arm of the study were instructed to apply the same amount of ointment they normally used. We estimate the amount generally to be about 15 gm. To estimate the amount of ointment necessary to apply a thin film to the entire skin surface, several investigators applied measured amounts of ointment. We found 15 gm to be adequate for total skin application when a thin film was applied. The purpose of this study was not to standardize the amount of ointment applied but rather to assess the adequacy of coverage achieved during the patients' daily routine. Patients were actually supplied with 30 gm of the ointment vehicle containing the fluorescent dye so that more than enough ointment was available to accommodate variations in individual patients' usage. We

estimated that 15 gm was the average amount applied. The exact amount applied by each patient was not calculated because that was not the point of the study. We should also note that all three of the patients participating in the ointment arm of this study were small. Obviously the amount of ointment necessary for application will vary depending on the size of the patient.

We hope these comments clarify any persisting questions about the methods or results of our study.

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Basal cell carcinoma in North American blacks

To the Editor: We read with interest the article by Abreo and Sanusi (J AM ACAD DERMATOL 1991;25:1005-11), and we were wondering how an albino patient could be included in a group of North American blacks. Even if he is of the black race, this patient with albinism has markedly reduced skin pigment. The albino skin is usually dry and often shows the stigmas of sun damage.[1] These characteristics are well-known predisposing factors for development of a basal cell carcinoma (BCC).

The importance of this article is due to the rarity of BCC in blacks. Pigmentary activity in blacks has two advantages. Blacks rarely have skin cancer, probably because pigmentation with melanosomal dispersion helps protect against the UV rays (290 to 320 nm) of the sun, the most incriminated causative factor in skin cancer.[2] In addition, black skin does not show aging changes as readily as white skin. However, the patient with the most tumors does not have the characteristics of black skin but those of patients with all the predisposing factors for BCC as accepted by the authors of this study.

Although the prevalence of BCC has been estimated to be only 36 in 100,000 for both sexes of albino Bantus (South Africa), this is much higher than the prevalence for nonalbino Bantus.[3] Moreover, of 43 tumors studied in this article, 12 were from the albino patient.

We believe that the inclusion of an albino patient is unfortunate and calls into question the statistical results.

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REFERENCES

1. McDonald C, Kelly AP. Dermatology in black skin. Clin Dermatol 1988;4:1-25.
2. Mora RG, Burris R. Cancer of the skin in blacks: a review of 128 patients with basal-cell carcinoma. Cancer 1981; 47:1436-8.
3. Urbach F. Incidence of nonmelanoma skin cancer. Dermatol Clin 1991;9:751-5.

Reply

To the Editor: Drs. Serna and Vázquez make a valid point when they wonder why we included an albino patient in our series of basal cell carcinomas in North American blacks, and we agree with their opinions. We did it for the sake of completeness and for comparing our data with those of others as can be seen in Tables I, II, and III of our article. In our review of the reported basal cell carcinomas in North American blacks, albino patients were also included by American authors,[1-3] including the series of Mora and Burris that was cited by Drs. Serna and Vázquez. In reviewing basal cell carcinomas in African blacks, albino patients were also included.[4-10] One would expect that albino patients in Africa would develop basal cell carcinoma readily, but for some unknown reason this does not happen. For each basal cell carcinoma, there are approximately 14 squamous cell carcinomas.[5] The skin cancers developing among Cuna albino Indians are almost always squamous cell carcinomas. The Caribbean coast of Lower Panama has the highest prevalence of albinism in the world, about 45 per 100,000.[11]

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REFERENCES

1. Mora RG, Burris R. Cancer of the skin in blacks: a review of 128 patients with basal cell carcinomas. Cancer 1981; 47:1436-8.
2. Burns JE, Eisenhauer ED, Jabaley ME, et al. Cellular immune deficiency in black patients with basal cell carcinoma. J Surg Oncol 1980;13:129-34.
3. Mora RG. Surgical and aesthetic considerations of cancer of the skin in the black American. J Dermatol Surg Oncol 1986;12:24-31.
4. Higginson J, Oettle AG. Cancer incidence in the Bantu and "Cape Colored" races of South Africa: report of a cancer survey in the Transvaal (1953-55). J Natl Cancer Inst 1960;24:589-671.
5. Oettle AG. Skin cancer in Africa. Monogr Natl Cancer Inst 1963;10:197-214.
6. Oluwasanmi JO, Williams AO, Alli AF. Superficial cancer in Nigeria. Br J Cancer 1969;23:714-28.
7. Shapiro MP, Keen P, Cohen L, et al. Skin cancer in the South African Bantu. Br J Cancer 1953;7:45-57.