

## Photoprotection in Vitiligo and Normal Skin

Sir,

We have read with great interest the article by Gniadecka et al. (1), titled "Photoprotection in vitiligo and normal skin", which assesses the quantitative roles in photoprotection of the stratum corneum, viable epidermis and pigmentation in a group of 14 vitiligo patients. The authors claim that the "stratum corneum was the main photoprotective factor not only in vitiligo but also in normally pigmented skin." We do not find this conclusion convincing, since – as we shall argue below – we believe that neither their measurements nor their analysis actually lends support to that claim.

A curious finding of the authors was that, while the "stratum corneum was thicker in vitiligo than in normally pigmented skin", the *total* photoprotection that they found that can be attributed to it is *the same* in both types of skin – this in spite of it being thicker in vitiligo. This fact alone should have warned them of the possibility of a fault in their analysis or, in any case, calls for an explanation to bring the result in line with their main conclusion.

An important factor one must keep in mind when studying the properties of skin, specially when one studies photoprotection, is the skin type or types of the different subjects in the studied population. They did not consider this factor in their study while, in fact, it has been shown that the contribution to photoprotection of melanin in the living epidermis and *stratum corneum* of an individual with skin type II or III is of an entirely different order of magnitude than that of a person with skin type VI (2). Their comparison of the photoprotection offered by "normal" pigmented skin adjacent to that of vitiligo cannot be properly interpreted if one does not know what the "normal" skin type was for each of the studied subjects, and neither can this factor be properly accounted for – or discounted – in the analysis that they performed. In our own studies on the role of constitutional skin type (determined by the amount of melanin), we have shown that the average MED of a population ranging from skin type I to VI shows a linearly increasing relation. From this result the amount of photoprotection offered by melanin can be readily assessed and properly quantified (3).

Gniadecka et al. also claim in their article that the photoprotective role of pigmentation has not yet been elucidated. In our own studies of the protective role of epidermal melanin in a patient with both porphyria variegata and vitiligo (4), we could demonstrate that the photosensitivity of vitiligo skin to UV light of 405 nm was *four* times as high as that of the normally pigmented skin of the same subject, while the sensitivity to both UV of 310 nm and visible light at 500 nm was also elevated by a factor of two. The test site was the lower arm, which was virtually never exposed to the sun because of the severe photosensitivity of the porphyria variegata patient to visible wavelengths of light.

Therefore, we assumed that the thickness of the viable epidermis and the stratum corneum was the same in vitiligo skin compared to normally pigmented skin. So in our experimental setup there was one variable, namely the presence or absence of melanin pigment. In view of our own findings, it is difficult for us to believe their claim that "the effect of

pigmentation in normal skin" was less important than that of the stratum corneum.

To support their claim they refer to the results of their analysis (Table I in Ref. 1), which yielded an estimated ratio of photoprotection of  $1.06 \pm 0.32$  SED – standard erythema dose – for the stratum corneum, while that of pigmentation would only be  $0.80 \pm 0.29$  SED. From these figures they conclude that the stratum corneum's photoprotection was 32% higher (i.e.  $1.06/0.80$ ). Leaving aside the question of skin type, which they never addressed in their study, as well as a number of methodological problems with their analysis, the significance of this ratio being exactly 1.32, in view of the size of the corresponding standard deviations of 0.32 and 0.29, respectively, is to be doubted. A simple arithmetic exercise shows that the actual ratios could be anywhere between  $(1.06 + 0.32)/(0.80 - 0.29)$  and  $(1.06 - 0.32)/(0.80 + 0.29)$ ; i.e. anywhere in the range of 2.71 to 0.68; even if one corrects these estimates, using a statistically appropriate method, one is left with an uncertainty of the *same order* as that of the value attributed to the ratio itself.

While Gniadecka et al. have made a worthy attempt to study simultaneously all three possible contributing variables to photoprotection – namely the thickness of viable epidermis, that of the stratum corneum and the amount of pigmentation – by a multiple regression analysis, their study appears, nevertheless, faulty. To begin with: their regression model is curiously inverted. While the only really independent variable in the experimental design is the actual UV dosis used to effect erythema (and this is also reflected in the fact that this variable is used for the abscissa of Fig. 1), their model expresses UV dosis as if it were the dependent variable, namely as a function of thickness of stratum corneum, of viable epidermis and pigmentation grade as well as of erythema grade. One would have expected to see "erythema grade" being the dependent variable plotted vs. UV dosis, while all other variables ought to play the role of parameters in this relation. While it is still possible to solve their "inverted model" mathematically by choosing the correct set of regression variables, the reader is at odds when trying to interpret both their model and the way the data is plotted.

Finally, we now come to the most important aspect in any study: the quality of the data and analysis. Simple examination of their plotted data (Fig. 1 in Ref. 1) shows a large spread of the measurements. While this is to be expected, due to the nature of such a study, the regression lines shown for the different degrees of erythema in both vitiligo and normal skin are anything but convincing: in Fig. 1A, for instance, the regression lines for grade +++ are almost completely determined by only *two* isolated extreme points near UV dosis 3 and 4, respectively. The line for grade ++ is even less convincing: it depends entirely on *one* point only – the one near UV dosis 3. If one were to eliminate those points in both cases, no regression whatsoever could have been determined, as the rest of the data cluster in an almost perfectly random way. The results shown in Fig. 1B are not much better: while the line for grade +++ is acceptable, that for grade ++ is not, because it depends entirely on the single point near UV

dosis 4.7, and that for grade+ is also totally determined by the single point at UV dosis 3.

In conclusion, the article by Gniadecka et al. shows such a number of methodological faults and poor quality of data and analysis that we have no reasons to believe or even accept as plausible the authors' claim that the stratum corneum offers as much photoprotection as pigment.

#### REFERENCES

1. Gniadecka M, Wulf HC, Mortensen NM, Poulsen T. Photoprotection in vitiligo and normal skin. *Acta Derm Venereol* (Stockh) 1996; 76: 429–432.
2. Everett MA, Jaegers E, Sayre RM, Olsen RL. Penetration of epidermis by ultraviolet rays. *Photochem Photobiol* 1966; 5: 533.
3. Westerhof W, Estevez Uscanga O, Meens J, Kammeyer A, Durocq

M, Cairo J. The relationship between constitutional skin color and photosensitivity estimated from UV-induced erythema and pigmentation close-response curves. *J Invest Dermatol* 1990; 94: 812–816.

4. Westerhof W, Beelaar D, Cormane RH, Langelaar J, Middelkamp-Hup J. The protective role of epidermal melanin in a patient with porphyria variegata and vitiligo. *Acta Derm Venereol* (Stockh) 1981; 61: 23–28.

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## Response to the Letter by Westerhof & Uscanga

*Sir*

Westerhof & Uscanga consider it surprising that the total photoprotection afforded by the stratum corneum is similar in vitiligo and normal skin, despite differences in the thickness of this layer (1). As explained in detail in Results and Discussion, the lower photoprotective capacity per thickness unit of stratum corneum in vitiligo is compensated for by its increased thickness.

The argument about the importance of skin types is irrelevant. Skin phototype offers a crude estimate of sensitivity to solar radiation and, as pointed out, strictly depends on pigmentation. We chose to measure skin pigmentation, which automatically excludes skin type evaluation (regression analysis does not permit one to have two or more explanatory variables which are dependent on each other). In view of the fact that we focused on Caucasians the notion about the role of melanin in skin type VI, although true, is not relevant.

We cannot consider the study of Westerhof et al. (4) as evidence against the role of stratum corneum, because: 1) the study was based on one (!) individual only; 2) the patient had porphyria variegata, which makes extrapolation to normal conditions very difficult; and 3) the thickness of stratum corneum was not measured but only assumed to be identical in vitiligo and "normal" skin. These deficiencies prevented us from discussing this work in our paper.

Westerhof's & Uscanga's objections to the data analysis are faulty. Their formula used to calculate the "error" of the ratio is incorrect, and the true significance of our data is very easy

to determine by calculating 95% confidence intervals. We will then obtain the values 0.44–1.68 SED for stratum corneum and 0.24–1.36 SED for pigmentation. We can immediately see that both ranges are significant and that stratum corneum is at least as important photoprotector as pigmentation in our group of Caucasians. However, in a population with a higher pigmentation grade, the relation between photoprotection afforded by stratum corneum and pigmentation may be different. We also want to stress that UV dosis is a dependent variable, because it is a dosis necessary to evoke an erythema reaction of a predetermined degree, which was assumed to depend on the explanatory variables given in equation 1. Thus plotting the UV dosis versus erythema grade, as suggested by Westerhof & Uscanga, does not make sense. The objection about the quality of the data is untrue: first it is improbable that single isolated points determine the slope of the lines in a coordinated pattern; second, slopes determined by single points will have an extremely large spread, which is not the case when one examines the standard errors given in Table I in our original paper.

In conclusion, none of the objections made by Westerhof & Uscanga are of relevance to the findings of our study.

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