In a recent report, Autier et al. described the correlation of nevi development with sunscreen use in children (1). This apparently counterintuitive finding will be the source of extensive discussion and perhaps some controversy. However, when the dynamics of skin biology are considered, it is important to recognize this study for what it really tells us. Specifically, it reminds us just how ignorant we are of all the complexities of skin biology and the impact of solar radiation. We are comfortable with the fact that the exposure of skin to sunlight causes sunburn and the unquestionable value of sunscreens for the prevention of sunburn (2). While it is tempting to extrapolate the protective effects of sunscreens to the prevention of skin cancers as well, it is important to recognize that the wavelengths (action spectra) that cause the effect on skin (sunburn) and those wavelengths that cause the induction of different types of skin cancer may be different. While good data exist that implicate sunburn-causing wavelengths of solar radiation in the development of squamous cell carcinoma, much less convincing evidence exists for the development of basal cell carcinoma and malignant melanoma in humans.

Protective clothing and sun avoidance drastically alter the effects of all wavelengths of sunlight on the skin. On the other hand, sunscreens are not impervious barriers to sunlight. Depending on the specific formulation, various wavelengths can be transmitted to underlying skin cells. A UVB (ultraviolet B)-blocking sunscreen, very effective at preventing sunburn, will permit the transmission of UVA (ultraviolet A) radiation. Even products claiming UVA protection will allow the penetration of varying amounts of UVA. While the ability of UVA radiation to directly damage DNA is far less than that of UVB, recent data suggest that energy
from these wavelengths (and those in the shorter portion of the visible spectrum) can be absorbed by endogenous photosensitizers and oxidize DNA bases (3). Since the technology to detect these latter effects has only been developed recently, it is too early to know the effect of sun exposure on human skin cells. The foregoing explanation thus highlights the extent of our ignorance concerning skin biology and the effects of solar radiation.

To begin to address this area, we need detailed studies of action spectra to elucidate the wavelength dependence for the following: 1) DNA damage, 2) immune suppression, and 3) genes that control important related activities, such as DNA repair and cell-cycle progression. Only then will we be able to design appropriate, preventive strategies for effects other than sunburn. An obvious question raised by Autier et al. is “Which wavelengths are responsible for nevi development?”

These questions can be answered by carefully designed photobiology experiments. In 1989 and 1998, the National Institutes of Health sponsored conferences on solar radiation and skin. After participating in the 1998 conference and reading the report on the 1989 conference, we thought that it is striking how similar the questions were a decade later. We have the tools to perform these experiments. We have the molecular biology insight to ask the right questions. What is needed is the following: 1) the desire to know this information, 2) the resources to conduct these experiments, and 3) the establishment of a consensus among the researchers, the Food and Drug Administration, funding sources, and industry that these experiments are important. In an era of “healthy people,” it would be expected that the number one environmental agent that affects human biology would have the highest priority for research.

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RESPONSE

In their letter, Gasparro and Berwick suggest that the increase in nevi number associated with sunscreen use that we observed in our study (1) is indicative of our general ignorance of the causal link that exists between sun exposure and nevi development or melanoma occurrence. We fully agree that this gap in our knowledge should be filled.

However, the link between sun exposure and melanoma could be more complex than just an issue of finding the relevant wavelength(s) responsible for nevi development. How ultraviolet radiation is delivered to the skin may also be of importance. For instance, it has been demonstrated that a given quantity of ultraviolet B radiation is more carcinogenic when administered in fractionated doses than in a few high doses or when doses are administered over a longer period of time (2).

Our data show that it is not sunscreen use that has a direct effect on nevi development, but the sun itself; sunscreen use probably allows higher amounts of sun exposure that would not be possible otherwise (1). Hence, sunscreen use would affect nevi development or melanoma risk more by a modification of the way wavelengths are delivered to the skin cells, rather than by a modification of wavelengths transmitted to the skin cells. In that respect, further work on the sunscreen–melanoma (or sunscreen–nevi) association could help to elucidate the mechanisms involved in the sunlight–melanoma association. Further research would also provide indications on how sunscreens should be formulated and used, for more efficient sun protection.

By discovering the nature of the sun–light–melanoma association, a constructive dialogue between basic and epidemiologic research could be very productive. Epidemiologic data tell us that it is the “intermittent” sun exposure that is mainly associated with melanoma occurrence, not the so-called “chronic” sun exposure pattern (3). Sunburn experience at all ages is associated with melanoma occurrence (3). However, sunburns are considered more and more as markers of natural susceptibility to sunlight and excessive sun exposure, rather than direct causes of melanoma (4). This last statement does not mean that avoiding sunburn is unimportant. Rather, it stresses that avoidance of sunburn (e.g., by using a sunscreen) does not necessarily equate to preventing all carcinogenic effects of solar radiation. Thus, epidemiologic data suggest that future experiments should try to mimic the sun exposure patterns mostly associated with melanoma occurrence (for instance, by examining in more detail the biologic effects of repeated suberythemal doses of ultraviolet radiation).

In their turn, epidemiologic researchers should adopt techniques developed within the framework of laboratory experiments. To date, measurements of sun exposures by means other than questionnaires have been limited (5,6). New technologies have now devised easy to use personal ultraviolet dosimeters that are able to record exposure to ultraviolet A and ultraviolet B. These dosimeters could be used to investigate the characteristics of sun exposures known to be more strongly associated with melanoma occurrence (e.g., sunbathing).

As Gasparro and Berwick rightly indicate, we possess the tools to perform such research. Now we just need to mobilize the necessary resources to perform the research.

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