Commentaries

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Cancer-preventive effects of sunscreens are uncertain

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Provocative findings have been published suggesting that the use of sunscreens may promote skin cancer. A recent meeting of international experts on the use of sunscreens and skin cancer was held at the International Agency for Research on Cancer in Lyon. The workshop concluded that the topical use of sunscreens reduces the risk of sunburn and that sunscreens probably prevent squamous-cell carcinoma of the skin when used mainly during unintentional sun exposure. No conclusion could be drawn about the cancer-preventive activity of topical sunscreens against basal-cell carcinoma and cutaneous melanoma. The use of sunscreens can extend the duration of intentional sun exposure, such as sunbathing. Such an extension may increase the risk for cutaneous melanoma. The workshop warned against relying solely on sunscreens for protection from ultraviolet radiation.

Key words basal-cell carcinoma, cancer, melanoma, prevention, skin cancer, squamous-cell carcinoma, ultraviolet radiation.

Sunscreens are chemicals that absorb ultraviolet (UV) radiation and attenuate the amount and nature of UV radiation reaching viable cells in the skin. They were originally developed to minimize erythema. The current major issue surrounding sunscreens involves their ability to prevent other potential deleterious effects of UV radiation on the skin, such as skin cancer and photoageing.

The incidence of all types of skin cancer (melanoma, basal-cell carcinoma, squamous-cell carcinoma) is increasing throughout the world (1). The incidence of non-melanocytic skin cancer is difficult to ascertain accurately because there are few registers in the world that consistently and carefully collect these data. However, its incidence appears to be rising at the same or a greater rate than melanoma throughout Caucasian populations in the world. The melanoma data are generally more accurate, and they show surprising similarity in various parts of the world.

Role of sun exposure

Exposure to the sun is regarded as a major cause of skin cancer (2). There has been a latitude gradient for the incidence of skin cancer among white populations in Australia and the United States, such that the highest rates are nearest the equator. In Europe this gradient has been confounded by the fact that those with the darker pigmentary phenotype live in the southern areas of Europe and those with the lighter phenotype reside in the northern parts so that the gradient is actually reversed. However, this switch does not explain the higher melanoma rates in Norway than in Sweden. Studies with migrant populations show that the risk of melanoma is related to sun exposure at the place of residence early in life. People migrating from low to heavy solar-exposure countries have, in fact, lower risk of skin cancer than people born in these countries; in addition, the risk becomes greater as the age at which this migration occurs decreases.

The role of sunburn in the development of melanoma is a critical consideration. This aspect of sun exposure is the one most often cited as the key to determining melanoma risk. In fact it can be argued that sunburn itself is not part of the pathway to the development of melanoma, but that it is an important marker for the combination of genetically susceptible phenotype and excessive sun exposure. However, recent data from Europe (3)

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support the concept that childhood sun exposure is not well represented by sunburning episodes.

Does the use of sunscreen protect against skin cancer?

An international workshop of leading cancer scientists on the use of sunscreens and sun protection was held recently at the International Agency for Research on Cancer (IARC) in Lyon. The summit reviewed all the studies currently available on skin cancer, sunscreens, and skin cancer protection, evaluated the effectiveness of sunscreens in preventing skin cancer, and produced public health advice. The deliberations of the meeting will be published as volume 5 of the *IARC Handbooks of Cancer Prevention* (4).

The workshop concluded that sunscreens prevent sunburns and do have the capacity to reduce squamous-cell carcinoma, but only if their use does not mislead people to extend their exposure to sunlight (4). No conclusions could be drawn regarding melanoma and basal-cell carcinoma. The picture seems different in cases of intentional exposure to sun, when the use of sunscreen does not seem to affect the occurrence of sunburn (5, 6). A double-blind randomized trial showed that the use of sunscreens with a higher sun protection factor may be related to intentional sun exposure of longer duration (6). The longer exposure to the sun is unconscious – that is, the ability of sunscreens to delay sunburn supports people's intention to stay in the sun. These findings may partly explain why several epidemiologic studies have reported moderately increased risks of cutaneous melanoma and basal-cell carcinoma in association with the use of sunscreens (4), a result suggesting that sunscreen use could be a risk factor, rather than a protective factor. Epidemiologic studies on the utility of sunscreens in preventing skin cancer are, however, flawed by poor reliability, potential confounders (including duration of sun exposure, sun sensitivity, history of skin cancer), inaccurate measurement of sunscreen application, and the use of other sun-protective behavior. This situation is consistent with the idea that sunburn is only a marker of the interaction between exposure and susceptibility and that eliminating sunburn will not necessarily affect the development of skin cancer.

Since high naevi counts are considered a strong predictor of melanoma, studies have been conducted on the ability of sunscreen use to prevent the formation of melanocytic naevi among children. One randomized trial showed that sunscreens reduced the formation of melanocytic naevi (7). Of the 4 cross-sectional studies performed, 2 studies (8, 9) did not report any statistical effect, and 2 others (10, 11) showed that sunscreens were associated with the development of naevi, possibly because sunscreen use may encourage prolonged sun exposure by delaying sunburn occurrence (6).

Mechanisms of cancer prevention by sunscreens

It has not been clearly established which part of the solar spectrum is responsible for the association between sun exposure and skin cancer, although there is evidence that UV radiation represents at least one of the causes. This evidence is consistent with molecular genetic evidence showing high frequencies (50—100%) of unique mutations, a C to T or a CC to TT transition, in the p53 tumor suppressor gene in UV-induced skin cancer among humans and mice (4). UV radiation can, in fact, cause specific DNA (deoxyribonucleic acid) damage that leads to mutations in tumor suppressor genes or protooncogenes and induces cell cycle arrest or DNA repair. UV radiation can also affect the host's immune system. These different pathways seem to interact to generate skin cancer.

Sunscreens prevent sunburn by stopping UV radiation from reaching the skin. Experiments with rodent models and humans have shown that, under certain circumstances, topical use of sunscreen prevents the toxicity induced in the skin by UV radiation, and it also reduces the occurrence of skin cancer in mice after exposure to solar-simulated radiation (4). Sunscreens decrease DNA damage induced by UV radiation and overexpression of wild-type p53 in epidermal keratinocytes. In addition, a single small study has also shown a reduction in p53 mutations in basal-cell carcinoma (12). Sunscreens also afford some protection from several end points of immunosuppression, including suppression of the elicitation of recall responses and suppression of the allostimulation of T cells with epidermal dendritic cells.

Recommendations

In order to avoid the scenario in which a sunscreen-promotion policy could increase rather than decrease the incidence of sun-related cancers, the workshop in Lyon put forward several recommendations in relation to the use of sunscreens (4). Principal among these is that the use of sunscreens be a part of a comprehensive sun avoidance strategy which includes taking advantage of natural shade and using appropriate clothing. In the context of a comprehensive sun-avoidance strategy, a sunscreen with a protection factor of ≥15 should be used. Where there is intentional exposure without control of time spent in the sun, sun seekers should be warned that the use of sunscreen could inadvertently increase the risk of cancer.

Increase in skin cancer risk due to "risk compensation"?

Drivers whose cars are equipped with spiked winter tires feel safer and drive faster or more carelessly than they would without these tires. The benefits of spiked tires for drivers could be offset by increases in the speed at

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which accidents occur. A similar "risk-compensation" mechanism has been suggested for condom users: increased condom use may reflect a person's decision to switch from inherently safer strategies of sex partner selection or fewer partners to the riskier strategy of developing or maintaining higher rates of partner change plus reliance on condoms (13).

Similarly, the use of sunscreens has not delivered all the protection benefits that were originally expected of them. A theory of "risk homeostasis" or "risk compensation" may explain why the obvious benefits of sunscreens do not necessarily translate into benefits when used by populations at large. If preventive intervention engenders compensatory changes in risk behavior (ie, prolonged stay in the sun) among intentional users of sunscreens, it is possible that intervention to reduce the risk involved in solar radiation would lead to a paradoxical increase in skin cancer risk.

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