

Prolonged exposure to the sun is considered to be the dominant risk factor for NMSC (U.S. EPA, 1987, ES-33). It has been observed that NMSC tends to develop on sites that are most frequently exposed to the sun (e.g., head, face, and neck). Outdoor workers, who are subject to greater exposure to solar radiation, tend to have higher incidence rates of NMSC. A latitudinal gradient exists for the flux of UV-B radiation (i.e., the amount of radiation transmitted through the atmosphere), with fluxes generally higher in lower latitudes. A similar latitudinal gradient is generally seen in incidence rates of NMSC. Skin pigmentation provides a protective barrier that reduces the risk of developing NMSC, such that light-skinned individuals, who are more susceptible to sunburn and have blue or green eyes, are more likely to develop NMSC.

Both types of NMSC result from the malignant transformation of keratinocytes, the major structural cells of the skin. Cumulative long-term exposure to UV radiation is the exposure of concern for both types of NMSC. More specifically, the incremental increase in cumulative lifetime exposure to UV-B radiation is the metric used to estimate the risk of increased incidence of NMSC (U.S. EPA, 1987, ES-3). Epidemiological evidence, however, also indicates that exposure to solar radiation may play different roles in the etiology of SCC and BCC. In particular, SCC is more likely to develop on sites receiving the highest cumulative UV radiation doses (e.g., nose), and the development of SCC is more strongly associated with cumulative exposure to UV radiation. Relative to SCC, BCC is more likely to develop on sites that are not normally exposed to the sun, such as the trunk. For a given cumulative level of exposure to solar radiation, the risk of developing SCC may be greater than the risk of developing BCC.

Dose-response relationships for NMSC are generally estimated in terms of a biological amplification factor (BAF), which is defined as the percent change in tumor incidence that results from a 1 percent change in UV-B radiation. While there is considerable uncertainty in such estimates, results from several studies have produced an overall BAF range that is 1.8 to 2.85 for all nonmelanoma skin tumors (U.S. EPA, 1987, ES-34). The BAF estimates are generally higher for males than females and for SCC than BCC, and generally increase with decreasing latitude. Key uncertainties in these estimates include, for example, uncertainties in the actual doses of UV-

B radiation received and in the underlying baseline incidence rates in populations. Additional uncertainty is introduced in estimating the change in mortality from NMSC associated with changes in UV-B radiation, reflecting in part discrepancies of reporting between death certificates and hospital diagnoses. Based on published estimates, rates of metastasis among SCCs and BCCs varied by one to two orders of magnitude, with rates estimated to be approximately 2 to 20 percent for SCC and 0.0028 to 0.55 percent for BCC. The overall fatality rate for NMSC has been estimated to be approximately 1 to 2 percent, with three-fourths to four-fifths of the deaths attributable to SCC (U.S. EPA, 1987, ES-34).⁴⁹

Melanoma is a serious, life-threatening skin cancer that is far rarer and generally much more aggressive than NMSC. The relationship between exposure to UV-B radiation and melanoma is not as clear as the relationship between exposure to UV-B radiation and NMSC. The EPA (1987) noted limitations in the evidence linking solar radiation to melanoma. For example, no animal models were identified in which exposure to UV-B radiation experimentally induces melanoma, and no *in vitro* models for malignant transformation of melanocytes. Despite these limitations, EPA (1987) recognizes that a large array of evidence does support the conclusion that solar radiation is one of the causes of melanoma. Melanin, the principal pigment in the skin, effectively absorbs UV radiation, such that darker skin provides more protection from UV radiation. Lighter-skinned individuals, whose skin contains less protective melanin, have higher incidence and mortality rates from melanoma than do darker-skinned individuals.

Sun exposure seems to induce freckling, which is an important risk factor for melanoma, and sun exposure leading to sunburn apparently induces melanocytic moles, which are also a risk factor for melanoma. Additional evidence suggests that melanoma risk may be associated with childhood sunburn. However, other evidence suggests that childhood sunburn may be a surrogate for an individual's pigmentation characteristics or be related to mole development, rather than being a separate risk factor (U.S. EPA, 1987, ES-37).

⁴⁹ More recent estimates of mortality rates from NMSC may be found on the American Cancer Society's Web site <http://www.cancer.org>, under cancer type "Skin, Nonmelanoma," then under "Nonmelanoma Skin Cancer—Overview."

Most studies that have used latitude as a surrogate for sunlight or UV-B exposure have found an increase in melanoma incidence or mortality correlated with proximity to the equator. Other evidence, however, creates uncertainty about the relationship between solar radiation and melanoma. Some ecologic epidemiology studies, conducted primarily in Europe or in countries close to the equator, have failed to find a latitudinal gradient for melanoma. In addition, outdoor workers generally have lower incidence and mortality rates from melanoma than indoor workers, which appears to be incompatible with the hypothesis that the cumulative dose from exposure to solar radiation causes melanoma. Unlike NMSC, most melanoma occurs on sites of the body that are not habitually exposed to sunlight. This evidence suggests that exposure to solar radiation, or UV-B, is not solely responsible for variations in the incidence and mortality from melanoma (U.S. EPA 1987, ES-37).

Considering the available evidence, EPA (1987) concluded that UV-B radiation is a likely component of solar radiation that causes melanoma, either through the initiation of tumors or through suppression of the immune system. The EPA (1987) also recognized that significant uncertainties exist in characterizing associations between solar radiation and melanoma, including the appropriate action spectrum to be used in estimating doses, the best functional form for a dose-response relationship, and the best way to characterize dose (e.g., peak value, cumulative summer exposure).

b. Effects on the Eyes

Evidence suggests that adverse effects on the eye are associated with exposure to UV-B radiation. Effects likely include increases in cataract incidence or severity and increased incidence of retinal disorders and retinal degeneration. Cataracts are characterized by the gradual loss of transparency of the lens due to the accumulation of oxidized lens proteins. Many possible mechanisms exist for the formation of cataracts, and UV-B radiation may play an important role in some mechanisms. Therefore, while epidemiological studies indicate that the prevalence of human cataracts varies with latitude and UV radiation in general (U.S. EPA, 1987, ES-40), significant uncertainty exists about the action spectrum to be used in any estimation of dose associated with variations in solar radiation. Epidemiological and laboratory evidence indicates that the exposure of