Review

Skin cancer as an occupational disease: the effect of ultraviolet and other forms of radiation

Claudia C. Ramirez, MD, Daniel G. Federman, MD, and Robert S. Kirsner, MD

From the Department of Dermatology and Cutaneous Surgery, Department of Epidemiology and Public Health, and Sylvester Cancer Center, University of Miami School of Medicine, Miami, Florida, Veterans Administration Medical Center, Miami, Florida, Department of Internal Medicine, Yale University School of Medicine, and Veterans Administration Medical Center, West Haven, Connecticut

Correspondence
Robert S. Kirsner, MD,
University of Miami/Veterans Administration Medical Center,
Department of Dermatology,
1201 NW 16th St., Miami, FL 33125
E-mail: Rkirsner@med.miami.edu

Introduction

Over 1 million Americans will be diagnosed with skin cancer this year, more than all other cancers combined.[1] Currently, it is estimated that one in five Americans will develop skin cancer during their lifetime, the majority diagnosed with non-melanoma skin cancer (NMSC), which includes basal cell (BCC) and squamous cell (SCC) carcinomas.[2] The incidence of both NMSC and melanoma is increasing and melanoma is increasing more rapidly than any other reported cancer.[3–5]

A number of risk factors are known to predispose persons to skin cancer. Skin cancer is more common in Caucasians who have light skin and eyes and in those who burn rather than tan when exposed to sunlight (Fitzpatrick skin types I and II). Ultraviolet (UV) exposure has been implicated in the development of all three of these malignancies, although the epidemiology of melanoma, BCC, and SCC differs. Although a number of environmental and genetic factors contribute to the development of NMSC and melanoma, UV exposure is considered to be the most important risk factor.[6–8] A combination of factors, including a predisposition of the immune system to be suppressed by UV radiation and a reduced capacity to repair UV-induced DNA damage, appears to increase the risk.[9]

Several studies have suggested that the lifetime cumulative sun exposure is responsible for the development of SCC. This epidemiologic pattern fits with the clinical presentation, as SCC occurs most frequently in areas maximally exposed to the sun (e.g. the face, back of the hands, and forearms).[8,10] On the other hand, the epidemiology of BCC suggests that it is related to both acute and chronic sun exposure, providing mixed effects of cumulative and intermittent sun exposure. Interestingly, the clinical presentation of BCC, although commonly located on the head and neck, tends to affect sun-protected areas (inner canthus) and occurs less commonly on the back of the hands.[8,11–14] Melanoma, however, is associated with intense intermittent sun exposure and tends to occur in areas exposed to sun sporadically (e.g. the back in men and lower legs in women).[15,16]

Exposure to other forms of radiation suggests that these may be risk factors for skin cancer development as well. Survivors of the atomic bomb explosions in Hiroshima and Nagasaki have an increased risk of developing NMSC, especially BCC, and this increased risk increases with the age of exposure.[17,18] Whether the increased risk of NMSC is also applicable for low-dose and chronic exposure remains unclear.

As increased occupational UV exposure through natural sunlight is assumed to be associated with skin cancer,[6,7,19,20] the goal of this paper is to describe the relationship between sun exposure, other occupational radiation exposures, and skin cancer.

Occupational exposure to UV and other forms of radiation and skin cancer

A study by Hannuksela-Svahn *et al.*,[21] using the Finnish national database, described the incidence and mortality rates of NMSCs from 1956 to 1995 in relation to gender, age, anatomical distribution, place of residence, and occupation. They found that traditional outdoor occupations, such as farming and forestry work, did not increase the risk of NMSC, but occupations requiring a high level of education or compulsory health controls, such as pilots, engine drivers, and those working in medical care, had an increased risk of BCC. They concluded that this might represent more frequent consultation for skin lesions amongst highly educated populations.

Farmers

As farmers are expected to spend more time outdoors than nonfarmers, they might be expected to have higher rates of skin cancer. Studying the mortality amongst farmers (9245 white and 3508 nonwhite male farmers) in North Carolina, Delzell and Grufferman[22] found that white farmers showed an increased relative frequency of deaths from NMSC [proportional mortality ratio (PMR) = 1.8 and odds ratio (OR) = 1.9)] compared with nonfarmers. Nonwhite farmers showed an increased frequency of deaths from melanoma (PMR = 2.3 and OR = 6), although the number of deaths was quite low ($n = 6$). The authors postulated that increased exposure to UV irradiation was the most likely reason for the farmers' increased risk of skin cancer.

Welders

Currie and Monk[23] reported five cases of NMSC occurring in welders, who have a potential for intense exposure to nonsolar UV irradiation. In a series of 296 consecutive patients with histologically proven NMSC, five reported a history of employment as welders. In these five, all white men, four of the lesions were located on the face and one on the forearm. In the welding process, high temperatures (up to 2000 °C) and UV irradiation (250–297 nm) are produced. The irradiation from the welding arc is in both the UVB (280–315 nm) and UVC (100–280 nm) range. Although there is evidence that implicates UVA, UVB, and UVC as carcinogenic,[24] nonsolar UV irradiation, from diverse sources such as welding torches to sunbeds, has also been implicated as a risk factor for malignant melanoma.[25]

Watermen

Vitasa *et al.*[20] examined the relationship between UVB radiation, NMSC and actinic keratosis (AK) in a cross-sectional prevalence study of 808 white watermen (who make their living from the water, i.e. fishing) in Maryland. Overall, 25% of subjects were diagnosed with AK, 4.3% with SCC and 4.1% with BCC. Watermen with SCC (OR = 2.05) or AK (OR = 1.55), but not BCC, had higher average annual UVB doses than matched controls. High cumulative UVB exposure was significantly associated with SCC, less strongly with AK, and was not associated with BCC. A comparison of the localization of the tumor types found that most of the AK, BCC and SCC occurred on exposed areas, such as the face, head, and neck. The low proportion of lesions on the trunk (which were predominantly BCC) was probably due to the fact that most watermen wore upper body clothing whilst working. This study suggests that watermen have higher levels of UVB exposure through natural sunlight, and this is associated with an increased risk of developing SCC.

Physical education (PE) teachers

A retrospective cohort study was performed on female PE teachers and language teachers to evaluate physical activity as a risk determinant of cancer.[26] The assumption was made that PE teachers represented a more physically active group. There were no significant differences in social status, general health status, nutrition, smoking, alcohol consumption, or diet between the two groups, although PE teachers reported higher amounts of life-long physical activity. There was an increased incidence of melanoma amongst PE teachers [standardized incidence ratio (SIR) = 2.01], but not language teachers (SIR = 0.84). The excess of melanoma in PE teachers was thought to be attributable in part to the increased occupational sun exposure during outdoor physical education activities.

Police officers

In a retrospective cohort cancer incidence study of 22,197 Ontario police officers, an excess of melanoma, prostate, and testicular cancer was found.[27] Using the Ontario Cancer Registry linked to the Ontario Mortality Database, SIRs were computed. For melanoma, 54 cases were diagnosed in police officers, compared with the 39.5 expected using population-based data [SIR = 1.37; 90% confidence interval (CI) = 1.08–1.72]. The anatomic distribution of melanoma involved the trunk (54%), upper limb (15%), and lower limb (9.25%), without significant differences compared with the distribution in the general population. Although for some police officers, outdoor work and sun exposure are common, this is not the case with all officers and this study did not control for job site (indoor vs. outdoor).

The National Institute for Occupational Safety and Health (NIOSH) reported that exposure to emissions from police radar might increase the risk of leukemia and testicular, brain, and skin cancers, and although few published studies have examined this potential association between police radar use and cancer, it has been implicated as a potential trigger.[28,29] The mechanism by which radar might cause cancer is unknown, although radar energy could reach the skin and testes, two of the target sites found to have an increase in

cancer in this population, as the frequencies utilized by police radar have been shown to penetrate body tissues by up to 1 cm.[30] Davis and Mostofi[28] reported a cluster of cases of testicular cancer: six cases in a cohort of 340 police officers (observed/expected = 6.9). A retrospective mortality study of male police officers from 1950 to 1990 (58,474 person-years follow-up) found higher than expected mortality rates for all malignancies [standardized mortality ratio (SMR) = 125; 95% CI = 1.10–1.41].[29]

World War II (WWII) veterans

A retrospective study including more than 5500 prisoners of war (POWs) and 3700 non-POW veteran control subjects evaluated melanoma mortality.[31] A history of military service in the Pacific or European theaters during WWII and POW status were examined, as POW camps in the Pacific (i.e. Philippines) had three times the ambient UV radiation of those located in Europe (Germany). Investigators found increased deaths from melanoma in POWs from the Pacific theater compared with non-POW veterans from the European theater (OR = 3.35) or non-POW veterans in the Pacific (OR = 3.22) These data are consistent with the hypothesis that exposure to high levels of solar radiation in young adulthood is associated with a higher risk of melanoma and subsequent mortality.

Another study compared skin cancer development in WWII veterans stationed in the Pacific and in Europe.[32] As the average troop strength in Europe was similar to that in the Pacific, it would be expected that the malignancy incidence would be equal between the two groups. Three hundred and seventy servicemen with skin cancer were studied, 66% of whom served in the Pacific; this was significantly greater ($P < 0.001$) than the number of veterans with these malignancies who served in Europe. This was consistent for BCC ($P < 0.001$) and SCC ($P < 0.01$) as well as for melanoma, where 70% occurred in Pacific veterans and 30% in European veterans. The latter did not reach statistical significance ($P < 0.2$), probably due to the small total number of melanomas in this study (10).

Pilots and cabin attendants

Pilots and cabin attendants may have an increased risk of skin cancer and this may highlight the potential role of cosmic radiation. Cosmic radiation is suspected to produce several types of cancer.[33–36] Airline pilots are occupationally exposed to cosmic radiation (mainly gamma and neutron radiation), with doses of 2–6 mSv per year, compared with a background radiation of 1 mSv per year.[37] The International Commission on Radiological Protection recommended in 1990 that the in-flight exposure of aircrew should be considered as an occupational exposure.[38]

In a retrospective study of commercial pilots in Iceland,[34] the number of person-years of pilot work was calculated for each pilot, in addition to the estimated dose of cumulative radiation and the flight length. Although there was an excess rate of melanoma amongst pilots (SIR = 10.20; 95% CI = 3.29–23.81), this was based on only a few cases (five cases) and thus the 95% confidence intervals were broad. The incidence of melanoma was higher in those who had flown over five time zones (SIR = 25.00) than in those who had flown over fewer than five time zones (SIR = 9.09). This suggests that other factors, rather than lifestyle behavior of excessive sunbathing, may have a role in the development of cutaneous malignancy in this population.

In a retrospective study of more than 10,000 male pilots by Pukkala *et al.*,[37] a significantly increased SIR for skin cancer, including melanoma (2.3; 95% CI = 1.7–3.0), NMSC overall (2.1; 95% CI = 1.7–2.8), and BCC (2.5; 95% CI = 1.9–3.2), was found. In this study, the number of hours in different types of flight was collected and converted into effective radiation doses (mSv). Airline pilots are exposed to ionizing radiation, with doses of 2–5 mSv per year,[39] compared with an annual dose from background radiation of approximately 1 mSv (excluding radon contribution).[40] Controlling for behavioral risk factors, the relative risk of melanoma increased significantly with increasing estimated radiation exposure during flight, especially for melanoma of the trunk amongst pilots with an exposure of greater than 20 mSv. Measurements of UV radiation have shown minimal exposure in the cockpit at high cruise altitudes.[41] In another retrospective study of 3701 male commercial pilots followed for more than 70,000 person-years, elevated risks were seen for both melanoma (SIR = 1.8) and NMSC (SIR = 2.4) (excluding BCC).[42]

The UV radiation exposure of airline pilots during flight was measured with UV-sensitive film badges worn on the epaulette nearest to the window by Diffey and Roscoe,[41] and found to be negligible. The distribution of skin cancers was compared with that of the total population, and cancers did not occur more often on the most exposed areas in the cockpit (heads, neck, and hands), suggesting that cosmic and not UV exposure may be causal. A trend of increasing SIR with exposure to cosmic radiation was observed for melanoma.

A review of five cohort studies of cancer incidence in commercial air pilots was published by Lynge.[44] Commercial pilots in Canada, Denmark, Iceland, and Norway were found to have an increased risk of melanoma (52 observed vs. 25.39 expected, SIR = 2.0). In addition, an increased risk of NMSC was found in the three cohorts for which this cancer type was reported (93 observed vs. 45.65 expected, SIR = 2.0).

Another retrospective study of cancer amongst 1690 cabin attendants (158 men and 1532 women) in Iceland was conducted by Rafnsson *et al.*[35] The SIRs of various cancer sites in relation to employment time and year of hiring were calculated, and an increased risk was seen for melanoma (7 observed vs.

2.34 expected, SIR = 3.0; 95% CI = 1.2–6.2). The SIR for melanoma increased with increasing employment time up to eight or more years of employment. Excess melanoma was most marked amongst those hired in 1971 or later, when the type of jet used (a Douglas DC-8) resulted in increased cosmic radiation exposure due to flying at higher altitudes. No information regarding the sunbathing habits of the cabin attendants was provided.

Haldorsen *et al.*[36] performed a retrospective cohort study of 3743 Norwegian airline cabin attendants (599 men and 3144 women), which was linked to the Cancer Registry of Norway. Compared with the expected number of cases, men showed an increased risk of melanoma (SIR = 2.9; 95% CI = 1.1–6.4) and SCC (SIR = 9.9; 95% CI = 4.5–18.8). Amongst women, there was also an increased risk for melanoma (SIR = 1.7; 95% CI = 1.0–2.7) and SCC (SIR = 2.9; 95% CI = 1.0–6.9). For melanoma, there was a trend towards increasing risk with increasing length of employment.

The increased risk of skin cancer amongst flight crew might be explained by lifestyle-related factors, such as excessive sunbathing; jetlag and disturbances in the circadian rhythm due to long-distance flights have also been suggested as risk factors for melanoma in this population.[34] The incidence of melanoma was highest amongst those who had flown routes that extended over five time zones, indicating that disturbance of the circadian rhythm (and thus melatonin homeostasis) may play a role in melanoma etiology. Melatonin has an oncostatic action and has been utilized in the treatment of metastatic melanoma.[44] Results from an experimental study indicate that melatonin can inhibit the growth of B16 mouse melanoma.[45] It has not been possible to separate the role of these risk factors in many studies.

Radiation technologists and physicians

A prospective study was conducted from 1983 to 1998 amongst 68,588 US radiologic technologists certified during 1926–82 to examine the risk of melanoma. Overall 207 cases were identified.[46] Technologists who began working prior to 1950, when radiation exposure was probably higher, had a relative risk for melanoma of 1.8 (CI = 0.6–5.5). No increased risk was found for those who began working after 1950. No association was found between the total number of years worked and the development of melanoma. The use of a lead apron appeared to protect against the development of melanoma to a small degree.

In China, Wang *et al.*[47] studied 27,011 diagnostic X-ray workers (radiologists and technicians) and compared their rate of skin cancer development with a control population of physicians of other specialties working at the same hospitals, during the same time period, but who did not use X-ray equipment. The incidence of all sites of cancer was 21% higher amongst diagnostic X-ray workers. For skin cancer, the relative risk was 2.8 ($P < 0.05$) and highest amongst workers employed for more than 15 years. Interestingly, most of the skin cancers occurred on the hands, where high exposure from the X-ray beam may occur during positioning of the patient. Other cancers found to be increased were leukemia, breast, and thyroid.

Conclusions

Members of several occupational groups appear to be at a higher risk of skin cancer. There is an increased risk of skin cancer amongst outdoor workers, such as farmers, welders, watermen, police officers, physical education teachers, pilots, and cabin attendants. Although sun exposure is thought to be a common etiologic factor, some studies have suggested alternative explanations, such as irradiation from the welding arc in welders, nonionizing microwave frequency radiation from radar use in police officers, and cosmic radiation in pilots and cabin attendants. Disturbances in circadian rhythm have also been suggested as having a role in the increased risk of skin cancer in pilots and cabin attendants and should be elucidated in future studies. Occupations in which there is an increased exposure to ionizing radiation, such as radiation technicians and radiologists, showed an increased risk for melanoma and NMSC. Surprisingly, there is a paucity of publications regarding skin cancer incidence amongst lifeguards, ski instructors, professional cyclists, and other professionals who spend time outside as part of their jobs. Ample evidence exists, however, that amongst selected occupations skin cancer is an important occupational disease.

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