Ultraviolet radiation

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The major source of ultraviolet radiation is solar radiation or sunlight. However, exposure to artificial sources particularly through tanning salons is becoming more important in terms of human health effects, as use of these facilities by young people, has increased. The International Agency for Research on Cancer has noted that there is sufficient evidence from studies in animals and in man to establish ultraviolet radiation as a human carcinogen.

Skin cancer has been the most commonly studied cancer site with respect to UV radiation. The nature and timing of sun exposure appear to be important determinants of both the degree of risk and the type of skin cancer. Cutaneous malignant melanoma and basal cell cancer are much more strongly related to measures of intermittent ultraviolet exposure (particularly those of childhood or adolescence) than to measures of cumulative exposure. In contrast, squamous cell cancer is more strongly related to constant or cumulative sun exposure. Lip cancer is causally related to lifetime sun exposure.

It has been estimated that solar ultraviolet radiation accounts for approximately 93 percent of skin cancers and about half of lip cancers. This translates to approximately 4,500 life-threatening cancers (cutaneous malignant melanoma) per year in Canada, as well as 65,000 less serious cancers (basal cell cancer, squamous cell cancer and lip cancer). Appropriate clothing use, care not to sunburn and judicious use of sunscreens could prevent at least half of these and save approximately 450 lives per year. In addition, physician and public education programs can significantly increase the proportion of melanomas diagnosed early. Lesions that have not yet penetrated deeply are associated with a mortality rate of less than five percent.

Several recent studies suggest a possible inverse relationship between ultraviolet radiation exposure and risk of non-Hodgkin lymphoma, colon, breast and prostate cancer, and investigators have speculated that this might be due to the higher serum levels of vitamin D stimulated by high lifetime sun exposure. Further, studies conducted within cohorts using stored pre-diagnostic serum suggest that those with high levels of vitamin D have lower incidence rates of a number of malignancies, particularly colon cancer. However, since serum vitamin D levels can be raised through the use of supplements without increasing risk for skin lip and other known UV-related cancers, changes to health policy with regard to exposure are not merited at this point. Further research is needed in this area.

Introduction

Optical radiation within the electromagnetic spectrum includes ultraviolet radiation (UVR), visible light and infrared radiation. UVR, as used in this review, is defined as that radiation between 100 and 400 nanometres (nm) in length (WHO 1994).[1] It is characterized further according to wave length into ultraviolet A (315–400nm), B (280–315nm) and C (100–280nm).

The major source of UVR is solar radiation or sunlight. Ultraviolet C (UV-C), from the sun, is virtually completely screened out by the Earth's atmosphere, and is thus a negligible source of adverse human health effects. Ultraviolet B (UV-B) is responsible for erythema (sunburn), and associated with an increased risk of skin cancer, and immunosuppression. However, solar UV-B is crucial in the synthesis of vitamin D, which some recent studies suggest may potentially reduce risk of colon, prostate and breast cancers. Ultraviolet A (UV-A) contributes to skin aging and has more recently been implicated, along with UV-B, in the development of skin cancers in animals and in immunosuppression in humans. Although the sun is the main source of UV-A exposure, use of UV-A-emitting lamps in sunbeds for recreational tanning has raised concern about artificial sources of human exposure.

The International Agency for Research on Cancer has noted that there is sufficient evidence from studies in animals and in man to establish UVR as a human carcinogen (IARC 1992).[2] For the most part, this review will focus on UVR as a single exposure without an attempt to separate the effects of the types noted above. This is because most of the human evidence concerning the health effects of UVR relates to reported sunlight exposure. When artificial sources of UVR are used in animal studies, distinguishing the separate effects of UV-A and UV-B is often possible. However, to date, this has not been possible in human epidemiological studies, most of which are retrospective and depend on subject recall. Animal studies will, in general, not be referred to in this review except where no alternative evidence is available.

Cancer and ultraviolet radiation

This review focuses initially on the positive relationship between UVR and the three major types of skin cancer: cutaneous malignant melanoma (CMM), basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). In addition, the potential relationship with cancer of the lip and with uveal (ocular) melanoma is discussed. Recent evidence has suggested a potential association between UVR and non-Hodgkin lymphoma. This hypothesis is examined, along with the hypothesis that solar exposure may reduce risk of colon, breast and prostate cancer through stimulation of increased serum vitamin D levels. Finally, all of the evidence is considered with a view to assessing the impact of UVR on the burden of cancer in Canada.

Cutaneous malignant melanoma

Solar ultraviolet radiation

The age-sex standardized incidence of CMM has increased markedly over the past 25 years in Canada (Gallagher et al., 1990; Gaudette and Gao, 1998)[3,4] such that it represents significant health problem from a population health based perspective.

Studies have revealed that the major environmental risk factor is solar and artificial UV exposure and that the principal modifying factor of this exposure is individual susceptibility as indicated by host pigmentation and sun sensitivity.

Solar UVR exposure is estimated to account for about 93 percent of melanomas in Canada (Armstrong and Kricker, 1993).[5] Early descriptive studies observed associations between the latitude of residence and melanoma incidence and mortality in Caucasian populations (Lancaster, 1956; Elwood et al., 1974; Fears et al., 1976).[6,7,8] The association, however, was not as strong as might have been predicted were there a simple and direct relationship between total UVR exposure and melanoma incidence. This led investigators to hypothesize that the character and timing of exposure might be more relevant than total lifetime exposure in inducing CMM (Elwood and Hislop, 1982; Holman et al., 1983).[9,10]

Over the following 15 years, more than 25 case-control and cohort studies addressed this and other hypotheses concerning solar ultraviolet radiation; these studies have been evaluated in in the review of Elwood and Jopson (1997).[11] Of the 29 studies outlined in Table 1, 22 evaluated at least one measure of intermittent solar exposure, usually defined as recreational time spent in the sun. A statistically significant positive association between intermittent exposure and melanoma risk was seen in 16 of the investigations ($p < 0.05$). In contrast, chronic or constant solar exposure, usually defined as occupational in origin, was assessed in 20 studies, the majority demonstrating either no increased risk or a reduced risk in those with the highest levels. Total sun exposure was studied in 11 investigations, with an absence of an association in all but two (those of Grob et al.[28] and Rodenas et al.[39]), which observed increased risk of melanoma among those with higher exposures. Both of these studies, however, were conducted among Mediterranean subjects which differ from Canadians as they are, on average in high sunlight areas and possibly with respect to other risk factors for melanoma. Therefore, the extrapolation of these findings to the Canadian population is not straightforward.

With respect to other risk factors for melanoma, differences in the populations in which studies of sun exposure and melanoma are conducted can affect risk estimates because pigmentation factors render some individuals more susceptible to melanoma than others. Individuals with light skin, hair and eye colour were consistently found to be at elevated risk of CMM in virtually all case-control and cohort studies of this tumour in the early 1980s.[12-45] Furthermore, the propensity of the skin to burn—rather than tan—in the sun also consistently increases risk.[20, 21,43-46] Finally, the presence of either freckling[41,47] or acquired melanocytic nevi (skin moles) substantially increases risk,[42-44,47,48] and at least one study reported a synergistic effect of these two factors.[45]

Overall, the results indicate that intermittent solar exposure is associated with an increased risk of melanoma in light-skinned populations, while constant or occupational exposure is associated with either no increase or a decrease in risk. Total solar exposure appears not to be associated with increased or decreased risk, except in Mediterranean populations, in which darker skin type may modify its effect. A cautious approach must be taken in interpreting the essentially negative findings for cumulative sun exposure. Most studies have been conducted in highly developed Western countries where indoor work predominates, effectively limiting the degree of cumulative exposure most people can accrue. Thus an effect for cumulative exposure might be missed due to limited range of exposure in these studies.

While the evidence indicates that the character of solar exposure is important in CMM, other findings, particularly those carried out in Australia, indicate that timing of exposure may also be important. Khlat et al.[49] demonstrated that migrants arriving in Australia after the age of 15 from low sunlight areas, such as the UK, had substantially lower mortality from CMM than those who arrived at a younger age. Other studies demonstrate a substantially reduced risk for melanoma in individuals coming to Australia after age nine, when compared to those who are native born, even after controlling for lifetime exposure.[43,44] A US study showed that early life spent in high sunlight southern states conferred an increased adult melanoma risk even among subjects who had later moved to low sunlight states.[50] Results of these investigations suggest that childhood may be a particularly susceptible period in relation to later risk of CMM.

In summary, as melanoma rates are substantially higher in white populations in high sunlight areas[51] than in low sunlight areas, ambient levels of solar irradiance are clearly important in accounting for melanoma incidence. However, the analytic studies indicate that character and timing of exposure are also important, particularly in accounting for risk at the individual level. Armstrong[52] has succinctly summarized the available information and hypothesized that for a particular intermittent pattern of exposure to solar UV, melanoma risk increases monotonically with increasing amount of exposure, and (for a given amount of exposure) risk of melanoma increases monotonically as exposure becomes more intermittent.

Recently, several studies have suggested that there may be at least two alternative etiologic pathways to melanoma.[53-55] These studies are potentially very important as they suggest that the relationship between host susceptibility factors (skin colour, sunsensitivity, nevus density, freckling density) and melanoma—and perhaps even the degree of solar exposure necessary for evolution of frank malignancy—may differ between the pathways. If this proves to be the case, it is likely that risk ratios associated with both susceptibility factors and solar exposure may have been substantially "diluted" in past epidemiologic studies due to inappropriate aggregation of etiologically distinct lesions.

Finally, a comparatively small proportion of malignant melanomas are due to what has been called either the atypical (dysplastic) nevus syndrome or familial atypical multiple mole-melanoma syndrome. Initially this was thought to be a phenotypic expression of a germline mutation

TABLE 1
Summary of case-control studies on solar UV radiation exposure and cutaneous malignant melanoma

Place of study	Diagnosis years	Overall no. cases/controls	OR (95% CI) in highest sun exposure category			
			Intermittent	Occupational	Total	Reference
Norway	1974-75	78/131	2.4 (1.0-5.8)	1.4 (0.6-3.5)	–	Klepp & Magnes 1979[12]
UK	1971-76	111/342	1.5 (0.9-2.5)	–	–	Adam et al. 1981[13]
Scotland	1978-80	113/113	0.6 (0.2-1.2)	0.4 (0.1-0.7)	–	MacKie & Aitchison 1982[14]
USA	1978-79	111/107	2.5 (1.1-5.8)	–	–	Lew et al. 1983[15]
USA	1978-81	114/228	2.4 (1.2-5.0)	–	1.6 (1.0-2.6)	Rigel et al. 1983[16]
Canada	1979-81	595/595	1.7 (1.1-2.7)	0.9 (0.6-1.5)	1.2 (0.7-2.0)	Elwood et al. 1985[17]
USA	1974-80	404/521	–	0.7 (0.3-1.3)	0.6 (0.4-0.9)	Graham et al. 1985[18]
UK	1980-82	58/333	6.5 (not given)	–	–	Sorahan & Grimley 1985[19]
USA	1972-82	1,103/585	1.7 (1.2-2.3)	2.5 (1.4-4.4)	1.1 (0.8-1.6)	Dubin et al. 1986[20]
UK	1981-84	83/83	–	1.7 (0.3-8.6)	–	Elwood et al. 1986[21]
Australia	1980-81	511/511	1.1 (0.7-1.8)	–	0.7 (0.4-1.1)	Holman et al. 1986[22]
Australia	1979-80	183/183	1.9 (0.5-7.4)	–	2.3 (0.9-6.1)	Green et al. 1986[23]
Italy	1983-85	103/205	0.9 (0.5-1.7)	–	0.6 (0.4-1.0)	Cristofolini et al. 1987[24]
Italy	1984-86	208/416	–	2.1 (0.6-6.8)	–	Zanetti et al. 1988[25]
Denmark	1982-85	474/926	1.8 (1.2-2.5)	0.7 (0.5-0.9)	–	Osterlind et al. 1988[26]
Germany	1987	200/200	–	5.5 (1.2-25.3)	–	Garbe et al. 1989[27]
France	1986-88	207/295	8.4 (3.6-19.7)	2.5 (1.2-5.1)	3.8 (2.2-6.5)	Grob et al. 1990[28]
Sweden	1978-83	523/505	1.8 (1.2-2.6)	0.6 (0.4-1.0)	–	Beitner et al. 1990[29]
USA	1979-82	289/527	1.5 (1.0-2.4)	1.8 (0.9-4.0)	1.7 (1.1-2.8)	Dubin et al. 1990[30]
Italy	–	260/416	2.3 (1.4-3.8)	–	–	Zanetti et al. 1992[31]
USSR	–	–	3.4 (0.6-17.4)	–	–	Zaridze et al. 1992[32]
USA	1977-79	324/415	2.0 (1.3-3.3)	0.7 (0.5-1.0)	–	Herzfeld et al. 1993[33]
Pan-European	1991-94	420/447	6.1 (1.8-20.3)	0.3 (0.1-0.9)	–	Autier et al. 1994[34]
Netherlands	–	128/168	2.4 (1.3-4.2)	–	–	Nelemans et al. 1994[35]
USA	1984-87	256/273	–	0.6 (0.3-1.2)	0.9 (0.5-1.6)	White et al. 1994[36]
Sweden	1988-90	400/640	1.2 (0.8-1.8)	0.8 (0.6-1.0)	–	Westerdahl et al. 1994[37]
USA	1981-86	452/930	0.8 (0.6-1.1)	0.8 (0.5-1.5)	–	Holly et al. 1995[38]
Spain	1988-93	105/138	4.9 (2.2-10.9)	3.7 (1.7-7.5)	5.4 (2.4-12.0)	Rodenas et al. 1996[39]
USA	1987-89	548/494	H&N 2.6 (1.2-5.6)	0.5 (0.2-1.1)	–	Chen et al. 1996[40]
			UL 2.4 (1.2-4.8)	0.6 (0.2-1.1)		
			LL 2.7 (1.2-5.8)	0.3 (0.1-0.9)		
			T 2.7 (1.6-4.5)	0.9 (0.6-1.3)		

Table 1 adapted from Elwood and Jopson; Int J Cancer,1997;73:198-203.

OR = Odds ratio; 95%
CI = 95% confidence intervals
H&N = Head and Neck
UL= Upper Limb
LL = Lower Limb
T = Trunk

predisposing to familial melanoma. More recently, a specific (CDKN2A) germline mutation on chromosome 9p21 has been found to be associated with melanoma in about 50 to 80 percent of families with very high incidence of melanoma.[56,57] At the present time, these germline mutations are thought to be transmitted from one generation to another in an autosomal dominant pattern, with variable penetrance, and individuals with them appear to be at high risk for the disease. However, such mutations account for fewer than 10 percent of the melanomas, and as population-based rather than family-study-based data on the mutation becomes available, this estimate will undoubtedly decline further. Interestingly, the presence of CDKN2A mutations does not appear to materially affect the relationship between solar UV and melanoma risk in carriers.[58] Reported family history of melanoma in a first degree relative (without testing for CDKN2A mutation) is only associated with approximately a twofold elevated risk of melanoma.[59]

Artificial ultraviolet radiation

A total of 14 studies have evaluated risk of melanoma in sunlamp and sunbed users,[21,22,26,37,38,46,60-67] although the relatively minimal data presented in four of them preclude a proper interpretation of their results.[21,22,46,67] Table 2 presents selected results from the ten studies with relatively complete data. Because most of the studies conducted to date have small numbers of exposed subjects, they have limited statistical power. This has resulted in unstable risk ratios, with wide confidence intervals surrounding the risk estimates. Because of this, a recent meta-analysis was conducted in an attempt to summarize current knowledge.[68] Ten studies provided estimates of risk for being exposed to sunbeds and sunlamps. Where possible, risk ratios adjusted for host susceptibility and sun exposure were used in the analysis. Compared to those with no exposure, those who had ever used sunlamps or sunbeds had a 25 percent increase in risk of CMM, which was statistically significant (95% CI: 1.05-1.49). Compared with subjects having no sunlamp or sunbed exposure, those with the "longest duration or highest frequency of exposure" had a relative risk of 1.61 (95% CI, 1.21-2.12). The analysis suggests that, overall, the existing body of epidemiological work indicates that use of sunbeds and sunlamps does increase risk of CMM.

Results of the meta-analysis must be interpreted with caution because there is likely to be at least some residual confounding due to host factors. Furthermore, individuals who use sunbeds to tan are also likely to engage in concomitant sunbathing. If this exposure is not adequately controlled for in the analyses, it is possible that the increased risk attributed to sunbed use may be explained in whole or in part by solar exposures. Finally, recreational exposure to artificial UV prior to the early 1980s entailed substantial UV-B exposure, whereas later (largely commercial) exposure was predominantly to UV-A. Thus, an analysis combining these exposures could conceivably be aggregating qualitatively different exposures. However, it should be noted that risk ratios from later studies do not appear to differ materially from those seen in earlier studies.

More research is necessary in this field to answer unresolved issues surrounding the relationship between artificial UV and CMM. Though contrary to some popular advertising, the body of available evidence does not suggest that artificial tanning reduces risk of CMM.

Solar UV-A

Solar UVR that reaches the Earth's surface comprises approximately 95% UV-A and 5% UV-B: UV-C is completely filtered out by the Earth's atmosphere.[2] Recent studies using the Xiphophorus fish model have demonstrated that UV-A radiation is effective in inducing malignant melanoma in this species.[69] In particular, melanoma induction showed particular sensitivity at the 365 and 405 nm wavelengths. Such findings have led to the suggestion that UV-A radiation may also induce CMM in humans.[70] This has led other investigators to suggest that the advent of effective UV-B sunscreens in the 1960s, and their adoption for common use shortly thereafter, may have inadvertently fueled the increase in CMM incidence as a result of increased UV-A exposure.[71] The authors propose that light-skinned individuals might expose themselves to the sun for much longer periods than previously because the onset of erythema is delayed by sunscreen use. This makes possible substantially more UV-A exposure in melanoma-susceptible individuals. A randomized trial conducted by Autier et al. tested the hypothesis that use of higher sun protection factor (SPF) sunscreens encourages longer exposure.[72] Study subjects were randomized to unlabelled SPF 10 or SPF 30 sunscreen prior to vacation with instruction to use the sunscreen as needed and record time in the sun. Both groups used similar amounts of sunscreen, recorded similar sunburn patterns and similar mean vacation days, but subjects randomized to the SPF 30 compound spent significantly more time in the sun each day than those randomized to the lower SPF sunscreen. Thus, though there is some empirical evidence to support the notion that sunscreen use increases time in the sun, the findings apply as strongly to UV-B as to UV-A. It should be noted that the increase in incidence of CMM began prior to the advent of sunscreens,[73] and that current incidence data suggest that age-standardized melanoma rates in young people are levelling off and perhaps beginning to decline.[74] This trend is happening in the face of increasing popularity of very high SPF sunscreens, which should be allowing greater UV-A (and UV-B) exposure than ever.

Non-melanocytic skin cancer

Solar ultraviolet radiation

Ecological data collected in the US in the 1970s on the relationship between solar UVR and the two major forms of non-melanocytic skin cancer (NMSC), namely basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), indicated an incidence gradient from north to south within the country among the white population. This gradient correlated well with indices of UVR obtained using Robertson-Berger meters situated close to the areas where the cancer incidence information was collected.[75] This close correlation reinforced the prevailing hypothesis that the two major forms of NMSC were directly related (in white individuals) to cumulative solar UV exposure. However, recent results from a number of well-conducted analytic studies

TABLE 2
Summary of case-control and cohort studies of sunlamp or sunbed use and cutaneous malignant melanoma

Place of study	Diagnosis years	No. of cases/ controls	Exposure	Summary OR		Reference
Eastern Denmark	1982-85	474/926	Sunlamp and sunbed use	0.7	(0.5-1.0)	Osterlind et al. 1988[26]
Scotland	1979-84	180/197	Sunlamp and sunbed use	2.9	(1.3-6.4)	Swerdlow et al. 1988[60]
Southern Ontario, Canada	1984-90	583/608	Sunlamp and sunbed use	Males: 1.9	(1.2-3.0)	Walter et al. 1990[61]
				Females: 1.5	(1.0-2.1)	
Germany	1984-87	856/705	Use of sunbeds	1.5	(0.9-2.4)	Garbe et al. 1993[63]
Pan-European	1991-93	420/447	Sunlamp or sunbed use	Overall: lamps: 1.3	(0.8-2.0)	Autier et al. 1994[62]
				Beds: 0.8	(0.6-1.2)	
				Tanning: lamps: 1.8	(1.0-3.2)	
				Beds: 1.0	(0.6-1.4)	
Southern Sweden	1988-90	400/640	Sunlamp or sunbed use	Overall: 1.3	(0.9-1.8)	Westerdahl et al. 1994[37]
California, USA	1981-86	452/930	Sunlamp use	0.9	(0.7-1.2)	Holly et al. 1995[38]
Connecticut, USA	1987-89	624/512	Sunlamp use	1.13	(0.8-1.5)	Chen et al. 1998[64]
South Sweden	1995-97	571/913	Sunbed use	1.2	(0.9-1.6)	Westerdahl et al. 2000[65]
Sweden and Norway	1991-99	Total cohort 106,379	Sunbed and sunlamp use	1.55	(1.0-2.3)	Veierod et al. 2003[66]

OR = Odds ratio

Odds ratios presented are adjusted for other known melanoma risk factors (susceptibility and sun exposure) where such adjustment was carried out in the study.

(Table 3) suggest that the relationship of SCC and BCC to UVR is as complex as that seen for CMM.

Most studies[76-88] have used relatively simple questions to elicit information on solar exposure from subjects. Results from one study[84] are difficult to interpret as BCC and SCC were combined in the analysis. In addition, the Egyptian population used in the study differs from other investigations in terms of pigmentary risk characteristics.

Later studies were designed specifically to separate the contributions of intermittent and constant solar exposure to risk, and appear to show differences between BCC and SCC.[89-93] Overall, the studies demonstrate little or no relationship between measures of intermittent recreational exposure and SCC, but significant associations with BCC. Indeed, the studies of Kricker et al.[89] and Gallagher et al.[90] both suggest a dose-response gradient in BCC risk with increasing exposure to recreational UVR, particularly in youth. For SCC, the weight of evidence appears to suggest that risk is related to measures of constant (occupational or cumulative) exposure. In the study of Gallagher et al.,[91] this form of skin cancer is related to exposures in the ten years prior to diagnosis, while the Rosso et al.[92] and English et al.[93] studies indicate a relationship with longer-term occupational exposure.

While results of these studies require confirmation, it appears that cutaneous malignant melanoma and BCC share a number of similarities in their relationships with solar UVR. Both appear much more strongly related to measures of intermittent UV exposure, particularly in early life, than to measures of cumulative lifetime exposure. Squamous cell carcinoma appears to be different in that it owes more to constant or cumulative sun exposure than to intermittent exposure. In addition, there is as yet little evidence which has reported that sun exposure in childhood or youth is strongly related to this disease.

Artificial UV exposure

There have been few studies specifically addressing the potential relationship between sunbed and sunlamp use and risk of NMSC.[76,94] The few investigations conducted to date are summarized in Table 4. Overall, they indicate little increased risk, with the exception of the study of Aubrey and MacGibbon.[76] However, the 13-fold increased risk of SCC seen in subjects using "long-tube sunlamps" is based on small numbers of study subjects, and so must be interpreted with caution. Well-conducted analytic studies with quantitative exposure data and good control for susceptibility factors and concomitant sun exposure are urgently needed to clarify risk.

Cancer of the lip

Cancer of the lip is rare in Canada and comprised only about 0.2 percent of cancers in females and 1.3 percent in males during the period 1984-1988, although by 2003 the rate in females had dropped to 0.1 percent and for males to 0.4 percent.[95,96] The decline among males is likely due to the reduced rates of smoking and the continuing reduction in outdoor occupations.[96,97] Both male and female proportional declines are also likely influenced by increases in incidence at other cancer sites. Evaluation of incidence rates in this cancer is complicated by the fact that diagnoses are a mixture of neoplasms of the external lip and the oral cavity.[2] Descriptive studies show that lip cancer is more common in males than females and that incidence rates are higher in light- than dark-skinned populations living in the same geographic area.[51] Evaluation of mortality and incidence data from Australia show that rates of lip cancer are

Table 3
Summary of case-control and cohort studies of solar UV radiation and non-melanocytic skin cancer

Place of study	Diagnosis years	Type of study	No. of cases	No. of comparison subjects	OR (95% CI) in highest sun exposure category			
					Intermittent	Occupational	Total	Reference
Canada	1977-78	Case-control	92	174	SCC: 4.6 (0.58-36.53)	SCC: 9.12 (0.99-84.47)		Aubrey & MacGibbon, 1985[76]
Australia	1987	Cross sectional	42	2,095 total subjects		SCC & BCC: 1.76 (0.77-4.05)		Green et al. 1988[77]
USA	1985-86	Cross sectional	33 BCC 35 SCC	808 subjects		BCC: 1.11 (0.5-2.44) SCC: 2.53 (1.18-5.40)		Strickland et al. 1989[78] Vitasa et al. 1990[79]
Canada	1988	Case-control	538 BCC	738		BCC: 1.29 (1.12-1.46)		Hogan et al. 1989[80]
Australia	1985-87	Cross sectional	66 BCC 21 SCC	1,770 total subjects	BCC: 0.6 (0.3-1.3) SCC: 3.9 (0.5-30.9)	BCC: 1.3 (0.6-2.8) SCC: 5.5 (1.1-28.2)		Green & Battistutta, 1990[81]
USA	1980-84	Cohort	771 BCC	73,366 total cohort			BCC[e]: ≈ 1.4 (calculated)	Hunter et al. 1990[82]
USA	1982-90	Cohort	197 SCC	107,900 total cohort			SCC[f]: ≈ 1.4 (calculated)	Grodstein et al. 1995[83]
Egypt	91	Case-control	136 BCC & SCC	145		BCC and SCC[b]: 7.7 (4.0-14.6)	BCC and SCC[d] 6.1 (2.3-16.0)	Khwsky et al. 1994[84]
Australia	1987	Case-control within a cohort	226 BCC	1,015	BCC: 3.86 (1.93-7.75)			Kricker et al. 1995[89]
Canada	1983-84	Case-control	226 BCC SCC	406	BCC: 2.6 (1.1-6.5)[c] SCC: 1.6 (0.6-4.5)[c]	BCC: 1.4 (0.8-2.4) SCC[a]: 4.0 (1.2-13.1)	BCC: 1.3 (0.7-2.4) SCC: 1.0 (0.4-2.1)	Gallagher et al. 1995[90,91]
Pan-European	1989-93	Case-control	1,549 BCC 228 SCC	1,795	BCC: 1.47 (1.18-1.83) SCC: 0.63 (0.39-1.03)	BCC: 0.84 (0.65-1.10) SCC: 1.60 (0.93-2.75)		Rosso et al. 1996[92]
Australia	1987	Case-control within a cohort	132 SCC	1,031	SCC on usually exposed sites: 1.3 (0.57–2.90) SCC on usually non-exposed sites 0.94 (0.36–2.60)	SCC on usually exposed sites: 1.3 (0.58–2.80) SCC on usually non-exposed sites 1.8 (0.55–5.60)		English et al. 1998[93]

OR = Odds ratio; 95% CI = 95% confidence intervals

[a] Occupational sunlight in the 10- years prior to diagnosis

[b] Outdoor vs. indoor occupation

[c] Recreational sunlight exposure age 0–19

[d] Heavy sun exposure vs. light exposure

[e] Subjects who used sunscreen and had 8 or more hours per week of sunlight compared to those with < 8 hours/week of exposure.

[f] Subjects who used sunscreen and had "regular time outdoors" compared to those without regular time outdoors.

TABLE 4
Summary of case-control or cross sectional studies of sunlamp & sunbed use and non-melanocytic skin cancer

Place of study	Diagnosis years	No. of cases/controls	Exposure	Summary OR in highest exposure category (95% CI)	Reference
Canada	1977-78	92/174	Sunlamp use	13.42 (1.38-130.48)	Aubrey & MacGibbon 1985[76]
Ireland	Unknown	63 SCC & 58 BCC/121	Artificial sunlight	0.3 ns (calculated)	O'Loughlin et al. 1985[85]
Ireland	1984-85	396 BCC & SCC /396	Sunlamp & sunbeds	0.7 ns (calculated)	Herity et al. 1989[86]
Canada	1960s to 1980s	857/2,753	Medical phototherapy or sunbed use	1.33 (1.04-1.70)	Hogan et al. 1991[87]
USA	1980-86	1,805	Sunbathing or sunlamp use	1.04 (0.67-1.63)	Karagas et al. 1992[88]
Canada	1984-85	226 BCC & 180 SCC/406	Sunlamp use	BCC: 1.2 (0.7-2.2) SCC: 1.4 (0.7-2.7)	Bajdik et al. 1996[94]

OR = Odds ratio; 95% CI = 95% confidence intervals

lower in migrants from low sunlight areas than they are in native-born Australians.[98,99] This finding is suggestive of the pattern seen in malignant melanoma in Australia[49] and may indicate the importance of sun exposure in youth for lip cancer.

Several studies have indicated that outdoor workers, such as farmers[100-102] and fishermen,[103] have elevated risks for lip cancer relative to the general male population or other males. A case-control study conducted in Los Angeles to evaluate risk factors associated with the sex differences in lip cancer incidence showed higher risk in those with fair complexion and in smokers.[104] Increased risks were strongly related to lifetime solar exposure (Relative Risk [RR] highest quartile 13.5, 95% CI: 4.5-40.6) and to annual time spent outdoors. Among those with high lifetime sun exposure, the risk was twice as high in women using lip protection once per day or less than those using it at least twice per day. These findings suggest that the stronger association between UV and cancer incidence observed among men, relative to women, may be explained, in part, by the increased use of lip protection by women. In summary, lip cancer appears to be causally related to lifetime sun exposure.

Melanoma of the eye

Ocular melanoma is a rare condition with an incidence rate in Canada of about seven per million population.[51] The rarity of this cancer has meant that few studies have been conducted and knowledge of the etiology is limited. Also, because subjects with this cancer are widely dispersed, the few studies have usually been restricted to telephone or postal questionnaires, which are probably inferior to in-person interviews for assessing important host susceptibility factors for melanoma.

The first case-control study[105] evaluated cumulative solar exposure as well as intermittent and constant exposure, and reported no differences between cases and controls, although odds ratios were not presented in the paper and this study had limited statistical power (65 cases and 65 controls). The study did indicate that subjects with light skin and blue or grey eyes were at an elevated risk of uveal melanoma; similar findings were seen in later studies.[106-108]

Tucker et al.[106] found an elevated risk of ocular melanoma in subjects born in the southern US (and thus perhaps exposed to higher levels of UVR in youth) by comparison with those born in the north. The Tucker study found elevated odds ratios for subjects who reported gardening outdoors, but similar associations were not seen with other outdoor activities. No elevated risks for solar exposure were seen in Holly et al. as assessed by tendency to tan or sunburn and vacation and leisure-time activities.[107] Seddon et al.[108] compared 197 patients with ocular melanoma with 385 controls recruited through random digit dialling and found an elevated but non-statistically significant risk of ocular melanoma among subjects with the highest reported outdoor exposure, relative to those with the lowest.

More recent evidence for an association between ocular melanoma and UVR came from a study conducted in Australia. A national case-control study of ocular melanoma cases diagnosed between 1996 and mid-1998, with controls frequency matched by age and sex, demonstrated higher risks in subjects with grey, hazel or blue eyes.[109] An increased risk of the cancer was found with increasing quartile of sun exposure up to 40 years of age (RR in highest quartile = 1.8 ;95% CI: 1.1-2.8), after controlling for phenotype susceptibility factors.[110] Interestingly, no indication of increased frequency of CDKN2A germline mutations was found in 62 ocular cases and their ethnically matched controls, suggesting that genetic predisposition is not the strong factor in ocular melanoma that it is in CMM.[111]

In general, evidence for associations between solar UVR and ocular melanoma has been weak to date. As the incidence of this cancer has not increased during the period in which cutaneous melanoma incidence has risen sharply, it seems unlikely that ocular melanoma will become a major public health hazard. Further studies of the relationship with solar UVR are unlikely to be productive until better measures of past solar exposure become available.

Three studies on sunlamp and sunbed use[106-108] have shown at least one measure of exposure to be related to increased risk of ocular melanoma; only two of these risk estimates are statistically significant. The exposure prevalence is very small, however, and these results should be interpreted

cautiously. More studies with better quantitative data on artificial UV exposure are necessary before firm conclusions about a causal relationship can be reached.

Non-Hodgkin lymphoma

Solar ultraviolet radiation

Non-Hodgkin lymphoma (NHL) is the fifth most important cancer in Canada in terms of incidence.[96] It is clear that the factors known to increase risk of NHL, including AIDS (Acquired Immune Deficiency Syndrome), can account for only a portion of the incidence rise[112-113] seen over the past 20 to 30 years in this group of cancers.

Recently a number of investigators using descriptive data have suggested that sunlight exposure may be important in the etiology of NHL. This hypothesis is based on a number of lines of evidence. First, the increase in incidence of NHL roughly parallels the increases seen for CMM and NMSC.[114-115] This suggests that the factors known to be responsible for the increases in skin cancers may also be involved in NHL. The most significant factor for both CMM and NMSC is sunlight exposure.[17,22,26,46,89-93]

The second line of evidence comes from parallel gradients of risk for NHL, CMM and SCC with proximity to the equator. Within the UK[116] there is an incidence gradient for NHL, with higher rates in the south similar to that seen with CMM. Mean daily duration of bright sunlight in southern UK is 50 percent greater than in the north.[117] Rates of NHL among countries in the northern hemisphere differ markedly; those whose population resides below 40 degrees north latitude have rates approximately 50 percent higher than those above 50 degrees north latitude.[118] Using tables of ambient solar irradiation, McMichael and Giles plotted incidence rates of NHL from 49 cancer registries against ambient solar UVR. A strong, statistically significant correlation was seen between ambient solar irradiation determined by latitude of population residence and age-standardized incidence of NHL and of CMM. This relationship was similar in both males and females. The authors point out that no gradient is seen within some countries, such as Canada. However, as the majority of the Canadian population resides in close proximity to the country's southern boundary, this is not unexpected. A separate study showed no latitude gradient in the US for NHL,[119] but this was based on mortality data only, as incidence data were not available for the whole country.

A further line of evidence originates in studies of second primary tumours arising in cohorts of both NHL and skin cancer patients. Adami et al.[114] showed a significantly increased risk of SCC (RR 5.5) and CMM (RR 2.8) among patients with NHL. In addition, an increased risk of NHL was seen in patients with prior SCC. In contrast to these findings, no other second primary tumours appeared to be elevated among the NHL and SCC cohorts, suggesting a similar causal agent in the two tumours. The authors noted the possibility of surveillance bias in the cohorts; however, the lack of elevated risk for other cancers argues against this explanation.

A further study carried out in Switzerland showed a twofold risk of subsequent NHL among a cohort of 11,878 BCC patients.[120] Of interest is that significantly increased risks of similar magnitude were seen also for cancer of the lip, for SCC and for CMM, each of which (along with BCC) is known to be strongly related to sunlight exposure. No other cancer sites showed significantly increased incidence rates in the BCC cohort. It is possible that such increases in second primaries are due solely to an underlying immunosuppression among the cohorts. It has been shown that SCC and NHL are both more common in individuals who are immune compromised, such as kidney transplant patients and AIDS patients. However, as will be discussed, solar and artificial UVR have been demonstrated to cause immune suppression. This suppression has been suggested as one of the reasons, along with its ability to damage DNA, that UVR causes skin cancer. Furthermore, little evidence of an excess of CMM and cancer of the lip has been seen among patients immune compromised by renal transplantation or AIDS. This suggests that the independent effects of DNA damage and immune suppression from UV might be at work in the excess of NHL seen in cohorts of skin cancer patients.

Studies of migrants are often helpful in assessing the importance of environmental factors, as exposure often dramatically changes by comparison with the country of origin. Thus, data comparing NHL rates in migrants from low sunlight areas (such as the UK) to high sunlight areas (such as Australia and New Zealand) and vice versa are instructive with the caveat that changes in sunlight are likely accompanied with changes in diet (or other lifestyle factors) which may relevant to NHL. Cancer incidence data from Australia show that rates of NHL in migrants from the UK are similar to those of native-born Australians, and substantially higher than those of nationals remaining in the UK and Wales.[121] The increase in risk for NHL in UK migrants is similar in magnitude to that seen for CMM. In UK migrants to New Zealand, a significant increased risk for NHL is seen in both males and females by comparison with their expected risk, based on rates in England and Wales.[122] By contrast, New Zealand males and females migrating to the UK experienced reduced risks for NHL by comparison with their expected risk, based on rates seen in New Zealand.

Several studies have noted an increased risk of NHL among farmers.[123] Although there is some evidence that this might be due to agricultural chemical use, the data are not compelling. Farmers also receive high cumulative solar UV exposures. Similarly, American soldiers having served in Vietnam have been reported by some—but not all—studies to have elevated rates of NHL.[124-125] Although it has been suggested that this is due to exposures to herbicides, high sunlight exposure in Vietnam may have played a role.

The mechanism by which UVR might increase risk of NHL is through systematic immune supression. There is a substantial body of evidence that suggests that UVR causes significant changes in human immune status. Chronic high levels of UV-B exposure have been reported to be immunosuppressive through induction of suppressor T-cells.[126] Hersey et al.[127] have also reported that exposure of human volun-

teers to UV-A radiation for 30 minutes per day over a twelve-day period provoked a reduction in natural killer cell activity, with an accompanying decline in the number of such circulating cells. It is also known that T-lymphocytes are substantially more sensitive to the cell killing effects of UV-B than are fibroblasts.[128] This indicates that, even at relatively low levels, an effect might be seen from UV exposure on the cells critical to human immune function. Granstein[129] and Murphy et al.[130] have also noted that fairly low doses of UVR result in depletion of epidermal Langerhans' cells and in reduced levels of activity. Langerhans' cells are important participants in the immune process as they present antigens to antibody producing cells in the body. Finally, there is animal evidence indicating that UVR produces suppressive effects on the immune systems of mice and impairs their ability to reject antigenic transplanted UV-related tumours,[131-132] including melanoma.[133] The evidence suggesting that UV-A might be nearly as effective as UV-B in inducing immune suppression could be particularly important, as use of UV-A sunbeds for tanning in Europe has increased rapidly in recent years, particularly among young people. It has been suggested that this could be related to the increases in NHL seen in Europe in young persons.[134]

Notwithstanding data from descriptive studies suggesting that sunlight exposure may be positively related to NHL, the evidence from carefully conducted case-control studies to date does not support this. A recently reported study in Australia found an inverse relationship between sun exposure and NHL.[135] Similar results were seen in a Scandinavian study.[136] After adjustment for potential confounders, a case-control study conducted in Sweden and Denmark also showed a reduced risk of NHL with increasing frequency of sun vacations abroad, and episodes of sunbathing at age 20 and 5 to 10 years prior to interview. A similar—though non-statistically significant association—was also detected for Hodgkin lymphoma. These results suggest that the increased frequency of skin cancer in those with prior NHL, and vice-versa, may not be related to UVR exposure, and also heighten the need for more studies of NHL, Hodgkin lymphoma and solar and artificial UV radiation.

Solar UVR and cancers of the colon, breast, ovary and prostate

Several review articles[137,138] examining primarily laboratory evidence, and also some epidemiological findings, have suggested that sunlight exposure may exert a protective effect against a number of cancers including colon, prostate, breast and perhaps other female cancers. The suggested mechanism of action is that the active metabolite of vitamin D ($1,25(OH)_2D$) inhibits proliferation and induces differentiation of cells that carry vitamin D receptors. This hypothesis is not new; in 1980, an ecological correlation study examining latitude of residence and colon cancer mortality found lower rates with declining latitude in North America.[139]

The role of solar UV-B in stimulating vitamin D synthesis is thought to be a potential mechanism by which sunlight might affect incidence of these internal cancers. Although some vitamin D is taken in food, principally through consumption of fish, eggs and vitamin-D-enriched milk, most vitamin D is synthesized from 7-dehydrocholesterol in the skin under the influence of UV-B radiation in sunlight.[140] It is then hydroxylated to 25(OH)D in the liver, and further, into biologically active $1,25\ (OH)_2\ D$ in the kidney. As noted above, this metabolite acts like a hormone and is taken up by many organs in the body. Receptors for vitamin D are present in breast and prostate tissue.[140] Furthermore, there is evidence that proliferation of cultured human prostate cancer,[141,142] breast cancer,[143,144] and colon cancer cells[145,146] are inhibited by Vitamin D. Finally, *in vivo* animal studies appear to show vitamin D induced inhibition of carcinogen induced colon[147] and mammary tumours[143] in rats.

Colon cancer

Garland and Garland[139] noted that colon cancer death rates were lower in areas of the US with high solar UV levels than in low sunlight areas. They hypothesized that this finding might be due to sunlight's ability to stimulate increased serum levels of vitamin D. A more detailed ecological correlation study which used incidence rates and also attempted some control for duration of residence in an area prior to diagnosis also found that risk of colon cancer appeared to be lower in high sunlight areas of the US.[148] Bostick et al.,[149] in an analysis of dietary intake among older women with colon cancer, found a modest protective effect for dietary calcium and vitamin D.

Intake of dietary vitamin D and calcium has been associated with lower risk of colon cancer and adenomatous polyps in a number of studies.[150-152] However, in at least one of these studies, vitamin D consumption is highly correlated with multivitamin use and the attendant concern that the effect attributed to vitamin D may actually be due to another vitamin.[152]

Several cohort studies have shown a reduced risk of colon cancer in subjects with high serum vitamin D levels.[153-158] A further investigation demonstrated a modest protective effect for high serum vitamin D, but only in certain sites in the colon.[159]

Not all studies of colon cancer and vitamin D have been positive. Several[160,161] (including cohort studies) have shown either no protective effect or suggestion of an effect which is not strong enough to be statistically significant.[162]

At the present time there is strong suggestive evidence that vitamin D, perhaps in conjunction with calcium, may reduce the risk of colon cancer and its precursor lesion, adenomatous polyps. Most of this evidence is based on studies of dietary intake of the vitamin. There is little direct evidence showing that increased sunlight exposure reduces risk. Any evidence comes from ecologic correlation studies, a relatively weaker form than that which analytic studies might provide.

Breast and ovarian cancer

Gorham et al.[163] examined mortality rates for breast cancer in the USSR and found the highest rates in the regions with the lowest sunlight levels. The relationship appeared

to persist after an attempt to control for socio-economic factors, but no control was possible for ethnic and dietary factors. The association could have been due to other factors. Studies by Garland et al.[164] and Freedman et al.[165] also suggested that mortality from breast cancer is lower in areas of the world with more sun exposure. However, data from the Nurses' Health study did not find a geographic gradient for breast cancer.[166] Again, these studies are of the ecologic correlation variety and no actual measurements of sunlight exposure were made.

Analysis of data from the US National Health and Nutrition Examination Survey (NHANES) suggested that sunshine exposure may reduce risk of breast cancer (RR in highest sun exposure group relative to the lowest was 0.54, 95% CI: 0.28-1.02).[167] The authors suggested that high serum levels of vitamin D, mediated through higher levels of sun exposure, might be responsible for this reduced risk. A further investigation carried out in Scandinavia suggested that women diagnosed with breast cancer in the summer months had longer survival than those diagnosed in winter.[168] The authors suggested that this might be due to a beneficial effect of sunlight.

Case-control data from North Carolina showed significantly lower serum levels of 1,25 dihydroxy vitamin D in breast cancer cases than in controls.[169] More recently, studies of dietary vitamin D have demonstrated that women with a high intake had lower risks of breast density[170] and breast cancer.[171] Neither of these examined exposure to UV radiation as a factor in vitamin D levels among the women.

Several studies of mortality from ovarian cancer[165,172] have demonstrated lower rates in high sunlight areas. The evidence for a protective effect of sunlight exposure in breast or ovarian cancer is, at present, modest. Furthermore, there is only scant evidence that either dietary intake of vitamin D, or serum levels of this vitamin, are associated with either cancer.

Prostate cancer

Several geographic studies of prostate cancer mortality in the US indicated decreased mortality in the southern US, consistent with an effect of sunlight exposure.[165,173] The authors hypothesized that the effect might be due to the effect of UVR on vitamin D production. Schwartz and Hulka noted an increased risk of prostate cancer in men with higher serum levels of vitamin D binding protein.[174] A study of prediagnostic serum levels of vitamin D found a higher risk of prostate cancer in men with low levels of 1,25 dihydroxy vitamin D, although there was no difference for levels of 25 dihydroxy vitamin D.[175] One further investigation showed similar results (Ahonen et al. 2000).[176] Several other studies have shown no association between serum levels of vitamin D or its metabolites and subsequent risk of prostate cancer.[177-181] The Scandinavian study noted earlier found a better prognosis in men diagnosed with prostate cancer in summer than in winter.[168] A study of vitamin D receptor polymorphisms, vitamin D levels and prostate cancer among US physicians found little effect of different variants of the *Bsm*I and *Taq*I polymorphisms on risk of prostate cancer.[182]

Two different investigations[183,184] conducted by John et al. have suggested a reduced risk of prostate cancer as sun exposure increases. The first, conducted using data from the NHANES I study, showed that inhabiting a more southernly located region of the US (rather than a northern one) might reduce risk of the disease.[183] The second was a case-control study in which the ratio of skin reflectance on a sun-exposed site of the body (i.e., forehead), compared to that on a non-exposed site (i.e., upper underarm), served as a measure of sun exposure.[184] However, it is possible that this metric is actually a better indicator of ability to tan vs burn in the sun, rather than a measure of solar exposure *per se*. A number of other sun exposure measures in the same study, showed little or no association with risk.

In summary, the results of studies linking sun exposure to subsequent risk of colon, prostate, breast and ovarian cancer have not yet demonstrated a convincing relationship between exposure and internal cancers. However, taken together, they do suggest a possible protective effect, at least for colorectal cancer, perhaps through the stimulation of higher serum levels of vitamin D. Many of the studies are descriptive or, if analytic, may suffer from incomplete control for confounders. The results from a recently published randomized clinical trial suggest that interventions designed to increase serum levels of vitamin D and calcium among postmenopausal women in order to reduce osteoporosis, might also reduce their risk of developing cancer (Lappe et al, 2007).[185] However, it should be noted that the follow-up of the women in the trial was very short, providing insufficient study power to assess individual cancers. Furthermore, there was no intervention arm dedicated to vitamin D alone, and so it is difficult to determine the effects of the vitamin in the absence of supplemental calcium. Finally, the reduced incidence of cancer was achieved without increasing exposure to solar or artificial UV, and so it appears clear that the benefits might be realized without increasing risk of UV related diseases. More research is needed, and it is clearly inappropriate at this point in time to suggest that more solar exposure, particularly in fair-skinned populations, is a rational cancer prevention strategy.

Impact of UVR on cancer incidence and mortality in Canada

Attributable fraction

The impact of UVR-related cancer in Canada can be estimated through reference to incidence and mortality data. The major cancer types known to be related to solar or artificial UVR are CMM and NMSC, as well as cancer of the lip. It was estimated that in 2007, 4,600 new cases of melanoma would be diagnosed.[96] In 2003 there were about 350 new cases of lip cancer.[96] In addition, it was estimated that about 69,000 new cases of basal cell, squamous cell and other non-melanocytic skin lesions would be diagnosed. Armstrong and Kricker[5] have estimated

that about 93 percent of CMM in Canada can be attributed to solar UVR. It is likely that the figure for SCC and BCC would be very similar.

Deriving an estimate of the burden of skin cancers caused by artificial UVR, in particular that from sunbed and sunlamp use, is more difficult. Although a recent meta-analysis has shown a positive association between sunbed exposure and CMM, the odds ratios are relatively low for most users.[68] Among those in the highest use categories, the risk ratios found in the meta-analysis are similar to those seen for reported sun exposure. However, with probable imperfect control for concomitant solar exposure, it is possible that at least some of the elevated risk in frequent users is due to outdoor sunbathing for tanning purposes. Marrett[186] has estimated the population attributable risk for CMM due to sunlamp and sunbed use at between 6 and 15 percent if true relative risk is about 1.2, which is compatible with the aggregated data seen in the meta-analysis. Thus, if sunlamp and sunbed exposure is causally related to CMM, then combined with solar exposure, most of the CMM incidence seen today in this country can be attributed to one form or another of UVR.

The studies carried out to date do not allow an estimate to be made of the proportion of non-melanocytic skin cancer attributable to sunbed and sunlamp use.

The proportion of lip cancer attributable to sunlight exposure is difficult to estimate, as other factors such as pipe and cigarette smoking are also etiologically significant. However, the study of Pogoda et al.[104] suggests that the use of lip covering (lipstick) among women more than once per day results in a 60 percent reduction in risk of the disease. It seems likely, then, that some 50 percent of the incident cases, probably in both sexes, are attributable to solar exposure. No studies have yet addressed the issue of artificial UV exposure and lip cancer risk, but the attributable fraction must be very small.

The original hypothesis that sunlight exposure might contribute to an increased incidence of non-Hodgkin lymphoma is of concern. However, the analytic studies conducted to date[135,136] appear to show a reduced—rather than increased—risk with high exposure. Further studies of a putative relationship are in the analysis phase and until the nature of the relationship is firmly established, no estimate can be made of the impact of UVR on the incidence or mortality of this disease.

Similarly, it is not possible to estimate the role of sunlight in the prevention of solid, internal cancers since a causal relationship has not been convincingly demonstrated. Further analytic studies are needed to illuminate the relationship between solar UV exposure, circulating vitamin D levels, and colon, prostate, and breast cancer.

In summary, some 4,500 life-threatening cancers per year are thought to be directly causally related to UVR, as well as some 64,000 less serious (basal and squamous cell) skin cancers and cancers of the lip. Melanoma of the eye, although very rare, is likely related to UVR, though its impact on the combined burden of cancer caused by UV radiation in Canada is probably negligible.

Primary prevention

Stern et al.[187] estimated that consistent regular use of sunscreens in childhood (up to 18 years of age) might reduce non-melanocytic skin cancer incidence by 78 percent. This estimate is certainly optimistic for several reason: first, sunscreens have not been shown to reduce incidence of BCC (or cutaneous melanoma) in humans, although they do appear to be effective in preventing squamous cell carcinoma of the skin.[188] Furthermore, the reduction is based on an estimated 80 percent of lifetime sunlight exposure occurring in childhood, which appears to be an unacceptably high estimate.[189] Nevertheless, with appropriate clothing use, care not to sunburn and judicious use of sunscreens, it is likely that 50 percent of these tumours are preventable. A similar figure is likely possible for CMM. Lip cancer incidence in females is only one-fifth that in males, likely due to lower levels of chronic UV exposure, but also to use of lip protection (lipstick and other UV-screening lip balms). In addition, females smoke less than males and female pipe-smoking is virtually non-existent. It is likely that some 30-40 percent of male lip cancers are preventable as occupational solar exposure declines in men, although this is an estimate only.

Mortality

Deaths from non-melanoma skin cancers are rare, and official mortality statistics are likely to overestimate deaths from NMSC by nearly 60% (Lewis and Weinstock 2004)[190] due to mistakes in completion of death registrations, or errors in cause of death coding. It is likely that no more than 100 deaths from SCC occur annually in Canada. In addition, there is evidence that many of the genuine NMSC deaths occur among individuals with comorbid psychiatric conditions,[190] perhaps associated with extreme delay in seeking medical care for their lesions. It is unlikely that public health campaigns designed to reduce mortality from skin cancer would affect these deaths. Mortality from lip cancer is also low, probably not exceeding 20 deaths per year. Recent cancer mortality estimates suggest that some 900 deaths will occur from CMM each year in Canada.[96] In total, then, probably about 850 to 870 deaths per year can reliably be attributed to UVR.

Secondary prevention

Most studies of CMM prognosis suggest that in lesions which are less than 0.76 mm in depth, mortality is only about five percent.[191] Physician and public education programs have been shown to significantly reduce the proportion of melanomas which are deeply penetrating at diagnosis.[192] Although declines in mortality from melanoma are being seen especially among the young in Canada,[4] it is difficult to attribute the decline to early detection or education programs. A randomized clinical trial of early detection is necessary to evaluate whether routine screening for CMM is cost effective, and such a trial is beginning in Australia, a high incidence area. Even though Marrett et al.[47] have shown that nearly 70 percent of melanomas could, in theory, be detected by screening only about 30 percent of the population in Canada, it is not clear that lay persons at high risk

would be able to self-select for entry into a surveillance program. Even if subjects could self-select appropriately, screening 30 percent of the population of Canada on a continuing basis would be prohibitively expensive. Thus, the magnitude of melanoma mortality reduction possible with some form of self- or physician-conducted screening is not clear. As noted above, mortality from BCC and SCC is low in Canada and screening for these lesions would prevent few deaths.

Mortality reductions from lip cancer early detection programs implemented by dentists and oral hygiene practitioners are likely to be low. Given the costs involved, programs to detect ocular melanomas early would not produce worthwhile mortality reductions.

In summary, with our present state of knowledge, primary prevention manoeuvres aimed at more rational UV exposure are likely to be most effective in reducing the cancer burden from UVR in Canada. At the same time, more intensive research is needed to determine whether the incidence rates of other malignancies such as cancer of the colon, prostate, breast and ovary, as well as non-Hodgkin lymphoma are related, inversely or otherwise, to UV exposure.

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