

Ultraviolet Radiation and Incidence of Non-Hodgkin's Lymphoma among Hispanics in the United States

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Abstract

Non-Hodgkin's lymphoma (NHL) is one of the most common cancers among American Hispanics. Several studies suggest that solar UV radiation (UVR) may be an environmental risk contributing to the rise of NHL over the past decades. These studies focused primarily on light-skinned Caucasian populations; it is unknown what role UVR plays in NHL for Hispanics. We described the incidence of NHL in Hispanics from selected states in the United States between 1989 and 2000. To evaluate the role of UVR, we correlated cancer rates with the UV index and latitude of residency. Variations in NHL incidence rates with estimated amount of UVR among whites and blacks from the selected states were also analyzed. We found that NHL occurred less frequently in Hispanics than in whites. Hispanic men had higher incidence of NHL than Hispanic women. Incidence rates of NHL in Hispanics were inversely associated with estimated amount of UVR as an increase in NHL was observed with decreasing UV index ($r = -0.7$ in men; $r = -0.41$ in women) or increasing latitude of residency ($r = 0.59$ in men; $r = 0.48$ in women). This trend, although it did not reach statistical significance, was also observed in whites and blacks. Our findings do not support previous reports of a positive association between solar radiation and NHL. The inverse relationship between UVR and incidence of NHL is unexplained but presents the need for generation of hypotheses regarding the epidemiology of causal factors for NHL in the United States. Additional studies should be conducted to clarify whether sunlight exposure contributes to the development of NHL.

Introduction

Non-Hodgkin's lymphoma (NHL) is a subgroup of neoplasms arising from the lymphopoietic system. It includes a wide range of either B-cell or T-cell lymphomas, with the exception of Hodgkin's disease. The incidence of NHL has risen by >100%

during the past 50 years in the United States and Western Europe (1–4). In the 1990s, this upward trend has persisted in most age groups in the United States (5). In contrast, the rates for Hodgkin's disease and leukemia appear to be stable or even declining (6). A small fraction of the overall rise in NHL incidence may be attributed to changes in diagnostic practices, and some of the recent increases are attributable to the AIDS epidemic or organ transplantation, however, most of this increase remains unaccounted for (6–10).

Chronic immunosuppression is the major risk factor for the development of NHL (11, 12). As reviewed in Baris *et al.* (11), immunosuppression can be from congenital immunodeficiency syndromes, or secondary to immunosuppressive medications, organ transplantation, HIV/AIDS infection, or human T-cell lymphotropic virus I infection. It has been suggested that UV radiation (UVR) may have a role in lymphomagenesis through immunosuppression (2, 13, 14). Solar radiation, particularly UV B radiation, causes reduced systemic immunity in both animal and human studies (15–17). Exposure to UVR is also a well-established risk factor for melanoma and nonmelanoma skin cancers. The increased population-based exposure to UVR, inferred from the widespread increases in skin cancers among fair-skinned populations over recent decades (18–20), has been postulated as one alternative explanation for the rise in the incidence of NHL. Supporting evidence for this hypothesis comes from epidemiology studies that found a positive association between the time trends of incidence of NHL and skin cancers (20–23). The incidence of NHL has also been shown to have a moderate inverse relationship with latitude (20, 24, 25), although several studies have not confirmed this (22, 26, 27). Additional support for the hypothesis comes from studies that demonstrated an increased relative risk for NHL after the diagnosis of melanoma and/or an increased incidence of melanoma after NHL (7, 21, 24, 28–30).

However, most of these studies evaluating the sunlight-NHL hypothesis have been conducted in white, Caucasian populations. Because cancer incidence and mortality vary significantly by race and ethnic origin (31), it is not known whether an association between NHL and UVR exists in variably pigmented populations such as Hispanics. The limited data on cancer among Hispanics is primarily due to the difficulty of classifying race/ethnicity. A few epidemiological studies have demonstrated that NHL occurs less frequently among Hispanic populations than among whites (18, 32, 33). Fewer studies have evaluated clinical patterns and risk factors of NHL in Hispanics.

From the public health and cancer control perspective, it is of value to better understand the epidemiological patterns of cancers in Hispanics. Hispanics are among the fastest growing minority populations in the United States. In 2000, approximately one in every eight Americans is of Hispanic origin (34). The Hispanic population is projected to reach 17% of total United States population by year 2020, becoming the largest racial/ethnic group (35). As the population of Hispanics con-

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Table 1 2000 United States Census Bureau Population profile by race/ethnicity in the six study states^a

	Hispanic count (percentage of population)	Non-Hispanic white count (percentage of population)	Black count (percentage of population)
United States	35,305,818 (12.5%)	194,552,774 (69.1%)	34,658,190 (12.3%)
New York	2,867,583 (15.1%)	11,760,981 (62.0%)	3,014,385 (15.9%)
New Jersey	1,117,191 (13.3%)	5,557,209 (67.8%)	1,141,821 (13.6%)
Illinois	1,530,262 (12.3%)	8,424,140 (67.8%)	1,876,875 (15.1%)
Florida	2,682,715 (16.8%)	10,458,509 (65.4%)	2,335,505 (14.6%)
Texas	6,669,666 (32.0%)	10,933,313 (52.4%)	2,404,566 (11.5%)
California	10,966,556 (32.4%)	2,263,882 (46.7%)	15,816,790 (6.7%)

^a Source: United States Census Bureau, Census 2000 Redistricting Data (P.L. 94-171) Summary File for states and Census 2000 Redistributing Summary File for Puerto Rico, Tables PL1 and PL2.

tinues to expand, their cancer experience will have a substantially greater impact on national cancer prevention and control.

Materials and Methods

We conducted a population-based epidemiological study of NHL incidence in United States Hispanics and compared cancer rates among different race/ethnicity groups. We also analyzed NHL incidence rates in relation to estimated annual UV index and latitude of residency.

Cancer Registry Selection. We selected states in the United States with large Hispanic populations and with readily accessible cancer data. California, Florida, Illinois, New Jersey, New York, and Texas met our selection criteria. According to the United States Census Bureau 2000 reports, these states are among the seven states (along with Arizona) with >1,000,000 in Hispanic population (Table 1); Hispanics residing in these states comprise 73% of total United States Hispanics (36). Additionally, cancer registries of these states are deemed by the National Program of Cancer Registries with high-quality data collection based on high proportion of histologically verified cases and low percentage identified from death certificates only. Texas Cancer Registry microscopically confirmed >92% of NHL cases, and the other five registries have >94% of NHL cases confirmed by microscopy (37). All six registries have no >4% of cases by death certificates only. These registries use multiple primary tumor standards set by the Surveillance, Epidemiology, and End Results program and the North American Association of Central Cancer Registries and International Classification of Disease-Oncology-Second Edition codes for coding data and grouping of cancer sites. The six states also represent the four distinctive regions of the United States, which are Northeast, Midwest, South, and West, therefore permitting the evaluation of the relationship between geographic location and cancer incidence. We extracted age-adjusted incidence rates to allow comparison of cancer incidence over time and across geographic regions and population subgroups, even when the age distributions are not comparable. The rates were adjusted to the 2000 United States standard population. Data sets with greatest similarity in time periods were selected for correlation analyses against UVR.

Exposure Calculation. We used annual mean UV index and latitude data for each state as surrogate estimates of potential UV exposure. Geographic latitude of residence is a routinely used proxy measure for UV exposure. The average north to south latitude of each state was obtained and designed as the representative latitude. The UV index is a composite measure of the expected risk of overexposure to UV from the sun, computed by the National Weather Service on a next-day basis for 58 cities. After accounting for local conditions,

UVR at different wavelengths is weighted so that the wavelengths more harmful to human skin have higher weights. The final value is converted to an index number that ranges from 0, where there is no sunlight, to the mid teens. For this study, we calculated the annual mean UV index of the major cities in the six study states from 1997, the only year for which monthly mean UV index was available (38). The annual mean UV index was the sum of monthly means; in the states containing data on more than one city, the average of all cities was used. Table 2 summarizes the mean annual UV index and latitude of each state.

Statistical Analysis. The standardized gender- and race/ethnicity-specific incidence data for NHL were summarized with 95% confidence intervals. Pearson's correlation analyses were performed to examine the correlation between the incidence rate of NHL and the UV index or latitude of the state of residency. Significance level was set at 0.05, two-sided, for all statistical analyses.

Results

We obtained all available cancer incidence data that included Hispanic ethnicity from the six state cancer registries. All six cancer registries determine Hispanic or Latino origin based on surname and maiden name in addition to self-reporting on medical record and death certificate (39–45). The protocol to impute Hispanic ethnicity from surname and maiden name varies within registries. The grouping of Hispanic or non-Hispanic population also differs. For instance, Hispanic, white, and black are three mutually exclusive populations in California and Texas (41, 45). In New Jersey, New York, Illinois, and Florida, "Hispanic" is an ethnicity variable; therefore, cancer data for Hispanics may overlap with those of whites and blacks.

Patterns of NHL Incidence Rates. Standardized incidence rates by race/ethnicity and gender with 95% confidence intervals that were used in our correlation analyses are detailed in Table 3 for females and Table 4 for males. Overall, men had

Table 2 Mean 1997 annual UV index and latitude by state^a

State	United States region	Mean annual UV index	Latitude
New York	Northeast	38	43
New Jersey	Northeast	48	40.3
Illinois	Midwest	47	39.8
Florida	South	75	27.5
Texas	South	67	31.3
California	West	67	37.3

^a Source: National Weather Service.

Table 3 Age-adjusted (to 2000 United States standard population) non-Hodgkin's lymphoma incidence rates/100,000 people with 95% confidence intervals (CIs) by race/ethnicity in females

State	Years	Black rate (95% CI)	Hispanic rate (95% CI)	White rate (95% CI)
New York (43) ^a	1995–1999	11.1 (10.3–11.9)	13.7 (12.7–14.7)	16.9 (16.5–17.3)
New Jersey (39) ^a	1996–2000	14.2 (12.8–15.8)	16.3 (14.4–18.4)	19.2 (18.6–19.8)
Illinois (44) ^a	1995–1999	9.8 (8.8–19.8)	11.3 (9.6–13.3)	16.3 (15.9–16.8)
Florida (40) ^a	1989–1995	8.7 (7.8–9.5)	11.6 (10.8–12.5)	14.0 (13.7–14.4)
Texas (42) ^b	1995–1999	11.5 (10.5–12.6)	12.7 (11.9–13.5)	15.7 (15.2–16.1)
California (45) ^b	1995–1999	11.3 (10.3–12.3)	12.9 (12.2–13.5)	15.6 (15.3–16.0)

^a Black, Hispanic, and white are not mutually exclusive.^b Black, Hispanic, and white are mutually exclusive.**Table 4** Age-adjusted (to 2000 United States standard population) non-Hodgkin's lymphoma incidence rates/100,000 people with 95% confidence intervals (CIs) by race/ethnicity in males

State	Years	Black rate (95% CI)	Hispanic rate (95% CI)	White rate (95% CI)
New York (43) ^a	1995–1999	19.0 (17.8–20.2)	21.6 (20.1–23.1)	24.2 (23.7–24.7)
New Jersey (39) ^a	1996–2000	20.7 (18.6–22.9)	22.0 (19.5–24.9)	26.6 (25.8–27.4)
Illinois (44) ^a	1995–1999	16.9 (15.4–18.6)	18.9 (16.4–21.7)	23.1 (22.5–23.8)
Florida (40) ^a	1989–1995	14.1 (12.9–15.4)	19.2 (18–20.5)	21.8 (21.4–22.3)
Texas (42) ^b	1995–1999	17.7 (16.2–19.2)	17.5 (16.4–18.6)	23.9 (22.4–23.7)
California (45) ^b	1995–1999	18.7 (17.3–20.2)	17.9 (17.1–18.8)	24.9 (24.5–25.4)

^a Black, Hispanic, and white are not mutually exclusive.^b Black, Hispanic, and white are mutually exclusive.

higher incidence of NHL than women. For both genders, incidence of NHL among Hispanics was significantly lower than that in whites. Hispanic females had higher rates of NHL than black females. These trends were observed in all six states. The differences in NHL incidence between Hispanic males and black males were less clear-cut. Black men had slightly higher incidence of NHL than Hispanic men in CA, while Hispanic men had greater rates of NHL than black men in Florida, Illinois, New Jersey, and New York. There was no statistically significant difference between the rates of NHL in Hispanic (17.5/100,000) and black men (17.7/100,000) in Texas for 1995–1999. Residents in New Jersey had the highest overall rates of NHL by both gender and race/ethnicity. For instance, Hispanic women in New Jersey had highest NHL rate (16.3/100,000 in 1996–2000) among female Hispanics, whereas Hispanic men in New Jersey had the highest rate (20.7/100,000 in 1996–2000) among Hispanic males. The rate of NHL in Hispanic men was lowest in California, Florida, Illinois because there was no statistically significant differences among them. The lowest rate of NHL in Hispanic females was observed in those residing in Florida and Illinois, 11.6/100,000 and 11.3/100,000, respectively, with no statistically significant difference. Florida also had the lowest NHL rate in blacks and whites, both female and male.

Correlation between NHL Incidence and UVR. Mean annual UV index and latitude of residency were correlated with the incidence of NHL by race/ethnicity for both genders (Table 5, Fig. 1–4). The correlation coefficient between NHL and UV

index was -0.41 in Hispanic females and -0.7 in Hispanic males, but this did not reach statistical significance. The negative correlation between NHL and mean annual UV index was consistently observed in whites and blacks, both females and males. The NHL incidence rates demonstrated an invariably positive association with latitude of residency state, meaning that the higher the latitude, the higher the NHL rates, in all racial/ethnic groups and in both sexes. The correlation coefficient between the rate of NHL and latitude was 0.48 in Hispanic women and 0.59 in Hispanic men, and again, this did not reach statistical significance.

Discussion

Our study is the first epidemiological study using large population-based cancer registries to evaluate for a possible causal role of UVR in the development of NHL among Hispanics in the United States. We did not find a positive association between NHL incidence and potential sunlight exposure in Hispanics. On the contrary, we found that the incidence of NHL increased as mean annual UV index decreased or the latitude of residency increased. This trend was uniformly observed in both genders and in all race/ethnicity groups (Hispanics, blacks, and whites). Using the similar methodology to analyze melanoma incidence rates from the same six states, we found a positive association between potential exposure to UVR and the risk of melanoma in Hispanics, blacks, and whites, which confirms the

Table 5 Correlation between age-adjusted to 2000 United States population, incidence rates of non-Hodgkin's Lymphoma, and mean annual UV index and latitude of residency by race/ethnicity and gender

	Female			Male		
	Black	Hispanic	White	Black	Hispanic	White
Correlation coefficient with UV index (<i>P</i>)	-0.38 (0.45)	-0.41 (0.42)	-0.72 (0.17)	-0.6 (0.2)	-0.7 (0.12)	-0.42 (0.48)
Correlation coefficient with latitude (<i>P</i>)	0.49 (0.32)	0.48 (0.34)	0.76 (0.14)	0.76 (0.08)	0.59 (0.21)	0.64 (0.24)

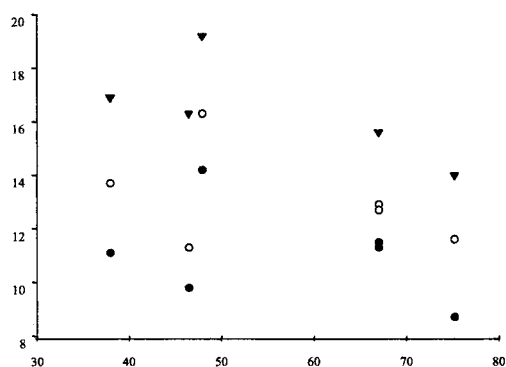


Fig. 1. Scatter plot for age-adjusted (to 2000 United States standard population) incidence of non-Hodgkin's lymphoma by race/ethnicity in women against estimated mean annual UV index (1997 value). Incidence data are from the state cancer registries of New York, New Jersey, Illinois, Florida, Texas, and California (black, ●; Hispanic, ○; white, ▼). X axis: mean annual UV index; y axis: age-adjusted rate/100,000 females

extant evidence on UVR as the major melanoma risk factor.⁵ Therefore, it appears that the role of solar radiation in the occurrence of NHL is dissimilar to that in the development of melanoma in populations in these six states.

This is the third United States study that examines the relationship between UVR and NHL and the first to examine incidence across populations and Hispanics in particular. The previous two studies evaluated mortality rates of NHL but not the incidence. Both focused on white populations (22) and only one included blacks (26). Interestingly, all of these studies, including ours, did not find solar radiation to be a possible risk factor in the development of NHL (22, 26, 27). One of these studies showed that mortality of NHL increased with higher latitude of residency even after controlling for occupational sun exposure and social economic class (26). In contrast, the incidence of NHL demonstrated an increasing gradient with decreasing latitude or more southerly residency in the United Kingdom (25), Sweden (24), and European nations combined (20). It is not clear if such differences in findings reflect inherent limitations in study designs or true variations in the epidemiology and risk factor profile of NHL among the United States and other Western countries. One distinguishing feature of NHL epidemiology in the United States is that the incidence is higher than any other developed countries. For instance, the rate of NHL in males in 2000 was 16.1/100,000 in the United States and 10.4/100,000 and 10.6/100,000 in United Kingdom and Sweden, respectively (46). Therefore, it is plausible that an unidentified etiologic factor (either associated with solar radiation or not) with a latitudinal gradient ubiquitous to the United States may have caused the apparent inverse association between NHL incidence and UVR. Whether UVR, possibly through stimulation of cutaneous production of vitamin D, is protective against NHL is not known. Vitamin D is known to induce differentiative markers, inhibit cell proliferation, and decrease cancer related gene expression *in vitro*, thus behaving both as a differentiation and an antiproliferative agent (47). Recent studies suggest that UVR has a protective effect against prostate cancer through production of vitamin D (48–50). It would be of interest to explore if such benefit of UVR plays a role in lymphomas.

Several etiologic factors related to NHL could have influenced the outcome of our analysis on the relationship between

NHL incidence and latitude of residence. The main risk factors of NHL include immunosuppression from HIV infection or organ transplantation and exposure to pesticides and organic solvents (11, 51, 52). According to data through December 2001 from the Centers for Disease Control and Prevention, New York, California, Florida, Texas, New Jersey, and Illinois are among the top 10 leading states with highest number of cumulative AIDS cases, in descending order (53). Among the states with confidential HIV infection reporting, Florida had the highest cumulative totals, followed by New York, New Jersey, and Texas. Our study indicated that New Jersey, the state with fifth highest cumulative AIDS cases, had the highest rates of NHL in all racial/ethnic groups, whereas Florida, where both AIDS and HIV prevalence are higher than New Jersey, had overall lower rates of NHL. Hence, the positive association between NHL incidence and latitude (higher the latitude, greater the incidence of NHL) that we found was unlikely due to a latitudinal gradient of AIDS or HIV infection. Our conclusion on NHL and latitude was also unlikely confounded by a possible latitudinal gradient of immunosuppression from organ transplantation (*i.e.*, increasing cases of transplants from south to north). On the basis of the Organ Procurement and Transplantation Network data as of June 10, 2003, the cumulative

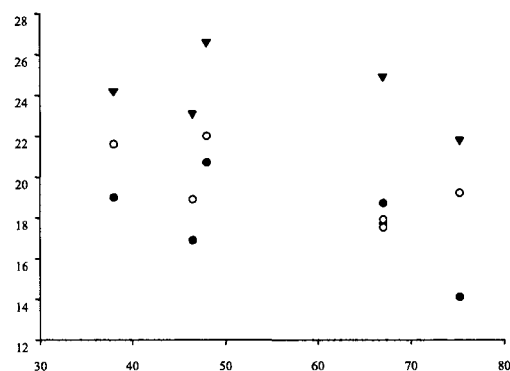


Fig. 2. Scatter plot for age-adjusted (to 2000 United States standard population) incidence of non-Hodgkin's lymphoma by race/ethnicity in men against estimated mean annual UV index (1997 value). Incidence data are from the state cancer registries of New York, New Jersey, Illinois, Florida, Texas, and California (black, ●; Hispanic, ○; white, ▼). X axis: mean annual UV index; y axis: age-adjusted rate/100,000 males.

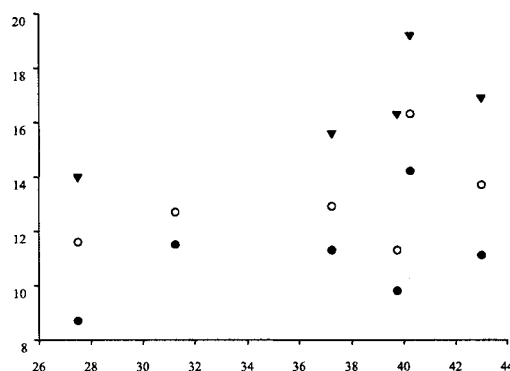


Fig. 3. Scatter plot for age-adjusted (to 2000 United States standard population) incidence of non-Hodgkin's lymphoma by race/ethnicity in women against latitude of residency state. Incidence data are from the state cancer registries of New York, New Jersey, Illinois, Florida, Texas, and California (black, ●; Hispanic, ○; white, ▼). X axis: degrees of latitude; y axis: age-adjusted rate/100,000 females.

⁵ S. Hu, F. Ma, F. Collado-Mesa, R. Kirsner, unpublished data.

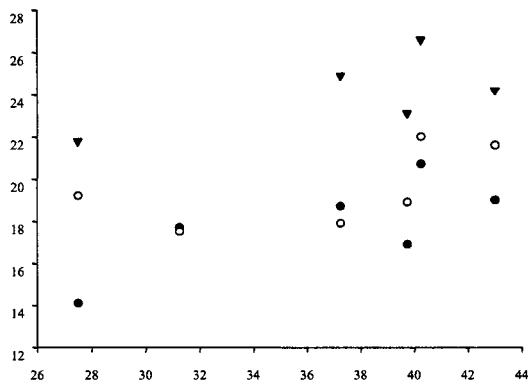


Fig. 4. Scatter plot for age-adjusted (to 2000 United States standard population) incidence of non-Hodgkin's lymphoma by race/ethnicity in women against latitude of residency state. Incidence data are from the state cancer registries of New York, New Jersey, Illinois, Florida, Texas, and California (black, ●; Hispanic, ○; white, ▼). X axis: degrees of latitude; y axis: age-adjusted rate/100,000 males.

cases of all transplants performed between 1988 and 2000 in each of the six study states did not demonstrate a south-to-north increasing gradient by race/ethnicity group (whites, blacks, and Hispanics; Ref. 54). For instance, California followed by Texas had the highest number of transplants performed in each of the three race/ethnicity groups, whereas New Jersey had the lowest cases of transplants in whites, blacks, and Hispanics. The geographic distribution and prevalence of immunosuppression from organ transplant do not explain our finding on the relationship between NHL incidence and UVR or latitude but may be causal in the higher rates of NHL in the United States compared with other developed countries. Overall, the consistency of the correlation between NHL incidence and UV index or latitude among all racial/ethnic groups and in both genders strengthens the validity of our results. It is unlikely that the confounders, if present, would have affected every gender and race/ethnic groups equally to yield uniform associations.

In our study population, the incidence of NHL in Hispanics was intermediate of that in whites and blacks. The lower incidence of NHL in Hispanic than in whites confirms the trend reported by the Surveillance, Epidemiology, and End Results program of National Cancer Institute (18, 19). Although Hispanic women had overall higher rates of NHL than black women, the difference in NHL incidence between Hispanic men and black men were less dramatic. It is not clear whether the overall lower risk of NHL in darker-pigmented populations reflect an effect of constitutive pigmentation protecting against UVR, similar to that in melanoma. Other factors that may be at play, which we were not able to control for in the study, include occupational exposure to sunlight, individual behavioral patterns, unknown cultural-environmental exposures or socioeconomic factors in addition to genetic predisposition specific to each race/ethnic group. It has been suggested that socioeconomic status is an independent risk factor for NHL in some populations (3, 20). Hence, the lower incidence of NHL in Hispanics and blacks may partially reflect the overall lower socioeconomic status of these two populations compared with whites according to the United States Census Bureau (34, 55).

Several inherent limitations related to cancer data from population-based registries exist. First, accuracy of race or ethnicity-specific rates relies on the quality of classification in cancer cases and in population estimates. Inconsistencies and difficulties associated with defining Hispanic ethnicity suggest

a general tendency for undercounts of both cancer cases and population under this variable. The term Hispanic also overlooks the differences in racial composition and migration patterns among the various subgroups of Hispanics. A person of Hispanic origin could be of any race or origin such as Mexican, Puerto Rican, Cuban, or Central or South American. For instance, Mexicans have more indigenous American heritage than Cubans, who have more of African genetic heritage (50). Therefore, the cancer incidence rates represent an average of a range of exposures experienced by a diverse population. This averaging may inadvertently result in obscured or negative association between NHL and sunlight in Hispanics.

We used NHL data from six states in the United States. Although these states are representative of the regions in the United States and contain >70% of total Hispanic population in the United States, evaluation of wider geographic areas will more accurately reflect the experience of Hispanic Americans. Incidence rates in some registries differed in time periods, and data from registries for a common time period was not available on Hispanics. Nevertheless, we believe our results are valid as time periods are all within the last decade, and rates of NHL in Hispanics and blacks have been relatively stable between 1992 and 2000 (19, 56).

Our analysis of NHL incidence against potential UVR is also complicated by the heterogeneity of NHL. NHL encompasses all lymphocytic malignancies except Hodgkin's disease. Clinical patterns and risk factors may vary by cell type (*T versus B cell*), histology subtype (follicular or diffuse), and tumor grade (57). Our study did not differentiate between NHL subtypes; therefore, it is possible that a positive association exists between UVR and a particular subtype of NHL. Because of the paucity of data, it is also unknown if certain patterns of sun exposure are associated with higher degree of immunosuppression or risk for NHL or if gradual skin adaptation in the chronically sun exposure is of importance. We also did not examine the role of other forms of UVR exposure such as sunlamp use and light therapy for dermatological diseases.

In summary, our study did not support the sunlight-NHL hypothesis in Hispanics, nor in whites or blacks. However given the heterogeneity of both NHL and the Hispanic population and multiple known risk factors for NHL, a possible, albeit weak, carcinogenic role of UVR in NHL should not be excluded. The consistently inverse relationship between UVR and NHL incidence in Hispanics, whites, and blacks demonstrated by our study, along with a similar positive trend between NHL mortality and latitude found by other United States studies, warrant a closer examination of other environmental factors that may have resulted in such a latitudinal pattern of NHL. Potential benefits of solar radiation against NHL, maybe at different exposure levels and patterns from those causing immune suppressions, should also be considered. Additional studies with broader population base, more accurate estimates of sun exposure, differentiation of various UVR exposure patterns, as well as stratification of NHL subtypes are needed to elucidate whether UVR truly has a role in the development of NHL.

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