Does Solar Ultraviolet Irradiation affect Cancer Mortality Rates in China?

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Abstract

Solar ultraviolet B (UVB; 290–315 nm) irradiance through production of vitamin D has been found to correlate with reduced risk for 14 types of cancer in three or more observational studies and another 14 in one-to-two observational studies. The beneficial role of UVB is thought to be mediated through vitamin D production. Few such studies have been conducted in Southeast Asia. Data on cancer mortality rates for 65 counties in China in 1978 and approximately 300 geographic, dietary, serum, occupation, and lifestyle factors from 1983–4 are available in Diet, Life-style and Mortality in China (Chen et al., Oxford University Press, 1990). The data for 39 counties away from the east coast of China were here used in multiple linear regression analyses. The indices of solar UV radiation (UVR), latitude and heat index, were correlated with reduced mortality rates for cervical, colorectal (females), esophageal, gastric, and lung (males) cancer. Latitude was inversely correlated with liver cancer (males) and nasopharyngeal carcinoma (NPC). Lung cancer, the index used for smoking, was correlated with all less lung (males), cervical, liver (males), and NPC. Several other factors were also correlated with some of the cancers. However, no other factors could explain the latitudinal variation for these seven cancers. Thus, it is concluded that solar UVB, through production of vitamin D, reduces the risk of some types of cancer in China. Liver cancer and NPC are linked to viruses, and UVB may increase the risk through immunosuppression. Further studies are warranted.

Keywords: Cancer - cervical/esophageal/liver/lung/nasopharyngeal - ecological study - ultraviolet - vitamin D

Introduction

Solar ultraviolet B (UVB; 290–315 nm) irradiance through production of vitamin D has been found to be a risk reduction factor for more than 20 types of cancer, largely through ecologic studies (Grant, 2002b; Freedman et al., 2002; Grant, 2003; Boscoe and Schymura, 2006; Grant 2006a,b; Grant and Garland, 2006). Such studies were favorably reviewed recently (Garland et al., 2006; Grant, 2006c; Kricker and Armstrong, 2006; van der Rhee et al., 2006), and confirmed in some cases by other epidemiologic studies (Hughes et al., 2004; Smedby et al., 2005; Giovannucci et al., 2006; Skinner et al., 2006). In addition, the dose-response relations have been determined for prevention of breast (Garland et al., 2007) and colorectal (Gorham et al., 2007) cancer, and mechanisms whereby vitamin D reduces the risk of cancer are well known (van den Bemd and Chang, 2002; Lamprecht and Lipkin, 2003). Generally, these ecologic studies use some index of solar UVB dose based on geographic location such as latitude (Grant, 2003),3 measured solar UVB doses (Leffell and Brash, 1996), or an index of solar UVB based on some combination or latitude, ozone, aerosols, and clouds (Mohr et al., 2006; Garland et al., 2006). Although critics object that geographic location may be confounded by different personal exposure practices or indices of other cancer risk factors, a recent study using nonmelanoma skin cancer (NMSC) as the index of population solar UVB irradiance obtained results similar to those in the same study using latitude (Grant, 2007). Using a geographic index for UVB irradiance is thus reasonably well justified.

On the other hand, solar UVR can increase the risk of disease, most notably NMSC and melanoma. More recently, attention has also turned to the role of UV in both skin- and systemic-immunosuppression and effect on defenses against viruses related to cancer risk (Schwartz, 2005, Norval, 2006). Many deaths in China are attributed to both cervical cancer and nasopharyngeal carcinoma (NPC), both of which have risk linked to viral infections (Cheng et al., 2002; Chang et al., 2006; Wu et al., 2006; Zhao et al., 2006;), so increasing the understanding of their risk factors is important.

Most of the ecologic studies of solar UVB and cancer risk reduction have been for white people (Grant, 2002b; Freedman et al., 2002; Grant, 2003; Boscoe and Schymura, 2006; Grant 2006a,b; Grant and Garland, 2006) or African Americans (Grant, 2006), with only two specifically targeting Southeast Asians (Kato et al., 1985; Mizoue et al., 2004). One study of cancer rates for females
in China did report a correlation with latitude, finding that cancer of the stomach, liver, and rectum increased with latitude for females in China and the United States, but attributed this finding to dietary variations with latitude (Archer, 1989). Thus, extending the analysis to China is useful.

The cancer mortality rate datasets in Diet, Life-style and Mortality in China (Chen et al., 1990a) from a nationwide survey in 1973-5 (Li et al., 1981) are quite useful, especially because they are coupled to more than 300 datasets on factors related to disease outcome including dietary factors, serum components and urinary by-products, physical and lifestyle parameters, and geographical data (Chen et al., 1981; Li, 1989). Thus, the analyses can include many other risk-modifying factors and examine possible confounding factors. However, to my knowledge, no one has yet used these datasets to examine the role of solar ultraviolet radiation (UVR) on risk of cancer and other diseases. The data in Chen et al., 1990a are used in a multifactorial ecologic study of cancer mortality rates in China.

**Materials and Methods**

The data were obtained from (Chen et al., 1990a). The annual cancer mortality rate data were for 65 rural counties included in the nationwide survey of all deaths in the 3-year period, 1973-5, and were age adjusted to the population of China. Data for some cancers, such as breast and esophageal, were considered highly reliable since the diagnosis was relatively straightforward, whereas for others, such as lung cancer or leukemia, there may be systematic differences in how the cancers were recorded in different regions of China. To limit the uncertainties of the data, the authors limited the data to those who died before the age of 65 years. The cancer data were reported for two age ranges: 0–64 years and 35–64 years. The truncated age range values were generally about three times those of the full age range data. This study used the truncated data.

The ancillary data were collected in the autumn of 1983 at the end of the harvest season from about 50 people aged 35–64 years, with approximately equal numbers of people in each 10-year age group, in each of two cities for each of the 65 counties. Five types of data were collected: intakes of foods and nutrients, levels of various blood constituents, excretion levels of a few urinary by-products, questionnaire-based information on lifestyle, and various constituent levels of virtually all plant foods identified and measured in the survey. Data on geographic and population factors were added later. Cross correlations between the data for the 65 counties were presented in that study.

Readily apparent from the maps in Chen et al., 1990a is that cancer rates on the southeast coast of China are generally much higher than for interior sites at the same latitudes. This effect is attributed to a more affluent lifestyle near the coast because of more interaction with foreign countries. For example, plasma albumin levels, alcohol consumption rates, and height were similar for all east coast counties but had latitudinal gradients in the interior counties. Since including such counties would probably mask any effect of solar UVB irradiance on cancer risk, the analysis presented here was based counties limited to the region between 102.9° and 114° E, which includes 40 counties. Two counties to the west, Dunhuang and Tuoli, were omitted from the reduced set since they were far from the other counties (40.1° N, 94.8° E and 46.0° N, 83.7° E, respectively) and were thought to have several differences from the other counties. Also, noncancer data for one county, Xuanwei, were often missing, so it, too, was omitted. Thus, the results presented here are based on 39 counties. A description of the cancer data used is presented in Table 1.

The data examined here include the data for cancers with geographic variations for people aged 35–64 years and most of the factors that were significantly linked to these cancers in the cross correlation analyses for all 65 counties, those reported correlated with cancer by other researchers (Lam, 1986; Campbell et al., 1990; Chen, 1991; Chen et al., 1990b; Forman et al., 1990; Guo et al., 1990; Hsing et al., 1991; Chen et al., 1992; Marshall et al., 1992; Guo et al., 1993, 1994; Chen et al., 2003), or those that exhibited a generally monotonic variation with latitude. The factors included in the model were varied until only those that were statistically significant or nearly so were identified. Stepwise regression analyses were conducted to guard against spurious results due to cross correlations of the data. The number of factors was generally limited to three since there were 39 counties. The Bonferroni criterion for significance at the 95% confidence level, p<0.05/n, where n is the number of factors in the model, was used, and factors not satisfying this criterion were generally omitted. Square roots of the values were used for most data to reduce the effect of extreme values. The data were used in multiple linear regression analyses using the SPSS 13.0 analysis program (SPSS, Chicago, IL). The term β is the normalized regression coefficient; r; in linear regression analysis, the two are identical.

**Table 1. Description of the Cancer Data for the 39-County Datasets for those Aged 35-64 Years.**

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Sex</th>
<th>Minimum*</th>
<th>Mean*</th>
<th>Maximum*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>M</td>
<td>34.7</td>
<td>262.0</td>
<td>625.3</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>35.2</td>
<td>186.1</td>
<td>430.2</td>
</tr>
<tr>
<td>All-lung</td>
<td>M</td>
<td>32.1</td>
<td>246.9</td>
<td>613.2</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>34.3</td>
<td>161.5</td>
<td>419.6</td>
</tr>
<tr>
<td>Breast</td>
<td>F</td>
<td>1.5</td>
<td>8.5</td>
<td>20.0</td>
</tr>
<tr>
<td>Cervical</td>
<td>F</td>
<td>4.4</td>
<td>34.4</td>
<td>97.0</td>
</tr>
<tr>
<td>Colorectal</td>
<td>M</td>
<td>1.3</td>
<td>10.2</td>
<td>38.6</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>2.1</td>
<td>7.1</td>
<td>19.6</td>
</tr>
<tr>
<td>Esophageal</td>
<td>M</td>
<td>1.4</td>
<td>75.9</td>
<td>435.5</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>0.0</td>
<td>38.2</td>
<td>285.8</td>
</tr>
<tr>
<td>Gastric</td>
<td>M</td>
<td>5.9</td>
<td>70.2</td>
<td>266.6</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>1.7</td>
<td>33.2</td>
<td>129.2</td>
</tr>
<tr>
<td>Liver</td>
<td>M</td>
<td>6.9</td>
<td>53.7</td>
<td>248.3</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>2.7</td>
<td>18.7</td>
<td>62.6</td>
</tr>
<tr>
<td>Lung</td>
<td>M</td>
<td>2.6</td>
<td>15.1</td>
<td>40.4</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>0.0</td>
<td>6.5</td>
<td>26.1</td>
</tr>
<tr>
<td>Nasopharyngeal</td>
<td>M</td>
<td>0.0</td>
<td>15.5</td>
<td>75.0</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>0.0</td>
<td>6.9</td>
<td>26.0</td>
</tr>
</tbody>
</table>

* deaths/100,000/year
Table 2. Regression Results for those Aged 35-64 Years for the 39-County Data Set

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Sex,</th>
<th>First term (β, p)</th>
<th>Second Term (β, p)</th>
<th>Third Term (β, p)</th>
<th>Adjusted R², F, p</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>F, M</td>
<td>-0.50, * Lipids</td>
<td>0.45, * Lung M</td>
<td>0.32, 0.01 Eggs</td>
<td>0.52, 15, *</td>
</tr>
<tr>
<td>All</td>
<td>F, M</td>
<td>-0.78, * Heat zone</td>
<td>0.29, 0.005 Eggs</td>
<td>0.65, 36, *</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>F, M</td>
<td>0.75, * Latitude</td>
<td>0.24, 0.03 Eggs</td>
<td>0.60, 29, *</td>
<td></td>
</tr>
<tr>
<td>All-lung</td>
<td>M</td>
<td>-0.53, * Lipids</td>
<td>0.40, 0.002 Lung M</td>
<td>0.32, 0.01 Eggs</td>
<td>0.49, 13, *</td>
</tr>
<tr>
<td>All-lung</td>
<td>F</td>
<td>-0.62, * Heat zone</td>
<td>0.38, * Eggs</td>
<td>-0.31, 0.006 Lipids</td>
<td>0.68, 28, *</td>
</tr>
<tr>
<td>All-lung</td>
<td>F</td>
<td>0.58, * Latitude</td>
<td>0.32, 0.003 Eggs</td>
<td>-0.30, 0.01 Lipids</td>
<td>0.63, 23, *</td>
</tr>
<tr>
<td>Breast</td>
<td>F</td>
<td>0.42, 0.02 Eggs</td>
<td>-0.35, 0.04 Iodine</td>
<td>0.24, 5.5, 0.01</td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>F</td>
<td>-0.61, * Heat zone</td>
<td>0.29, 0.02 Lung M</td>
<td>0.54, 23, *</td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>F</td>
<td>0.69, * Latitude</td>
<td></td>
<td>0.46, 33, *</td>
<td></td>
</tr>
<tr>
<td>Colorectal</td>
<td>M</td>
<td>0.52, 0.001 Lung M</td>
<td>0.43, 0.001 Refined carb</td>
<td>0.25, 14, 0.001</td>
<td></td>
</tr>
<tr>
<td>Colorectal</td>
<td>F</td>
<td>-0.54, * Heat zone</td>
<td>0.36, 0.01 Refined carb</td>
<td>0.45, 16, *</td>
<td></td>
</tr>
<tr>
<td>Colorectal</td>
<td>F</td>
<td>0.41, 0.005 Latitude</td>
<td>0.36, 0.01 Refined carb</td>
<td>0.28, 8.4, 0.001</td>
<td></td>
</tr>
<tr>
<td>Esophageal</td>
<td>M</td>
<td>0.67, * Latitude</td>
<td>0.40, 26, *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophageal</td>
<td>F</td>
<td>0.64, * Latitude</td>
<td>0.49, 26, *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric</td>
<td>M, 25</td>
<td>0.54, 0.002 Latitude</td>
<td>0.39, 0.02 C. pylori</td>
<td>0.56, 11, *</td>
<td></td>
</tr>
<tr>
<td>Gastric</td>
<td>F, 25</td>
<td>0.73, * Latitude</td>
<td>0.26, 0.05 C. pylori</td>
<td>0.63, 21, *</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>M</td>
<td>-0.54, 0.001 Latitude</td>
<td>0.43, 0.005 Lung M</td>
<td>0.28, 8.6, 0.001</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>M</td>
<td>-0.60, * Latitude</td>
<td>0.34, 0.04 Lung M</td>
<td>0.30, 6.5, 0.001</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>M</td>
<td>-0.53, * Agriculture</td>
<td>0.43, 0.02 Latitude</td>
<td>0.37, 12, *</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>F</td>
<td>0.52, 0.001 Plasma copper</td>
<td>0.47, * Lung M</td>
<td>0.25, 14, *</td>
<td></td>
</tr>
<tr>
<td>Nasopharyngeal</td>
<td>M</td>
<td>-0.92, * Latitude</td>
<td>0.47, * Lung M</td>
<td>0.76, 61, *</td>
<td></td>
</tr>
<tr>
<td>Nasopharyngeal</td>
<td>F</td>
<td>-0.82, * Latitude</td>
<td>0.54, * Lung, M</td>
<td>0.64, 35, *</td>
<td></td>
</tr>
<tr>
<td>Nasopharyngeal</td>
<td>F</td>
<td>-0.80, * Latitude</td>
<td>0.49, * Lung, F</td>
<td>0.59, 28, *</td>
<td></td>
</tr>
</tbody>
</table>

N, number of counties, = 39 unless otherwise stated; * p<0.001; _, normalized regression coefficient; agriculture, agricultural employment; carb, carbohydrates; F, females; lung, lung cancer; M, males

Three indices can be used for solar UVB and UVR in China: latitude, heat zone, and elevation. Annual average UVB and UVR decrease with increasing latitude. The temperature of the heat zones decreases with latitude, and the cross correlation between heat zones and latitude is very high. There were only six heat zones tabulated in China, so it is a much coarser index than latitude. The atmosphere blocks less solar UVB at higher altitudes, leading to more UVR irradiance (Deng et al., 2006); however, elevation may not be an independent indicator of solar UVB since elevation is highly correlated with several factors including fiber, weight, and wheat. Since food was not fortified with vitamin D in China in the 1970s and 1980s, and since animal sources of vitamin D such as oily cold-water ocean fish are not an important source of vitamin D in rural China, solar UVB was the primary source of vitamin D in China.

Lung cancer was used as the index of adverse health outcome due to inhaled smoke (Leistikow, 2004; Grant and Garland, 2006). Although cigarette smoking is the primary risk factor for lung cancer in Western developed countries, home cooking fires were a major source of inhaled smoke in continental China in the 1970s and early 1980s. However, the ratio of female to male lung cancer mortality rates had a mean value of 0.44 with a range from 0.0 to 1.11. This finding indicates that smoking probably played an important role in the etiology of lung cancer of both men and women because (i) women would be indoors more than men and (ii) men were 10–100 times more likely to smoke than women in the past six months (Table 6006 in Chen et al., 1990a). Thus, there were probably effects of secondhand smoke.

Factors used in the analysis but for which no significant results were found in multiple linear regressions include the following: albumin, animal protein, arsenic, green vegetables, height, industrial employment, lipid peroxide, longitude, moldy peanuts, rice, salt, selenium, urea, vegetable protein, and wheat flour. Alcohol consumption by females was low, so this index was not used for females.

Results

The results of the multiple linear regression analyses are presented in Table 2. In the analyses, five cancers plus all and all less lung cancer (females) were found to have mortality rates increasing with increasing latitude or varying inversely with heat zone: cervical, colorectal (females), esophageal, gastric, and lung (males) cancer. Lung cancer mortality rates for males were correlated with all less lung (males), cervical, colorectal (males), lung cancer (males), and NPC. Presence of Campylobacter pylori antibodies was correlated with gastric cancer risk. Latitude was inversely correlated with liver cancer (males) and NPC.

Several dietary factors were also correlated with cancer rates. Egg consumption was correlated with all, all less lung, and breast cancer. Agricultural employment was inversely correlated with lung cancer (males), while plasma copper was directly correlated with lung cancer (females). Refined carbohydrates and sugar was correlated with colorectal cancer (females). Iodine was weakly inversely correlated with breast cancer.

Discussion

All the cancers for which at least one of the stronger
UVB-linked indices was correlated—colorectal, esophageal, gastric, and lung cancer—have been identified as vitamin D sensitive in one or more studies (Grant, 2002b; Freedman et al., 2002; Grant, 2003; Boscoe and Schymura, 2006; Grant 2006a,b; Grant and Garland, 2006). Three of these, colorectal, esophageal, and gastric cancer, were among the five identified in an ecologic study in Japan (Mizoue, 2004). Pancreatic cancer rates were also found to increase in Japan (Kato et al., 1985; Mizoue, 2004), but there were no data available for China. Thus, these results both add to previous findings that solar UVB reduces the risk of many types of cancer and suggest that cancer rates in China could be reduced if vitamin D production or oral intake were higher.

That male lung cancer mortality rates were more highly correlated with all, all less lung, cervical, colorectal, and NPC indicates that smoking tobacco products had a more significant impact on cancer rates than did indoor cooking fires. Smoking is a well-known risk factor for many types of cancer (Sasco et al., 2004). In addition, the results might indicate the effects of secondhand smoke (Sasco et al., 2004).

The results for cervical cancer are consistent with those from a recent study in the U.S. (Grant and Garland, 2006). However, no other study has found that UVB or vitamin D reduces the risk of cervical cancer, so this finding should be treated cautiously.

Agricultural employment often correlates with lower mortality rates for lung and other cancers in other studies (Keller and Howe, 1993). Perhaps agricultural workers spend more time outdoors and thus are exposed to less indoor pollution and more solar UVB irradiance (Xu et al., 1989).

Although breast cancer is generally found to be UVB- and vitamin D sensitive, it was not in this study: breast cancer rates were low in China because of low-risk factors such as a diet high in animal products (Grant, 2002a), which increases levels of both estrogen and insulin-like growth factor-I (IGF-I). One of the effects of vitamin D is to attenuate growth-inducing signals such as from estrogen and IGF-I (van den Bemd and Chang, 2002; Lamprecht and Lipkin, 2003). However, the correlation with eggs is consistent with animal products’ being an important risk factor (Grant, 2002a), and the literature supports the inverse correlation with iodine (Smyth, 2003).

Total energy consumption (higher weight) and refined carbohydrates are thought to be associated with increased risk of colorectal cancer (Giovannucci, 2001; Gunter and Leitzmann, 2006), in agreement with the results of this study, although more likely through weight gain than insulin (Larsson et al., 2007) since sugar consumption is correlated with increased weight (Grant, 2004).

The etiology of NPC has been puzzling (Chang and Adami, 2006). Intake of preserved foods at an early age, smoking, and occupational exposure to formaldehyde and wood are significant risk factors (Yu and Yuan, 2002). However, NPC rates are high in Guangdong Province, but the reasons for these high rates have not been determined (Jia et al., 2004). In the United States, NMSC correlates strongly with NPC, as does lung cancer and urban residence, whereas UVB is inversely correlated.
may not have been risk-modifying factors. A potential problem with the datasets is that the non-cancer data were obtained five years after the cancer data. This problem is thought to be minor since at that time, the rural Chinese were not very mobile, and changes in diet and lifestyle were slow (Food and Agriculture Organization, 1996). Another problem is that aerosols from fossil fuel combustion and sandstorms as well as clouds also reduce the amount of solar UVR reaching the surface in an irregular variation with latitude, but these factors were not included in the analysis.

The primary advantage of this study is that data for a great many factors are available, which helps to either include or rule out confounding factors. An important advancement for studying cancer risks in China was the use of a 39-county subset of the data less affected by increased affluence and contact with the West. There may be other subsets that could also be used to shed more light on cancer risks in China. As with any observational study, these results should be investigated using other approaches.

Summary and conclusion

This ecologic study found significant inverse correlations with indices of solar UVB irradiance for cervical, colorectal (females), esophageal, gastric, lung (males) and all and all cancers other than lung cancer (females). These results are generally consistent with ecologic studies in other countries. Most of the other correlations found here are in general agreement with the literature, such as risk associated with smoking, diet, and microorganisms. Thus, this work indicates that cancer incidence and mortality rates could be reduced if population-level serum calcidiol levels were higher, especially at the higher latitudes and for those who do not spend enough time in the sun, as well as during the winter when producing vitamin D from solar UVB irradiance is difficult or impossible (Webb and Engelsen, 2006).

The incidence and mortality rates for cancers previously common in China such as cervical, esophageal, and gastric cancer are trending down, whereas those more common in Western developed countries such as female breast, colorectal, lung, prostate, and renal cancer are increasing (Gu, 2003; Yang et al., 2003, 2005; Chen et al., 2006; Tian and Chen, 2006). Dietary changes may explain some of these trends. Since the cancers with increasing incidence rates are vitamin D sensitive, investigating the role of vitamin D in health and making appropriate policy recommendations would be worthwhile for China.

References


