Leukemia and Background Radiation
in Northern New England

By ASCHER SEGALL

OF THE RADIATION-induced malignant neoplasms in man, leukemia has been best characterized in terms of the dose-response relationship. It has been suggested on the basis of studies of Japanese atomic bomb survivors, patients receiving radiotherapy for ankylosing spondylitis, radiologists exposed occupationally to radiation and children irradiated over the mediastinum in infancy, that for high level single dose exposure of man the incidence of leukemia is approximately linear with dose. At dose levels of 100 rads or greater, the estimated incidence has been postulated to lie within the range of from one to six cases per million persons at risk per year per rad. Below 100 rads, neither the linear non-threshold nor any of the alternative dose-response functions has been firmly demonstrated, nor is it known whether a dose rate dependency exists. Current estimates of the possible leukemogenic effects of exposure to such sources of low level radiation as radioactive fallout from nuclear testing are based on extrapolation from findings obtained at considerably higher doses. The bone marrow dose from nuclear fallout from 1954–1961 has been estimated as the equivalent of 1.2 years of exposure to natural background radiation.

One direct approach to the problem of assessing the possible hazard of chronic exposure to low level radiation is the study of variation in leukemia mortality associated with geographic differences in the dose rate from natural background radiation. Yet, despite the growing interest in the biological effects of low level radiation, relatively few studies of leukemia and background radiation have been reported. Roubault et al. in 1958 reported a sixfold higher leukemia mortality among adults (1941 to 1958) in a French district located on bedrock rich in granite than in neighboring communities built on geological formations other than granite. No measurements of the dose rate from natural radioactivity received by the residents were made and demographic parameters were not specified. It is therefore difficult to evaluate the significance of these findings. The authors recommended further investigations in this geographical area but to date none has been traced in the literature.

Court-Brown et al., in 1960, conducted a geographical study of leukemia mortality from 1939 through 1956 in relation to background radiation in Scotland. The maximum interareal difference in the mean bone marrow dose

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rates from background radiation was estimated at 21 mrads per year, assuming no variation in the contribution from internal emitters. Concomitant variations in leukemia mortality and radiation levels were observed. However, it did not appear plausible to the authors to interpret these in terms of a causal relationship. A major methodologic drawback was the choice of a study population within which the diagnosis and reporting of leukemia differed considerably.

In 1961, Craig and Seidman examined the 1949–1951 leukemia and lymphoma mortality rates for 163 metropolitan areas in the United States, classified by elevation, as an approximate index of the intensity of cosmic radiation. No estimates of the interareal difference in dose rate were made nor was variation in the dose rate from other background sources considered. No increase in mortality with rise in elevation was observed. The influence of demographic factors of possible leukemogenic significance was not discussed. Cosmic flux under usual conditions accounts for a relatively small proportion (25 per cent) of the total exposure from natural sources.

The limitations of these studies reflect both the difficulties inherent in the measurement of background radiation and the caution with which interpretation of any findings must be tempered. The measurement problem presents two facets. The first is related to the degree of dosimetric sensitivity required to detect environmental variation in both the external and internal components of background radiation. Methods that are sufficiently sensitive and that are at the same time suitable for large scale use required in epidemiologic studies are only now becoming available. A second major difficulty lies in relating differences in potential exposure as measured in the environment to variation in the dose rate delivered to the human skeleton. The skeletal dose rate from terrestrial and cosmic sources, for example, is a function not only of the local dose rate as usually measured in the air 3 feet above the ground but also of such factors as the proportion of time spent out of doors and the shielding effect of building materials. Similarly, in the case of internal emitters, nutritional and metabolic patterns constitute important determinants of the skeletal-dose rate from natural radioisotopes which may be present in water and food supplies. Thus, the magnitude of geographic variation in the skeletal dose rate from background radiation does not necessarily correspond to differences in potential exposure from these sources as measured in the environment.

The present study represents an endeavor to determine whether geographic variation in background radiation in the states of Maine, New Hampshire and Vermont is associated with differences in leukemia mortality from 1925 to 1954. Northern New England was selected for several reasons. Geological surveys had revealed the presence of inhabited granitic areas in New Hampshire where the dose rate from terrestrial gamma radiation might be expected to be elevated. A preliminary study of well waters had demonstrated relatively high concentrations of several radioisotopes in certain parts of Maine and New Hampshire. In addition, marked local variation in leukemia mortality over the past decade had been noted. It therefore appeared reasonable to measure in greater detail the magnitude of geographic variation in back-
ground radiation and to explore the possibility that it is sufficiently large to produce a detectable effect on mortality from leukemia over a 30-year period in the mean annual tri-state population of approximately 1,700,000 persons.

**Method**

The basic geographic units used in the study are minor civil divisions. These are the primary political divisions into which counties are divided and constitute the smallest administrative units for which vital statistics are routinely tabulated. There are 1,178 minor civil divisions in Maine, New Hampshire and Vermont.

Estimates of bedrock radioactivity were obtained for each minor civil division. For comparative purposes, the radioactivity of bedrock may be expressed in terms of equivalent uranium in parts per million. This is the amount of uranium which, by itself, would yield the same quantity of gamma radiation in roentgens as the uranium, thorium and potassium in the particular rock.

Boundaries of the minor civil divisions were plotted on state geological maps and the percentage area overlying each specific geological formation was determined. In this way, an average equivalent uranium value for the minor civil division, weighted by the proportion of the total area overlying each geological formation, was calculated.

The minor civil divisions were grouped into four categories according to bedrock radioactivity and into three categories according to population size. In selecting boundaries for the radiogeologic groups, an effort was made to provide a reasonable distribution of the total population among the four categories and concomitantly to maximize the between category differences in the weighted mean equivalent uranium values. Analysis by population size was introduced to control for those factors related to degree of urbanization which might affect reported leukemia mortality rates.

The radiogeological method as described above yields only indirect inferences as to the existence and magnitude of differences between populations characterized in this manner with respect to dose rate from natural background sources. To determine if under conditions of the present study the population-dose rate from external radiation is related to bedrock radioactivity, a personnel monitoring survey was conducted in eight selected areas of Vermont and New Hampshire overlying representative geological formations. The terrestrial component was measured simultaneously using a pressurized ion chamber. The relationship between the dose rate from internal emitters and local bedrock radioactivity was examined by analysis of radium, polonium, and radium in teeth extracted from life or long-time residents of the same eight geological areas which were surveyed for external radiation.

The association between radiogeologic estimates and the measured population dose rates in these areas has been described elsewhere in detail. A significant relationship between exposure to external background radiation and the equivalent uranium concentration of underlying geological formations was found. It was therefore possible to estimate differences in the mean annual dose from external emitters between the four radiogeological categories defined in the present study. Although teeth of residents in areas with high equivalent uranium content tended to have higher levels of radium and polonium, this trend was not statistically significant.

Transcripts of vital records pertaining to the earlier years included in the study are on file at the State Health Departments of Maine, New Hampshire and Vermont. These were microfilmed and searched for resident-deaths from leukemia on two occasions by different observers. Transcripts of death certificates meeting the criteria specified below were identified and information concerning cause of death, age, sex and place of usual residence was abstracted, coded and punched onto standard punch cards. For the more recent years, punch cards containing the same information had been prepared by the respective state health departments and were made available to the study.

Coding procedure was uniform for all microfilm transcripts from the three states, these
being processed centrally by the author. The punch cards which were prepared by the individual states are, however, subject to interstate variability in coding procedures. Table 1 shows the type of document used in the study by state and year. The selection was such as to minimize the extent of interstate variation.

Mortality records on file at the State Health Department, Boston, Mass., and at the City Health Department, Montreal, Canada, were also examined. Deaths from leukemia occurring to residents of Maine, New Hampshire and Vermont during the period 1945 through 1954 were identified. In the event that no duplicate was found in the relevant state files, the transcript was allocated to the state of residence.

Both nomenclature and statistical classification of neoplastic diseases of the lymphatic and hematopoietic systems have undergone considerable revision during the past several decades. For purposes of the present study, all certificates were included which listed under “cause of death,” whether primary or contributory, terms codeable to rubric 204 of the Sixth Revision of the International Classification of Diseases. Terms employed in previous years which do not appear in the Sixth Revision were ceded to the rubric consistent with their former assignment.

Deaths were allocated on a de jure basis according to the place of usual residence of the deceased person as reported on the death certificate. When there was no mention of place of “usual residence” and if the place of previous residence was stated to be different from the place of death, the place of residence as stated was coded provided the “length of stay” in the place of death was less than 1 year. If the “length of stay” was more than 1 year, the decedent was coded as a resident of the place of death. If the “length of stay” was not stated, the place of residence was coded as given. In the event that the transcript contained no entry for place of residence, the decedent was coded as a resident of the place of death.

Observed deaths were tabulated by successive census period, minor civil division and age. Of the 1,178 minor civil divisions recognized by the United States Census, 74 unorganized places, representing 0.56 per cent of the entire population are excluded from the state geographic codes used to allocate place of residence of decedents. Deaths for which the usual place of residence was entered as falling within a non-codeable minor civil division were omitted from the final analysis.

Age specific mortality rates were calculated for the tri-state region for each census period. These were used for age standardization. Expected deaths by minor civil division were obtained by applying the age and census period specific standardizing rates to the minor civil division population in the respective age categories for each census period. For this phase of the analysis, a 7090 I.B.M. computer was used.

Observed and expected deaths were summed over all minor civil divisions in each of the 12 radiation-population categories by state and by census period. The age-adjusted standard mortality ratio for each category was obtained. Differences between the observed and expected values were tested for statistical significance at the 5 per cent level using the Chi-square method.

RESULTS

Fig. 1 shows an isorad map delineating by contour lines the distribution of equivalent uranium in northern New England. In figure 2 the distribution of minor civil divisions by the equivalent uranium concentration of underlying bedrock is shown. Values range from 5 parts per million in the limestone areas of Vermont to 46 parts per million in the Conway Granite Region of New Hampshire. The clustering at 17 parts per million is due to the large number of minor civil divisions located on sedimentary and metamorphic rocks in Maine.

The set of boundaries used to define the four radiogeological categories and
Table 1.—Source of Leukemia Mortality Data by State and Year: 
Northern New England, 1925–1954

<table>
<thead>
<tr>
<th>State</th>
<th>Microfilm</th>
<th>State Punch Cards</th>
</tr>
</thead>
</table>

selected demographic characteristics are shown in table 2. The mean equivalent uranium concentration for each category was calculated as a weighted average, taking into account the population of the total intracategory population exposed to the respective concentration of equivalent uranium. Figure 3 illustrates the geographic repartition of equivalent uranium for minor civil divisions. Boundaries between adjacent minor civil divisions of the same radiogeological category are not shown. Of the average annual tri-state population, 8.4 per cent is classified in the lowest exposure category and 16.0 per cent in the highest. The remaining 75.6 per cent is assigned to the intermediary categories.

The distribution of resident leukemia deaths by decade and by state is shown in table 3. Of the 1,970 deaths identified, three were excluded from the
analysis because the place of residence was not codeable. Age-specific leukemia mortality rates are tabulated by decade in table 4.

Table 5 shows the distribution of observed and expected deaths from leukemia as well as the standard mortality ratios by radiogeological and population size categories for the tri-state region from 1925 through 1954. There is no significant association between mortality from leukemia and the estimated level of population exposure to background radiation. The standard mortality ratios for radiogeological categories 3 and 4, over-all population categories combined, are slightly higher than those for categories 1 and 2, but the differences are not statistically significant. This trend is not evident when each population category is considered separately.

The data were also analyzed by individual state, no consistent trend of mortality related to radiogeology being observed. Nor was any association noted when each decade was examined separately for the tri-state region or within individual states.

The distribution of mortality from acute and myeloid leukemia was con-
Fig. 3.—Mean equivalent uranium for minor civil divisions in northern New England. Boundaries between adjacent minor civil divisions of the same radiogeological category are not shown.

Considered separately in view of the high relative frequency with which these forms of the disease have been found to appear in populations exposed to high doses of radiation. The results are shown in table 6. Differences between the four radiogeological categories are not statistically significant.

Demographic Characteristics and Radiogeology

Previous studies have shown that certain demographic characteristics are associated with geographic variation in the reported mortality from leukemia. Of particular importance are ethnic and racial group, socioeconomic factors, urban-rural differences and the quality of medical care. Knowledge of the distribution of these factors relative to the distribution of exposure
levels to background radiation is necessary in order to determine whether they may be considered as uncontrolled random variables or whether their effect is confounded with that due to natural radioactivity.

The geographic distribution of the proportion of foreign born was examined relative to radiation exposure level by county using the Spearman rank correlation method. The correlation coefficient is +0.3308 with a probability value greater than 0.01 and less than 0.05. Thus, at the 5 per cent level, the proportion of foreign born shows significant positive correlation with radio-geology. However, since in no county does the proportion of foreign born exceed 16 per cent of the total population, the excess mortality attributable to this segment of the population is minimal. The situation is similar with respect to the Jewish population which represents a maximum of 0.8 per cent of the total, and for the nonwhite population comprising about 0.2 per cent.17

The Spearman rank correlation coefficient between level of radiation exposure and median effective buying income, as an index of socio-economic level, is +0.012 indicating no significant correlation at the 5 per cent level. To control for urban-rural differences, minor civil divisions were classified by size of population as well as by exposure to background radiation. It will be noted that there is a significant association between leukemia mortality and population size for the tri-state region over a period of 30 years. As population size increases, there is a concomitant increase in the mortality rate.

The quantity and quality of medical care may be presumed to influence both population exposure to medical sources of ionizing radiation and the reliability of diagnostic statements appearing on the death certificate.14 Physician density, as a rough index of medical care, was therefore examined for
Table 5.—Standard Mortality Ratios for Leukemia by Radiogeological and Population Size Categories: Tri-State Region, 1925–1954

<table>
<thead>
<tr>
<th>Radiogeological Category</th>
<th>Population Size 1 (under 1,000)</th>
<th>Population Size 2 (1,000–10,000)</th>
<th>Population Size 3 (over 10,000)</th>
<th>Population Size 1, 2, 3 Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ob. 15,000</td>
<td>exp. 19,408</td>
<td>SMR 0.77</td>
<td>1 exp. 19,408</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ob. 104,000</td>
<td>exp. 123,088</td>
<td>SMR 0.94</td>
<td>3 exp. 56,044</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ob. 116,000</td>
<td>exp. 123,088</td>
<td>SMR 0.94</td>
<td>4 exp. 56,044</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ob. 48,000</td>
<td>exp. 56,044</td>
<td>SMR 0.86</td>
<td>radiogeological categories 1, 2, 3, 4 combined</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ob. 283,000</td>
<td>exp. 328,583</td>
<td>SMR 0.86</td>
<td></td>
</tr>
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<td></td>
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<td></td>
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</tr>
</tbody>
</table>

Chi square for differences between radiogeological categories: 1.131; p > .05.
Chi square for differences between population size categories: 10.733; .001 < p < .01.
*Difference between observed and expected values is due to computer rounding to two decimal places.

association with level of exposure to background radiation. The Spearman rank correlation coefficient is +0.069 indicating no significant correlation at the 5 per cent level. There is therefore no indication that the geographic distribution of error in the designation of cause of death in vital records is related to the distribution of radiogeology. If this is so, the statistical effect of misclassification is to decrease the probability of demonstrating an association between the two variables under study.10

Discussion

Few contiguous populated areas of the U.S.A. have been identified which exhibit the amount of variation in external background radiation present in northern New England. This fact, together with the previous observation of substantial geographic variation in leukemia mortality within the area, prompted the present investigation of the relationship between the two observations.

However, it was recognized at the outset that in view of the magnitude of differences in background radiation as inferred from the distribution of equivalent uranium, the size of the tri-state population was adequate to test the hypothesis which specifies a linear dose-effect relationship only in the order of the upper limit which has been postulated (6 cases per million persons per rad per year). In addition, direct dosimetric evaluation of interareal variability in population exposure to external and internal emitters, conducted simultaneously with the mortality survey, indicated that although radiogeological characterization was a reasonable method of separating probably high and probably low areas with respect to terrestrial radioactivity, the differences between such areas in the actual dose rates of population exposure are considerably lower than those inferred from differences in equivalent uranium.
Table 6.—Mortality from Acute and Myeloid Leukemia: Tri-State Region, 1925-1954

<table>
<thead>
<tr>
<th>Radiogeological Category</th>
<th>Observed</th>
<th>Expected</th>
<th>Standard Mortality Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>81.000</td>
<td>76.800</td>
<td>1.055</td>
</tr>
<tr>
<td>2</td>
<td>388.000</td>
<td>396.972</td>
<td>0.977</td>
</tr>
<tr>
<td>3</td>
<td>308.000</td>
<td>304.174</td>
<td>1.013</td>
</tr>
<tr>
<td>4</td>
<td>154.000</td>
<td>153.032</td>
<td>1.006</td>
</tr>
<tr>
<td>Total</td>
<td>931.000</td>
<td>930.978</td>
<td></td>
</tr>
</tbody>
</table>

Estimates of the differences between the four radiogeological categories used in this study in the mean annual dose from external background sources, as derived from the personnel monitoring survey, are shown in Table 7; analysis of teeth revealed no significant relationship between local bedrock radioactivity and the estimated skeletal concentration of natural radioisotopes. Under these conditions the size of the population of these three states is insufficient and the observed absence of association between level of exposure to background radiation and leukemia mortality does not permit rejection of the hypothesis as stated above.

In view of these findings, the identification in the United States of populations of sufficient size and with sufficient variability in background exposure to test adequately the hypothesis of relationships between leukemia and background radioactivity is considered unlikely. Such studies would appear to be more feasible in areas where geographic variation in dose rate is considerably higher such as the monozite region of Kerala, India.¹

**Summary**

A survey of background radiation and mortality from leukemia was conducted in the states of Maine, New Hampshire and Vermont. The radioactivity in bedrock underlying each of 1,178 minor civil divisions was estimated on the basis of radiogeological analysis. Values were found to range from 5 parts per million equivalent uranium in the limestone areas of Vermont to 45 parts per million equivalent uranium in the Conway granite region of New Hampshire.

Mortality records from the tri-state study area for the period 1925-1954 were examined. One thousand nine hundred and seventy deaths from leukemia were identified and tabulated by minor civil division. An expected number of deaths by decade was calculated for each minor civil division using the tri-state age specific rates for standardization. Minor civil divisions were grouped into four categories according to mean equivalent uranium concentration in underlying bedrock. The difference in annual dose rate from external background sources was estimated to be 14.65 mrad per year. No significant difference in exposure to internal emitters was noted.

The observed and expected numbers of deaths were compared within each of the four radiogeological categories. No statistically significant association was observed between mortality from leukemia and radiogeological category either for the entire 30-year study period or within successive decades.

These data do not allow rejection of the hypothesis that leukemia mortality...
Table 7.—Estimated Mean Annual Dose from External Background Radiation* in Northern New England by Radiogeological Category

<table>
<thead>
<tr>
<th>Radiogeological Category</th>
<th>Mean Annual Dose mrad/year</th>
<th>Most probable value</th>
<th>lower estimate†</th>
<th>Upper estimate†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>133.26</td>
<td>5.85</td>
<td>2.88</td>
<td>8.83</td>
</tr>
<tr>
<td>2</td>
<td>139.12</td>
<td>3.02</td>
<td>1.48</td>
<td>4.55</td>
</tr>
<tr>
<td>3</td>
<td>142.14</td>
<td>5.78</td>
<td>2.85</td>
<td>8.73</td>
</tr>
<tr>
<td>4</td>
<td>147.93</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Excluding the cosmic neutron dose.
†At the 95 per cent confidence level.

varies with background radioactivity if the dose response relationship is of the order of that estimated from studies in humans at doses of 100 rads or greater. It seems unlikely that such a hypothesis could be adequately tested in the United States where geographic variation in background radiation is relatively small.

SUMMARIO IN INTERLINGUA

Un studio del radiation de fundo e del mortalitate ab leucemia esseva executate pro le statos de Maine, New Hampshire, e Vermont. Le radioactivitate in le rocca native sub cata un de 1.178 minor divisiones civil esseva estimate a base de analyses radiogeologic. Esseva trovate valores variante inter 5 pro million de equivalente de uranium in le areas de petra de calce de Vermont e 45 pro million de equivalente de uranium in le region granitic de Conway in New Hampshire.

Esseva examinate le registros de mortes pro le areas del studio pertinent al periodo inter 1925 e 1954. Mille novem centos septanta mortes ab leucemia esseva identificote e tabulate secundo le minor divisiones civil. Esseva calculate le expectate numero de mortes per decennio pro cata un del minor divisiones civil le quales esseva gruppate in quatro categorias secundo le valores medie de equivalente de uranium in le subjacente petra native.

Le observate e le expectate numeros de mortes esseva comparate in cata un del quatro categorias radiogeologic. Nulle statisticamente significative association esseva observate inter mortalitate ab leucemia e categoria radiologic. Isto vale etiam pro le decennios individual del periodo total de 30 annos del studio.

Iste datos non permitte le rejection del hypothese que le mortalitate ab leucemia varia con le radioactivitate de fundo quando le relation de dose e responsa es del ordine de illo estimate a base de studios in humanos con doses de 100 rad o plus. Il pare pauc pro probable que iste hypothese pote esser testate adequatemente in le Statos Unite que es un pais de relativamente minor variationes geographic del radiation de fundo.

REFERENCES
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