Geographic Variation in Leukemia Mortality in the United States

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DIFFERENCES BETWEEN countries in the recorded death rate from leukemia are considerable. Notable differences are evident even when countries with reasonably complete death registration are compared. For example, the United States, Denmark, and Sweden experience death rates from leukemia 1½ times as high as those of Canada, Great Britain, and France, which again have much higher rates than Ireland, Italy, or Finland (*1*).

Geographic variation within countries has also been noted. Hewitt (*2*), examining death registration data for England and Wales, noted a fairly regular gradient from a relatively low level in the north to a level about half as high again in the south. Material from the Danish Cancer Registry (*3*) showed highest rates in the capital and lowest in the rural areas. Otherwise, there were no definite topographical differences in Denmark. Higher rates for the urban compared with the rural population have been noted also in the United States (*4*). Death registration data for leukemia in the United States have been examined on a number of occasions (*5–8*), but no study of geographic variation between regions or States within the United States has been reported.

The National Office of Vital Statistics of the Public Health Service has published annually data on deaths from leukemia in the United States, classified according to State of residence, sex, race, and age, since 1949 (*9*). Prior to 1949 the reports did not include a breakdown by age for deaths from this cause in the individual States. The present study is based in the main, therefore, on data for the 5 years 1949–53. Attention is confined to the white population. Age-standardized death rates are shown in table 1 for the male, female, and total populations of each State and each division. The standard population used was the total white population of the United States in 1950; nine age groups were used in the standardizations.

In addition to the standardized rates, comparative mortality indexes for the individual States are given in table 1. These indexes express the observed number of deaths in each area as a percentage of the number of deaths expected in the area on the basis of (*a*) the age and sex distribution of the population of the area, and (*b*) the age-specific and sex-specific death rates from leukemia observed in the total United States white population.

Differences Between Divisions

The nine divisions into which the States are grouped are those used by the Bureau of the Census. Differences between them in leukemia death rate were not great. The highest division, Pacific, with a mean annual death rate of 69.9 per million, was 20 percent higher than the lowest, East South Central, with a rate of 58.4.

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Table 1. Leukemia death rates and characteristics for the white population of States and divisions of the United States, 1949–53 and 1938–42

Division and State	Number of leukemia deaths 1949–53			Standardized death rate per million, 1949–53			Corrected sex ratio 1949–53 (percent male)	Comparative mortality index 1949–53	Comparative mortality index 1938–42	Percentage increase from 1938–42 to 1949–53	Mean yearly increment in leukemia death rate [1]		Physicians per 100,000 population, 1949
	Male	Female	Total	Male	Female	Total					1938–45	1946–53	
New England	**1,687**	**1,331**	**3,018**	**71.8**	**52.7**	**62.2**	**57.7**	**97**	**67**	**45**	**1.8**	**2.0**	**151**
Maine	136	108	244	56.5	43.5	50.0	56.5	78	55	42	1.5	−.2	97
New Hampshire	97	84	181	67.2	54.2	60.7	55.4	95	47	102	2.6	1.8	126
Vermont	80	69	149	80.3	67.4	73.8	54.4	114	57	100			140
Massachusetts	881	683	1,564	75.0	52.6	63.7	58.8	99	73	36	1.5	2.6	170
Rhode Island	111	87	198	58.9	42.5	50.7	58.1	78	59	32	.8	1.6	118
Connecticut	382	300	682	77.6	58.2	67.9	57.1	105	69	52	2.8	1.5	152
Middle Atlantic	**5,400**	**4,171**	**9,571**	**75.9**	**56.5**	**66.2**	**57.3**	**103**	**75**	**37**	**1.4**	**2.5**	**161**
New York	2,908	2,177	5,085	82.4	59.0	70.6	58.3	110	83	33	1.7	2.4	196
New Jersey	862	645	1,507	77.0	55.3	66.1	58.2	103	72	43	1.6	2.6	128
Pennsylvania	1,630	1,349	2,979	66.2	53.5	59.8	55.3	93	65	43	2.0	2.5	128
East North Central	**5,516**	**3,875**	**9,391**	**75.1**	**53.2**	**64.1**	**58.5**	**100**	**68**	**47**	**2.0**	**2.5**	**118**
Ohio	1,473	1,077	2,550	76.7	55.4	66.0	58.1	103	63	63	1.6	3.8	116
Indiana	691	478	1,169	71.1	49.2	60.1	59.1	93	58	60	2.0	1.2	103
Illinois	1,551	1,122	2,673	74.1	53.4	63.5	58.1	99	76	30	1.5	1.7	141
Michigan	1,096	708	1,804	75.0	50.3	62.6	59.9	97	66	47	1.4	2.7	106
Wisconsin	705	490	1,195	78.2	56.7	67.4	58.0	105	75	40	2.5	3.2	104
West North Central	**2,948**	**2,056**	**5,004**	**79.7**	**58.1**	**68.8**	**57.8**	**107**	**71**	**51**	**2.0**	**3.5**	**113**
Minnesota	749	481	1,230	94.3	64.2	79.2	59.5	124	90	38	−.5	3.7	132
Iowa	572	393	965	78.6	55.6	67.1	58.6	105	67	57	4.0	3.7	105
Missouri	711	510	1,221	71.4	50.3	60.8	58.7	95	61	56	1.9	2.7	120
North Dakota	101	85	186	63.7	63.1	63.4	50.2	97	74	31	2.7	1.9	75
South Dakota	141	82	223	83.5	55.7	69.5	60.0	108	69	57	1.6	2.4	73
Nebraska	287	193	480	79.6	55.7	67.6	58.8	106	70	51	4.0	3.9	113
Kansas	387	312	699	77.5	63.7	70.6	54.9	110	67	64	1.1	4.9	103
South Atlantic	**2,444**	**1,804**	**4,248**	**67.6**	**50.3**	**58.9**	**57.3**	**91**	**56**	**63**	**1.9**	**2.1**	**96**
Delaware	56	35	91	83.2	49.7	66.4	62.6	103	66	56			126
Maryland	290	238	528	64.9	49.7	57.2	56.6	89	62	44	1.7	2.1	136
District of Columbia	99	73	172	84.0	52.2	67.9	61.7	104	95	9	−.3	−1.3	267
Virginia	356	283	639	62.0	48.6	55.2	56.1	87	55	58	2.6	1.5	91
West Virginia	307	195	502	69.3	46.1	57.6	60.1	90	49	84	1.9	2.5	84
North Carolina	382	317	699	61.0	49.8	55.4	55.1	89	54	65	1.9	1.8	79
South Carolina	175	136	311	70.1	49.6	59.8	58.6	89	45	98	2.1	1.5	69
Georgia	373	268	641	72.2	50.4	61.2	58.9	95	58	64	1.5	2.2	84
Florida	406	259	665	71.7	46.1	58.8	60.9	92	51	80	1.8	3.9	91
East South Central	**1,372**	**1,003**	**2,375**	**67.9**	**49.1**	**58.4**	**58.0**	**93**	**48**	**94**	**1.7**	**2.7**	**79**
Kentucky	418	307	725	63.1	47.4	55.2	57.1	86	43	100	2.1	3.0	84
Tennessee	425	343	768	68.4	53.0	60.6	56.3	102	52	96	1.6	3.0	90
Alabama	332	227	559	72.0	47.7	59.7	60.2	92	43	114	1.9	2.8	68
Mississippi	197	126	323	71.6	45.9	58.7	60.9	91	56	63	.8	1.3	64
West South Central	**2,053**	**1,434**	**3,487**	**73.5**	**51.1**	**62.2**	**59.0**	**97**	**53**	**83**	**1.7**	**3.3**	**95**
Arkansas	240	161	401	65.7	46.4	56.0	58.6	87	40	118	2.8	3.7	82
Louisiana	316	209	525	81.2	50.6	65.8	61.6	102	55	85	1.6	3.3	104
Oklahoma	376	267	643	73.6	53.3	63.4	58.0	98	44	123	2.4	4.8	94
Texas	1,121	797	1,918	74.3	52.2	63.2	58.7	98	59	66	1.0	2.8	95
Mountain	**850**	**609**	**1,459**	**72.4**	**55.8**	**64.1**	**55.9**	**100**	**56**	**79**	**.9**	**3.9**	**110**
Montana	130	85	215	81.8	64.6	73.2	55.9	113	67	69	1.6	5.5	94
Idaho	127	77	204	85.7	59.5	72.5	59.0	114	50	128	.8	8.1	77
Wyoming	36	27	63	51.8	48.7	50.3	51.5	75	53	42			83
Colorado	229	187	416	69.3	57.6	63.4	54.6	99	59	68	.3	3.4	158
New Mexico	79	60	139	56.7	49.1	52.9	53.6	85	46	85	1.6	.0	73
Arizona	102	78	180	69.0	53.1	61.0	56.5	96	51	88	−.2	4.7	97
Utah	117	77	194	80.1	50.7	65.3	61.2	102	55	85	2.4	4.5	115
Nevada	30	18	48	75.0	57.2	66.1	56.7	103	52	98			110
Pacific	**2,802**	**2,077**	**4,879**	**80.5**	**59.3**	**69.9**	**57.6**	**107**	**75**	**43**	**2.6**	**2.3**	**132**
Washington	477	312	789	77.3	54.7	65.9	58.6	97	70	39	3.4	2.0	106
Oregon	337	195	532	84.4	52.7	68.5	61.6	107	71	51	3.6	4.3	109
California	1,988	1,570	3,558	81.0	61.3	71.0	56.9	110	77	43	1.6	2.0	142

[1] Values are not calculated for States with less than 500,000 white population in 1950.

All three southern divisions (East South Central, West South Central, and South Atlantic) had rates lower than any other area. By contrast, rates were highest in the west. The Pacific, Mountain, and West North Central divisions ranked first, second, and fourth in order of leukemia death rates.

Since Meadors (*4*) found the leukemia death rate approximately 1½ times higher in the urban than in the rural population of the United States, some relationship between leukemia death rate and degree of urbanization of the area might be expected. The lower leukemia death rate in the three southern divisions is consistent with this expectation. However, among the other six divisions, the death rates showed little relationship to the pattern of urbanization. The two divisions with the highest leukemia rates, Pacific and West North Central, were third and seventh in a listing according to urbanization. The two most urban divisions, Middle Atlantic and New England, ranked third and sixth according to leukemia death rates. Meadors' finding was based on a direct comparison of the urban and rural populations and is therefore in no way invalidated by the finding of high leukemia rates in areas with low urbanization, or vice versa. It seems likely, however, that the urban-rural difference in leukemia death rates was operating during the period of the present study to reduce some of the geographic differences between divisions.

Adjustment of the divisional death rates is possible on the basis of the known percentage of the population of the division classified as urban, and the assumption that the rates for the urban population were 1½ times higher than those for the rural population in each division. This assumption was made on the basis of Meadors' findings for the whole United States. After adjustment on this basis, divisional death rates were West North Central 72.7, Pacific 66.8, Mountain 66.3, East South Central 64.9, West South Central 64.3, East North Central 63.1, South Atlantic 62.6, Middle Atlantic 61.9, and New England 59.1. The adjustment has raised the rates for the southern divisions relative to divisions in the northeast, suggesting that the originally low rates in the south may result from the lower percentage of urban population there. However, the adjustment has accentuated the difference between the west and the northeast. The three western divisions now rank first, second, and third in order of leukemia death rates.

Differences Between States

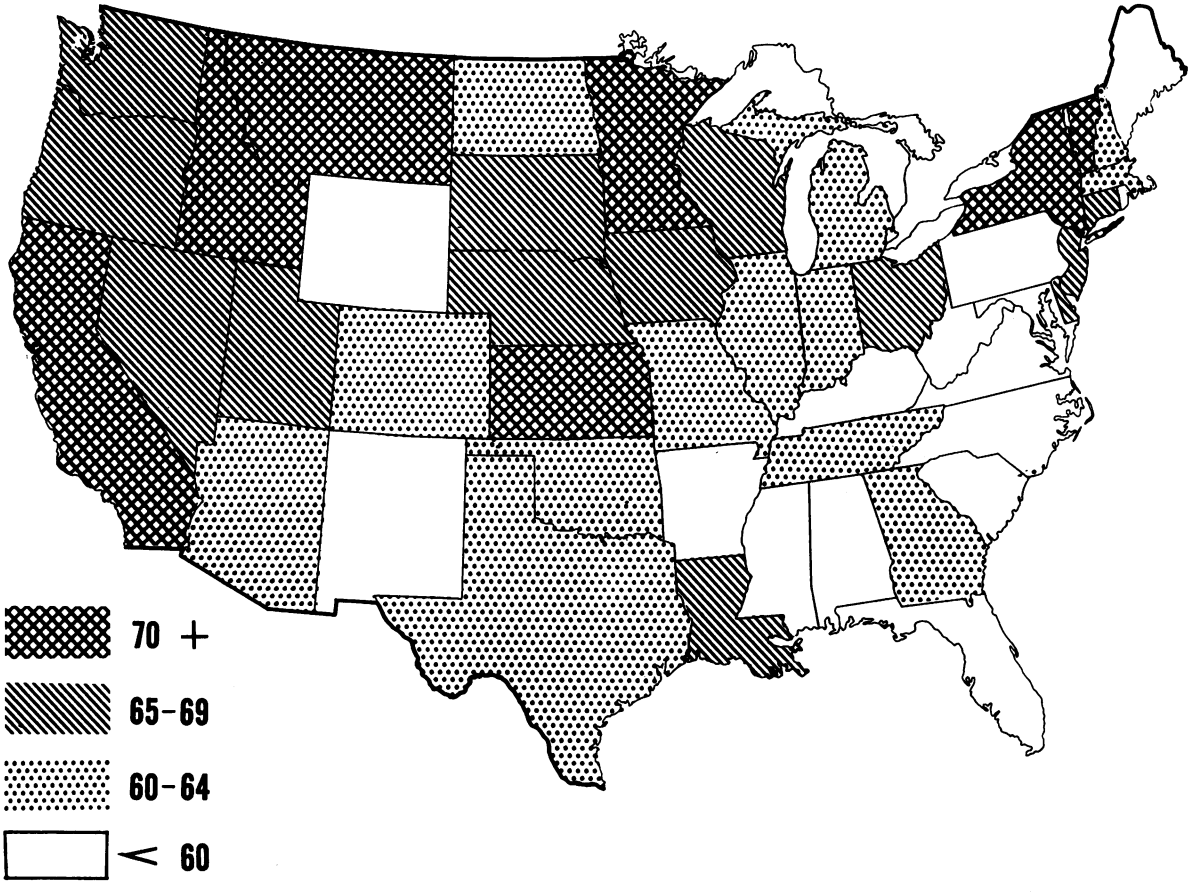
The individual States showed greater variation in leukemia death rates than the divisions (table 1, fig. 1). States with the highest rates in 1949–53 were Minnesota (79.2), Vermont (73.8), Montana (73.2), Idaho (72.5), California (71.0), New York (70.6), and Kansas (70.6). Lowest rates were in Maine (50.0), Wyoming (50.3), Rhode Island (50.7), and New Mexico (52.9).

Greatest variation in leukemia death rates was between States constituting the New England and Mountain divisions. New England included the second highest State (Vermont) as well as the 46th and 48th (Rhode Island and Maine). In the Mountain division there was disparity between the four northwestern States with the rates of 73.2, 72.5, 65.3, and 66.1, and the four southeastern States with rates of 63.4, 61.0, 52.9, and 50.3. The three Middle Atlantic States showed less variation, from 70.6 in New York to 59.8 in Pennsylvania.

On the other hand, the States constituting the three southern divisions showed fair uniformity in their low individual rates. Of the 17 States (including the District of Columbia) in these divisions, only the District of Columbia, Delaware, and Louisiana, with rates of 67.9, 66.4, and 65.4, respectively, had rates higher than the overall rate for the country (64.4). Similarly, the States of the Pacific and the West North Central divisions showed almost uniformly high rates. Of the 10 States in these divisions, only North Dakota and Missouri, had rates lower than the national average.

Once again it might be expected that some of these geographic variations could be attributed to differences between States in variables which are known to affect leukemia death rates, such as urban dwelling (*3*, *4*) and income (*5*, *10*, *11*). Coefficients have been calculated for the correlation of the comparative mortality index in each State with the percentage of the white pop-

Figure 1. Mean annual age- and sex-standardized leukemia deaths per 100,000 white persons for each State, 1949–53.



ulation of the State classified as urban in 1950, the median income of the white population in 1949, and the number of active non-Federal physicians per 100,000 population in 1949. The correlation with the percentage of urban population was small and insignificant ($r=0.13\pm 0.14$), but higher correlations were found with both median income ($r=0.27\pm0.14$) and density of physicians ($r=0.35\pm0.14$). Partial correlation suggested closer association of the leukemia death rate with density of physicians when income was kept constant ($r=0.24$) than with income with physician density constant ($r=0.06$).

The interpretation of these associations is discussed below. It is clear however that they account for only a part of the geographic variation. In sharp contrast to this trend are, for example, the high leukemia rates noted in certain Mountain and other western States in spite of low physician: population ratios, and the relatively low leukemia rates found in the industrial middle west.

Variations by Age and Sex

The general pattern of the distribution of death rates among States was similar for males and females. The coefficient of correlation between the rates for males and females in the same States was 0.55 ± 0.14. There is a suggestion that the sex ratio tended to be high in those States with high total death rates ($r=0.26\pm 0.14$). However, the correlation coefficient is not significant. In general, sex ratios were constant at about 58 percent male from division to division, and, even between States, differences were small (table 1). In the few States in which the proportion of males affected was higher than average, the age trend was not such as to suggest any specific occupational risk.

Numbers are too small for reliable examina-

tion of age trends in the individual States, but divisional age-specific rates are examined in table 2. The rate for each age group for each division is shown as a percentage of the rate for the United States in the same age group. The rates in the Pacific division were particularly high (compared with total United States rates) in the age groups 0–14 and to a lesser extent in the older age groups. In the West North Central division, on the other hand, rates were relatively highest in the older age groups. Two divisions, Middle Atlantic and East South Central, were characterized by relatively high rates in the age groups 15–44.

The different pathological varieties of leukemia have different age and sex trends (*12*). It may be, therefore, that these age differences in rates for divisions are indicative of variations in the proportions of the different types of leukemia. On the other hand, local circumstances may affect the shape of the age trend through changes in the age-specific risks for a specific pathological diagnosis. No data permitting examination of this question are available.

Secular Changes

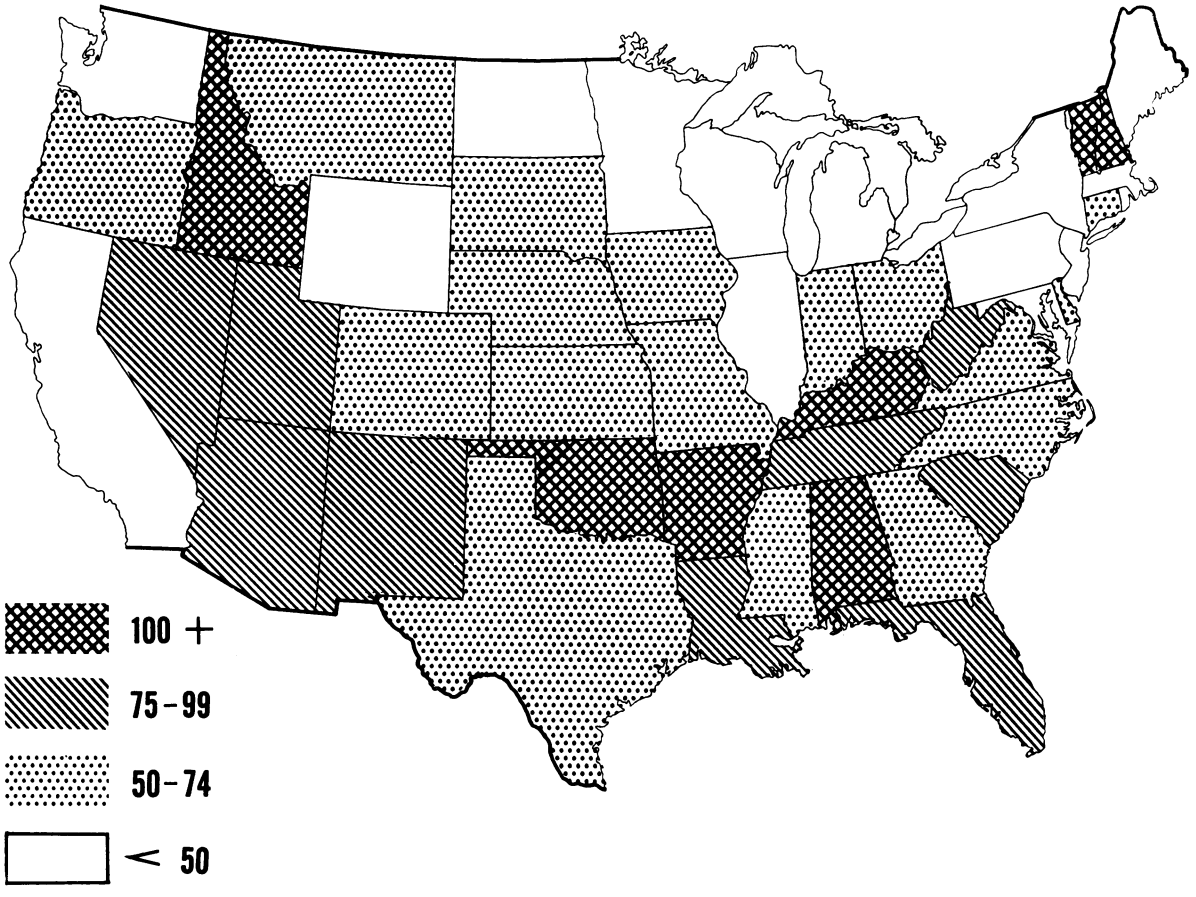
To determine whether these geographic patterns have undergone any recent changes, data have been assembled for the 5 years surrounding the census of 1940 (1938–42). As mentioned previously, data on leukemia deaths in individual States are not available by age for this period, and age-standardized death rates cannot be calculated. The measurement of secular change in mortality in individual States has therefore been approached in two ways. First, comparative mortality indexes have been calculated for each State for 1938–42, using the total age-specific and sex-specific rates of 1949–53 for the calculation of expected numbers. The increase in the index between 1938–42 and 1949–53 is then expressed as a percentage of the 1938–42 index in the same State (table 1). Second, regression lines have been fitted to the annual crude leukemia death rates in each State separately for the two periods 1938–45 and 1946–53. From these, the regression coefficient is shown as the mean annual increment in table 1. This second method does not allow for age changes in population but gives a crude measure of the rate of increase of leukemia mortality in the two halves of the time period.

In examining the comparative mortality indexes for 1938–42, we may note that the overall pattern is similar to that of the later period, 1949–53. However, there is a suggestion that the physician-income-urbanization complex was more influential in determining leukemia death rates in the early period. Coefficients of correlation of the comparative mortality indexes for 1938–42 with density of physicians and percentage of urban population in 1940 were 0.62 ± 0.14 and 0.60 ± 0.14, respectively. Data on median income of the white population were not published by State for the 1940 census. The stronger association with the urbanization com-

Table 2. Age-specific leukemia death rates in each division, as a percentage of the United States rate for the same age group, 1949–53

Age	Pacific	West North Central	Middle Atlantic	East North Central	Mountain	New England	West South Central	South Atlantic	East South Central	Death rate per million, United States
0–4	114	101	95	106	97	99	102	89	89	58. 7
5–14	126	98	105	98	103	107	92	89	87	31. 7
15–24	106	101	109	99	89	101	89	88	110	20. 8
25–34	107	100	111	94	107	89	93	91	111	22. 5
35–44	100	103	112	98	102	85	96	89	101	33. 2
45–54	103	106	104	96	98	99	96	97	97	62. 3
55–64	102	105	107	99	97	97	98	89	89	129. 7
65–74	108	112	103	105	102	92	92	87	88	238. 7
75+	119	123	95	99	103	105	108	104	79	339. 1
Total	107	105	101	98	98	96	95	90	90	64. 4

Figure 2. Percentage increase in the mean annual age-standardized leukemia death rate in white persons between 1938–42 and 1949–53.



plex found in the earlier time period is largely the result of comparatively higher rates in the States in the East North Central division and lower rates in the Mountain States.

The percentage increase in leukemia between 1938–42 and 1949–53 is illustrated in figure 2. The increase in recorded death rates between the two periods was greatest in those areas in which initial rates were lowest. For the southern States, this increase may be interpreted as due to a leveling out of those factors, diagnostic or otherwise, which were responsible for the initial low rates. In two areas, however, Vermont and the Mountain States, such a leveling out cannot be accepted as the whole explanation of the high percentage increase between the two periods since the process has gone beyond the point of equalization. Vermont in 1949–53, for instance, had the second highest leukemia death rate. Similarly, of the five Mountain States with increases above 75 percent, three (Idaho, Utah, and Nevada) had rates in 1949–53 well above the national average.

The probability that the increase in leukemia death rates in certain of the Mountain States is of different origin from that observed in other States with initially low rates is further suggested by the observation that in the Mountain States the rise has affected the second half of the period almost exclusively. This is shown in the two columns of table 1 which give mean annual increments in leukemia death rate for 1938–45 and for 1946–53. In the southern States with large increases, the increase has occurred in both time periods, whereas in Utah, Arizona, Idaho, and Montana the increase has affected the second period predominantly. During 1946–53, two of these States experienced a rate of increase greater than that experienced by any other State in the same or the preceding 8-year period.

Discussion

In the period 1949–53, the leukemia death rate recorded in certain States of the United States was more than 1½ times as high as that in other States. It is not to be expected that the geographic pattern should be explained in terms of any one variable or influence or even that there should be any one overall pattern. In fact, several separate trends are evident.

First, reference has been made to the partial consistency of the findings with previous reports of high leukemia incidence associated with the social complex which includes urbanization, higher income, better medical care, and more accurate diagnosis. How much of the association of leukemia with this complex is directly attributable to the last component, more accurate diagnosis, is conjectural.

The fact that leukemia death rates in the individual States were more closely correlated with physician: population ratios than with either income or urbanization suggests that diagnostic differences are important. However, the difference between the correlation coefficients for physician density and income was not significant. In addition, while close association with measures of medical care suggests, first of all, differences in diagnostic standards, the possibility mentioned elsewhere (*13*) that some feature of medical care is itself leukemogenic cannot be overlooked.

It is evident, however, that as a determinant of the geographic pattern of leukemia death rate, the importance of this association has diminished over the time period 1938–53. Correlation coefficients measuring the association in the period 1949–53 were almost half those for 1938–42. This is consistent with the wider distribution of medical care occurring during this period.

A second feature of the geographic pattern is the belt of relatively high leukemia death rates covering the northern half of the United States west of the Mississippi River. This belt is seen in both time periods, although it is more marked in the second. It is clearly not the result of the association with physician density or urbanization discussed in the previous paragraph; in fact it would appear to be evident in spite of this, notably, for example, in Montana and Idaho, both of which have leukemia death rates of more than 72 per million, and only 94 and 77 physicians per 100,000 population, respectively. Highest rates in this belt were in Minnesota. In fact, in both time periods, Minnesota had the highest death rate of all the States, and by a comfortable margin. Minnesota is, of course, the seat of important medical graduate and postgraduate teaching centers. These could explain the especially high rate in this State on a diagnostic basis, but it could not account for the much wider plateau of high leukemia incidence of which the Minnesota rate is the peak. It should be noted that Minnesota as a whole has a physician: population ratio no higher than the national average.

A third area of interest centers around certain of the Mountain States, particularly Nevada, Utah, Arizona, Idaho, and Montana. The interesting feature here is not so much the present level of the death rate as its recent rate of increase. The leukemia death rate in the area covered by these States almost doubled in the 8 years 1946–53. The rate of increase in this period was high in each of these States, and in two of them (Montana and Idaho) exceeded that experienced by any other State in the same or in the preceding 8 years.

The increase is not explained by changes in the age distribution of the population although there has been considerable migration into certain of these areas during the period concerned. To what extent the increase can be attributed to improvement of diagnostic facilities is uncertain. Examination of the trends for certain other causes of death (duodenal ulcer, diabetes, cancer of the stomach, uterus, and breast), diagnosis of which is also dependent on laboratory facilities, did not reveal any short-term change during this period. Of course, this does not eliminate the possibility of changes in the specific type of facility upon which the diagnosis of leukemia depends.

In 4 of these 5 States, Eisenbud and Harley noted the greatest levels of radioactivity deposited from atomic tests in spring 1952 (*14*). This fact suggests at first sight the possibility that this source of radioactivity has contributed to the increase in leukemia death rates. The possibility is eliminated however by closer consideration. First, after the initial explosion in New Mexico in 1945, a relatively small one, no

tests were conducted in the United States until 1951 according to the Office of Public Information, United States Atomic Energy Commission. The upward trend in leukemia death rates commenced about 1947–48. Second, a later publication of Eisenbud and Harley showing cumulative radioactive fallout to January 1955 discloses much less correspondence to the pattern of leukemia increases than did the pattern from the single test series recorded previously (*15*). Third, as reviewed by the same authors, the presently available evidence suggests that the biological effect of fallout in the amounts observed is trivial.

The trend of leukemia mortality in these States in the next few years deserves continued attention.

Summary

United States vital statistics for 1949–53 are used to compare age-standardized death rates from leukemia in the different States and divisions of the United States. Areas are also compared with respect to the increase in leukemia death rate noted since an earlier period (1938–42). The following features are noted:

1. Some of the geographic pattern of leukemia mortality is explicable in terms of the association of leukemia with urbanization, higher income, and better medical care. The importance of this association seems to have diminished in the decade between the two periods examined.

2. Independent of this, there is a belt of high leukemia death rates in States in the northern half of the country west of the Mississippi.

3. In an area covered by five contiguous Mountain States (Nevada, Utah, Arizona, Idaho, and Montana) the leukemia death rate almost doubled in the 8 years 1946–53. Two of these States individually had greater rates of increase during this period than any other State in the same or in the preceding 8 years.

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