The Relation of Socioeconomic Factors To Incidence of Childhood Leukemia

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AN INCREASING NUMBER of studies have suggested a relationship between certain social or economic factors and the incidence of leukemia. In 1947 Sacks and Seeman (*1*) showed a rising rate for leukemia paralleling a rise in economic status in Baltimore from 1939 to 1943. Their study included both adults and children. In 1956 Walter and Gilliam (*2*) found that the leukemia mortality rate in the United States for nonwhite and white children under 1 year of age was similar but that the rate of the nonwhite children decreased throughout the childhood years while that of the white children increased until 4 years of age and then declined. Slocumb and MacMahon (*3*) also demonstrated a difference between white and nonwhite children between 1950 and 1959.

Phillips (*4*) reported a statistical study in 1959 which showed the death rate for leukemia in Britain to be higher in the more prosperous southern counties than in the economically poorer northern ones. He also found the rate to be high in urban areas and low in most rural areas. Stewart (*5*) did not find an urban-rural difference in the childhood leukemia rate in Britain. The recent study by Pinkel and Nefzger (*6*) in Buffalo, N.Y., showed a significantly higher rate for childhood leukemia from 1943 to 1956 in the upper economic census tracts of that city. These findings support the fact that there appears to be a higher incidence of both childhood and adult leukemia in economically more favored nations and races (*7*).

While interviewing families of recently diagnosed leukemia patients in Colorado, it was our impression that the majority lived in cities and in the better parts of town. The present study was initiated to investigate the validity of this impression.

Methods

To study the relation between certain social and economic factors and the incidence of childhood leukemia in the State of Colorado, the necessary identifying data were obtained from death certificates of the 258 children, 14 years old and under, reported to have died from leukemia from 1941 through 1959. The 1940, 1950, and 1960 U.S. Bureau of the Census figures (*8–11*) were used to determine the child population. For most of the tabulations, the 1950 census figures (*9*, *10*) were used to represent the median child population for this period and to obtain certain social and economic information about the geographic area in which the child had lived. Seventy-five of the leukemia patients had lived within the census tracts of Denver, and more detailed social and economic data were available for this group.

The mortality was determined as the 19-year rate (1941–59) when the 1950 census figures were used to represent the median child population. The annual leukemia death rate was determined by calculating the child population for each year.

The population for the years between census

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counts were calculated by using the 1940, 1950, and 1960 census counts according to the formula

$$Y = Y_2 + \frac{(Y_3 - Y_1)}{2}x + \left[\frac{(Y_1 + Y_3)}{2} - Y_2\right]x^2$$

where

x = any given year. For convenience of calculation, arbitrary values of -1, 0, $+1$ were assigned to 1940, 1950, and 1960, with intervening years being given values of -0.1, -0.2, 0.1, 0.2, and so on; 1949, for example, would have an x value of -0.1, 1948 of -0.2, and so on; 1951 would have an x value of 0.1, 1952 of 0.2, and so on.

Y = population for any given year x
Y_1 = population by census count, 1940
Y_2 = population by census count, 1950
Y_3 = population by census count, 1960

Results

Total mortality trends by year. The total death rates for childhood leukemia in Colorado each year from 1941 through 1959 are shown in table 1. The statewide mortality varied from a low 0.6 per 100,000 in 1948 to a high of 7.3 per 100,000 in 1957. Although the rates varied considerably from year to year, the general trend was toward an increasing reported incidence. The average mortality rate from childhood leukemia for the first 5 years of this period (1941–45) in Colorado was 1.7 as compared with a rate of 4.6 for the last 5 years (1955–59), representing a 2.7-fold increase.

If the total rates are ranked and correlated with the years in table 1 (Spearman rank order correlation), an R of 0.74 is obtained. This is significant at less than 0.01 for the hypothesis that the reported death rate for leukemia among children 14 years old and under has increased in Colorado in the period 1941–59. This reflects the nationwide increase in reported deaths from leukemia in children over 1 year of age for most of this period, and in particular from 1941 to 1950 (*3, 12*).

Urban-rural differences. Urban and rural death rates were compared by using the 1950 U.S. Bureau of the Census definition for urban

Table 1. Population of children through 14 years and number of leukemia deaths and rates, by urban and rural areas, Colorado, 1941–59

Year	Total			Rural			Urban		
	Population [1]	Number deaths	Rate [2]	Population [1]	Number deaths	Rate [2]	Population [1]	Number deaths	Rate [2]
1941	289.8	4	1.4	160.9	3	1.9	128.9	1	0.8
1942	292.9	2	.7	160.9	0	0	132.0	2	1.5
1943	297.3	6	2.0	161.0	1	.6	136.3	5	3.7
1944	303.0	3	1.0	161.0	1	.6	142.0	2	1.4
1945	309.9	11	3.5	161.0	2	1.2	148.9	9	6.0
1946	318.2	10	3.1	161.0	1	.6	157.2	9	5.7
1947	327.7	12	3.7	161.0	4	2.5	166.7	8	4.8
1948	338.5	2	.6	160.9	0	0	177.6	2	1.1
1949	350.7	11	3.1	160.9	5	3.1	189.8	6	3.2
1950	364.1	15	4.1	160.8	3	1.9	203.3	12	5.9
1951	378.8	15	4.0	160.7	5	3.1	218.1	10	4.6
1952	394.7	23	5.8	160.5	6	3.7	234.2	17	7.3
1953	412.0	16	3.9	160.4	6	3.7	251.6	10	4.0
1954	430.6	13	3.0	160.2	5	3.1	270.4	8	3.0
1955	450.5	18	4.0	160.0	4	2.5	290.5	14	4.8
1956	471.6	16	3.4	159.8	1	.6	311.8	15	4.8
1957	494.0	36	7.3	159.6	9	5.6	334.4	27	8.1
1958	517.8	22	4.2	159.4	4	2.5	358.4	18	5.0
1959	542.8	23	4.2	159.1	4	2.5	383.7	19	5.0

[1] Colorado, in thousands.
[2] Death rates per 100,000.

SOURCES: Population as of April 1 each year is calculated by formula given in text. The U.S. Bureau of the Census 1950 definition of urban is used. Deaths are classified by residence shown on certificates filed at the Colorado Department of Public Health.

NOTE: The urban rate exceeds the rural rate for 17 of the 19 years. The one-tailed sign test shows that $P < 0.001$ for such an occurrence.

Table 2. Leukemia death rates per 100,000 population of children through 14 years, by economic indexes, Denver, 1941–59

Census tracts, by economic division	19-year death rate [1]	
	Census tracts, by income [2]	Census tracts, by rent [3]
Upper half	94. 2	94. 7
Lower half	58. 4	61. 5
Upper 10 percent	122. 9	124. 3
Lower 10 percent	57. 2	54. 0

[1] U.S. Bureau of the Census child population for year 1950 was used to represent the median annual population.
[2] Data include all 50 census tracts of Denver.
[3] Data include 49 tracts. (Median rent not available for 1 tract.)

and rural (*9*). The urban group included primarily those towns and cities with a population of 2,500 or more plus the suburbs of large cities.

Table 1 indicates that the increasing incidence of reported deaths from childhood leukemia for the State as a whole occurred in both the urban and rural child populations. However, the peak incidence appears to be in the early 1950's for the rural group as compared with the late 1950's for the urban children. Table 1 also indicates that the urban rate was higher than the rural rate for 17 of the 19 years. A sign test of the hypothesis that the Colorado urban leukemia death rate among children 14 years old and under is higher than the rural death rate produced a P value of less than 0.001.

The 19-year difference in the urban and rural death rate was determined for the total group of 258 children who were reported to have died from leukemia during this period. The 1950 child population was used to represent the median number. By this method of comparison, the rate of urban deaths per 100,000 children from 1941 to 1959 was 95.5 as compared with 38.4 in rural areas.

Correlation with other economic and social factors. More detailed social and economic data were available from the census reports (*8*, *9*) for a group of 75 leukemia patients that had lived in the 50 census tracts of Denver. Using this information, an attempt was made to determine the leukemia death rate in childhood for different census tracts by grouping them according to selected social and economic factors. For this aspect of the study, the 19-year mortality rate was determined by using the 1950 child population to represent the median for the period. The 1950 census data also were used to provide information regarding the social and economic aspects of the census tracts.

Table 2 lists the incidence of childhood leukemia in Denver according to the same economic indexes that had been studied by Pinkel and Nefzger (*6*) in Buffalo, N.Y., to compare these two geographic areas. The 19-year leukemia death rate was first determined in the higher and lower census tracts by income. The higher tracts are those with the average income above the median and the lower, those below the median. The leukemia death rate in the upper income census tracts was 94.2 as compared with 58.4 in the lower half. The five tracts comprising the upper 10 percent in average income had a rate of 122.9 as compared with 57.2 in the five tracts with the lowest average income.

Table 2 also shows similar findings in the incidence of leukemia when the census tracts are divided according to the median rent paid in the area. Census tracts above the median monthly rent show a mortality of 94.7 per 100,000 as compared with 61.5 for those below the median. A greater difference occurs if the census tracts are divided into tenths and the extremes are used, with a rate of 124.3 in the upper 10 percent of census tracts and 54.0 in the lower 10 percent. If the tracts are divided into thirds by income and rent paid, the differences in leukemia death rates show the same trend.

An attempt was made to determine whether certain social factors might show a more critical difference than the economic indexes. It is possible from U.S. Bureau of the Census data to obtain information on the general condition of the home and the plumbing facilities and on the extent of crowding in the dwellings for each city census tract.

Table 3 shows the incidence of deaths from childhood leukemia in census tracts in which the condition of the home or the standard of plumbing was below the median as compared with the tracts above the median. The Census Bureau definition is based on the presence or absence of a private bath or running water and the general state of repair of the home. In the half of the

census tracts with homes of better condition and better plumbing, the death rate was 97.5 as compared with 54.0 in those with the poorer plumbing or more dilapidated homes. In the 10 percent of tracts with the best homes and best plumbing, the rate was 95.8, compared with 40.5 in the 10 percent of the tracts with the least adequate housing and plumbing facilities.

Table 3 also shows the leukemia death rate in relation to crowding in the home. The Census Bureau definition was used as the index of crowding. The death rate from childhood leukemia was 91.9 per 100,000 in the half of the tracts with less crowding and 63.9 in the half with more crowding. The 10 percent of tracts with the least crowding had a mortality of 122.9 as compared with only 33.8 in the 10 percent of tracts with the most crowding. Again, analysis of these data by dividing the tracts into thirds showed the same trend.

Rank order correlations were determined to attempt a statistical approach to these data. In table 4 the rank order of tracts with respect to the number of deaths is correlated with the condition of the housing and plumbing and with the degree of crowding in the dwelling unit. It will be noted that the rank order correlation is a perfect −1.0 and significant at the 0.01 level for both of these social factors.

Table 3. Leukemia death rates per 100,000 population of children through 14 years, by selected social indexes, Denver, 1941–59

Census tracts, by social division	19-year death rate [1]	
	Census tracts, by dilapidated homes with inadequate plumbing	Census tracts, by crowding
Upper half [2]	97.5	91.9
Lower half [3]	54.0	63.9
Upper 10 percent [2]	95.8	122.9
Lower 10 percent [3]	40.5	33.8

[1] Data include all 50 census tracts of Denver.
[2] Upper half or upper 10 percent denotes census tracts with smallest percentage of dilapidated homes with inadequate plumbing or the least crowding.
[3] Lower half or lower 10 percent are those with the greatest number of dilapidated homes with inadequate plumbing or the most crowding.

Table 4. Rank order of the 50 census tracts of Denver with respect to death correlations, by selected social data, average percent [1]

Number deaths	Number tracts	Dilapidated dwellings with inadequate plumbing	Crowded dwellings
0	14	37.1	8.8
1	14	21.0	5.7
2	13	20.1	5.1
3	3	15.1	3.3
4	4	11.9	2.7
5	2	3.7	1.0

[1] The rank order correlation for both social indexes is a perfect −1.0, significant at the 0.01 level.

The same pattern of rank order correlations was found for other social and economic indexes using median monthly rent, income, educational level of the father, and adequacy of the water supply for the house.

Discussion

Interpretation of the results of such a study must first take into account whether all the cases of childhood leukemia were diagnosed and reported with equal reliability for each census area. Pinkel and Nefzger (*6*) clearly pointed out that any interpretation of such data depends on the assumption that the majority of cases of childhood leukemia during this period were diagnosed and reported by death certificate. The severity and fatal nature of leukemia almost invariably results in hospitalization, and it would seem improbable that many cases of childhood leukemia would have remained undiagnosed in the State of Colorado between 1941 and 1959. The possibility exists that an occasional patient with leukemia could have died without his case being diagnosed. Although the likelihood of this is greater for rural than for urban areas, it is hard to believe that this could be true of enough cases to significantly alter the rather large urban-rural difference.

In the city of Denver during most of this period, the medical care of the majority of indigent patients was under the supervision of the University of Colorado Medical Center, and very good diagnostic facilities were available at

all the private hospitals. Therefore, it seems unlikely that many diagnoses of leukemia were missed in any of the economic groups within the city. However, it is possible that early treatment of infectious diseases may have been less adequate in the rural areas and among poorer children, thus creating a difference in the competing risks of death.

Statistical analysis of these types of data is difficult. The annual incidence of the disease is too low for adequate analysis, and yet the use of a 19-year period gives a statistical advantage. Because the deaths during the 19-year period have been compared with the average child population for a single year, the death rate has been magnified. Differences in rate of growth of rural and urban populations could also influence these results. For this reason, it was believed that the application of chi square was not appropriate. The rank order correlations were therefore carried out in an effort to evaluate these data by another statistical approach. There was a highly significant correlation between the leukemia death rate and all the social and economic factors that were studied by this method.

It is apparent from these several approaches that there is a high degree of consistency in the relationship of childhood leukemia and these socioeconomic factors regardless of how the data are analyzed. The degree of significance of the differences, however, is difficult to determine.

The childhood leukemia death rate in Denver was correlated with housing and certain social as well as economic factors in the hope that either of the first two factors might show a higher degree of sensitivity and thus suggest a more definite clue to the etiology of acute leukemia. However, it was found that a high degree of correlation existed between all the socioeconomic factors themselves. A calculation of Kendall's coefficient of concordance based on the rank order of six factors (rent, income, education of the father, plumbing facilities, crowding, and water supply) produced a W value of 0.84. This indicates a high degree of association among these factors in Denver in 1950. Thus in attempting to trace the degree of association between any of these factors and the death rate from leukemia among children 14 years old and under, it does not make a great deal of difference which of these factors were used since all should have about the same association with leukemia deaths.

Although this type of epidemiologic study utilizes rather crude data and the true significance of the differences is hard to determine, the death rate among urban children in Colorado appeared to be about 2½ times higher than in rural areas. For children living under the most favorable social conditions within the large urban area of Denver, the incidence of leukemia deaths was from two to almost four times higher than for children in low-income families living under the poorest housing conditions. It is of interest that the higher incidence of childhood leukemia deaths in the better economic areas of Denver is almost identical to that found by Pinkel and Nefzger (*6*) in their study of the Buffalo area.

These epidemiologic findings suggest the desirability of further study of a wide variety of factors that might have produced such a pattern. They include the genetic or ethnic background of the families, the possible influence of diet, and a difference in the exposure of these children to physical agents such as fuel fumes or diagnostic X-rays. In view of the increasing evidence for a virus in acute leukemia, it should be noted that the lower incidence of clinical disease in poor economic areas is similar to that for paralytic poliomyelitis in the period before the widespread use of vaccines for this disease. These findings would be expected for a disease associated with a virus that is widely distributed through the population and to which passive-active immunity may be acquired in infancy, particularly under insanitary living conditions. Although it is difficult to interpret human disease on the basis of animal studies, it is of interest that maternal antibodies have been shown to have a protective effect in chicken lymphomatosis (*13*), suggesting that the mechanism of passive-active immunity is possible in a malignant disease in the fowl.

Summary

The relationship between certain social and economic factors and the incidence of childhood leukemia in Colorado was studied for the 19-year period from 1941 through 1959. Identifying information was obtained from death

certificates of 258 children, and U.S. Bureau of the Census reports were used to obtain data on the social and economic backgrounds and population.

The rate of reported cases of childhood leukemia in the State increased from 1941 to 1959. The last 5 years (1955–59) showed a 2.7-fold increase over the first 5 years (1941–45) of this period.

The leukemia death rate appeared to be about 2½ times higher for urban children than for those living in rural Colorado. In the large urban area of Denver, the incidence of leukemia was two to almost four times higher in children living in the census tracts that were socially and economically more favored compared with children of low-income families from census tracts with the poorest housing conditions. No single social factor among those studied showed a significantly higher correlation than the others.

A consistent relationship of childhood leukemia with these social and economic factors was found by various methods of analysis. Although the true significance of these differences is difficult to determine, a number of possible etiologic factors might explain such a pattern. These include the genetic or ethnic background of the children, the influence of variations in diet and in exposure to various physical agents such as X-rays, and differences in exposure to infections including enteric viruses.

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