Childhood Cancer Mortality in U.S.A. and Japan

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Study was made of mortality rates for 5 leading childhood cancers over 2 time intervals in the U.S. and 3 in Japan. The U.S. rates changed very little over time, and, though the Japanese rates increased progressively, they still were well below those for the U.S. for each site considered. A peak in leukemia mortality appears to be emerging at 3 years of age in Japan as it did 25 years ago among U.S. white children. Kidney neoplasia (principally Wilms' tumor) appears from mortality data to be much less frequent and to have an earlier peak in Japan than in the U.S. The explanation of this difference awaits the accumulation of additional information through Japanese childhood cancer registries. Preliminary results from these registries suggest that the large differences between the U.S. and Japan in mortality from neuroblastoma may be a consequence of dissimilar diagnostic or classification practice.

The U.S. national data have revealed dynamic changes in childhood mortality rates for certain forms of cancer.¹ These variations, more apparent when the data are examined by single year of age than by the usual 5-year age groups, may provide substantial clues to the origins of the neoplasia. An example is the racial distinction in the age patterns for leukemia mortality in the United States; there is an immense peak at about 4 years of age among white children, but none among the non-white. The interpretation is that non-white children are either not exposed or not susceptible to some leukemogen which affects white children.

In addition to comparing mortality rates for groups within a country, some further understanding of a disease may be obtained by comparing the data from various countries. While such comparisons have been made for cancers during adult life, much less has been done with respect to childhood neoplasia. This deficiency is due in part to the lack of readily available data on childhood cancer mortality by single year of age and to the relatively small numbers of cases by site and age except in the most populous countries. Japan is the most populous country with published vital statistics available in a form which allows comparison with those of the U.S. This presentation concerns an examination of the data from the two countries with respect to five of the most common forms of neoplasia in childhood.

Received for publication, October 5, 1966.

METHODS

The U.S. data were derived from punch cards provided by the National Vital Statistics Division, USPHS, pertaining to all death certificates of children who died of cancer in the 48 states or the District of Columbia, 1950–1959, before 15 years of age. Annual mortality rates per 100,000 were computed from population estimates obtained according to the methods described in a previous report.² The Japanese data came from annual reports of Vital Statistics, 1950–1963, published by the Ministry of Health and Welfare. Cancer deaths are shown in these volumes by single year of age through the first 5 years of life, and by 5-year age groups thereafter. Annual mortality rates were calculated through the use of population estimates for each age studied as given in the same volumes. The forms of childhood cancer studied, with the International List Numbers given in parenthesis, were leukemia (204), cancer of the brain and nervous system (193), lymphoma (200–203), cancer of the kidney (180) and cancer of bone (196).

RESULTS

Fig. 1 depicts the site-specific cancer mortality rates for two time intervals in the U.S. and for three in Japan. There was little difference over time in the U.S., whereas in Japan there was generally a progressive and substantial increase in rates.

Leukemia. In 1950–1954 the leukemia mortality rates in Japan were lower than those in the U.S. throughout childhood. Since that time, the Japanese rates have increased rapidly, and the most recent data (1960–1963) indicate a peak at three years of age, still much less pronounced than the U.S. peak at four years of age. Beyond five years of age the Japanese rates now equal those in the U.S.

The emergence of a peak is of great interest because it may signify that the Japanese experience is duplicating that of U.S. white children, whose peak in leukemia mortality first emerged in about 1940.³ The rise in rates for all ages may result from underdiagnosis in years past or from the increasing use of antibiotics to control infections which might otherwise claim the lives of children prior to the development or recognition of leukemia.

Lymphoma. The U.S. lymphoma mortality experience, unlike that for leukemia, shows no peak during childhood. In Japan the lymphoma rates in the first three years of life were slightly higher than they were later in childhood and adolescence. After five years of age the lymphoma mortality rates increased over time. The only hint of a recent increase among U.S. children occurred at 10–14 years of age. The Japanese mortality pattern suggests that there may be some difficulty in distinguishing lymphoma from other diseases of early childhood, whereas recognition of the disease is increasing later in life for the reasons above-mentioned under the section on leukemia.

Fig. 1. Mortality rates by age for 5 childhood cancers in the United States (whites; 1950-1959) and Japan (1950-1963).

Kidney. Renal neoplasia in children consists almost entirely of Wilms' tumor (nephroblastoma). The U.S. experience revealed a very great peak at about four years of age. The Japanese rates, though they have been climbing rapidly since 1950, are still far below those of the U.S., and the most recent data show the peak to be surprisingly early: at one year of age. It is noteworthy that the Japanese rates after five years of age are about the same as those in the U.S. and have changed little in the last 14 years. Again the pattern suggests that

there was perhaps difficulty in the past in separating Wilms' tumor from other serious diseases of early childhood. The constancy of the rates after five years of age and their similarity to those in the U.S. suggests that there has been little difficulty in recognizing the neoplasm later in childhood.

Brain and nervous system. Childhood cancer of the brain and nervous system is a very mixed category. Early in life it consists largely of neuroblastomas with some ependymomas, whereas in midchildhood it is composed principally of gliomas and medulloblastomas. The patterns of mortality in the U.S. are much different from those in Japan. Although the Japanese rates have more than tripled since 1950-1954, the U.S. rates are still five to ten times greater. The difference may in part be due to less easily available neurosurgery in Japan as compared with the U.S. This would not, however, explain the dissimilarity in rates early in childhood when neuroblastoma, a relatively easily diagnosed neoplasm, is most prevalent. Perhaps in Japan most neuroblastomas are classified by location, such as the abdomen, whereas in the United States the vast majority are classified by cell type (neural tissue).

Bone cancer. The two countries have about the same bone cancer mortality rates early in life, followed by a progressive rise through adolescence, more pronounced in the U.S., despite increasing rates over time in Japan. Bone cancer is usually quite obvious in children so improvement in diagnosis or increased use of antibiotics to control concomitant infection seem unlikely explanations in this instance. While the similar rise in Japanese rates for each of the cancers considered above suggest that one explanation applies to all, the possibility cannot be excluded that the progressive increase in stature of Japanese children in recent years has influenced bone cancer mortality. A correlation between stature and bone cancer mortality is indicated by the 100-fold greater relative risk among giant breeds of dogs as compared with small breeds,⁴ and by the increase in rates among U.S. children as stature increases, the effect being greater and continuing longer among males than females.⁵

DISCUSSION

Neoplasia at each site considered here was reported as a cause of death more often in the U.S. than in Japan, but one must ask if there is a real difference in disease occurrence, or are the discrepancies observed due to dissimilar diagnostic practice. This question might be resolved through study of information from childhood tumor registries, which concern cancer morbidity—not mortality. Such registries have recently been established in Hiroshima City and in the Tokyo Metropolitan Area. Registry information will not suffer the variation in diagnostic practice that occurs when nationwide data are used. Early results from the registries suggest that there may be substantially less Wilms' tumor in

Japan than in the U.S., but, as Takatsu to be published has pointed out, because registry cases are ascertained through pediatricians, there may be underrepresentation of Wilms' tumor, which in Japan is commonly the responsibility of urologists.

Registry data thus far suggest that the relative frequency of neuroblastoma is substantially greater than that indicated by national mortality data. Also, hepatoblastoma appears from registry data to be much more common among Japanese children than mortality statistics indicate. Childhood hepatoblastoma may, in fact, occur more often in Japan than in Western countries, an observation which would be of etiologic importance.

For a given cancer, there was little difference in the U.S. mortality rates from 1950-1954 as compared with those for 1955-1959. In contrast, corresponding Japanese rates climbed progressively from 1950 through 1963 not only for children, but also for adults (data not shown). This rapid change over time must be taken into account when Japanese rates are used in international comparisons.

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