Geographic Aspects of Malignant Lymphoma and Multiple Myeloma

Select Comparisons Involving Japan, England and the United States

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IN RECENT YEARS, geographic variations in the prevalence of the various types of malignant lymphoma have engendered considerable interest. Much of the stimulus for this interest came from the description of a distinctive lymphoma in African children [1] and the suggestion that an arthropod vector and/or host-related immunologic deficit might be related to the selective geographic distribution of this tumor. Since Burkitt's original description, there have been scattered reports from other parts of the world of tumors that mimic the Burkitt lymphoma, but the high prevalence of this peculiar tumor in a small geographic region remains impressive.

Insofar as is known, there is no lymphoma peculiar to Japan; however, a comparison of several large independent studies from multiple Japanese and American institutions suggests differences in the relative frequencies of the various lymphomas. There has been a tendency to ascribe these apparent discrepancies to differences between Japanese and American pathologists with respect to the histologic interpretation and classification of lymphomas. The present study attempts to apply Western diagnostic criteria, as defined by Rappaport,[2] to a large series of Japanese cases in an attempt to define putative differences in the relative frequency of reticulum cell sarcoma, Hodgkin's disease and lymphosarcoma in the United States, Great Britain and Japan. Although not universally accepted as a form of lymphoma, comparable data for multiple myeloma are included because of the apparent close immunologic relationship between this entity and lymphosarcoma.

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Materials and Methods

The morphologic review of the material reported herein is described elsewhere.[3] In summary, 682 cases from the 1945–1965 period with a diagnosis of lymphoma or related conditions, established at the Atomic Bomb Casualty Commission (ABCC) in Hiroshima and Nagasaki, were reviewed. Only cases with adequate available morphologic material (biopsy or necropsy) felt to represent definite or probable lymphoma were included herein. Histologic examination was performed independently by at least two pathologists and cases were classified as reticulum cell sarcoma, Hodgkin's disease and lymphosarcoma according to the diagnostic criteria outlined by Rappaport.[2] All other types of lymphoma were classified as "other"; included in this heterogeneous group were several transitional cases (mixed lymphoma of Rappaport), a number of cases of undifferentiated lymphoma, and one example of malignant histiocytic medullary reticulosis of Robb-Smith.[4] Follicular lymphoma was classified according to Rappaport.[5] Diagnoses of multiple myeloma were based on standard diagnostic criteria and included an evaluation of immunoglobulin production and roentgenographic appearance of the skeleton and bone marrow morphology. One case each of extraosseous plasmacytoma (biopsy), osseous plasmacytoma (biopsy) and so-called "plasma cell leukemia" was included with the multiple myeloma group. All pathologic material was considered independently; therefore an individual with lymphoma as demonstrated by both biopsy and necropsy material was retained in both series; however, a person with two or more temporally independent biopsies was counted as only one case.

The prevalence of malignant lymphoma may be increased in closely exposed survivors of the atomic bomb explosions.[3,6] Because of possible radiation-related discrepancies in this group of individuals, persons exposed at less than 1600 m from the hypocenter of the explosion were not included in the present study. Thus, the maximum estimated dose (T65D estimates)[7] absorbed by an individual included herein is 15 rad.

The population under evaluation at ABCC has been described elsewhere.[8] Of particular interest with respect to the present report is the existence at ABCC of a surgical pathology program that draws a large volume of material from physicians in the environs of Hiroshima and Nagasaki. Thus, approximately 65% of the surgical specimens reviewed at ABCC are obtained from persons located in neither city at the time of the bombs and only 15% of the specimens are obtained from individuals in the matched mortality sample, which forms the basis of the majority of the studies at this institution. The remaining 85% of cases will henceforth be referred to as nonstudy material. On the other hand, the majority of the necropsies involve members of the mortality sample in which various categories of exposed persons are matched by age, sex, etc with individuals who were in neither city at the time of the bombs. It is also important to note that the mortality sample is markedly skewed by the fact that the majority of healthy young men were in the military in 1945 and therefore away from Hiroshima and Nagasaki at the time of the bombs.

Representative studies from Japan,[9–14] the United States [15–18] and Great Britain [19–22] were selected to establish a balance between necropsy and biopsy material that would approach the experience at ABCC and to prevent reduplication of case material. Despite the latter precaution, there may be a small amount of overlap in the combined Japanese experience. Other unrecognized sources of bias are probably also present. For this reason, statistical analysis was very limited and major emphasis was attached only to striking dissimilarities between the involved countries.

Results

Included in the ABCC component of the study as definite or probable lymphoma were 246 biopsies and 121 necropsies from a total of 317 individuals. Table 1 summarizes the distribution of this case material by city and by diagnostic category. It is evident that in this sample, reticulum cell sarcoma is the most prevalent form of lymphoma in Japan, followed by lymphosarcoma, Hodgkin's disease and multiple myeloma in that order. Intercity differences of varying magnitude are apparent in all diagnostic categories: reticulum cell sarcoma is relatively more prevalent in Hiroshima than Nagasaki (43.5 versus 36.7%) as is Hodgkin's disease (23.2 versus 15.3%) and multiple myeloma (8.7 versus 7.5%) while the reverse is true with respect to lymphosarcoma (21.0 versus 34.9%). These differences are not statistically signifi-

Table 1. Composition of ABCC Data by City, Diagnosis and Type of Morphologic Material Accepted as Lymphoma

Diagnosis	Biopsy	Necropsy	Total No.	Total (%)
HIROSHIMA				
Reticulum cell sarcoma	45	15	60	(43.5)
Hodgkin's disease	24	8	32	(23.2)
Lymphosarcoma	20	9	29	(21.0)
Multiple myeloma	6	6	12	(8.7)
Other	5	0	5	(3.6)
Total			138	100.0
NAGASAKI				
Reticulum cell sarcoma	51	33	84	(36.7)
Hodgkin's disease	19	16	35	(15.3)
Lymphosarcoma	57	23	80	(34.9)
Multiple myeloma	9	8	17	(7.5)
Other	10	3	13	(5.6)
Total			229	100.0
TOTAL				
Reticulum cell sarcoma	96	48	144	(39.2)
Hodgkin's disease	43	24	67	(18.3)
Lymphosarcoma	77	32	109	(29.7)
Multiple myeloma	15	14	29	(7.9)
Other	15	3	18	(4.9)
Total	246	121	367	100.0

Table 2. Representative Expèrience with Malignant Lymphoma in Japan, United States and Great Britain

Source	Total No. of cases	Composition of case material	No. of Cases*			
			Reticulum cell sarcoma	Lymphosarcoma	Hodgkin's disease	Other
JAPAN						
Wakisaka[8]	112	Biopsy	36	26	50	—
Ota[9]	237	Biopsy	204	19	7	7
Otsuka[10]	186	Biopsy	157	2	11	16
Nishio[11]	1154	Biopsy (763), necropsy (391)	661	189	174	130
Yoshida[12]	1232	Biopsy (890), necropsy (342)	886	154	192	—
Necropsy statistics[13]	1911	Necropsy	1167	299	348	97
Total	4832		3111	689	782	250
			(64.4%)	(14.3%)	(16.2%)	(5.2%)
JAPAN—ABCC						
ABCC—Hiroshima[3]	126	Biospy (94), necropsy (32)	60	29	32	5
ABCC—Nagasaki[3]	212	Biopsy (137), necropsy (75)	84	80	35	13
Total	338		144	109	67	18
			(42.6%)	(32.2%)	(19.8%)	(5.4%)
UNITED STATES						
Gall and Mallory[14]	618	Biopsy (580), necropsy (135)	127	220	229	42
Hellwig[15]	196	? All necropsy	33	106	48	9
Jackson and Parker[16]	717	Biopsy and necropsy	116	233	329	39
Williams et al[17]	3725	Biopsy and necropsy	—1733—		1992	—
Total	5256		854	1712	2598	90
			(16.2%)	(32.6%)	(49.7%)	(1.7%)
GREAT BRITAIN						
Lumb[18]	347	Biopsy and necropsy	29	63	194	61
Hilton and Sutton[19]	363	Biopsy—some with follow-up necropsy	85	87	152	39
Hancock[20]	515		102	207	206	—
Symmers[21]	977		269	222	486	—
Total	2202		485	579	1038	100
			(22.0%)	(26.3%)	(47.2%)	(4.5%)

* Figures in parenthesis indicate percentages by country for individual types of lymphoma.

cant although the values with respect to lymphosarcoma are somewhat equivocal ($0.2 > P > 0.1$).

Table 2 compares the relative frequencies of the various lymphomas in the ABCC series of cases, the remainder of Japan, the United States and Great Britain. As might be expected, the differences between the latter two countries are minimal and subsequently, data from these countries will be grouped and referred to as *Western*. Intracountry discrepancies of varying magnitude are apparent; this is not unexpected in a study of this type and probably reflects personal bias of individual observers. However, inclusion of a sufficient number of observers should dilute such bias to a nonpivotal level.

Similar comparisons between Western countries and Japan, excluding ABCC, involving the relative distribution of lymphoma cases reveal marked differences, as summarized in Table 3. Reticulum cell sarcoma comprises the majority of Japanese lymphoma experience with most of the remainder of the cases approximately equally divided between lymphosarcoma and Hodgkin's disease. The latter is the most frequent lymphoma in the United States and Great Britain and is almost three times as prevalent as reticulum cell sarcoma; in these latter countries, lymphosarcoma prevalence occupies an intermediate position between the other two forms of lymphoma.

The ABCC data, if it is representative of Japan, suggest that a portion of the above described differences may be due to discrepancies between Eastern and Western pathologists with respect to diagnostic criteria and/or classification; however, it is equally apparent that such differences are not entirely artifactual and that the relative frequencies of reticulum cell sarcoma, lymphosarcoma and Hodgkin's disease are apparently not the same in Japan as in the United States and Great Britain; this is also shown in Table 3, wherein the relative frequency of reticulum cell sarcoma is somewhat less at ABCC than the remainder of Japan but still impressively larger than the comparable figure for the United

Table 3. Distribution of Lymphoma by Cell Type

	% of cases in group		
	Japan		
	ABCC	Other series	England and United States
Reticulum cell sarcoma	42.6	64.6	17.9
Hodgkin's disease	19.8	16.2	48.7
Lymphosarcoma	32.2	14.3	30.8
Other	5.4	5.2	2.6

States and Great Britain. There is an attendant increase in the relative frequency of lymphosarcoma in the ABCC data, in comparison with the remainder of Japan, which approximates the corresponding Western data. Thus, it would appear that the major discrepancy between Western and Japanese pathologists with respect to the histologic diagnosis of malignant lymphoma involves the reticulum cell sarcoma-lymphosarcoma group of cases and that some cases that were interpreted as lymphosarcoma in the present study would have been diagnosed as reticulum cell sarcoma at other Japanese institutions. This may be due to the emphasis in Japan on the reticulum cell as the focal point in malignant disease of the reticuloendothelial system.

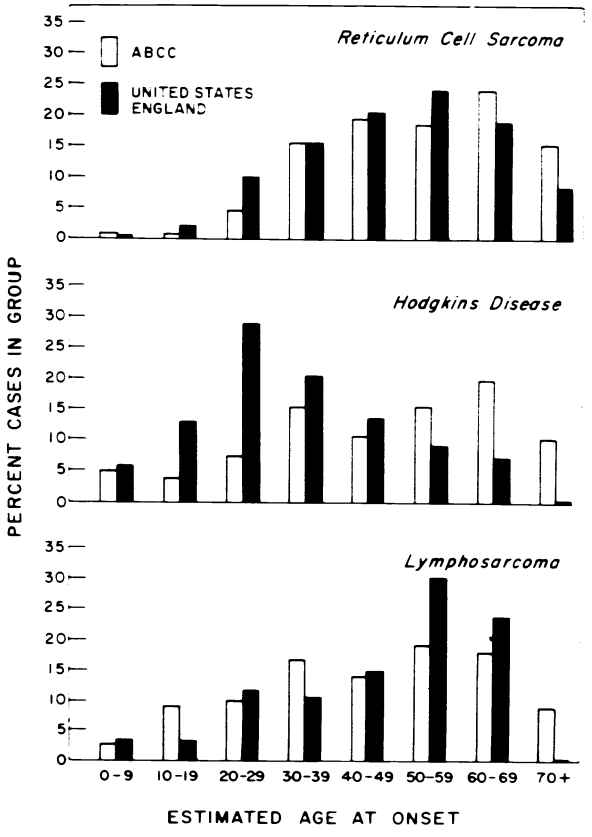
Most reports relevant to lymphoma do not include data pertaining to multiple myeloma; immunologic similarities between multiple myeloma and lymphosarcoma and apparent transitional disease (*ie*, Waldenstrom's macroglobulinemia) have only recently been appreciated. Therefore, it is difficult to make meaningful geographic comparisons with this form of lymphoma, and multiple myeloma has not been uniformly included in the results of Table 2 and 3. However, reference is made to sporadic reports that include this disease. On the basis of this data, it would appear that there is an increased prevalence of this form of lymphoma in Japan, although the magnitude of this difference is difficult to determine.

Text-figure 1 shows the distribution of the ABCC and Western material by estimated age at onset of symptomatology suggestive of lymphoma, the symptoms generally being painless asymmetrical lymphadenopathy. The age distribution of the two series is remarkably similar with respect to reticulum cell sarcoma and lymphosarcoma; however, the Japanese case material fails to mirror the peak prevalence of Hodgkin's disease in early adulthood (*circa* 20–30 years), which conspicuously characterizes Western series.

Some of the above discrepancies are also apparent in Table 4 which compares the case material of ABCC and that of Gall and Mallory [15] with respect to age at onset and death; estimated total duration of symptomatic disease; and male to female ratio. Several differences between these two series of cases are readily apparent. A male preponderance is evident with respect to reticulum cell sarcoma, Hodgkin's disease and lymphosarcoma in the ABCC case material but is considerably less pronounced than that noted by Gall and Mallory. Although there is a relative paucity of middle-aged males in the mortality sample followed at ABCC—such men were in the Armed Forces at the time of the bombs—evaluation of the nonstudy cases shows essentially

the same ratios noted in Table 4. For the three major forms of lymphoma, the average age at onset and death is older among the Japanese than the Americans: this difference is especially pronounced with respect to Hodgkin's disease where it approximates 10 years. Average estimated survival (estimated onset until time of death) is also uniformly shorter among the Japanese with lymphoma: again this difference is most pronounced with respect to Hodgkin's disease. The paucity of young exposed males may be a factor here too, especially with respect to Hodgkin's disease where disease that develops in younger persons is known to be associated with a more favorable prognosis than Hodgkin's disease with an onset later in life.

Comparisons involving survival data are complicated by discrepancies in therapy. This is undoubtedly a factor in the data presented in Table 4. However, the study of Gall and Mallory was selected for com-



TEXT-FIG 1. Distribution of ABCC and Western case material by estimated age at onset.

Table 4. Average Estimated Age at Onset, Duration of Disease, Age at Death and Sex Ratio in Japan versus the United States

		Japan (ABCC)				United States (Gall and Mallory)			
Diagnosis	ABCC subsample	Age at onset (yr)	Estimated duration (mo)	Age at death (yr)	Male:female ratio	Age at onset (yr)	Estimated duration (mo)	Age at death (yr)	Male:female ratio
Hodgkin's disease	Study cases	48.0	15.0	49.3	1.9:1	37.9	45.6	41.7	2.6:1
	Nonstudy cases	47.6	13.3	48.5					
Reticulum cell sarcoma	Study cases	53.6	12.3	54.6	1.4:1	47.7	22.8	49.6	2.0:1
	Nonstudy cases	53.8	12.5	54.8					
Lymphosarcoma	Study cases	45.8	10.0	47.6	1.4:1	42.9	31.2	45.5	2.7:1
	Nonstudy cases	46.2	8.6	47.5					

parison because the therapy employed during the period of that study approximated the average Japanese physician's approach to lymphoma during the 1946–1966 period represented by the ABCC series. Therapy in the latter series of cases is discussed in more detail elsewhere.[3] An additional form of bias exists in the ABCC material. As noted previously, much of the latter, and virtually all of the necropsies, are drawn from the mortality sample, a defined population of exposed persons matched with individuals who were in neither city at the time of the bombs. This population is fixed and therefore progressively ages; thus, at the present time, there are no persons in this sample less than 24 years of age. However, with respect to lymphoma, a comparison of study and nonstudy case material, as summarized in Table 4, fails to confirm the suspicion that the progressive aging of the ABCC study sample is responsible for the temporal differences, as described above, between the ABCC and American series.

Putative histologic differences between individual cases or groups of cases that apparently represent a single disease entity are often subtle and difficult to quantitate. Conclusions based on such comparisons often are rightly viewed with suspicion. These comments are especially valid with respect to malignant lymphoma, a spectrum of diseases with a potpourri of morphologic expressions. However, based on the review of the cases reported herein and experience with similar material from US institutions, a few conclusions appear warranted. Eosinophilia is vanishingly rare in lymphosarcoma and reticulum cell sarcoma in the United States and generally alerts the observer suspicious of lymphoma to the possibility of Hodgkin's disease. Eosinophilia in association with lymphomas other than Hodgkin's disease, especially reticulum cell sarcoma, is considerably more common in Japan. This association might raise the possibility that some cases of Hodgkin's disease have been misdiagnosed as reticulum cell sarcoma; however, extensive examinations of such cases, with up to 20 sections of an involved lymph node, failed to reveal a Reed-Sternberg cell.

In contrast with the above, eosinophilia in Hodgkin's disease, although generally present, is considerably less florid in the average Japanese case than in comparable material in the United States. Fibrosis, spontaneous necrosis and neutrophilic and plasma cell infiltration, although generally present, are often not prominent among the Japanese cases reviewed at ABCC. As a result of the above, the histology of the average case of Hodgkin's disease in Japan merges with that of reticulum cell sarcoma, the primary difference being the presence of Reed-Sternberg cells in the former and the absence of these characteristic cells in

reticulum cell sarcoma. Finally, lymphosarcoma in Japan is almost exclusively of the lymphoblastic type in contradistinction to the United States where the lymphocytic form predominates.

Discussion

The present report presents evidence to suggest that there are rather impressive differences between Japan on the one hand and the United States and Great Britain on the other with respect to the relative frequencies of the various malignant lymphomas. Experimentation in this regard is not possible and indeed it is difficult to design experiments that would define the genesis of the described differences. Therefore, at least at the present time, interpretation must be largely speculative and the following should be viewed in this context.

Assuming that the ABCC data is representative of the entire country, the relative frequency of lymphosarcoma is approximately the same in Japan as in Western countries but in common with all forms of lymphoma is associated with a much shorter estimated clinical course in the former country. There are recognized morphologic similarities between lymphosarcoma and lymphocytic leukemia and often the former appears to terminate as an expression of the latter (leukolymphosarcoma). Chronic lymphocytic leukemia is rare in Japan and constitutes at most 2–3% of all leukemia (versus 20–30% in the United States). Lymphocytic lymphosarcoma is also rare in Japan, where the vast majority of cases of this form of lymphoma are of the lymphoblastic type; this is reflected in the short average survival times of the Japanese with this form of lymphoma. As far as Japan is concerned, there appears to be an increased prevalence of chronic lymphocytic leukemia in Nagasaki [23] and nearby Kumamoto prefecture [24] which has been attributed, at least by some observers,[23] to a possible Western influence since Nagasaki was the only Japanese port continuously open to Western shipping between 1637 and 1859. In this connection, it is of interest that the relative frequency of lymphosarcoma is also greater in Nagasaki than in Hiroshima although this difference is of equivocal statistical significance.

Hodgkin's disease is the most prevalent form of lymphoma in the United States and Great Britain and the least prevalent of the major forms of lymphoma in Japan. Furthermore, the characteristic peak in prevalence of this form of lymphoma in early adulthood, especially in the third decade, noted in virtually all Western series of cases, is not apparent in Japan and the male preponderance, although present, is not as marked as in the United States and Great Britain. Finally, Hodgkin's disease in Japan is not associated with an enhanced progno-

sis, in comparison with lymphosarcoma and reticulum cell sarcoma, as it is in Western countries. Of interest in this connection is the minimal evidence of spontaneous necrosis, fibrosis and inflammatory infiltration in the majority of the Japanese case material. If, as is commonly stated, these tissue reactions are manifestations of the host response, the Japanese in general would appear to be less able to mobilize an effective tissue response than Westerners to the agent(s) responsible for this type of lymphoma. This is also reflected in the survival data; Hodgkin's disease in Japan is associated with an estimated clinical course of approximately 1 year compared with almost 4 years in comparable Western series. Indeed, the attenuated survival of persons with Hodgkin's disease in Japan approaches that reported for Hodgkin's sarcoma in the United States. In addition, similarities between Hodgkin's disease and reticulum cell sarcoma in histopathology, distribution of cases by age at death and survival data among the Japanese suggest a close relationship between these forms of lymphoma.

Reticulum cell sarcoma is the most prevalent form of lymphoma in Japan. The relative incidence is somewhat less when Western diagnostic criteria are applied to Japanese case material, presumably because of discrepancies in morphologic interpretation involving the lymphoblastic lymphosarcoma-reticulum cell sarcoma cases. The average estimated duration of survival among the Japanese approaches that reported by Gall and Mallory but is still approximately 10 months less. Of interest, and contrary to Western experience, reticulum cell sarcoma in Japan is not associated with the shortest clinical survival among Japanese with lymphoma; the latter distinction belongs to lymphosarcoma.

The genesis of these apparent discrepancies in the relative frequencies of the malignant lymphomas is difficult to define. Similar geographic differences with respect to chronic lymphocytic leukemia suggest the possibility that discrepancies in host reactivity, presumably genetically governed, may be partially or totally responsible for the described differences. Predisposing or synergistic disease(s) might be indigenous to Japan but thus far none has been described. The agent or agents responsible for lymphoma might be susceptible to geographic influences but this appears a less attractive hypothesis in terms of modern communication and the accelerated contact between populations unless there is a long latent period between contact (? infection) and the clinical expression of disease.

Summary

The present study concerns the relative frequency of reticulum cell

sarcoma, lymphosarcoma and Hodgkin's disease in Japan, the United States and Great Britain. Application of Western diagnostic technics to Japanese case material suggests that a portion of the apparent differences between East and West in this respect may be due to discrepancies in classification and/or histologic interpretation but that not all such differences can be explained on this basis. Reticulum cell sarcoma is the most prevalent form of malignant lymphoma in Japan with a relative frequency (42%) that approaches Hodgkin's disease in Western series (49%). Conversely, Hodgkin's disease is the least frequently encountered form of lymphoma in Japan with a relative frequency (20%) not far removed from reticulum cell sarcoma (18%) in the West. There is little difference in relative prevalence of lymphosarcoma in Japanese and Western experience. Finally, each type of lymphoma in Japan appears to be associated with a shorter estimated clinical course than the comparable disease in the United States. It is suggested that these geographic differences may be related to the close interrelationships of the lymphomas and genetically governed variations in host reactivity.

References

1. Burkitt D, O'Conor GT: Malignant lymphoma in African children. I. A clinical syndrome. Cancer 14:258–269, 1961
2. Rappaport H: Tumors of the Hematopoietic System. Washington, DC, Armed Forces Institute of Pathology, 1966
3. Nishiyama H, Anderson RE, Ishimaru T, Ishida K, Ii Y, Okabe N: Malignant lymphoma and multiple myeloma in atomic bomb survivors in Hiroshima and Nagasaki. Atomic Bomb Casualty Commission Technical Report (in press)
4. Scott, RB, Robb-Smith AHT: Histiocytic medullary reticulosis. Lancet 2: 194–198, 1939
5. Rappaport H, Winter WJ, Hicks EB: Follicular lymphoma. A re-evaluation of its position in the scheme of malignant lymphoma, based on a survey of 253 cases. Cancer 9:792–821, 1956
6. Anderson RE, Ishida K: Malignant lymphoma in survivors of the atomic bomb in Hiroshima. Ann Intern Med 61:853–862, 1964
7. Milton RC, Shohoji T: Tentative 1965 Radiation Dose (T65D) Estimation for A-Bomb Survivors, Hiroshima and Nagaski. Atomic Bomb Casualty Commission Technical Report 1–68
8. Zeldis LJ, Matsumoto VS: NIH-ABCC Pathology Studies in Hiroshima and Nagaski: Provisional Research Plan. Atomic Bomb Casualty Commission Technical Report 04–61
9. Wakisaka G: Statistics of malignant lymphoma in Japan. Saishin Igaku 19: 1799–1813, 1964
10. Ota K: Pathology of reticulum cell sarcoma. Saishin Igaku 19:1686–1692, 1964
11. Otsuka H: Malignant lymphoma: Statistical and histologic observation of

reticulum cell sarcoma and Hodgkin's disease. Nichibyo-Kaishi 47:256–272, 1958

12. Nishio S: Statistical and histologic study of malignant lymphoma in Japan based on autopsy and biopsy cases. Handai Ishi 11:5273–5283, 1959
13. Yoshida T: Study of malignant lymphoma. General Research Report of the Ministry of Education, No 259, 1956, 301, 1957. Atomic Bomb Casualty Commission Technical Report (in press)
14. Ii Y: Unpublished observations obtained from Annual Summary of Autopsy Cases in Japan (1958–65). Japanese National Institute of Health of the Ministry of Health and Welfare.
15. Gall EA, Mallory TB: Malignant lymphoma. A Clinico-Pathologic Survey of 618 Cases. Amer J Path 18:381–429, 1942
16. Hellwig CA: Malignant lymphoma. Analysis of 202 cases. Amer J Clin Path 16:564–573, 1946
17. Jackson H Jr, Parker F Jr: Hodgkin's Disease and Allied Disorders. London, Oxford University Press, 1947, pp 17–34
18. Williams HM, Diamond HD, Craver LF, Parsons H: Neurological Complications of Lymphomas and Leukemias. Springfield, Illinois, Charles C. Thomas, 1959
19. Lumb G, Newton KA: Prognosis in tumors of lymphoid tissue. An analysis of 602 cases. Cancer 10:976–993, 1957
20. Hilton G, Sutton PM: Malignant lymphomas: Classification, prognosis and treatment. Lancet 1:283–287, 1962
21. Hancock PET: Malignant lymphoma:clinico-pathologic correlation, Cancer. Edited by RW Raven. Vol 4. London, Butterworth and Co, Ltd, 1958, pp 412–428
22. Symmers WSTC: Primary malignant diseases of the lymphoreticular system, Cancer. Edited by RW Raven. Vol 2. London, Butterworth and Co, Ltd, 1958, pp 448–483
23. Finch SC, Hoshino T, Itoga T, Ishimaru M, Ingram R: Chronic Lymphocytic Leukemia in Hiroshima and Nagasaki. Atomic Bomb Casualty Commission Technical Report (in press)
24. Kawakita Y: Clinical and statistical research of leukemia in Kyushu, especially in the Kumamoto District. Acta Haemat Jap 21:295–300, 1958

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