Clinical and Statistical Studies of Tumors of Reticuloendothelial System in Japan*

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Statistical and clinical studies were carried out in 1443 patients with tumors of reticuloendothelial system (RES) and 2188 patients with tumors of lymphoid tissue treated between 1953 and 1962 at universities and other hospitals in Japan. It is noteworthy that the incidence of lymphoid reticulum cell sarcoma is high in Japan. However, the incidence of tumors of RES and lymphoid tissue is still lower than that in most of other countries. As to the age distribution there was a significant difference between Japan and other countries, and it has been suggested that the incidence of lymphoid reticulum cell sarcoma in over 55 years of age was actually increasing. There were some differences in frequency of initial symptom, presenting symptoms and signs between tumors of RES except lymphoid reticulum cell sarcoma and lymphoid tissue. The characteristic hematologic findings have not been observed at the initial phase of tumors of RES and lymphoid tissue. Also in this paper pathophysiology, effects of therapies and survival time of patients with tumors of RES and lymphoid tissue have been reported.

Statistical and clinical studies were carried out in 1443 patients with tumors of reticuloendothelial system (RES) and 2188 patients with tumors of lymphoid tissue treated between 1953 and 1962 at universities and other hospitals in Japan. Each case was histologically verified. The patterns of tumors of RES according to the histological classification of Prof. Akazaki¹⁻⁴) were as follows: 1169 cases of reticulum cell sarcoma of lymphoid tissue (18.0%), 130 cases of reticulum cell sarcoma of various organs (9.0%), 58 cases of Ewing's sarcoma (4.0%), 54 cases of reticuloendothelioma (3.7%) and 32 cases of reticulum cell sarcoma of bone (2.2%) as shown in Table I.

Also distributions of tumors of lymphoid tissue were as follows: 1169 cases of reticulum cell sarcoma of lymphoid tissue (53.4%), 459 cases of Hodgkin's disease (21.0%), 313 cases of lymphosarcoma (14.3%), 156 cases of lymphatic

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TABLE I. Varieties of Tumors of RES

	Total		Male		Female	
	No. of cases	%	No. of cases	%	No. of cases	%
Total cases	1443	100.0	948	100.0	495	100.0
Ewing's sarcoma	58	4.0	36	3.7	22	4.4
Reticulum cell sarcoma of bone	32	2.2	21	2.2	11	2.2
Reticulum cell sarcoma of lymphoid tissue	1169	81.0	775	81.8	394	79.5
Reticulum cell sarcoma of various organs	130	9.0	84	8.9	46	9.3
Reticuloendothelioma	54	3.7	32	3.3	22	4.4

leukemia (7.1%), 38 cases of follicular lymphoblastoma (1.7%) and 53 cases of unclassified malignant lymphoma as shown in Table II. It is noteworthy that the incidence of reticulum cell sarcoma of lymphoid tissue in Japan is higher than that in most of other countries⁵⁻⁸).

Death rate:

According to the report of Prof. Hibino⁹) the death rate from tumors of lymphoid tissue per 1,000,000 population in Tokai district, Japan was 3.37 in 1950 and 8.06 in 1955. But the annual death rate from tumors of lymphoid tissue per 1,000,000 population for all Japan was 9.36 in 1946 and 14.6 in 1959 as shown in Fig. 1. And since 1952 it showed remarkable increase. However, the incidence of tumors of lymphoid tissue in Japan is still lower than that in most of other countries¹⁰).

Sex incidence:

Sex incidence was given in Table III. Males were more frequently affected

TABLE II. Varieties of Tumors of Lymphoid Tissue

	Total		Male		Female	
	No. of cases	%	No. of cases	%	No. of cases	%
Total cases	2188	100.0	1472	100.0	716	100.0
Reticulum cell sarcoma of lymphoid tissue	1169	53.4	775	52.6	394	55.0
Hodgkin's disease	459	21.0	333	22.6	126	17.6
Lymphosarcoma	313	14.3	200	13.6	113	15.8
Follicular lymphoblastoma	38	1.7	25	1.7	13	1.8
Lymphocytic leukemia	156	7.1	114	7.7	42	5.9
Malignant Lymphoma*	53	2.4	25	1.7	28	3.9

* Not classified

than females in both tumors of RES and lymphoid tissue^{11,12).}

Age incidence:

Age distribution was shown in Fig. 2. Reticulum cell sarcoma was most frequently observed in the age group of 55-65, and reticulum cell sarcoma of bone seen in the age groups of 20-30 and 55-60. Ewing's sarcoma occurred frequently in the age group under 25. As to the age distribution there was a significant difference between Japan and other countries.

A comparison of the age incidence of reticulum cell sarcoma of lymphoid tissue during the periods of 1950-1953, 1954-1958 and 1959-1963 was given in Fig. 3.

It has been suggested that the incidence of reticulum cell sarcoma in over 55 years of age was actually increasing. This result was almost similar to that of leukemia in Japan^{13,14).}

Fig. 1. Death rate from tumors of lymphoid tissue in Japan, 1949~1959.

TABLE III. Sex Incidence of Tumors of RES and Lymphoid Tissue

	Male	Female	Male : Female
Reticulum cell sarcoma of lymphoid tissue	775	394	1.9 : 1
Hodgkin's disease	333	126	2.6 : 1
Lymphosarcoma	200	113	1.8 : 1
Reticulum cell sarcoma of bone	25	13	1.9 : 1
Follicular lymphoblastoma	21	11	1.9 : 1
Ewing's sarcoma	36	22	1.6 : 1

Fig. 2. Age distribution of tumors of RES and lymphoid tissue

Period \ Age	Age																Unknown	No. of cases
	~5	5~9	10~14	15~19	20~24	25~29	30~34	35~39	40~44	45~49	50~54	55~59	60~64	65~69	70~74	75~		
1959~1963	13	14	16	27	23	30	33	40	36	70	65	88	62	57	31	18	7	630
1954~1958	4	10	10	17	16	20	28	28	41	58	65	48	49	28	15	12	5	454
1950~1953	—	1	2	5	5	1	6	4	11	13	4	11	2	3	1	—	1	70

Fig. 3. Age incidence of reticulum cell sarcoma of lymphoid tissue during periods of 1950~1953, 1954~1958 and 1959~1963.

TABLE IV. Analysis of Past Illness and Familial Influences

	Hereditary influences							Familial influences				
	Total cases	Tuberculosis	Syphilis	Anemia	Radiation injury	Atomic bomb survivors	Trauma	Cancer	Sarcoma	Leukemia	Banti's syndrome	Hemorrhagic diathesis
Reticulum cell sarcoma of lymphoid tissue	1169	71	19	1	1	4	15	92	2	1	1	1
Hodgkin's disease	459	31	7	1	1	3	5	47	1			
Lymphosarcoma	313	22	6			2	2	26	1			
Follicular lymphoblastoma	38	1						4				
Reticulum cell sarcoma of various organs	130	4	2				2					
Reticulum cell sarcoma of bone	32	1	1					3	1	1		
Ewing's sarcoma	58	2					2	3				

Past illness:

In tumors of RES and lymphoid tissue, tuberculosis and syphilis were relatively frequently encountered in the past history as shown in Table IV. There is no evidence that these diseases were responsible for the development or proliferation of tumors of RES and lymphoid tissue in individual cases.

Initial and presenting symptoms:

Initial symptoms of tumors of RES and lymphoid tissue were given in Table V. In tumors of lymphoid tissue lymphadenopathy was observed in 76.2% of the patients with reticulum cell sarcoma, 73.2%, Hodgkin's disease, 73.2%, lymphosarcoma and 81.6%, follicular lymphoblastoma, respectively. But in reticulum

TABLE V. Initial Symptoms of Tumors of RES and Lymphoid Tissue

	Reticulum cell sarcoma of lymphoid tissue	Hodgkin's disease	Lymphosarcoma	Follicular lymphoblastoma	Reticulum cell sarcoma of bone	Ewing's sarcoma
Lymphadenopathy	76.2%	73.2%	73.2%	81.6%	25.0%	6.9%
Anemia	2.5	7.2	5.1	—	3.1	—
Fever	11.2	25.5	8.1	7.9	6.2	25.0
Pain	13.9	5.9	8.9	5.3	40.6	51.7
Others	16.4	12.2	5.4	7.9	46.8	37.9
No. of cases	1169	459	313	38	32	58

cell sarcoma of bone, it was found only in 25.0% and 6.9%, in Ewing's sarcoma and pain was most frequently experienced¹⁵⁾.

Presenting symptoms and signs:

There were some differences in frequency of presenting symptoms and signs, as shown in Table VI. In tumors of lymphoid tissue including reticulum cell sarcoma, lymphadenopathy and anemia were the presenting symptoms encountered relatively frequently, while in reticulum cell sarcoma of bone and Ewing's sarcoma, anemia, pain, involvement of bones and joints, and abnormal finding of bones were commonly manifested symptoms and signs besides the lymphadenopathy¹⁵⁻¹⁸⁾.

Primary sites of lymphnodes:

Primary sites of lymphnodes in tumors of RES and lymphoid tissue were given in Table VII. Enlargement of cervical lymphnodes was most frequently observed in tumors of lymphoid tissue.

Physical signs:

In children splenomegaly and hepatosplenomegaly were observed in 8.2%.

TABLE VI. Presenting Symptoms and Signs of Tumors of RES and Lymphoid Tissue

	Reticulum cell sarcoma of lymphoid tissue	Hodgkin's disease	Lymphosarcoma	Follicular lymphoblastoma	Reticulum cell sarcoma of bone	Ewing's sarcoma
Lymphadenopathy	98.2%	85.8%	91.1%	87.4%	53.1%	25.8%
Anemia	41.9	54.8	44.1	57.9	43.7	63.8
Fever	12.7	8.3	13.1	7.9	6.2	31.0
Tiredness	9.1	16.1	9.6	13.2	3.1	8.6
Pain	16.3	12.4	15.0	7.9	56.2	48.3
Involv. of G.I. tract	1.5	18.5	16.0	5.3	3.1	6.9
Involv. of respiratory and circulatory systems	1.2	12.9	14.4	2.6	6.2	6.9
Mediastinal tumor*	2.1	3.1	6.7	—	—	1.7
Enlarged hilar lymphnodes*	2.1	7.2	5.8	—	—	—
Involv. of skin	1.8	8.7	4.8	2.6	3.1	3.4
Involv. of mouth	2.1	1.5	2.2	—	6.2	1.7
Involv. of bone and joint*	2.1	0.9	1.6	—	75.0	62.0
Abnormal findings of bone*	2.1	0.4	—	—	68.7	31.0
Involv. of genital organ	2.2	0.4	0.6	—	—	—
Involv. of nervous system	1.7	2.2	2.9	2.6	31.2	13.8
Involv. of urinary tract	2.2	0.4	0.6	—	—	1.7
Others	1.5	5.2	0.4	2.6	15.6	32.7
No. of cases	1169	459	313	38	32	58

* Observed by X-ray examination

TABLE VII. Primary Sites of Lymphnodes in Tumors of RES and Lymphoid Tissue

	Reticulum cell sarcoma of lymphoid tissue	Hodgkin's disease	Lymphosarcoma	Follicular lymphoblastoma	Reticulum cell sarcoma of bone	Ewing's sarcoma
	Bi.,* Uni.**	Bi., Uni.	Bi., Uni.	Bi., Uni.	Bi., Uni.	Bi., Uni.
Nasopharyngeal	0.4% 0.1% 1.0 : 0.25	—% —%	—% —%	—% —%	—% —%	1.7% —%
Tonsil	1.4 5.9 : 4.2	— 0.4	0.3 1.3 : 4.3	— 2.6	— —	—
Infraauricular	0.4 3.5 : 8.7	— 1.6	0.3 1.9 : 6.3	2.6 —	— —	1.7
Submaxillary	1.6 6.7 : 4.2	1.3 4.0 : 3.0	1.6 5.2 : 3.3	2.6 5.3 : 2.0	— —	1.7
Cervical	9.2 30.0 : 3.3	13.0 30.6 : 2.3	8.8 33.1 : 3.8	10.5 13.2 : 1.3	6.3 3.1 : 0.5	1.7
Supraclavicular	0.3 2.3 : 7.6	1.3 3.6 : 2.8	0.3 3.0 : 1.3	2.6 —	— —	1.7
Hilar	0.1 0.5 : 5.0	— —	1.0 0.3 : 3.0	— —	— —	—
Axillary	0.9 5.5 : 6.1	1.1 4.7 : 4.3	2.6 6.2 : 2.4	— 2.6	— —	3.4
Cubital	— 0.3	— —	— —	— —	— —	— —
Inguinal	2.1 6.6 : 3.1	3.8 7.4 : 1.9	2.3 4.5 : 1.9	2.6 2.6 : 1.0	6.3 6.3 : 1.0	6.9 3.4 : 0.5
Femoral	0.1 0.5 : 5.0	— 0.7	0.3 0.6 : 2.0	— 2.6	3.1 —	1.7 —
Others	3.5 2.7 : 0.8	4.5 —	2.6 2.9 : 1.1	10.5 —	— —	1.7
	21.0 64.6 : 3.0	25.0 53.0 : 2.1	20.1 59.9 : 3.0	31.4 28.9 : 0.9	15.7 9.4 : 0.6	22.2 3.4 : 0.2
Generalized	6.9%	9.8%	3.6%	39.5%	—%	3.4%
not observed	8.7	12.3	16.2	—	75.0	70.7
No. of cases	1111	448	308	38	32	58

* Bilateral

** Unilateral

47.8%, 20.4%, 33.4% of reticulum cell sarcoma of lymphoid tissue, Hodgkin's disease, lymphosarcoma and follicular lymphoblastoma respectively, but in adults in 11.2%, 19.7%, 9.9%, 10.0% of reticulum cell sarcoma of lymphoid tissue, Hodgkin's disease, lymphosarcoma, and follicular lymphoblastoma respectively. However, in reticulum cell sarcoma of bone and Ewing's sarcoma hepatosplenomegaly was less frequently observed, as shown in Table VIII.

TABLE VIII. Presence of Splenomegaly and Hepatomegaly

		Reticulum cell sarcoma of lymphoid tissue	Hodgkin's disease	Lymphosarcoma	Follicular lymphoblastoma	Reticulum cell sarcoma of bone	Ewing's sarcoma
Children (~15yrs.)	Hepatomegaly	16 24.6%	7 15.9%	20 40.8%	2 33.3%	—	5 18.5%
	Splenomegaly	1 1.5%	5 11.4%	1 2.0%	1 16.7%	—	—
	Hepatosplenomegaly	5 7.7%	16 36.4%	9 18.4%	1 16.7%	—	—
	Total cases	65	44	49	6	2	27
Adults (16yrs.~)	Hepatomegaly	116 14.3%	97 28.6%	48 22.6%	5 25.0%	4 19.0%	3 9.7%
	Splenomegaly	21 2.6%	17 5.0%	4 1.9%	—	1 4.8%	—
	Hepatosplenomegaly	70 8.6%	50 14.7%	17 8.0%	2 10.0%	—	—
	Total cases	814	339	212	20	21	31

TABLE IX. Analysis of Fever as Initial Symptom of Tumors of RES and Lymphoid Tissue

	Reticulum cell sarcoma of lymphoid tissue	Hodgkin's disease	Lymphosarcoma	Follicular lymphoblastoma	Reticulum cell sarcoma of bone	Ewing's sarcoma
36°	1,201	299	262	35	32	50
37°	46 31.1%	42 26.3%	11 22.0%	—	—	3 37.5%
38°	35 23.6%	37 23.1%	21 42.0%	3 99.9%	—	4 50.0%
39°	14 9.5%	8 5.0%	8 16.0%	—	—	1 12.5%
Fever of unknown degree	53 35.8%	73 45.6%	10 20.0%	—	—	—
Total cases	1,349	459	313	38	32	58

Fever:

Fever was more frequently observed in Hodgkin's disease than in tumors of RES, as shown in Table IX.

Hematological findings:

Hematological findings at the initial and terminal phases of tumors of RES and lymphoid tissue were given in Tables X-XVI.

The leukocyte count showed no significant variation from normal range at the initial phase of tumors of RES and lymphoid tissue, but at the terminal phase leukopenia was found in most cases of tumors of lymphoid tissue.

The percentage of atypical lymphocytes and immature cells appeared in peripheral blood less than 1.0% except reticulum cell sarcoma of bone.

Moderate anemia was observed in most cases of tumors of RES and lymphoid tissue at the initial and terminal phases.

The reduction of platelet count was observed in few cases of tumors of RES and lymphoid tissue.

As for the bone-marrow findings at the initial phase the reduction of nucleated cell count and percentage of erythrocytic series were observed in most cases of tumors of lymphoid tissue, while an increase of percentage of reticulum cells and lymphocytic series was seen¹⁹⁻²⁶).

TABLE X. Hematological Findings during Initial Phase

		Reticulum cell sarcoma of lymphoid tissue	Hodgkin's disease	Lymphosarcoma	Follicular lymphoblastoma	Reticulum cell sarcoma of bone	Ewing's sarcoma
WBC/mm ³	4,000>	12.8%	13.2%	14.9%	23.5%	19.4%	9.6%
	4,000~	73.0	65.8	69.6	61.8	70.9	65.4
	10,000~	13.8	21.0	15.5	14.7	9.6	25.0
	No. of cases	997	424	286	34	31	52
RBC×10 ⁴ /mm ³	300>	12.0	17.1	11.7	2.6	23.3	12.7
	300~	38.6	44.5	40.8	38.2	30.0	27.3
	400~	28.0	24.7	25.2	26.5	13.3	30.9
	450~	13.8	10.8	11.7	20.6	13.3	20.0
	500~	7.5	2.9	10.6	11.8	20.1	9.1
	No. of cases	968	409	282	34	30	55
Pl×10 ⁴	3>	4.1	2.1	4.0	—	25.0	—
	7>	20.8	18.6	14.7	—	—	—
	15>	39.8	39.2	25.3	40.0	—	33.3
	15~	46.2	40.2	56.0	60.0	75.0	66.7
	No. of cases	195	97	75	5	4	3

TABLE XI. Hematological Findings at the Terminal Phase of Tumors of Lymphoid Tissue

		Reticulum cell sarcoma of lymphoid tissue	Hodgkin's disease	Lymphosarcoma
WBC/mm ³	4,000>	42.0%	47.4%	52.2%
	4,000~	42.0	36.8	30.7
	10,000~	15.9	15.8	17.1
	Total cases	69	38	23
RBC/10 ⁴ mm ³	300>	30.8	45.7	36.4
	300~	41.5	40.0	40.9
	400~	13.8	5.7	18.2
	450~	7.7	5.7	4.5
	500~	6.2	2.9	—
	Total cases	65	35	22
Pl/×10 ⁴	~ 3	21.1	33.3	37.5
	~ 7	5.3	22.2	37.5
	~ 15	52.6	45.5	25.0
	15<	21.1	—	—
	Total cases	19	9	8

TABLE XII. Hematological Findings during Initial Phase of Tumors of RES and Lymphoid Tissue

		Reticulum cell sarcoma of lymphoid tissue	Hodgkin's disease	Lymphosarcoma	Follicular lymphoblastoma	Reticulum cell sarcoma of bone	Ewing's sarcoma
No. of cases		805	397	245	32	30	47
Band cells %	5>	31.2%	18.6%	30.0%	37.5%	40.0%	27.5%
	5~	27.5	25.3	23.5	40.5	20.0	38.5
	10~	41.4	56.1	46.5	22.0	40.0	34.0
Neutrophils %	50>	37.4	43.6	47.5	47.0	35.0	38.5
	50~	46.6	42.0	39.5	43.0	45.0	50.0
	70~	16.0	14.4	13.0	10.0	20.0	11.5
Eosinophils %	2>	43.9	42.3	52.5	37.5	33.0	51.0
	2~	45.2	32.0	34.5	37.5	50.0	40.5
	6~	11.8	25.4	13.0	25.0	17.0	8.5
Basophils %	0	85.8	78.1	87.0	97.0	93.4	91.5
	2>	11.4	18.9	10.5	—	3.3	—
	2~	2.8	3.0	2.5	3.0	3.3	8.5
Lymphocytes %	20>	34.5	43.1	26.0	15.5	26.5	25.5
	20~	48.3	43.6	49.0	56.0	60.0	59.5
	40~	17.1	13.4	25.0	28.5	13.5	15.0
Monocytes %	5>	56.5	59.9	61.5	59.5	50.0	57.5
	5~	31.6	30.5	31.0	28.5	33.0	32.0
	10~	11.9	9.6	7.5	12.0	17.0	10.5

TABLE XIII. Hematological Findings during Terminal Phase of Tumors of RES and Lymphoid Tissue

		Reticulum cell sarcoma of lymphoid tissue	Hodgkin's disease	Lymphosarcoma
No. of cases		55	28	19
Band cells %	5>	20.8%	28.6%	31.5%
	5~	20.8	53.6	16.0
	10~	58.4	17.8	52.5
Neutrophils %	50>	45.3	46.4	52.5
	50~	47.2	42.9	21.0
	50~	7.5	10.9	26.5
Eosinophils %	2>	87.3	71.4	100.0
	2~	12.7	21.4	—
	6~	—	7.2	—
Basophils %	0	90.9	89.3	100.0
	2>	7.3	3.6	—
	2~	1.8	7.1	—
Lymphocytes %	20>	49.1	53.6	42.0
	20~	32.7	28.6	31.5
	40~	18.2	17.8	26.5
Monocytes %	5>	58.2	57.1	68.0
	5~	21.8	32.0	10.0
	10~	20.0	10.8	21.5

TABLE XIV. Presence of Atypical Lymphocytes in Peripheral Blood

	Reticulum cell sarcoma of lymphoid tissue	Hodgkin's disease	Lymphosarcoma	Follicular lymphoblastoma	Reticulum cell sarcoma of bone	Ewing's sarcoma
-	798 99.1%	394 99.2%	243 99.2%	32 100.0%	29 96.7%	47 100.0%
±	7 0.9%	3 0.7%	1 0.4%	—	1 3.3%	—
+	—	—	1 0.4%	—	—	—
No. of cases	805	397	245	32	30	47

- Not observed.

± Occasionally observed.

+ Observed throughout course of illness.

TABLE XV. Presence of Immature Cells in Peripheral Blood

	Reticulum cell sarcoma of lymphoid tissue	Hodgkin's disease	Lymphosarcoma	Follicular lymphoblastoma	Reticulum cell sarcoma of bone	Ewing's sarcoma
-	764 94.9%	386 97.2%	226 92.2%	32	29 99.7%	46 99.8%
±	38 4.7%	11 2.8%	18 7.3%	-	1 0.3%	-
+	3 0.4%	-	1 0.5%	-	-	1 0.2%
No. of cases	805	397	245	32	30	47

- Not observed.

± Occasionally observed.

+ Observed throughout course of illness.

TABLE XVI. Initial Bone Marrow Findings in Tumors of RES and Lymphoid Tissue

		Reticulum cell sarcoma of lymph- oid tissue	Hodgkin's disease	Lympho- sarcoma	Follicular lympho- blastoma	Reticulum cell sarcoma of bone	Ewing's sarcoma
Nucleated cell count × 10 ⁴	14 >	12 cases	6	2		-	1
	14 ~	2	3	2		-	-
	40 ~		3			-	-
Reticu- lum cells %	3 >	11	14	6		2	1
	3 ~	4	1	3		-	-
	6 ~	4	3	1		-	-
Erythro- cytic series %	20 >	12	9	7		2	1
	20 ~	7	7	3		-	-
	40 ~		2	0		-	-
Granulo- cytic series %	50 >	4	6	5		2	1
	50 ~	13	9	5		-	-
	80 ~	2	3	0		-	-
Monocy- tic series %	1 >	2	9	3		2	-
	1 ~	13	3	5		-	1
	4 ~	4	6	2		-	-
Lympho- cytic series %	4 >	2	5	2		1	-
	4 ~	4	10	2		-	-
	15 ~	13	3	6		1	1

Fig. 6. Lactic acid dehydrogenase and isocitric acid dehydrogenase activities in reticulum cell sarcoma of lymphoid tissue.

Results of clinical laboratory examination:

Elevation of erythrocyte sedimentation rate was observed in most cases of tumors of RES and lymphoid tissue.

Urinalysis revealed no Bence-Jones protein in any instances as shown in Fig. 4.

Total plasma protein and albumin-globulin ratio were lower than normal value in most cases of RES and lymphoid tissue.

The results of chemical assay of excreted 17-hydroxycorticosteroid and 17 ketosteroid before and after ACTH infusion revealed no significance as shown in Fig. 5, which was performed in 9 cases of reticulum cell sarcoma of lymphoid tissue.

Serum lactic acid dehydrogenase activities were increased in 12 out of 15 cases of reticulum cell sarcoma of lymphoid tissue, while serum isocitric acid dehydrogenase activities were not increased in most instances, as shown in Fig. 6.

Response to therapies:

In 505 cases of tumors of RES and lymphoid tissue, the effects of various kinds

TABLE XVII. Effects of Various Therapies
(in cases treated in universities and other hospitals)

Effective cases + (Slightly effective cases) / Total cases

		Reticulum cell sarcoma of lymphoid tissue	Hodgkin's disease	Lymphosar- coma	Follicular lympho- blastoma	Reticulum cell sarcoma of bone	Ewing's sarcoma
Alkylating agents	Nitromin	18 + (22) / 86 46.5%	12 + (19) / 60 51.7%	3 + (10) / 29 44.9%	0 + (1) / 2	—	2 + (1) / 5 60.0%
	Thio-TEPA	3 + (9) / 31 38.8%	5 + (4) / 14 63.3%	3 + (7) / 18 55.6%	0 + (1) / 2	—	0 + (0) / 2
	Endoxan	4 + (2) / 14 42.8%	6 + (4) / 12 83.3%	2 + (0) / 3 66.6%	1 + (1) / 3	—	1 + (0) / 1
Anti meta- bolite	6MP	0 + (2) / 6 33.3%	1 + (0) / 2	0 + (1) / 1	—	—	—
Antibiotics	MMC	6 + (13) / 37 51.4%	1 + (4) / 8 62.5%	1 + (1) / 8 25.0%	0 + (1) / 1	0 + (0) / 2	0 + (2) / 2
	Actino- mycin-J	8 + (5) / 24 54.2%	0 + (0) / 3	0 + (0) / 2	1 + (1) / 2	—	0 + (0) / 1
Steroid hormones	Steroid H. alone	6 + (3) / 19 47.4%	9 + (8) / 25 68.0%	2 + (1) / 10 30.0%	0 + (2) / 3	—	—
	With other agents	2 + (1) / 7 42.8%	5 + (8) / 18 72.4%	1 + (1) / 3	—	—	—
Other	MH	1 + (2) / 12 25.0%	0 + (2) / 4 50.0%	1 + (1) / 5 40.0%	—	—	—
Total		48 + (59) / 236 45.3%	39 + (49) / 146 60.3%	13 + (22) / 79 44.3%	1 + (7) / 13 61.5%	0 + (0) / 2	3 + (3) / 11 54.5%

TABLE XVIII. Effects of Various Therapies
(in cases treated in National Cancer Center Hospital)

		Reticulum cell sarcoma of lymphoid tissues					Lymphosarcoma			
		III**			I*			III**		
		Effec- tive cases	Slightly effec- tive cases	Total cases	Effec- tive cases	Slightly effective cases	Total cases	Effec- tive cases	Slightly effective cases	Total cases
Endoxan		3/5	2/5	5/5	—	—	—	0/2	1/2	1/2
Uracil-M		—	—	—	—	—	—	0/1	1/1	1/1
MMC		—	—	—	1/1	0/1	1/1	—	—	—
MH		0/1	0/1	0/1	—	—	—	—	—	—
ST. H.		0/2	2/2	2/2	—	—	—	0/2	1/2	1/2
Combined therapy	ST. H., Endoxan	0/1	1/1	1/1	—	—	—	—	—	—
	ST. H., MMC	0/1	1/1	1/1	—	—	—	1/1	0/1	1/1
	ST. H., En- doxan,6MP	—	—	—	—	—	—	1/1	0/1	1/1
Total		3/10	6/10	9/10	1/1	0/1	1/1	2/7	3/7	5/7
Radiation		1/3	2/3	3/3	2/2	0/2	2/2	1/1	0/1	1/1

of treatments were analyzed from hospital records as shown in Tables XVII and XVIII.

In reticulum cell sarcoma of lymphoid tissue remission was observed relatively frequently following the treatment with Actinomycin-J, Mitomycin C (MMC),

	Age	Life span yrs								Total cases
		~ 0.5	0.5 ~	1 ~	2 ~	3 ~	4 ~	5 ~	6 ~	
Chemotherapy	~15	8	6	1	—	—	—	—	—	15
	16~	69	36	21	8	6	1	1	1	143
	Total cases	77	42	22	8	6	1	1	1	(158)
Radiation therapy	~15	2	2	1	—	—	—	—	—	5
	16~	44	41	33	7	5	2	—	1	133
	Total cases	46	53	34	7	5	2	—	1	(138)
Combined therapy	~15	10	4	4	1	—	—	—	1	20
	16~	58	56	53	10	9	7	2	2	197
	Total cases	68	60	57	11	9	7	2	3	(217)
Symptomatic treatment	~15	1	1	—	—	—	—	—	—	2
	16~	28	13	6	1	1	1	—	—	50
	Total cases	29	14	6	1	1	1	—	—	(52)

Fig. 7. Life span in reticulum cell sarcoma of lymphoid tissue.

steroid hormones (ST. H.) and alkylating agents.

In Hodgkin's disease, alkylating agents, especially Endoxan, MMC and ST.H. with or without other agents produced remission in more than one half of the cases treated by these drugs.

In lymphosarcoma, remission was relatively frequently obtained following the treatment with alkylating agents²⁷⁻³⁵).

Influence of therapies on survival time:

Using 565 cases with reticulum cell sarcoma of lymphoid tissue, survival time was estimated from the onset of the initial symptoms which were attributable to

	Life span yr								M.S* (Mon- ths)
		<0.5	0.5~	1~	2~	3~	4~	5~	
Chemotherapy	Effective	cases 13	19	19	4	1	1	—	11.1
	Non effective	32	11	7	5	2	—	1	5.5
Radiation therapy	Effective	14	19	11	3	2	—	—	9.4
	Non effective	7	4	4	1	—	—	—	8.3
Combined therapy	Effective	24	34	31	4	7	3	2	11.1
	Non effective	12	14	2	3	—	2	—	8.5
Symptomatic treatment		30	13	6	3	1	—	2	5.6

* Median survival

Fig. 8. Life span in reticulum cell sarcoma with and without therapeutic effects.

reticulum cell sarcoma. These cases were divided into several groups according to the age and treatments, and no significant difference among the groups was observed, as shown in Fig. 7. But as shown in Fig. 8, the survival time of the patients, to whom the therapy was judged as effective through their hospital records and who went into the remissions was longer than that of patients who did not respond to the therapies³⁶⁾.

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