Distribution of Lymphoid Neoplasms in China

Analysis of 4,638 Cases According to the World Health Organization Classification

Jian Sun, MD,[1] Qunpei Yang, MD,[2*] Zhaohui Lu, MD, PhD,[1] Miaoxia He, MD,[3] Li Gao, MD,[3] Minghua Zhu, MD, PhD,[3] Lu Sun, MD,[4] Lixin Wei, MD, PhD,[4] Min Li, MD,[5] Cuiling Liu, MD,[5] Jie Zheng, MD, PhD,[5] Weiping Liu, MD, PhD,[2] Gandi Li, MD, PhD,[2] and Jie Chen, MD, PhD[1]*

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Abstract

To estimate the distribution of lymphoid neoplasms in China, we conducted a comprehensive analysis, based on subtype, age, sex, and lesion, of primary and resected biopsy specimens of 4,638 lymphoid neoplasms diagnosed from 2004 to 2008 at 5 large hospitals. Of the 4,638 patients, mature B-cell neoplasms accounted for 64.3% of all lymphoid neoplasms, mature T/NK-cell neoplasms for 23.3%, and Hodgkin lymphoma for 8.6%. The most common subtype was diffuse large B-cell lymphoma (36.2%), followed by extranodal NK/T-cell lymphoma, nasal type (11.0%), classic Hodgkin lymphoma (8.4%), extranodal marginal zone B-cell lymphoma (7.7%), plasmacytic neoplasm (5.0%), and peripheral T-cell lymphoma, not otherwise specified (3.9%). For most lymphoid neoplasm subtypes, male subjects showed higher rates than female subjects. In summary, our study showed that the epidemiologic features of lymphoid neoplasms in China are distinct from those in Western countries and similar in many ways to those in other countries of the Far East.

Lymphoid neoplasms comprise a group of closely related yet heterogeneous diseases. Categorizing the various lymphoid neoplasms has proven to be enormously challenging, and has resulted in the evolution of numerous clinical and pathologic classification schemes over the past 50 years.[1-3] Recent revolutionary advances in immunology, genetics, and molecular biology have resulted in extensive changes in the classifications of these tumors, culminating in the Revised European-American classification (1994)[4] and its successor, the World Health Organization (WHO) classification (2001 and 2008).[5,6]

Together, lymphoid neoplasms comprise the sixth most common group of malignancies worldwide in men and women,[7] but there are marked geographic variations, with the highest rates observed in North America and Australia, followed by Europe, and lower rates throughout Asia.[8,9] Ethnic and regional differences are seen in the distribution of subtypes. For example, Asian populations have higher proportions of mature T/NK-cell neoplasms and extranodal marginal zone B-cell lymphoma and lower proportions of follicular lymphoma and chronic lymphocytic leukemia/small lymphocytic lymphoma than Western populations.[5,6,10-17]

The strongest known risk factor for lymphoid neoplasm is severe immunodeficiency, but the causes of most lymphomas remain unknown.[10,16,18] Thus the comparison of incidence rates and patterns of specific subtypes may provide critical clues for future etiologic investigations.

To date, only a few small descriptive analyses have focused on the subtype, age, sex, and lesion of primary and resected biopsy specimens and their distribution patterns in China for all of the lymphoid neoplasm subtypes defined by the WHO classification.[11,19-21] To describe the epidemiologic features of the entire spectrum of lymphoid neoplasms in

China according to the WHO classifications, we examined the subtype, age, sex, and lesion of 4,638 primary and resected biopsy specimens of lymphoid neoplasms diagnosed from 2004 to 2008 at 5 large hospitals.

Materials and Methods

The records of all patients with lymphoid neoplasms found on tissue samples from 2004 to 2008 at the following hospitals were retrieved: the Department of Pathology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (Beijing, China); the Department of Pathology, West China Hospital, Sichuan University (Chengdu, China); the Department of Pathology, Health Science Center, Peking University (Beijing); the Department of Pathology, Chinese PLA General Hospital (Beijing); and the Department of Pathology, Changhai Hospital, Second Military Medical University (Shanghai, China).

To determine the exact distribution, cases that were referred only for consultation were excluded. The diagnosis was made using a comprehensive diagnostic system that included morphology, immunohistochemistry, in situ hybridization for Epstein Barr virus–encoded RNA, polymerase chain reaction–based techniques for the analysis of clonality, and fluorescence in situ hybridization. Patients suspected of having a lymphoid neoplasm based on morphologic findings, with ambiguous immunostaining results or insufficient tissue sample for full characterization, were excluded. A total of 4,638 lymphoid neoplasm patients were enrolled in the study.

When patients had 2 or more tissue samples collected at different times, the diagnosis was based on the first sample. All cases were histologically reconfirmed and grouped into subtypes according to the 2001 and 2008 WHO classification system. When applicable, the International Lymphoma Epidemiology Consortium (InterLymph) guideline[15] was used. Clinical information obtained from medical records for the calendar year of the diagnosis included patient sex and age and the site of tissue sampling.

Differences were assessed using independent samples *t* test. *P* values of less than .05 were considered statistically significant. All statistical analyses were performed using SPSS software for Windows, version 17.0 (SPSS, Chicago, IL). The ethics committee of the Peking Union Medical College Hospital approved this study.

Results

Subtype Distribution of Lymphoid Neoplasms

Of the 4,638 patients diagnosed with lymphoid neoplasms from 2004 to 2008, 2,983 (64.3%) had mature B-cell neoplasms, 1,082 (23.3%) had mature T/NK-cell neoplasms, 399 (8.6%) had Hodgkin lymphomas, and 174 (3.8%) had precursor lymphoid neoplasms **Table 1**. The most common subtype was diffuse large B-cell lymphoma (36.2%), followed by extranodal NK/T-cell lymphoma, nasal type (11.0%); classic Hodgkin lymphoma (8.4%); extranodal marginal zone B-cell lymphoma (7.7%); plasmacytic neoplasm (5.0%); and peripheral T-cell lymphoma, not otherwise specified (NOS; 3.9%). There were 111 (2.4%) anaplastic large cell lymphomas, including 68 anaplastic lymphoma kinase (ALK)+ cases and 43 ALK– cases.

Of the 399 patients with Hodgkin lymphoma, 8 (2.8%) had nodular lymphocyte predominance type and 391 (97.2%) had classic Hodgkin lymphoma, with mixed cellularity Hodgkin lymphoma being the most common subtype (211 patients, 52.9%).

Age and Sex Distribution

Lymphoid neoplasm subtypes were seen more often in male subjects than in female subjects. The male-female (M/F) ratio was 1.7 for all lymphoid neoplasms, 1.7 for non-Hodgkin lymphomas, 2.2 for precursor lymphoid neoplasms, 1.6 for mature B-cell neoplasms, and 2.2 for mature T/NK-cell neoplasms. The highest male predominance was observed in patients with non-Hodgkin lymphoma with Burkitt lymphoma (5.7), extranodal NK/T-cell lymphoma, nasal type (2.6), mantle cell lymphoma (2.5), and plasmacytic neoplasm NOS (2.5). In contrast, female predominance was seen in splenic B-cell marginal zone lymphoma (0.5). In Hodgkin lymphoma, the overall M/F ratio was 1.8; male predominance was seen for lymphocyte-rich Hodgkin lymphoma (2.8) and mixed cellularity Hodgkin lymphoma (2.5).

Most mature lymphoid neoplasms were diseases of adults. The mean age was 32.9 years for Hodgkin lymphomas, 54.4 years for mature B-cell neoplasms, and 43.7 years for mature T/NK-cell neoplasms. Patients with mature T/NK-cell neoplasms were significantly younger than patients with mature B-cell neoplasms (mean age, 43.7 vs 54.4 years, $P < .001$), and patients with Hodgkin lymphomas were significantly younger than those with mature non-Hodgkin lymphomas (mean age, 32.9 vs 51.6 years; $P < .001$).

Among the 318 pediatric lymphomas, mixed cellularity Hodgkin lymphoma was the most common (57 patients, 17.9%), followed by T-lymphoblastic leukemia/lymphoma (50 patients, 15.7%), diffuse large B-cell lymphoma (34 patients, 10.7%), and extranodal NK/T-cell lymphoma, nasal type (28 patients, 8.8%) **Table 2**.

The mean ages for Burkitt lymphoma (25.6 years) and mediastinal (thymic) large B-cell lymphoma (34.9 years) were less than those for major mature B-cell neoplasms, including diffuse large B-cell lymphoma (mean age, 54.5 years), plasmacytic neoplasm (mean age, 55.4 years), extranodal marginal zone B-cell lymphoma (mean age, 55.6 years),

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Table 1
Distribution of Lymphoid Neoplasms According to the World Health Organization Classification

Lymphoid Neoplasms	M/F Ratio	Mean Age (y)	No. of Cases	% of Total	% of HL	% of NHL
Hodgkin lymphoma	258/141	32.9	399	8.6	100	
Nodular lymphocyte predominant Hodgkin lymphoma	8/3	40.9	11	0.2	2.8	
Nodular sclerosis Hodgkin lymphoma	69/61	31.5	130	2.8	32.6	
Lymphocyte-rich Hodgkin lymphoma	11/4	32.5	15	0.3	3.8	
Mixed cellularity Hodgkin lymphoma	151/60	33.6	211	4.6	52.9	
Lymphocyte depleted Hodgkin lymphoma	1/2	35.0	3	0.1	0.8	
Hodgkin lymphoma, NOS	18/11	30.9	29	0.6	7.3	
Non-Hodgkin lymphoma	2,678/1,561	50.5	4,239	91.4		100
Precursor lymphoid neoplasms	120/54	24.7	174	3.8		4.1
B-lymphoblastic leukemia/lymphoma	18/11	22.7	29	0.6		0.7
T-lymphoblastic leukemia/lymphoma	102/43	25.1	145	3.1		3.4
Mature B-cell neoplasms	1,817/1,166	54.4	2,983	64.3		70.4
Chronic lymphocytic leukemia/small lymphocytic lymphoma	120/53	59.6	173	3.7		4.1
Follicular lymphoma	76/59	56.3	135	2.9		3.2
Mantle cell lymphoma	81/32	59.7	113	2.4		2.7
Plasmacytic neoplasm (plasma cell myeloma and plasmacytoma)	166/67	55.4	233	5.0		5.5
Lymphoplasmacytic lymphoma	8/8	57.9	16	0.3		0.4
Hairy cell leukemia	3/1	54.8	4	0.1		0.1
Burkitt lymphoma	40/7	25.6	47	1.0		1.1
Diffuse large B-cell lymphoma	1,003/677	54.5	1,680	36.2		39.6
Mediastinal (thymic) large B-cell lymphoma	31/31	34.9	62	1.3		1.5
Extranodal marginal zone B-cell lymphoma	193/162	55.6	355	7.7		8.4
Splenic B-cell marginal zone lymphoma	6/12	58.1	18	0.4		0.4
Nodal marginal zone B-cell lymphoma	7/2	63.8	9	0.2		0.2
B-cell lymphoid neoplasm, NOS	83/55	53.6	138	3.0		3.3
Mature T-cell and NK-cell neoplasms	741/341	43.7	1,082	23.3		25.5
T-cell prolymphocytic leukemia	0/1	39.0	1	0.0		0.0
Adult T-cell lymphoma/leukemia	1/0	39.0	1	0.0		0.0
Aggressive NK-cell leukemia	6/1	32.1	7	0.2		0.2
Enteropathy associated T-cell lymphoma	7/1	42.5	8	0.2		0.2
Extranodal NK/T-cell lymphoma, nasal type	368/141	43.1	509	11.0		12.0
Hepatosplenic T-cell lymphoma	12/4	29.5	16	0.3		0.4
Anaplastic large cell lymphoma	70/41	33.7	111	2.4		2.6
Primary cutaneous anaplastic large cell lymphoma	7/8	48.0	15	0.3		0.4
Angioimmunoblastic T-cell lymphoma	44/24	62.9	68	1.5		1.6
Mycosis fungoides/Sézary syndrome	3/3	52.0	6	0.1		0.1
Peripheral T-cell lymphoma, NOS	119/63	48.5	182	3.9		4.3
Subcutaneous panniculitis-like T-cell lymphoma	21/8	34.6	29	0.6		0.7
T/NK-cell lymphoid neoplasms, NOS	83/46	41.6	129	2.8		3.0
Total	2,936/1,702	49.0	4,638	100		

HL, Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; NOS, not otherwise specified.

follicular lymphoma (mean age, 56.3 years), and chronic lymphocytic leukemia/small lymphocytic lymphoma (mean age, 59.6 years; $P < .001$).

For mature T/NK-cell neoplasms, patients with anaplastic large cell lymphoma (mean age, 33.7 years) were significantly younger than patients with extranodal NK/T cell lymphoma, nasal type (mean age, 43.1 years, $P = .005$), and peripheral T-cell lymphoma, NOS (mean age, 48.5 years, $P < .001$). Furthermore, patients with angioimmunoblastic T-cell lymphoma (mean age, 62.9 years) were significantly older than patients with extranodal NK/T-cell lymphoma, nasal type, and peripheral T-cell lymphoma, NOS ($P < .001$).

Distribution of Lesions With Primary and Resected Biopsies

The anatomic sites of sampling in the primary diagnosis of lymphoid neoplasms are shown in **Table 3**. The common

Table 2
Subtype Distribution of Lymphoid Neoplasms of Pediatric Cases

Subtypes	No. (% of Total)
Mixed cellularity Hodgkin lymphoma	57 (17.9)
T-lymphoblastic leukemia/lymphoma	50 (15.7)
Diffuse large B-cell lymphoma	34 (10.7)
Extranodal NK/T-cell lymphoma, nasal type	28 (8.8)
Anaplastic large cell lymphoma	27 (8.5)
Burkitt lymphoma	25 (7.9)
Nodular sclerosis Hodgkin lymphoma	17 (5.4)
T-cell lymphoid neoplasm, NOS	16 (5.0)
B-lymphoblastic leukemia/lymphoma	14 (4.4)
Peripheral T-cell lymphoma, NOS	13 (4.1)
Others	37 (11.6)
Total	318 (100)

NOS, not otherwise specified.

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sites of diagnosis were lymph nodes (36.6%), gastrointestinal tract (15.5%), nasal cavity/sinus (8.3%), and Waldeyer ring (7.3%). Diffuse large B-cell lymphoma was the most common type (32.2%) for lymph node lesions, followed by mixed cellularity Hodgkin lymphoma (11.1%), chronic lymphocytic leukemia/small lymphocytic lymphoma (6.9%), and T-lymphoblastic leukemia/lymphoma (6.1%).

Among the 2,943 extranodal lymphomas, diffuse large B-cell lymphoma was the most common (1,117 patients, 38.0%), followed by extranodal NK/T-cell lymphoma, nasal type (498 patients, 16.9%), extranodal marginal zone B-cell lymphoma (340 patients, 11.6%), and plasmacytic neoplasm (227 patients, 7.7%) **Table 4**. For the 720 gastrointestinal sites, diffuse large B-cell lymphoma was the most common (379 patients, 52.6%), followed by extranodal marginal zone B-cell lymphoma (196 patients, 27.2%) and extranodal NK/T-cell lymphoma, nasal type (31 patients, 4.3%). For the 385 nasal cavity/sinus sites, extranodal NK/T-cell lymphoma, nasal type, was the most common (286 patients, 74.3%), followed by diffuse large B-cell lymphoma (48 patients, 12.5%) and peripheral T-cell lymphoma, NOS (16 patients, 3.1%).

Among the 399 patients with Hodgkin lymphoma, most cases (338 patients, 84.7%) were diagnosed by examination of lymph nodes; 32 cases (8.0%) were found in the mediastinum.

Table 3
Distribution of Sampling Sites for the Primary Diagnosis of Lymphoid Neoplasms

Sampling Sites	No. (% of Total)
Lymph node	1,695 (36.6)
Gastrointestinal tract	720 (15.5)
Nasal cavity/sinus	385 (8.3)
Waldeyer ring	340 (7.3)
Skin	167 (3.6)
Abdominopelvic cavity	155 (3.3)
Bone marrow	140 (3.0)
Bone	139 (3.0)
Mediastinum	134 (2.9)
Spinal cord and brain	121 (2.6)
Spleen	106 (2.3)
Others	536 (11.6)
Total	4,638 (100)

Table 4
Subtype Distribution of Extranodal Lymphomas

Subtypes	No. (% of Total)
Diffuse large B-cell lymphoma	1,117 (38.0)
Extranodal NK/T-cell lymphoma, nasal type	498 (16.9)
Extranodal marginal zone B-cell lymphoma	340 (11.6)
Plasmacytic neoplasm	227 (7.7)
B-cell lymphoid neoplasm, NOS	105 (3.6)
Peripheral T-cell lymphoma, NOS	86 (2.9)
T/NK-cell lymphoid neoplasms, NOS	86 (2.9)
Mediastinal (thymic) large B-cell lymphoma	62 (2.1)
Chronic lymphocytic leukemia/small lymphocytic lymphoma	56 (1.9)
Mantle cell lymphoma	44 (1.5)
T-lymphoblastic leukemia/lymphoma	42 (1.4)
Anaplastic large cell lymphoma	38 (1.3)
Follicular lymphoma	34 (1.2)
Nodular sclerosis Hodgkin lymphoma	29 (1.0)
Burkitt lymphoma	28 (1.0)
Subcutaneous panniculitis-like T-cell lymphoma	27 (0.9)
Mixed cellularity Hodgkin lymphoma	23 (0.8)
B-lymphoblastic leukemia/lymphoma	18 (0.6)
Splenic B-cell marginal zone lymphoma	18 (0.6)
Hepatosplenic T-cell lymphoma	16 (0.5)
Primary cutaneous anaplastic large cell lymphoma	15 (0.5)
Others	34 (1.2)
Total	2,943 (100)

NOS, not otherwise specified.

Discussion

The distribution of lymphoid neoplasms shows marked variation in different parts of the world, reflecting etiologic heterogeneity and the participation of both genetic and environmental factors in lymphomagenesis. To estimate the distribution of lymphoid neoplasms in China and the differences between China and other countries, we conducted a comprehensive analysis, based on the subtype, age, sex, and lesion, of primary and resected biopsy specimens of 4,638 lymphoid neoplasms. Our findings are in agreement with previous results showing relatively higher proportions of patients with T/NK-cell neoplasms and relatively lower proportions of patients with follicular lymphoma and chronic lymphocytic leukemia/small lymphocytic lymphoma among Chinese individuals compared with Western populations.[13,15,16]

Mature B-cell neoplasms comprise more than 90% of lymphoid neoplasms in Western countries.[6] The most common types are follicular lymphoma and diffuse large B-cell lymphoma. However, mature B-cell neoplasms only accounted for 64.3% of all lymphoid neoplasms in our study, which was much lower than in Western countries. Diffuse large B-cell lymphoma is the most prevalent histologic subtype of lymphoid neoplasms worldwide.[5,6] The proportion of diffuse large B-cell lymphoma in our study is similar to that reported in the literature for Asian and Western populations.[14-17,22,23] In our study, follicular lymphoma accounted for 2.9% of all lymphoid neoplasms. This proportion is similar to that seen in Korean data[17] but much lower than in Japanese data.[14] Japan studies have found a relatively high rate of follicular lymphoma (19%),[14] which is similar to that of Western countries (11%-30%).[10] For extranodal marginal zone B-cell lymphoma, the frequency observed in this study is similar to that of previous Korean data[17] and higher than the Japanese or US data.[14,16] The high proportion of extranodal marginal zone B-cell lymphoma is likely because of the high prevalence of *Helicobacter pylori* infections in China.[24]

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Chronic lymphocytic leukemia is the most common leukemia of adults in Western countries.[6] In the United States, chronic lymphocytic leukemia/small lymphocytic lymphoma accounts for 14.8% of all lymphoid neoplasms,[14] whereas previous results have shown that it is very rare in far-eastern countries. In the current study, chronic lymphocytic leukemia/small lymphocytic lymphoma accounted for only 3.7% of all lymphoid neoplasms; this result is similar to that seen in studies from Japan and Korea.[14,17] The low incidence in East Asians is maintained in migrant populations in the United States.[25] These observations strongly suggest that host-related genetic factors play an important role in the pathogenesis of this disease. However, all cases in this study were diagnosed based on tissue samples. Some cases of chronic lymphocytic leukemia/small lymphocytic lymphoma might be diagnosed based only on blood samples, making the number of chronic lymphocytic leukemia/small lymphocytic lymphoma small.

T/NK-cell neoplasms show significant variations in incidence in different geographical regions and racial populations. In our study, mature T/NK-cell neoplasms accounted for 23.3% of all lymphoid neoplasms. This result is similar to that of other Asian countries, including Japan,[14] Thailand,[26] Korea,[17] and India,[27] but much higher than the rates in Western countries.[15,16] The most common types were extranodal NK/T-cell lymphoma, nasal type, which made up almost half of all mature T/NK-cell neoplasms in our study.

Extranodal NK/T-cell lymphoma is more prevalent in Asia and is closely related to Epstein Barr virus (EBV) infection.[28] In Hong Kong, extranodal NK/T-cell lymphoma is one of the more common subtypes, accounting for 8% of cases.[28] By contrast, in Europe and North America, it accounts for fewer than 1% of all lymphoid neoplasms. In our study, extranodal NK/T-cell lymphoma, nasal type, accounted for 11.0% of all lymphoid neoplasms, which is close to the rate in Korea[17] and Hong Kong.[28] These results suggest that genetic susceptibility could therefore reflect an inherited or acquired impaired immunity against EBV.

Most mature non-Hodgkin lymphomas in our study were diseases of adults (mean age, 51.6 years), whereas precursor lymphoid neoplasms were found in young individuals (mean age, 24.7 years). The mean age of mature non-Hodgkin lymphomas in our study is much lower than that of Western countries.[15] This characteristic is likely because of the higher proportions of mature T/NK-cell lymphomas in China, which tends to be diagnosed at younger ages.

In agreement with previous studies,[14,16,17,29,30] most subtypes of lymphoid neoplasms in our study showed a male predominance, with an average M/F ratio of 1.7. Among B-cell neoplasms, roughly equal numbers of male and female patients were diagnosed with follicular lymphoma and with extranodal marginal zone B-cell lymphoma, but the sex ratio for most other B-cell lymphomas showed a male predominance (Burkitt lymphoma, 5.7; mantle cell lymphomas, 2.5; plasmacytic neoplasm, 2.5; chronic lymphocytic leukemia/small lymphocytic lymphoma, 2.3). Among T/NK-cell neoplasms and Hodgkin lymphoma, male predominance was seen for extranodal NK/T-cell lymphoma, nasal type (2.6), mixed cellularity Hodgkin lymphoma (2.5), and T-lymphoblastic leukemia/lymphoma (2.4).

Compared with Western countries and Japan,[14,31,32] our study found a higher rate of extranodal lymphoma. Extranodal lymphomas were found in 2,943 (63.5%) of the 4,638 patients in our study. Of these patients, approximately one quarter had gastrointestinal tract involvement. These findings are consistent with a previous study from China[33] in which the incidence of extranodal lymphomas was 61.4% of all non-Hodgkin lymphoma, and gastrointestinal tract involvement accounted for 34.8% of the extranodal lymphoma cases. The high rate of gastrointestinal tract involvement is likely because of the high prevalence of *H pylori* infections in China.

In summary, our study showed that the epidemiologic features of lymphoid neoplasms in China are distinct from those seen in Western countries but are similar to those seen in the Far East. These results strongly suggest an etiologic heterogeneity among lymphoid neoplasms and participation of both genetic and environmental factors, thus supporting the pursuit of epidemiologic analysis by subtype.

From the [1]Department of Pathology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [2]Department of Pathology, West China Hospital, Sichuan University, Sichuan, China; [3]Department of Pathology, Changhai Hospital, Second Military Medical University, Shanghai, China; [4]Department of Pathology, Chinese PLA General Hospital, Beijing; [5]Department of Pathology, Health Science Center, Peking University, Beijing.

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Address reprint requests to Dr Chen: Department of Pathology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, 1 Shuai Fu Yuan Hu Tong, Beijing 100730, China; xhblk@163.com.

[*] These authors contributed equally to this work.

References

1. Aisenberg AC. Historical review of lymphomas. *Br J Haematol*. 2000;109:466-476.
2. National Cancer Institute sponsored study of classifications of non-Hodgkin's lymphomas: summary and description of a working formulation for clinical usage—The Non-Hodgkin's Lymphoma Pathologic Classification Project. *Cancer*. 1982;49:2112-2135.
3. Herrinton LJ. Epidemiology of the revised European-American lymphoma classification subtypes. *Epidemiol Rev*. 1998;20:187-203.

DOI: 10.1309/AJCP7YLTQPUSDQ5C

4. Harris NL, Jaffe ES, Stein H, et al. A revised European-American classification of lymphoid neoplasms: a proposal from the International Lymphoma Study Group. *Blood*. 1994;84:1361-1392.
5. Jaffe ES, Harris NL, Stein H, et al, eds. *Pathology and Genetics of Tumors of Haematopoietic and Lymphoid Tissues*. Lyon, France: IARC Press; 2001.
6. Swerdlow SH, Campo E, Harris NL, et al. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*. 4th ed. Lyon, France: IARC Press; 2008.
7. Jemal A, Siegel R, Xu J, et al. Cancer statistics, 2010. *CA Cancer J Clin*. 2010;60:277-300.
8. Parkin DM, Whelan SL, Ferlay J, et al, eds; International Agency for Research on Cancer, International Association of Cancer Registries. *Cancer Incidence in Five Continents, Vols I-VIII*. Lyon, France: IARC Press; 2005.
9. Curado MP, Edwards MP, Shin B, et al, eds; International Agency for Research on Cancer, International Association of Cancer Registries. *Cancer Incidence in Five Continents, Vol IX*. Lyon, France: IARC Press; 2007.
10. Muller AM, Ihorst G, Mertelsmann R, et al. Epidemiology of non-Hodgkin's lymphoma (NHL): trends, geographic distribution, and etiology. *Ann Hematol*. 2005;84:1-12.
11. Gross SA, Zhu X, Bao L, et al. A prospective study of 728 cases of non-Hodgkin lymphoma from a single laboratory in Shanghai, China. *Int J Hematol*. 2008;88:165-173.
12. Anderson JR, Armitage JO, Weisenburger DD. Epidemiology of the non-Hodgkin's lymphomas: distributions of the major subtypes differ by geographic locations: Non-Hodgkin's Lymphoma Classification Project. *Ann Oncol*. 1998;9:717-720.
13. Sant M, Allemani C, Tereanu C, et al. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. *Blood*. 2010;116:3724-3734.
14. Aoki R, Karube K, Sugita Y, et al. Distribution of malignant lymphoma in Japan: analysis of 2260 cases, 2001-2006. *Pathol Int*. 2008;58:174-182.
15. Morton LM, Turner JJ, Cerhan JR, et al. Proposed classification of lymphoid neoplasms for epidemiologic research from the Pathology Working Group of the International Lymphoma Epidemiology Consortium (InterLymph). *Blood*. 2007;110:695-708.
16. Morton LM, Wang SS, Devesa SS, et al. Lymphoma incidence patterns by WHO subtype in the United States, 1992-2001. *Blood*. 2006;107:265-276.
17. Yoon SO, Suh C, Lee DH, et al. Distribution of lymphoid neoplasms in the Republic of Korea: analysis of 5318 cases according to the World Health Organization classification. *Am J Hematol*. 2010;85:760-764.
18. Morton LM, Wang SS, Cozen W, et al. Etiologic heterogeneity among non-Hodgkin lymphoma subtypes. *Blood*. 2008;112:5150-5160.
19. Xiao C, Su ZL, Wu QL, et al. Clinical and pathological reassessment of 493 cases of non-Hodgkin's lymphomas according to current WHO classification of lymphoid neoplasms [in Chinese]. *Zhonghua Bing Li Xue Za Zhi*. 2005;34:22-27.
20. Yin HF, Li T, Li JX. Retrospective analysis of 304 cases of malignant lymphomas in pathology: study and practice of the WHO classification of lymphoid neoplasms [in Chinese]. *Zhonghua Yi Xue Za Zhi*. 2003;83:1556-1560.
21. Yang QP, Zhang WY, Yu JB, et al. Subtype distribution of lymphomas in Southwest China: analysis of 6,382 cases using WHO classification in a single institution. *Diagn Pathol*. 2011;6:77.
22. Luminari S, Cesaretti M, Rashid I, et al. Incidence, clinical characteristics and survival of malignant lymphomas: a population-based study from a cancer registry in northern Italy. *Hematol Oncol*. 2007;25:189-197.
23. Chang KC, Huang GC, Jones D, et al. Distribution and prognosis of WHO lymphoma subtypes in Taiwan reveals a low incidence of germinal-center derived tumors. *Leuk Lymph*. 2004;45:1375-1384.
24. Mitchell HM, Li YY, Hu PJ, et al. Epidemiology of *Helicobacter pylori* in southern China: identification of early childhood as the critical period for acquisition. *J Infect Dis*. 1992;166:149-153.
25. Carreon JD, Morton LM, Devesa SS, et al. Incidence of lymphoid neoplasms by subtype among six Asian ethnic groups in the United States, 1996-2004. *Cancer Causes Control*. 2008;19:1171-1181.
26. Sukpanichnant S. Analysis of 1983 cases of malignant lymphoma in Thailand according to the World Health Organization classification. *Hum Pathol*. 2004;35:224-230.
27. Naresh KN, Srinivas V, Soman CS. Distribution of various subtypes of non-Hodgkin's lymphoma in India: a study of 2773 lymphomas using R.E.A.L. and WHO classifications. *Ann Oncol*. 2000;11(suppl 1):63-67.
28. Jaffe ES, Chan JK, Su IJ, et al. Report of the Workshop on Nasal and Related Extranodal Angiocentric T/Natural Killer Cell Lymphomas: definitions, differential diagnosis, and epidemiology. *Am J Surg Pathol*. 1996;20:103-111.
29. Zhang YN, Zhou XG, Zhang SH, et al. Clinicopathologic study of 369 B-cell non-Hodgkin lymphoma cases, with reference to the 2001 World Health Organization classification of lymphoid neoplasms [in Chinese]. *Zhonghua Bing Li Xue Za Zhi*. 2005;34:193-197.
30. Wang JF, Wang YZ, Chen ZW, et al. Prevalence of lymphoma subtypes in Shanxi according to latest WHO classification [in Chinese]. *Zhonghua Bing Li Xue Za Zhi*. 2006;35:218-223.
31. Otter R, Gerrits WB, vd Sandt MM, et al. Primary extranodal and nodal non-Hodgkin's lymphoma. A survey of a population-based registry. *Eur J Cancer Clin Oncol*. 1989;25:1203-1210.
32. d'Amore F, Christensen BE, Brincker H, et al. Clinicopathological features and prognostic factors in extranodal non-Hodgkin lymphomas: Danish LYFO Study Group. *Eur J Cancer*. 1991;27:1201-1208.
33. Chen Y, Du H, Hu WW, et al. Clinicopathologic analysis and classification of 365 cases of non-Hodgkin's lymphomas according to the new WHO criteria. *Chin J Diagn Pathol*. 2004;11:304-307.

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