New Approach to Classifying Non-Hodgkin's Lymphomas: Clinical Features of the Major Histologic Subtypes

By James O. Armitage and Dennis D. Weisenburger for the Non-Hodgkin's Lymphoma Classification Project

Increasing knowledge about the biology of the non-Hodgkin's lymphomas has led to new approaches in classification. Rather than grouping lymphomas simply based on cell size, cell shape, and growth pattern, it is now possible to identify distinctive clinicopathologic entities. In many cases, the existence of specific immunologic and/or genetic features has confirmed the existence of these distinctive types of lymphoma. Since patients will be given these diagnoses by pathologists, it is important that clinicians be knowledgeable with regard to their clinical characteristics. The findings for the 13 most common lymphoma types that will be encountered in clinical practice are presented hem.

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NON-HODGKIN'S LYMPHOMAS are increasing in incidence and will be diagnosed in more than 55,000 patients this year in the United States." These malignancies have been increasing in incidence at a rapid pace, approximately 4% per year since 1950.[1] and the mortality rate has been increasing in a parallel manner.

The classification of non-Hodgkin's lymphoma has been modified several times in this century and has often been a source of confusion and frustration for clinicians. Gall and Mallory[3] proposed the first widely used lymphoma classification. but this classification was not useful clinically. In the 1950s, Rappaport et al[4] recognized the importance of lymphoma-cell growth pattern and subdivided the non-Hodgkin's lymphomas based on this characteristic. which led to the clinically relevant classification that bears Rappaport's name. In the 1970s. it became apparent that non-Hodgkin's lymphomas were tumors of the immune system and were derived from T or B lymphocytes. This knowledge led to the classifications of Lukes and Collins[5] and Lennert et al[6,7] (Kiel classification). The Working Formulation was proposed in 1982 in an attempt to unify the complex and confusing lymphoma terminology and improve communication between pathologists and clinicians in different parts of the world.[8] The Working Formulation became the most popular classification used in North America, whereas the Kiel classification dominated clinical practice in Europe.

The 1980s and 1990s have been a time of rapid increase in our knowledge of the biology of the immune system. New insights into immunology and genetics have allowed the recognition of a number of previously unrecognized types of non-Hodgkin's lymphoma: In some cases, biologic observations confirmed the existence of entities that were suspected on clinical and/or morphologic grounds. In 1994, the International Lymphomas Study Group recognized the existence of these new entities and proposed a new classification that has been referred to as the Revised European-American Lymphoma (REAL)classification.[9] These observations will form the basis for a new World Health Organization classification of lymphomas that will soon become available.

A recent retrospective study of the REAL classification confirmed the clinical relevance of this approach.[10] This study was performed in eight countries throughout the world and demonstrated that this new approach could be applied more accurately than previous classification systems.[10] The data from that study form the basis of this report.

METHODS OF THE INTERNATIONAL LYMPHOMA CLASSIFICATION PROJECT

The methods used have been published in detail[10] and are summarized here. Nine institutions in eight countries were chosen to provide up to 200 consecutive cases of previously untreated non-Hodgkin's lymphoma that were representstive of the geographic region during the time between January 1, 1988 and December 31. 1990. The first 200 cases at each site that fulfilled the following criteria were selected for the study. In all cases. tissue biopsy samples that wen? adequate for diagnosis and classification were required and all diagnostic pathology materials obtained before initial therapy, including positive bone marrow specimens. were included in the pathology review. Immunologic characterization as to B- or T-cell origin. by whatever means in use at the institution, was also required in all cases. Clinical data were also required in all cases. The nine study sites provided a total of 1.403 cases.

At each institution. the pathology slides and reports for each case were carefully reviewed by a designated site

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pathologist. Five expert hematopathologists then traveled as a group to each of the nine sites to review and classify each case in each of the three major classifications.[7-9] In each case, the expert was then presented with the immunophenotypic profile, along with any available cytogenetic and molecular genetic data, and the immunostains and/or flow cytometry report. After review. a second diagnosis was rendered in each classification. In addition to the independent diagnoses rendered by each of the expert pathologists. a consensus diagnocis mas also reached in each case.

The International Prognostic Index" was used to stratify patients within the various disease entities. Treatment outcome was measured using failure-free survival and overall survival. Failure-free survival was defined as the time from diagnosis to the first occurrence of progression. relapse after response. or death from any cause. Follow-up evaluation of patients who did not experience one of these events was censored at the date of last contact Overall survival was measured from diagnosis to death from any cause. with surviving patient follow-up data censored at the last contact date. Estimates of failure-free survival and overall survival distribution were calculated using the method of Kaplan and Meier.[12] Time-to-event distributions were compared using the log-rank test."

MAJOR LYMPHOMA SUBTYPES

The I3 most frequent clinical entities that are recognized in the new lymphoma classification are diffuse large B-cell lymphoma, follicular lymphoma, small lymphocytic lymphoma. mantle cell lymphoma, peripheral T-cell lymphoma, marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) type, primary mediastinal large B-cell lymphoma. anaplastic large T-/null-cell lymphoma, lymphoblastic lymphoma (T/B), Burkitt-like lymphoma, marginal zone B-cell lymphoma of nodal type. lymphoplasmacytic lymphoma. and Burkitt's lymphoma. These are the diagnoses that will be provided by pathologists to clinicians who care for patients with lymphoma for the ensuing years. Therefore, it is important that clinicians be acquainted with the clinical characteristics of these lymphoma types. Summaries of their frequency. clinical characteristics, biologic characteristics, and clinical course are presented in the following tables for easy reference.

The lymphomas are presented in order of their frequency of occurrence. Composite lymphomas are excluded, resulting in a total of less than 100%. A previous study has shown that expert hematopathologists can diagnose most subtypes accurately (ie, > 85%) when adequate material. immunophenotype. and clinical information are available.[10] The exceptions are Burkitt-like lymphoma: nodal marginal zone lymphoma. and lymphoplasmacytic lymphoma. In these subtypes. lack of clear definitions are probably at fault. Burkitt-like lymphoma is probably a mixture of Burkitt's lymphoma and a variant more closely related to diffuse large B-cell lymphoma. with the former more frequent in pediatric cases and the latter more likely in older adults.

In conclusion. it is extremely important that clinicians recognize that the correct diagnosis of each of these lymphoma entities is only one of many important pieces of information necessary for planning patient care. The clinical prognostic characteristics as identified in the International Prognostic Index" are also vitally important. since the prognosis of any particular patient is related to the biology of the specific lymphoma type and the patient's clinical prognostic characteristics. Combining this information will facilitate an accurate estimate of the prognosis and makes possible the development of a rational treatment plan for an individual patient.

This progress is not the last change in the classification of lymphomas we will see. New insights into the biology of lymphoma will continue to elucidate new clinicopathologic entities. Certainly, the large group of diffuse large B-cell lymphomas will be subdivided into more specific entities. The future for clinical investigation in the non-Hodgkin's lymphomas is promising. Hopefully, new insights into the biology of this group of disorders will lead to improved therapies.

APPENDIX
Study Participants

The pathologists and clinicians at each institution were as follows Wing C Chan and James O Armitage (Omaha, NE). Rand) Gascoyne and Joseph Connors (Vancouver, Canada). Pauline Close and Peter Jacobs (Capetown, South Africa); Andrew Norton and T. Andreu Lister (London, United Kingdom). Ennio Pedrinis and Franco Cavalli (Locarno, Switzerland), Francoise Berger and Bertrand Coiffier (Lyon, France). Faith Ho and Raymond Liang (Hong Kong); German Ott/Alfred Schauer and Wolfgang Hiddemann (Würzburg/Göttingen, Germany)

The five visiting expert hematopathologists were as follows Jacques Diebold (Pans France). Kenneth A MacLennan (Leeds, United Kingdom), H Konrad Müller-Hermelink (Würzburg. Germany). Bharat N Nathwani (Los Angeles. CA). and Dennis D Weisenburger (Omaha, NE)

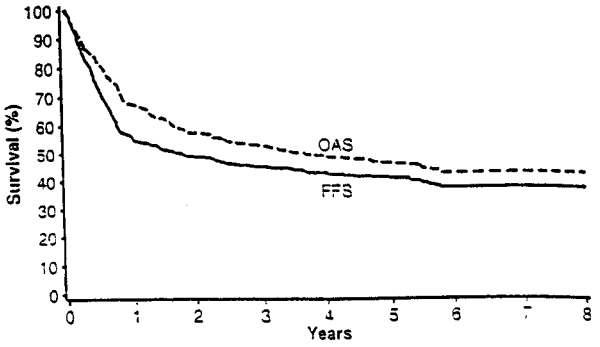
Nancy L Harris (Boston. MA) participated as a consultant regarding application of the International Lymphoma Stud) Group classification James R. Anderson (Omaha. NE) and Pascal Roy (Lyon. France) provided statistical expertise regarding the study design and data analysis

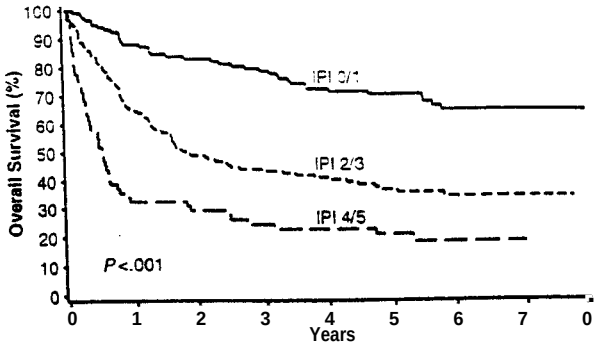
DIFFUSE LARGE B-CELL LYMPHOMA

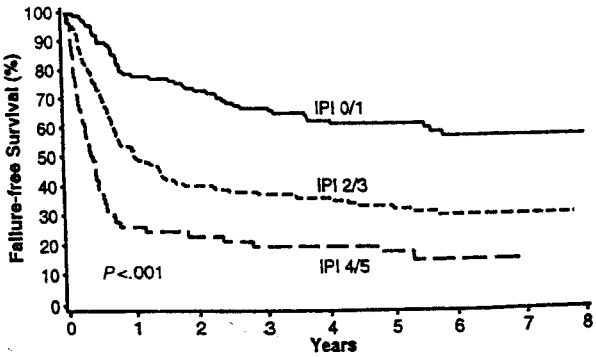
This is the most frequently occurring non-Hodgkin's lymphoma. It contains predominantly lymphomas classified as diffuse large cell, diffuse mixed cell, or immunoblastic in the Working Formulation and lymphomas classified as diffuse centroblastic, diffuse centroblastic/centrocytic, and immunoblastic in the Kiel classification. In the Non-Hodgkin's Lymphoma Classification Project using histology, immunophenotyping, and clinical information, diffuse large B-cell lymphoma was diagnosed accurately 87% of the time. Immunophenotyping improved the accuracy of diagnosis by **14%.** Diffuse large B-cell lymphoma is a chemotherapy-curable lymphoma.

Frequency	31%(n = 422)
Age, years	
Median	64
Range	14-98
Male	55%
Stage	
I	12%
IE	13%
II	13%
IIE	16%
III	13%
IV	33%
B symptoms	33%
Elevated LDH	53%
Kamahky score ≤ 70	24%
Tumor bulk, cm	
≥ 5	76%
≥ 10	30%
Any extranodal site	71%
> 1 extranodal site	29%
Bone marrow involved	16%
GI tract involved	18%
IPI score	
0/1	35%
2/3	46%
4/5	19%
Typical immunophenotype	$CD20^+$, $CD3^-$
Characteristic cytogenetics	t(14;18)(q32;q21)
	t(8;14)(q24;q32)
	t(3;14)(q27;q32)
Oncogenes frequently involved	*BCL-2*
	C-MYC
	BCL-6

Abbreviations: LDH, lactate dehydrogenase; GI, gastrointestinal; IPI, International Prognostic Index



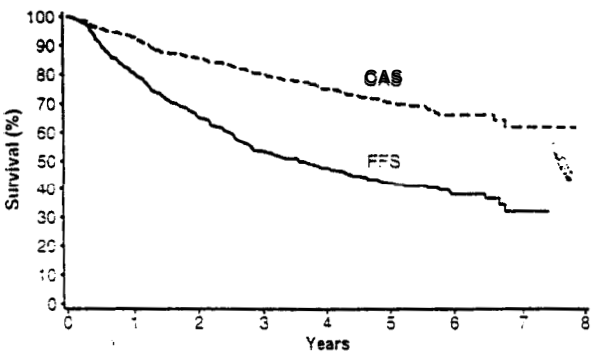


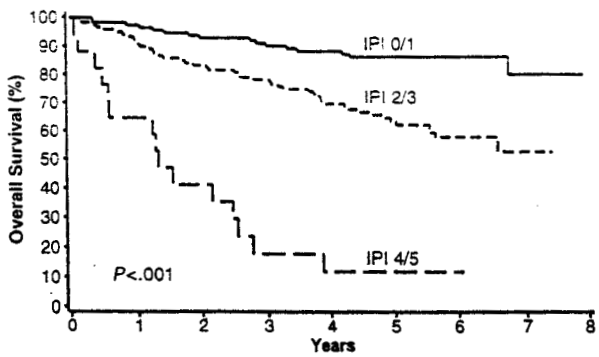


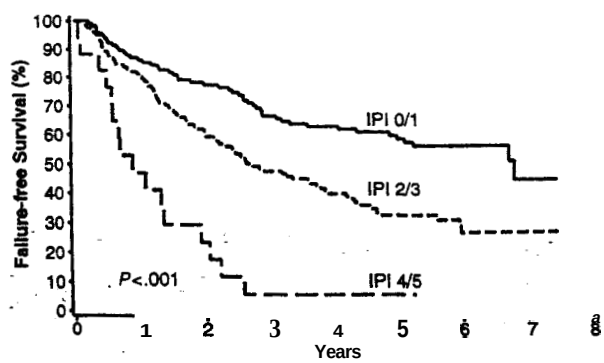
FOLLICULAR LYMPHOMA

The combined group of follicular lymphoma makes up the second most frequent type of non-Hodgkin's lymphoma. These lymphomas are classified as follicular small cleaved cell, follicular mixed cell, and follicular large cell lymphoma in the Working Formulation and predominantly as follicular centroblastic/centrocytic or follicular centroblastic lymphoma in the Kiel classification. In the Non-Hodgkin's Lymphoma Classification Project using histology, immunophenotyping, and clinical information. follicular lymphoma was diagnosed accurately 94% of the time. However, subtyping of follicular lymphomas was less accurate. Immunophenotyping improved the accuracy of diagnosis by only 1%. Although there was an overall 5-year survival rate of approximately 72%, patients with a high International Prognostic Index score had a poor survival.

Frequency	22% (n = 306)
Age, years	
Median	59
Range	23-90
Male	42%
Stage	
I	16%
IE	2%
II	11%
IIE	4%
III	16%
IV	51%
Symptoms	28%
Elevated LDH	30%
Karnofsky score ≤ 70	9%
Tumor bulk, cm	
≥ 5	61%
≥ 10	28%
Only extranodal site	64%
1 extranodal site	23%
Bone marrow involved	42%
GI tract involved	4%
IPI score	
0/1	45%
2/3	48%
4/5	7%
Typical immunophenotype	CD20+, CD3- CD10+, CD5-
Characteristic cytogenetics	t(14;18)(q32;q21)
Oncogenes involved	*BCL-2*



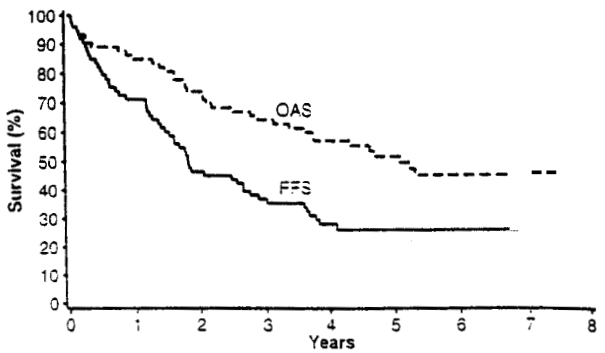


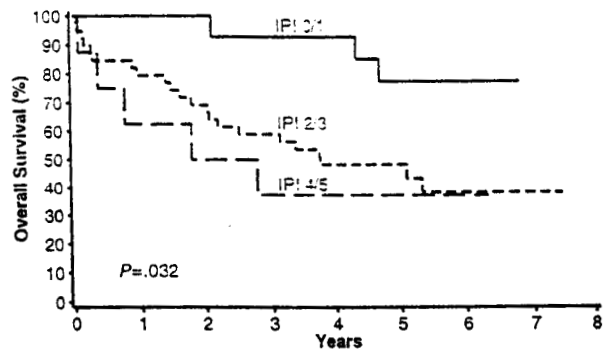


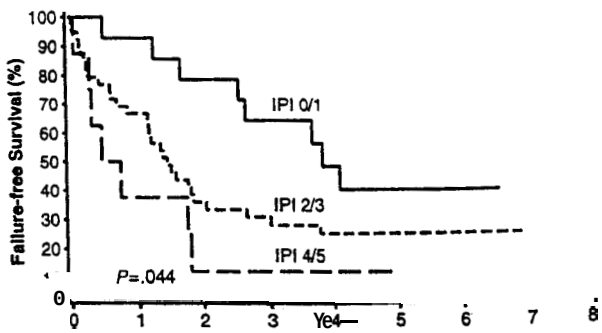
SMALL LYMPHOCYTIC LYMPHOMA

Small lymphocytic lymphoma makes up *6%* of all non-Hodgkin's lymphomas. Since this often is the tissue manifestation of chronic lymphocyte leukemia, if patients who present with leukemia and predominantly blood and bone marrow involvement are included, the actual incidence would be higher. It contains predominantly lymphomas classified as small lymphocytic in the Working Formulation, but is called chronic lymphocytic leukemia in the Kiel classification. In the Non-Hodgkin's Lymphoma Classification Project using histology, immunophenotyping, and clinical information, small lymphocytic lymphoma was diagnosed accurately **87%** of the time. Immunophenotyping added only 3% to the diagnostic accuracy.

Frequency	6%(n = 88)
Age, years	
Median	65
Range	21-91
Male	53%
Stage	
I	4%
IE	0%
II	2%
IIE	3%
III	8%
IV	83%
B symptoms	33%
Elevated LDH	41%
Karnofsky score ≤ 70	11%
Tumor bulk, cm	
≥ 5	59%
≥ 10	13%
Any extranodal site	80%
> 1 extranodal site	29%
Bone marrow involved	72%
GI tract involved	3%
IPI score	
0/1	23%
2/3	64%
4/5	13%
Typical immunophenotype	CD20+, CD3-, CD10-, CD5+, CD23+
Characteristic cytogenetics	del (13q), +12
Oncogenes involved	Unknown



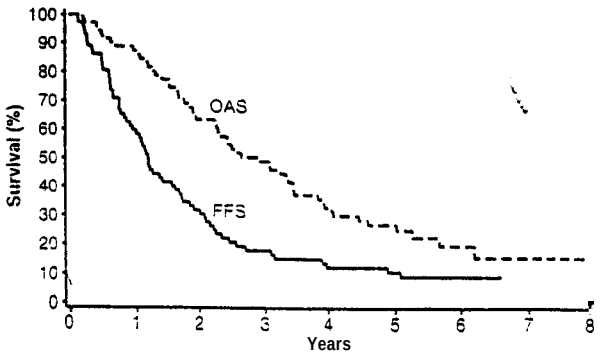


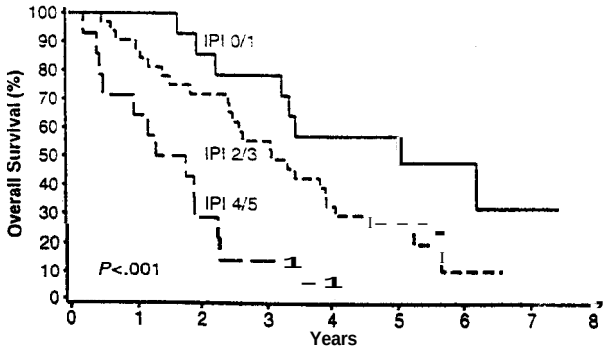


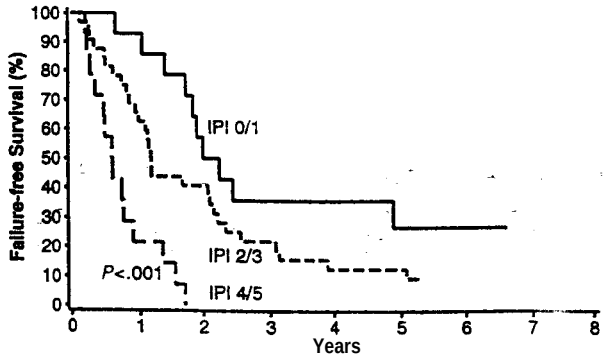
MANTLE CELL LYMPHOMA

Mantle cell lymphoma is among the most frequent of the newly recognized subtypes of non-Hodgkin's lymphoma. In the Working Formulation, mantle cell lymphoma is classified as diffuse small cleaved cell lymphoma most frequently, but also as follicular small cleaved cell lymphoma, small lymphocytic lymphoma, diffuse large cell lymphoma, and lymphoblastic lymphoma. In the Kiel classification, this lymphoma is most frequently classified as centrocytic lymphoma or centrocytoid centroblastic lymphoma. In the Non-Hodgkin's Lymphoma Classification Project using histology, immunophenotyping, and clinical information, mantle cell lymphoma was diagnosed accurately 87% of the time. Immunophenotyping added 10% to the accuracy of diagnosis. Patients with mantle cell lymphoma have a striking male predominance, usually advanced disease, and a poor overall and failure-free survival, which belies the good survival usually anticipated with small cell lymphomas.

Frequency	6%(n = 83)
Age, years	
Median	63
Range	37-02
Male	74%
Stage	
i	10%
f	3%
II	6%
HE	1%
III	9%
IV	71%
symptoms	28%
evated LDH	40%
rnofsky score ≤ 70	21%
mor bulk, cm	
≥ 5	69%
≥ 10	25%
y extranodal site	81%
1 extranodal site	51%
ne marrow involved	64%
tract involved	9%
score	
0/1	23%
2/3	54%
4/5	23%
ical immunophenotype	CD20⁺, CD⁻ CD10⁻, CD5⁺ CD23⁻, PRAD1⁺
aracteristic cytogenetics	t(11;14)(q13;q32)
ogenes involved	*BCL-1*(PRAD1)



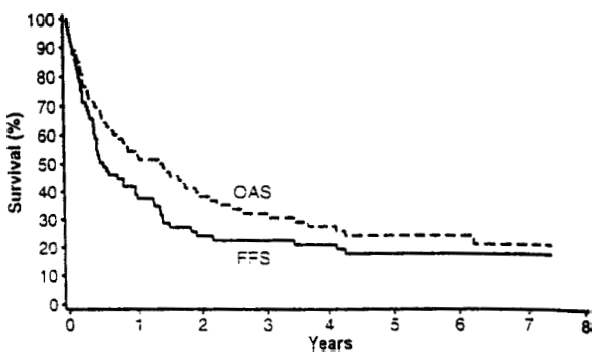


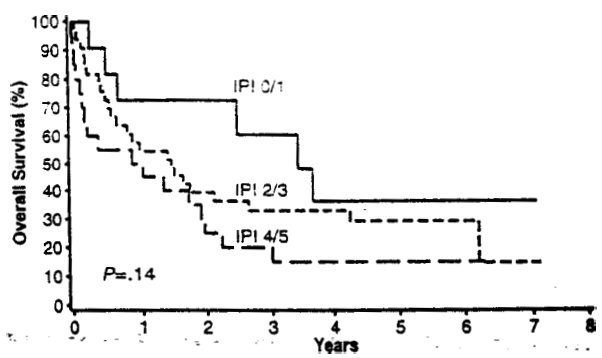


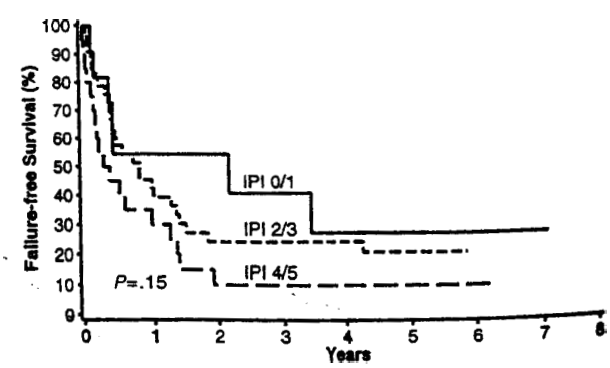
PERIPHERAL T-CELL LYMPHOMA

The subgroup of peripheral T-cell lymphoma not otherwise specified represents the largest group of T-cell lymphomas in the REAL classification. For this report, angiocentric nasal lymphomas and human T-lymphotropic virus type 1 (HTLV-1)–associated lymphomas were excluded, which makes the results typical for those seen in most western countries. Peripheral T-cell lymphoma includes lymphomas with a wide variety of histologic appearances. Tumors in this subgroup were classified as diffuse small cleaved cell, diffuse mixed cell, diffuse large cell, and immunoblastic in the Working Formulation. In the Non-Hodgkin's Lymphoma Classification Project using histology, immunophenotyping, and clinical information, peripheral T-cell lymphoma was diagnosed accurately 86% of the time. However, this was only true when immunophenotyping was available. Immunophenotyping improved the accuracy of diagnosis by 45%. Peripheral T-cell lymphomas have one of the lowest overall and failure-free survival rates.

Frequency	6%(n = 76)
Age, years	
Median	61
Range	17-90
Male	55%
Stage	
I	1%
IE	7%
II	6%
IIE	6%
III	15%
IV	65%
B symptoms	50%
Elevated LDH	64%
Karnofsky score ≤ 70	32%
Tumor bulk, cm	
≥ 5	65%
≥ 10	12%
Any extranodal site	82%
> 1 extranodal site	45%
Bone marrow involved	36%
GI hod involved	15%
IPI score	
0/1	17%
2/3	52%
4/5	31%
Typical immunophenotype	CD20 , CD3
Characteristic cytogenetics	Variable
Oncogenes involved	Unknown



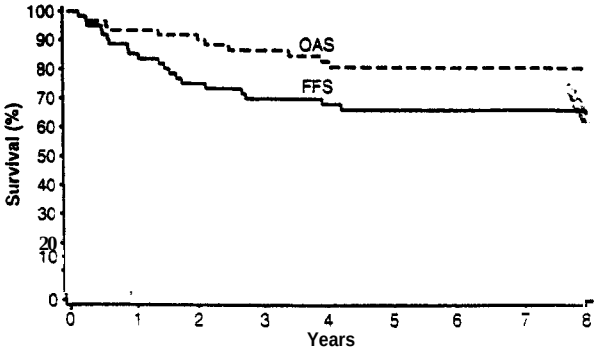


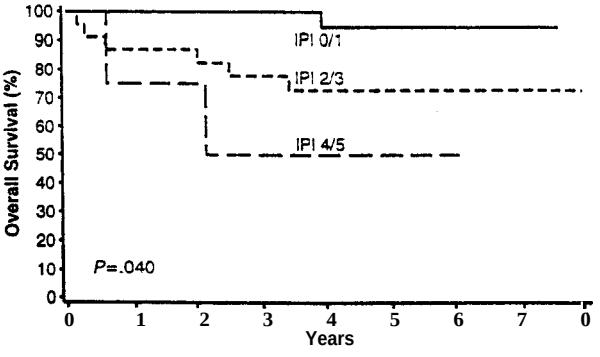


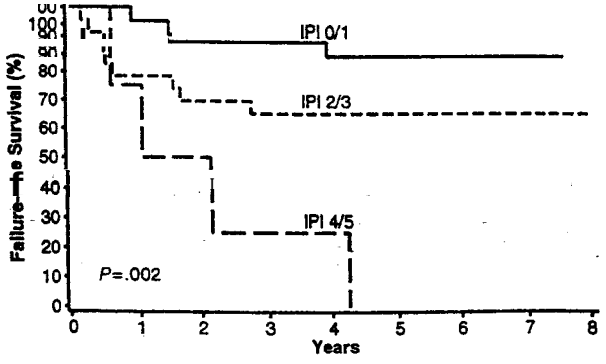
MARGINAL ZONE B-CELL LYMPHOMA, MALT TYPE

This is among the most frequent of the newly recognized subtypes of non-Hodgkin's lymphoma. In this report, only low-grade **MALT** lymphomas are included. In the Working Formulation, **MALT** lymphomas were most commonly diagnosed as small lymphocytic lymphoma or small lymphocytic lymphoma with plasmacytoid characteristics, although some were called diffuse small cleaved cell lymphoma. In the Non-Hodgkin's Lymphoma Classification Project using histology, immunophenotyping. and clinical information, marginal zone lymphoma of the **MALT** type was diagnosed accurately 86% of the time. Immunophenotyping added only 2% to the accuracy of the diagnosis. **MALT** lymphomas have one of the highest survivals of any subtype and even patients with a high International Prognostic Index score have a 5-year overall survival rate of 40%.

Frequency	5%(n = 72)
Age, years	
Median	60
Range	19-91
Male	48%
Stage	
I	0%
IE	39%
II	0%
IIE	28%
III	2%
IV	31%
B symptoms	19%
Elevated LDH	27%
Karnofsky score ≤ 70	15%
Tumor bulk, cm	
≥ 5	68%
≥ 10	8%
Any extranodal site	98%
> 1 extranodal site	31%
Bone marrow involved	14%
GI tract involved	50%
PI score	
0/1	44%
2/3	48%
4/5	8%
Typical immunophenotype	$CD20^+$, $CD3^-$, $CD10^-$, $CD5^-$, $CD23^-$
Characteristic cytogenetics	t(11;18)(q21;q21) +3,+18
Oncogenes involved	Unknown



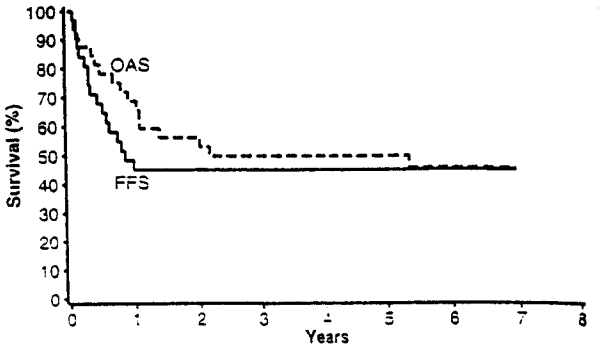


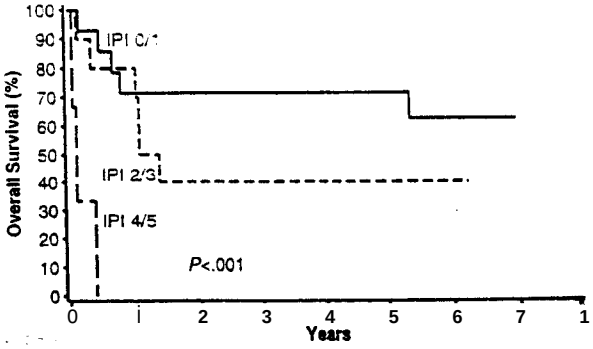


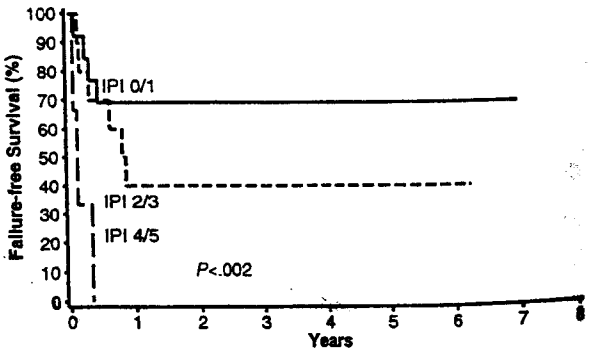
PRIMARY MEDIASTINAL LARGE B-CELL LYMPHOMA

Primary mediastinal large B-cell lymphoma represents a diffuse large B-cell lymphoma that cannot be distinguished histologically, but presents as a clinical syndrome due to the presence of a large mediastinal mass. This syndrome is clinically distinctive in that it occurs predominantly in younger patients and has a female predominance. In the International Non-Hodgkin's Lymphoma Classification Project using histology, immunophenotyping, and clinical information, mediastinal large B-cell lymphoma was diagnosed accurately 85% of the time. Immunophenotyping added 7% to the accuracy of diagnosis. The clinical course of these patients differed little from that of other patients with diffuse large B-cell lymphoma, although mediastinal radiotherapy may play an important role in their treatment.

Frequency	2% (n = 33)
Age, years	
Median	37
Range	21-84
Male	34%
Stage	
I	10%
IE	0%
II	34%
IIE	22%
III	3%
IV	31%
B symptoms	38%
Elevated LDH	81%
Karnofsky score ≤ 70	22%
Tumor bulk, cm	
a 5	90%
≥ 10	52%
Any extranodal site.	56%
> 1 extranodal site	19%
Bone marrow involved	3%
GI tract involved	0%
IPI score	
0/1	52%
2/3	37%
4/5	11%
Typical immunophenotype	CD20+, CD3-
Characteristic cytogenetics	Variable
Oncogenes involved	Unknown



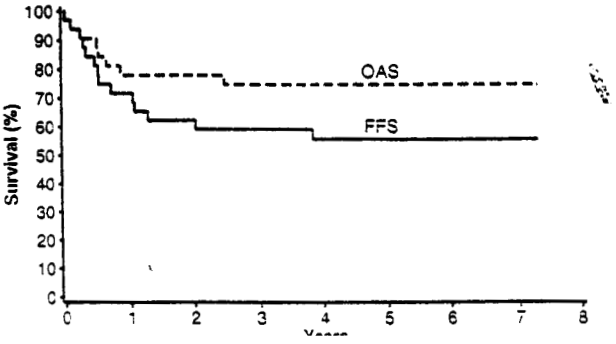


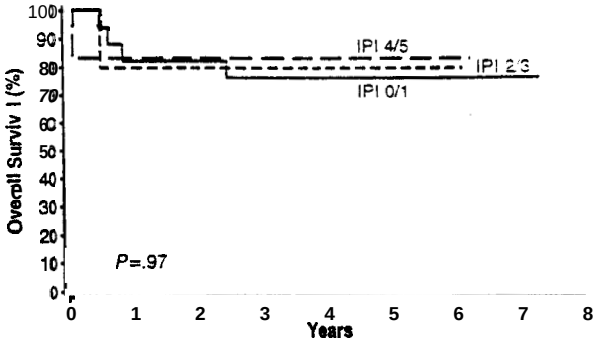


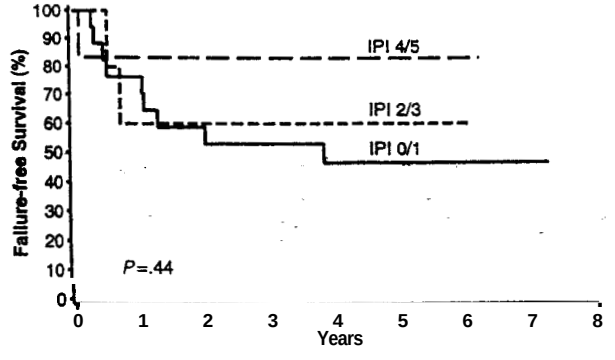
ANAPLASTIC LARGE T-/NULL-CELL LYMPHOMA

Anaplastic large T-hull-cell lymphoma represents the second most common T-cell lymphoma in the REAL classification. Patients with anaplastic large T-hull-cell lymphoma were often classified as having anaplastic carcinoma or an undifferentiated malignant neoplasm before staining for the CD30 antigen and discovery of the characteristic chromosomal translocation between chromosomes 2 and 5 led to its recognition as a distinctive non-Hodgkin's lymphoma. In the REAL classification, only anaplastic large-cell lymphomas with T or null immunophenotype are included in this category. In the Non-Hodgkin's Lymphoma Classification Project using histology, immunophenotyping, and clinical information, anaplastic large T-hull-cell lymphoma was diagnosed accurately *85%* of the time. Immunophenotyping contributed 39% to the accuracy of diagnosis. Patients with this subtype **of** lymphoma have a young median age and a male predominance, and have the best overall and failure-free survival rates of any large cell lymphoma.

Frequency	2% (n = 33)
Age, years	
Median	34
Range	10-100
Male	69%
Stage	
I	16%
IE	3%
II	22%
IIE	10%
III	10%
IV	39%
B symptoms	53%
Elevated LDH	45%
Karnofsky score ≤ 70	26%
Tumor bulk, cm	
≥ 5	76%
≥ 10	17%
Any extranodal site	59%
> 1 extranodal site	28%
Bone marrow involved	13%
GI tract involved	9%
IPI score	
0/1	61%
2/3	18%
4/5	21%
Typical immunophenotype	CD20 , $CD3^+$ $CD30^+$, $CD15^-$ EMA^+, ALK^+
Characteristic cytogenetics	t(2;5)(p23;q35)
Oncogenes involved	*ALK*



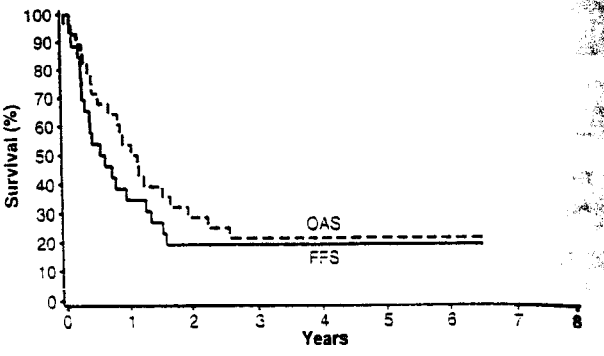


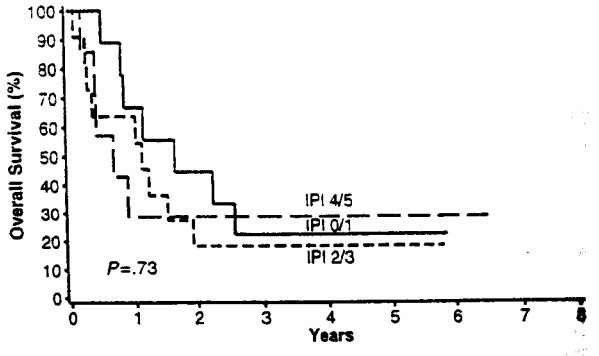


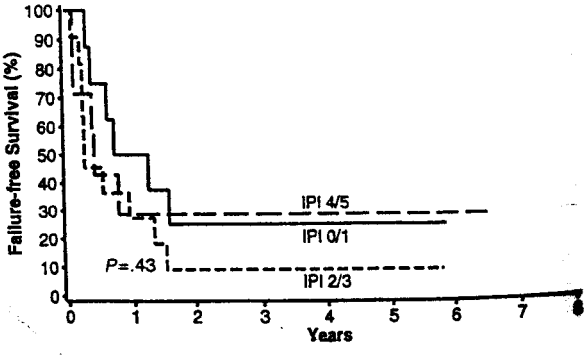
LYMPHOBLASTIC LYMPHOMA (T/B)

The lymphoblastic lymphomas make up a small proportion of all non-Hodgkin's lymphomas and are associated with a low median age, male predominance, and advanced stage. In the Non-Hodgkin's Lymphoma Classification Project using histology, immunophenotyping, and clinical information, lymphoblastic lymphomas were diagnosed accurately **89%** of the time. Immunophenotyping contributed 35% to the accuracy of diagnosis. This is an aggressive lymphoma with **low** overall and failure-free survival rates.

Frequency	2% (n = 26)
Age, years	
Median	20
Range	4-65
Male	64%
Stage	
I	0%
IE	0%
II	11%
IIE	0%
III	14%
IV	75%
B symptoms	21%
Elevated LDH	70%
Karnofsky score ≤ 70	29%
Tumor bulk, cm	
≥ 5	06%
≥ 10	32%
Any extranodal site	82%
> 1 extranodal site	43%
Bone marrow invoked	50%
GI tract involved	A%
IPI score	
0/1	33%
2/3	41%
4/5	26%
Typical immunophenotype	CD20⁻, CD3⁺
(T-cell only)	Tdt⁺
Characteristic cytogenetics	Variable
Oncogenes involved (T-cell only)	*TCL1*-3



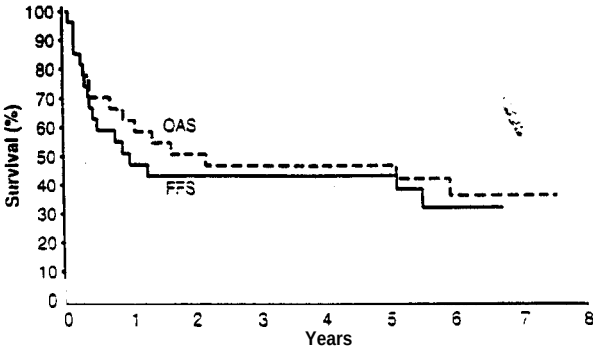


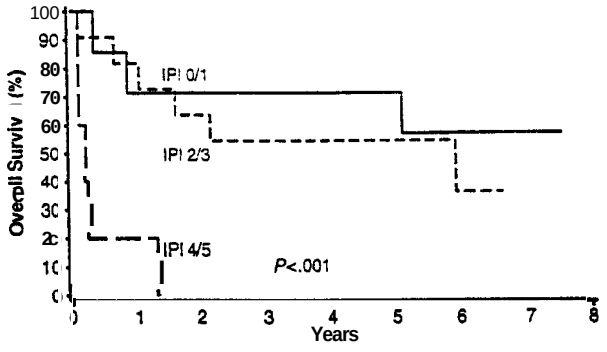


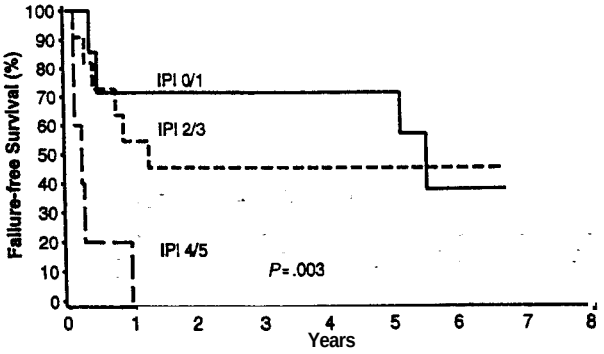
BURKITT-LIKE LYMPHOMA

Burkitt-like lymphomas could not be diagnosed accurately in the Non-Hodgkin's Lymphoma Classification Project. Using histology, immunophenotyping, and clinical information, the diagnostic accuracy was only 53%. The problem was the lack of precise definitions to separate this group from the diffuse large B-cell category or true Burkitt's lymphoma. The median age and clinical characteristics of this subgroup were intermediate between patients with diffuse large B-cell lymphoma and Burkitt's lymphoma, but more closely approximated diffuse large B-cell lymphoma.

Frequency	2% (n = 29)
Age, years	
Median	57
Range	20-92
Male	59%
Stage	
I	19%
IE	7%
II	4%
IIE	22%
III	7%
IV	41%
B symptoms	39%
Elevated LDH	61%
Karnofsky score ≤ 70	27%
Tumor bulk, cm	
≥ 5	92%
≥ 10	42%
Any extranodal site	79%
>1 extranodal site	43%
Bone marrow involved	21%
GI tract involved	29%
IPI score	
0/1	30%
2/3	48%
4/5	22%
Typical immunophenotype	CD20+, CD3- CD10-, CD5- Tdt-
Characteristic cytogenetics	t(14;18)(q32;q21) t(8;14)(q24;q32)
Oncogenes involved	*BCL-2*, *C-MYC*



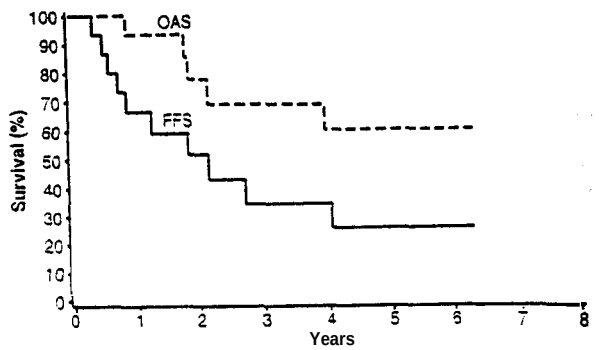


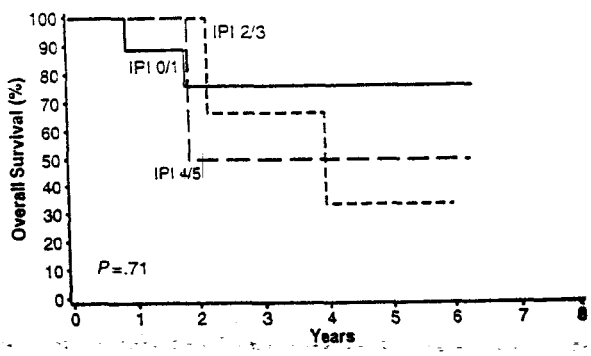


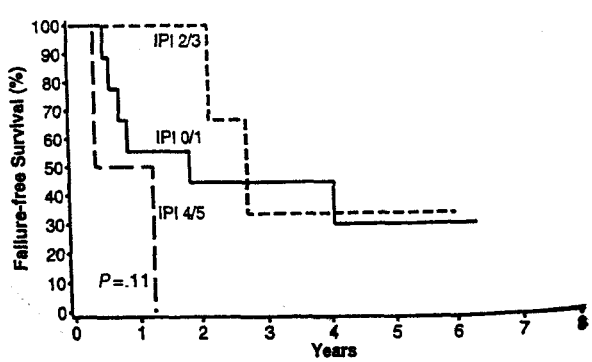
MARGINAL ZONE B-CELL LYMPHOMA, NODAL TYPE

Marginal zone B-cell lymphoma of the nodal type is one of the new forms of non-Hodgkin's lymphoma not recognized in the Working Formulation. In the Working Formulation, these lymphomas were most commonly found in the small lymphocytic subcategory, but were also sometimes diagnosed as diffuse small cleaved cell lymphoma, small lymphocytic lymphoma with plasmacytoid characteristics, or diffuse mixed cell lymphoma. In the non-Hodgkin's Lymphoma Classification Project using histology, immunophenotype, and clinical information, marginal zone B-cell lymphoma of the nodal type was diagnosed accurately **63%** of the time. Immunophenotyping added 8% to the accuracy of diagnosis. These patients had an overall and failure-free survival similar to small lymphocytic lymphoma. These lymphomas are often currently diagnosed as monocytoid B-cell lymphoma.

Frequency	1%(n = 20)
Age, years	
Median	58
Range	27-90
Mole	42%
Stage	
I	13%
IE	0%
II	13%
IIE	0%
III	34%
IV	40%
B symptoms	37%
Elevated LDH	40%
Karnofsky score ≤ 70	7%
Tumor bulk, cm	
≥ 5	36%
≥ 10	0%
Any extranodal site	47%
> 1 extranodal site	16%
Bone marrow involved	32%
GI tract involved	5%
IPI score	
0/1	60%
2/3	27%
4/5	13%
Typical immunophenotype	$CD20^+$, $CD3^-$ $CD10^-$, $CD5^-$ $CD23^-$
Chorocteristiccytogenetics	+3,+18
Oncogenes involved	Unknown





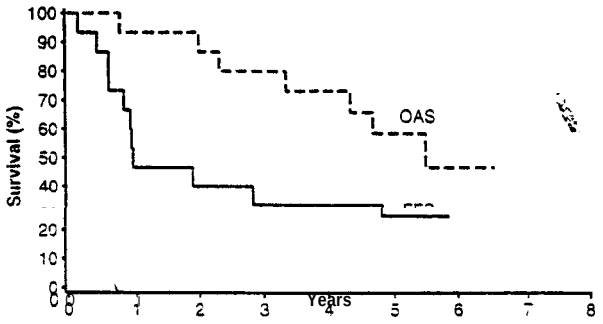


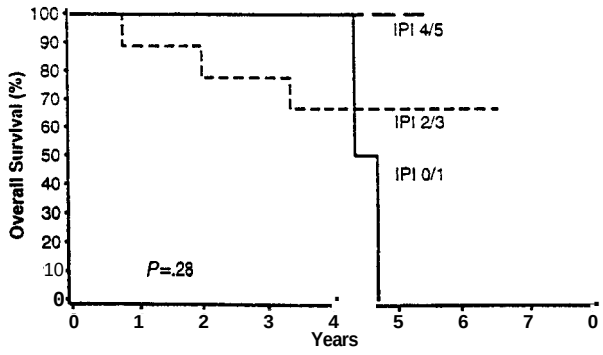
LYMPHOPLASMACYTIC LYMPHOMA

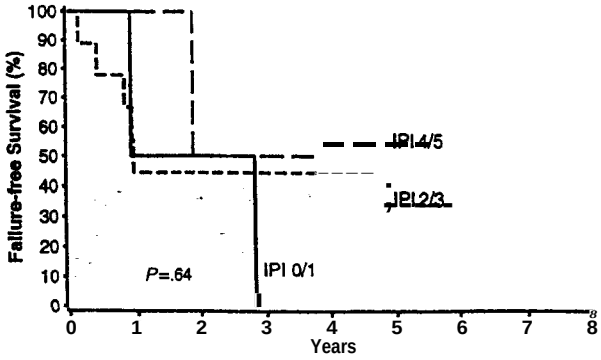
Lymphoplasmacytic lymphoma is an uncommon diagnosis in the **REAL** classification, and includes patients that might **also** be diagnosed with Waldenstrom's macroglobulinemia. In the Non-Hodgkin's Lymphoma Classification Project using histology, immunophenotyping, and clinical information, lymphoplasmacytic lymphoma was diagnosed accurately 56% of the time. Immunophenotyping contributed 3% to the diagnostic accuracy. The clinical characteristics of this lymphoma were similar to those of **small** lymphocytic lymphoma.

Frequency	1% (n = 15)
Age, years	
Median	63
Range	37-81
Male	53%
Stage	
I	7%
IE	0%
II	0%
IIE	13%
III	7%
IV	73%
B symptoms	13%
Elevated LDH	15%
Karnofsky score ≤ 70	27%
Tumor bulk, cm	
≥ 5	50%
≥ 10	25%
Any extranodal site	100%
> 1 extranodal site	40%
Bone marrow involved	73%
GI tract involved	7%
IPI score	
0/1	16%
2/3	69%
4/5	15%
Typical immunophenotype	$CD20^+$, $CD3^-$ $CD10^-$, $CD5^-$ $CD23^-$, cyto Ig^+
Characteristic cytogenetics	t(9;14)(p13;q32) del 6(q23)
Oncogenes involved	Unknown

Abbreviation: cyto Ig, cytoplasmic immunoglobulin.



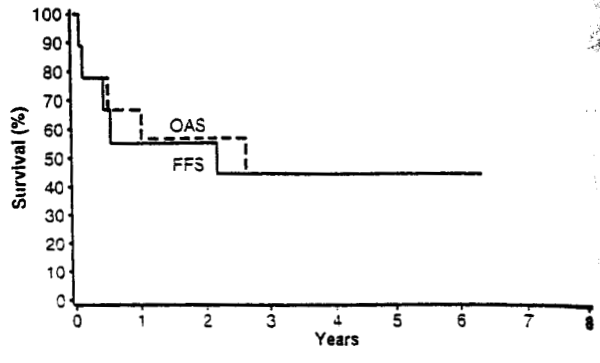


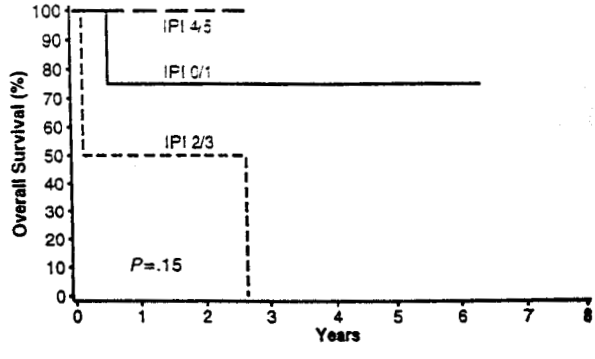


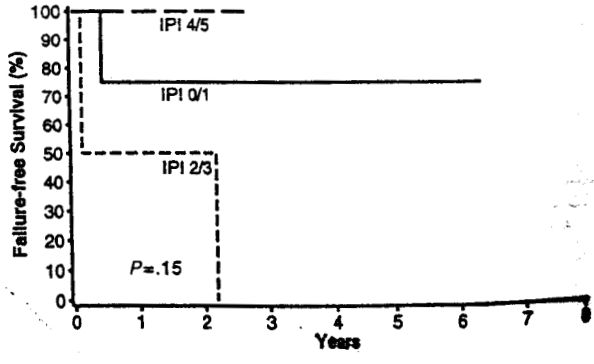
BURKITT'S LYMPHOMA

This is a rare lymphoma in a clinical series that includes predominantly adults. Although this is a highly aggressive and clinically distinctive lymphoma requiring unique treatment approaches, the overall and failure-free survival rates are similar to diffuse large B-cell lymphoma.

Frequency	<1% (n = 10)
Age, years	
Median	31
Range	2-60
Male	89%
Stage	
I	25%
IE	12%
II	13%
IIE	12%
III	0%
IV	38%
B symptoms	22%
Elevated LDH	75%
Karnofsky score ≤ 70	44%
Tumor bulk, cm	
≥ 5	56%
≥ 10	22%
Any extranodal site	78%
< 1 extranodal site	56%
Bone marrow involved	33%
GI tract involved	11%
IPI scare	
0/1	57%
2/3	29%
4/5	14%
Typical immunophenotype	CD20⁺, CD3⁻ CD10⁺, CD5⁻ Tdt⁻
Characteristic cytogenetics	t(8;14)(q24;q32) t(2;8)(p12;q24) t(8;22)(q24;q11)
Oncogenes involved	C-MYC







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