

Non-Hodgkin Lymphoma Around the World: Distribution of Major Types Differs by Geographic Region

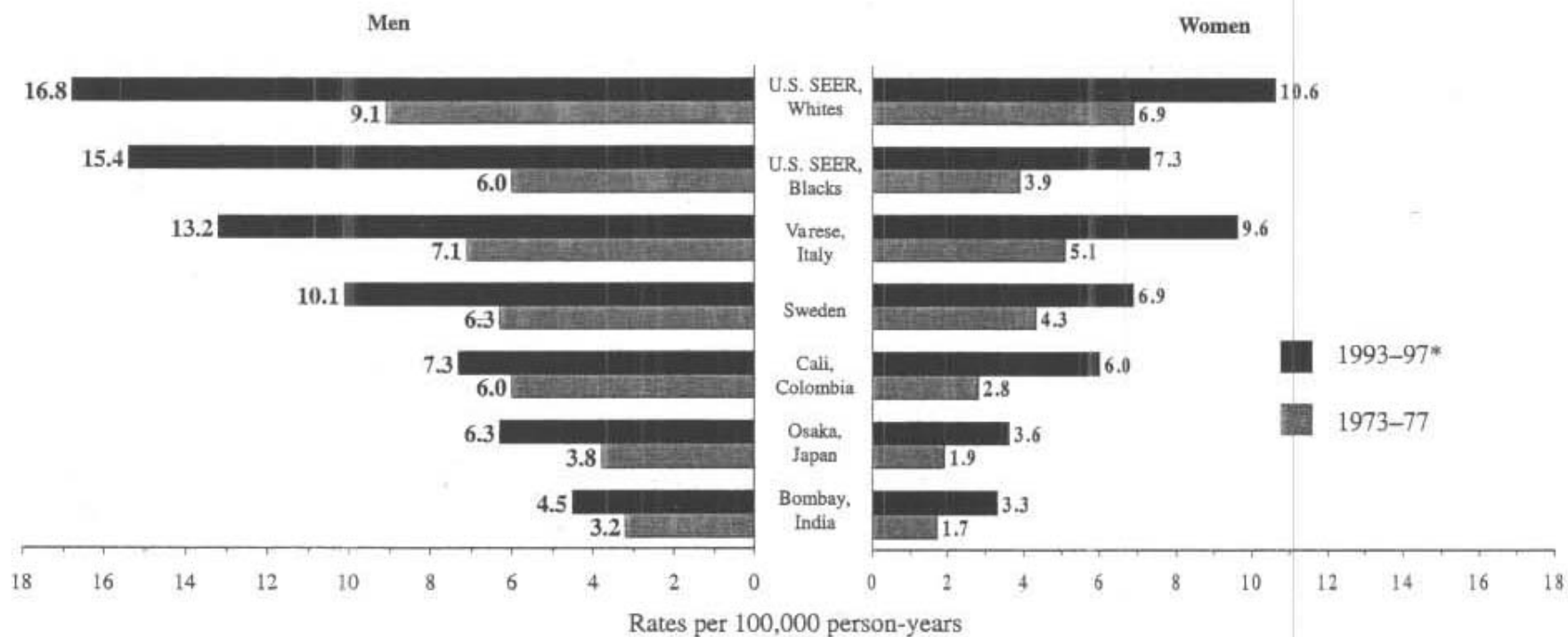
Dennis D. Weisenburger, M.D.

for the

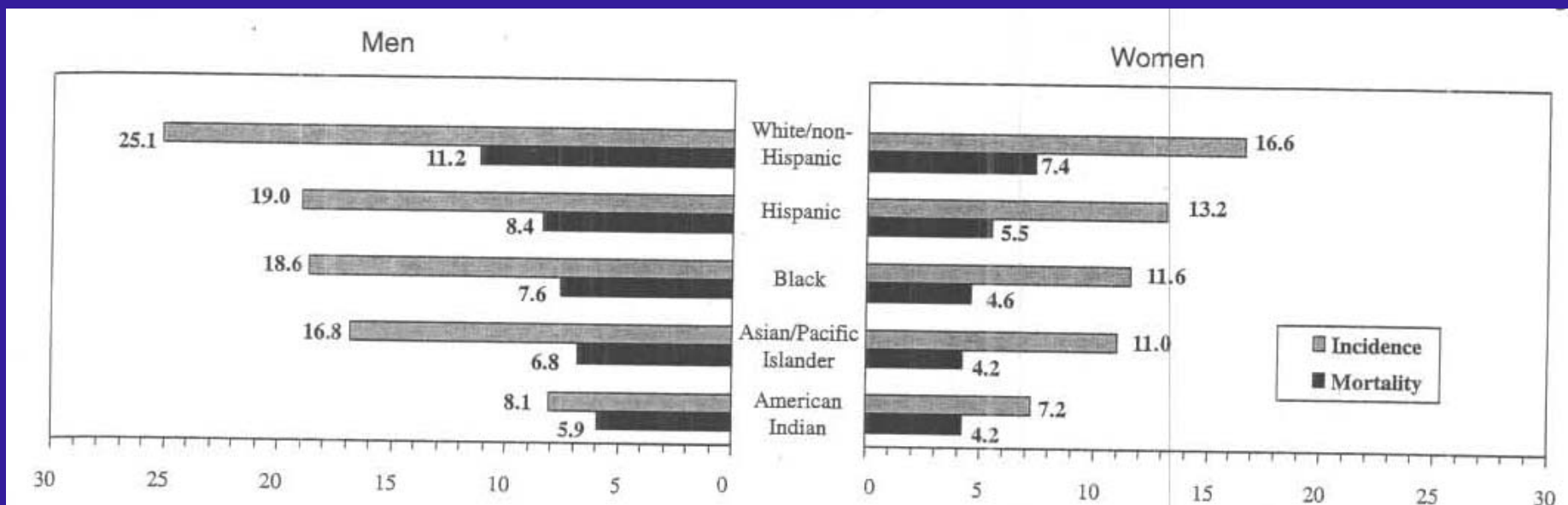
Non-Hodgkin Lymphoma Classification

Project

Age-adjusted Incidence Rates of Non-Hodgkin's Lymphoma, 1993-97



Incidence and Mortality Rates of Non-Hodgkin's Lymphoma, 1996-2000



Introduction

- **Non-Hodgkin lymphoma (NHL) subtypes differ by geographic location around the world**
- **No systematic, comparative study of NHL subtypes by geographic region has been done to date**
- **Non-Hodgkin Lymphoma Classification Project (1995) to evaluate the REAL Classification (Annals of Oncology 9:717, 1998)**

Methods and Materials

- **Between 1995 and 2004, a team of 5 expert hematopathologists traveled to various sites to review NHL cases representative of that geographic region**
- **Phase 1, 1995-96, the team reviewed 1403 consecutive cases from 8 lymphoma centers in mostly developed countries**
- **Phase 2, 1998-2004, the team reviewed 1406 consecutive cases from 8 centers in various developing countries**
- **Phenotyping was required and a consensus diagnosis was reached in all cases (Blood 89:3909, 1997)**

Geographic Sites and Cases

<u>Phase 1</u>		<u>Phase 2</u>	
Omaha	200	Cairo	177
Vancouver	202	Kuwait City	205
London	120	Riyadh	191
Locarno	80	Bombay	200
Lyon	195	Johannesburg	132
Würzburg	210	Harare	201
Cape Town	196	Bangkok	100
Hong Kong	200	Jakarta	200

Phase 1: Epidemiology of NHL

- Follicular lymphoma was highest in North America (32%) compared to Europe (11-18%) and Hong Kong (8%)
- High frequency of mantle cell lymphoma (14%) and mediastinal large B-cell lymphoma (9%) was found in the Locarno/Bellinzona region
- Peripheral T-cell lymphoma was highest in Hong Kong (10%) and Cape Town (8%) compared to other sites (1-6%)
- High frequency of nasal NK/T-cell lymphoma (8%) in Hong Kong compared to other sites (0-2%)

Groupings by Geographic Region

N. America (399)

Omaha

Vancouver

Europe (678)

London, Locarno

Lyon, Würzburg

Cape Town (whites)

S. Africa (397)

Cape Town (blacks)

Johannesburg

Harare

Middle East (695)

Cairo, Kuwait City

Riyadh, Bombay

Far East (450)

Hong Kong

Bangkok, Jakarta

Major NHL Types by Region

<u>Percent</u>	<u>NA</u>	<u>EU</u>	<u>SA</u>	<u>ME</u>	<u>FE</u>
Low-grade B-cell	55.9	54.0	28.7	27.2	23.2
High-grade B-cell	34.6	36.6	55.4	59.3	59.5
T/NK-cell	9.5	9.4	15.9	13.5	17.4

Low-grade B-cell NHL by Region

<u>Percent</u>	<u>NA</u>	<u>EU</u>	<u>SA</u>	<u>ME</u>	<u>FE</u>
Follicular	32.1	22.7	11.8	11.9	6.4
Mantle cell	7.0	7.2	2.0	2.2	2.4
Marginal zone, MALT	6.3	8.1	2.8	3.5	7.8
Small lymphocytic (CLL)	5.0	9.4	8.8	5.5	1.8
Other low-grade B-cell	3.6	5.5	2.8	3.2	3.6

High-grade B-cell NHL by Region

<u>Percent</u>	<u>NA</u>	<u>EU</u>	<u>SA</u>	<u>ME</u>	<u>FE</u>
Diffuse large B-cell	28.6	29.5	38.5	46.6	51.6
Mediastinal large B-cell	1.0	3.0	1.5	1.7	1.8
Burkitt	0.7	0.7	2.0	3.5	2.4
Burkitt-like	2.5	2.0	10.1	1.7	1.6
Lymphoblastic	0.5	0.3	0.0	1.3	0.4

T/NK-cell NHL by Region

<u>Percent</u>	<u>NA</u>	<u>EU</u>	<u>SA</u>	<u>ME</u>	<u>FE</u>
Peripheral T-cell	2.3	5.5	7.6	3.5	6.9
Anaplastic large cell	2.8	1.8	1.8	3.6	2.0
Nasal NK/T-cell	0.0	0.4	0.5	0.6	5.3
Lymphoblastic	2.0	0.7	4.5	4.2	3.1

High Frequencies by Site

- Marginal zone lymphoma, MALT, in Lyon (13%)
- Diffuse large B-cell lymphoma in Riyadh, Bangkok and Jakarta (58-60%)
- Burkitt lymphoma in Cairo (7.6%) and Jakarta (6.0%)
- Burkitt-like lymphoma in Harare (18%)
- T-lymphoblastic lymphoma in Cairo, Bombay, Johannesburg, and Harare (5-7%)
- Plasmacytoma of the head and neck in Jakarta (4%)

Other Diagnosis by Region

<u>Percent</u>	<u>NA</u>	<u>EU</u>	<u>SA</u>	<u>ME</u>	<u>FE</u>
Diagnoses other than NHL	0.0	1.3	5.0	7.7	6.6
Unclassifiable cases	0.5	1.0	2.5	2.5	3.2

Clinical Features by Region

<u>Percent</u>	<u>NA</u>	<u>EU</u>	<u>SA</u>	<u>ME</u>	<u>FE</u>
Median age (yrs)	65.0	61.0	44.0	50.0	52.0
Males	52.9	48.9	60.9	66.2	63.2
Stage III/IV	58.2	59.2	81.6	47.8	53.2
Tumor >10 cm.	20.5	16.3	31.3	17.3	14.6
IPI scores 3-5	30.7	39.1	55.4	27.2	36.8
5-year survival	53.0	55.0	32.0	67.0	52.0

Low-grade B-cell NHL by Region

<u>Percent</u>	<u>NA</u>	<u>EU</u>	<u>SA</u>	<u>ME</u>	<u>FE</u>
Median age (yrs)	64.0	62.0	54.0	48.0	58.0
Males	46.4	47.2	55.2	65.5	62.1
Stage III/IV	66.2	67.0	80.0	58.1	56.3
Tumor >10 cm.	18.1	14.0	19.1	6.9	9.5
IPI scores 3-5	27.4	35.1	39.1	25.6	30.3
5-year survival	58.0	63.0	56.0	77.0	62.0

High-grade B-cell NHL by Region

<u>Percent</u>	<u>NA</u>	<u>EU</u>	<u>SA</u>	<u>ME</u>	<u>FE</u>
Median age (yrs)	68.0	62.0	41.0	53.0	49.0
Males	59.1	48.8	61.5	65.4	61.5
Stage III/IV	42.3	44.0	79.9	39.6	47.7
Tumor >10 cm.	26.9	21.0	44.4	22.5	17.8
IPI scores 3-5	36.0	39.2	56.6	26.4	38.2
5-year survival	44.0	48.0	19.0	61.0	49.0

T/NK-cell NHL by Region

<u>Percent</u>	<u>NA</u>	<u>EU</u>	<u>SA</u>	<u>ME</u>	<u>FE</u>
Median age (yrs)	44.0	60.0	37.0	37.0	49.0
Males	68.4	58.6	69.6	71.3	70.1
Stage III/IV	68.4	72.7	91.1	69.8	62.3
Tumor >10 cm.	11.4	11.1	14.0	11.4	9.7
IPI scores 3-5	31.6	58.3	82.2	35.3	42.3
5-year survival	55.0	33.0	18.0	63.0	43.0

International PTCL Study

<u>Study Sites</u>	<u>Number</u>	<u>Cases</u>	<u>%</u>
North America	6 sites	333	25.2
Europe	7 sites	452	34.2
Far East	8 sites	535	40.6

International PTCL Study Contributing Sites

- **North America – Omaha, Vancouver, Bethesda, Boston, Los Angeles, Tucson**
- **Europe – Barcelona, Madrid, London, Oslo, Lyon, Wuerzburg, Bologna**
- **Far East – Seoul, Hong Kong, Singapore, Bangkok, Tokyo, Nagoya, Okayama, Fukuoka**

International PTCL Study

Major NHL Types by Region

<u>Percent</u>	<u>NA</u>	<u>EU</u>	<u>FE</u>
PTCL, unspecified	34.2	21.4	22.3
Angioimmunoblastic	15.9	31.4	17.8
Anaplastic, ALK+	16.3	9.2	3.6
Anaplastic, ALK-	7.8	11.8	2.6
NK/T-cell	5.1	5.5	22.3
ATLL	2.0	1.5	24.8

International PTCL Study

Major NHL Types by Region

<u>Percent</u>	<u>NA</u>	<u>EU</u>	<u>FE</u>
Enteropathy-type	5.8	11.8	1.9
Hepatosplenic	3.0	3.0	0.2
Subcut panniculitis	1.4	0.7	1.3
Cutaneous anaplastic	5.4	1.1	0.9
Unclassifiable T-cell	3.0	2.6	2.3

International PTCL Study

Major NHL Types by Region

<u>Percent</u>	<u>NA</u>	<u>EU</u>	<u>JF</u>	<u>JO</u>	<u>FE</u>
PTCL, unspecified	34.2	21.4	19.1	31.2	19.1
Angioimmunoblastic	15.9	31.4	18.0	26.2	11.1
NK/T-cell	5.1	5.5	6.6	17.2	43.8
ATLL	2.0	1.5	50.1	18.9	0.0

Incidence of Non-Hodgkin's Lymphoma by Country

(Herrinton et al, Cancer Causes Control 7: 224, 1996)

	<u>Males</u>	<u>Females</u>
White, US, 1973-86	10.7	7.4
Chinese, US, 1973-86		
US-born	7.8	2.6
Asia-born	5.5	3.1
Chinese		
Shanghai, 1978-82	3.5	2.1
Tianjin, 1981-82	3.1	2.5
Hong Kong, 1978-82	6.5	5.0
Singapore, 1978-82	5.1	2.9

Incidence of Lymphoma by Country, 1970-83

(Yanagihara et al, Hematol Oncol 7: 219, 1989)

	<u>Japan</u>	<u>Hawaiian Japanese</u>	<u>US Whites</u>
Follicular lymphoma	0.5	1.5	3.8
Diffuse lymphomas	4.3	3.3	4.8
Total NHL	4.8	4.8	8.6
Hodgkin's disease	0.3	0.4	3.5

Incidence of Follicular Lymphoma by Race and Birthplace, 1973-86

(Herrinton et al, Cancer Causes Control 7: 224, 1996)

<u>Race</u>	<u>Birthplace</u>	<u>RR</u>	<u>95% CI</u>
White	US	1.00	--
Chinese	US	0.84	(0.51-1.40)
	China	0.11	(0.05-0.23)
Japanese	US	0.36	(0.23-0.56)
	Japan	0.15	(0.04-0.54)

Conclusions

- Frequency of the various types of NHL differs significantly in different parts of the world
- Clinical features of the various types of NHL are also different in various parts of the world
- Epidemiologic and molecular biologic studies of risk factors and host response factors are needed to better understand these differences and to elucidate complex etiologies
- Studies of specific NHL types in certain countries may provide important new insights regarding the etiology and pathogenesis of NHL