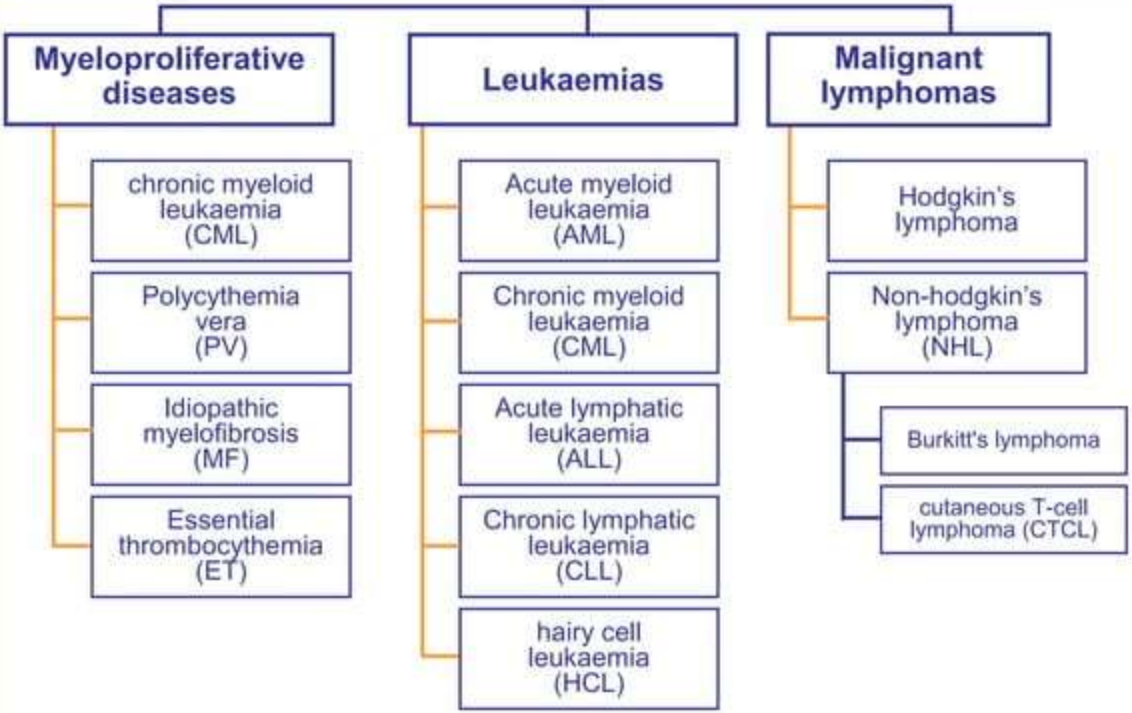
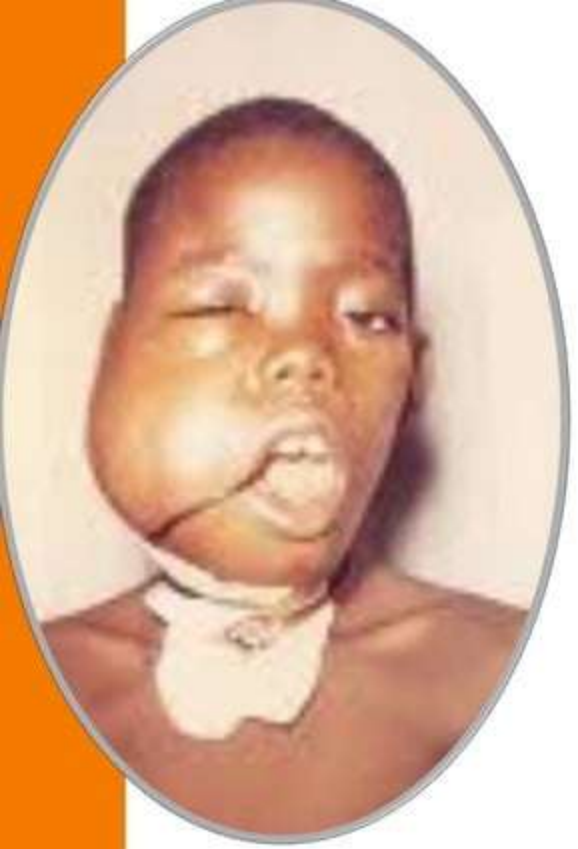
Non-Hodgkin's Lymphoma

Epidemiology, Disease and Staging

Haematopoietic Malignancies





Non-Hodgkin's Lymphoma

Oliveros francis!!!!!!!!!!!!!!!!!

Haematopoietic Malignancies

Myeloproliferative diseases

- Family of chronic neoplastic diseases
- Due to a clonal disorder arising at the level of the pluripotent stem cell
- Characterised by abnormal proliferation of 1 or more blood cell lines

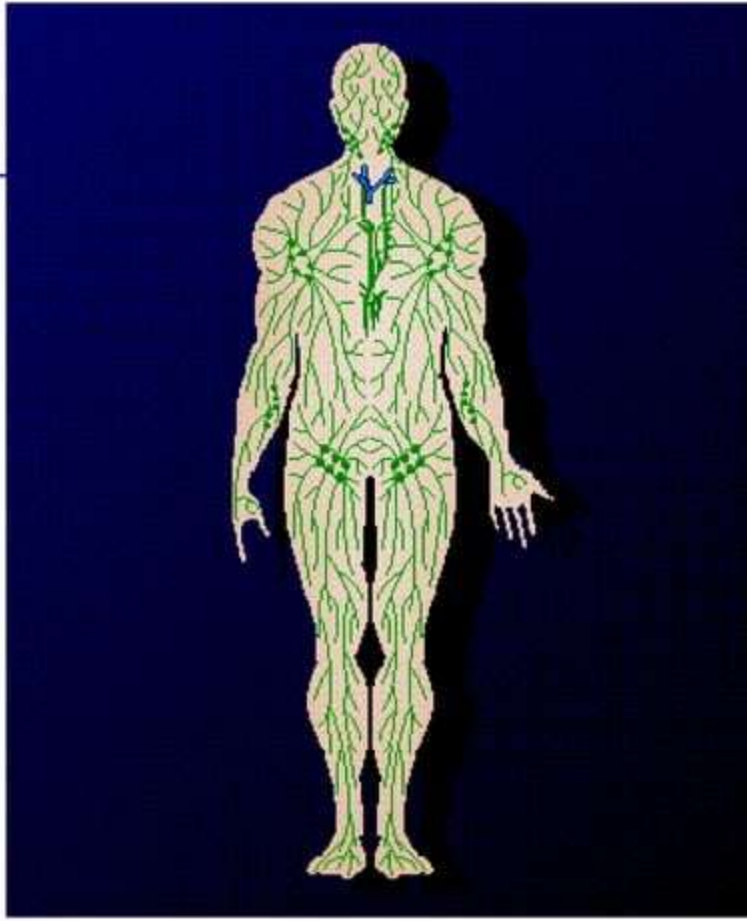
Leukaemias

- Neoplastic disease of a haematopoietic precursor cell
- Characterised by replacement of normal bone marrow
- Often infiltration into other organs
- Malignant clones suppress normal cell formation

Malignant lymphomas

- Neoplastic disease of lymphatic tissue
- Originates in lymph node or spleen
- Hodgkin's (15%)
- non-Hodgkin's (85%)

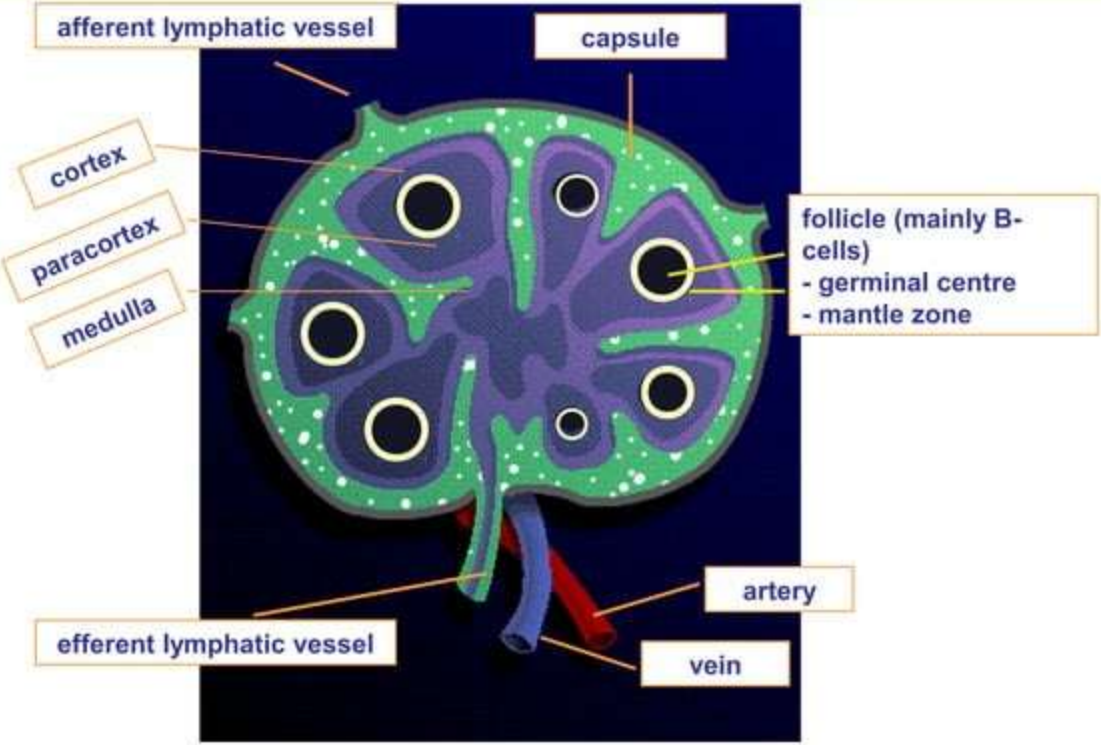
The Lymphatic System



Lymphatic Tissue

- Lymph nodes, spleen, liver, skin and the respiratory, GI and GTU tract
- Lymphocytes undergo further proliferation and differentiation in lymphoid tissue
  - B-lymphocytes
    - tend to reside in lymph nodes & spleen
  - T-lymphocytes
    - tend to circulate throughout the lymphatic system

Lymph Node - normal histology



Hodgkin's Lymphoma

- 15% of lymphomas
- First described by Thomas Hodgkin in 1832
- Originally had a very poor prognosis (<10% survival at 5 years)
- Improved staging techniques and understanding of the pattern of spread helps direct management
- Now curable in over 70% of cases through the use of radiotherapy and chemotherapy

Non-Hodgkin's Lymphoma (NHL): Definition and Indication

A heterogeneous group of B- and T-cell malignancies that are diverse in cellular origin, morphology, cytogenetic abnormalities, response to treatment, and prognosis

Non-Hodgkin's Lymphoma (NHL)

- 85% of lymphomas
- 6th major cause of cancer deaths yearly
  Heterogeneous group of malignant diseases arising from lymphoid tissue
  - lymph nodes, spleen
- Various immune cell types
  - principally B-cells derivation (>85%)
  - T-cells derivation
  - Histiocytes (very rarely)
  - Various stages of differentiation and maturation

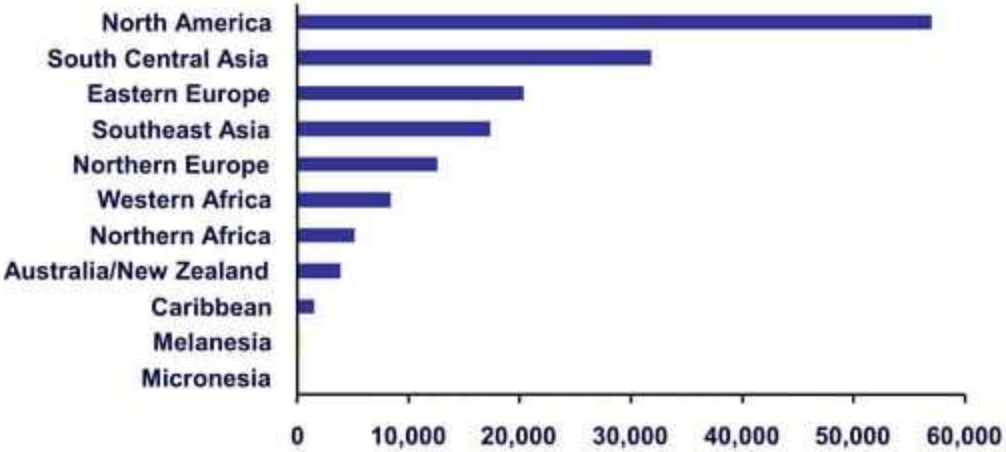
NHL Incidence

- Incidence of 13.3/100,000 per year (Aust)
- Predominates in the 40-70 years age group
  - most common neoplasm in the 20-40 age group
- Incidence is rising
  - 150% growth over the past 30 years
  - increasing by 4% annually since 1970's
- Mortality rate is also rising
  - 2% rise per year
  - third highest rise, exceeded only by lung cancer in women and malignant melanoma

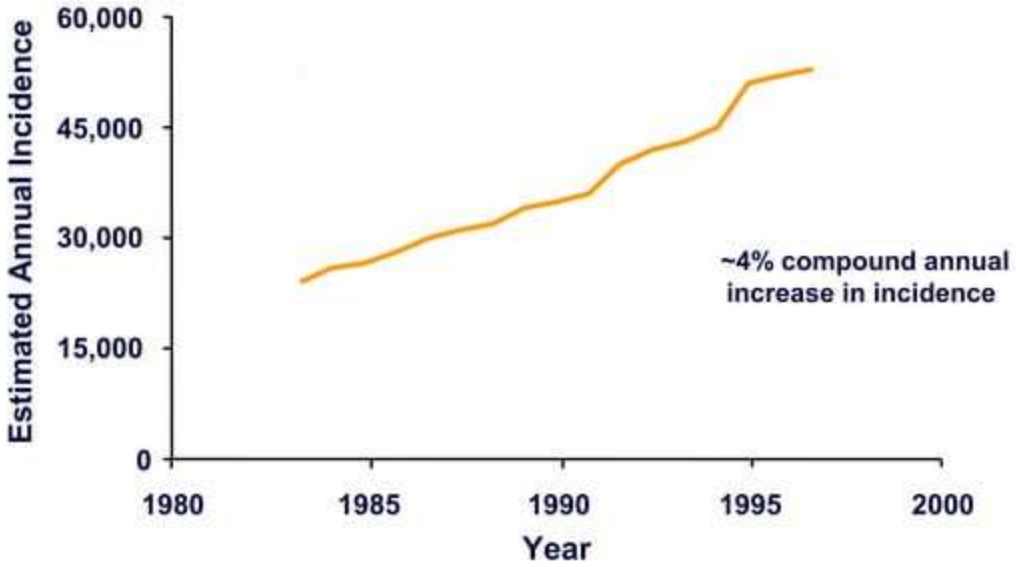
NHL Incidence

- Increases with age
  - implications
- Slight male predominance overall
- Striking male predominance for several subtypes
- Incidence of certain subtypes varies greatly around the world
  - Burkitt's Lymphoma in African children
  - T-cell type more common in Japan

Estimated Incidence of NHL in the Year 2000 (Worldwide)



Estimated Incidence of NHL (US)



Adapted from Greenlee et al. *CA Cancer J Clin.* 2001;51:15.

Revised European-American Lymphoma (REAL) Classification: B-Cell Neoplasms

Indolent	Aggressive	Very Aggressive
■ CLL/SLL	■ PLL	■ Precursor B-lymphoblastic lymphoma/ Leukemia
■ Lymphoplasmacytic/ IMC/WM	■ Plasmacytoma/ Multiple myeloma	■ Burkitt's lymphoma/ B-cell acute leukemia
■ HCL	■ MCL	■ Plasma cell leukemia
■ Splenic marginal zone lymphoma	■ Follicle centre lymphoma, follicular, grade III	
■ MZL - Extranodal (MALT) - Nodal	■ DLCL	
■ Follicle center lymphoma, follicular, grade I-II	■ Primary mediastinal large B-cell lymphoma	
	■ High-grade B-cell lymphoma/Burkitt's-like	

Hiddemann. *Blood*. 1996;88:4085.

World Health Organization (WHO) Classification of Lymphoid Neoplasms: B-Cell Neoplasms

- **Precursor B-cell neoplasm**
  - Precursor B-lymphoblastic leukemia/lymphoma (precursor B-cell acute lymphoblastic leukemia)
- **Mature (peripheral) B-cell neoplasms**
  - B-cell CLL/SLL
  - B-cell PLL
  - Lymphoplasmacytic lymphoma
  - Plasmacytoma, plasma cell myeloma
  - HCL
- **Marginal zone B-cell lymphoma**
  - Marginal zone B-cell lymphoma of MALT
  - Nodal marginal zone lymphoma (+/- monocytoid B-cells)
  - Splenic marginal zone B-cell lymphoma
- **FL**
  - Grade 1, 0-5 centroblasts/hpf
  - Grade 2, 6-15 centroblasts/hpf
  - Grade 3, >15 centroblasts/hpf
    - 3a, >15 centroblasts, but centrocytes still present
    - 3b, centroblasts from solid sheets with no residual centrocytes
  - Variants
    - Cutaneous follicle center
- **MCL**
- **DLCL**
  - Mediastinal (thymic) large B-cell lymphoma
  - Intravascular lymphoma
  - Primary effusion lymphoma
- **Burkitt's lymphoma/Burkitt cell leukemia**

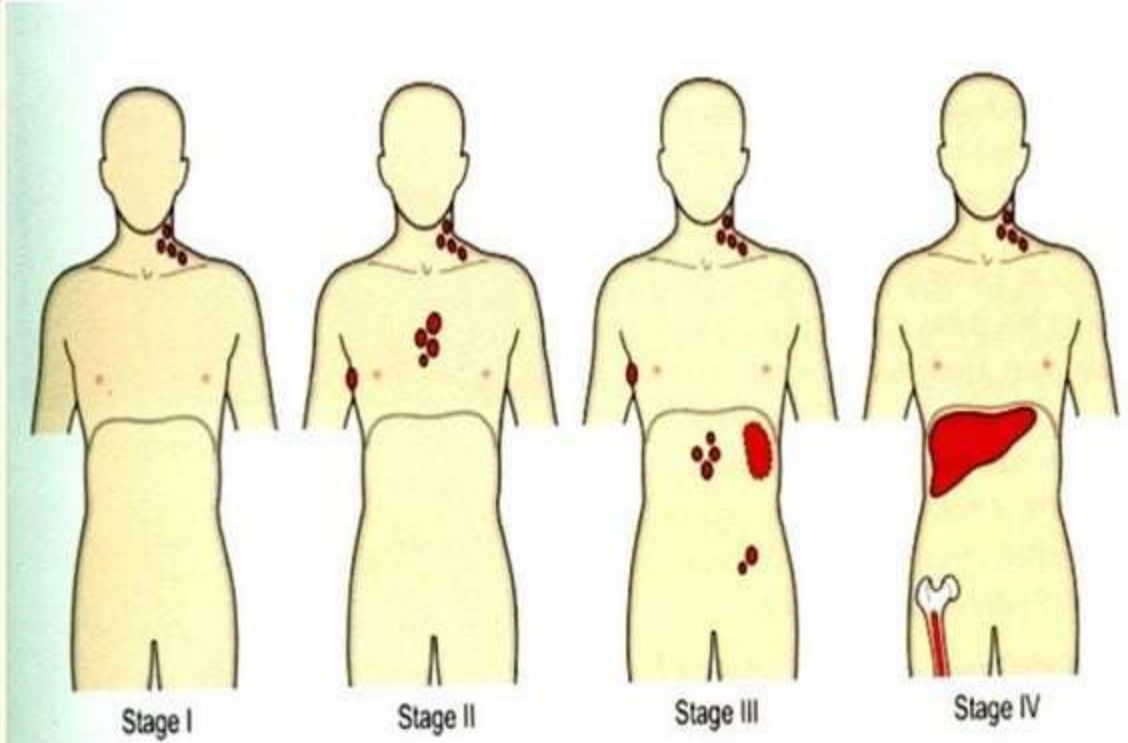
Jaffe et al. *Ann Oncol.* 1998;9 (suppl 5):S25.

Modified Ann Arbor Staging of NHL

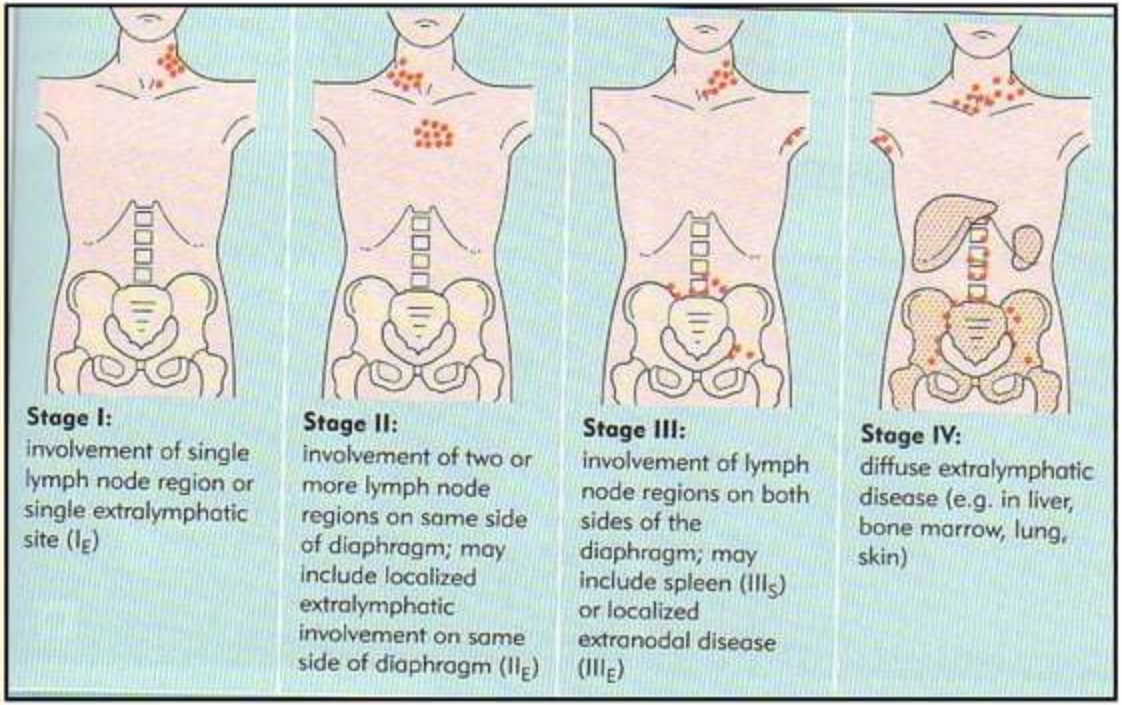
Stage I	Involvement of a single lymph node region
Stage II	Involvement of ≥2 lymph node regions on the same side of the diaphragm
Stage III	Involvement of lymph node regions on both sides of the diaphragm
Stage IV	Multifocal involvement of ≥1 extralymphatic sites ± associated lymph nodes or isolated extralymphatic organ involvement with distant nodal involvement

The Non-Hodgkin's Lymphoma Pathologic Classification Project. *Cancer.* 1982;49:2112.

Staging of NHL



Staging of NHL



Stage I: involvement of single lymph node region or single extralymphatic site (I_E)

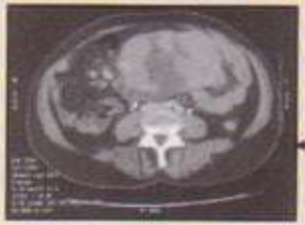
Stage II: involvement of two or more lymph node regions on same side of diaphragm; may include localized extralymphatic involvement on same side of diaphragm (II_E)

Stage III: involvement of lymph node regions on both sides of the diaphragm; may include spleen (III_S) or localized extranodal disease (III_E)

Stage IV: diffuse extralymphatic disease (e.g. in liver, bone marrow, lung, skin)

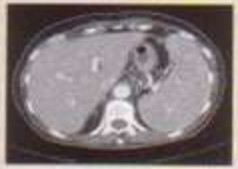
Enlarged lymph nodes
Single/multiple

Peripheral
Cervical
Axillar
Inguinal



Profound
Mediastinal
Lombo-aortic
Mesenteric
Iliac

Splenomegaly

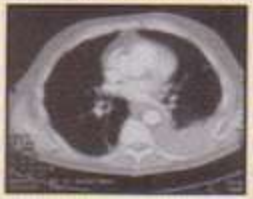


Diagnosis of lymphoma

Atypical symptoms
Weight loss
Fever
Fatigue

Extranodal tumors

Typical of lymphoma
Skin
Stomach
Orbit
Similar to any other solid tumor
Effusion



Follicular non-Hodgkin's Lymphoma

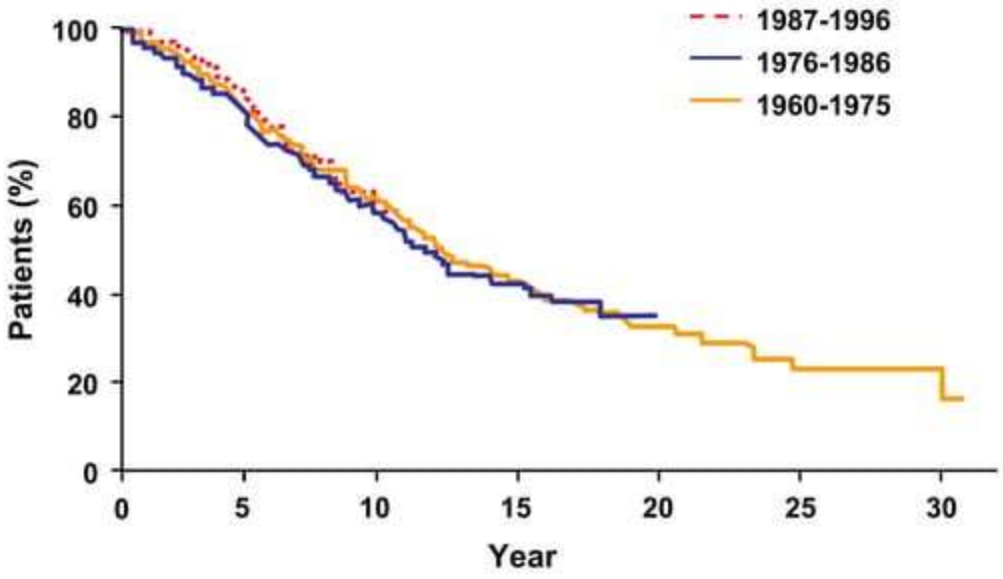
Classification and survival

Classification of Indolent NHL: International Working Formulation (IWF)

Class	% of NHL Patients	Median Survival (y)
A. Small lymphocytic	3.6	5.8
B. Follicular, predominantly small cleaved cell	22.5	7.2
C. Follicular, mixed small and large cell	7.7	5.1
D. Follicular, predominantly large cell	3.8	3.0

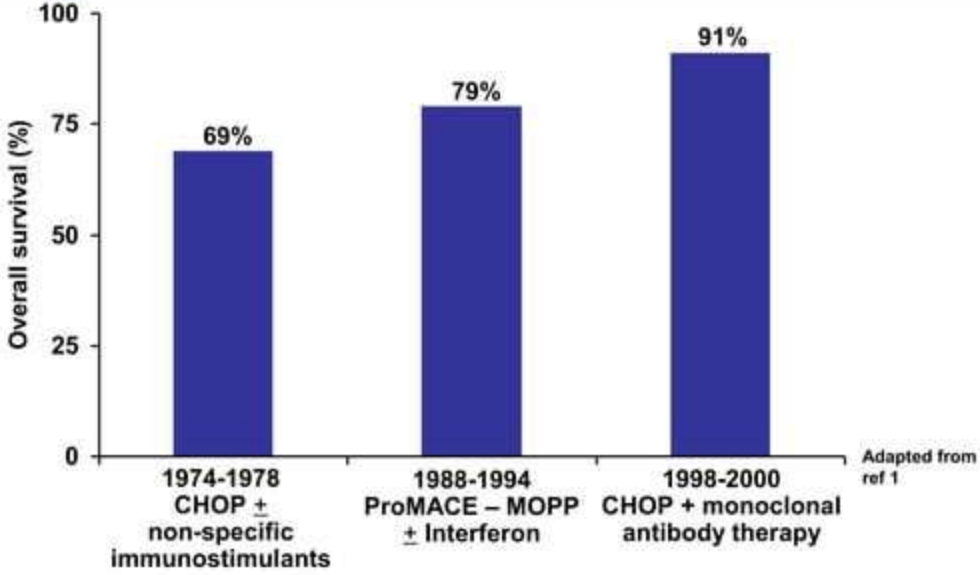
The Non-Hodgkin's Lymphoma Pathologic Classification Project. *Cancer.* 1982;49:2112.

Survival of Patients with Indolent Lymphoma: The Stanford Experience, 1960-1996



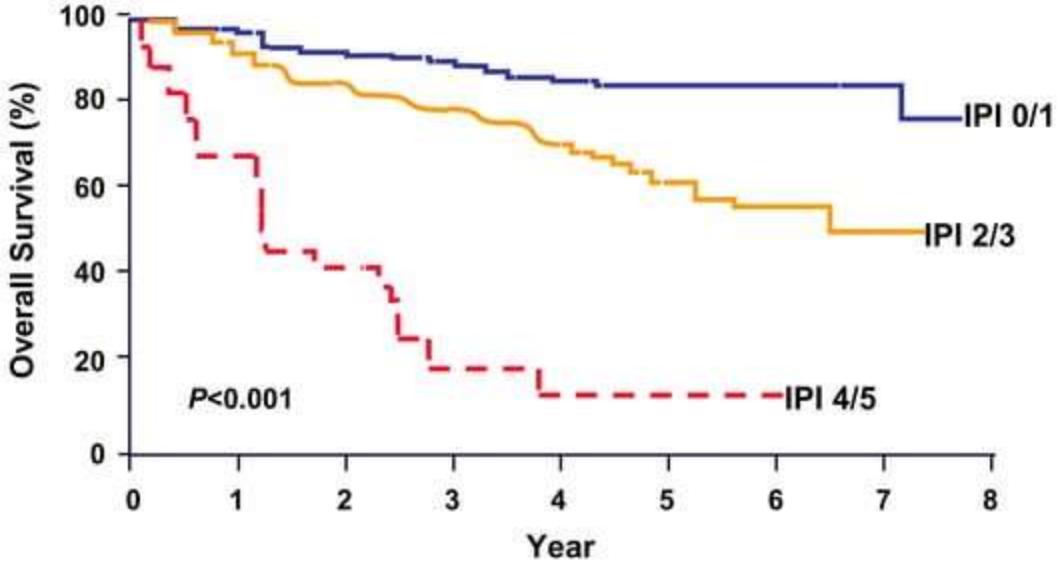
Adapted from Horning. *Semin Oncol.* 1993;20(5 suppl 5):75.

SWOG Finding: New treatment options have changed the natural history of follicular lymphoma[1]



Impact of new treatment options on the natural history of follicular lymphoma determined by SWOG via retrospective analysis of three sequential treatment approaches. 1:Fisher et al Blood 2004;104 Abstract 583

Follicular Lymphoma: Overall Survival

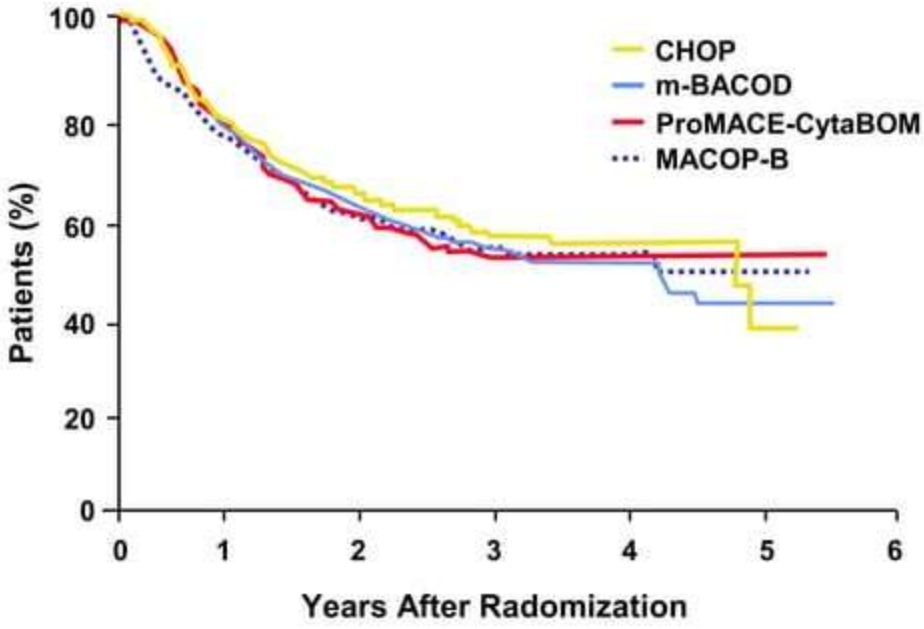


Adapted from Armitage and Weisenburger. *J Clin Oncol.* 1998;16:2780.

Aggressive non-Hodgkin's Lymphoma

Classification and Survival

National High-Priority Lymphoma Study: Overall survival for aggressive lymphoma



Fisher et al. *N Engl J Med.* 1993;328:1002.

International Prognostic Index (IPI)

Patients of all ages	Risk Factors
Age	>60 years
PS	2-4
LDH level	Elevated
Extranodal involvement	>1 site
Stage (Ann Arbor)	III-IV
Patients ≤60 years (age-adjusted)	
PS	2-4
LDH	Elevated
Stage	III-IV

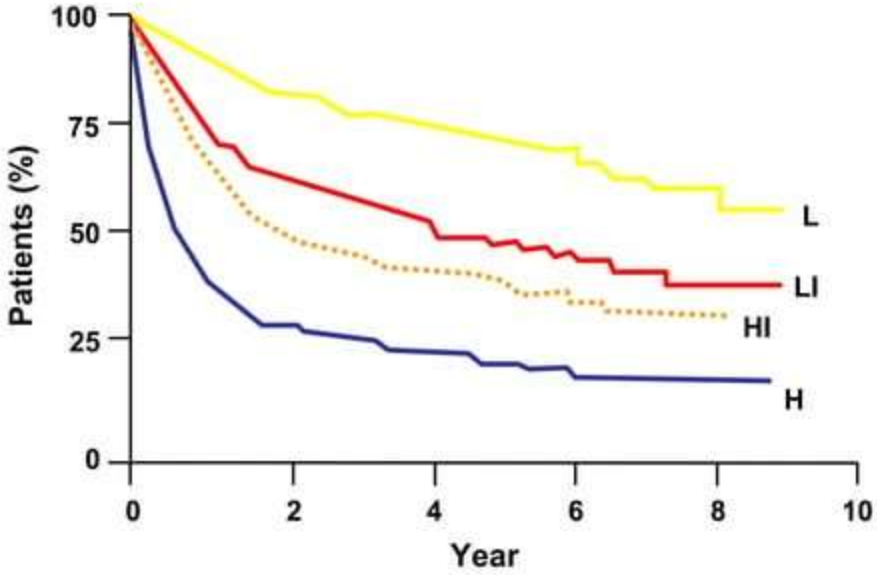
Shipp. *N Engl J Med.* 1993;329:987.

IPI Risk Strata

	Risk Group	Risk Factors
All ages	Low (L)	0-1
	Low-intermediate (LI)	2
	High-intermediate (HI)	3
	High (H)	4-5
Age-adjusted	L	0
	LI	1
	HI	2
	H	3

Shipp. *Blood*. 1994;83:1165.

IPI: Overall Survival by Risk Strata



Adapted from Shipp. *N Engl J Med.* 1993;329:987.