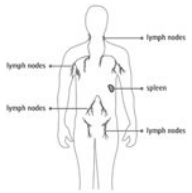
Lymphoma

Jasmine Zain
2008

Lymphoma

- Malignancies arising from lymphoid tissue
- Hodgkin's Lymphoma/Disease
- Non-Hodgkin's Lymphoma

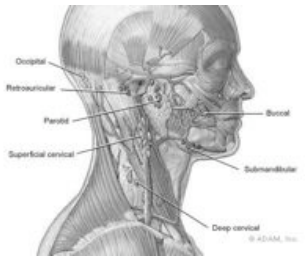


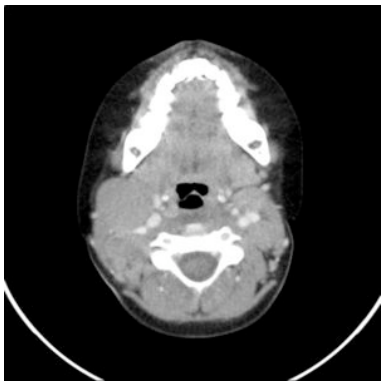
Statistical facts of 2007 in U.S

- 71,380 cases of NHL
- 8190 cases of H.D
- 5th most common cancer in males and females in the U.S
- Age adjusted incidence rose by 84% from 1974-2004
- Incidence increases by age

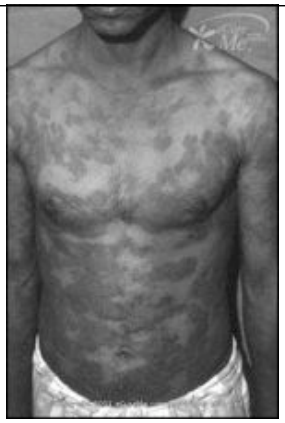
Clinical Features

- Enlarged lymph nodes
- Weight loss
- Fever
- Night sweats
- Itching





Mycosis Fungoides



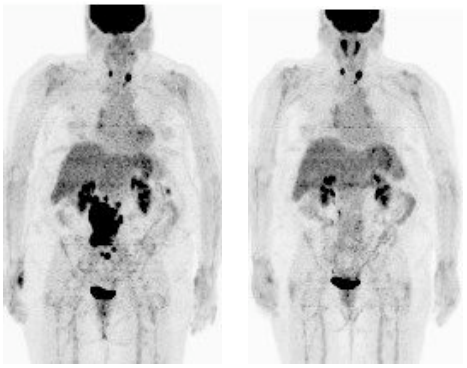
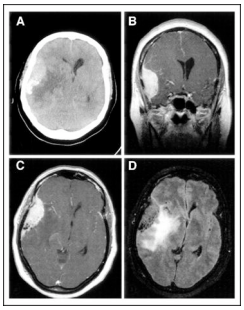


Fig 1. Radiologically, this marginal zone B-cell lymphoma presented as (A) a dura-based mass with hyperdense signal on computed tomography scan; (B, C) homogeneous contrast enhancement and a dural tail sign, mimicking meningioma, on the T1-weighted magnetic resonance images (MRIs)



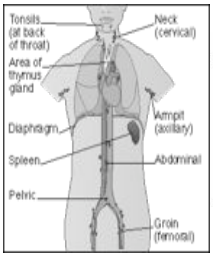
Tu, P.-h. et al. J Clin Oncol; 23:5718-5727 2005

JOURNAL OF CLINICAL ONCOLOGY

Diagnosis

- Tissue biopsy must be an adequate sample with intact tissue architecture
  - Excision biopsies
  - Core biopsy
- Fine needle aspirate acceptable only for recurrent disease or for hard to reach areas

Staging for H.D and Nodal NHL



Ann Arbor Staging System

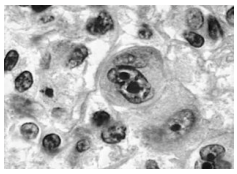
Stage	Distribution of Disease
I	Involvement of a single lymph node region (I) or involvement of a single extralymphatic organ or site (I_E)
II	Involvement of two or more lymph node regions on the same side of the diaphragm alone (II) or with involvement of limited contiguous extralymphatic organ or tissue (II_E)
III	Involvement of lymph node regions on both sides of the diaphragm (III), which may include the spleen (III_S) and/or limited contiguous
IV	Multiple or disseminated foci of involvement of one or more extralymphatic organs or tissues with or without lymphatic involvement.

Diagnostic work up

- Biopsy and pathology review
- Complete blood counts
  - Anemia, pancytopenia
  - Lymphocytosis, abnormal cells on the smear
- Serum chemistries including LDH
- Staging scans
  - CT scans, PET scans, PET/CT
- Bone marrow biopsies

Hodgkin's Disease/Lymphoma

Characterized by the presence of Reed Sternberg cell



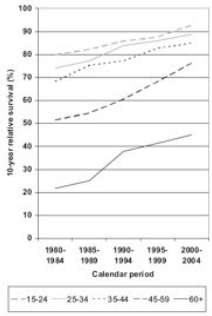
Classification of Hodgkin's Disease

Type	Percentage
• Nodular sclerosing	• 55
• Mixed cellularity	• 25
• Lymphocyte rich classical Hodgkin's disease	• 5
• Lymphocyte depleted	• 2
• Not classifiable	• 5

Hodgkin's Disease

- Curable in over 85% of cases
- Combination of chemotherapy and radiation therapy
- Monitor for secondary malignances

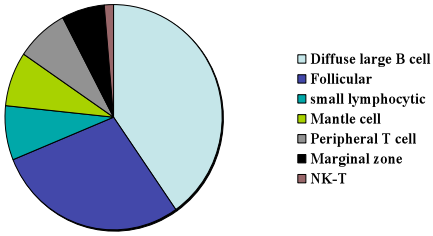
Survival rates in H.D over time



Hodgkin's Lymphoma

- Different pattern of growth
- Response to therapy is different
- Curable in over 85% of cases with a combination of chemotherapy and radiation
- Monitor for secondary malignancies

Relative frequency of Non-Hodgkin's lymphomas



NHL

Clonal expansion of B, T or NK cells

Arise from lymph nodes or any lymphoid tissue including brain, skin, breast

Etiology of NHL

- Association with infection
  - EBV------ Burkitt's, NK-T, PTLD
  - HTLV-1---- HTLV1 associated ATL
  - Helico bacter pylori- Gastric MALTs
  - Borrelia Bergdorfi--- B cell lymphomas of skin
- Immunosuppression
  - Increased incidence in HIV infected
  - Organ transplantation
- Autoimmune states
  - Psoriasis
  - Schojern's syndrome
- Previous history of Lymphoma or H.D

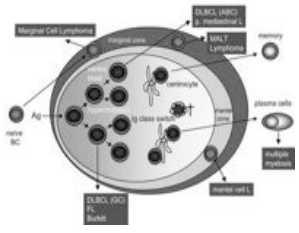
Table 1.2: WHO Classification of NHL

	B-cell
Mature B-cell lymphomas	
Precursor B-cell lymphoma	Small lymphocytic lymphoma
	Lymphoplasmacytic lymphoma
	Splenic marginal zone lymphoma
	Hairy cell leukaemia
	Plasma cell neoplasms
	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
	Nodal marginal zone B-cell lymphoma
	Follicular lymphoma (grades 1, 2, 3a and 3b)
	Diffuse follicle centre lymphoma
	Mantle cell lymphoma
	Diffuse large B-cell lymphoma
	Mediastinal (thymic) large B-cell lymphoma
	Intravascular large B-cell lymphoma
	Primary effusion lymphoma
	Burkitt lymphoma
B-cell proliferations of uncertain malignant potential	Lymphomatoid granulomatosis
	Post-transplant lymphoproliferative disorder, polymorphic
	T-cell and NK-cell
Precursor T- and NK-cell lymphomas	Precursor T lymphoblastic lymphoma
	Blastic NK-cell lymphoma
Mature T-cell and NK-cell lymphomas	T-cell prolymphocytic leukaemia
	T-cell large granular lymphocytic leukaemia
	Aggressive NK-cell leukaemia
	Adult T-cell lymphoma/leukaemia
	Extranodal NK-/T-cell lymphoma, nasal type
	Enteropathy-type T-cell lymphoma
	Hepatosplenic T-cell lymphoma
	Subcutaneous panniculitis-like T-cell lymphoma
	Mycosis fungoides
	Peripheral T-cell lymphoma unspecified
	Angioimmunoblastic T-cell lymphoma
	Anaplastic large cell lymphoma

Practical points

- B vs T vs NK-T cell lymphoma
- B NHL more common
  - Working formulation
    - Low grade (slow growing, poorly responsive to treatment
    - Aggressive (fast growing, more likely to be cured with chemotherapy
    - High grade (aggressive, life threatening behave like acute leukemias)

Origin of B cell lymphoma



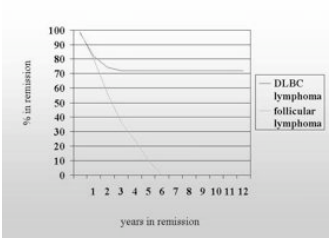
Prognosis of NHL

- Histological subtype determines clinical behavior and prognosis
- Accurate diagnosis
- Staging
- Age
- LDH
- Performance status
- Other prognostic factors unique to histological subtype

Immunophenotyping

- B cell malignanices—CD19, CD20, kappa/ lambda light chain restriction
- Tcell malignancies-----CD3, CD4, CD5, CD4, CD8, Tcell gene rearrangements
- NK-T cell---- CD56, CD16 usually EBV positive

Diffuse large B cell lymphoma vs Follicular lymphoma



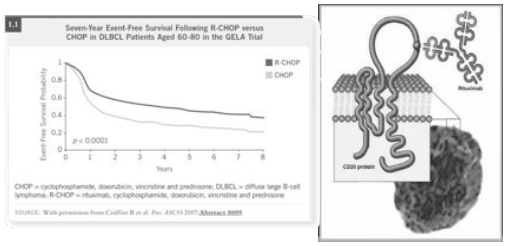
Treatment

- Tailored to the type of NHL
- B cells vs T cells
  - Different therapeutic approaches
- Low grade vs aggressive or high grade
  - Immediate treatment vs wait and watch
- General condition of the patient
- Site of origin
  - Skin
  - brain

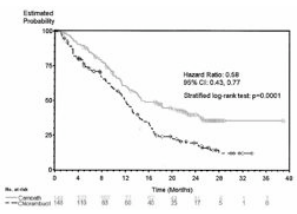
Chemotherapy

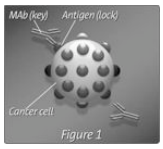
- Combination chemotherapy has shown the best results for both HD and NHL
- Most active drugs are
  - Alkylating agents
  - Anthracyclins
  - Topoisomerase I and II inhibitors
  - Steroids

Rituximab
anti - CD20

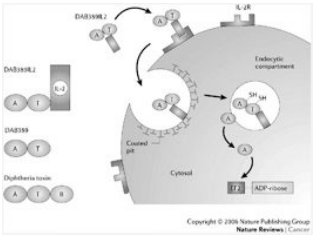


Alemetuzemab (Campath)
Anti- CD52





Denileukin Diftitox
Ontak



Radiation therapy

- External beam radiation
- Radioimmunotherapy
  - Ibritumomab Tiuxetan (Zevelin)
  - I-131 Tositumomab

Targeted therapies

- HDAC inhibitors
- Hypomethylating agents
- Syk inhibitors
- M-TOR inhibitors

Principles of Underlining Cure by BMT

1. AUTOLOGOUS	Ablation of host normal hematopoiesis and malignancy (hematologic and solid tumor) Re-establishment of host hematopoeisis Host immune reconstitution (stem cell derived)
2. ALLOGENEIC	Ablation of host hematopoiesis, normal and malignant Re-establishment of donor hematopoiesis Donor immune resconstitution (stem cell derived) Donor anti-tumor effect (GVL)