LYMPHOMA
RESEARCH • FOUNDATION

LYMPHOMA OVERVIEW

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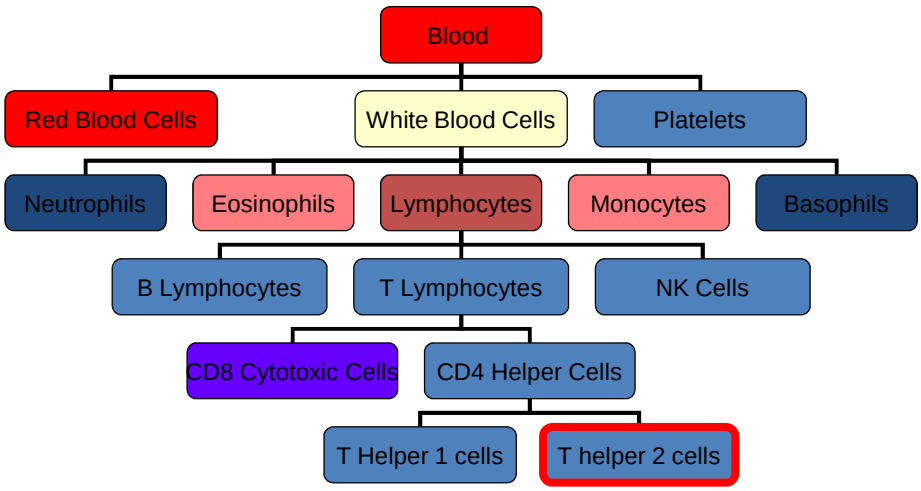
DEFINITION

Lymphoma is a cancer of the lymphoid cells arising in the lymphatic system

WHAT IS A LYMPHOCYTE



PRESENTATION

- Lymph nodes are the most common sites of origin but they can arise from any organ in the body that has lymphoid tissue- skin, gastrointestinal tract, liver, spleen, bone marrow, brain, nasal passages
- Can arise from B cells, T cells or NK cells- all important in the immune response

LYMPHOMA IN ANIMALS

Lymphoma is the most common malignancy diagnosed in dogs – cause is mostly GENETIC
The golden retriever has a life time risk of 1:8 for developing lymphoma

Lymphoma is also the most common tumor seen in cats.- commonly due to the association with the FELINE LEUKEMIA virus

It can occur in other animals as well including ferrets,

MAJOR TYPES

HODGKIN'S DISEASE

Nodular Lymphocyte Predominance

Classical HD

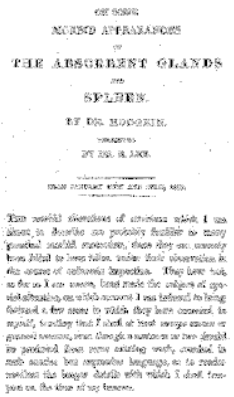
NON- HODGKIN'S LYMPHOMA

B cell lymphomas

T cell lymphomas

NK/ NK-T cell lymphomas

HISTORICAL FACTS



ON SOME
MORBID APPEARANCES
OF
THE ABSORBENT GLANDS
AND
SPLEEN.
BY DR. HODGKIN.
COMMUNICATED
BY DR. M. LEE.

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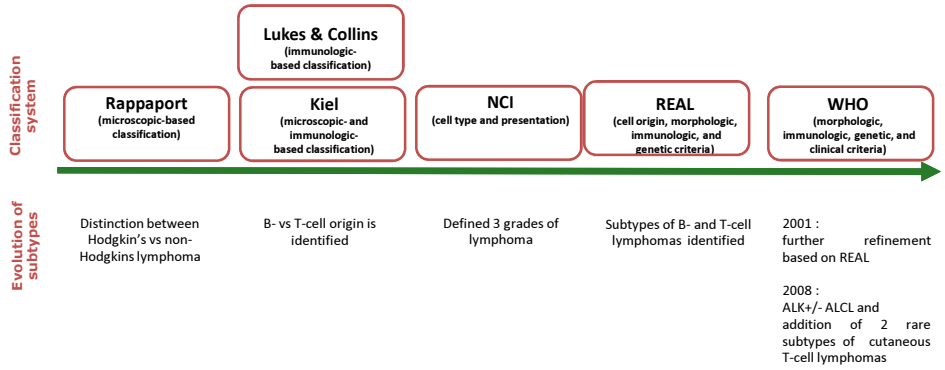
MILESTONES IN THE CLASSIFICATION OF LYMPHOID NEOPLASMS

1832	T. Hodgkin	First clinical report of a case of Hodgkin disease
1845, 1863	R. Virchow	Describes both leukemia and lymphoma
1898,1902	C. Strenberg, D.Reed	Define the microscopic features of the neoplastic cells of Hodgkin Disease
1958	D. Burkitt	Describes the clinical syndrome if Burkitt's lymphoma in African children
1956, 1966	H. Rappoport	Alternative classification for NHL
1974	K.Lennert	Proposes the Kiel classification of lymphomas- recognizes B and T cells
1975		Working Formulation proposed by the NCI
1994		Revised European –American Classification of the lymphoid Neoplasm (REAL)
2001		WHO classification
2008		WHO classification

CLASSIFICATION SYSTEMS OF NHL

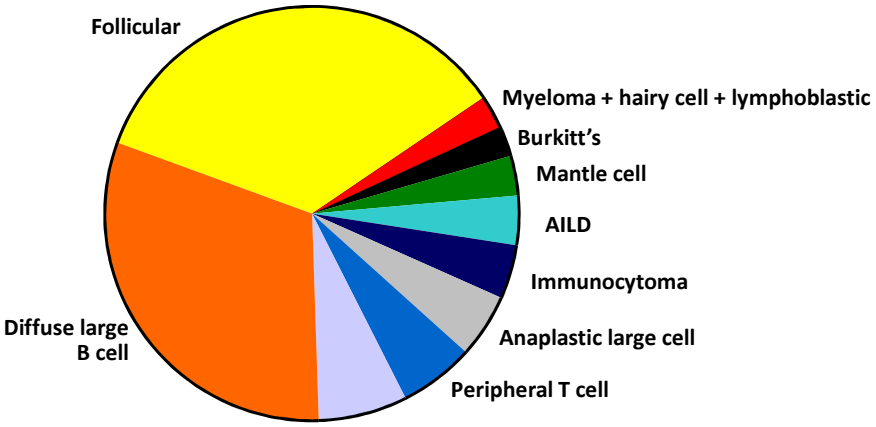
- NHL classification schemes have evolved based on growing understanding of cancer cell characteristics[1]
- Subclassifications are driving more specific clinical trials and therapeutic approaches[2]



EPIDEMIOLOGY

- Most common hematologic cancer
- Prevalence ~300,000 patients
- ~53,000 new cases/year
- ~23,000 deaths/year
- Increasing incidence of non–AIDS-associated NHL
- Demographic shift accounts for most of increase

FREQUENCY OF SUBTYPES OF LYMPHOMA IN BIOPSIES



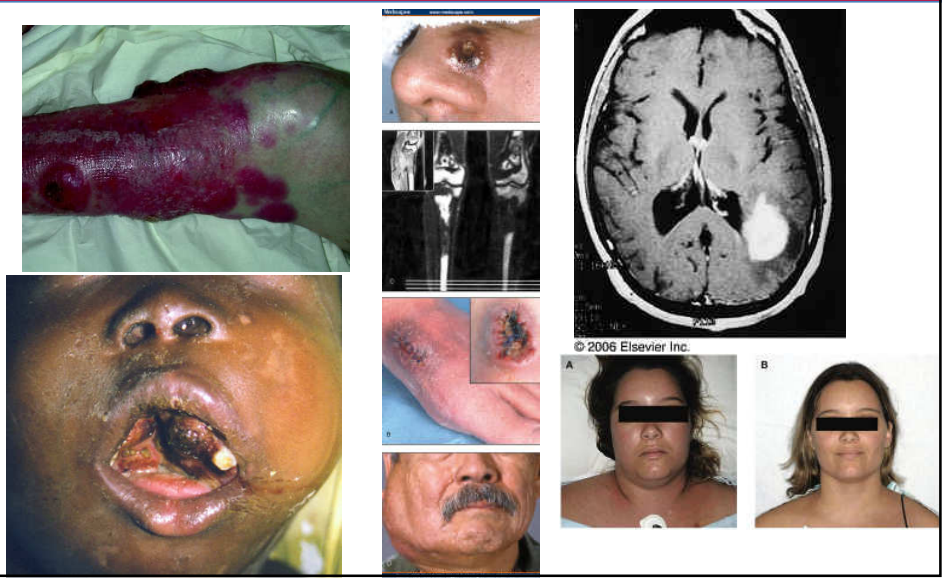
INCIDENCE OF SUBTYPES

LYMPHOMA SUB-TYPE	RELATIVE FREQUENCY	EST. # CASES/YEAR
Large B-Cell	**~ 31%**	**16,709**
Follicular (I-III)	**~ 22%**	**11,858**
Marginal Zone	**~ 8%**	**4,312**
PTCL	**~ 7%**	**3,773**
Mantle Cell	**~ 6%**	**3,234**
SLL/CLL	**~ 6%**	**3,234**
Mediastinal	**~ 6%**	**3,234**
Anaplastic L Cell	**~ 2%**	**1,078**
Hodgkin's	**~ 11%**	**7,500**

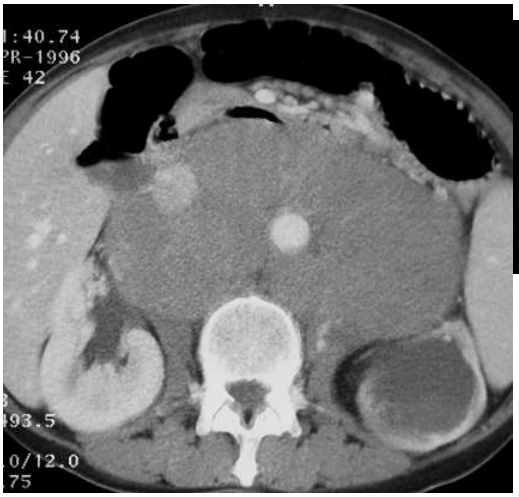
SIGNS AND SYMPTOMS

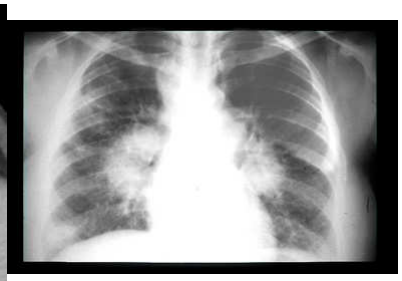
- Swollen lymph nodes
- Fevers not related to infections
- Night sweats
- Itching
- Unexplained weigh loss
- Abnormal blood counts
- Elevated LDH, paraproteins in the blood
- Organ specific symptoms based on site of origin of lymphoma

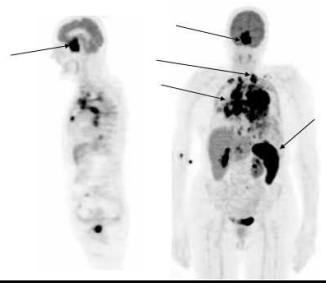
CLINICAL PRESENTATIONS



RADIOLOGICAL FINDINGS







ETIOLOGY

- Infections
- Immune deficiency
  - HIV
  - Immunosuppressive agents
  - Congenital immune deficiency states
  - Post transplantation
- Environmental factors
  - Hair dyes
  - Exposure to radiation
  - Insecticides

INFECTIOUS AGENTS ASSOCAITED WITH LYMPHOMAS

EPSTEIN BARR VIRUS	BURKITT'S LYMPHOMA
	POST ORGAN TRASNPLANT LYMPHOPROLIFERATIVE DISORDER
	PRIMARY CNS DIFFUSE LARGE CELL LYMPHOMA
	HODGKIN'S DISEASE
	EXTRANODAL NK/T CELL LYMPHOMA, NASAL TYPE
HTLV-1	ADULT T-CELL LEUKEMIA/LYMPHOMA
HIV	DIFFUSE LARGE B CELL LYMPHOMA
	BURKITT'S LYMPHOMA
HEPATITIS C VIRUS	LYMPHOPLASMACYTIC LYMPHOMA
HELICOBACTER PYLORI	GASTRIC MALT LYMPHOMA
HUMAN HERPES VIRUS 8	PRIMARY EFFUSION LYMPHOMA
	MULTICENTRIC CASTLEMAN'S DISEASE

HOST SUSCEPTIBILITY FACTORS

TYPE OF LYMPHOMA	HOST FACTORS
Enteropathy associated T cell lymphoma	Genetics, gliadin allergy
Hepatosplenic T cell lymphomas	EBV?
Lymphomatoid granulomatosis	EBV?
Burkitt's lymphoma	EBV
Post transplant lymphoproliferative disorder	Immunosuppression, EBV

DISEASES ASSOCIATED WITH AN INCREASED RISK OF LYMPHOMA

INHERITED IMMUNODEFICIENCY STATES
KLEINFELTER'SSYNDROME
CHEDIAK-HIGASHI SYNDROME
ATAXIA-TELENGECTASIA
COMMON VARIABLE IMMUNODEFICIENCY

AUTOIMMUNE DISEASES
SJOGERN'SSYNDROME
CELIAC SPRUE
RHEUMATOID ARTHIRITIS
SLE

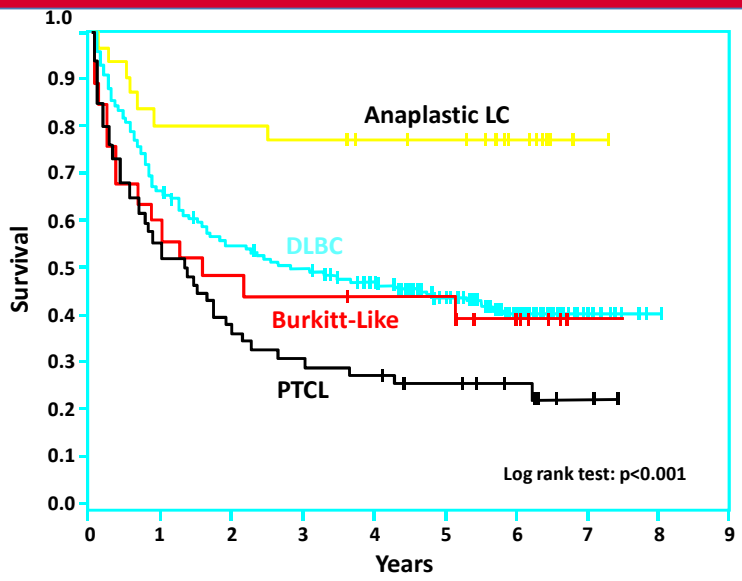
ACQUIRED IMMUNODEFICIENC STATES
IATROGENIC IMMUNOSUPPRESSION
HIV-1 INFECTION
AQUIRED HYPOGAMMAGLOGULINEMIA

CHEMICAL OR DRUG EXPOSURE
PHENYTOIN
DIGOXIN,PHENOXYHERBICIDES
RADIATION
PRIOR CHEMOTHERAPY
RADIATION THERAPY

INITIAL EVALUATION

- History and physical
- Diagnostic biopsy (excisional or incisional)
- Lab studies, CBC, diff, chem profile, LDH, B2 microglobulin, consider SPEP
- Bone marrow biopsy (bilateral?)
- Radiological studies, CT scans , PET? Gallium? MRI if indicated
- Viral serologies- hepatitits B,C, HIV, HTLV1? EBV?

NOT ALL LYMPHOMAS ARE CREATED EQUAL



COMMON MARKERS FOR DIAGNOSING LYMPHOMA SUBTYPES

T	B	NK	NK/T	HODGKIN'S DISEASE
CD 2	CD 20	CD 56	CD 56	CD 15
CD 3	CD 19	CD 16	CD 16	CD30
CD 4			CD3,4	CD20?
CD 8				
CD 7				
CD 10				
CD 30				
T cell gene rearrangements	B cell gene rearrangements			

Chronic lymphocytic leukemia/small lymphocytic lymphoma
B-cell prolymphocytic leukemia
Splenic marginal zone lymphoma
Hairy cell leukemia
Splenic lymphoma/leukemia, unclassifiable*
- Splenic diffuse red pulp small B-cell lymphoma*
- Hairy cell leukemia-variant*

Lymphoplasmacytic lymphoma
Waldenström macroglobulinemia
Heavy chain diseases
- Alpha heavy chain disease
- Gamma heavy chain disease
- Mu heavy chain disease

Plasma cell myeloma
Solitary plasmacytoma of bone
Extraosseous plasmacytoma
Extranodal marginal zone lymphoma of mucosa-associated
Lymphoid tissue(MALT lymphoma)
Nodal marginal zone lymphoma
Pediatric nodal marginal zone lymphoma*
Follicular lymphoma
Pediatric follicular lymphoma*
Primary cutaneous follicle center lymphoma
Mantle cell lymphoma

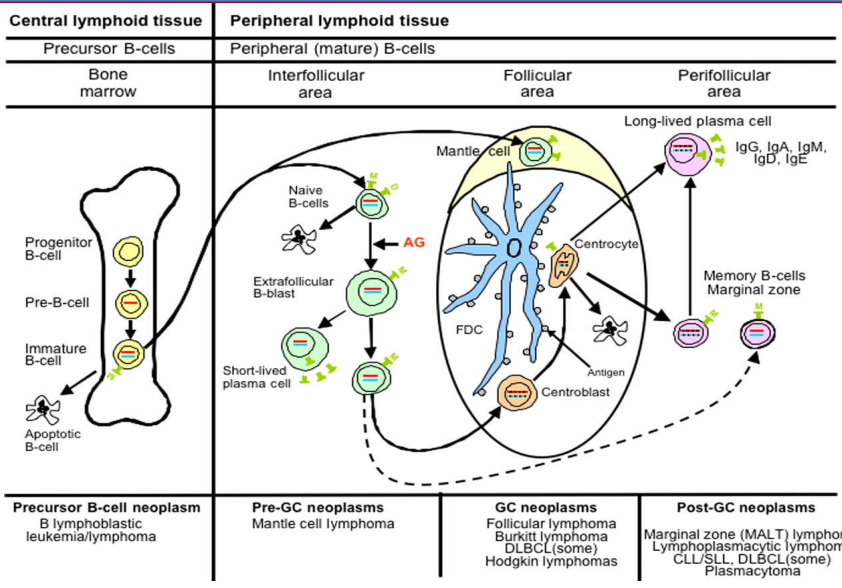
Diffuse large B-cell lymphoma (DLBCL), NOS
- T-cell/histiocyte rich large B-cell lymphoma
- Primary DLBCL of the CNS
- Primary cutaneous DLBCL, leg type
- EBV+ DLBCL of the elderly*

DLBCL associated with chronic inflammation
Lymphomatoid granulomatosis
Primary mediastinal (thymic) large B-cell lymphoma
Intravascular large B-cell lymphoma
ALK+ large B-cell lymphoma
Plasmablastic lymphoma
Large B-cell lymphoma arising in HHV8-associated multicentric Castleman disease
Primary effusion lymphoma
Burkitt lymphoma
B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt
B-cell lymphoma,

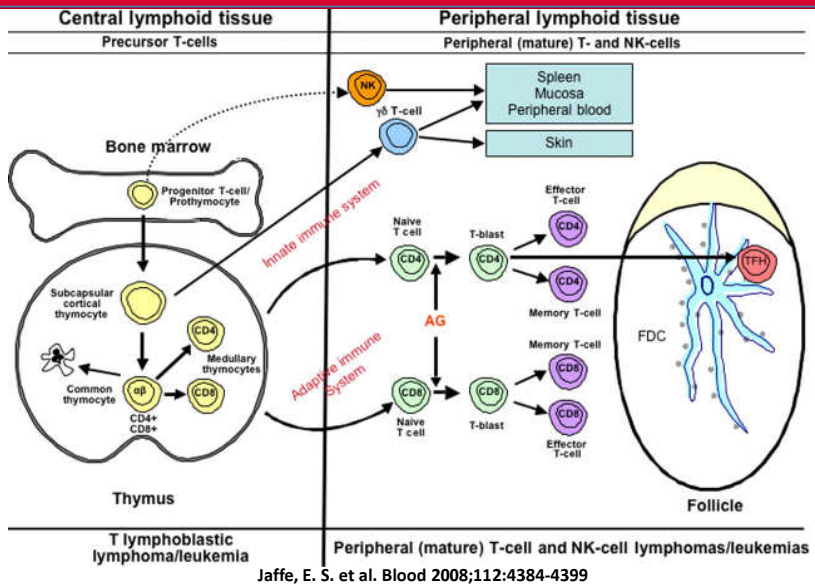
B- cell lymphoma unclassifiable with features intermediate between
diffuse large B-cell lymphoma and classical Hodgkin lymphoma

MATURE B CELL LYMPHOMAS

B CELL DIFFERENTIATION AND LYMPHOMA SUBTYPES



T-cell differentiation and lymphoma subtypes



Jaffe, E. S. et al. Blood 2008;112:4384-4399

MATURE T-CELL AND NK CELL NEOPLASMS

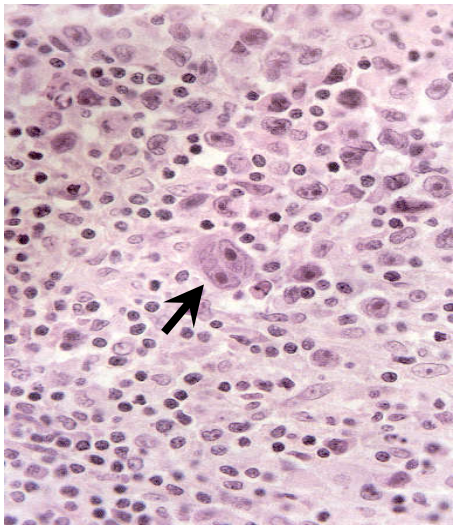
- T-cell prolymphocytic leukemia
- T-cell large granular lymphocytic leukemia
- Chronic lymphoproliferative disorder of NK cells*
- Aggressive NK cell leukemia
- Systemic EBV+ T-cell lymphoproliferative disease of childhood
- Hydroa vacciniforme-like lymphoma
- Adult T-cell leukemia/lymphoma
- Extranodal NK/T-cell lymphoma, nasal type
- Enteropathy-associated T-cell lymphoma
- Hepatosplenic T-cell lymphoma
- Subcutaneous panniculitis-like T-cell lymphoma
- Mycosis fungoides
- Sézary syndrome
- Primary cutaneous CD30+ T-cell lymphoproliferative disorders
  - Lymphomatoid papulosis
  - Primary cutaneous anaplastic large cell lymphoma
- Primary cutaneous gamma-delta T-cell lymphoma
- Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma*
- Primary cutaneous CD4+ small/medium T-cell lymphoma*
- Peripheral T-cell lymphoma, NOS
- Angioimmunoblastic T-cell lymphoma
- Anaplastic large cell lymphoma, *ALK*+
- Anaplastic large cell lymphoma, ALK–*

A BIOLOGIC APPROACH TO LYMPHOMAS

Very aggressive lymphomas	**Burkitt's lymphoma Diffuse large cell lymphomas – high proliferative index Hepatosplenic T cell lymphoma Blastic mantle cell lymphoma Gamma delta T cell lymphomas**	**Respond to chemotherapy and radiation therapy. Curable if treated aggressively**
Aggressive	Diffuse large B cell lymphomas PTCL except cutaneous T cell lymphomas Mantle cell lymphoma (high ki-67) Transformed lymphomas	Chemosensitive, high dose therapy and stem cell transplant can cure relapsed disease
Indolent	Follicular Marginal zone lymphomas, MALTS CTCL Mantle cell lymphoma (low ki-67) CLL/SLL	Slow growing, may be observed for a while. Not curable with chemotherapy alone

HODGKIN'S DISEASE

- Nodular Lymphocyte Predominance (5%)
- Classical HD (95%)
  - **Nodular sclerosis**
  - **Mixed cellularity**
  - **Lymphocyte depletion**
- Cell type
  - **typical H/RS**



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THANK YOU