LYMPHOMA CANADA

Lymphoma 101

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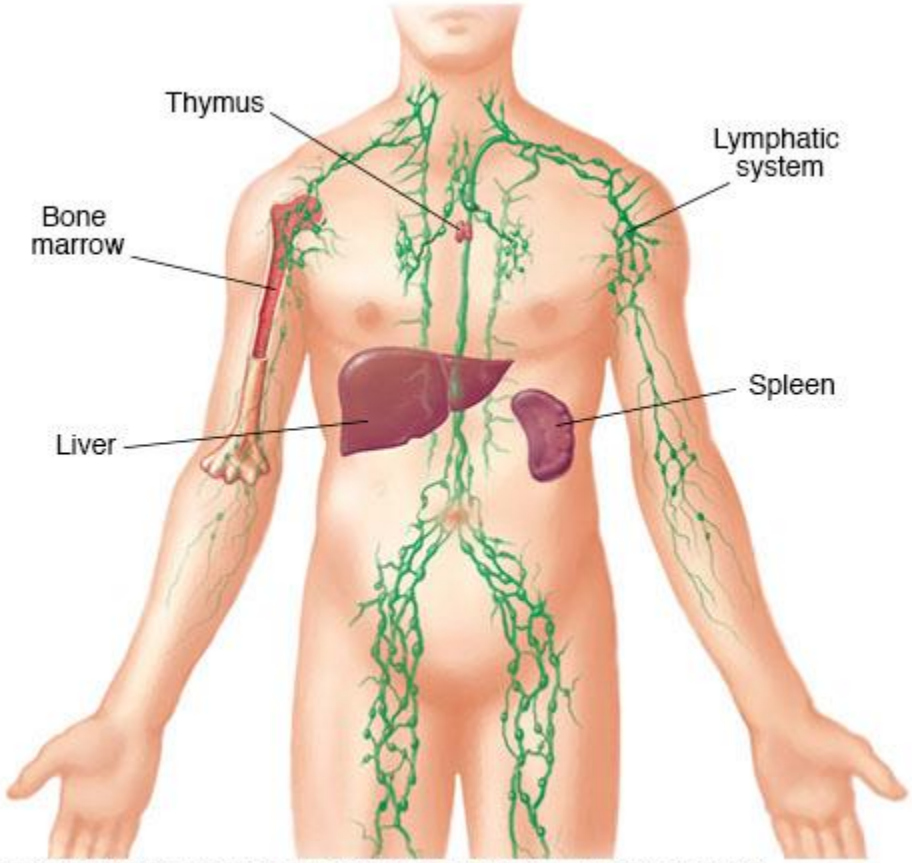
Declaration of potential conflit of interests

- Have received honorarium as advisor and/or speaker for :
  - Amgen
  - Bristol Myers Squibb
  - Celgene
  - Novartis
  - Paladin Laboratories

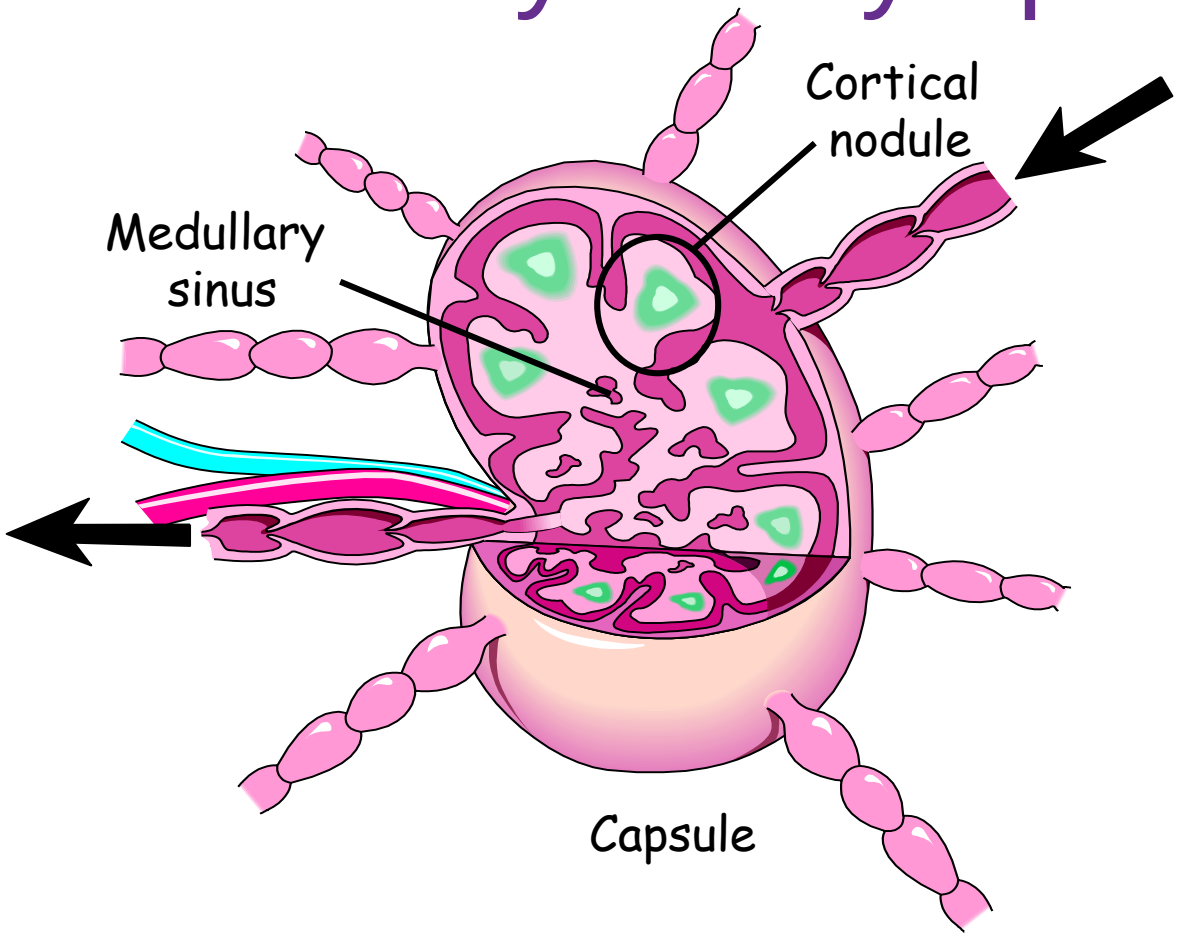
Lymphomas

- Group of cancers that originate in the lymphatic system (bone marrow, lymph nodes and other lymphoid organs such spleen and thymus)
  - A network of drainage vessels paralleling blood vessels
  - Bean shaped glands (lymph nodes)
  - This system of vessels ultimately meets and drains into the blood vessels in the neck
- Lymph vessels transport:
  - A normally clear liquid (lymph)
  - Lymphocytes, cells primarilly fighting infections

The Lymphatic System

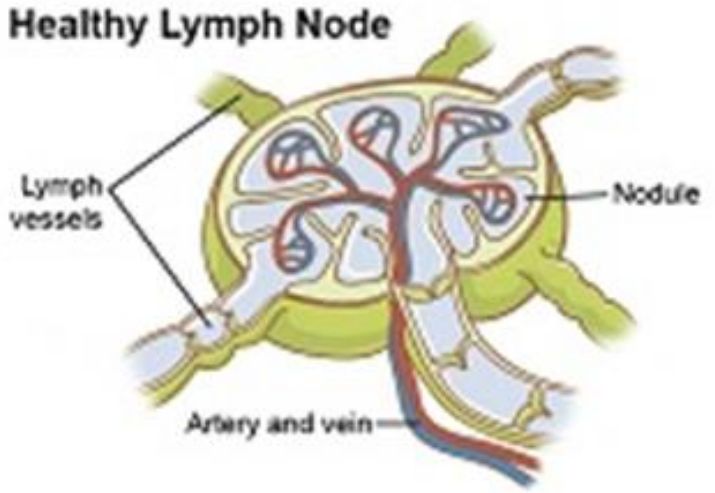


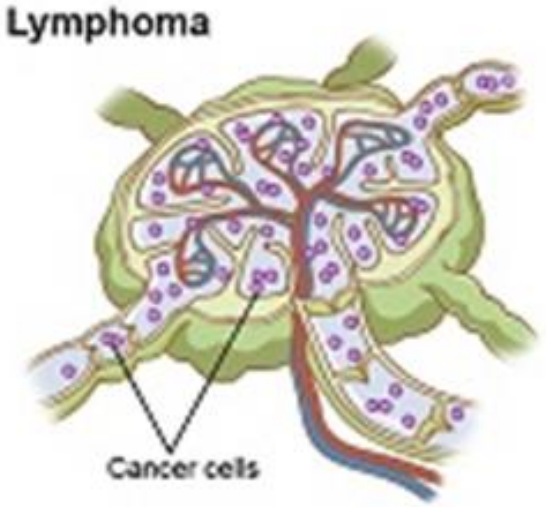
Anatomy of a lymph node



Lymphocytes

- B-cells develop in the bone marrow and key players of the immune system.
  - Produce antibodies, a protein, that circulates in blood and other body fluids capable of specifically targeting different structures on cells (infected or cancerous), microbes, other proteins (e.g. hormones)
- T-cells develop and mature in the thymus gland. Killer T-cells destroy virus infected cells and cancers. Helper T-cells orchestrate an immune response.
- NK (natural killer) cells destroy virus infected cells and cancers non specifically without delay. Can gain specificity by using antibodies that are produced by the B lymphocyte.

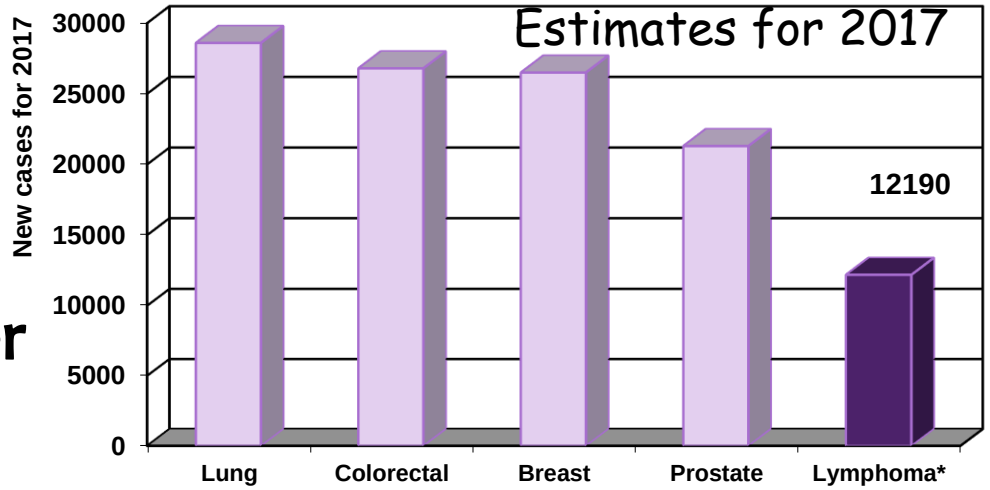

Healthy Lymph Node
Lymph vessels
Nodule
Artery and vein


Lymphoma
Cancer cells

Causes of lymphoma

- For the majority of cases, there is no known cause and no pre-existing risk factor
- Predisposition has been seen with:
  - Congenital immunodeficiencies;
  - Immunosuppression (e.g. HIV, post transplantation);
  - Auto-immune disorders;
  - Prior chemotherapy or radiation therapy;
  - Exposition to certain pesticides;
  - Alterations in lymphocytes following certain viral infections

Lymphoma in Canada

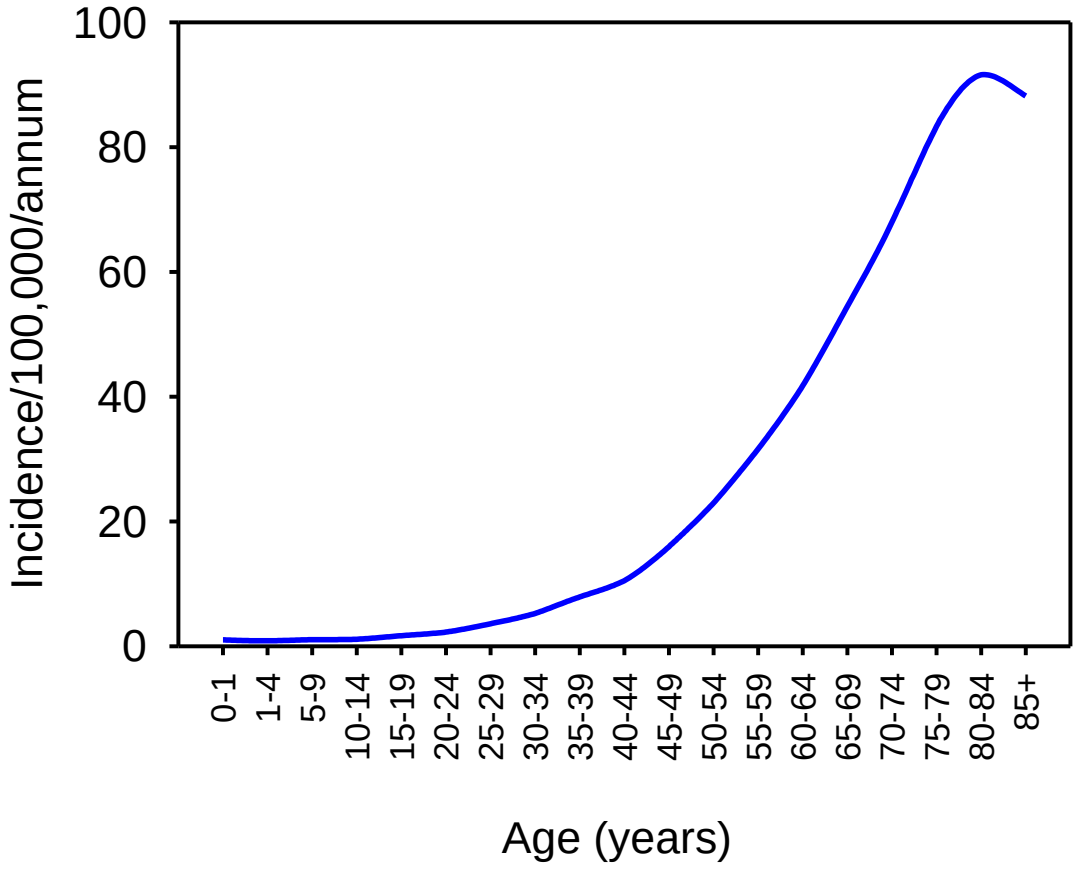


- 5th most common cancer
- In 2017 (estimates):
  - ~ 12 190 new cases* (Cf. ~ 206 200 total)
  - ~ 3590 deaths* (Cf. ~80 800 total)
  - Slight male predisposition (~ 55% of cases)
- NHL deaths have declined in ♂ by 2,3%/yr & in ♀ by 2,5%/yr during 2000 to 2012

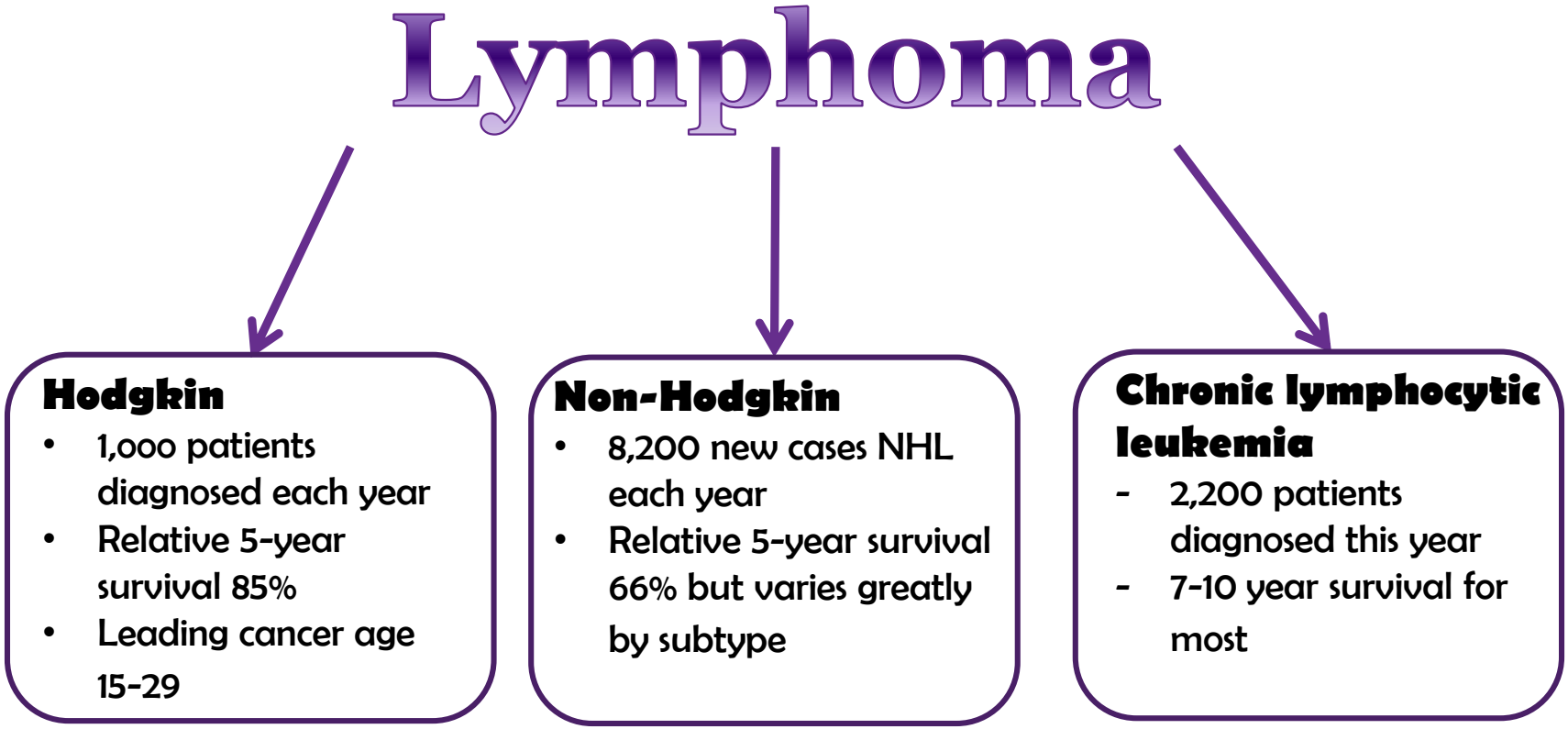
* Includes CLL representing ~ 47% new leukemia cases and ~ 26% of leukemia deaths in Canada

Canadian Cancer Society/National Cancer Institute of Canada: Canadian Cancer Statistics 2017

Increasing age is a risk factor for NHL



Lymphoma Types



Lymphomas can present with many different clinical manifestations.

- Variable
  - Severity: asymptomatic to extremely ill
  - Time course: evolution over weeks, months, or years
- Systemic manifestations
  - fever, night sweats, weight loss, anorexia, pruritis
- Local manifestations
  - lymphadenopathy, splenomegaly most common
  - any tissue potentially can be infiltrated

Lymphomas don't just arise in lymph nodes.

Nodal Sites	Extranodal
Neck	GI tract (stomach)
Supraclavicular	Bone
Axillary	Liver
Groin	Skin
Spleen	Head and neck
Bone marrow	

Other Complications of Lymphoma

- Bone marrow failure (low blood counts)
- CNS infiltration
- Immune hemolysis or thrombocytopenia
- Compression of adjacent structures (e.g. spinal cord, ureters) by bulky disease
- Pleural/pericardial effusions, ascites

Diagnosis of Lymphoma

- History:
  - Unwell non specifically (or not)
  - Lumps/bumps
  - Short of breath, abdominal pain/symptoms
  - B symptoms:
    - Fever
    - Drenching Night Sweats
    - Weight loss (>10% of baseline weight)

Classifying lymphomas by their clinical behaviour

Indolent NHL or CLL

- Slow growth
- Often asymptomatic
- Long natural history possible

- Incurable with standard therapy

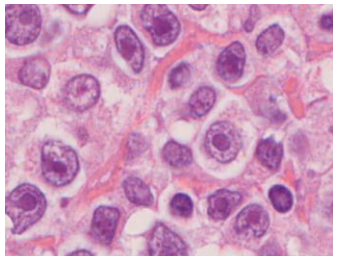
Aggressive NHL or HL

- Rapid growth
- Often symptomatic
- Fatal in months (if untreated)

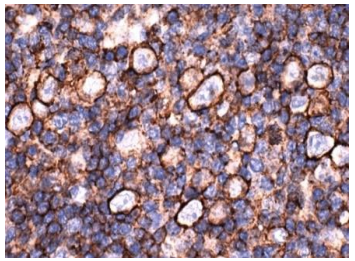
- Potential for cure with standard therapy

Lymphoma Classification

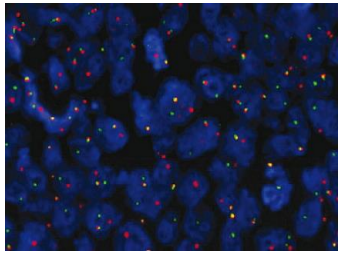
- Morphology



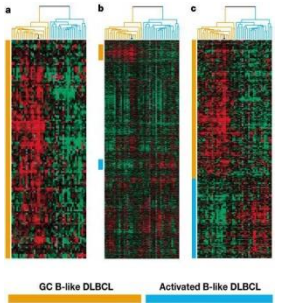
- Immunohistochemistry



- Cytogenetics



- (gene expression profiling)



Current Lymphoma Classification WHO – 2016 Revision

There are over 60 types of lymphoma.

Hodgkin lymphoma

- Classical Hodgkin lymphomas (4)
- Nodular lymphocyte predominant Hodgkin lymphoma (1)

Mature B-cell neoplasms (41 types)

Mature T-cell & NK-cell neoplasms (27 types)

Hodgkin Lymphoma

Classical Hodgkin Lymphoma

Nodular sclerosis classic Hodgkin lymphoma

Lmphocyte-rich classical Hodgkin lymphoma

Mixed-cellularity classical Hodgkin lymphoma

Lymphocyte-depleted classical Hodgkin Lymphoma

Non-classical Hodgkin lymphoma

Nodular lymphocyte-predominant Hodgkin lymphoma (low grade with watch and wait)

B cell Non Hodgkin

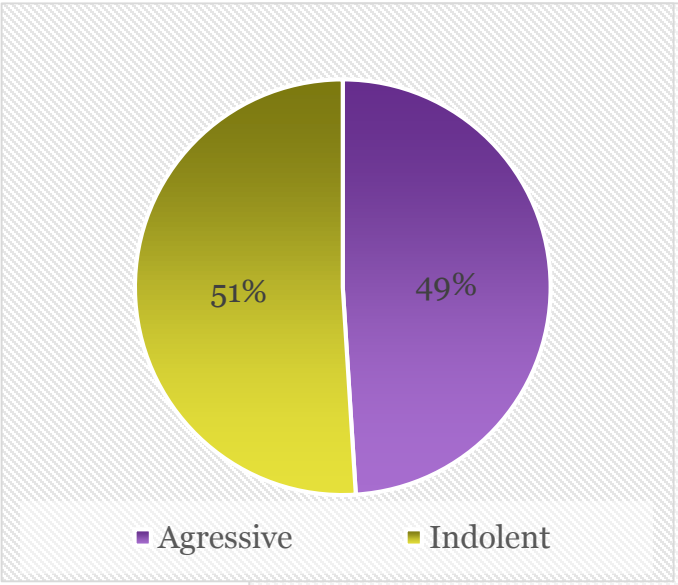
- Chronic lymphocytic leukemia/small lymphocytic lymphoma
- Monoclonal B-cell lymphocytosis*
- B-cell prolymphocytic leukemia
- Splenic marginal zone lymphoma
- Hairy cell leukemia
  - Splenic B-cell lymphoma/leukemia, unclassifiable
  - Splenic diffuse red pulp small B-cell lymphoma
  - Hairy cell leukemia-variant
- Lymphoplasmacytic lymphoma
  - Waldenström macroglobulinemia
- Monoclonal gammopathy of undetermined significance (MGUS), IgM*
- μ heavy-chain disease
- γ heavy-chain disease
- α heavy-chain disease
- Monoclonal gammopathy of undetermined significance (MGUS), IgG/A*
- Plasma cell myeloma
- Solitary plasmacytoma of bone
- Extraosseous plasmacytoma
- Monoclonal immunoglobulin deposition diseases*
- Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
- Nodal marginal zone lymphoma
  - Pediatric nodal marginal zone lymphoma
- Follicular lymphoma
  - In situ follicular neoplasia*
  - Duodenal-type follicular lymphoma*
- Pediatric-type follicular lymphoma*
- Large B-cell lymphoma with IRF4 rearrangement*
- Primary cutaneous follicle center lymphoma
- Mantle cell lymphoma
- In situ mantle cell neoplasia*
- Diffuse large B-cell lymphoma (DLBCL), NOS
- Germinal center B-cell type*
- Activated B-cell type*
- T-cell/histiocyte-rich large B-cell lymphoma
- Primary DLBCL of the central nervous system (CNS)
- Primary cutaneous DLBCL, leg type
- EBV+ DLBCL, NOS*
- EBV+ mucocutaneous ulcer*
- 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
- Primary effusion lymphoma
- HHV8+ DLBCL, NOS*
- Burkitt lymphoma
- Burkitt-like lymphoma with 11q aberration*
- High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements*
- High-grade B-cell lymphoma, NOS*
- B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma

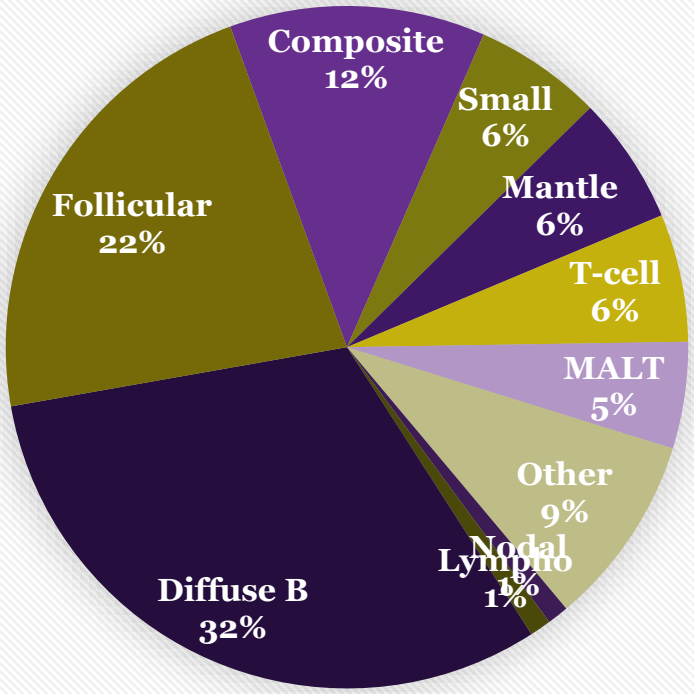
T cell Non Hodgkin

T-cell prolymphocytic leukemia
T-cell large granular lymphocytic leukemia
Chronic lymphoproliferative disorder of NK cells
Aggressive NK-cell leukemia
Systemic EBV+ T-cell lymphoma of childhood*
Hydroa vacciniforme–like lymphoproliferative disorder*
Adult T-cell leukemia/lymphoma
Extranodal NK-/T-cell lymphoma, nasal type
Enteropathy-associated T-cell lymphoma
Monomorphic epitheliotropic intestinal T-cell lymphoma*
Indolent T-cell lymphoproliferative disorder of the GI tract*
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 γδ T-cell lymphoma
Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma
Primary cutaneous acral CD8+ T-cell lymphoma*
Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder*
Peripheral T-cell lymphoma, NOS
Angioimmunoblastic T-cell lymphoma
Follicular T-cell lymphoma*
Nodal peripheral T-cell lymphoma with TFH phenotype*
Anaplastic large-cell lymphoma, ALK+
Anaplastic large-cell lymphoma, ALK−*
Breast implant–associated anaplastic large-cell lymphoma*

Non Hodgkin Lymphoma





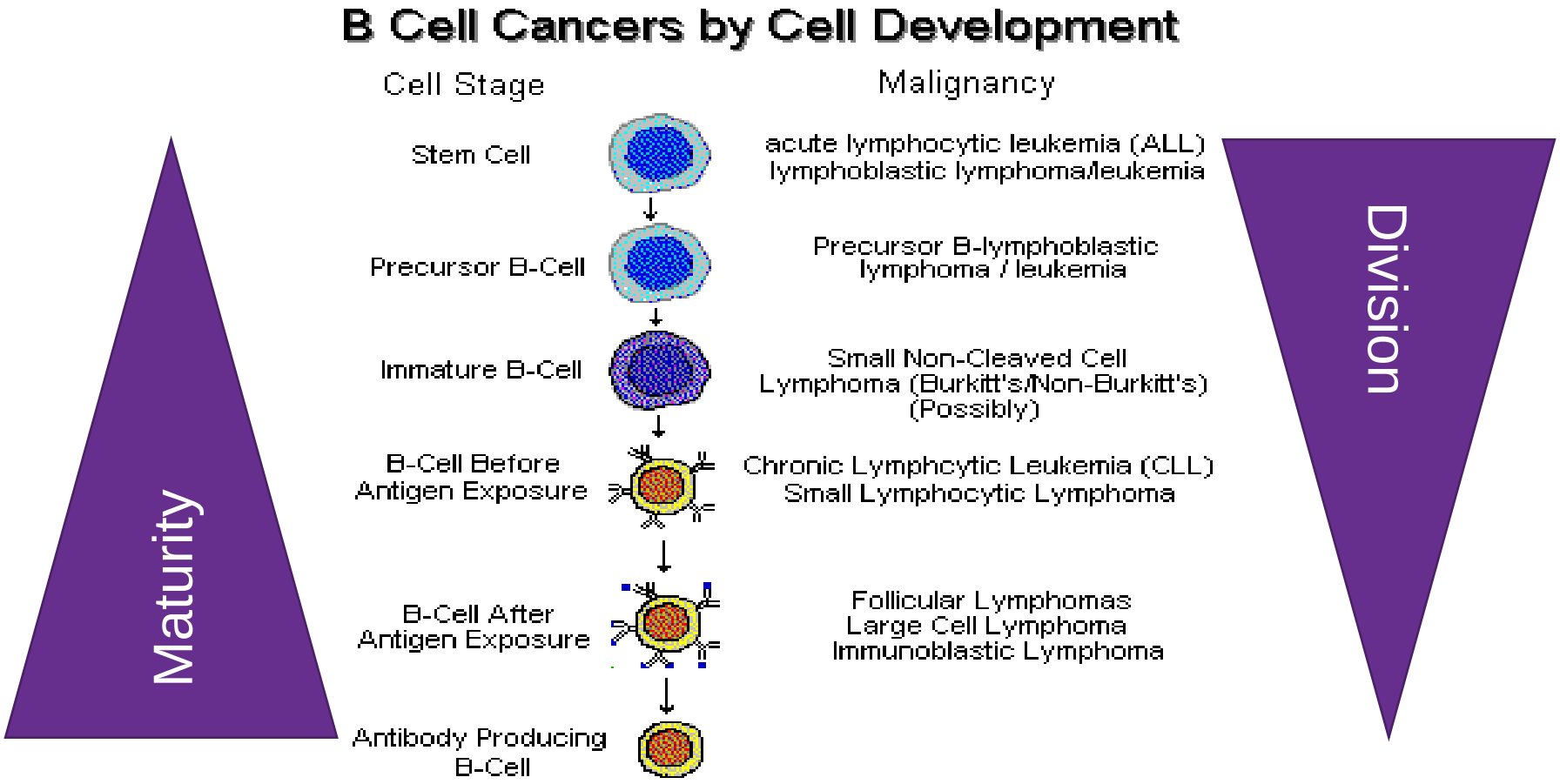
Composite Small Mantle T-cell MALT
Other Nodal Lympho Diffuse B Follicular

LYMPHOMA CANADA

lymphoma.ca

Armitage *et al*. *J Clin Oncol* 1998;16:2780–2795

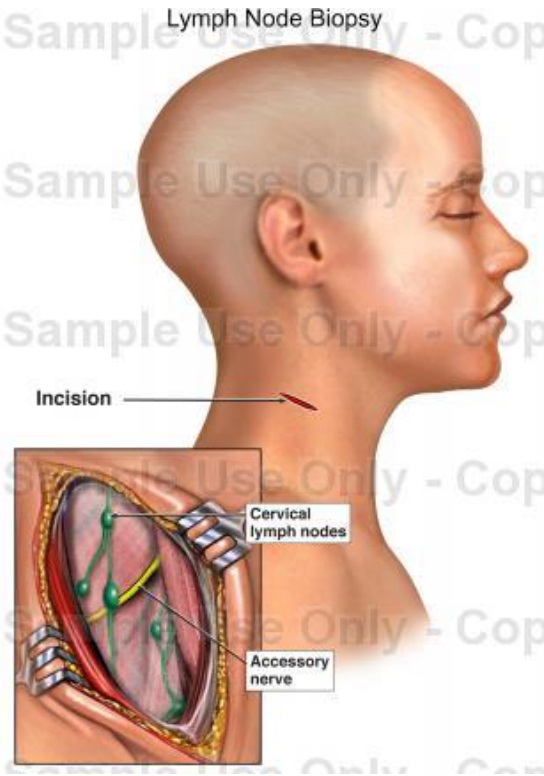
The different lymphomas originate at different levels of lymphocyte maturation.



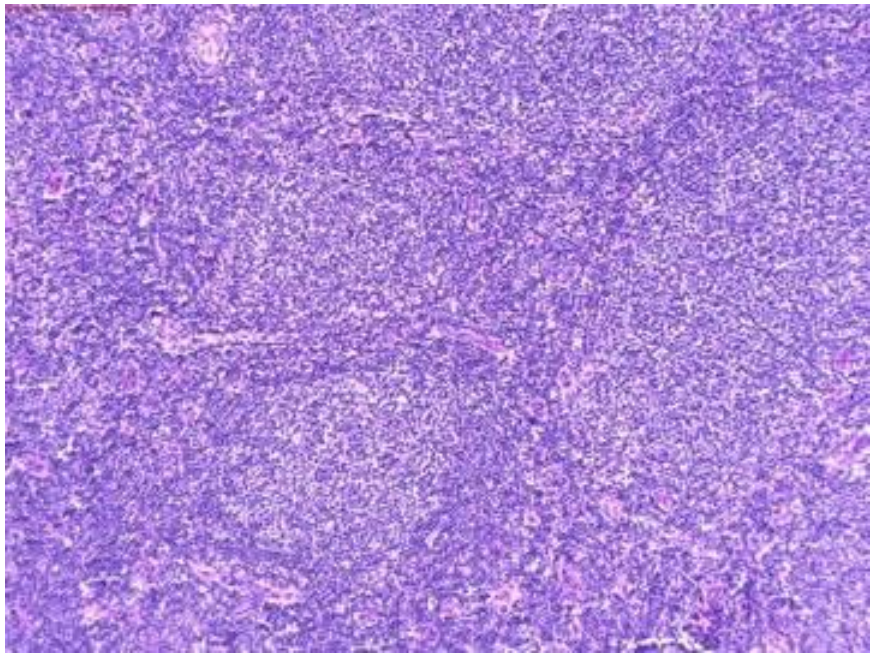
Lymphoma: How do we figure out what type you have?

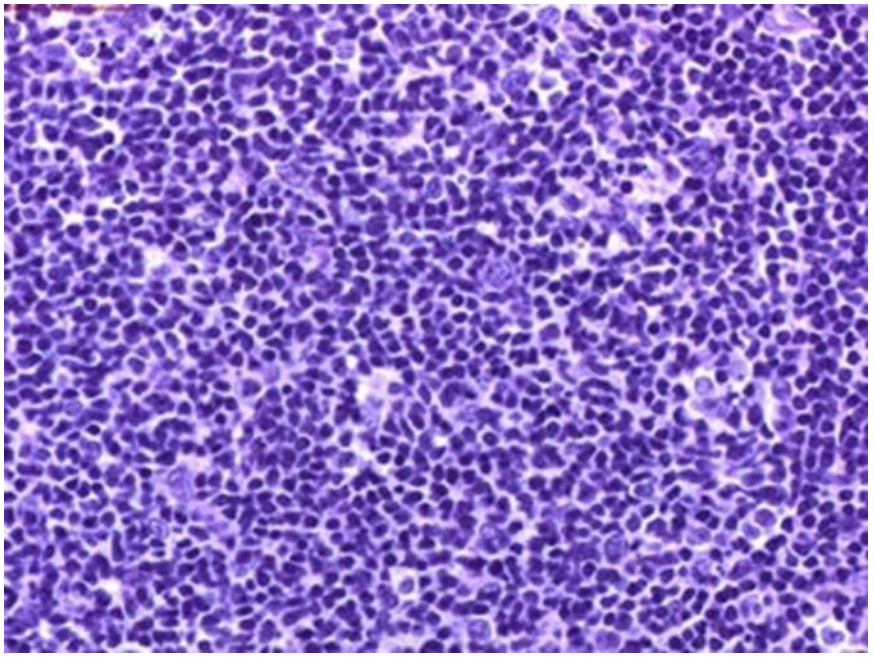
- **Physical Exam**
  - Cardiac, respiratory, abdominal,
  - Lymph nodes
- **Biopsy**
  - FNA
  - Incisional biopsy
  - Excisional biopsy
- **Laboratory:**
  - CBC and differential
  - LDH (prognostic marker in NHL)
  - ESR (important in HD)
  - Bone marrow aspirate/biopsy
- **Imaging:**
  - Chest X-ray
  - Ultrasound
  - CT scan neck/ chest/ abdomen/pelvis
  - Gallium Scan
  - PET
- **Other:**
  - LP – if CNS symptoms, or in certain high risk cases of aggressive lymphoma (sinus, testicle, bone marrow)

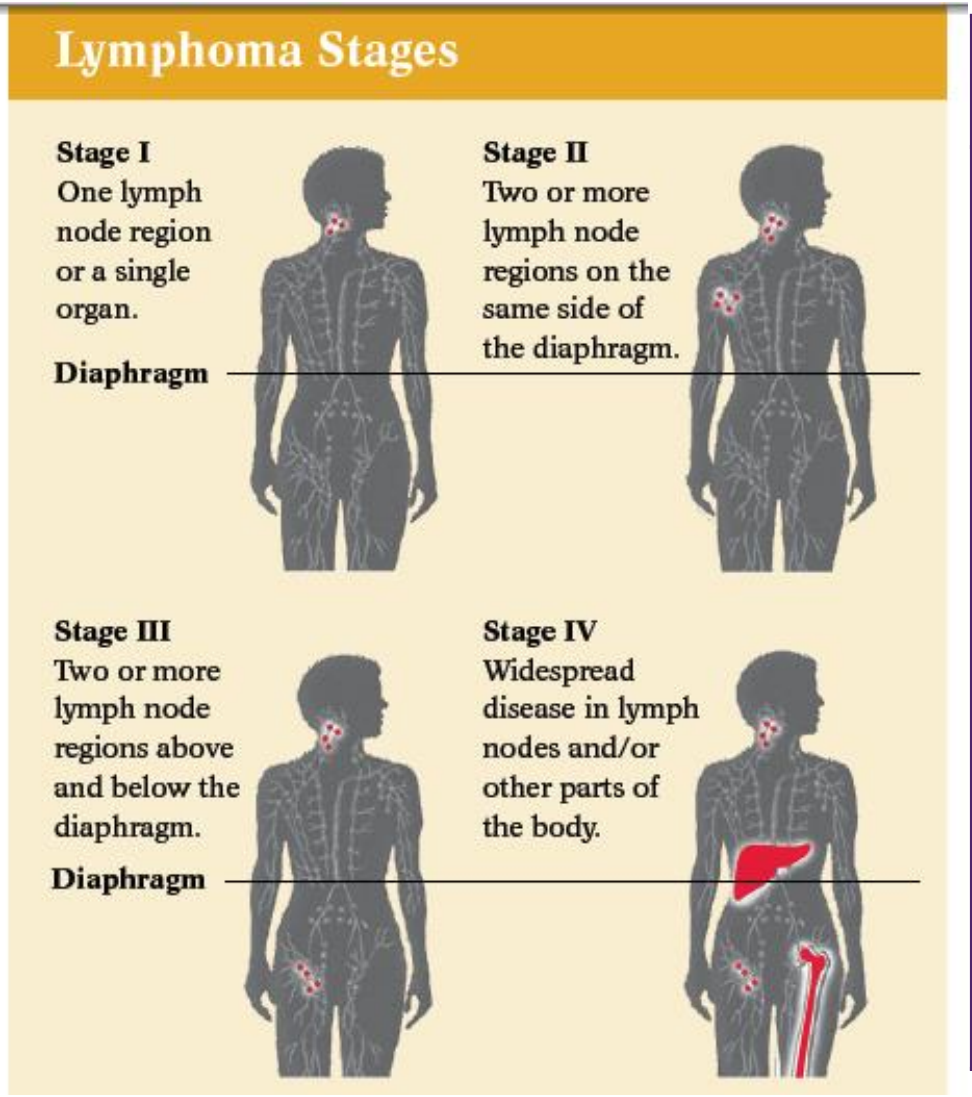
Pathology remains the absolute most critical piece of the diagnostic work-up….



Biopsies are Examined to Classify the Lymphoma







Designation	Characteristic
A:	Have no constitutional ('B') symptoms
B:	Have constitutional (fever, weight loss, night sweats) symptoms
E:	Involvement of areas other than lymph nodes
S:	Spleen involvement
X	Bulky disease

CLL staging system – Rai classification

Rai Stage	Risk	lymphocytes	RBC	Platelets	Lymph nodes enlarged?	Spleen enlarged?
0	Low	High	Normal	Normal	No	No
1	Intermediate	High	Normal	Normal	Yes	No
2	Intermediate	High	Normal	Normal	Maybe	Yes
3	High	High	Low	Normal	Maybe	Maybe
4	High	High	Low	Low	Maybe	Maybe

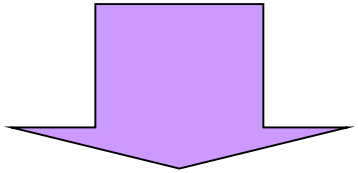
With all of the information formulation of treatment plan and prognosis.

Initial Evaluation:

Specific Histologic Sub-type

Extent of disease

General health status of patient



Treatment Plan

Prognosis

The importance of classification

- There is more than one treatment for each lymphoma
- The subtype of lymphoma dictates the thrapeutic approach
- Treatment is tailored to each patient
- Statistics are useful to predict the results for a group
- It is impossible to predict the results for a specific person accurately

Category		Survival of untreated patients	Curability	To treat or not to treat
Non-Hodgkin lymphoma	Indolent	Years	Generally not curable	Generally defer Rx if asymptomatic
	Aggressive	Months	Curable	Treat at Dx
	Very aggressive	Weeks	Curable	Treat at DX
Hodgkin lymphoma	All types	Variable – months to years	Curable	Treat at Dx

- Many lymphoma subtypes with different treatments and different outcomes.
- It is important you know exactly what your diagnosis is.
- If you don't know, ask your doctor.

Thank you for your attention