LYMPHOMA CANADA

Lymphoma/CLL 101: Know your Subtype

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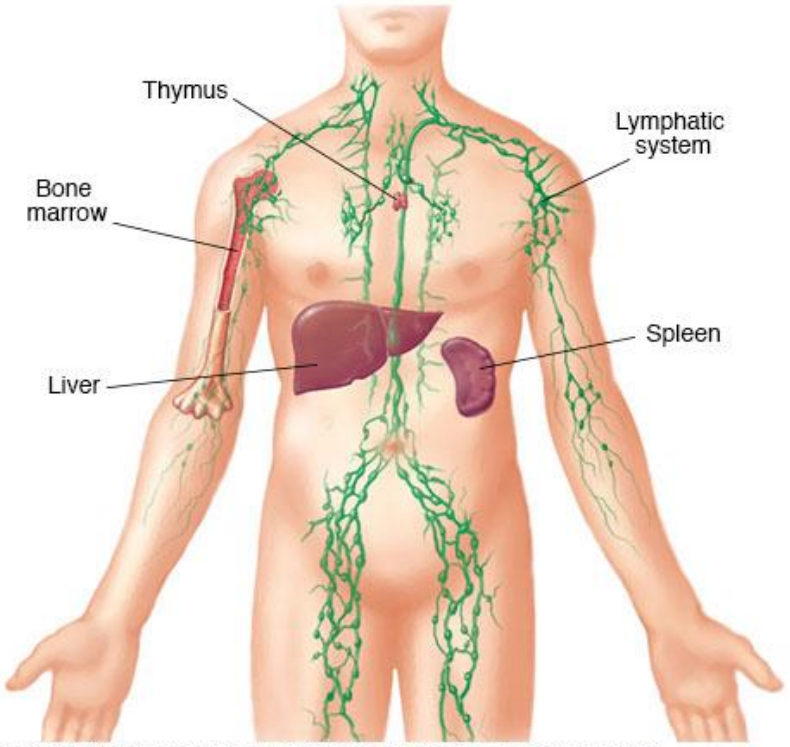
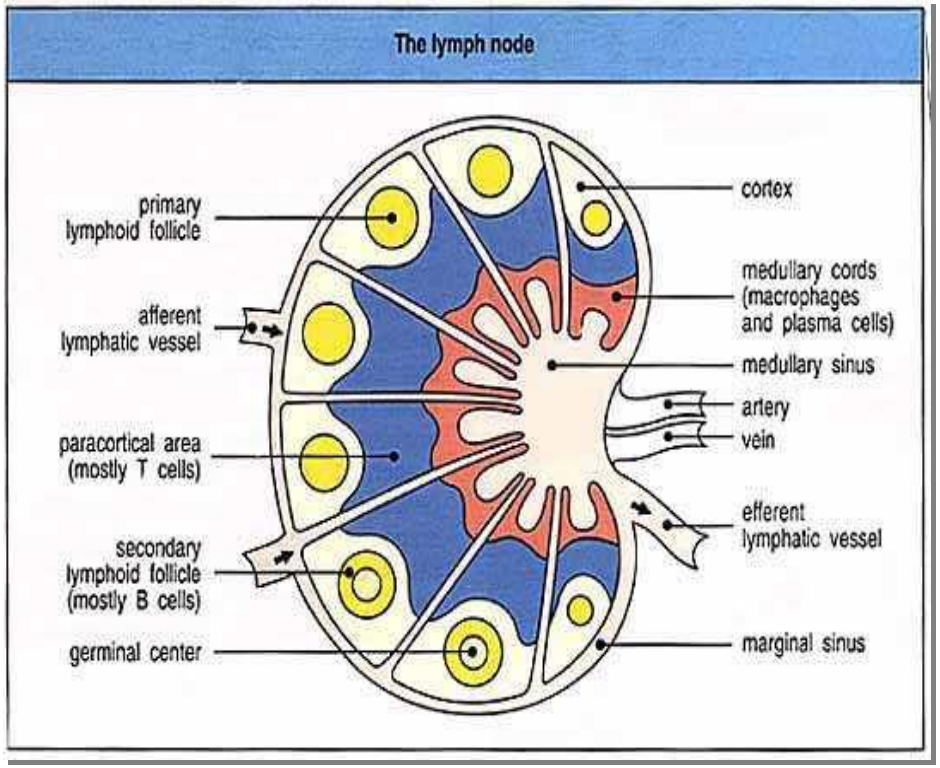
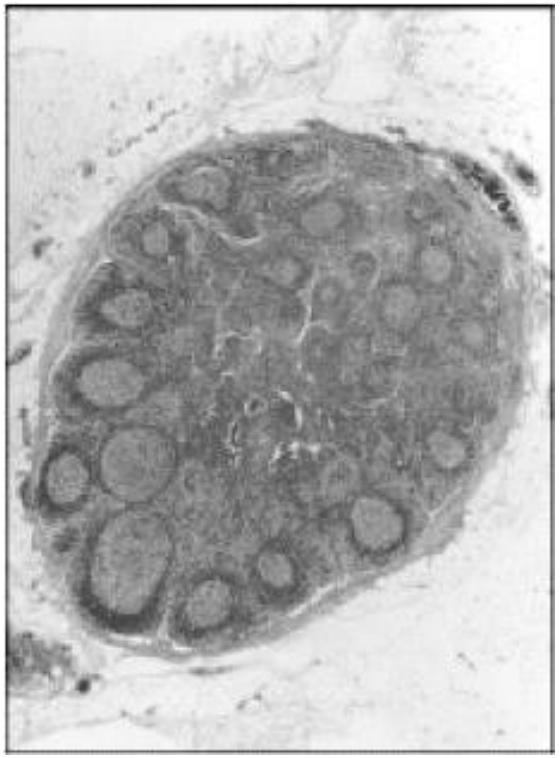
Function of the Lymph System



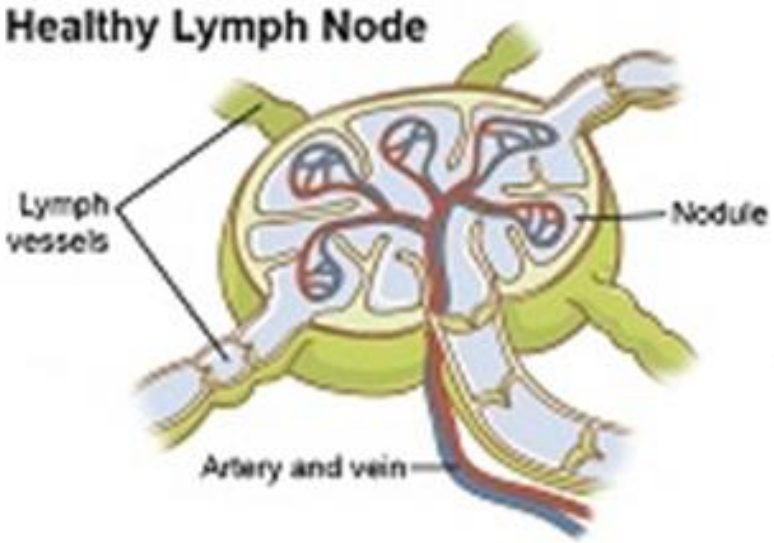
Lymph Node

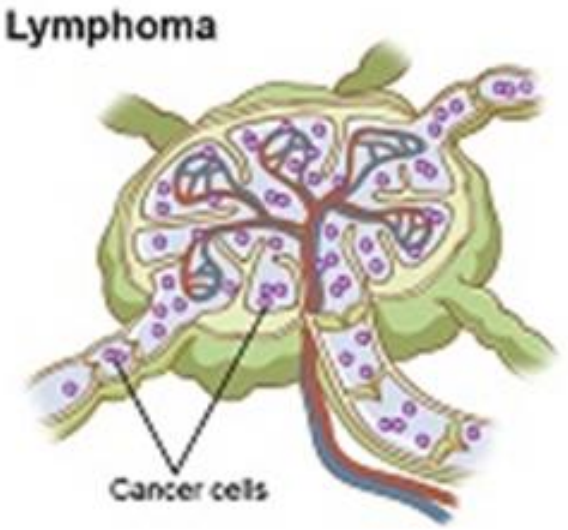

The lymph node
primary lymphoid follicle
afferent lymphatic vessel
paracortical area (mostly T cells)
secondary lymphoid follicle (mostly B cells)
germinal center
cortex
medullary cords (macrophages and plasma cells)
medullary sinus
artery
vein
efferent lymphatic vessel
marginal sinus

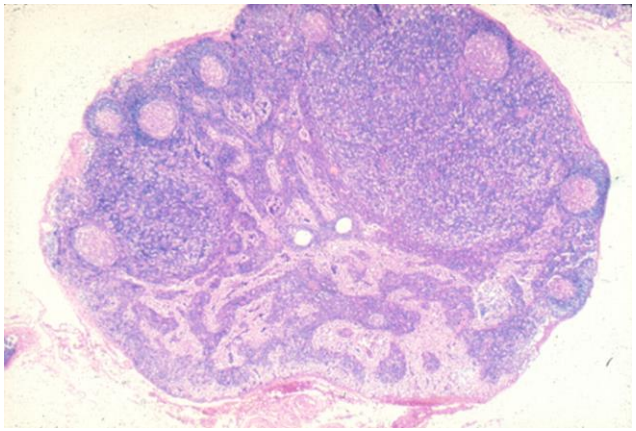


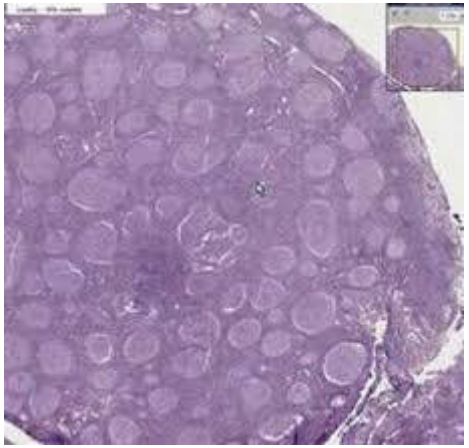
Lymphocytes

- B-cells develop in the bone marrow and influence the immune system by helping cells recognize infection.
- T-cells develop and mature in the thymus gland. Killer T-cells destroy viruses and cancers. Helper T-cells orchestrate an immune response.
- NK (natural killer) cells destroy viruses and cancers.

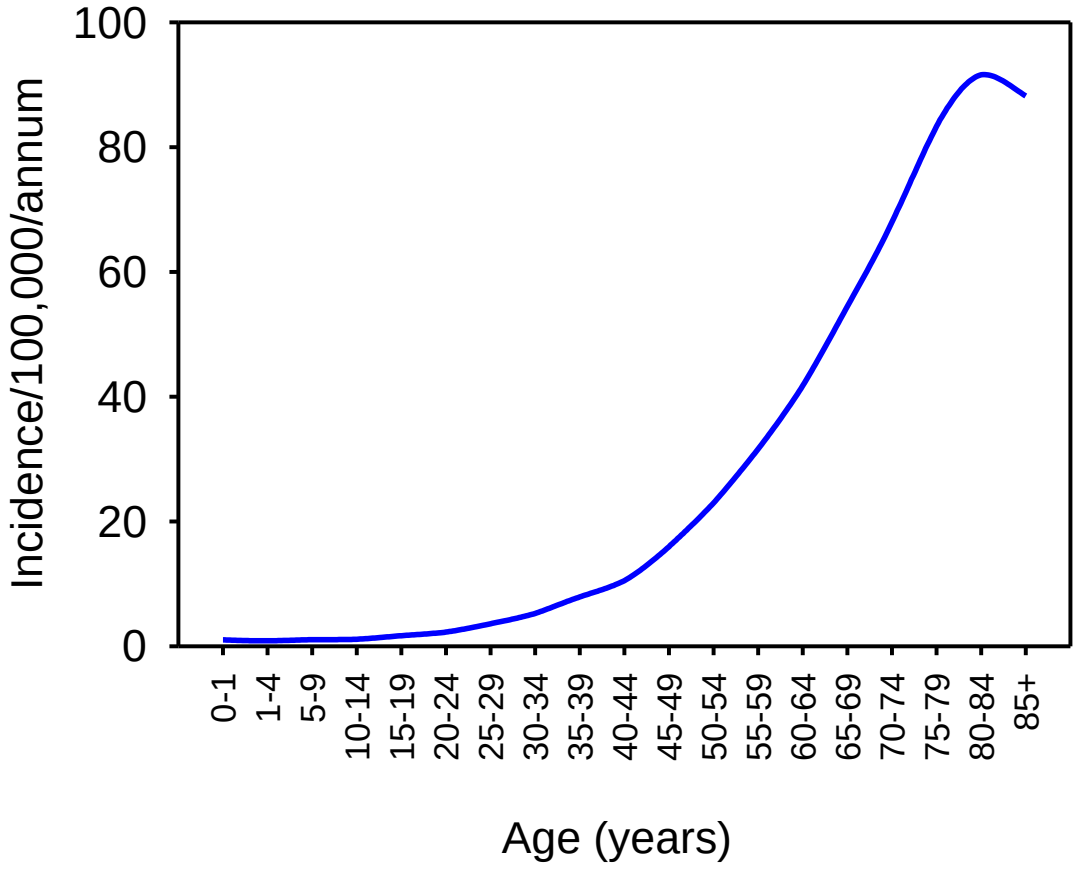

Healthy Lymph Node
Lymph vessels
Nodule
Artery and vein


Lymphoma
Cancer cells





Increasing age is a risk factor for NHL



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 marrow
axillary	liver
groin	skin
(spleen)	head and neck
bone	

Other Complications of Lymphoma

- Bone marrow failure (infiltration)
- CNS infiltration
- Immune hemolysis or thrombocytopenia
- Compression of structures (eg spinal cord, ureters) by bulky disease
- Pleural/pericardial effusions, ascites

Diagnosis of Lymphoma

- History:
  - Unwell
  - Lumps/bumps
  - Short of breath, abdominal pain/symptoms
  - B symptoms:
    - Fever
    - Drenching Night Sweats
    - Weight loss (>10% of baseline weight)

Lymphoma Types

Hodgkin

- 1,000 patients diagnosed each year
- Relative 5-year survival 85%
- Leading cancer age 15-29

Non-Hodgkin

- 8,200 new cases NHL each year
- Relative 5-year survival 66% but varies greatly by subtype

Chronic lymphocytic leukemia

- 2,200 patients diagnosed this year
- 7-10 year survival for most

Distinguishing lymphomas by 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

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

1. Nodular sclerosis classical Hodgkin lymphoma
2. Lymphocyte-rich classical Hodgkin lymphoma
3. Mixed cellularity classical Hodgkin lymphoma
4. Lymphocyte-depleted classical Hodgkin lymphoma

Non-classical Hodgkin Lymphoma

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

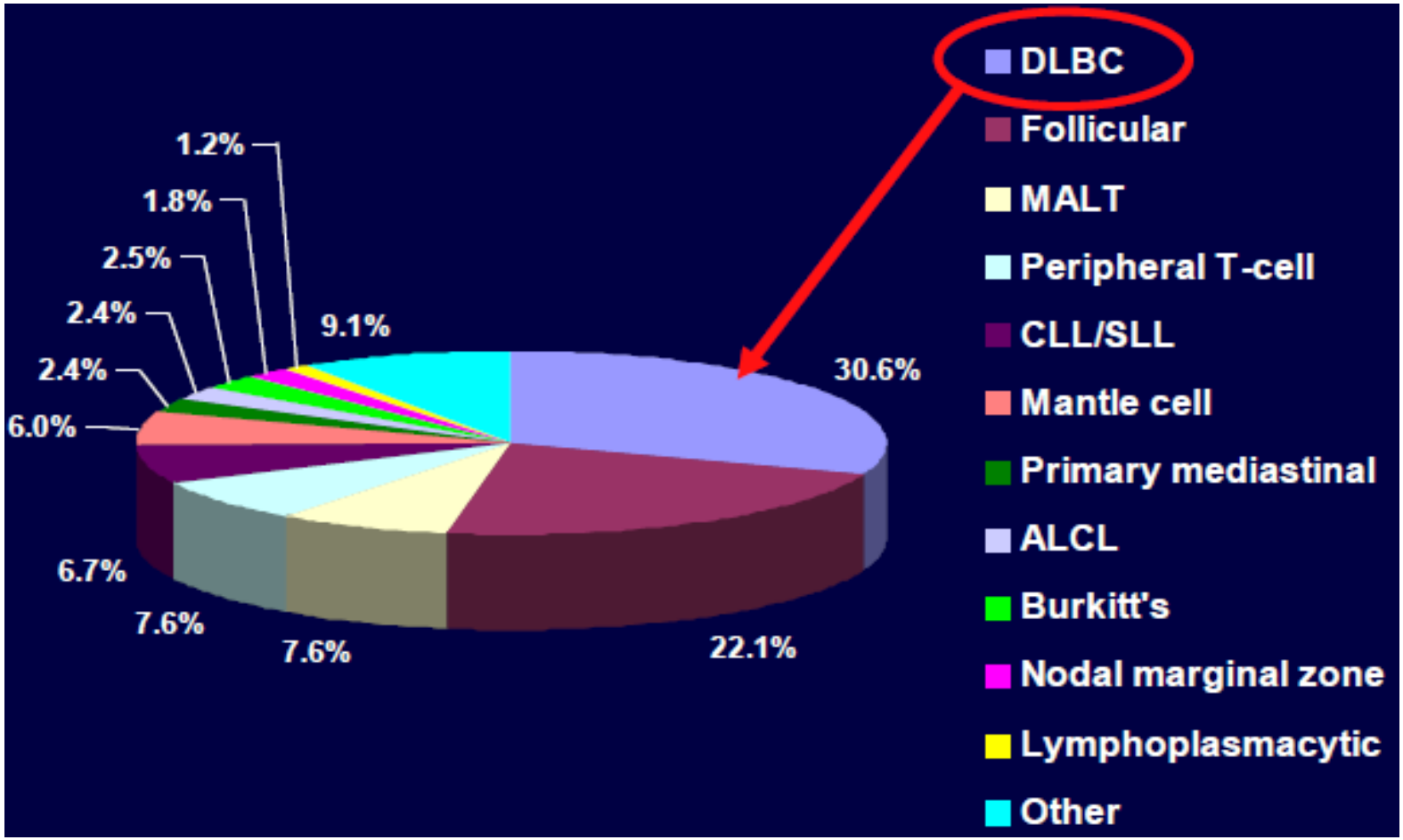
Non Hodgkin B Cell

- 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

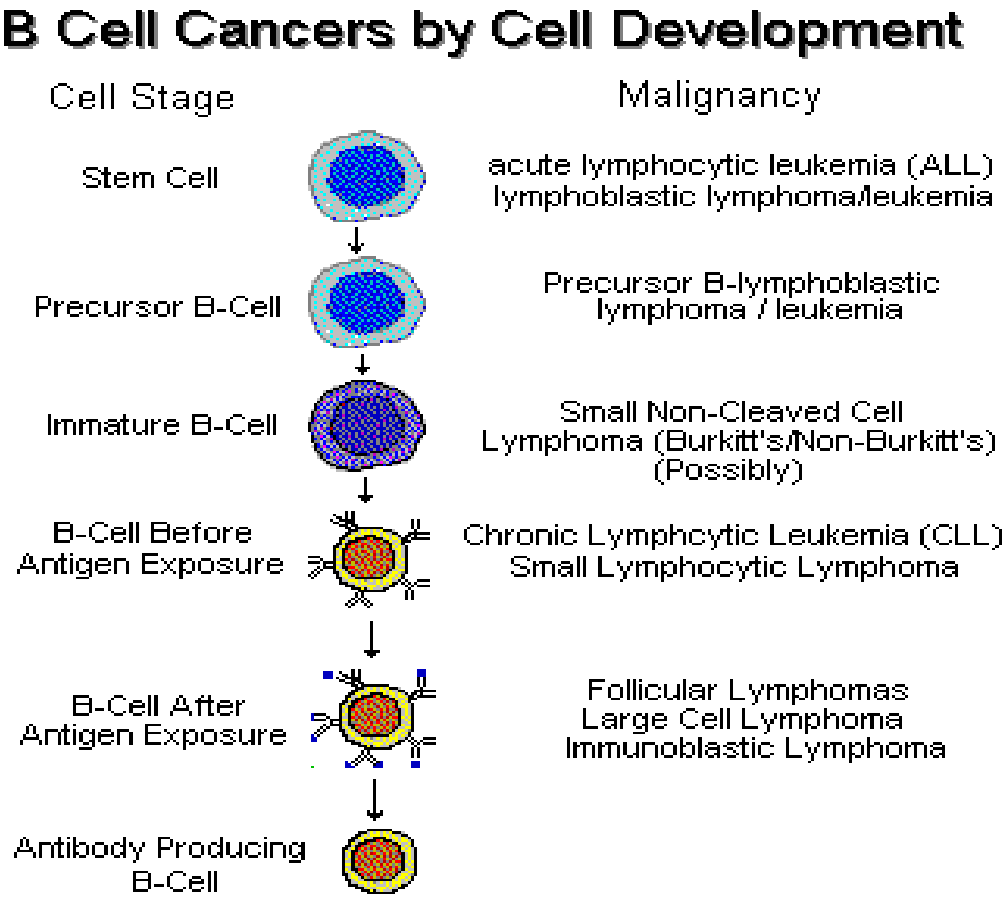
Non Hodgkin T Cell

- 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*

Current Lymphoma Classification



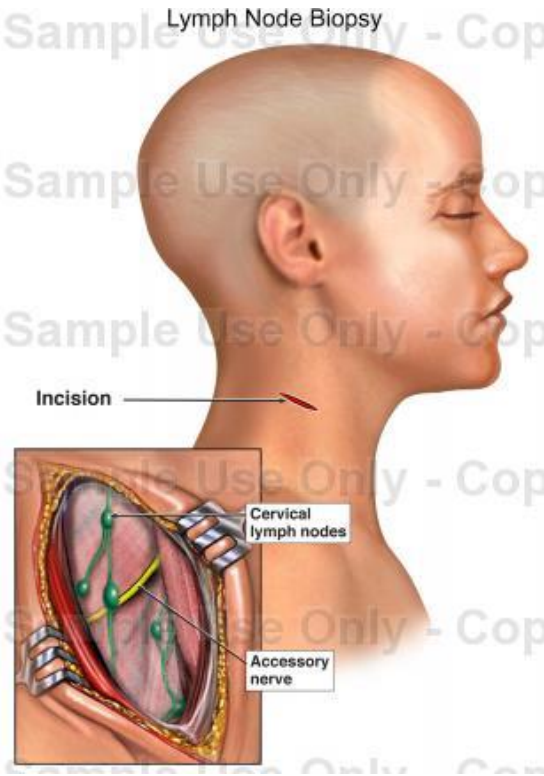
The different lymphomas originate at different levels of lymphocyte maturation.



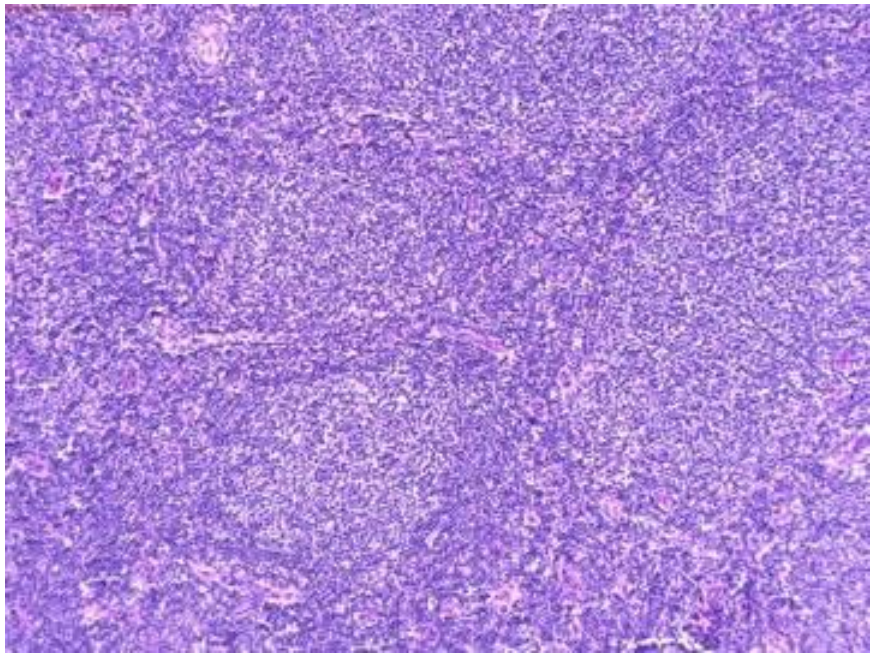
Lymphoma: How do we figure out what type you have?

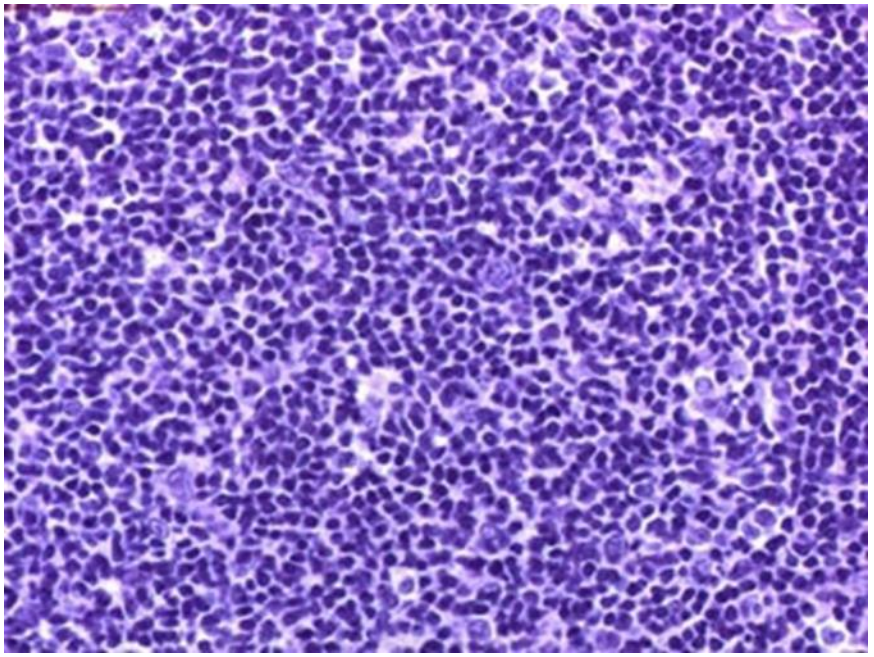
- **Physical Exam**
  - Cardiac, respiratory, abdominal,
  - Lymph nodes
- **Biopsy**
  - FNA
  - Incisional biopsy
  - Excisional biopsy
- **Laboratory:**
  - CBC and differential
  - LDH (prognostic marker in NHL)
  - ESR (important in HD)
  - Bone marrow aspirate/biopsy
- **Imaging:**
  - Chest X-ray
  - 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….



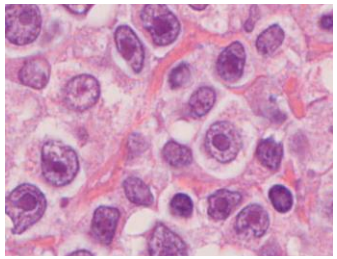
Biopsies are Examined to Classify the Lymphoma



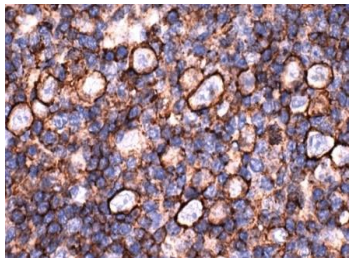


Lymphoma Classification

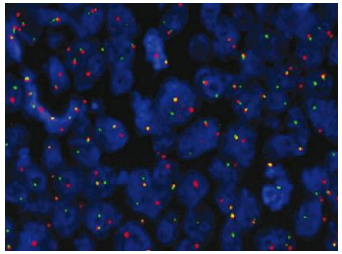
- Morphology



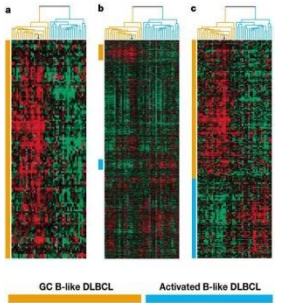
- Immunohistochemistry



- Cytogenetics



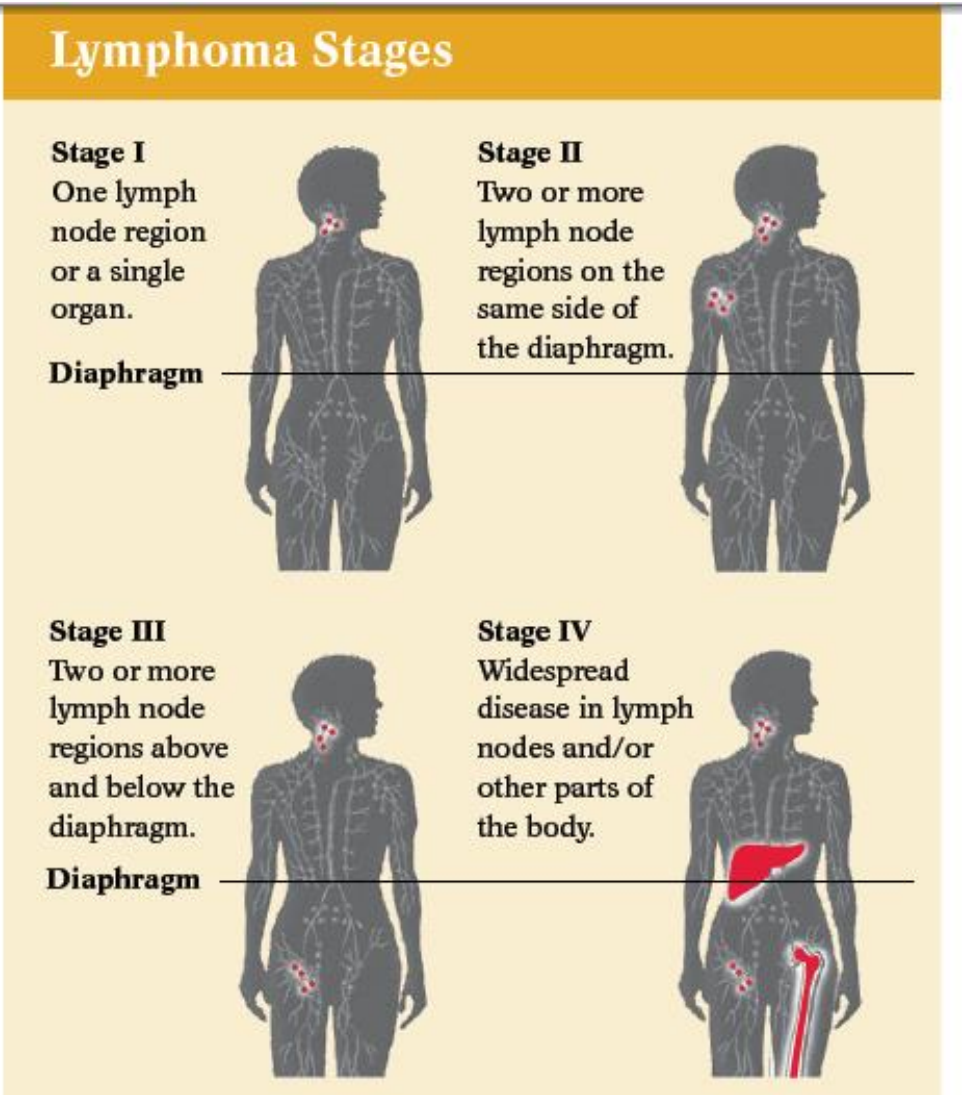
- (gene expression profiling)



Staging of Lymphoma and CLL

- Stage might influence prognosis
- Stage might influence how we choose to treat

- But…we DO NOT USE the term “metastatic”

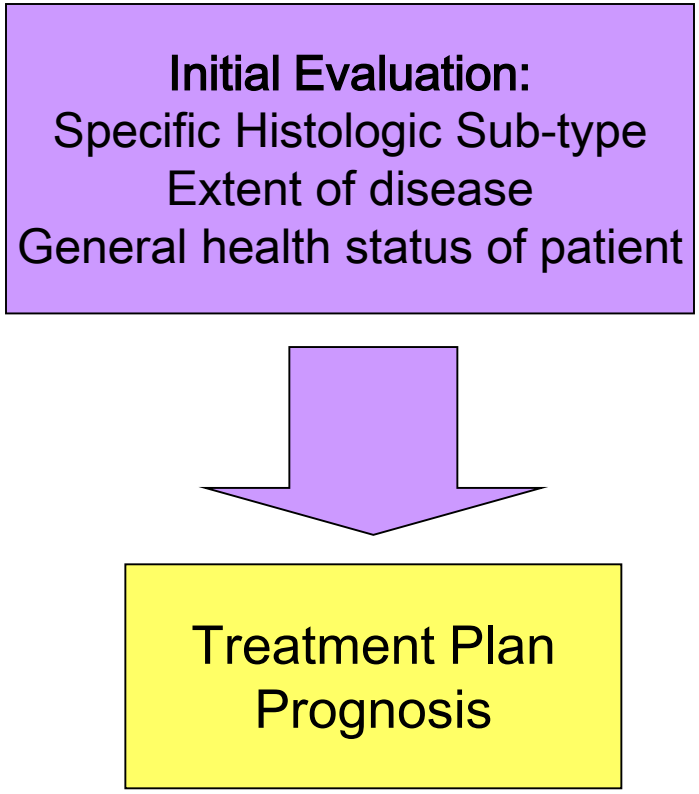


- **"A"** means that you have no “B” symptoms
- **"B"** reported fever, night sweats, & weight loss = ‘B’ symptoms
- **"E"** parts of your body other than the lymph nodes are involved

CLL Staging – Rai Staging System

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 we are now able to formulate a treatment plan and discuss prognosis.



- 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.

Know Your Subtype

- Is it Hodgkin or Non Hodgkin?
  - If it is Hodgkin, is it Classic or not?
  - If it is Non Hodgkin, is it T-cell or B-cell
    - If it is T-cell, is it Skin (Cutaneous) or Body (Systemic)
    - If it is B-cell, is it Indolent or Aggressive

Treating lymphomas according to subtype

Indolent NHL or CLL

- Slow growth
- Often asymptomatic
- Long natural history possible

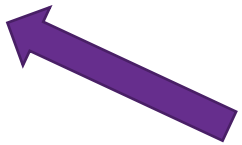
- Incurable with standard therapy

- Watch and Wait if no symptoms
- Goal of treatment intitially is to get long remission without too many side effects
- More difficult to treat each time it comes back
- Goal of later treatment is to control disease symptoms

Treating lymphomas according to subtype

Aggressive NHL or HL

- Rapid growth
- Often symptomatic
- Fatal in months (if untreated)
- Potential for cure with standard therapy



- Treat right away
- Goal of initial treatment is to try to cure
- More toxic treatments may be necessary
- Not everyone will be cured