LYMPHOMA 101

Causes and detection

Topics of discussion

- Research into the causes of lymphoma
- What are the steps and tests to detect lymphoma?
- Why does it take some patients a long time to receive their lymphoma diagnosis?

What is cancer?

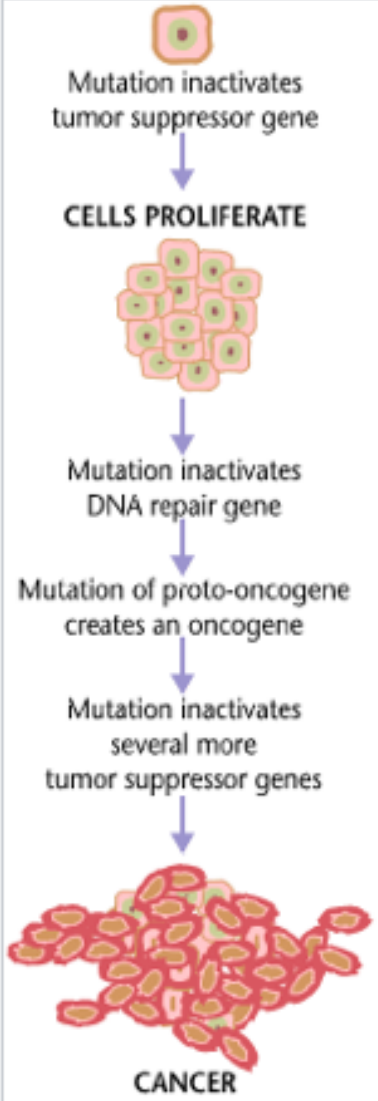
-cells that divide in an uncontrolled way

-cells normally grow, divide and die

-cancer occurs when the genes that control the cell life cycle are altered

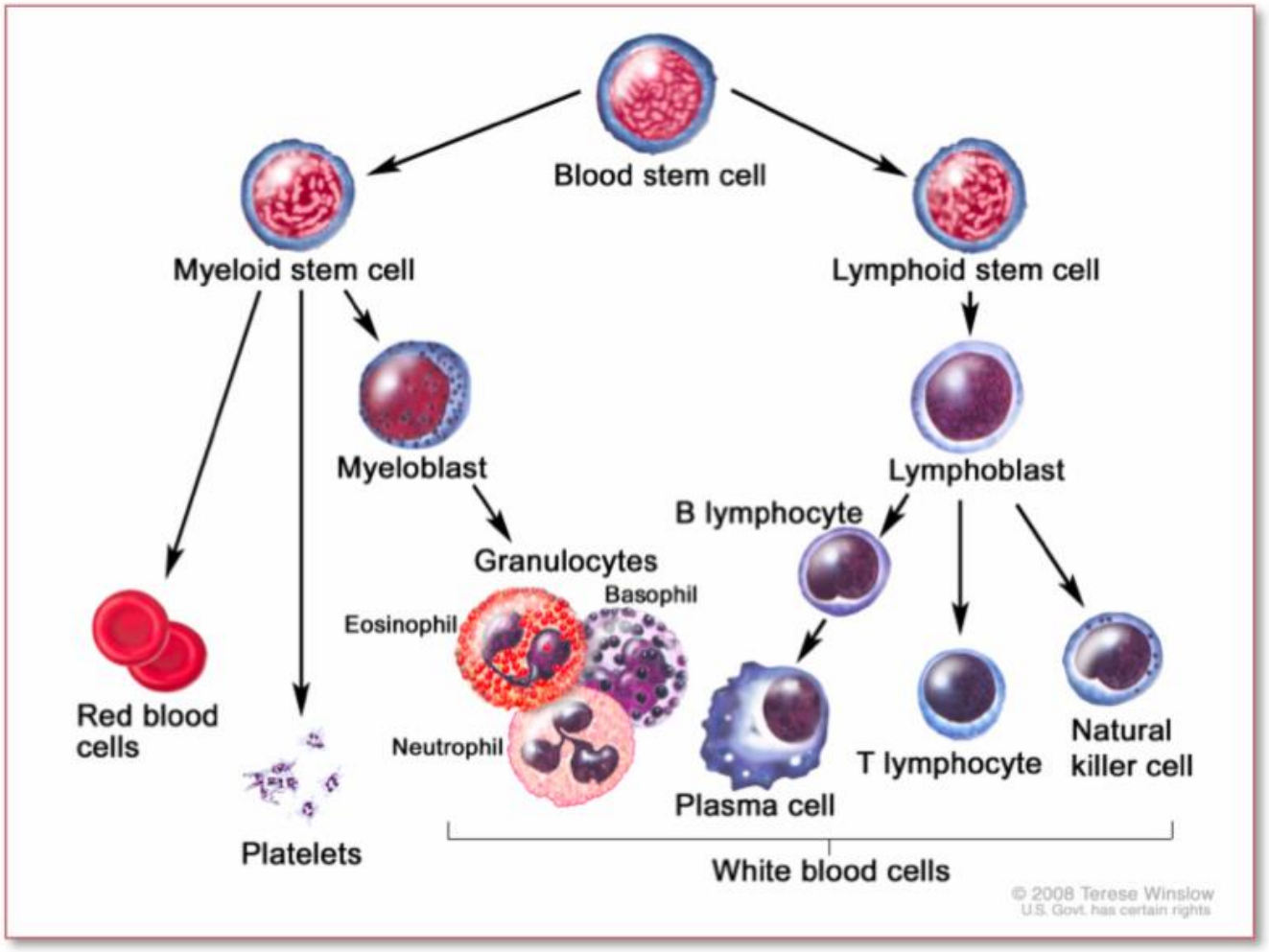
-these include genes that promote cell growth, that turn off cell division, or that play a role in repairing damaged DNA

cancerhealth.com



Cancers are caused by a series of mutations. Each mutation alters the behavior of the cell somewhat.

Lymphoma – cancer cell = lymphocyte



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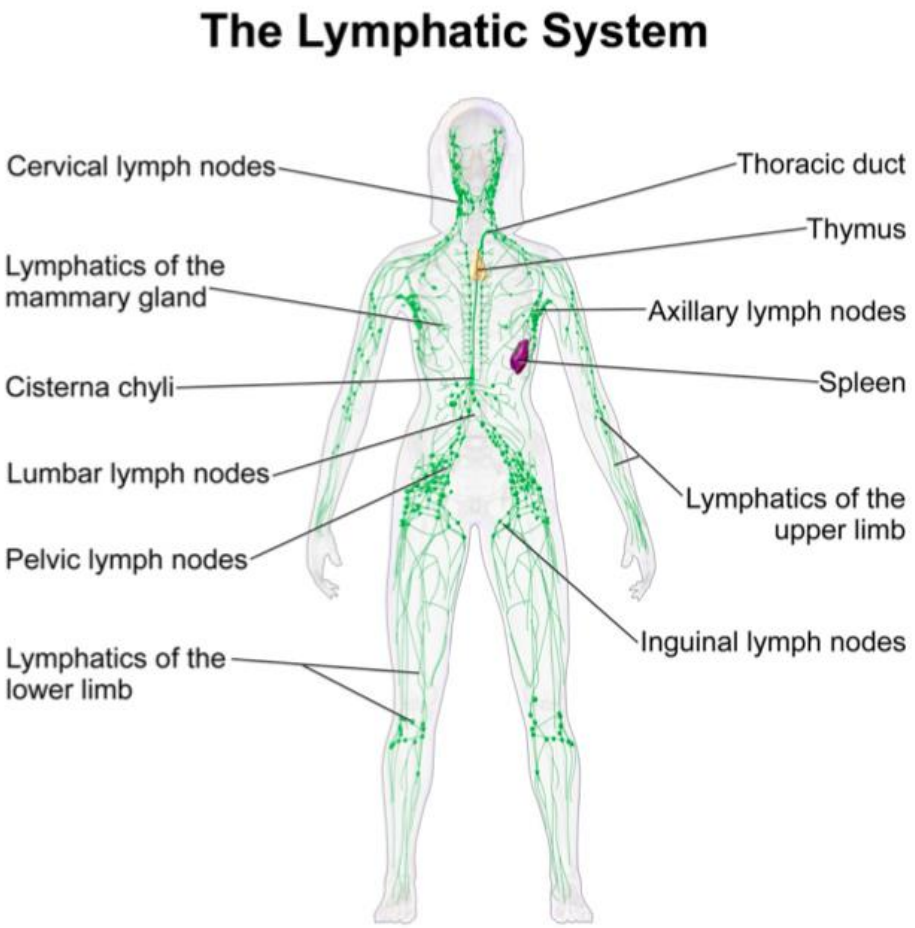
-Lymphocytes play a role in the immune system

-They circulate through our lymphatic system

-B-cells develop in the bone marrow and produce antibodies

-T-cells develop and mature in the thymus – they help destroy virus-infected cells and orchestrate an immune response



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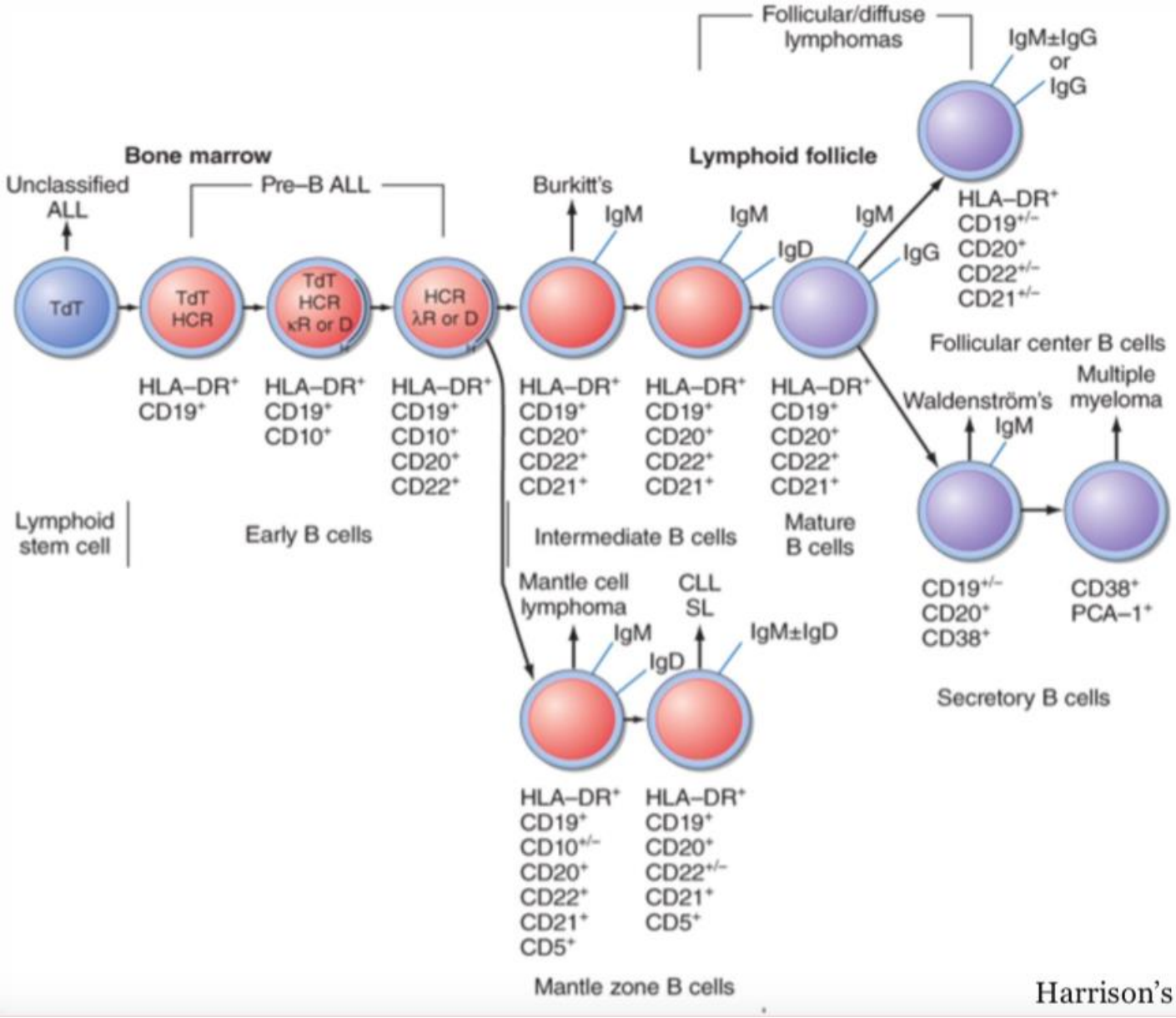
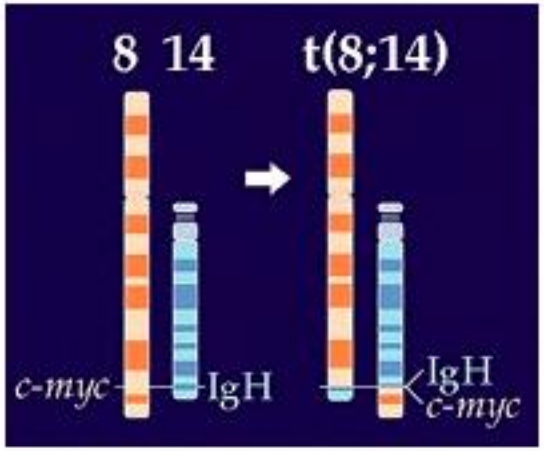
B-cell maturation

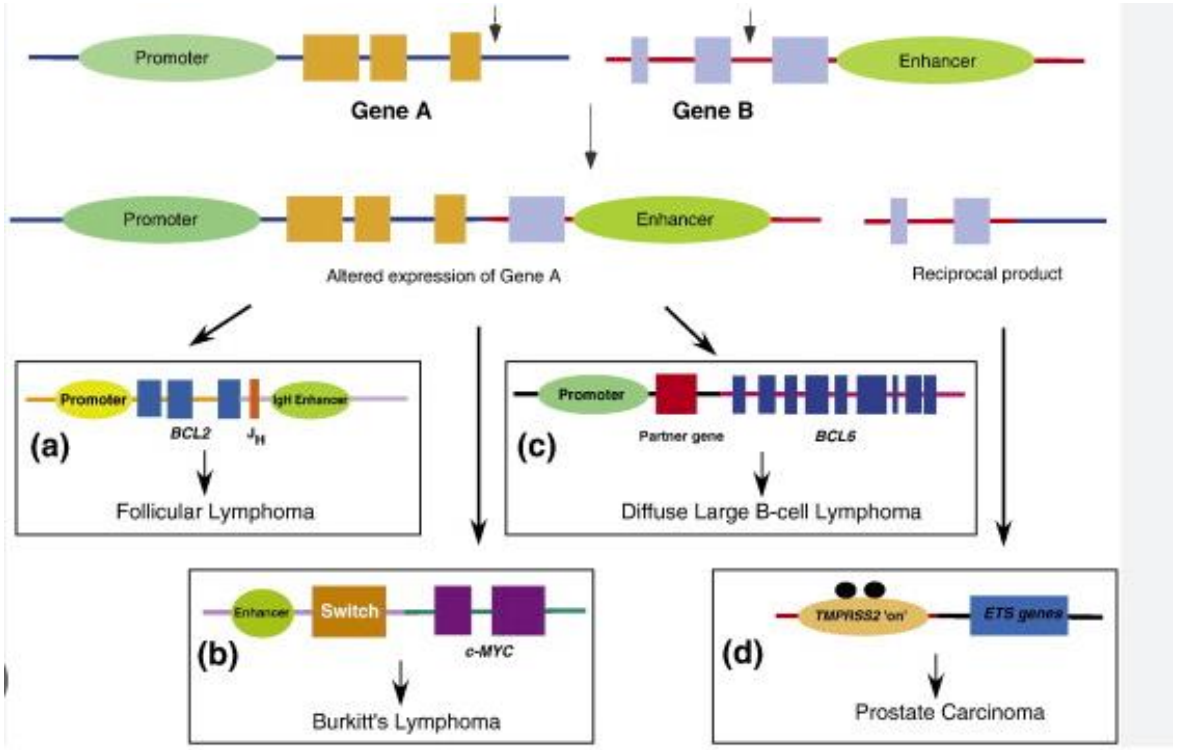


Harrison's Principles of Internal Medicine

Why does this happen? – DNA level



In Burkitt lymphoma, Myc, which is normally found on chromosome 8, is transferred to chromosome 14. This is known as chromosome translocation and can be characteristic of a cancer type. [image credit: Gregory Schuler, NCBI, NLM, NIH.]

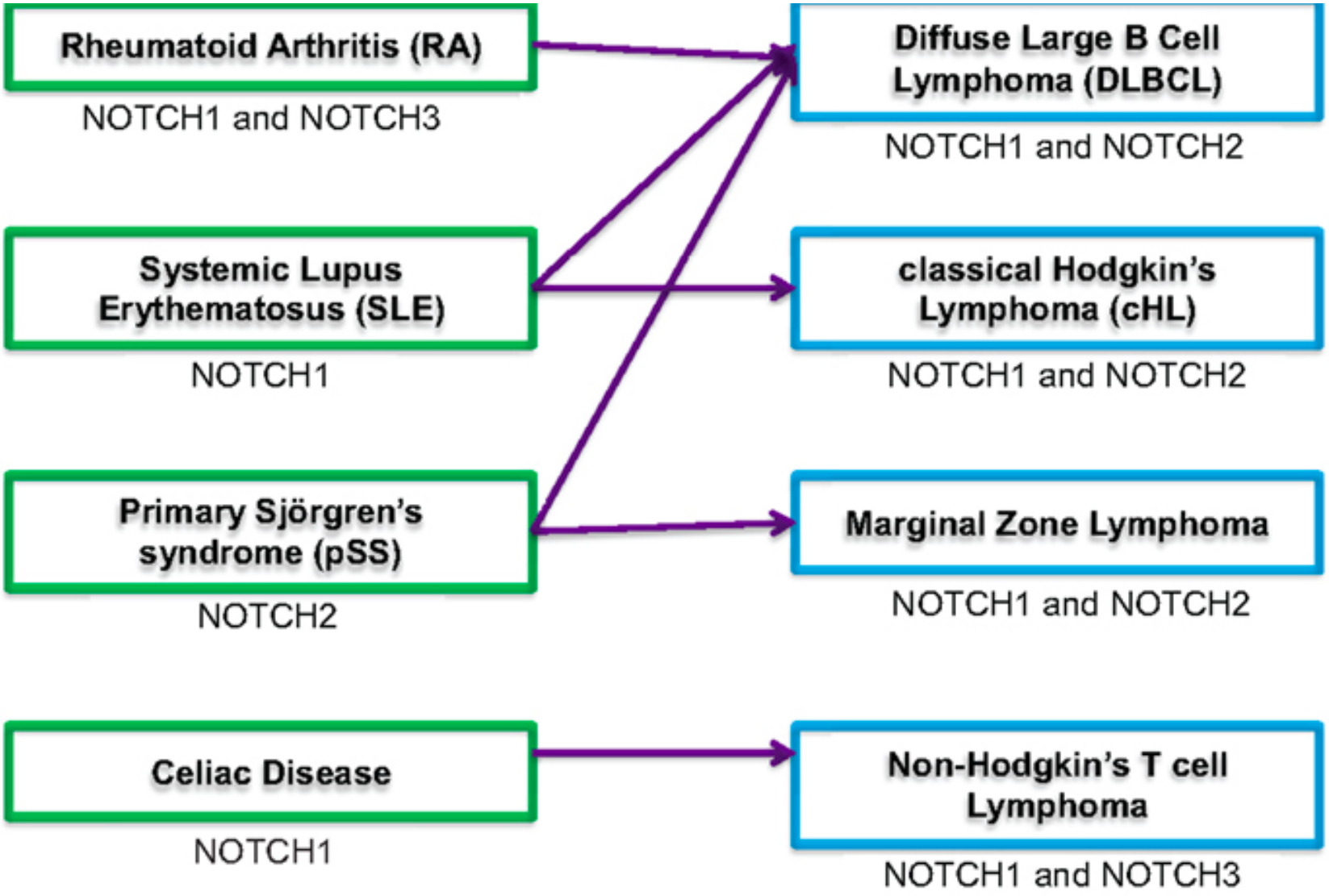


Causes of lymphoma

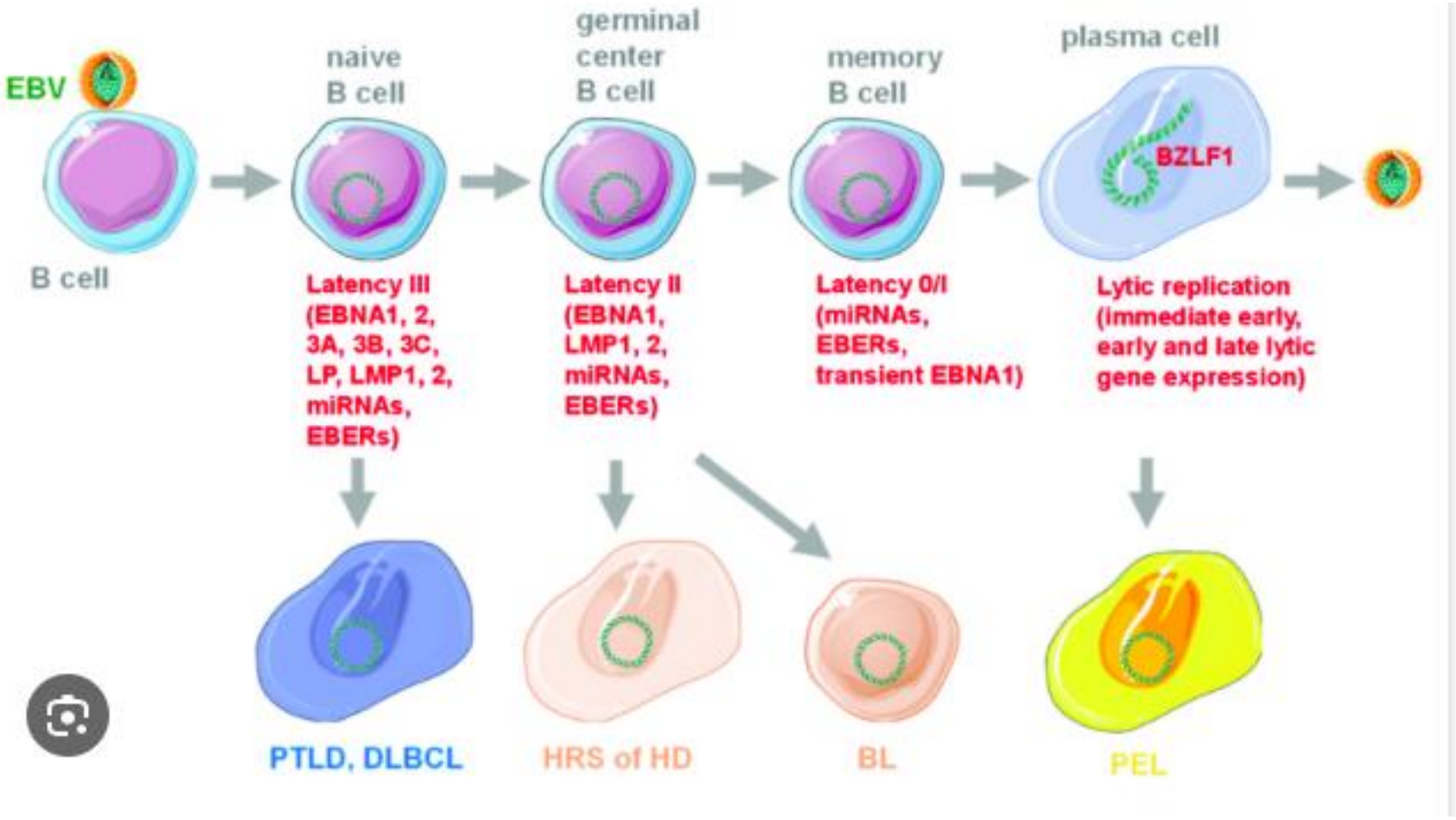
- For the majority, there is no known cause and no pre-existing risk factor (age)

- Risk factors:
  - Congenital immunodeficiencies
  - Acquired immunodeficiencies (HIV, post-transplant)
  - Autoimmune disorders
  - Prior chemo or radiation
  - Exposure to certain pesticides or chemicals
  - Alterations in lymphocytes following certain viral infections (EBV, hepatitis C)
  - Exposure to certain medications (Imuran)

Autoimmune disease and risk of lymphoma



Role of EBV infection in lymphomagenesis



Steps and tests to detect lymphoma

- Most often present in lymph nodes but can present in any organ in the body
  - Spleen
  - Bone marrow
  - GI tract
  - Brain
  - Liver
  - Lungs

Detection

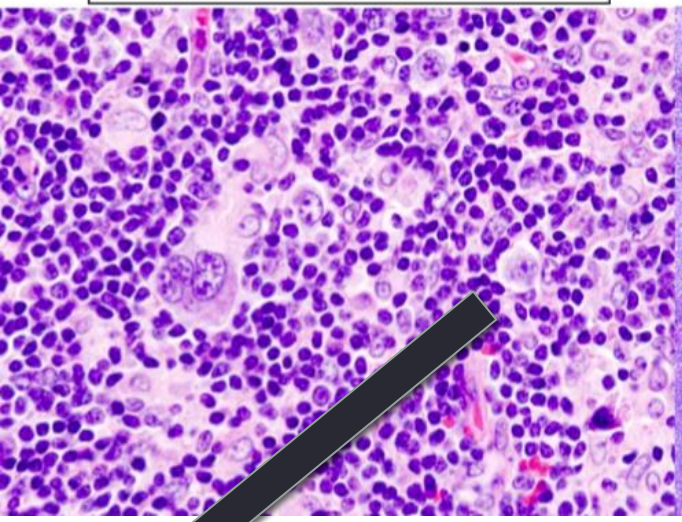
- Physical exam – lymph nodes, spleen, masses
- Bloodwork – CBC, LDH, ESR, liver and kidney function, calcium
- Imaging – CXR, U/S, CT scans, PET scan
- Biopsy – lymph node, other affected organ, splenectomy, lumbar puncture, bone marrow biopsy

How do we diagnose lymphoma

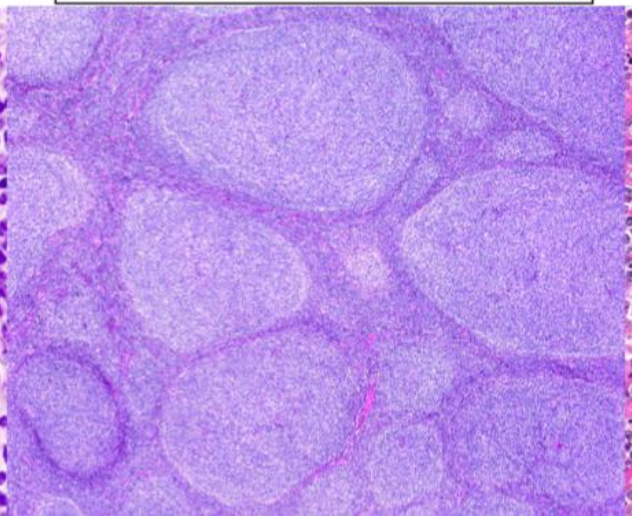
- Biopsy (core, excisional)

- Immunohistochemistry
- Flow cytometry
- Cytogenetics

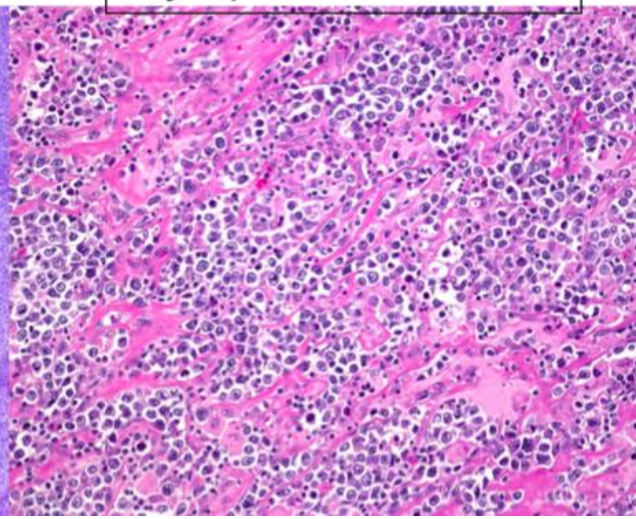
Hodgkin Lymphoma



Follicular Lymphoma

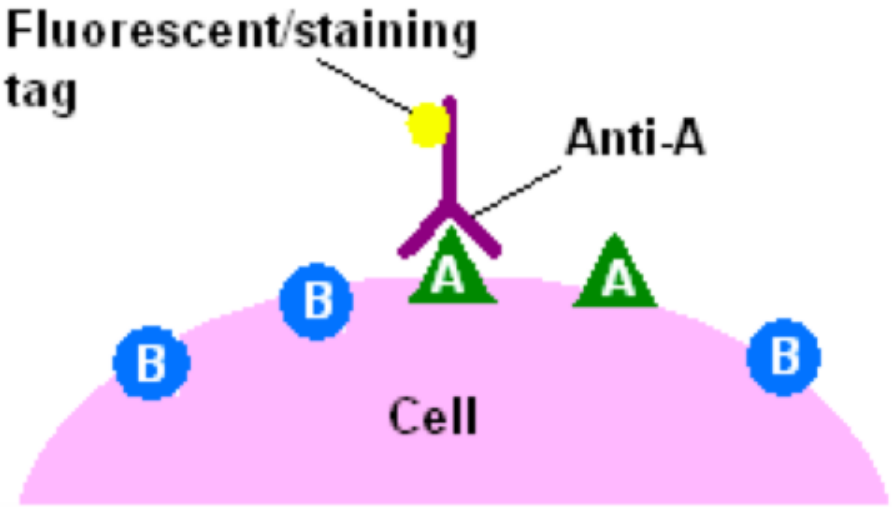


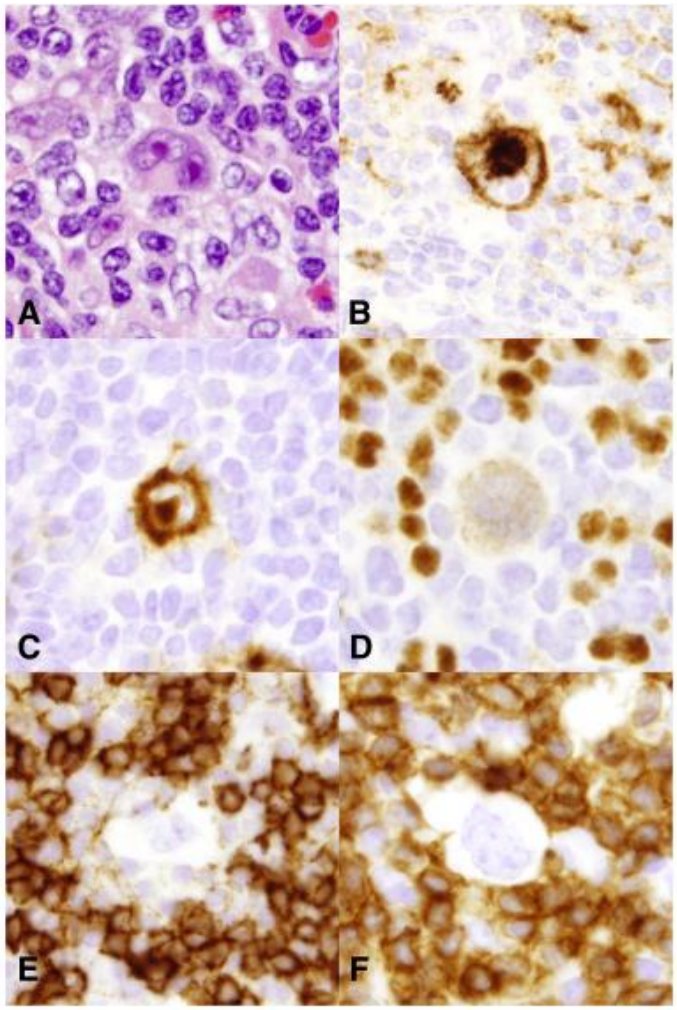
Diffuse Large B Cell Lymphoma



Immunohistochemistry

-Use an antibody against a protein on the cell
-Antibody is tagged with dye or fluorescence
-Look at stained cells on the slide





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Why does it take some patients a long time to receive their diagnosis?

- Because lymphoma can affect any organ in the body, symptoms can be non-specific
- Enlarged lymph nodes can be “hidden” (deep inside the body)
- Harder to reach those lymph nodes with a needle – sometimes you can’t
- Needle biopsy may “miss” the cancer cells
- Excisional biopsy can be delayed – time to see the surgeon, time to have operating room space
- Some lymphomas notoriously difficult to diagnose from a pathology perspective (cells may not express abnormal proteins)

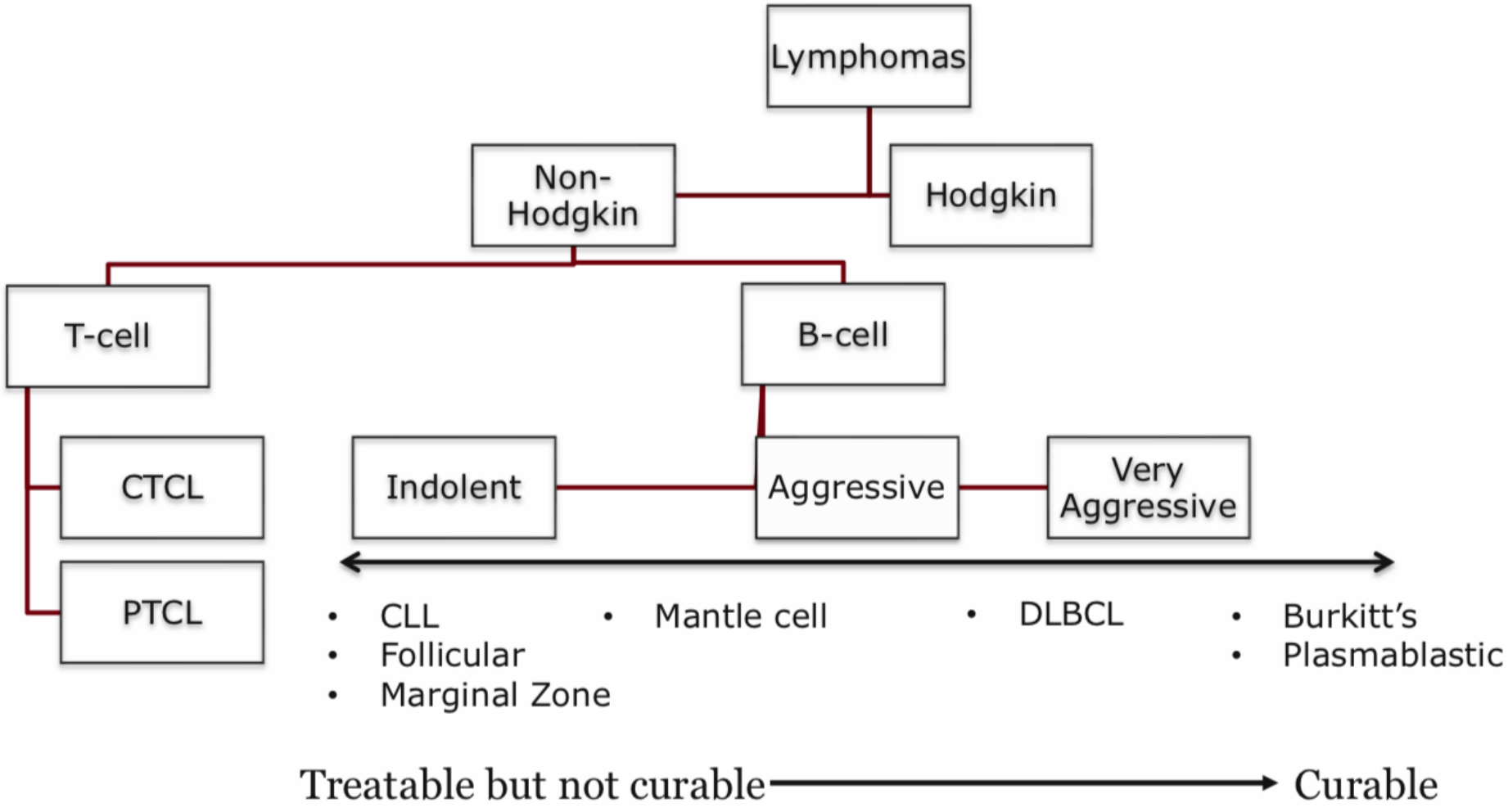
Extra questions

- “Knowing there are so many types of lymphoma, how does this determine which type of test will be used to confirm a lymphoma diagnosis?”

  - Bloodwork – everyone
  - Imaging – everyone (CT scans, PET)

  - Biopsy
    - Preferably excisional
    - May not be feasible depending on location
    - Pathologists will then determine what additional tests need to be run on the biopsy – IHC, flow, genetic tests (FISH, TCR rearrangements)

- “Around 2001 when I was diagnosed, there were 35 types of lymphoma. I believe now there are at least 60. What are these new lymphomas that have been added to the list? How are they different from the original ones first identified?”


Lymphomas
Non-Hodgkin
Hodgkin
T-cell
B-cell
CTCL
PTCL
Indolent
Aggressive
Very Aggressive
• CLL
• Follicular
• Marginal Zone
• Mantle cell
• DLBCL
• Burkitt's
• Plasmablastic
Treatable but not curable
Curable

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*

- “Is a chronic food sensitivity now a recognized cause of lymphoma?”
  - Celiac disease - EATL