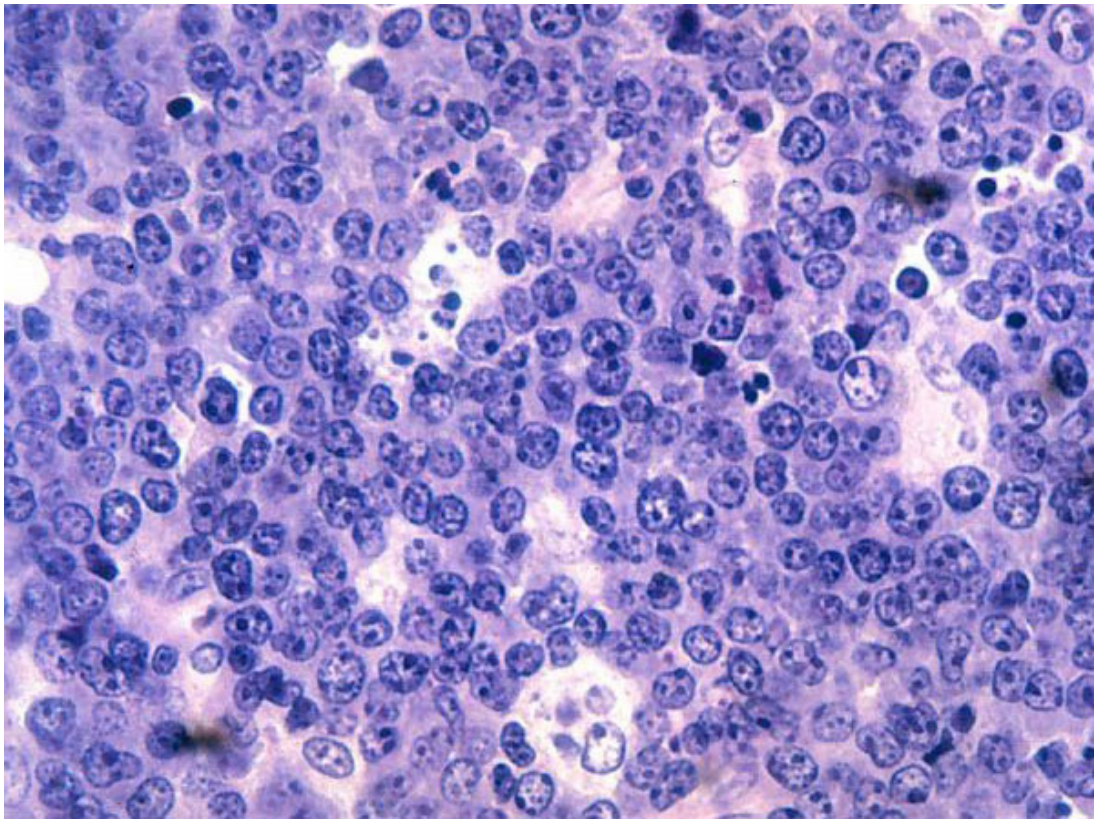
Non-Hodgkin’s Lymphoma

See online here



Non-Hodgkin lymphoma (NHL) is a malignant proliferation of lymphocytes (B and T cells). Like Hodgkin lymphoma, NHL often presents with constitutional signs; however, NHL is associated with painless lymphadenopathy. B cell NHL’s include Burkitt lymphoma, diffuse large B cell lymphoma, mantle cell lymphoma, and marginal zone lymphoma. T cell NHL’s include adult T cell lymphoma and mycosis fungoides. Management is primarily through chemotherapy.

Epidemiology and Etiology

Lymphoma is a neoplastic proliferation of lymphoid cells.

- Non-Hodgkin lymphoma (60%)
- Hodgkin lymphoma (40%)

Epidemiology

- Accounts for 4% of all cancers
    - Most common hematopoietic cancer

- Occurs in both children and adults
- Risk of developing NHL increases with age
    - > 50% of cases are in those > 65 years old

Etiology

Malignant proliferation of mature or progenitor B cell, T cells, and (rarely) natural killer cells associated with

- Genetic translocations that result in the overexpression of transcription factors
    - t(14;18) causes ↑ Bcl-2
    - t(8;14) causes ↑ *c-myc*
    - t(11;14) causes ↑ Cyclin D1
- Infections
    - Epstein-Barr virus (EBV)
    - Human T cell leukemia virus (HTLV)
    - *H. pylori*
- Chronic inflammatory conditions
    - Hashimoto thyroiditis
    - Sjögren syndrome
    - Chronic gastritis

Video Gallery

Non-hodgkin Lymphomas – Lymphoma by Paul Moss, PhD
Lymphoma in Children by Brian Alverson, MD

Clinical Presentation and Types of NHL

The clinical presentation varies depending on the type of lymphoma. The hallmark symptom of Non-Hodgkin lymphoma is **painless lymphadenopathy**.

Indolent lymphomas, insidious onset of

- Lymphadenopathy
- Hepato or splenomegaly
- Cytopenias
    - Anemia
    - Neutropenia
    - Thrombocytopenia

Aggressive lymphomas

- Constitutional, “B” symptoms
    - Low-grade fever
    - Night sweats
    - Weight loss
- Rapidly growing mass
    - May result in SVC obstruction
        - Facial swelling and congestion
        - Venous distension in the upper limbs/neck
        - Pleural effusion
- Elevated LDH and uric acid

Common Non-Hodgkin lymphomas			
	Type	Risk Factors and Genetics	Notes
B cell origin (85–90%)	**Follicular lymphoma**	Driven by • **t(14;18)** • Overexpression of **Bcl-2**	**Population:** late adulthood **Classic presentation:** • Indolent onset/course • Painless lymphadenopathy **Complications:** progression to diffuse large B cell lymphoma
	Diffuse large B cell lymphoma (most common NHL)	Arrises sporadically or from transformation of low-grade lymphoma (e.g., follicular lymphoma)	**Population:** late adulthood **Classic presentation:** • Enlarging lymph node or extranodal mass • Extremely aggressive
	Burkitt lymphoma	Associated with • **EBV** Driven by • **t(8;14)** • Overexpression of ***c-myc***	**Population:** adolescents or young adults **Classic presentation:** extranodal mass • African form: jaw mass • Sporadic form: abdominal mass • Aggressive **Histology:** "Starry sky" appearance
	Mantle cell lymphoma	Driven by • **t(11;14)** • Overexpression of **Cyclin D1**	**Population:** late adulthood, males **Classic presentation:** • Painless lymphadenopathy • Highly aggressive, often presents in late-stage disease
	Marginal zone lymphoma	Associated with • ◦ Hashimoto thyroiditis ◦ Sjögren syndrome • *H. pylori*	**Population:** adults with chronic inflammatory conditions **Clinical presentation:** • Indolent onset • Painless lymphadenopathy **MALToma:** marginal zone lymphoma of mucosal sites • Symptoms may mimic gastritis • Gastric MALToma may regress with treatment of *H. pylori*
T cell origin (10–15%)	**Adult T cell lymphoma**	Associated with • HTLV	**Population:** adults **Geographic location:** Japan, West Africa, Caribbean **Clinical presentation:** • Cutaneous lesions • Lytic bone lesions • Hypercalcemia
	Mycosis fungoides	Associated with • *Staphylococcus aureus* • *Borrelia* species	**Population:** adults **Clinical presentation:** • Skin patches/plaques **Histology:** atypical CD4+ cells with cerebriform nuclei **Complications:** progression to T cell leukemia

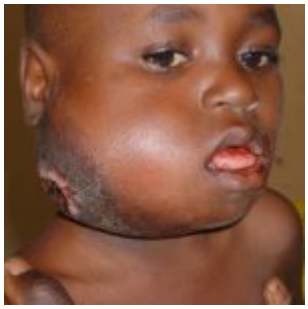


Image: “Large facial Burkitt’s Lymphoma” This seven-year-old boy presented with a several month history of jaw swelling which had been treated with antibiotics. The tumor was ulcerated and draining. By Mike Blyth. License: CC BY-SA 2.5

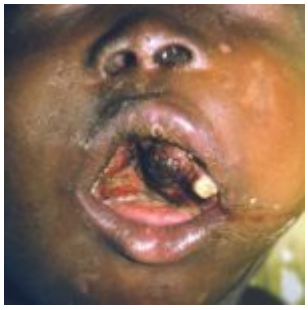


Image: “Picture of a mouth of a patient with Burkitt lymphoma showing disruption of teeth and partial obstruction of airway.” By Mike Blyth – Own work. License: CC BY-SA 2.5

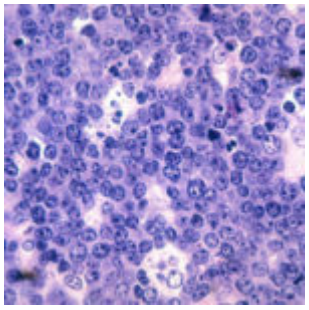


Image: “Malignant B cell lymphocytes seen in Burkitt lymphoma, stained with hematoxylin and eosin (H&E) stain.” License: Public Domain

Video Gallery

Lymphadenopathy: Non-Hodgkin Lymphoma (NHL) – White Blood Cell Pathology by Carlo Raj, MD
Lymphadenopathy: Follicular Lymphoma and Lymphoid Hyperplasia – White Blood Cell Pathology by Carlo Raj, MD
Lymphadenopathy: Burkitt Lymphoma – White Blood Cell Pathology by Carlo Raj, MD

Diagnostics and Staging

Diagnostics

- **Excisional lymph node biopsy**
    - Can be excised or core-needle
    - Histology is key.
- Initial laboratory work-up
    - CBC with white cell differential and platelet count
    - Electrolytes, BUN, and Cr
    - LFTs
    - LDH
    - Uric acid
- Imaging: CT and PET
    - Staging
    - Guided biopsy
    - Measuring response to therapy
- Unique circumstances

- Endoscopy/gastroscopy
    - If suspected MALToma
- Lumbar Puncture
    - If CNS symptoms
- Thoraco or paracentesis
    - If suspected pleural effusion or ascites
- Bone Marrow biopsy
    - If aggressive lymphoma suspected

Staging

- Has limited importance for treatment of NHL
- More important for targeting therapies for Hodgkin lymphoma
- **Subclasses: E: extranodal extension**
    I. Involvement of **1** lymph node group
    II. Involvement of 2 or more lymph node groups on the same side of the diaphragm
    III. Involvement of lymph node groups on both sides of the diaphragm
    IV. Disseminated, widespread disease

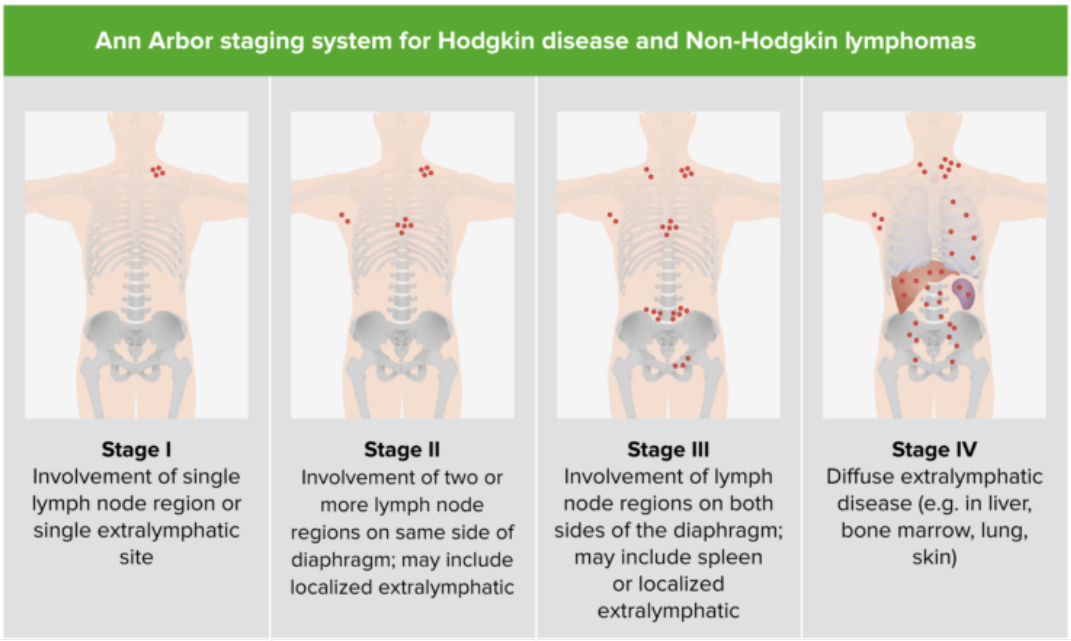


Image: Hodgkin disease staging. By Lecturio.

Treatment

Treatment is based on many factors including histological subtype, stage, and patient comorbidities.

- For localized disease (stage I or II)
    - Local radiation
    - Small course of chemotherapy
- For advanced disease (stage III, IV, or “B” symptoms)
    - Rituximab and CHOP
        - **C** – cyclophosphamide
        - **H** – adriamycin (hydroxydaunorubicin)

        - **O** – vincristine (oncovin)
        - **P** – prednisone
- Before beginning treatment, patients may need a baseline evaluation of their
    - Cardiac function
    - Pulmonary function
    - Fertility goals (if childbearing age)

Prognosis

- International prognostic index (IPI) for NHL assigns 1 point for each of the following:
    - Age > 60 years
    - Stage III or IV disease
    - Elevated **serum LDH**
    - Performance status
    - More than 1 extranodal site

IPI Scoring		
Risk	**Points**	**5-year survival**
Low	0—1	73 %
Low-intermediate	2	51 %
High-intermediate	3	43 %
High	4—5	26 %

Clinical Relevance

- **Hodgkin Lymphoma:** Neoplastic proliferation of Reed-Sternberg cells (B cells) within the lymph nodes that classically presents with “B” symptoms. Histology is positive for CD15 and CD30.
- **Multiple Myeloma:** The most common primary tumor of the bone in people aged 40–50 years old; occurs secondary to monoclonal plasma cell proliferation. Associated with monoclonal M protein spike, hypercalcemia, lytic bone lesions/back pain, renal involvement, and blood smear showing rouleaux formation.

Notes