Aggressive Lymphomas

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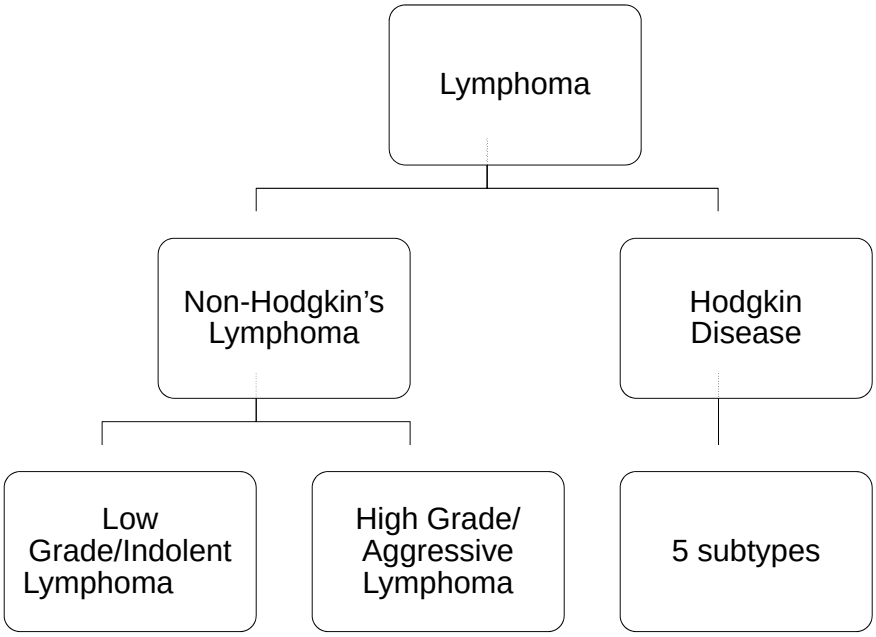
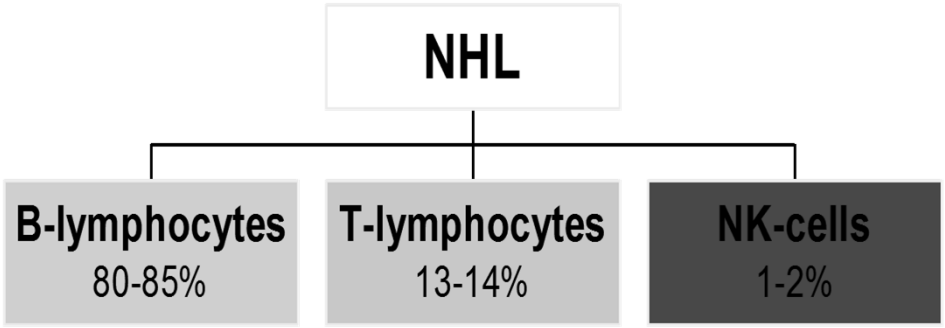


Cellular Origin of Non-Hodgkin's Lymphoma (U.S. and Europe)



Cancer statistics, 2018

Estimated New Cases

	Males			Females	
Prostate	164,690	19%		Breast	266,120	30%
Lung & bronchus	121,680	14%		Lung & bronchus	112,350	13%
Colon & rectum	75,610	9%		Colon & rectum	64,640	7%
Urinary bladder	62,380	7%		Uterine corpus	63,230	7%
Melanoma of the skin	55,150	6%		Thyroid	40,900	5%
Kidney & renal pelvis	42,680	5%		Melanoma of the skin	36,120	4%
Non-Hodgkin lymphoma	41,730	5%		Non-Hodgkin lymphoma	32,950	4%
Oral cavity & pharynx	37,160	4%		Pancreas	26,240	3%
Leukemia	35,030	4%		Leukemia	25,270	3%
Liver & intrahepatic bile duct	30,610	4%		Kidney & renal pelvis	22,660	3%
All Sites	**856,370**	**100%**		**All Sites**	**878,980**	**100%**

Estimated Deaths

	Males			Females	
Lung & bronchus	83,550	26%		Lung & bronchus	70,500	25%
Prostate	29,430	9%		Breast	40,920	14%
Colon & rectum	27,390	8%		Colon & rectum	23,240	8%
Pancreas	23,020	7%		Pancreas	21,310	7%
Liver & intrahepatic bile duct	20,540	6%		Ovary	14,070	5%
Leukemia	14,270	4%		Uterine corpus	11,350	4%
Esophagus	12,850	4%		Leukemia	10,100	4%
Urinary bladder	12,520	4%		Liver & intrahepatic bile duct	9,660	3%
Non-Hodgkin lymphoma	11,510	4%		Non-Hodgkin lymphoma	8,400	3%
Kidney & renal pelvis	10,010	3%		Brain & other nervous system	7,340	3%
All Sites	**323,630**	**100%**		**All Sites**	**286,010**	**100%**

CA: A Cancer Journal for Clinicians
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Non-Hodgkin's Lymphoma

- 4% of all cancers
- 7th most common cancer in men & women
- ~ 74,680 people (41,730 males and 32,950 females) diagnosed
- ~ 19,910 people will die of this disease (11,510 and 8,400)
- Risk of developing NHL is 1 in 47
- One of the more common cancers among children, teens and young adults but risk of developing NHL increases throughout life with half the patients ≥ 65 years of age

Hodgkin Disease

- ~ 8,500 new cases (3,660 in females and 4,840 in males)
- ~ 1,050 deaths (430 females, 620 males)
- Most common in early adulthood but bimodal
  - Peak patients aged 15-34
  - Risk rises again > 55 years old
- ~ 10-15% of cases diagnosed in children and teenagers
- 5-year relative survival rate for all comers is 86%

Risk Factors

- Age
- Benzene, herbicides and insecticides
- Immune deficiency
  - Solid organ transplant
  - HIV/AIDS
  - Congenital Immunodeficiency
- Autoimmune diseases
  - RA
  - SLE
  - Sjogren's
  - Celiac Disease
- Chronic Infections
  - Helicobacter pylori
  - Hepatitis C
  - EBV
  - HHV8
  - HTLV-1
- Immunosuppressive Medications
- Chemotherapy drugs
- Radiation

Screening

There is no routine screening for NHL or Hodgkin disease

Patient Presentations

- Enlargement of a lymph node
- Symptoms from bulky lymphadenopathy
  - Dependent on location – pain, dyspnea, early satiety, renal dysfunction
- Abnormal blood counts
- Some patients present with “B” symptoms
  - Fevers, night sweats, weight loss
  - Pruritus in Hodgkin Disease

How is Lymphoma Diagnosed?

- An excisional biopsy is ideal
- Fine needle aspirations are generally non-diagnostic
  - Even if indicative of lymphoma, not necessarily of subtype
- A core biopsy often does not obtain enough tissue for all diagnostic studies
- A bone marrow biopsy and aspirate can help make the diagnosis and is used in staging

Nodal versus Extranodal

Lymphoid Tissues

- Lymph nodes
- Spleen
- Thymus
- Mucosa-associated lymphoid tissue (MALT)
  - Marginal zone lymphoma of mucosa associated tissue

Non-lymphatic Tissue

- Skin
  - Cutaneous T-cell lymphoma
- Organs
  - GI tract
  - Lung
  - Liver
  - Renal or adrenal
- Central nervous system

Evaluation and Staging Studies'

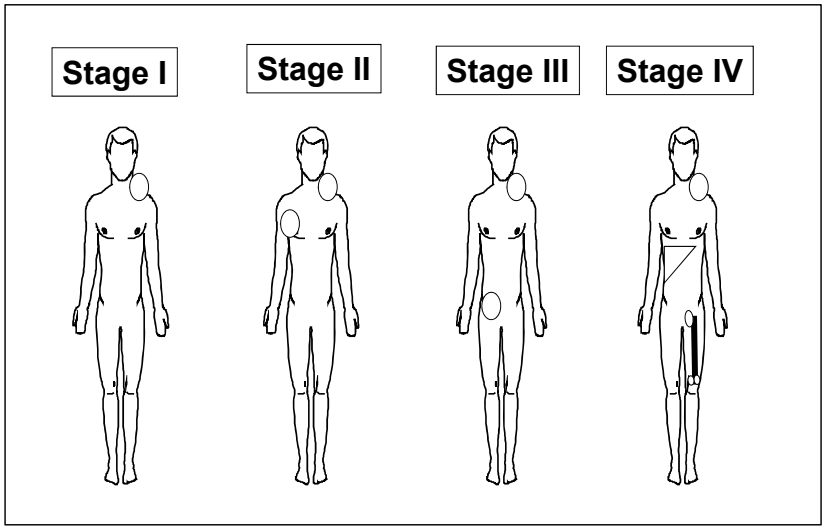
- Laboratory studies including CBC with differential, lactate dehydrogenase (LDH), uric acid, liver function
- HIV
- Imaging
  - Chest X-ray (HD)
  - Computed tomography (CT) scans
  - Positron emission tomography (PET) scans – all aggressive lymphomas
- Bone marrow biopsy and aspirate
- Additional potential testing:
  - Hepatitis
  - ESR (HD)
  - Echocardiogram
  - PFT's with DLCO (HD)
  - Brain MRI and LP

Ann Arbor Staging System

Stage I	Involvement of a single lymph node region or lymphoid structure, or involvement of a single extra lymphatic site (I_E).
Stage II	Involvement of two or more lymph node regions on the same side of the diaphragm which may be accompanied by localized contiguous involvement of an extra lymphatic site or organ (II_E).
Stage III	Involvement of lymph node regions on both sides of the diaphragm which may also be accompanied by involvement of the spleen (III_S) or by localized contiguous involvement of an extra lymphatic site or organ (III_E).
Stage IV	Diffuse or disseminated involvement of one or more extra lymphatic organs or tissues, with or without lymph node involvement.

*** The absence or presence of fever (> 38°C), unexplained weight loss (> 10% body weight), or night sweats should be donated by the suffix letters A or B, respectively.**

Ann Arbor Staging System



Subtypes

- Non-Hodgkin's Lymphoma
  - Diffuse Large B Cell Lymphoma
  - Burkitt Lymphoma
  - Mantle Cell Lymphoma
  - Peripheral T Cell Lymphoma
- Hodgkin Lymphoma

Diffuse Large B-cell NHL

- Epidemiology
  - Most common, constitutes 30-40% of adult NHL
  - Usually presents in middle aged and older adults, male predominance
  - Median age 7th decade
- Clinical Features
  - 30-40% of cases present with early stage disease
  - Usually symptomatic and not incidental
  - Symptoms noticed over weeks to a few months
  - 1/3 cases arise from low grade process

Diffuse Large B-cell NHL

- Rapid growth (weeks) enlarging tumor
  - Usually rapidly enlarging, symptomatic mass at a single nodal or extranodal site
    - bulky palpable mass(es)
  - thoracic and abdominal adenopathy without superficial lymph nodes
  - Extranodal extension or involvement common
  - Most common extranodal site is gastrointestinal region, but CNS, bone, thyroid, testis, lung, kidney, and liver involvement all occur
- Symptoms
  - Dependent on site of disease involvement
  - "B" symptoms (fevers, sweats, weight loss)

Diffuse Large B-cell NHL

- Laboratory abnormalities
  - Cytopenias if disease involvement of BM or enlarged spleen
  - Elevated lactate dehydrogenase
  - Elevated uric acid
  - Spontaneous tumor lysis

Hodgkin Presentation

- Painless adenopathy
  - 75% neck, left > right
  - 25% axillary
  - 10% inguinal and iliac
- Rarely, alcohol ingestion can induce pain in node
- Pruritus very common
  - Can predate lymphadenopathy by months, can delay diagnosis as patient travels to and from dermatologists
  - Intense, refractory to topical and oral antihistamines

Hodgkin Presentation

- Cough, SOB, DOE in patients with mediastinal disease
  - Hemoptysis rarely
- Usually tracks
- Subdiaphragmatic presentations uncommon
- 1/3 have B-symptoms (fever, NS, weight loss)
  - Frequently cause of FUO in older males, very difficult to diagnose in these patients as they often have stage IV disease and small nodes

Treatment

- Chemotherapy based
  - R-CHOP standard chemotherapy in most diffuse large B cell lymphoma
    - Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone
  - ABVD standard chemotherapy in Hodgkin Disease
    - doxorubicin, bleomycin, vinblastine and dacarbazine
  - More aggressive/intensive regimens used in some of the other rare but more aggressive lymphomas
- XRT in select cases
  - Early/limited stage Diffuse Large B cell lymphoma
  - Select cases of Early Stage HD
  - Bulky Hodgkin Disease

Toxicities

- R-CHOP
  - Infusion reactions, cytopenias, infections, need for transfusion, GI toxicity (nausea/vomiting/diarrhea/constipation/mucositis), alopecia, anorexia, peripheral neuropathy, cardiotoxicity, small risk of secondary malignancy including acute leukemia
- ABVD
  - Cytopenias, infections, alopecia, muscle cramps, GI toxicity (nausea/vomiting/diarrhea/constipation/mucositis), phlebitis, peripheral neuropathy, cardiotoxicity, pulmonary toxicity
- Radiation
  - Dependent on location – local symptoms
  - Fatigue, cytopenias, skin burn/irritation
  - CAD or CHF (HD – mediastinal)
  - Secondary malignancies

Lymphoma Emergencies

- **Presentation**
  - **Cord Compression**
  - **SVC Syndrome**
  - **CNS Lymphoma**
  - **Spontaneous Tumor Lysis**
- **Treatment**
  - **Neutropenic Fever**

Infectious Complications

- **Most common cause of morbidity and mortality in the cancer patient**
- **Neutropenia major risk factor for infection**
- **Hematologic diseases associated with inherent immune defects**

Neutropenia

- Chemotherapy induced, bone marrow involvement and heavily pretreated
- Correlation between neutrophil count (both duration and rate of decline) and frequency and severity of infection
  - 20% patients ANC ≤ 100 bloodstream infection
- Infectious complications combination of neutropenia, disruption of mucosal barriers, microbial flora shifts

Neutropenic Fever

- Fever
  - Single oral temperature 38.3 C (101) or higher
  - 38.0 C (100.4) or higher for an hour
- Neutropenia
  - ANC less than 500/mcL
  - ANC less than 1000/mcL with a predicted decline in the next 48 hours
- Weakness, hypotension, syncope, pain, localized symptoms
- Mortality highest among
  - Initial neutrophil counts ≤ 100
  - Prolonged neutropenia (≥ 7 days)
  - Delay in treatment with broad spectrum antibiotics

Neutropenic Fever

- 2/3 patients with fever have occult infection
- Bacteria most common early pathogen
  - Coag negative staph, S. aureus, viridans strep, entrerococci
  - E. coli, klebsiella, enterobacter, pseudomonas
  - HSV, RSV, influenza
- Antibiotic-resistant bacteria, yeast, other fungi, virus common causes of subsequent infections
  - Candida, aspergillus

Evaluation and Treatment

- Exam with localizing signs (vascular access, mucosal membranes)
- CBC with differential, Chemistry Panel, Liver Function, Urinalysis/culture, Blood cultures, Chest x-ray
- Intravenous antibiotic therapy
  - IV broad spectrum monotherapy usually sufficient
    - Anti-pseudomonal cephalosporin (cefepime or ceftazidime)
    - Piperacillin/tazobactam
    - Imipenem/cilastatin or meropenem
  - Vancomycin consideration
    - Apparent catheter related infections
    - Gram-positive bacteremia
    - Known colonization with MRSA
    - Soft tissue infection
    - Clinically unstable
  - Double gram-negative coverage
    - High risk for pseudomonas infections
    - Clinically unstable

Evaluation and Treatment

- Persistent febrile neutropenia
  - Anti-fungal coverage after 4 days
  - CT scans to investigate for source
- Treatment duration dependent on infection but should continue until ANC recovers to ≥ 500
- Removal of vascular access
  - Immediate in unstable patient
  - Fungal or mycobacterial bloodstream infections
  - S. aureus, P. aeruginosa and VRE strongly consider

Follow-up

- Hematologic follow up every 3 months for 2 years, every 4-6 months from years 3-5 and then yearly dependent on patient preference
  - Physical exam and blood tests (CBC, LDH in NHL, sedimentation rate in HD if initially elevated

Survivor

“ An individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life”

Survivorship

- **Many survivors experience physical and/or psychosocial effects of cancer and its treatment**
  - **Some evident during anti-cancer therapy (long-term effects)**
  - **Some manifest months or years after therapy (late effects)**
    - **Recent review suggests 50% of survivors suffer from late effects of cancer therapy**
  - **Incidence increases with longer follow up time**
  - **May occur less with new therapies and standards**

Standards for Survivorship

- Prevention of new and recurrent cancers and other late effects
- Surveillance for cancer spread, recurrence or second cancers
- Assessment of late psychosocial and medical effects
- Intervention for consequences of cancer and treatment
- Coordination of care between primary care providers and specialists to ensure all health needs are met

Long-term effects

- Long-term physical effects
  - Cardiac effects, reproduction, pain, fatigue
  - Male and female sexual dysfunction
  - Cognitive decline
- Secondary Malignancies
  - 2-10% of patients develop
  - Dependent on chemotherapeutic agents and radiation therapy
- Psychosocial issues
  - Anxiety, depression, sleep disorders
  - Employment, finances, insurance
  - Exercise

Secondary Malignancies

- Multifactorial (decreased immune surveillance, treatment related, virally mediated)
- Solid tumors most common
  - XRT > combined modality > chemotherapy alone
  - Breast and lung cancer most common (esp in HD)
- Risk of secondary acute leukemia in both HD and NHL and risk of secondary NHL in HD
  - Higher risk with chemotherapy
    - Alkylating agents
      - Highest risk 5-10 years
    - Topoisomerase II inhibitors, anthracyclines
      - Highest risk 2-3 years

Screening for second malignancy

- AGE APPROPRIATE SCREENING and SKIN EXAMS
  - Referral to dermatology
  - Colonoscopy, prostate, mammogram, PAP smear
  - SMOKING CESSATION
- Yearly chest imaging in patients with history of smoking or chest irradiation
- Annual breast screening 5-8 years after completion of therapy or age 40 if history of chest or axillary radiation
  - MRI for those receiving between the ages of 10-30

Cardiovascular disease

- Mediastinal irradiation and anthracycline-based chemotherapy
- Radiation-induced toxicity usually > 5-10 years after completion of therapy
- Coronary disease and cardiomyopathy
- Annual blood pressure monitoring and aggressive management of risk factors
- Baseline stress test or echocardiogram (chest irradiation) and carotid ultrasound (neck irradiation) 10 years after therapy

Hypothyroidism

- 50% of long-term survivors, greatest with neck or upper mediastinal irradiation
- Thyroid exam
- Yearly thyroid function tests

Myelosuppression

- Usually resolves with time from therapy
- Some delayed myelosuppression
- Concern if new cytopenias develop
- Appropriate immunizations and prevention of infection

Resources

- Leukemia and Lymphoma Society
- Lymphoma Research Foundation

Stem cell transplant in aggressive lymphomas

How do you define “cured”?

Indolent Non-Hodgkin Lymphoma

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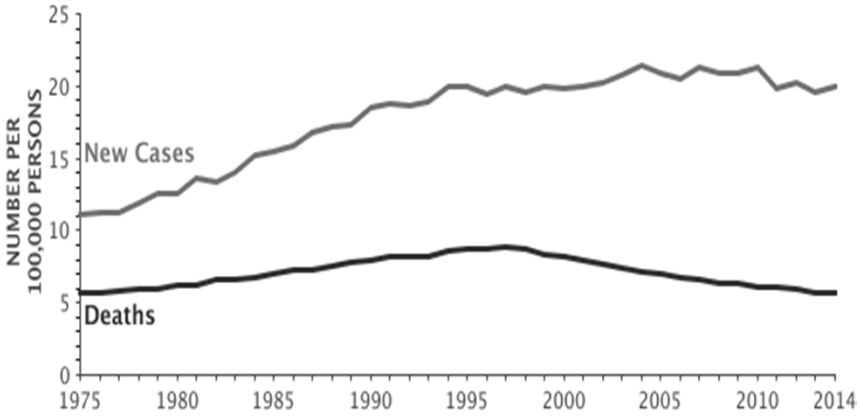
Indolent lymphoma

- **A heterogeneous group of malignancies derived from mature B lymphocytes**
- **Overview the common subtypes**
  - **Follicular lymphoma**
  - **Marginal zone lymphoma, 3 varieties**
  - **Lymphoplasmacytic lymphoma**

Non-Hodgkin Lymphoma



- **4% new cancer cases**
- **5 year overall survival (2007-2013) was 71%**

seer.cancer.gov

Precursor B-cell: bone marrow

⇩

Naïve B-cell: peripheral blood

⇩

Germinal Center B-cell:
Lymph node, follicular region
Follicular lymphoma

⇩

Memory B-cell:
Lymph node, Perifollicular region
Marginal zone lymphoma
Lymphoplasmacytic lymphoma

Pathologic Diagnosis

- Morphology
  - Appearance of the malignant cells
  - Pattern of involvement within a lymph node
- Immunophenotype or pattern of antigens expressed on the cell surface
  - Flow cytometry
  - Immunohistochemistry
- Cytogenetics

Indolent Lymphoma

- Characterized by slow growth over years
- Severe symptoms are uncommon
- Advanced stage indolent lymphoma is not cured with standard therapy
- Therapy for advanced stage indolent lymphoma is given with the goal of treating or preventing complications of the disease

Indolent Lymphoma – Complications

- Increased risk of infection
  - Importance of immunizations: pneumococcal, influenza
  - Avoidance of live vaccines
  - Hypogammaglobulinemia
- Increase risk of secondary malignancies
  - Age-appropriate cancer screening
- Complications of treatment
  - Risk of cardiovascular disease
  - Radiation

Follicular Lymphoma

Follicular Lymphoma

- 2nd most common non-Hodgkin lymphoma, 20%
- 70% of indolent lymphoma
- Median age of diagnosis = 60 years
- Symptoms: enlarged lymph nodes, uncommon to have severe symptoms associated with disease
- Bone marrow involvement at diagnosis 60-70%
- "B symptoms" at diagnosis 20%
  - Fevers, night sweats, or weight loss

Follicular lymphoma - Pathology

- Grade 1-2, 3A,and 3B – number of centroblasts
- Immunophenotype: monotypic immunoglobulin light chain, CD20, CD19, CD10, and BCL-2
- Cytogenetics: t(14;18)

Indolent lymphoma can transform into aggressive lymphoma

Follicular Lymphoma – Treatment

Treatment decisions are primarily made to improve the quality of a patient's life:

Questions:

1. **How can life be made better with treatment?**
2. **Is the benefit of treatment greater than the side effects?**
3. **What treatment is the right one at this point in the patient's course?**

Follicular Lymphoma - Treatment

- **Early Stage – radiation or observation**
- **Advanced Stage**

"Watch and Wait" – Criteria for treatment

- **Involvement of ≥3 nodal sites, each with a diameter of ≥3 cm**
- **Any nodal or extranodal tumor mass with a diameter of ≥7 cm**
- **B symptoms**
- **Splenomegaly**
- **Pleural effusions or peritoneal ascites**
- **Cytopenias or leukemic involvement**

Treatment Milestones in Follicular Lymphoma FDA Approvals

Early era: CHOP, CVP

- **1997 – rituximab, the first monoclonal antibody**
- **2002 – ibritumomab tiuxetan (Zevalin®)**
- **2008 – bendamustine**
- **2014 – idelalisib**
- **2016 – obinutuzumab**
- **2017 – rituximab plus hyaluronidase - subQ copanlisib**

2018…

Follicular Lymphoma - Treatment

Initial Therapy

- **Chemotherapy with an anti-CD20 monoclonal antibody**
- **Maintenance therapy with an anti-CD monoclonal antibody**
- **Rituximab**

Relapse(s)

- **Chemotherapy with an anti-CD20 monoclonal antibody**
- **Immunomodulatory drug - lenalidomide***
- **PI3 Kinase inhibitors – idelalisib, copanlisib**
- **Stem cell transplant**

*** Off label use**

Rituximab

- First monoclonal antibody approved for treatment
- Chimeric – both mouse and human components
- Binds to CD20 on B-cells, normal and malignant
- Antibody-dependent cell-mediated cytotoxicity
  - Natural killer cells recognize the antibody bound to the cancer cell and release cytokines and cytotoxic granules
- Complement-dependent cytotoxicity
  - The antibody activates complement and the membrane attack complex destroys the cell
- Depletes B-cells for up to 6 months

Rituximab

- A major advance in the treatment of follicular lymphoma
- First targeted treatment
- Side effects
  - Infusion reactions
  - Rash, potentially severe
  - Increased risk for infections
  - Hepatitis B reactivation
- Model for the development of all monoclonal antibody therapy
  - Obinutuzumab

Follicular Lymphoma

- The prognosis of follicular lymphoma continues to improve
- A chronic disease, requiring intermittent treatment
- Median overall survival ~ 20 years
- Allogeneic stem cell transplant is a potentially treatment
- Clinical Trials

Marginal Zone Lymphoma

MALT, gastric
MALT, non-gastric
Splenic MZL
Nodal MZL

Marginal Zone Lymphoma

- 5% non-Hodgkin lymphoma
- Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue lymphoma = MALT lymphoma: most common type 70%
- Splenic MZL – 20%
- Nodal MZL – 10%

Marginal Zone Lymphoma

Associated with chronic immune stimulation

- H pylori – gastric
- Hashimoto's thyroiditis - thyroid
- Sjogren's syndrome - salivary glands, ocular adnexa
- Chlamydia psittaci – ocular adnexa
- Campylobacter jejuni – small intestine
- Hepatitis C – splenic

Gastric MALT Lymphoma

- The majority are localized and associated with H. pylori
- Eradication of H. pylori can result in remission and cure of the lymphoma
- Median time to complete response = 15 months
- Up to 1/3 associated with t(11;18), unlikely to respond to antibiotics
- Local radiation is an alternative therapy

MALT Lymphoma

- Non gastric sites: salivary glands, skin, lacrimal glands, orbit and conjunctiva, lung, thyroid, upper airway, breast, other GI sites, liver
- Stage I-II
  - 10 year recurrence free survival: 76%
  - 10 year cause specific survival: 98%
- Transformation is uncommon, <10%
- Localized disease is commonly treated with radiation
- Up to 1/3 of patients will present with or develop disseminated disease

Splenic Marginal Zone Lymphoma

- Median age diagnosis – 69 years
- Splenic enlargement with localized LAD
- Bone marrow / peripheral blood involvement 95%
- Often associated with a monoclonal protein
- Autoimmune complications
  - AIHA
  - ITP
  - Cold agglutinin disease
  - Cryoglobulinemia

SMZL - Treatment

Indicated for cytopenias or symptomatic splenomegaly

- Treatment of Hepatitis C
- Splenectomy – historical
- Rituximab* – response rate ~ 90%
- Chemotherapy with rituximab*
- Ibrutinib

* Off label use

Marginal Zone Lymphoma

- Ibrutinib – the first and only FDA approved therapy (2017)
- Bruton's tyrosine kinase inhibitor
- Side effects
  - Increased bleeding risk
  - Diarrhea
  - Rash
  - Atrial fibrillation
  - Infection

Nodal MZL

- 1% of NHL, 10% of MZL
- Median age of diagnosis: 50-64 years
- Bone marrow involvement in approximately 1/3
- Association with Hepatitis C
- Transformation occurs in approximately 15%

Nodal MZL – Pathology

- Plasmacytic features in 20-40%
- Higher portion of large blastoid cells and high Ki-67 can occur
- CD19, CD20, CD79a, BCL2
- Frequent genetic abnormalities:
  - Gain chromosome 3
  - 18q23

Nodal MZL -Treatment

- Approach is similar to follicular lymphoma
- Localized disease – radiation
- Advance stage disease
  - Watch and Wait
  - Rituximab and chemotherapy*
  - Ibrutinib
  - Treatment for Hepatitis C

* Off label use

Lymphoplasmacytic Lymphoma

Waldenström macroglobulinemia

Lymphoplasmacytic lymphoma & Waldenström macroglobulinemia (WM)

- 1% of Non-Hodgkin Lymphoma
- Median age diagnosis: 73 years
- Male:Female 1.6:1
- Lymphoplasmacytic lymphoma with an IgM monoclonal protein = Waldenström macroglobulinemia
- Non-IgM associated LPL is very rare
- Familial association

WM - Pathology

Immunophenotype

- **sIgM, CD19, CD20, CD22, CD79**
- **Up to 20% can express CD5, CD10, or CD23**

Cytogenetics

- **Chromosome 6q deletions in up to half of patients**
- **MYD88 somatic mutations are present in >90%**

WM – Signs/Symptoms

- **Anemia – most common presentation**
- **Elevated total protein and a monoclonal protein**
- **Bone marrow involvement is very common**
- **Lymphadenopathy: 15%**
- **Splenomegaly: 10%**
- **AIHA, ITP**
- **Cryglobulinemia, Cold agglutinin disease**

WM – Signs/Symptoms

- Neuropathy
  - 20% patients at presentation
  - distal, symmetric, and slowly progressive sensorimotor peripheral neuropathy causing paresthesias and weakness
  - Antibodies: Anti-myelin-associated glycoprotein and GM1 ganglioside
- Renal complications
  - Direct infiltration
  - Immune mediated glomerulonephritis
- Amyloid
- Skin involvement / vasculitis
- Bing Neel Syndrome = CNS involvement

WM – Signs/Symptoms

IgM

- Pentamer and the largest antibody
- Accumulation of IgM can result in increased blood viscosity
  - IgM ~ 6000 mg/dL but can vary
- There is no definitive viscosity level where symptoms occur but typically ~ 4 cP
- Use caution with PRBC transfusions – increasing hematocrit will increase viscosity

WM – Signs/Symptoms

Symptomatic hyperviscosity is an emergency

Symptoms:

- **Visual – blurred vision, retinal hemorrhage, papilledema**
- **Mucocutaneous – epistaxis, gingival bleeding**
- **Neurologic – headache, tinnitus, vertigo, seizures**

Treatment:

- **Plasmapheresis**
- **Treatment of the lymphoma**

WM – Indications for Treatment

- **Anemia - Hemoglobin < 10 (11) g/dL**
- **Platelets < 100 (120) x 10^9 /L**
- **Symptomatic hyperviscosity**
- **Bulky adenopathy / organomegaly**
- **Moderate to severe neuropathy**
- **Amyloidosis**
- **Cryoglobulinemia**
- **Cold agglutinin disease**

WM - Treatment

- Chemotherapy*
  - Cyclophosphamide
  - Bendamustine
- Anti-CD20 monoclonal antibodies – rituximab*
- Bruton's tyrosine kinase inhibitor - ibrutinib
- Proteosome inhibitors – bortezomib, carfilzomib*
- Stem cell transplant

* Off label use

Indolent Lymphoma: Summary

Common Signs / Symptoms of Indolent Lymphoma

- Cytopenias
- Slowly progressive lymphadenopathy
- Splenomegaly
- Elevated total protein with presence of a monoclonal protein
- New onset of autoimmune cytopenias

Indolent Lymphoma: Summary

- The mainstay of therapy is to only treat when needed
- The prognosis of indolent lymphomas is very good and improving over time
- We are less reliant on traditional chemotherapy and have increasing options for treatment
- Clinical trials – new options are on the horizon
- Allogeneic stem cell transplant offers a potentially curative option