Staging of Hematologic Malignancies

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Objectives

- Broad overview of hematologic malignancies
  - Leukemia
  - Myelodysplastic Syndrome
  - Myeloproliferative Neoplasms
  - Multiple Myeloma
  - Lymphomas
- Discuss staging classifications
- Address some of the complexities

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How Common Is This Cancer?

	Common Types of Cancer	Estimated New Cases 2018	Estimated Deaths 2018
1.	Breast Cancer (Female)	266,120	40,920
2.	Lung and Bronchus Cancer	234,030	154,050
3.	Prostate Cancer	164,690	29,430
4.	Colorectal Cancer	140,250	50,630
5.	Melanoma of the Skin	91,270	9,320
6.	Bladder Cancer	81,190	17,240
7.	Non-Hodgkin Lymphoma	74,680	19,910
8.	Kidney and Renal Pelvis Cancer	65,340	14,970
9.	Uterine Cancer	63,230	11,350
10.	Leukemia	60,300	24,370
	-	-	-
	Cancer of Any Site	1,735,350	609,640

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Estimated New Cases

Males			Females		
Prostate	220,800	26%	Breast	231,840	29%
Lung & bronchus	115,610	14%	Lung & bronchus	105,590	13%
Colon & rectum	69,090	8%	Colon & rectum	63,610	8%
Urinary bladder	56,320	7%	Uterine corpus	54,870	7%
Melanoma of the skin	42,670	5%	Thyroid	47,230	6%
Non-Hodgkin lymphoma	39,850	5%	Non-Hodgkin lymphoma	32,000	4%
Kidney & renal pelvis	38,270	5%	Melanoma of the skin	31,200	4%
Oral cavity & pharynx	32,670	4%	Pancreas	24,120	3%
Leukemia	30,900	4%	Leukemia	23,370	3%
Liver & intrahepatic bile duct	25,510	3%	Kidney & renal pelvis	23,290	3%
All Sites	**848,200**	**100%**	**All Sites**	**810,170**	**100%**

Estimated Deaths

Males			Females		
Lung & bronchus	86,380	28%	Lung & bronchus	71,660	26%
Prostate	27,540	9%	Breast	40,290	15%
Colon & rectum	26,100	8%	Colon & rectum	23,600	9%
Pancreas	20,710	7%	Pancreas	19,850	7%
Liver & intrahepatic bile duct	17,030	5%	Ovary	14,180	5%
Leukemia	14,210	5%	Leukemia	10,240	4%
Esophagus	12,600	4%	Uterine corpus	10,170	4%
Urinary bladder	11,510	4%	Non-Hodgkin lymphoma	8,310	3%
Non-Hodgkin lymphoma	11,480	4%	Liver & intrahepatic bile duct	7,520	3%
Kidney & renal pelvis	9,070	3%	Brain & other nervous system	6,360	2%
All Sites	**312,150**	**100%**	**All Sites**	**277,280**	**100%**

FIGURE 1. Ten Leading Cancer Types for the Estimated New Cancer Cases and Deaths by Sex, United States, 2015.
Estimates are rounded to the nearest 10 and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

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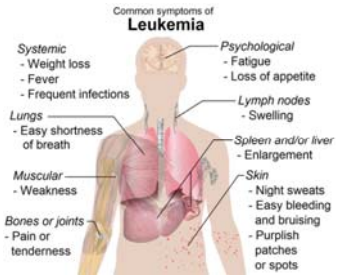
Table 1. WHO classification of myeloid neoplasms and acute leukemia

WHO myeloid neoplasm and acute leukemia classification	Acute myeloid leukemia (AML) and related neoplasms
Myeloproliferative neoplasms (MPN)	AML with recurrent genetic abnormalities
Chronic myeloid leukemia (CML), *BCR-ABL1*+	AML with t(8;21)(q22;q22.1);*RUNX1-RUNX1T1*
Chronic neutrophilic leukemia (CNL)	AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22);*CBFB-MYH11*
Polycythemia vera (PV)	APL with *PML-RARA*
Primary myelofibrosis (PMF)	AML with t(9;11)(p21.3;q23.3);*MLLT3-KMT2A*
PMF, prefibrotic/early stage	AML with t(6;9)(p23;q34.1);*DEK-NUP214*
PMF, overt fibrotic stage	AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2, MECOM*
Essential thrombocythemia (ET)	AML (megakaryoblastic) with t(1;22)(p13.3;q13.3);*RBM15-MKL1*
Chronic eosinophilic leukemia, not otherwise specified (NOS)	*Provisional entity: AML with BCR-ABL1*
MPN, unclassifiable	AML with mutated *NPM1*
Mastocytosis	AML with biallelic mutations of *CEBPA*
Myeloid/lymphoid neoplasms with eosinophilia and rearrangement of *PDGFRA, PDGFRB,* or *FGFR1*, or with *PCM1-JAK2*	*Provisional entity: AML with mutated RUNX1*
Myeloid/lymphoid neoplasms with *PDGFRA* rearrangement	AML with myelodysplasia-related changes
Myeloid/lymphoid neoplasms with *PDGFRB* rearrangement	Therapy-related myeloid neoplasms
Myeloid/lymphoid neoplasms with *FGFR1* rearrangement	AML, NOS
Provisional entity: Myeloid/lymphoid neoplasms with PCM1-JAK2	AML with minimal differentiation
Myelodysplastic/myeloproliferative neoplasms (MDS/MPN)	AML without maturation
Chronic myelomonocytic leukemia (CMML)	AML with maturation
Atypical chronic myeloid leukemia (aCML), *BCR-ABL1*−	Acute myelomonocytic leukemia
Juvenile myelomonocytic leukemia (JMML)	Acute monoblastic/monocytic leukemia
MDS/MPN with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T)	Pure erythroid leukemia
MDS/MPN, unclassifiable	Acute megakaryoblastic leukemia
Myelodysplastic syndromes (MDS)	Acute basophilic leukemia
MDS with single lineage dysplasia	Acute panmyelosis with myelofibrosis
MDS with ring sideroblasts (MDS-RS)	Myeloid sarcoma
MDS-RS and single lineage dysplasia	Myeloid proliferations related to Down syndrome
MDS-RS and multilineage dysplasia	Transient abnormal myelopoiesis (TAM)
MDS with multilineage dysplasia	Myeloid leukemia associated with Down syndrome
MDS with excess blasts	
MDS with isolated del(5q)	
MDS, unclassifiable	
Provisional entity: Refractory cytopenia of childhood	
Myeloid neoplasms with germ line predisposition	

Arbor, et al. Blood; 2016

Leukemia

- Blood Cancer
- Varied presentation at diagnosis
- Most common type of childhood cancer
- 90% are adult
- Risks:
  - h/o radiation, prior chemotherapy, smoking, Down syndrome
- Diagnosis includes peripheral blood smear and bone marrow biopsy



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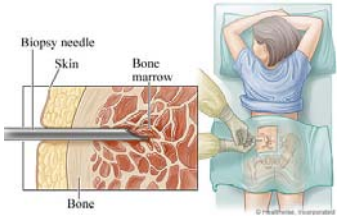
Bone Marrow Biopsy and Aspiration



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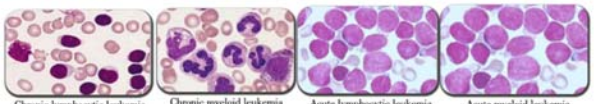
Leukemia Types:

Four major kinds of leukemia

Cell type	Acute	Chronic
Lymphocytic leukemia (or "lymphoblastic")	Acute lymphoblastic leukemia (ALL)	Chronic lymphocytic leukemia (CLL)
Myelogenous leukemia ("myeloid" or "nonlymphocytic")	Acute myelogenous leukemia (AML or myeloblastic)	Chronic myelogenous leukemia (CML)



Chronic lymphocytic leukemia (CLL) | Chronic myeloid leukemia (CML) | Acute lymphocytic leukemia (ALL) | Acute myeloid leukemia (AML)

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picture from Lloyd Healthcare

Classification: Acute Myeloid Leukemia:

- Previously FAB Classification

FAB subtype	Name
M0	Undifferentiated acute myeloblastic leukemia
M1	Acute myeloblastic leukemia with minimal maturation
M2	Acute myeloblastic leukemia with maturation
M3	Acute promyelocytic leukemia (APL)
M4	Acute myelomonocytic leukemia
M4	Acute myelomonocytic leukemia with eosinophilia
M5	Acute monocytic leukemia
M6	Acute erythroid leukemia
M7	Acute megakaryoblastic leukemia

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Updated AML diagnoses by WHO 2016

Staging???

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AML with t(9;11)(p21.3;q23.3);*MLLT3-KMT2A*
AML with t(6;9)(p23;q34.1);*DEK-NUP214*
AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2, MECOM*
AML (megakaryoblastic) with t(1;22)(p13.3;q13.3);*RBM15-MKL1*
Provisional entity: AML with BCR-ABL1
AML with mutated *NPM1*
AML with biallelic mutations of *CEBPA*
Provisional entity: AML with mutated RUNX1
AML with myelodysplasia-related changes
Therapy-related myeloid neoplasms
AML, NOS
AML with minimal differentiation
AML without maturation
AML with maturation
Acute myelomonocytic leukemia
Acute monoblastic/monocytic leukemia
Pure erythroid leukemia
Acute megakaryoblastic leukemia
Acute basophilic leukemia
Acute panmyelosis with myelofibrosis
Myeloid sarcoma
Myeloid proliferations related to Down syndrome
Transient abnormal myelopoiesis (TAM)
Myeloid leukemia associated with Down syndrome

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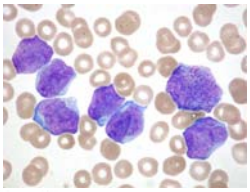
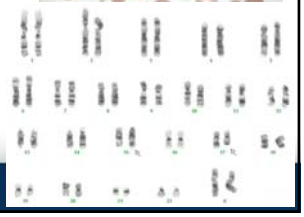
Acute Promyelocytic Leukemia (APL)

- Previously "M3" disease
- Hallmark chromosome t(15;17)
  - PML/RARA mutation
- Classification based on WBC ct:
  - Low-Risk Disease (≤10K)
  - High-Risk Disease (>10K)
- CURABLE
- Mortality = mismanagement +/- delayed diagnosis
  - Coagulation dysfunction
  - Differentiation syndrome





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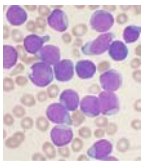
Acute Lymphoblastic Leukemia

- Is it B-cell or T-cell disease? Or is it both?
- Staging – not really
- Presence of t(9;22) = Philadelphia chromosome
- Age?
  - Adolescent Young Adult (AYA) protocols
- CNS disease – presumed involvement
  - CNS-1: No lymphoblasts in CSF
  - CNS-2: WBC <5/mcl in CSF w/ presence lymphoblasts
  - CNS-3: WBC ≥5/mcl in CSF w/ presence lymphoblasts



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Myelodysplastic Syndrome

WHO (2008) Classification for MDS
Refractory anemia
Refractory neutropenia
Refractory thrombocytopenia
Refractory anemia with ring sideroblasts
MDS associated with isolated del(5q)
Refractory cytopenia with multilineage dysplasia
Refractory anemia with multilineage dysplasia with ring sideroblasts
Refractory anemia with excess blasts-1
Refractory anemia with excess blasts-2
MDS, unclassified
WHO (2016) Classification for MDS
MDS with single lineage dysplasia (MDS-SLD)
MDS with multilineage dysplasia (MDS-MLD)
MDS with ringed sideroblasts and single lineage dysplasia (MDS-RSSLD)
MDS with ringed sideroblasts and multilineage dysplasia (MDS-RSMLD)
MDS with excess blasts-1 (MDS-EB1)
MDS with excess blasts-2 (MDS-EB2)
MDS, unclassified

INTERNATIONAL PROGNOSTIC SCORING SYSTEM (IPSS)

Survival and AML Evolution					
	Score Value				
Prognostic variable	0	0.5	1.0	1.5	2.0
Marrow blasts (%)[2]	<5	5-10	—	11-20	21-30
Karyotype[6]	Good	Intermediate	Poor	—	—
Cytopenia[8]	0/1	2/3	—	—	—

IPSS Risk category (% IPSS pop.)	Overall score	Median survival (y) in the absence of therapy	25% AML progression (y) in the absence of therapy
LOW (33)	0	5.7	9.4
INT-1 (38)	0.5-1.0	3.5	3.3
INT-2 (22)	1.5-2.0	1.1	1.1
HIGH (7)	≥2.5	0.4	0.2

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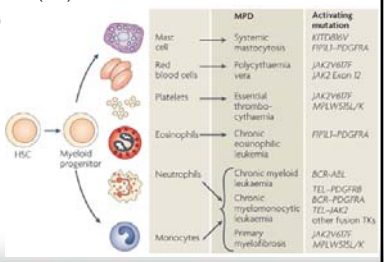
Myeloproliferative Neoplasms

- Chronic Myelogenous Leukemia (CML)
- Essential Thrombocythemia (ET)
- Polycythemia Vera (PV)
- Myelofibrosis (MF)



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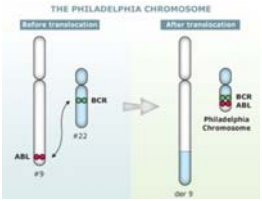
Medscape

Chronic Myeloid Leukemia:

- Hallmark is chromosome t(9;22) – Philadelphia chromosome
- Classification based on blast count:
  - Chronic Phase
  - Accelerated Phase (≥15%)
  - Blast Phase (≥30%)
- Oral chemotherapy – tyrosine kinase inhibitors (TKI)
  - Imatinib, Dasatinib, Ponatinib, Bosutinib, Potatinb



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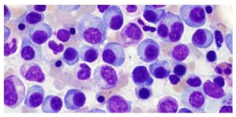
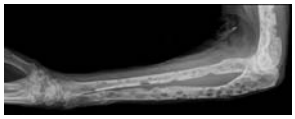
Multiple Myeloma



- Plasma Cell Myeloma (PCM)
- CRAB criteria
  - Hypercalcemia
  - Renal failure
  - Anemia
  - Bone lesions



- Secrete abnormal immunoglobulins
  - Measurable in blood and urine
- Rare subset – Solitary Plasmacytoma

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Cancer Stat Facts: Myeloma

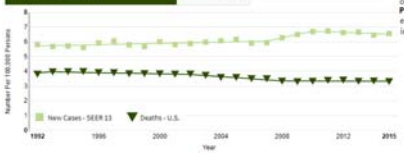
Estimated New Cases in 2018	30,770
% of All New Cancer Cases	1.8%
Estimated Deaths in 2018	12,770
% of All Cancer Deaths	2.1%

Percent Surviving 5 Years: **50.7%** (2008-2014)

Number of New Cases and Deaths per 100,000: The number of new cases of myeloma was 6.7 per 100,000 men and women per year. The number of deaths was 3.3 per 100,000 men and women per year. These rates are age-adjusted and based on 2011-2015 cases and deaths.

Lifetime Risk of Developing Cancer: Approximately 0.8 percent of men and women will be diagnosed with myeloma at some point during their lifetime, based on 2013-2015 data.

Prevalence of This Cancer: In 2015, there were an estimated 124,733 people living with myeloma in the United States.



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Multiple Myeloma

Stage	Durie-Salmon Criteria[1]	ISS Criteria[2]
I	All of the following: • Hemoglobin value > 10 g/dL • Serum calcium value normal or ≤ 12 mg/dL • Bone x-ray, normal bone structure) or solitary bone plasmacytoma only • Low M-component production rate ▸ IgG value < 5 g/dL; ▸ IgA value < 3 g/dL ▸ Bence Jones protein < 4 g/24 h	Serum beta-2 microglobulin < 3.5 mg/L Serum albumin ≥ 3.5 g/dL
II	Neither stage I nor stage III	Neither stage I nor stage III
III	One or more of the following: • Hemoglobin value < 8.5 g/dL • Serum calcium value > 12 mg/dL • Advanced lytic bone lesions • High M-component production rate ▸ IgG value > 7 g/dL; ▸ IgA value > 5 g/dL ▸ Bence Jones protein > 12 g/24 h	Serum beta-2 microglobulin ≥ 5.5 mg/L
Subclassification Criteria A Normal renal function (serum creatinine level < 2.0 mg/dL) B Abnormal renal function (serum creatinine level ≥ 2.0 mg/dL)		

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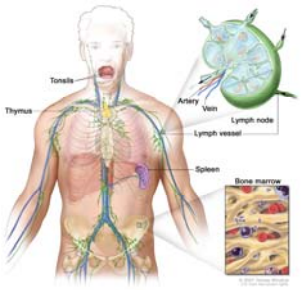
Lymphoma

- Hematologic malignancy
- Spans a lifetime
- Not typically hereditary
- Pretty uncommon
- Spectrum of disease
- More than just ONE disease
- Lots of treatment options



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picture from cancer.gov

Table 1. 2016 WHO classification of mature lymphoid, histiocytic, and dendritic neoplasms

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

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Swerdlow, et al. Blood, 2016.

Mature T and NK neoplasms	**Hodgkin lymphoma**
T-cell prolymphocytic leukemia	Nodular lymphocyte predominant Hodgkin lymphoma
T-cell large granular lymphocytic leukemia	Classical Hodgkin lymphoma
Chronic lymphoproliferative disorder of NK cells	Nodular sclerosis classical Hodgkin lymphoma
Aggressive NK-cell leukemia	Lymphocyte-rich classical Hodgkin lymphoma
Systemic EBV$^+$ T-cell lymphoma of childhood*	Mixed cellularity classical Hodgkin lymphoma
Hydroa vacciniforme–like lymphoproliferative disorder*	Lymphocyte-depleted classical Hodgkin lymphoma
Adult T-cell leukemia/lymphoma	**Posttransplant lymphoproliferative disorders (PTLD)**
Extranodal NK-/T-cell lymphoma, nasal type	Plasmacytic hyperplasia PTLD
Enteropathy-associated T-cell lymphoma	Infectious mononucleosis PTLD
Monomorphic epitheliotropic intestinal T-cell lymphoma*	Florid follicular hyperplasia PTLD*
*Indolent T-cell lymphoproliferative disorder of the GI tract**	Polymorphic PTLD
Hepatosplenic T-cell lymphoma	Monomorphic PTLD (B- and T-/NK-cell types)
Subcutaneous panniculitis-like T-cell lymphoma	Classical Hodgkin lymphoma PTLD
Mycosis fungoides	**Histiocytic and dendritic cell neoplasms**
Sézary syndrome	Histiocytic sarcoma
Primary cutaneous CD30$^+$ T-cell lymphoproliferative disorders	Langerhans cell histiocytosis
Lymphomatoid papulosis	Langerhans cell sarcoma
Primary cutaneous anaplastic large cell lymphoma	Indeterminate dendritic cell tumor
Primary cutaneous $\gamma\delta$ T-cell lymphoma	Interdigitating dendritic cell sarcoma
Primary cutaneous CD8$^+$ aggressive epidermotropic cytotoxic T-cell lymphoma	Follicular dendritic cell sarcoma
*Primary cutaneous acral CD8$^+$ T-cell lymphoma**	Fibroblastic reticular cell tumor
*Primary cutaneous CD4$^+$ small/medium T-cell lymphoproliferative disorder**	Disseminated juvenile xanthogranuloma
Peripheral T-cell lymphoma, NOS	Erdheim-Chester disease*
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**	

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Swerdlow, et al. Blood, 2016.

Lymphoma

Non-Hodgkin's Lymphoma (NHL)

B-cell | T-cell | NK-cell

Hodgkin's Lymphoma (HL)

Classical HL:
- Nodular sclerosis
- Mixed cellularity
- Lymphocyte-rich
- Lymphocyte-depleted

Nodular Lymphocyte-Predominate HL

Aggressive B-cell NHLs

Diffuse Large B-cell Lymphoma (DLBCL)
Mantle Cell Lymphoma (MCL
Burkitt's Lymphoma (BL)
Plasmablastic Lymphoma

Indolent B-cell NHLs

Follicular Lymphoma (FL)
Marginal Zone Lymphoma (MZL)
- Gastric/Nongastric MALT Lymphomas
- Nodal/Splenic MZL

Small Lymphocytic Lymphoma (CLL/SLL)
Lymphoplasmacytic Lymphoma (LPL)
Waldenström's Macroglobulinemia (WM)
Hairy Cell Leukemia

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Precursor Lymphoid Neoplasms

T-Lymphoblastic Leukemia/Lymphoma

Mature T/NK-cell Neoplasms

Cutaneous	Extranodal	Nodal	Leukemic
Mycosis Fungoides Sezary Syndrome Primary Cutaneous CD30+ Primary Cutaneous γ / δ	NK/TCL Nasal Type Enteropathy Associated Hepatosplenic T-cell Subcutaneous Panniculitis-like	Peripheral Tcell, NOS Anaplastic Large Cell - ALK + and ALK – Angioimmunoblastic	Adult T-cell Leukemia / Lymphoma Aggressive NK-cell Leukemia T-cell Prolymphocytic Leukemia T-cell LGL Leukemia

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Cancer Stat Facts: Non-Hodgkin Lymphoma

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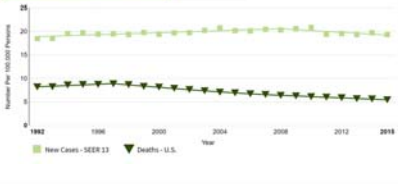
Estimated Deaths in 2018	19,910
% of All Cancer Deaths	3.3%

Percent Surviving 5 Years
71.4%
2008-2014



Number of New Cases and Deaths per 100,000: The number of new cases of non-Hodgkin lymphoma was 19.4 per 100,000 men and women per year. The number of deaths was 5.7 per 100,000 men and women per year. These rates are age-adjusted and based on 2011-2015 cases and deaths.

Lifetime Risk of Developing Cancer: Approximately 2.1 percent of men and women will be diagnosed with non-Hodgkin lymphoma at some point during their lifetime, based on 2013-2015 data.

Prevalence of This Cancer: In 2015, there were an estimated 686,042 people living with non-Hodgkin lymphoma in the United States.

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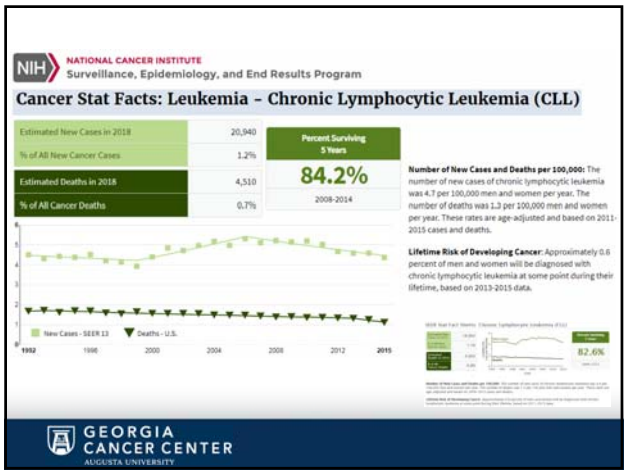
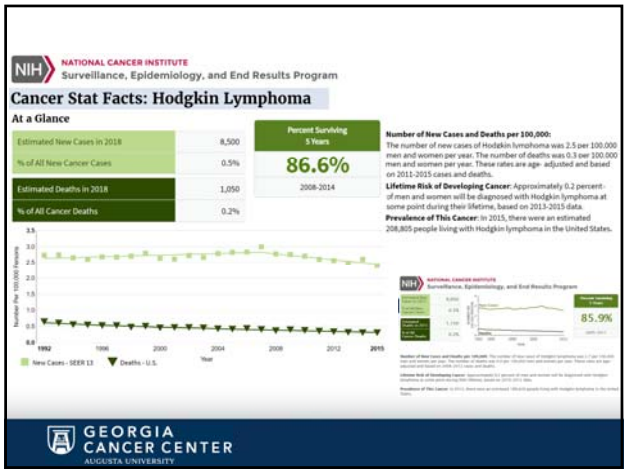
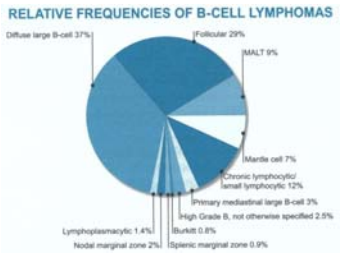
Excludes CLL/SLL





Key Features: B-cell Non-Hodgkin's Lymphoma

- Most common – 85%
- CD20 expression
- Well characterized mechanisms of disease
- Spectrum of diseases
- Disease of all ages
- 50:50 split for aggressive vs indolent lymphoma



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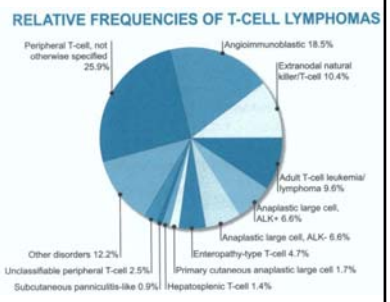
Key Features: T-cell Non-Hodgkin's Lymphoma

- Rare – 10% of NHL
  - 50% CTCL
- CD30 expression
- Odd presentations in certain subpopulations



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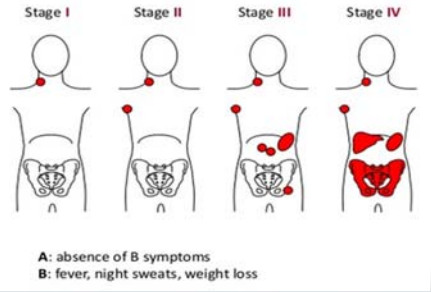
Lymphoma Staging: Ann Arbor Classification



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But to add some complexity…

- Modifiers
  - E – Involvement of a single, extranodal site contiguous or proximal to known nodal disease
  - S – Splenic involvement
  - X – Bulky disease (mass >10 cm)
- Note: Tonsils, Waldeyer's ring, Spleen are considered nodal tissue
- Special Considerations
  - Stage I and II = Limited disease
  - Stage III and IV = Advance disease
- Removal of A vs B modifier in the Lugano Modification of Ann Arbor Staging

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CLL / SLL: Rai Classification

- CLL/SLL
  - Defined as > $5x10^9$/L +/- lymphadenopathy

Stage	Description	Risk Status
0	Lymphocytosis, peripheral lymphocyte count >15,000/mcL and >40% lymphocytes in bone marrow	Low
I	Stage 0 disease with enlarge lymph node(s)	Intermediate
II	Stage 0-I with splenomegaly and/or hepatomegaly	Intermediate
III	Stage 0-II with Hgb <11 g/dL or Hct <33%	High
IV	Stage 0-III with platelet count <100,000/mcL	High

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Rai, et al. Blood; 1975

CLL / SLL: Binet Classification

Stage	Description
A	Hemoglobin ≥10 g/dL and Platelets ≥100,000/mm³ and <3 enlarged areas
B	Hemoglobin ≥10 g/dL and Platelets ≥100,000/mm³ and ≥3 enlarged areas
C	Hemoglobin <10 g/dL and/or Platelets <100,000/mm³ and any number of enlarged areas

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Binet, et al. Cancer; 1981

Evolution of Treatment for CLL/SLL

Before 1985
Single-agent alkylators

1985-1990
Single-agent purine analogs

1990-2000
Combinations of purine analogs with alkylators

2000-2013
Chemoimmunotherapy

After 2014
Small molecule inhibitors of critical survival pathways

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Staging: Mycosis Fungoides / Sezary Syndrome

NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2018
Mycosis Fungoides/Sezary Syndrome

TNMB		TNMB Classification and Staging of Mycosis Fungoides and Sezary Syndrome[h,j]
Skin	T1	Limited patches,[m] papules, and/or plaques[n] covering <10% of the skin surface
	T2	Patches,[m] papules, and/or plaques[m] covering ≥10% of the skin surface
	T2a	Patch only
	T2b	Plaque ± patch
	T3	One or more tumors[o] (≥1 cm in diameter)
	T4	Confluence of erythema ≥80% body surface area
Node	N0	No abnormal lymph nodes; biopsy not required
	N1	Abnormal lymph nodes; histopathology Dutch Gr 1 or NCI LN 0-2
	N2	Abnormal lymph nodes; histopathology Dutch Gr 2 or NCI LN 3
	N3	Abnormal lymph nodes; histopathology Dutch Gr 3-4 or NCI LN 4
	NX	Abnormal lymph nodes; no histologic confirmation
Visceral	M0	No visceral organ involvement
	M1	Visceral involvement (must have pathology confirmation and organ involved should be specified)
	MX	Abnormal visceral site; no histologic confirmation
Blood	B0	Absence of significant blood involvement: ≤5% of peripheral blood lymphocytes or <250/mcL are atypical (Sezary) cells or <15% CD4+/CD26- or CD4+/CD7- cells of total lymphocytes
	B1	Low blood tumor burden: >5% of peripheral blood lymphocytes are atypical (Sezary) cells or ≥15% CD4+CD26- or CD4+CD7- of total lymphocytes but do not meet the criteria of B0 or B2
	B2	High blood tumor burden: ≥1000/mcL Sezary cells[l] (CD4+/CD26- or CD4+/CD7- cells by flow cytometry) or CD4/CD8 ≥10 or ≥40% CD4+/CD7- or ≥30% CD4+/CD26- cells of total lymphocytes

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Staging: MF / SS

NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2018
Mycosis Fungoides/Sezary Syndrome

Clinical Staging of MF and SS[k]

	T	N	M	B
IA	1	0	0	0,1
IB	2	0	0	0,1
IIA	1–2	1,2	0	0,1
IIB	3	0–2	0	0,1
IIIA	4	0–2	0	0
IIIB	4	0–2	0	1
IVA_1	1–4	0–2	0	2
IVA_2	1–4	3	0	0–2
IVB	1–4	0–3	1	0–2

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Changes on the horizon?

- Subtypes of diagnoses
- Moving beyond histologic diagnosis
  - Detection / determination of driver mutations
  - Targetable protein expression

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