Abstracting and Coding Lymphoid Neoplasms

BACKGROUND MATERIAL
2014 HEMATOPOIETIC MANUAL AND DATABASE CODING RULES AND INSTRUCTIONS
TREATMENT GUIDELINES
STAGING

FCDS 2013-2014 Educational Webcast Series

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February 20, 2014

Outline

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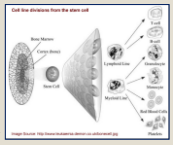
- Background and Characteristics
- Causes/Risk Factors/Signs/Symptoms
- Overview of the Immune System
- Hematopoiesis and Lymphoid Cell Line Derivation
- Anatomy of Two Circulatory Systems
- Complex Disease Processes
  - Confirming the Diagnosis
  - The Clinical Workup
  - Immunophenotype Studies
  - Identifying Disease Progression/Transformation



Outline

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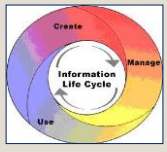
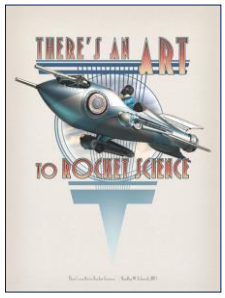
- 2014 Updates to Tools & Rules
- Determining the Primary Site
- Determining the Histology
- Determining the Grade
- Staging Lymphoid Neoplasms
- Treatment for Lymphoid Neoplasms
- Text Documentation



Why Are These Cases So Challenging?

4



Source: http://shop.webomator.com/retropolis/prints/ArtToRocketScience.jpg

Why Are These Cases So Challenging?

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- Not the same as when many of us started as registrars
- Terminology can be confusing and complicated
- Terms don't always match up with codes
- What is leukemia/lymphoma?
- Is multiple myeloma a type of leukemia?
- Are some lymphomas also leukemia and vice versa?
- Why are some lymphomas in lymph nodes but not all?

Inter-Lymph Classification Comparisons

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Table 2. Comparison of the Proposed Classification With the Kiel Classification and Working Formulation

Kiel Classification	Revised European American Lymphoma Classification	Working Formulation
B-lymphoblastic	Precursor B-lymphoblastic lymphoma/ leukemia	Lymphoblastic
B-Lymphocytic, CLL B-lymphocytic, prolymphocytic leukemia Lymphoplasmacytoid immunocytoma	B-cell chronic lymphocytic leukemia/ prolymphocytic leukemia/small lymphocytic lymphoma	**Small lymphocytic, consistent with CLL** Small lymphocytic, plasmacytoid
Lymphoplasmacytic immunocytoma	Lymphoplasmacytoid lymphoma	**Small lymphocytic, plasmacytoid**
Centrocytic Centroblastic, centrocytoid subtype	Mantle cell lymphoma	Diffuse, mixed small and large cell Small lymphocytic **Diffuse, small cleaved cell** Follicular, small cleaved cell Diffuse, mixed small and large cell Diffuse, large cleaved cell
Centroblastic-centrocytic, follicular Centroblastic, follicular Centroblastic-centrocytic, diffuse	Follicular center lymphoma, follicular —Grade I —Grade II —Grade III Follicular center lymphoma, diffuse, small cell (provisional)	**Follicular, predominantly small cleaved ce** **Follicular, mixed small and large cell** Follicular, predominantly large cell **Diffuse, small cleaved cell** Diffuse, mixed small and large cell
—	Extranodal marginal zone B-cell lymphoma (low-grade B-cell lymphoma of MALT type)	**Small lymphocytic** Diffuse, small cleaved cell Diffuse, mixed small and large cell
Monocytoid, including marginal zone Immunocytoma	Nodal marginal zone B-cell lymphoma (provisional)	**Small lymphocytic** Diffuse, small cleaved cell Diffuse, mixed small and large cell
—	Splenic marginal zone B-cell lymphoma (provisional)	Unclassifiable **Small lymphocytic** Diffuse small cleaved cell
Hairy cell leukemia	Hairy cell leukemia	—
Plasmacytic **Centroblastic** (monomorphic, polymorphic and multilobated subtypes) **Immunoblastic** B-large cell anaplastic (Ki-1+)	Plasmacytoma/myeloma Diffuse large B-cell lymphoma	Extramedullary plasmacytoma **Diffuse, large cell** Large cell immunoblastic Diffuse, mixed small and large cell

Pediatric Neoplasms

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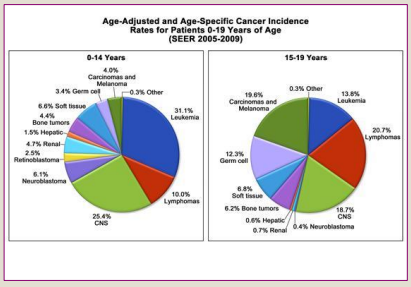

Source: NCI SEER Program

Adult Neoplasms

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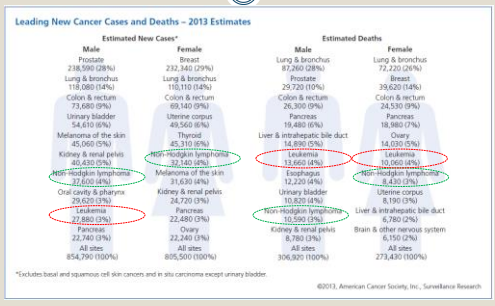

Source: American Cancer Society

WHO Definition

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- "B cell and T/NK cell neoplasms are clonal tumors of mature and immature B cells, T cells or natural killer (NK) cells at various stages of differentiation."
- Cells can be circulating lymphocytes such as lymphoid leukemia or cells in aggregate similar to a solid tumor but tumor made up of all the same type of cells (lymphoma).
- Features of clonality are most often used to identify and establish histologic type for most lymphoid neoplasm.

Lymphoid Neoplasm Characteristics

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- **2013 estimates in the United States**
  - 79,030 new lymphoma cases
    - 9,290 Hodgkin Lymphoma
    - 69,740 Non-Hodgkin Lymphoma
  - 20,200 lymphoma deaths
    - 1,180 Hodgkin Lymphoma Deaths
    - 19,020 Non-Hodgkin Lymphoma Deaths

- **2013 estimates in Florida**
  - 5,060 Non-Hodgkin Lymphoma Cases
  - 1,450 Non-Hodgkin Lymphoma Deaths

Source: American Cancer Society Cancer Facts and Figures 2013

Lymphoid Neoplasm Characteristics

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- **2013 estimates in the United States**
  - 15,680 Chronic Lymphocytic Leukemia
    - 4,580 CLL Deaths
  - 6,070 Acute Lymphocytic Leukemia
    - 1,430 ALL Deaths

- **2013 estimates in Florida**
  - 3,490 Leukemia Deaths
    - Lymphoid – CLL and ALL
    - Myeloid – CML and AML

Source: American Cancer Society Cancer Facts and Figures 2013

Common Lymph Node Chains for Lymphoma

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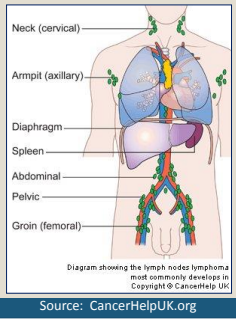

Source: CancerHelpUK.org

Extra-Nodal Lymphoma

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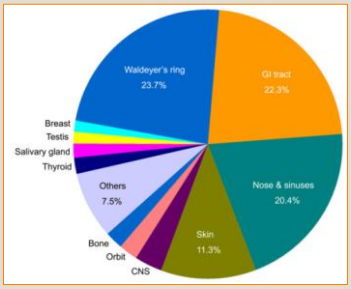

Source: nlm.nih.gov

Common Types of Lymphoma

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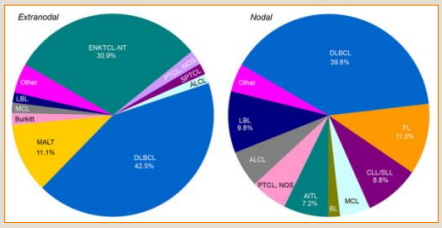

Source: nlm.nih.gov

Causes and Risk Factors

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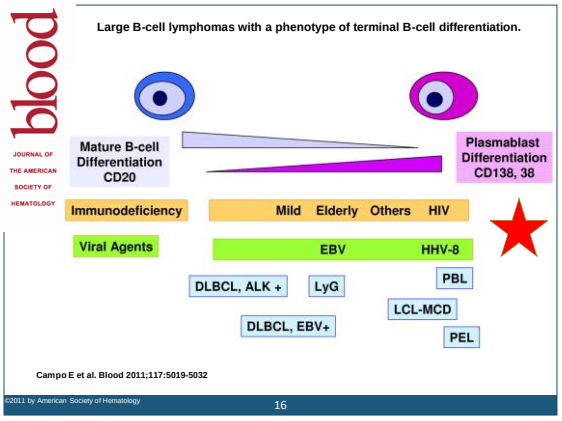
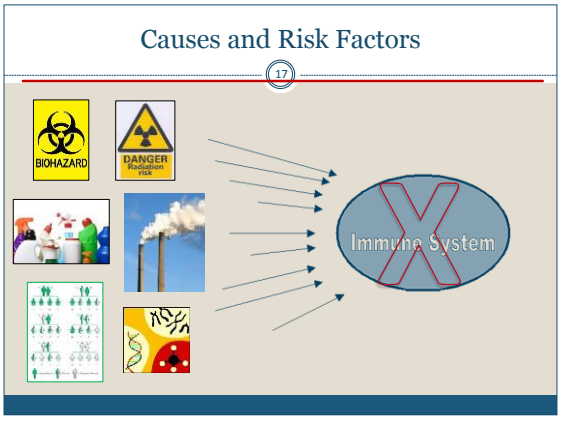
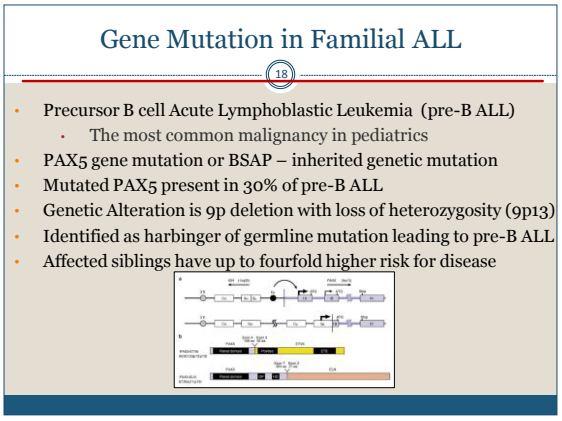
- Genetic Abnormalities (inherited/acquired)
- Conditions Causing Lowered Immunity
- Chemicals Causing Lowered Immunity
- History of Organ Transplant
- History of Viral or Bacterial Infection
  - HTLV1/HIV/EBV/HHV8/HepC/Helicobacter Pylori
- Auto Immune Condition
  - Rheumatoid Arthritis
  - Systemic Lupus Erythematous
- Family History of Lymphoma

http://cancer.gov/


blood
JOURNAL OF THE AMERICAN SOCIETY OF HEMATOLOGY
Large B-cell lymphomas with a phenotype of terminal B-cell differentiation.
Mature B-cell Differentiation CD20
Plasmablast Differentiation CD138, 38
Immunodeficiency
Mild
Elderly
Others
HIV
Viral Agents
EBV
HHV-8
DLBCL, ALK +
LyG
PBL
LCL-MCD
DLBCL, EBV+
PEL
Campo E et al. Blood 2011;117:5019-5032
©2011 by American Society of Hematology
16


Causes and Risk Factors
17
BIOHAZARD
DANGER
Radiation Risk
Immune System


Gene Mutation in Familial ALL
18
Precursor B cell Acute Lymphoblastic Leukemia (pre-B ALL)
The most common malignancy in pediatrics
PAX5 gene mutation or BSAP – inherited genetic mutation
Mutated PAX5 present in 30% of pre-B ALL
Genetic Alteration is 9p deletion with loss of heterozygosity (9p13)
Identified as harbinger of germline mutation leading to pre-B ALL
Affected siblings have up to fourfold higher risk for disease

Signs and Symptoms

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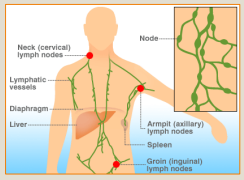
- Enlarged Lymph Node(s)
  - Neck
  - Armpit
  - Groin
- Swollen Abdomen
- Chest Pain/Pressure
- Shortness of Breath
- Fever
- Weight Loss
- Night Sweats
- Fatigue

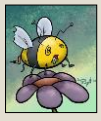


Source: b4tea.com

"B" Symptoms

20

- What is Significance of "B" Symptoms
- What are "B" Symptoms
  - Fevers
  - Night Sweats
  - Weight Loss > 10% of Body Weight
- Minor Symptoms
  - Malaise
  - Fatigue
  - Pruritis
  - Alcohol Intolerance
  - Frequent Infections
- **Do Not Code Minor Symptoms as "B" Symptoms**



Not a "B"

Immune System

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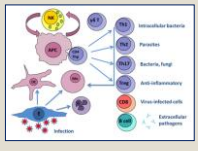
- Primary Function Lymphatic System – Fluid Retrieval
- Primary Function Immune System – Protect from infection
  - Bacteria
  - Viruses
  - Fungi
  - Injury
  - Parasites
- Interacts with Nervous System
- Protects via immune response from;
  - **Innate Immunity**
  - **Adaptive Immunity**



Source: http://static.abdserotec.com/2013images/figure1.jpg

Immune System

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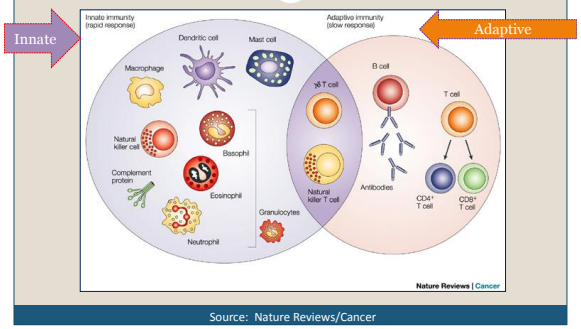
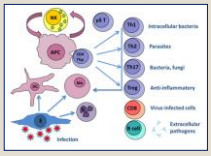


Source: Nature Reviews/Cancer

Immune System

23

- Causes of Lymph Node Enlargement:
  - Non-specific reactive hyperplasia
  - Inflammatory Reaction
    - Foreign Body
    - Tuberculosis
    - Infection
    - Injury
  - Neoplasm
    - Primary – Lymphoma (Hodgkin or Non-Hodgkin)
    - Secondary – Metastatic Ds. via Lymph Node Drainage

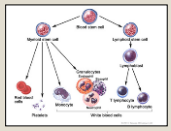


Source: http://static.abdserotec.com/2013images/figure1.jpg

Hematopoiesis

24

- What is a hematopoietic stem cell?
- Where are hematopoietic stem cells found?
- Hematopoietic stem cells give rise to ALL blood cells in a process called Cell Line Differentiation
  - Lymphoid cell line (lineage)
  - Myeloid cell line (lineage)
- Cell Line Differentiation
- Cell Line Proliferation
- Regulating Proliferation and Differentiation



Regulatory Function of Cells

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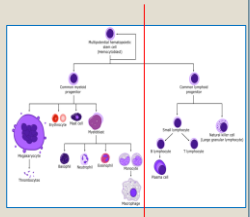
- Regulation of proliferation
- Regulation of differentiation
- Turn on/Turn off
  - Growth factors
  - Genes (including mutations)
  - Proteins
- Disregulation disrupts normal development of cell line
- Ongogenesis – becoming malignant

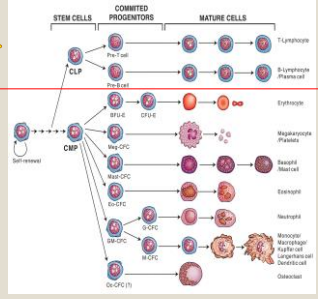


Hematopoietic stem cells give rise to two major progenitor cell lineages, myeloid and lymphoid progenitors
Regenerative Medicine. 2006. http://www.dentalarticles.com/images/hematopoiesis.jpg

Lymphoid Cell Line Differentiation

26

Lymphoid



Blood Lines – Donald Metcalf, AlphaMED Press, 2005
Figure 3.2 The eight major hematopoietic lineages generated by self-renewing multipotential stem cellsB

Cell Line Differentiation

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- Cellular differentiation is the process by which an immature cell becomes a more mature cell
- Differentiation changes a cell's size, shape, membrane potential, metabolic activity, and responsiveness to signals or signal pathways
- Regulatory function of cells (regulates cell line proliferation and cell line differentiation) so you have right mix of different types of hematopoietic cells being produced by the bone marrow…and circulating in the blood and/or lymph.
- Over/Under Production by bone marrow of one cell line (clonal)
- Too many or too few cells may lead to chronic/acute condition

B-cell Differentiation

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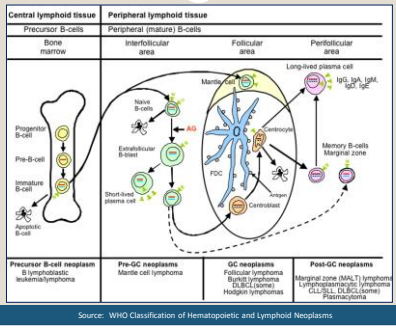

Source: WHO Classification of Hematopoietic and Lymphoid Neoplasms

T-cell Differentiation

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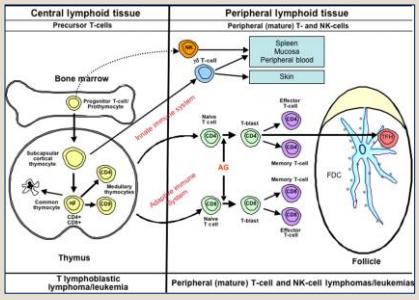

Source: WHO Classification of Hematopoietic and Lymphoid Neoplasms

Differentiation and Immune Function

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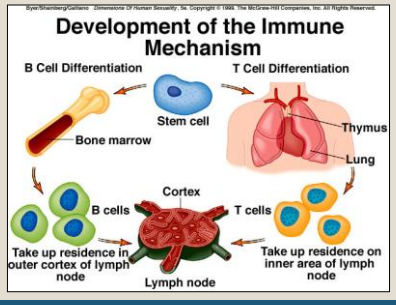

Source: www..mhhe.com/science

Blood Circulatory System

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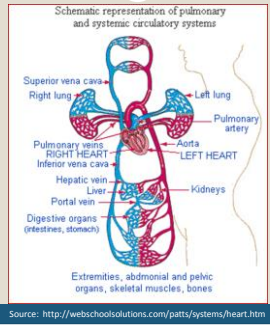
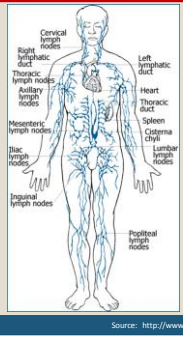
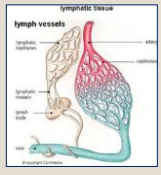


Source: http://webschoolsolutions.com/patts/systems/heart.htm

Lymphatic Circulatory System

32





Source: http://www.gorhams.dk/html/the_lymphatic_system.htm

Lymphatic Circulatory System

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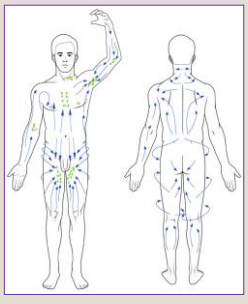

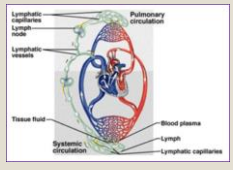

Source: Nature Reviews Immunology http://www.nature.com/nri/journal/v4/n5

The Lymphatic System

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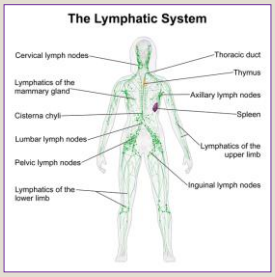

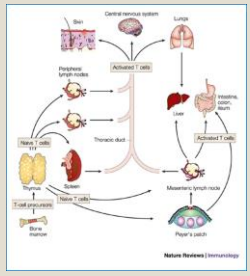

Lymphatic Organs

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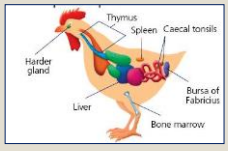
- Primary Organs
  - Bone Marrow
  - Thymus



- Secondary Organs
  - Spleen – process blood
    - Red Pulp
    - White Pulp
  - Tonsils (Waldeyer's Ring)
  - Lymph Nodes – process extracellular fluids
  - MALT (mucosa-associated lymphoid tissue) – process mucosa
    - GALT (gut-associated lymphoid tissue)
    - Peyer's Patches
  - Skin

Lymphatic Organs

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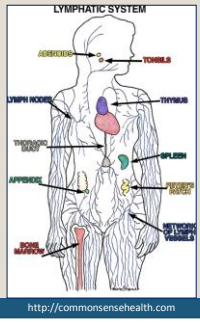

http://commonsensehealth.com

Lymphatic Organs

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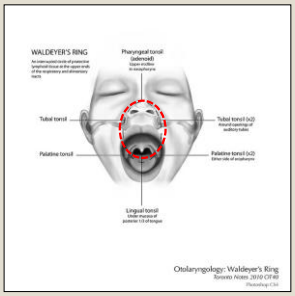

http://www.flickr.com/photos

Lymph Node

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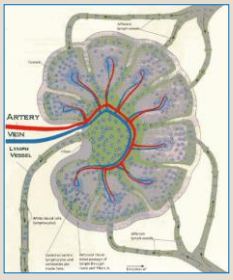

Source: http://www.bcb.uwc.ac.za/SCI_ED/grade10/manphys/plan.htm

Lymph Node Chains

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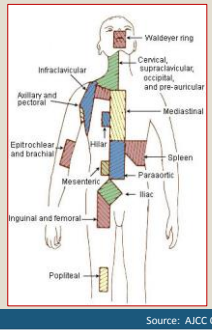

Lymph nodes above the diaphragm

1. Waldeyer's ring
2. Cervical, supraclavicular, occipital, and pre-auricular
3. Infraclavicular
4. Axillary and pectoral
5. Mediastinal
6. Hilar
7. Epitrochlear and brachial

Lymph nodes below the diaphragm

8. Spleen
9. Mesenteric
10. Paraaortic
11. Iliac
12. Inguinal and femoral
13. Popliteal

Source: AJCC Cancer Staging Form, 7th edition

Appendix C
Lymph Node/Lymph Node Chain Reference Table

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Use this table with the Primary Site and Histology Rules to determine whether involved lymph nodes are in a single ICD-O-3 lymph node region or in multiple ICD-O-3 lymph node regions.
This table contains the names of lymph nodes that have the capsule and sinus structure of true lymph nodes. Lymphoid tissue such as that in the GI tract, tonsils, etc., is not represented in this table.
Note: Pathology reports may identify lymph nodes within most organs, the most common being breast, parotid gland, lung, and pancreas. The lymph nodes in these organs are called intra-(organ name) lymph nodes such as intramammary lymph nodes. We have included the most common intra-organ lymph nodes on this table. For an intra-organ lymph node not listed on the table, code to the ICD-O-3 topography code for that organ's regional lymph node chain(s).

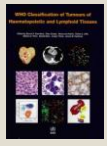
Table C1: Lymph Node/Lymph Node Chain Reference Table

Lymph Node/Lymph Node Chain	Use for MP/H	ICD-O-3 Lymph Node Region(s)	AJCC/CS Staging
Abdominal	C772	Intra-abdominal	Mesenteric
Anorectal	C772	Pelvic	Pelvic, right and left*
Anterior axillary	C773	Axilla or arm	Axillary, right and left*
Anterior cecal	C772	Intra-abdominal	Mesenteric
Anterior deep cervical	C770	Head, face and neck	Cervical, right and left*
Anterior jugular	C770	Head, face and neck	Cervical, right and left*
Aortic NOS; ascending aortic lateral aortic; lumbar aortic; para-aortic; peri-aortic	C772	Intra-abdominal	Para-aortic
Aortico-pulmonary window (subaortic)	C772	Intra-abdominal	Para-aortic
Appendiceal	C772	Intra-abdominal	Mesenteric
Ascending aortic	C772	Intra-abdominal	Para-aortic
Auerbach's glands (nodes near pancreas)	C772	Intra-abdominal	Para-aortic
Auricular NOS; infra-auricular, pre-auricular, post-auricular; retro-auricular	C770	Head, face and neck	Cervical, right and left*
Axillary, lateral;	C773	Axilla or arm	Axillary, right and left*
Axillary, anterior	C773	Axilla or arm	Axillary, right and left*
Azygos (lower paratracheal)	C771	Intrathoracic	Mediastinal
Brachial	C773	Axilla or arm	Axillary, right and left*
Bronchial, bronchopulmonary; hilar, proximal lobar; pulmonary root	C771	Intrathoracic	Hilar
Bronchopulmonary	C771	Intrathoracic	Hilar
Bronchopulmonary; bronchial hilar, proximal lobar; pulmonary root	C771	Intrathoracic	Hilar
Buccal	C770	Head, face and neck	Cervical, right and left*
Buccinator (facial)	C770	Head, face and neck	Cervical, right and left*
Calot's node (cysto-hepatic triangle or hepato-biliary triangle)	C772	Intra-abdominal	Para-aortic
Cardiac	C771	Intrathoracic	Mediastinal

Classification of Lymphoid Neoplasms

41

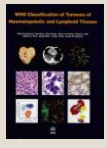
- Development of a World Standard
  - 1951 – Dameshek – clinical phenotype
  - 1960 – Philadelphia (Ph1) chromosome
  - 1966 – Rappaport Classification
  - 1974 – Kiel Classification System
  - 1974 – Lukes and Collins System
  - 1976 – Revised Rappaport Classification
  - 1976 – French – American – British Classification



Classification of Lymphoid Neoplasms

42

- Development of a World Standard
  - 1982 – Working Formulation
  - 1994 –Revised European-American Classification of Lymphoid Neoplasms
  - 2001 – WHO Classification of Tumors of Hematopoetic and Lymphoid Tissues, 3rd edition, 2001
  - 2008 – WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues, 4th edition, October 2008



2008 WHO Classification of Lymphoid Neoplasms

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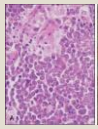
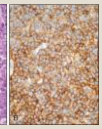
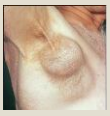
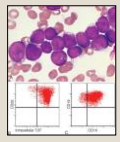
Incorporates:

- ✓ Histology/Morphology
- ✓ Stage of Differentiation
- ✓ Immunophenotype
- ✓ Genotypic features
- ✓ Clinical features

2008 WHO Classification - Lymphoid

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Precursor Lymphoid Neoplasm

Table B7: Precursor Lymphoid Neoplasms

WHO Preferred Term	
Adult T-cell leukemia/lymphoma	9837/3
B lymphoblastic leukemia/lymphoma with hyperdiploidy	9815/3
B lymphoblastic leukemia/lymphoma with hypodiploidy (hypodiploid ALL)	9816/3
B lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities	No Code
B lymphoblastic leukemia/lymphoma with t(1;19)(q23;p13.3); E2A-PBX1 (TCF3-PBX1)	9818/3
B lymphoblastic leukemia/lymphoma with t(12;21)(p13;q22); TEL-AML1 (ETV6-RUNX1)	9814/3
B lymphoblastic leukemia/lymphoma with t(5;14)(q31;q32); IL3-IGH	9817/3
B lymphoblastic leukemia/lymphoma with t(9;22)(q34;q11.2); BCR-ABL1	9812/3
B lymphoblastic leukemia/lymphoma with t(v;11q23); MLL rearranged	9813/3
B lymphoblastic leukemia/lymphoma, NOS	9811/3

Mature B-Cell Neoplasm

Table B8: Mature B-Cell Neoplasms

WHO Preferred Term	
ALK positive large B-cell lymphoma	9737/3
B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and classical Hodgkin lymphoma	9596/3
B-cell prolymphocytic leukemia	9833/3
Burkitt lymphoma	9687/3
Chronic lymphocytic leukemia/small lymphocytic lymphoma	9823/3
Diffuse large B-cell lymphoma (DLBCL)	9680/3
Extranodal marginal zone lymphoma of mucosal-associated lymphoid tissue (MALT lymphoma)	9699/3
Extraosseous plasmacytoma	9734/3
Follicular lymphoma	9690/3
Hairy cell leukemia	9940/3

2008 WHO Classification - Lymphoid

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Mature B-Cell Neoplasm (con't)

WHO Preferred Term	
Heavy chain disease	
Intravascular large B-cell lymphoma	9712/3
Large B-cell lymphoma arising in HHV8-associated multicentric Castleman disease	9738/3
Lymphomatoid lesion	9766/1
Lymphoplasmacytic lymphoma	9671/3
Mantle cell lymphoma	9673/3
Non-Hodgkin lymphoma, NOS; splenic B-cell lymphoma/leukemia, unclassifiable	9591/3
Plasma cell myeloma	9732/3
Plasmablastic lymphoma	9735/3
Primary cutaneous follicle center lymphoma	9597/3
Primary effusion lymphoma	9678/3
Primary mediastinal (thymic) large B-cell lymphoma	9679/3
Solitary plasmacytoma of bone	9731/3
Splenic marginal zone lymphoma	9689/3
T-cell/histiocyte rich large B-cell lymphoma	9688/3
Waldenström Macroglobulinemia	9761/3

Mature T-Cell and NK-Cell Neoplasm

Table B9: Mature T-Cell and NK-Cell Neoplasms

WHO Preferred Term	
Adult T-cell leukemia/lymphoma (HTLV-1 positive)	9827/3
Aggressive NK-cell leukemia	9948/3
Anaplastic large cell lymphoma, ALK positive	9714/3
Angioimmunoblastic T-cell lymphoma	9705/3
Enteropathy-associated T-cell lymphoma	9717/3
Extranodal NK/T-cell lymphoma, nasal type	9719/3
Hepatosplenic T-cell lymphoma	9716/3
Hydroa vacciniforme-like lymphoma	9725/3
Lymphomatoid papulosis	9718/1
Mycosis fungoides	9700/3
Peripheral T-cell lymphoma, NOS	9702/3
Primary cutaneous CD30 positive T-cell lymphoproliferative disorders	9718/3
Primary cutaneous T-cell lymphoma	9709/3
Primary cutaneous gamma-delta T-cell lymphoma	9726/3
Sezary syndrome	9701/3
Subcutaneous panniculitis-like T-cell lymphoma	9708/3
Systemic EBV positive T-cell lymphoproliferative disease of childhood	9724/3
T-cell large granular lymphocytic leukemia	9831/3
T-cell prolymphocytic leukemia	9834/3

2008 WHO Classification - Lymphoid

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Hodgkin Lymphoma

Table B10: Hodgkin Lymphoma	
WHO Preferred Term	ICD-O-3
Classical Hodgkin lymphoma	9650/3
Lymphocyte-depleted classical Hodgkin lymphoma	9653/3
Lymphocyte-rich classical Hodgkin lymphoma	9651/3
Mixed cellularity classical Hodgkin lymphoma	9652/3
Nodular sclerosis classical Hodgkin lymphoma	9663/3

Histiocytic /Dendritic Cell Neoplasm

Table B11: Histiocytic and Dendritic Cell Neoplasms	
WHO Preferred Term	
Disseminated juvenile xanthogranuloma	No Code
Fibroblastic reticular cell tumor	9759/3
Follicular dendritic cell sarcoma	9758/3
Histiocytic sarcoma	9755/3
Interdigitating dendritic cell tumor	9757/3
Langerhans cell histiocytosis	9751/3
Langerhans cell sarcoma	9756/3

PTLD (Post-Transplant)

Table B12: Post-Transplant Lymphoproliferative Disorders (PTLD)	
WHO Preferred Term	ICD-O-3
Early lesions	No Code
Classical Hodgkin lymphoma type PTLD	*
Monomorphic PTLD (B- and T/NK-cell types)	*
Plasmacytic hyperplasia	9971/1
Post-transplant lymphoproliferative disorder	9971/3

Understanding Complex Disease Processes

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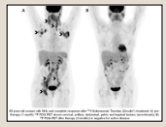
- Lymph Node Biopsy
- Extranodal Site Biopsy
- Diagnostic Imaging (CT/PET/MRI)
- Bone Marrow Aspirate
- Bone Marrow Biopsy

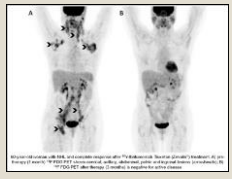


- Histology/Morphology
- Immunohistocytohemistry
- Flow Cytometry (Immunophenotype)
- Cytyogenetics
- Molecular Genetic Studies
  - FISH
  - PCR

The Clinical Workup

48

- Disease Definition
- Risk Factors
- Signs and Symptoms
- Diagnostic Work Up
  - Clinical Evaluation
  - History and Physical
  - CBC – What is Normal
  - Immunophenotype
  - Imaging Studies (CT/PET/MRI and PET/CT)
  - Tissue Biopsy – Histologic Type and Staining
  - Bone Marrow Biopsy – Histologic Type and Staining
  - Molecular Cytogenetics – Genetic Testing



Disease Definition

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Table 2
Diagnostic criteria for plasma cell myeloma

Symptomatic plasma cell myeloma	
	M-protein in serum or urine*
	BM clonal plasma cells or plasmacytoma†
	Related organ or tissue impairment heavy chain disease‡ (CRAB)
Asymptomatic (smoldering) myeloma	
	M-protein in serum at myeloma levels (> 30 g/L) and/or ≥ 10% clonal plasma cells in BM
	No related organ or tissue impairment end-organ damage or bone lesions [CRAB] or myeloma-related symptoms

Source: BLOOD, 12 MAY 2011 VOLUME 117, NUMBER

Plasma Cell Neoplasms

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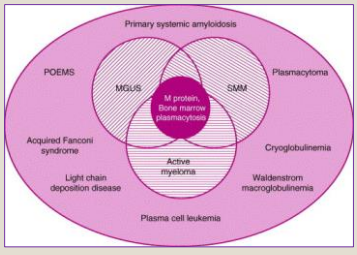
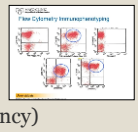
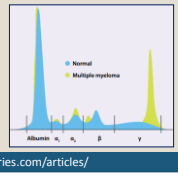


Immunophenotype

51

- Study of proteins expressed by cells
- Evaluates or Designates
  - Proliferation (myeloid or lymphoid)
  - Differentiation (category of malignancy)
- Antibodies "cluster of differentiation" or "CD"
- Immunophenotyping methods
  - Immunohistochemistry
  - Immunofluorescence
  - Flow cytometry
  - Electrophoresis

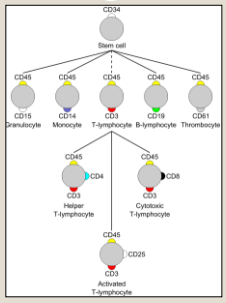




Source: http://www.mayomedicallaboratories.com/articles/

Cluster of Differentiation

52



Source: Schorschski @ de.wikipedia

Cluster of Differentiation Markers – B Cell

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B-cell CD markers

Marker Status										
Type	CD5	CD10	CD19	CD20	CD21	CD22	CD23	CD43	CD79a	sIg
Follicular	1	3	4	4		4	2	1	4	4
Nodal marginal zone	1	1	4	4		4	1	2	4	M4, D1
MALT	1	1	4	4		4	1	2	4	M4
Splenic Marginal zone	1	1	4	4		4	1	0	4	M4
CLL/SLL	4	0	4	4		4	4	4	4	D3
Lymphoplasmacytic Waldenstroms	1	1	4	4		4	0	3	4	M4, D2
Mantle Cell	4	1	4	4		4	1	4	4	MBD 4
Precursor B-cell (lymphoblastic)	4	3	4	4		4	0	0	4	0
Diffuse large B-cell	2	2	4	4		4	0	1	4	
Mediastinal large cell	2									
Burkitt's	1	4								
Intravascular B-cell										

Footnote: 0 = negative, 1 = <10% positive, 2 10-50% positivity, 3 = 50-90% positivity and 4 = >90% positive

Source: http://www.nhlcyberfamily.org/tests/cdmarkers.htm

Cluster of Differentiation Markers – T Cell

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T-cell CD markers

Marker Status							
Type	CD3	CD5	CD7	CD4	CD8	CD30	NK16/56
T-prolymphocytic leukaemia	+	-	+	+(-)	-(+)	-	-
T-large granular lymphoproliferative	+	-	+	-	+	-	+(-)
Mycosis Fungoides	+	+	+	-	-(+)	-(+)	-
Cutaneous ALCL	+	+(-)	+(-)	+(-)	-	++	-(+)/-(+)
Primary systemic ALCL	+(-)	+(-)	+(-)	-(+)	-(+)	++	-
Peripheral T-cell lymphoma, unspecified	+(-)	+(-)	-(+)	+(-)	-(+)	-(+)	-(+)/-(+)
Subcutaneous panniculitis-like T-cell	+	+	+	-(+)	+(-)	-(+)	-/-(+)
Hepatosplenic T-cell lymphoma	+	-	+	-	-	-	+/+(-)
Angioimmunoblastic T-cell lymphoma	+	+	-	+(-)	-(+)	-	-
Extranodal NK/Tcell lymphoma	S-, C+	-	-(+)	-(+)	-	-	-/+
Enteropathy-associated T-cell lymphoma	+	+	+	-(+)	+(-)	+(-)	-
Adult T-cell leukaemia/lymphoma	+	+	-	+(-)	-(+)	+(-)	-

Footnote: + = >90% positive; +(-) = >50% positive; -(+) = <50% positive; - = <10% positive.
ALCL-Anaplastic large cell lymphoma; C=Cytoplasmic; S-Surface.

Source: http://www.nhlcyberfamily.org/tests/cdmarkers.htm

Dx Confirmation - Codes

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Codes Hematopoietic or Lymphoid Tumors (9590-9992)

Code	Description	Definition
1	Positive histology	Histologic confirmation (tissue microscopically examined)
2	Positive cytology	Cytologic confirmation (no tissue microscopically examined; fluid cells microscopically examined)
3	Positive histology PLUS • Positive immunophenotyping AND/OR • Positive genetic studies	Histology is positive for cancer, and there are also positive immunophenotyping and/or genetic test results. For example, bone marrow examination is positive for acute myeloid leukemia (9861/3) Genetic testing shows AML with inv(16)(p13.3q22) (9871/3).
4	Positive microscopic confirmation, method not specified	Microscopic confirmation is all that is known. It is unknown if the cells were from histology or cytology.
5	Positive laboratory test/marker study	A clinical diagnosis of cancer is based on laboratory tests/marker studies which are clinically diagnostic for cancer.
6	Direct visualization without microscopic confirmation	The tumor was visualized during a surgical or endoscopic procedure only with no tissue resected for microscopic examination.
7	Radiography and other imaging techniques without microscopic confirmation	The malignancy was reported by the physician from an imaging technique report only.
8	Clinical diagnosis only, other than 5, 6 or 7	The malignancy was reported by the physician in the medical record.
9	Unknown whether or not microscopically confirmed	A statement of malignancy was reported in the medical record, but there is no statement of how the cancer was diagnosed (usually nonanalytic).

Dx Confirmation - Instructions

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Coding Instructions for Hematopoietic or Lymphoid Tumors (9590-9992)

1. There is no priority hierarchy for coding *Diagnostic Confirmation* for hematopoietic and lymphoid tumors. Most commonly, the specific histologic type is diagnosed by immunophenotyping or genetic testing. See the *Hematopoietic Database (DB)* for information on the definitive diagnostic confirmation for specific types of tumors.
2. Code 1 when the microscopic diagnosis is based on tissue specimens from biopsy, frozen section, surgery, or autopsy or bone marrow specimens from aspiration or biopsy.
3. For leukemia only, code 1 when the diagnosis is based only on the complete blood count (CBC), white blood count (WBC) or peripheral blood smear. Do not use code 1 if the diagnosis was based on immunophenotyping or genetic testing using tissue, bone marrow, or blood.
4. Code 2 when the microscopic diagnosis is based on cytologic examination of *cells* (rather than tissue) including but not limited to spinal fluid, peritoneal fluid, pleural fluid, urinary sediment, cervical smears and vaginal smears, or from paraffin block specimens from concentrated spinal, pleural, or peritoneal fluid. These methods are rarely used for hematopoietic or lymphoid tumors.
5. Code 3 when there is a histology positive for cancer AND positive immunophenotyping and/or positive genetic testing results. Do not use code 3 for neoplasms diagnosed prior to January 1, 2010.

Dx Confirmation - Instructions

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6. Code 5 when the diagnosis of cancer is based on laboratory tests or marker studies which are clinically diagnostic for that specific cancer, but no positive histologic confirmation.
7. Code 6 when the diagnosis is based only on the surgeon's report from a surgical exploration or endoscopy or from gross autopsy findings without tissue or cytological findings.
8. Code 8 when the case was diagnosed by any clinical method that can not be coded as 6 or 7.
9. A number of hematopoietic and lymphoid neoplasms are diagnosed by tests of exclusion where the tests for the disease are equivocal and the physician makes a clinical diagnosis based on the information gfrom the equivocal tests and the patient's clinical presentation.

Disease Progression

58

- The worsening of a disease over time
- Advancing stage of disease with/out treatment
- Progression from a solitary site of involvement to multiple sites of involvement.
- May be used to describe the progression of a chronic state of disease to an acute state.

Hematopoietic Disease Progression

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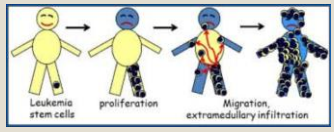
- Same
  - Cell type
  - "Function"
  - Genetics
- Change
  - Symptoms
  - Treatment Approach
  - Prognosis or Life Expectancy



Source: www.haematologica.org

Hematopoietic Disease Progression

60

- Solitary plasmacytoma to plasma cell myeloma
- Smoldering myeloma to plasma cell myeloma
- Early stage/asymptomatic Small Lymphocytic Lymphoma (SLL) or Chronic Lymphocytic Leukemia (CLL) to late stage/symptomatic CLL requiring tx

Transformation

61

- Change in nature, function, or condition of cells
- Change in cell's potential or type; cell undergoing genetic transformation
- Most transformations are myeloid neoplasms transforming from chronic myeloproliferative or myelodysplastic disease into acute myeloid leukemia
- Chronic Lymphocytic Leukemia (CLL) to Acute Lymphoblastic Leukemia (ALL) is rare - new primary

Hematopoietic Disease Transformation

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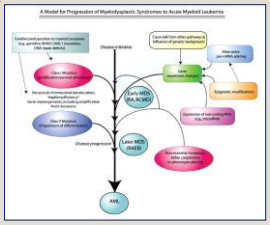
- Rare in Lymphoid Neoplasms
- Different
  - Cell type
  - "Function"
  - Genetics
- Change
  - Symptoms
  - Treatment Approach
  - Prognosis or Life Expectancy



Source: www.haematologica.org

Cutaneous Lymphomas

63

- Most primary skin lymphomas are T-cell lymphoma
  - Often multiple skin sites involved - plaque
  - Mycosis Fungoides
  - Sezary Syndrome
- Primary B-cell lymphoma of skin is rare
  - Cutaneous Follicle Center Lymphoma
  - Cutaneous Marginal Zone B-cell lymphoma
  - Cutaneous Diffuse Large B-cell lymphoma
- Diffuse Large B-cell lymphoma of skin is very rare

CUTANEOUS LYMPHOMA FOUNDATION

Tools and Rules

2014 UPDATES 2014

HEMATOPOIETIC DATA BASE

HEME/LYMPH RULES AND INSTRUCTIONS

2014 Data Base Updates 2014

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- New Format
- New User's Guide
- Content Updates
  - Typos fixed
  - Additional information added
  - MP Calculator Algorithm Updated
  - Information resorted (alphabetical)
  - Transformations Corrected/Enhanced
    - Transformation "to"
    - Transformation "from"
- Enhanced Search Gives Score for Match
- Enhanced Internal Links to Related Rules

2014 Data Base Updates 2014

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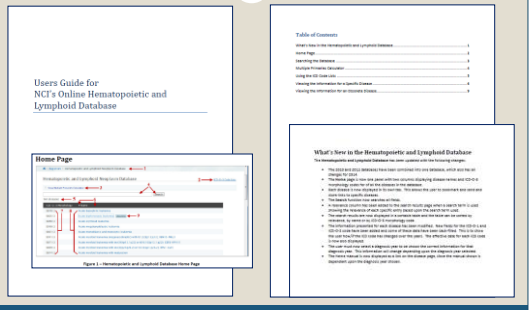

2014 Updates 2014

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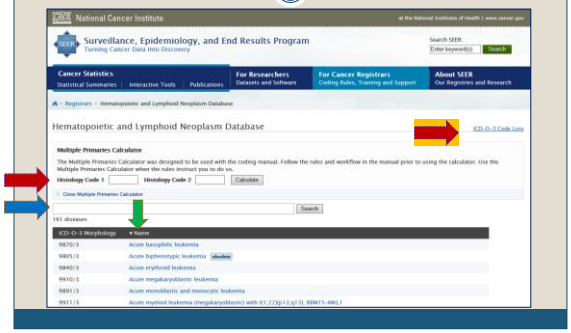

2014 Updates 2014

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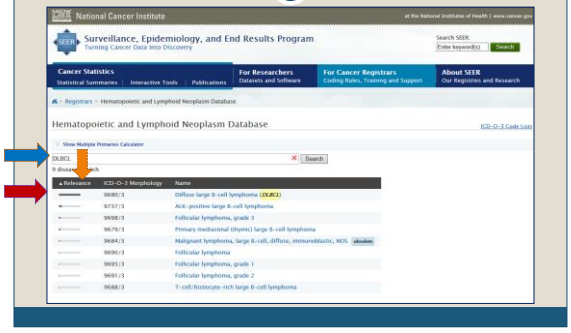

2014 Updates 2014

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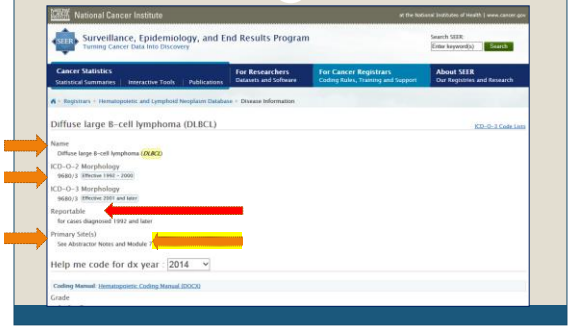

2014 Updates 2014

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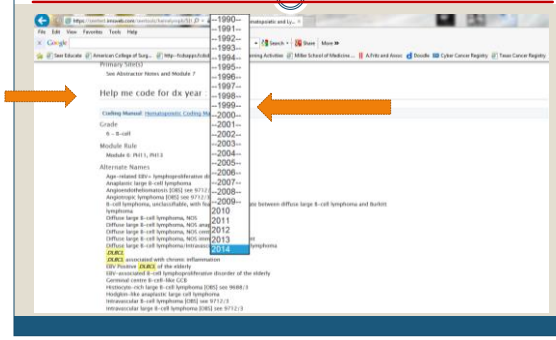

2014 Updates 2014

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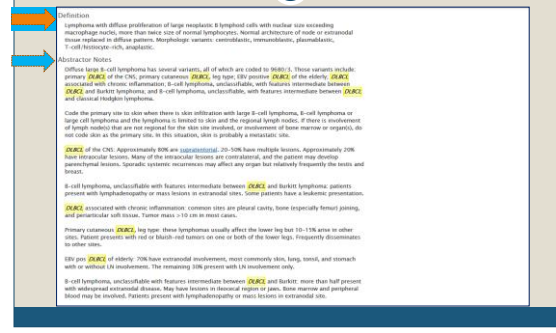

2014 Updates 2014

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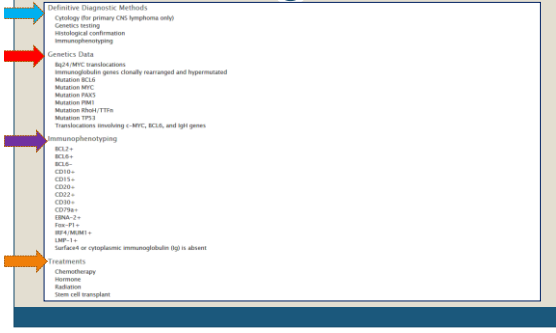

2014 Updates 2014

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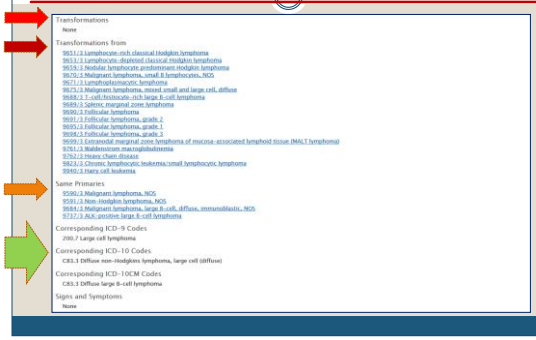

What's In The Manual/Database

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Manual (Rules/Instructions)	Database (Dx Yr)
• Introduction	• Neoplasm Name/Definition
• General Instructions	• Alternate Names
• Diagnostic Confirmation	• MP Calculator/Special Rules
• Reportability Instructions	• Primary Site(s)
• Multiple Primary Rules	• Diagnostic Method(s)
• Primary Site Rules	• Abstractor Notes
• Histology Coding Rules	• Immunophenotype
• Grade Coding Rules	• Genetic Tests
• Glossary	• Standard Treatment(s)
• Appendix A – Hx of Coding	• Transformation(s) "to" and "from"
• Appendix B – WHO Lineages	• ICD-O/ICD-9/ICD-10 Codes
• Appendix C – Nodal Chains	• Signs and Symptoms
• Appendix D – Terms / Codes	• Diagnostic Exams
• Appendix E – Obsolete Codes	• Recurrence and Metastases
• Appendix F – Not Reportable	• Epidemiology/Mortality

2014 Rule Updates 2014

75

- Only 1 Format – TEXT
- All Changes to Rules are Effective for Cases Dx 2010>
  - Some Rules Combined
  - Duplicate Rules Removed
  - Corrections to Some Rules
  - Clarifications to Some Rules
  - Example: Review of 2010 and 2011 data shows multiple occurrences of patients with multiple MDS histologies (9980/3, 9982/3, 9983/3, 9984/3, 9985/3, 9986/3, 9989/3, 9991/3, 9992/3)
- Improved (embedded) Navigation to Related Rules
  - Example: See Module 5, PH9 and PH10 for information regarding primary site and histology

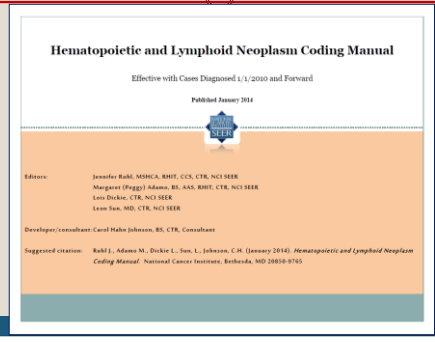
2014 Rule Updates 2014

76

- PH Rules Reduced from 43 to 31
- Primary Site Coding Rules for Lymphoma are More Clear
- Lymphoid Combinations Clarified
  - DLBCL with any other lymphoma coded to DLBCL
  - Other mixed lymphomas handled differently
- OBS (obsolete) codes
  - All OBS codes are obsolete as of 1/1/2010
  - OBS codes are now date driven
  - Instruction to use for "DCO's, path only and minimal information" cases removed

2014 Updates 2014

77



Hematopoietic and Lymphoid Neoplasm Coding Manual

Effective with Cases Diagnosed 1/1/2010 and Forward

Published January 2014

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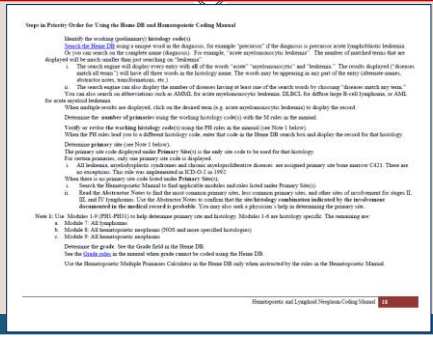
2014 Updates 2014

78



Steps in Priority Order for Using the Heme DB and Hematopoietic Coding Manual

Identify the working (preliminary) histology code(s).
Search the Heme DB using a unique word in the diagnosis, for example "precursor" if the diagnosis is precursor acute lymphoblastic leukemia.
Or you can search on the complete name (diagnosis). For example, "acute myelomonocytic leukemia". The number of matched terms that are displayed will be much smaller than just searching on "leukemia".
i. The search engine will display every entry with all of the words "acute" "myelomonocytic" and "leukemia." The results displayed ("diseases match all terms") will have all three words in the histology name. The words may be appearing in any part of the entry (eliminate names, abstractor notes, transformations, etc.)
ii. The search engine can also display the number of diseases having at least one of the search words by choosing "diseases match any term."
You can also search on abbreviations such as AMML for acute myelomonocytic leukemia. DLBCL for diffuse large B-cell lymphoma, or AML for acute myeloid leukemia.
When multiple words are displayed, click on the desired term (e.g. acute myelomonocytic leukemia) to display the record.
Determine the **number of primaries** using the working histology code(s) with the M rules in the manual.
Verify or revise the working **histology** code(s) using the PH rules in the manual (see Note 1 below).
When the PH rules lead you to a different histology code, enter that code in the Heme DB search box and display the record for that histology.
Determine **primary site** (see Note 3 below).
The primary site code displayed under **Primary Site(s)** is the only site code to be used for that histology.
For certain primaries, only one primary site code is displayed.
i. All leukemia, myelodysplastic syndromes and chronic myeloproliferative diseases are assigned primary site bone marrow C421. There are no exceptions. This rule was implemented in ICD-O-2 in 1992.
When there is no primary site code listed under **Primary Site(s)**,
i. Search the Hematopoietic Manual to find applicable modules and rules listed under Primary Site(s).
ii. Read the Abstractor Notes to find the most common primary sites, less common primary sites, and other sites of involvement for stages II, III, and IV lymphomas. Use the Abstractor Notes to confirm that the site/histology combination indicated by the **involvement documented in the medical record** is probable. You may also seek a physician's help in determining the primary site.
Note 1: Use Modules 1-9 (PH1-PH31) to help determine primary site and histology. Modules 1-6 are histology specific. The remaining are:
a. Module 7: All lymphomas
b. Module 8: All hematopoietic neoplasms (NOS and more specified histologies)
c. Module 9: All hematopoietic neoplasms
Determine the **grade**. See the Grade field in the Heme DB.
See the Grade rules in the manual when grade cannot be coded using the Heme DB.
Use the Hematopoietic Multiple Primaries Calculator in the Heme DB only when instructed by the rules in the Hematopoietic Manual.

Hematopoietic and Lymphoid Neoplasm Coding Manual 18

How to Use and Follow the Rules

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Rules Basics

80

1. Is the condition reportable?
2. How many cases do I abstract?
3. How do I code the primary site?
4. How do I code the histology?
5. How do I code the grade?

Determining Primary Site

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Primary Site and Histology Coding Rules

1. The primary site and histology coding rules are divided into nine modules. The first six cover primary site and histology, while the last three cover coding primary site only. Each **module** covers a group of **related** hematopoietic or lymphoid neoplasms. However, a specific histology may be covered in more than one module.
2. Go to the first module that fits the case being abstracted. If the situation in the case is not covered in that module, **continue** on to the next module.
   Note: The modules are NOT hierarchical, but the rules within each module are in hierarchical order. Apply the rules within each module in order. Stop at the first rule that applies.

Module 1: Post-Transplant Lymphoproliferative Disorder PH1

Post-transplant lymphoproliferative disorder (9971/3)

Rule PH1 Code the primary site to the site **of origin**, lymph node(s) or lymph node region(s), tissue(s), or organ(s), and code the **histology of the accompanying lymphoma or plasmacytoma/myeloma when the diagnoses of post-transplant lymphoproliferative disorder and any B-cell lymphoma, T-cell lymphoma, Hodgkin lymphoma, or plasmacytoma/myeloma occur simultaneously.**

Note 1: These neoplasms are monomorphic post-transplant lymphoproliferative disorders. The diagnosis may or may not include the word "monomorphic". For polymorphic PTLD, see the database (9971/3).
Note 2: The patient must have a history of a solid organ transplant or an allogeneic bone marrow transplant.
Note 3: Most cases of PTLD occur within a year of transplantation; however, they can occur anytime after the transplant.
Note 4: Monomorphic PTLD is also caused by the immunosuppressant drugs. Patients are treated for the lymphoma or plasmacytoma/myeloma.
Example: Previous history of kidney transplant. Now presents for bone marrow biopsy. BM positive for B-cell lymphoma. Abdominal mass biopsy was positive for PTLD, monomorphic type and aggressive B-cell malignancy. Immunohistochemistry shows the B-cell malignancy to be Burkitt lymphoma. Code the histology to Burkitt lymphoma and primary site to the abdominal lymph nodes, (C77.2).

Determining Primary Site

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Module 2: Plasmacytomas PH2 – PH4

Extraosseous plasmacytoma (9734/3)
Solitary plasmacytoma of bone (9731/3)

Rule PH2 Code the primary site to the **site of origin**, lymph node(s) or lymph node region(s), tissue(s), or organ(s), and code the histology **extramedullary plasmacytoma (9734/3)** when any of the following occur in a site **other than bone**
- Extraosseous (extramedullary) plasmacytoma
- Multiple extraosseous (extramedullary) plasmacytomas
- Multiple plasmacytomas
- Plasmacytoma, NOS
- Solitary plasmacytoma

Note 1: Extramedullary and extraosseous mean outside of bone.
Note 2: 80% of extramedullary plasmacytomas occur in the upper respiratory tract (oropharynx, nasopharynx, sinuses, and larynx) although they may occur in numerous other sites including the GI tract, lymph nodes, bladder, CNS, breast, thyroid, testis, parotid, and skin.
Note 3: Do not code to blood (C420), bone marrow (C421), reticuloendothelial system, NOS (C423), or the hematopoietic system, NOS (C424).
Example 1: Pathology reports a solitary plasmacytoma wrapped around L4 vertebrae, no invasion of vertebrae. Code the primary site as soft tissue of back (C490) and histology to plasmacytoma (9734/3).
Example 2: Scan shows two plasmacytomas in the nasopharyngeal wall. Biopsy confirms plasmacytoma. Code the primary site nasopharynx (C119) and histology to plasmacytoma (9734/3).

Rule PH3 Code the primary site to the **specific bone (C400-C419)** where the plasmacytoma originated and code the histology **solitary plasmacytoma** of bone (9731/3) when the diagnosis is
- Multiple medullary plasmacytomas
- Multiple plasmacytomas
- Multiple plasmacytomas of bone
- Solitary medullary plasmacytoma
- Solitary plasmacytoma
- Solitary plasmacytoma of bone

Note 1: Plasma cell neoplasm has been removed from the alternate names list for 9731/3. See abstractor notes for 9731/3 or the non-reportable list, Appendix F.
Note 2: The most common sites are bones with active bone marrow hematopoiesis; in order of frequency these include vertebrae, ribs, skull, pelvic, femur, clavicle, and scapula.
Note 3: When multiple bone sites are involved that are not included in the same ICD-O-3 code, code primary site to C419.
Note 4: Do not code primary site to blood (C420), bone marrow (C421), reticuloendothelial system, NOS (C423), or the hematopoietic system, NOS (C424).

Rule PH4 Code the primary site **bone, NOS (C419)** and histology **solitary plasmacytoma, NOS (9731/3)** when the only information is that the patient had a **plasmacytoma, NOS** or a **solitary plasmacytoma, NOS**.
Note1: When the only information available is that the patient had a plasmacytoma, default to coding plasmacytoma of bone. "Plasmacytoma, NOS" is an Alternate Name in the Bone DB for 9734/3.
Example: Death-certificate-only case (central or regional registry only) with underlying cause of death listed as plasmacytoma.

Determining Primary Site

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Module 4: Lymphoma/Leukemia (Specific neoplasms that can manifest as either leukemia or lymphoma or both leukemia and lymphoma) PH7 – PH8
(9727/3, 9811/3-9818/3, 9827/3, 9837/3)

Adult T-cell leukemia/lymphoma (HTLV-1 positive) (9827/3)
Adult T-cell leukemia/lymphoma (9837/3)
B lymphoblastic leukemia/lymphoma with hyperdiploidy (9815/3)
B lymphoblastic leukemia/lymphoma with hypodiploidy (Hypodiploid ALL) (9816/3)
B lymphoblastic leukemia/lymphoma with t(1;19)(q23;p13.3); ***E2A-PBX1 (TCF3-PBX1)*** **(9818/3)**
B lymphoblastic leukemia/lymphoma with t(5;14)(q31;q32); ***IL3-IGH*** **(9817/3)**
B lymphoblastic leukemia/lymphoma with t(9;22)(q34;q11.2); ***BCR-ABL1*** **(9812/3)**
B lymphoblastic leukemia/lymphoma with t(12;21)(p13;q22); ***TEL-AML1 (ETV6-RUNX1)*** **(9814/3)**
B lymphoblastic leukemia/lymphoma, NOS (9811/3, 9812/3-9818/3)
Blastic plasmacytoid dendritic cell neoplasm (Blastic natural killer leukemia/lymphoma) (9727/3)
Lymphoblastic leukemia/lymphoma with t(v;11q23); ***MLL rearranged*** **(9815/3)**

Note 1: ICD-9-CM, ICD-10 and ICD-10-CM have separate codes for leukemia and lymphoma.
Note 2: Lymphoma commonly originates in lymph nodes, tissue, or an organ although it will metastasize to the bone marrow when the stage is IV or disseminated.
Note 3: Primary liver lymphomas are possible; however, most of the time liver is a metastatic site.

Rule PH7 For the histologies listed above, code the primary site to bone marrow (C421) when the **only** site involved is bone marrow.
Note 1: If **lymph node(s), lymph node region(s), organ(s)** or tissue(s) are involved, see Rule PH8.
Note 2: Do not change primary site code because the spleen is involved with infiltrate. The infiltrate refers to deposit of leukemia in the spleen as a result of the spleen filtering the blood.

Rule PH8 For the histologies listed above, code the primary site to the site of origin when lymph node(s) or lymph node region(s), tissue(s) or organs are involved.
Note 1: Do not simply code the site of a biopsy; also use the information available from scans to determine the correct primary site.
Note 2: Bone marrow may or may not be involved. If bone marrow is involved, code this information in CS Extension.
Note 3: See Appendix C for help identifying lymph node names, chains, regions and codes.
Note 4: See Module 7 for more information on coding primary site for lymphomas.

Determining Primary Site

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Module 7: Coding Primary Site for Lymphomas Only PH15 – PH27

9590/3-9729/3, 9735/3-9738/3, 9811/3-9818/3, 9823/3, 9827/3, 9837/3

Note 1: Primary liver lymphomas are possible, however, most of the time liver is a metastatic site.
Note 2: Do not simply code the site of a biopsy; use the information available from scans to determine the correct primary site.

Rule PH15 Code the primary site to the specified **lymph node region** when the site of **lymphoma** is described only as a **mass.**
- Mediastinal lymph nodes (C771) when the site of the lymphoma is described only as a **mediastinal mass.**
- Intra-abdominal lymph nodes (C772) when the site of the lymphoma is described only as a **retroperitoneal mass** or **mesenteric mass.**
- Inguinal lymph nodes (C774) when the site of the lymphoma is described only as an **inguinal mass.**
- Pelvic lymph nodes (C773) when the site of the lymphoma is described only as a **pelvic mass.**

Rule PH19 Code the primary site to the **specific lymph node region** when only **one lymph node** or **one lymph node region** is involved.

Rule PH20 Code the primary site to the **specific lymph node region** when **multiple** lymph node **chains** within the **same region** as defined by ICD-O-3 are involved.
Note 1: Use this rule when there is bilateral involvement of lymph nodes.
Note 2: See Appendix C for help identifying lymph node names, chains, regions, and codes.
Example 1: Code involvement of intra-abdominal lymph node chain, hepatic lymph node chain, and para-aortic lymph node chain to intra-abdominal lymph nodes (C772).
Example 2: Code involvement of cervical lymph node chain and mandibular lymph node chain to lymph nodes of head, face and neck (C770).
Example 3: Code to mediastinal lymph nodes (C771) when bilateral mediastinal lymph nodes are involved.

Rule PH21 Code the primary site to **multiple lymph node regions, NOS (C778)** when multiple lymph node regions, as defined by ICD-O-3, are involved and it is **not possible to identify the lymph node region where the lymphoma originated.**
Note 1: See Rule PH24 when there is also organ involvement.
Note 2: Do not simply code the site of a biopsy; use the information available from scans to determine the correct primary site. See Primary Site Coding Instructions for more information on coding primary site for lymphoma.
Note 3: See Appendix C for help identifying lymph node names, chains, regions, and codes.
Example 1: Cervical (C770) and antethoracic (C771) lymph nodes involved with B-cell lymphoma. Code the primary site to lymph nodes of multiple regions C778.
Example 2: CT scans showed involvement of the cervical lymph nodes C770 and the mediastinal lymph nodes C771. No additional involvement was identified during the work-up. Biopsy of a cervical lymph node confirmed lymphoma. Code the primary site to lymph nodes of multiple regions C778.

Rule PH22 Code the primary site to **lymph nodes, NOS (C779)** when
- Lymphoma is present in an organ and lymph nodes that are **not** regional for that organ and the origin of the lymphoma cannot be determined even after consulting the physician OR
- Lymphoma is present in more than one organ and the regional nodes for all organs involved OR

Single Node Station/Multiple LN/Extranodal

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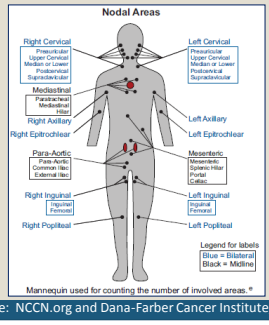
- Biopsy Site
- Single Node Station
- Bilateral - Same Node Station?
- Multiple Node Stations
- No nodal involvement

Number of Involved Nodal Areas

86



Source: NCCN.org and Dana-Farber Cancer Institute, Inc.

Determining Histologic Type

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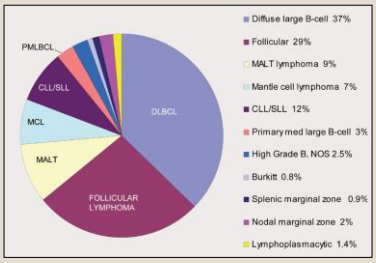
- Code the non-specific (NOS) histology when – PH28
- Code the specific histology when – PH29
- Use the Heme Data Base in Most Cases – PH30
- Code the Numerically Higher – PH31

B-Cell Lymphoid Histology Distribution in Adults

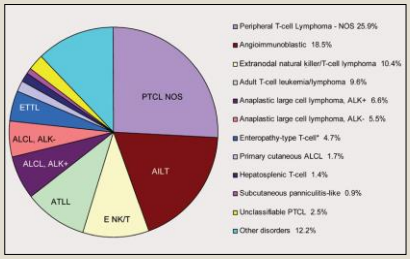
88



Source: WHO Classification of Hematopoietic and Lymphoid Neoplasms

T-Cell Lymphoid Histology Distribution in Adults

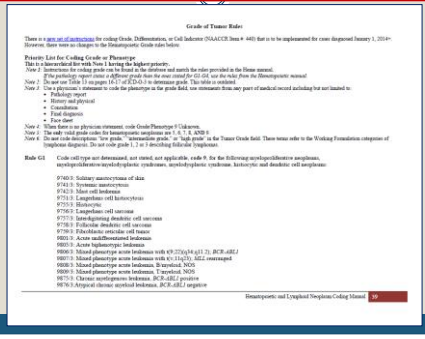
89



Source: WHO Classification of Hematopoietic and Lymphoid Neoplasms

Determining Grade/Differentiation

90



Grade of Tumor Rules

There is a new set of instructions for coding Grade, Differentiation, or Cell Indicator (NAACCR Item # 440) that is to be implemented for cases diagnosed January 1, 2014+. However, there were no changes to the Hematopoietic Grade rules below.

Priority List for Coding Grade or Phenotype

Rule G1 Instructions for coding grade can be found in the database and match the rules provided in the Heme manual.
If the pathology report states a different grade than the ones stated for G1-G4, use the value from the Hematopoietic manual.
Note 1: Do not use Table 11 on pages 16-17 of ED-O-3 to determine grade. This table is outdated.
Note 2: Use a physician's statement to code the phenotype in the grade field, use statements from any part of medical record including but not limited to:
- Pathology report
- History and physical
- Consultation
- Final diagnosis
- Op Note

Note 3: When there is no physician statement, code Grade/Phenotype 9 Unknown.
Note 5: The only valid grade codes for hematopoietic neoplasms are 1, 6, 7, 8, AND 9.
Note 6: Do not code descriptions "low grade," "intermediate grade," or "high grade" in the Tumor Grade field. These terms refer to the Working Formulation categories of lymphoma diagnosis. Do not code grade 1, 2 or 3 describing follicular lymphoma.

Rule G1 Code cell type not determined, not stated, not applicable, code 9, for the following myeloproliferative neoplasms, myeloproliferative/myelodysplastic syndromes, myelodysplastic syndromes, histiocytic and dendritic cell neoplasms:

9740/3: Solitary mastocytoma of skin
9741/3: Systemic mastocytosis
9742/3: Mast cell leukemia
9751/3: Langerhans cell histiocytosis
9755/3: Histiocytic
9756/3: Langerhans cell sarcoma
9757/3: Interdigitating dendritic cell sarcoma
9758/3: Follicular dendritic cell sarcoma
9759/3: Fibroblastic reticular cell tumor
9801/3: Acute undifferentiated leukemia
9805/3: Acute biphenotypic leukemia
9806/3: Mixed phenotype acute leukemia with t(9;22)(q34;q11.2); *BCR-ABL1*
9807/3: Mixed phenotype acute leukemia with t(v;11q23); *MLL* rearranged
9808/3: Mixed phenotype acute leukemia, B-myeloid, NOS
9809/3: Mixed phenotype acute leukemia, T-myeloid, NOS
9875/3: Chronic myelogenous leukemia, *BCR-ABL1* positive
9876/3:Atypical chronic myeloid leukemia, *BCR-ABL1* negative

Hematopoietic and Lymphoid Neoplasms Coding Manual 39

Appendices

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- Appendix A - History of Hematopoietic /Lymphoid Coding
- Appendix B - WHO Classification - Lineage Tables
- Appendix C - Lymph Node/Lymph Node Chain Table
- Appendix D - New Histology Terms and Codes
- Appendix E – Obsolete Hematopoietic Codes
- Appendix F – Non-Reportable Terms - NEW

Training

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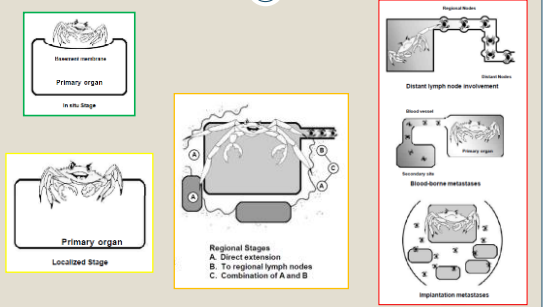
NEW Hematopoietic and Lymphoid Neoplasm Training
https://educate.fhcrc.org

Solid Tumor Staging

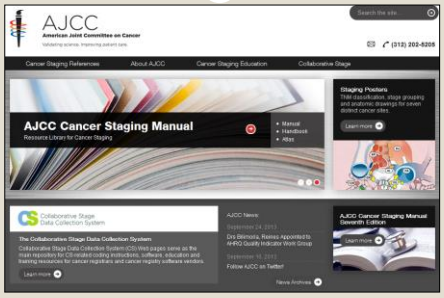
93



Source: SEER Summary Staging Manual 2000

AJCC Cancer Staging - TNM

94



http://www.cancerstaging.org

AJCC Cancer Staging - TNM

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http://www.cancerstaging.org

COLLABORATIVE STAGE DATA COLLECTION SYSTEM

CS Schemas for Lymphoid Neoplasms:

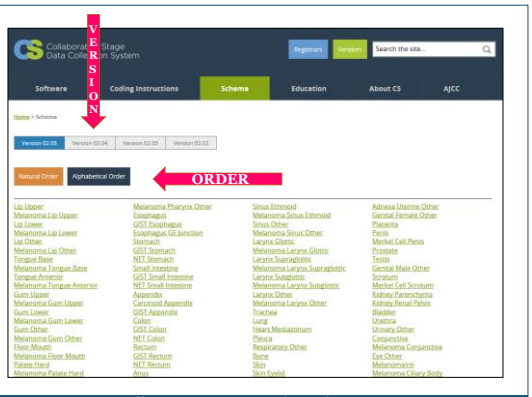
- Heme/Retic

- Lymphoma
- Lymphoma Ocular Adnexa
- Mycosis Fungoides

- Myeloma Plasma Cell Disorder

http://www.cancerstaging.org/cstage/index.html

http://www.cancerstaging.org/cstage/index.html



http://www.cancerstaging.org/cstage/index.html

HemeRetic Schema

Hematopoietic, Reticuloendothelial, Immunoproliferative, and Myeloproliferative Neoplasms

- M-Sea list of specific histologies below. All primary sites (C00.0-C80.9) are included unless otherwise specified.
- Schema includes only preferred terms from ICD-O-3.
- Plasmacytomas (9731 and 9734) and Multiple Myeloma (9732), except for cases with primary site C441, C690 and C695-C696, have been moved to the MyelomaPlasmaCellDisorder schema in V0203.
- 9733 Plasma cell leukemia [except C441, C690, C695-C696]
- 9740 Mast cell sarcoma
- 9741 Malignant mastocytosis
- 9742 Mast cell leukemia
- 9750 Malignant histiocytosis
- 9752 Langerhans cell histiocytosis, unifocal* (see new reportable code 9751/3)
- 9753 Langerhans cell histiocytosis, multifocal* (see new reportable code 9751/3)
- 9754 Langerhans cell histiocytosis disseminated
- 9755 Histiocytic sarcoma
- 9756 Langerhans cell sarcoma
- 9757 Interdigitating dendritic cell sarcoma
- 9758 Follicular dendritic cell sarcoma
- 9760 Immunoproliferative disease, NOS
- 9761 Waldenstrom macroglobulinemia
- 9762 Heavy chain disease, NOS
- 9764 Immunoproliferative small intestinal disease
- 9765 Monoclonal gammopathy of undetermined significance*
- 9766 Angiocentric immunoproliferative lesion*
- 9767 Angioimmunoblastic lymphadenopathy*
- 9768 T-gamma lymphoproliferative disease*
- 9769 Immunoglobulin deposition disease*
- 9800 Leukemia, NOS
- 9801 Acute leukemia, NOS
- 9805 Acute biphenotypic leukemia
- 9820 Lymphoid leukemia, NOS [except C441, C690, C695-C696]
- 9823 B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma [C420, C421, or C424 ONLY]
- 9826 Burkitt cell leukemia leukemia [except C441, C690, C695-C696]
- 9827 Adult T-cell leukemia/lymphoma (HTLV-1 positive)[C420, C421, or C424 ONLY]
- 9832 Prolymphocytic leukemia, NOS [except C441, C690, C695-C696]
- 9833 Prolymphocytic leukemia, B-cell type [except C441, C690, C695-C696]

http://www.cancerstaging.org/cstage/index.html

HemeRetic Schema

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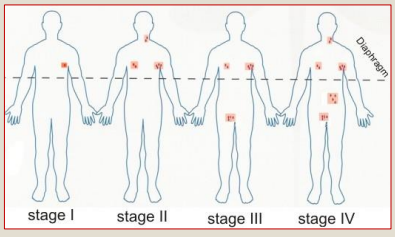
Code	Description
100	Localized disease: (Single/solitary/unifocal/isolated): May be coded for: Mast cell sarcoma (9740) Malignant histiocytosis (9750) Langerhans cell histiocytosis (9751) Histiocytic sarcoma (9755) Langerhans cell sarcoma (9756) Dendritic cell sarcoma (9757, 9758) Myeloid sarcoma (9930)
800	Systemic disease (All histologies including those in 100)
999	Unknown; extension not stated Primary tumor cannot be assessed Not documented in patient record

http://www.cancerstaging.org/cstage/index.html

Lymphoma Staging

101



Source: http://cancer.gov

Lymphoma Staging

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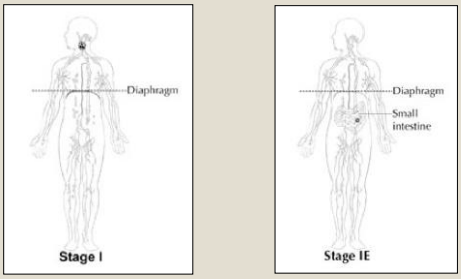
Stage	Description
Reprinted with permission from AJCC: Hodgkin and non-Hodgkin lymphomas. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 607-11.[15]	
I	Involvement of a single lymphatic site (i.e., nodal region, Waldeyer's ring, thymus, or spleen) (I); or localized involvement of a single extralymphatic organ or site in the absence of any lymph node involvement (IE).
II	Involvement of two or more lymph node regions on the same side of the diaphragm (II); or localized involvement of a single extralymphatic organ or site in association with regional lymph node involvement with or without involvement of other lymph node regions on the same side of the diaphragm (IIE).
III	Involvement of lymph node regions on both sides of the diaphragm (III), which also may be accompanied by extralymphatic extension in association with adjacent lymph node involvement (IIIE) or by involvement of the spleen (IIIS) or both (IIIE,S).
IV	Diffuse or disseminated involvement of one or more extralymphatic organs, with or without associated lymph node involvement; or isolated extralymphatic organ involvement in the absence of adjacent regional lymph node involvement, but in conjunction with disease in distant site(s). Stage IV includes any involvement of the liver or bone marrow, lungs (other than by direct extension from another site), or cerebrospinal fluid.
Designations applicable to any stage	
A	No symptoms.
B	Fever (temperature >38°C), drenching night sweats, unexplained loss of >10% of body weight within the preceding 6 months.
E	Involvement of a single extranodal site that is contiguous or proximal to the known nodal site.
S	Splenic involvement.

Source: http://cancer.gov

Lymphoma Staging

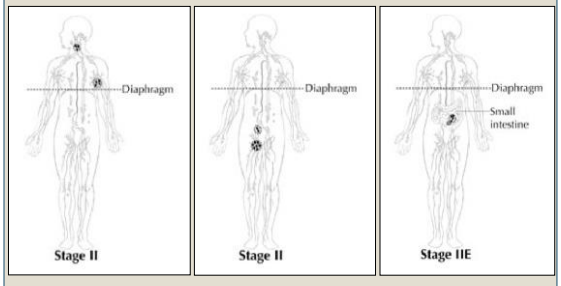
103



Source: AJCC Cancer Staging Atlas, 2nd edition

Lymphoma Staging

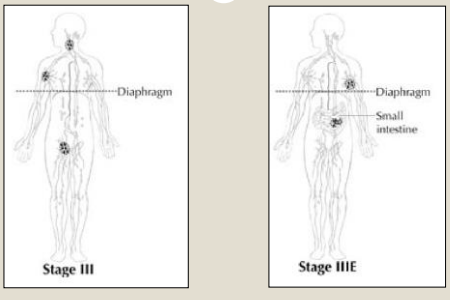
104



Source: AJCC Cancer Staging Atlas, 2nd edition

Lymphoma Staging

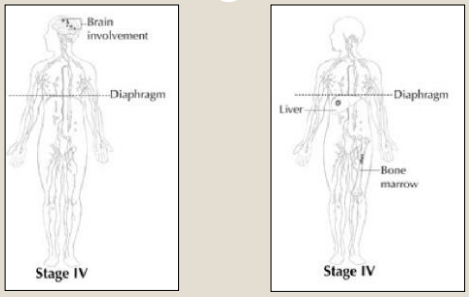
105



Source: AJCC Cancer Staging Atlas, 2nd edition

Lymphoma Staging

106



Source: AJCC Cancer Staging Atlas, 2nd edition

Lymphoma Schema

107

Collaborative Stage for TNM 7 - Revised 10/25/2011

Lymphoma

Hodgkin and Non-Hodgkin Lymphomas of All Sites (excluding Mycosis Fungoides and Sezary Disease)

- M-9590,9699,9702-9729,9735,9737,9738 (EXCEPT C44.1, C69.0, C69.5-C69.6)
- M-9811-9818,9823,9827,9837 (EXCEPT C42.0, C42.1, C42.4, C44.1, C69.0, C69.5-C69.6)

CS Tumor Size = **988**	CS Site-Specific Factor 7 = **988**
CS Extension	CS Site-Specific Factor 8 = **988**
CS Tumor Size/Ext Eval	CS Site-Specific Factor 9 = **988**
CS Lymph Nodes	CS Site-Specific Factor 10 = **988**
CS Lymph Nodes Eval = **9**	CS Site-Specific Factor 11 = **988**
Regional Nodes Positive = **99**	CS Site-Specific Factor 12 = **988**
Regional Nodes Examined = **99**	CS Site-Specific Factor 13 = **988**
CS Mets at DX	CS Site-Specific Factor 14 = **988**
CS Mets Eval = **9**	CS Site-Specific Factor 15 = **988**
CS Site-Specific Factor 1	CS Site-Specific Factor 16 = **988**
Associated with HIV/AIDS	CS Site-Specific Factor 17 = **988**
CS Site-Specific Factor 2	CS Site-Specific Factor 18 = **988**
Systemic Symptoms at Diagnosis	CS Site-Specific Factor 19 = **988**
CS Site-Specific Factor 3	CS Site-Specific Factor 20 = **988**
International Prognostic Index (IPI)	CS Site-Specific Factor 21 = **988**
CS Site-Specific Factor 4	CS Site-Specific Factor 22 = **988**
Follicular Lymphoma Prognostic Index (FLIPI)	CS Site-Specific Factor 23 = **988**
CS Site-Specific Factor 5	CS Site-Specific Factor 24 = **988**
International Prognostic Score (IPS)	CS Site-Specific Factor 25 = **988**

Source: http://cancerstaging.org

Lymphoma Schema

108

100	Involvement of a single lymph node region Stated as Stage I
110	Localized involvement of a single extralymphatic organ/site in the absence of any lymph node involvement Multifocal involvement of one extralymphatic organ/site Stated as Stage IE
120	Involvement of spleen only Stated as Stage IS
200	Involvement of two or more lymph node regions on the SAME side of the diaphragm Stated as Stage II
210	Localized involvement of a single extralymphatic organ/site WITH involvement of its regional lymph node(s) WITH or WITHOUT involvement of other lymph node(s) on the SAME side of the diaphragm Direct extension to adjacent organs or tissues Stated as Stage IIE
220	Involvement of spleen PLUS lymph node(s) BELOW the diaphragm Stated as Stage IIS

http://www.cancerstaging.org/cstage/index.html

Plasma Cell Neoplasm Staging

109

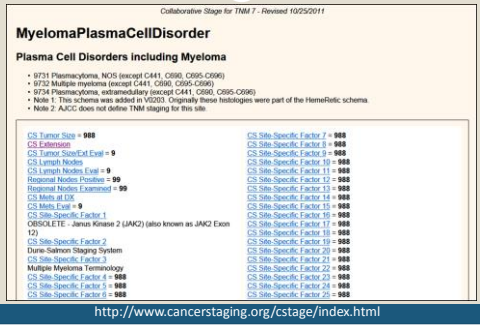
Table 1: The Durie-Salmon Staging System for Multiple Myeloma

Stage	Hemoglobin	Calcium	Myeloma Protein	Bone Lesions
I[a]	>10 g/dL	Normal or ≤12 g/dL	IgG peak <5 g/dL IgA peak <3 g/dL Bence-Jones protein <4 g/24 h	None or solitary bone plasmacytoma only
II[b]	Not I or III	Not I or III	Not I or III	Not I or III
III[c]	<8.5 g/dL	>12 mg/dL	IgG peak >7 g/dL IgA peak >5 g/dL Bence-Jones protein >12 g/24 h	>3 lytic lesions

[a] *Stage I must demonstrate all of the criteria.*
[b] *Stage II defined as all patients who do not qualify as Stage I or III.*
[c] *Stage III must demonstrate one or more of the criteria.*
Source: Reference 7.

MyelomaPlasmaCellDisorder Schema

110



Collaborative Stage for TNM 7 - Revised 10/25/2011

MyelomaPlasmaCellDisorder

Plasma Cell Disorders including Myeloma

- 9731 Plasmacytoma, NOS (except C441, C690, C695-C696)
- 9732 Multiple myeloma (except C441, C690, C695-C696)
- 9734 Plasmacytoma, extramedullary (except C441, C690, C695-C696)
- Note 1: This schema was added in V0203. Originally these histologies were part of the HemeRetic schema.
- Note 2: AJCC does not define TNM staging for this site.

CS Tumor Size = 988
CS Extension
CS Tumor Size/Ext Eval = 9
CS Lymph Nodes
CS Lymph Nodes Eval = 9
Regional Nodes Positive = 99
Regional Nodes Examined = 99
CS Mets at DX
CS Mets Eval = 9
CS Site-Specific Factor 1
OBSOLETE - Janus Kinase 2 (JAK2) (also known as JAK2 Exon 12)
CS Site-Specific Factor 2
Durie-Salmon Staging System
CS Site-Specific Factor 3
Multiple Myeloma Terminology
CS Site-Specific Factor 4 = 988
CS Site-Specific Factor 5 = 988
CS Site-Specific Factor 6 = 988
CS Site-Specific Factor 7 = 988
CS Site-Specific Factor 8 = 988
CS Site-Specific Factor 9 = 988
CS Site-Specific Factor 10 = 988
CS Site-Specific Factor 11 = 988
CS Site-Specific Factor 12 = 988
CS Site-Specific Factor 13 = 988
CS Site-Specific Factor 14 = 988
CS Site-Specific Factor 15 = 988
CS Site-Specific Factor 16 = 988
CS Site-Specific Factor 17 = 988
CS Site-Specific Factor 18 = 988
CS Site-Specific Factor 19 = 988
CS Site-Specific Factor 20 = 988
CS Site-Specific Factor 21 = 988
CS Site-Specific Factor 22 = 988
CS Site-Specific Factor 23 = 988
CS Site-Specific Factor 24 = 988
CS Site-Specific Factor 25 = 988

http://www.cancerstaging.org/cstage/index.html

MyelomaPlasmaCellDisorder Schema

111

- Note 1: Osseous plasmacytomas are localized tumors occurring in the bone. There may be soft tissue extension.
- Note 2: Extraosseous (extramedullary) plasmacytomas are plasma cell neoplasms that arise in tissues other than bone. The most common sites are the upper respiratory tract, the gastrointestinal tract, lymph nodes, bladder, central nervous system (CNS), breast, thyroid, testis and skin.

http://www.cancerstaging.org/cstage/index.html

MyelomaPlasmaCellDisorder Schema

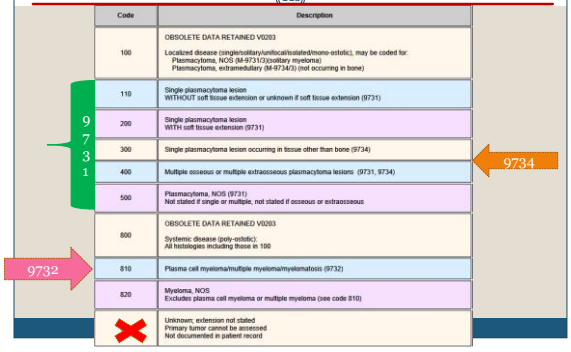
112

- Note 3: Criteria for the diagnosis of multiple myeloma include: presence of clonal bone marrow plasma cells or plasmacytoma, presence of an M-protein in serum and/or urine, and the presence of related organ or tissue impairment. Do not use this criteria to determine the diagnosis of multiple myeloma. Code according to histologic confirmation or physician statement according to the AJCC 7th edition.
- Note 4: Multiple myeloma or plasma cell myeloma is a widely disseminated plasma cell neoplasm, characterized by a single clone of plasma cells derived from B cells that grows in the bone marrow. It is always coded to 810 or 820 for systemic involvement.

http://www.cancerstaging.org/cstage/index.html

MyelomaPlasmaCellDisorder Schema

113



Site Specific Factors - Lymphoma

114

- SSF1 – Associated with HIV/AIDS
- SSF2 – Systemic Symptoms at Diagnosis
- SSF3 – International Prognostic Index (IPI)
- SSF4 – Follicular Lymphoma Prognostic Index (FLIPI)
- SSF5 – International Prognostic Score (IPS)

Site Specific Factors – Plasma Cell Tumors

115

- SSF1 – OBSOLETE
- SSF2 – Durie-Salmon Staging System
- SSF3 – Multiple Myeloma Terminology

000	Multiple myeloma/Plasma cell myeloma with no other modifiers Multiple myeloma, NOS; Myeloma, NOS
010	Asymptomatic myeloma
020	Early or evolving myeloma
030	Inactive, indolent, or smoldering myeloma
080	Other terminology describing myeloma
100	Any combination of terms in codes 010-080

Treatment Options – Lymphoid Neoplasms

116

- Hodgkin Lymphoma
- Non-Hodgkin Lymphoma
- Chronic Lymphocytic Leukemia
- Acute Lymphocytic Leukemia
- Other Lymphoid Neoplasm

Source: Mosaic Rainbow and Woodland Forest - http://www.etsy.com

Treatment Options – Basic Concepts

117

- Surgery
- Chemotherapy
- Radiation Therapy
- Hormonal Therapy
- Combination Therapy
- Continuation Therapy
- Bone Marrow/Stem Cell Transplant

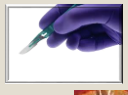


Image Source: http://greenplanetparadise.com and http://avinoamlerner.com

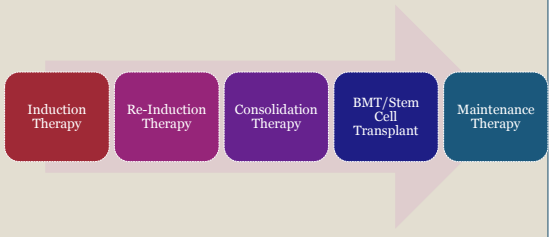
Treatment Options – Basic Concepts

118

- Pre-Induction Risk Assessment
- Induction Therapy
- Post-Induction Assessment
- Re-Induction Therapy
- Intensification/Consolidation Therapy
- Post-Consolidation Assessment
- BMT/Stem Cell Transplant
- Maintenance Therapy
- Maintenance Assessment

Treatment Options – Basic Concepts

119

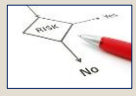


Source: http://cancer.gov – Pediatric Myeloid Neoplasm NCI PDQ for Health Professionals

Treatment Options – Basic Concepts

120

- Risk-Based Treatment – Pre-Induction Risk
  - Patient Characteristics
    - Performance Status
    - Age at Diagnosis
    - Comorbidities
    - B-Symptoms
  - Neoplasm Characteristics
    - Morphology
    - Immunophenotype
    - Stage of Differentiation
    - Molecular/Cyto-Genetics
  - Special Characteristics of Neoplasm or Patient

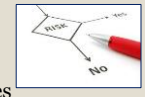


Source: http://cancer.gov – Pediatric Lymphoid Neoplasm NCI PDQ for Health Professionals

Treatment Options – Basic Concepts

121

- Risk-Based Treatment – Induction Failure
  - Identify patients at highest risk of induction failure:
    - T-cell phenotype (especially without a mediastinal mass)
    - B-precursor ALL with very high presenting leukocyte counts
    - Bulky Disease
- Risk-Based Treatment – Re-Induction/Consolidation
  - Re-Induction
  - Intensification
  - Consolidation
- Risk-Based Treatment – Sanctuary Sites
- Risk-Based Treatment – Maintenance Therapy

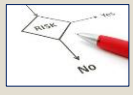


Source: http://cancer.gov – Pediatric Lymphoid Neoplasm NCI PDQ for Health Professionals

Treatment Options – Basic Concepts

122

- Risk-Based Treatment Assessment Examples
  - Low Risk Disease – Stage I, II – no B symptoms, no bulky disease
  - Intermediate Risk Disease – Stage I, II with B symptoms
  - Intermediate Risk Disease – Stage I, II with bulky disease
  - Intermediate Risk Disease – Stage IIIA, IVA
  - High Risk Disease – Stage IIIB, IVB
  - High Risk Disease – Poor response to initial chemotherapy

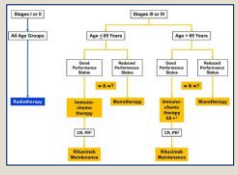


Source: http://cancer.gov – Pediatric Lymphoid Neoplasm NCI PDQ for Health Professionals

Treatment - Surgery

123

- Surgery – when do you code for lymphoma?
- Surgery – when do you NOT code for lymphoma?
- Why the difference?
- When is Surgery = TX
- Why so seldom?



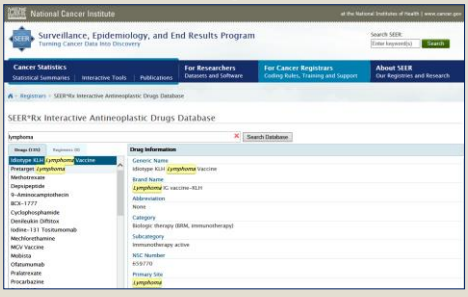
Treatment - Chemotherapy

124

- Chemotherapy Regimens
- REMINDER: Many regimens contain Prednisone which is to be coded under Hormone Therapy – in addition to the combination Chemotherapy

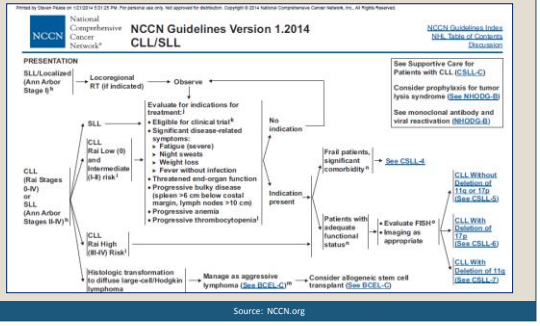
Treatment - Chemotherapy

125



Treatment Options – CLL/SLL

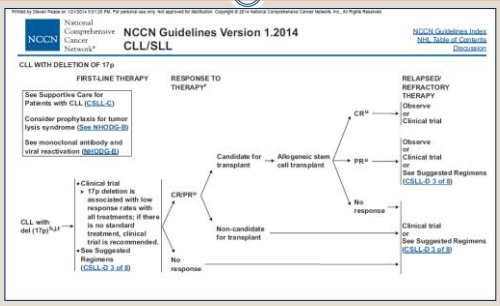
126



Source: NCCN.org

Treatment Options – CLL/SLL (del 17p)

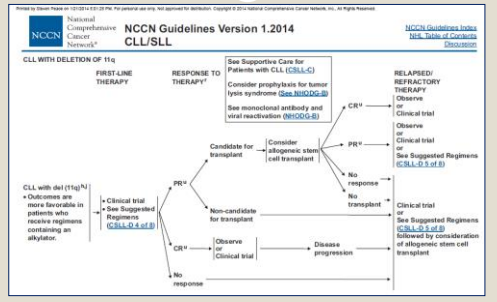
127



Source: NCCN.org

Treatment Options – Lymphoma

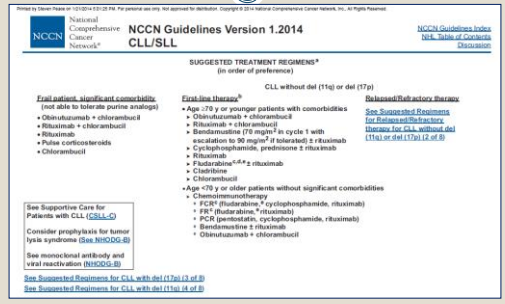
128



Source: NCCN.org

Treatment Options – Lymphoma

129



Source: NCCN.org

Treatment Options – Lymphoma

130

SUGGESTED TREATMENT REGIMENS[a]

CLL with del (17p)

First-line therapy[b] (in alphabetical order)
- Alemtuzumab[c] ± rituximab
- FCR[c,e]
- FR[c,e]
- HDMP + rituximab
- Obinutuzumab + chlorambucil

Relapsed/Refractory therapy[b] (in alphabetical order)
- Alemtuzumab[c] ± rituximab
- RCHOP
- CFAR[c] (cyclophosphamide, fludarabine,[e] alemtuzumab, rituximab)
- HDMP ± rituximab
- Ibrutinib[g]
- Lenalidomide[h] ± rituximab
- Ofatumumab[i]
- OFAR[c,e]

SUGGESTED TREATMENT REGIMENS[a]
(in order of preference)

CLL with del (11q)

First-line therapy[b]
- Age ≥70 y or younger patients with comorbidities
  - Obinutuzumab + chlorambucil
  - Rituximab + chlorambucil
  - Bendamustine (70 mg/m^2 in cycle 1 with escalation to 90 mg/m^2 if tolerated) ± rituximab
  - Cyclophosphamide, prednisone ± rituximab
  - Reduced-dose FCR[c,e,k]
  - Rituximab
  - Chlorambucil
- Age <70 y or older patients without significant comorbidities
  - Chemoimmunotherapy
    - FCR[c,e]
    - Bendamustine ± rituximab
    - PCR
    - Obinutuzumab + chlorambucil

Relapsed/Refractory therapy[b]

See Suggested Regimens for Relapsed/Refractory therapy for CLL with del (11q) (5 of 8)

Source: NCCN.org

FDA Approved Agents for HL / NHL (A-L)

131

Abitrexate (Methotrexate)	Cyclophosphamide
Adcetris (Brentuximab Vedotin)	Cytoxan (Cyclophosphamide)
Adriamycin PFS (Doxorubicin Hydrochloride)	Denileukin Diftitox
Adriamycin RDF (Doxorubicin Hydrochloride)	DepoCyt (Liposomal Cytarabine)
Ambochlorin (Chlorambucil)	Doxorubicin Hydrochloride
Amboclorin (Chlorambucil)	DTIC-Dome (Dacarbazine)
Arranon (Nelarabine)	Folex (Methotrexate)
Bendamustine Hydrochloride	Folex PFS (Methotrexate)
Bexxar (Tositumomab and Iodine I 131 Tositumomab)	Folotyn (Pralatrexate)
Blenoxane (Bleomycin)	Ibritumomab Tiuxetan
Bleomycin	Ibrutinib
Bortezomib	Imbruvica (Ibrutinib)
Brentuximab Vedotin	Intron A (Recombinant Interferon Alfa-2b)
Chlorambucil	Istodax (Romidepsin)
Clafen (Cyclophosphamide)	Lenalidomide

Source: www.cancer.gov/cancertopics/druginfo

FDA Approved Agents for HL / NHL (M-Z)

132

Leukeran (Chlorambucil)	Revlimid (Lenalidomide)
Linfolizin (Chlorambucil)	Rituxan (Rituximab)
Liposomal Cytarabine	Rituximab
Matulane (Procarbazine Hydrochloride)	Romidepsin
Methotrexate	Tositumomab and Iodine I 131 Tositumomab
Methotrexate LPF (Methotrexate)	Treanda (Bendamustine Hydrochloride)
Mexate (Methotrexate)	Velban (Vinblastine Sulfate)
Mexate-AQ (Methotrexate)	Velcade (Bortezomib)
Mozobil (Plerixafor)	Velsar (Vinblastine Sulfate)
Nelarabine	Vinblastine Sulfate
Neosar (Cyclophosphamide)	Vincasar PFS (Vincristine Sulfate)
Ontak (Denileukin Diftitox)	Vincristine Sulfate
Plerixafor	Vorinostat
Pralatrexate	Zevalin (Ibritumomab Tiuxetan)
Recombinant Interferon Alfa-2b	Zolinza (Vorinostat)

Source: www.cancer.gov/cancertopics/druginfo

Common Chemo Regimens in NHL

133

Regimen	Regimen
CHOP	EPOCH
COPP	ICE
CVP	R-CHOP

C	Cyclophosphamide
H	Doxorubicin Hydrochloride
O	Vincristine Sulfate (Oncovin)
P	Prednisone
P	Procarbazine Hydrochloride
V	Vincristine Sulfate (Oncovin)
E	Etoposide
I	Ifosfamide
C	Carboplatin
R	Rituximab

Source: www.cancer.gov/cancertopics/druginfo

Chemo Regimens in Hodgkin Lymphoma

134

Regimen	Regimen
ABVD	ICE
ABVE	MOPP
ABVE-PC	OEPA
BEACOPP	OPPA
COPP	Stanford V
COPP-ABV	VAMP

A	Adriamycin
B	Bleomycin
V	Vinblastine Sulfate
D	Dacarbazine
E	Etoposide
P	Prednisone
C	Cyclophosphamide
V	Vincristine Sulfate (Oncovin)
P	Procarbazine Hydrochloride
I	Ifosfamide
C	Carboplatin
M	Methotrexate

Source: www.cancer.gov/cancertopics/druginfo

Treatment - BRM

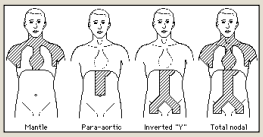
135

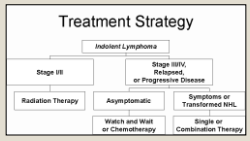
- Biological Response Modifiers – when and why?
- SEER*Rx is Primary Reference
- Examples:
  - Rituximab – cytostatic monoclonal antibody – CLL, NHL
  - Belinostat – histone deacetylation inhibitor – CLL, MM, NHL
  - Thalidomide – antiangiogenic agent – MM, leukemia
  - Epratuzumab – NOT BRM – Radioisotope – Code RT – NHL
  - Zevalin – NOT BRM – Radiolabeled monoclonal antibody – NHL

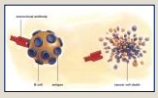
Treatment - Radiation

136

- Radiation Therapy – when and why?







Treatment - Radiation

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NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2014
Non-Hodgkin's Lymphomas

NCCN Guidelines Index
NHL Table of Contents
Discussion

PRINCIPLES OF RADIATION THERAPY®

Field:
- Treatment with photons, electrons, or protons may all be appropriate, depending upon clinical circumstances.
- Involved-site radiation therapy (ISRT) for nodal sites
  - ISRT is recommended as the appropriate field for NHL. Planning for ISRT requires modern CT-based simulation and planning capabilities. Incorporating other modern imaging like PET and MRI often enhances field determination.
  - ISRT targets the site of the originally involved lymph node(s). The field encompasses the original suspicious volume prior to chemotherapy or surgery. Yet, it spares adjacent uninvolved organs (like lungs, bone, muscle, or kidney) when lymphadenopathy regresses following chemotherapy.
  - The pre-chemotherapy or pre-biopsy gross tumor volume (GTV) provides the basis for determining the clinical target volume (CTV). Concerns for questionable subclinical dispase and uncertainties in original imaging accuracy or localization may lead to expansion of the CTV and are determined individually using clinical judgment. Possible movement of the target by respiration as determined by 4D-CT or fluoroscopy (internal target volume- ITV) should also influence the final CTV.
  - The planning treatment volume (PTV) is an additional expansion of the CTV that accounts only for setup variations (see ICRU definitions).
  - Organs at risk (OAR) should be outlined for optimizing treatment plan decisions.
  - The treatment plan is designed using conventional, 3-D conformal, or IMRT techniques using clinical treatment planning considerations of coverage and dose reductions for OAR.
- ISRT for extranodal disease
  - Similar principles as for ISRT nodal sites (see above).
  - For most organs and particularly for indolent disease, the whole organ alone is the CTV (eg, stomach, salivary gland, orbit, thyroid, breast, testis).
  - For bone/spine, localized skin, only the involved part of the organ is irradiated with adequate margins.
  - For most NHL subtypes no radiation is required for uninvolved lymph nodes.

General Dose Guidelines:
- Localized CLL/SLL: 24-30 Gy
- Follicular lymphoma: 24-36 Gy
- Marginal zone lymphoma:
  - Gastric: 30 Gy
  - Other extranodal sites: 24-30 Gy
  - Nodal MZL: 24-30 Gy
- Early-stage mantle cell lymphoma: 30-36 Gy
- Mini-dose RT (2 Gy x 2 may be repeated) for palliation/local control of SLL, FL, MZL, MCL
- Diffuse large cell lymphoma or PTCL
  - Consolidation after chemotherapy CR: 30-36 Gy
  - Complementary after PR: 40-50 Gy
  - RT as primary treatment for refractory or noncandidates for chemotherapy: 45-55 Gy
  - Salvage pre- or post-stem cell transplantation: 30-40 Gy
- Primary cutaneous anaplastic large cell lymphoma: 30-36 Gy

Treatment - Radiation

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NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2014
Follicular Lymphoma (grade 1-2)

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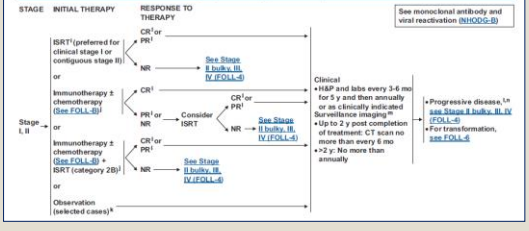

Treatment - Other

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- Other Therapy – when and why?
- PUVA for cutaneous lymphoma

Text Documentation

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DATA ITEMS REQUIRING COMPLETE TEXT DOCUMENTATION	
Date of DX	RX Summ – Surg Prim Site
Seq No	RX Summ – Scope Reg LN Surgery
Sex	RX Summ – Surg Oth Reg/Distant
Primary Site	RX Date – Surgery
Subsite	RX Summ – Radiation
Laterality	Rad Rx Modality
Histologic Type	RX Date – Radiation
Behavior Code	RX Summ – Chemo
Grade	RX Date – Chemo
	RX Summ – Hormone
CS Tumor Size	RX Date – Hormone
CS Ext	RX Summ – BRM/Immunotherapy
CS Tumor Ext/Eval	RX Date – BRM/Immunotherapy
Regional Nodes Positive	RX Summ – Transplant/Endocrine
Regional Nodes Examined	RX Date – Transplant/Endocrine
CS LN	RX Summ – Other
CS LN Eval	RX Date - Other
CS Mets	
CS Mets Eval	Any Unusual Case Characteristics
All FCDS Req'd SSFs	Any Pertinent Patient/Family History

References

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- **2014 Hematopoietic and Lymphoid Neoplasm Case Reportability and Coding Manual**, J. Ruhl, M. Adamo, C. Hahn Johnson, L. Dickie, NCI SEER, 2014
- **Classification, Characteristics, and Behavior of Myeloid Neoplasms,** G.M. Dores, NCI, 2010
- **WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues , 4th ed**, S. Swerdlow, E. Campo, N. Lee Harris, E. Jaffe, S. Pileri, H. Stein, J. Thiele, J. Vardiman, IARC, Lyon, FR, 2008
- **National Comprehensive Cancer Network (NCCN)** 2014 Clinical Practice Guidelines – NHL, ALL, Myeloma, and Hodgkin Lymphoma
- **The 2008 WHO Classification of Lymphoid Neoplasms and Beyond;** E. Campo, S. Swerdlow, NL Harris, E Jaffe; Blood 2011 117
- **A Revised European-American Classification of Lymphoid Neoplasms;** NL Harris, E Jaffe, H Stein; Blood 1994 84
- **FCDS Data Acquisition Manual**

Questions

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