2016 WHO CLASSIFICATION OF TUMOURS OF HAEMATOPOIETIC AND LYMPHOID TISSUES, 4TH ED., VOL 2

LEUKEMIA, LYMPHOMA, MYELOMA = Blood Cancer

2017-2018 FCDS WEBCAST SERIES

OCTOBER 19, 2017

STEVEN PEACE, CTR

1

CDC & Florida DOH Attribution

"We acknowledge the Centers for Disease Control and Prevention, for its support of the Florida Cancer Data System, and the printing and distribution of the materials for the 2017-2018 FCDS Webcast Series under cooperative agreement 1NU58DP006350 awarded to the Florida Department of Health. The findings and conclusions in this series are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention".

CDC Centers for Disease Control and Prevention

Florida HEALTH

FCDS would also like to acknowledge the Florida Department of Health for its support of the Florida Cancer Data System, including the development, printing and distribution of materials for the 2017-2018 FCDS Webcast Series under state contract CODJU. The findings and conclusions in this series are those of the author(s) and do not necessarily represent the official position of the Florida Department of Health.

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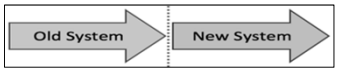
FLCCSC LMS – CEU QUIZ –FCDS IDEA ACCESS

- FLORIDA HAS CHANGED HOW WE TRACK WEBCAST ATTENDANCE
- FLORIDA HAS CHANGED HOW WE AWARD CEUS FOR OUR WEBCAST SERIES
- ATTENDEES MUST TAKE AND PASS A 3-5 QUESTION CEU QUIZ TO BE AWARDED CEUS
- ONLY REGISTERED FLCCSC USERS WILL BE GIVEN ACCESS TO THE CEU QUIZ
- FLORIDA ATTENDEES MUST HAVE A FLORIDA FLCCSC ACCOUNT & PASS THE QUIZ TO GET CEUS
- SOUTH CAROLINA ATTENDEES MUST HAVE A SOUTH CAROLINA FLCCSC ACCOUNT & PASS THE QUIZ TO GET CEUS
- OTHER ATTENDEES CAN ATTEND THE LIVE WEBCASTS BUT CANNOT RECEIVE CEUS FOR ATTENDANCE AT THIS TIME
- PLEASE REMEMBER THIS IS A NEW SYSTEM WITH NEW REQUIREMENTS - SOME STILL BEING WORKED OUT

FLCCSC
Fundamental Learning Collaborative for the Cancer Surveillance Community



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OUTLINE

- INTRODUCTION TO WHO CLASSIFICATION & BASIC ANATOMY
- MILESTONES IN THE CLASSIFICATION OF TUMORS OF HEMATOPOIETIC TISSUES
- MILESTONES IN THE CLASSIFICATION OF TUMORS OF LYMPHOID TISSUES
- THE 2010 HEMATOPOIETIC MPH RULES MANUAL AND DATABASE
- 2016 UPDATES TO WHO CLASSIFICATION OF MYELOID NEOPLASMS & ACUTE LEUKEMIA
- 2016 UPDATES TO WHO CLASSIFICATION OF LYMPHOID NEOPLASMS
- THE **2019** HEMATOPOIETIC MPH RULES MANUAL & DATABASE
- STAGING MYELOID NEOPLASMS + 2018 MYELOID SSDI'S
- STAGING LYMPHOID NEOPLASMS + 2018 LYMPHOID SSDI'S
- QUESTIONS

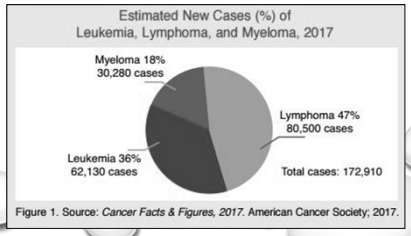
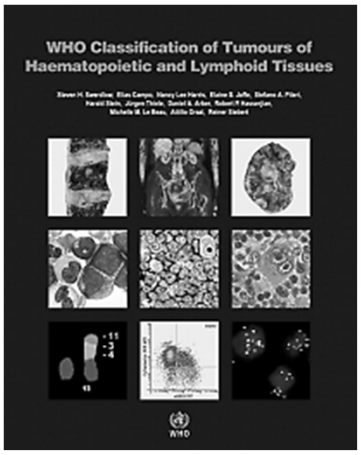


Figure 1. Source: *Cancer Facts & Figures, 2017.* American Cancer Society; 2017.

2016 WHO CLASSIFICATION OF TUMOURS OF HAEMATOPOIETIC AND LYMPHOID TISSUES, 4TH ED.



4TH EDITION WHO CLASSIFICATION OF TUMORS

- **CENTRAL NERVOUS SYSTEM (2007)**
- **HEMATOPOIETIC AND LYMPHOID (2008)**
- **DIGESTIVE SYSTEM (2010)**
- **BREAST (2012)**
- **SOFT TISSUE AND BONE (2013)**
- **FEMALE REPRODUCTIVE ORGANS (2014)**
- **LUNG, PLEURA, THYMUS & HEART (2015)**
- **URINARY SYSTEM & MALE GENITAL (2016)**
- **CENTRAL NERVOUS SYSTEM (2016 REVISION)**
- **HEMATOPOIETIC & LYMPHOID (2016 REVISION)**
- **HEAD & NECK (2017)**

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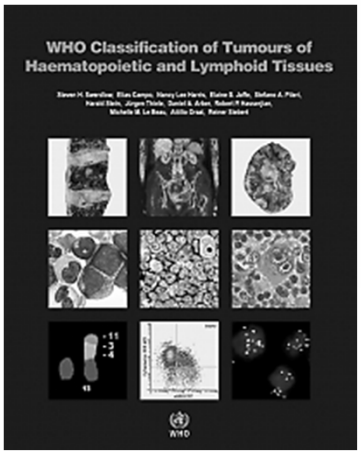
2016 WHO CLASSIFICATION OF TUMOURS OF HAEMATOPOIETIC AND LYMPHOID TISSUES, 4TH ED.



- **WHO CLASSIFICATION OF TUMOURS, REVISED 4TH EDITION, VOLUME 2, LYON: IARC; 2017**
  - **INTERNATIONAL STANDARD FOR PATHOLOGISTS AND ONCOLOGISTS**
  - **DIAGNOSTIC CRITERIA**
  - **PATHOLOGICAL FEATURES**
  - **ASSOCIATED GENETIC ALTERATIONS**
  - **NEW ICD-O CODES**
  - **EPIDEMIOLOGY**
  - **CLINICAL FEATURES**
  - **MACROSCOPY**
  - **PROGNOSTIC & PREDICTIVE FACTORS**

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2016 WHO CLASSIFICATION OF TUMOURS OF HAEMATOPOIETIC AND LYMPHOID TISSUES, 4TH ED.

- "CLASSIFICATION IS THE LANGUAGE OF MEDICINE: DISEASES MUST BE DESCRIBED, DEFINED AND NAMED BEFORE THEY CAN BE DIAGNOSED, TREATED AND STUDIED."
- "A CONSENSUS ON DEFINITIONS AND TERMINOLOGY IS ESSENTIAL FOR BOTH CLINICAL PRACTICE AND INVESTIGATIONS."
- THE 2016 EDITION REPRESENTS A REVISION OF THE PRIOR CLASSIFICATION RATHER THAN AN ENTIRELY NEW CLASSIFICATION AND ATTEMPTS TO INCORPORATE NEW CLINICAL, PROGNOSTIC, MORPHOLOGIC, IMMUNOPHENOTYPIC, AND GENETIC DATA THAT HAVE EMERGED SINCE THE LAST EDITION.

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INTRODUCTION
ADULT MYELOID AND LYMPHOID NEOPLASMS

Figure 3. Leading Sites of New Cancer Cases and Deaths – 2017 Estimates

Estimated New Cases

Male			Female		
Prostate	161,360	19%	Breast	252,710	30%
Lung & bronchus	116,990	14%	Lung & bronchus	105,510	12%
Colon & rectum	71,420	9%	Colon & rectum	64,010	8%
Urinary bladder	60,490	7%	Uterine corpus	61,380	7%
Melanoma of the skin	52,170	6%	Thyroid	42,470	5%
Kidney & renal pelvis	40,610	5%	Melanoma of the skin	24,940	4%
Non-Hodgkin lymphoma	40,080	5%	Non-Hodgkin lymphoma	32,160	4%
Leukemia	36,290	4%	Leukemia	25,840	3%
Oral cavity & pharynx	35,720	4%	Pancreas	25,700	3%
Liver & intrahepatic bile duct	29,200	3%	Kidney & renal pelvis	23,380	3%
All sites	836,150	100%	All sites	852,630	100%

Estimated Deaths

Male			Female		
Lung & bronchus	84,590	27%	Lung & bronchus	71,280	25%
Colon & rectum	27,150	9%	Breast	40,610	14%
Prostate	26,730	8%	Colon & rectum	23,110	8%
Pancreas	22,300	7%	Pancreas	20,790	7%
Liver & intrahepatic bile duct	19,610	6%	Ovary	14,080	5%
Leukemia	14,300	4%	Uterine corpus	10,920	4%
Esophagus	12,720	4%	Leukemia	10,200	4%
Urinary bladder	12,240	4%	Liver & intrahepatic bile duct	9,310	3%
Non-Hodgkin lymphoma	11,450	4%	Non-Hodgkin lymphoma	8,690	3%
Brain & other nervous system	9,620	3%	Brain & other nervous system	7,080	3%
All sites	318,420	100%	All sites	282,500	100%

Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

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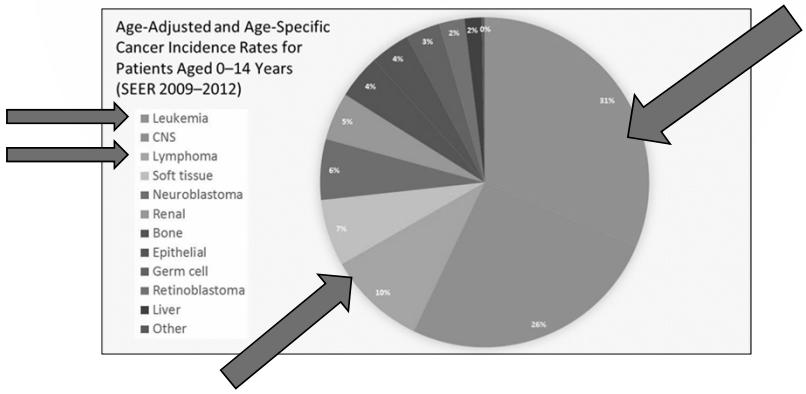
2017 Cancer Facts & Figures – American Cancer Society

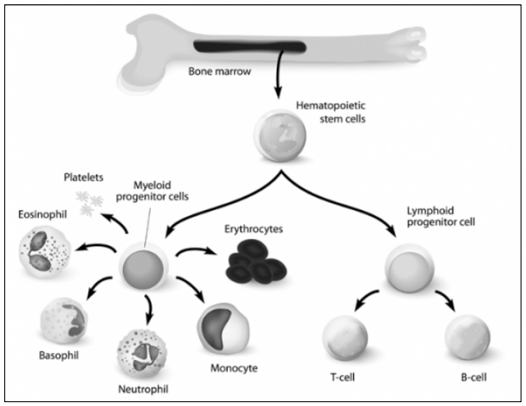
INTRODUCTION
PEDIATRIC MYELOID AND LYMPHOID NEOPLASMS

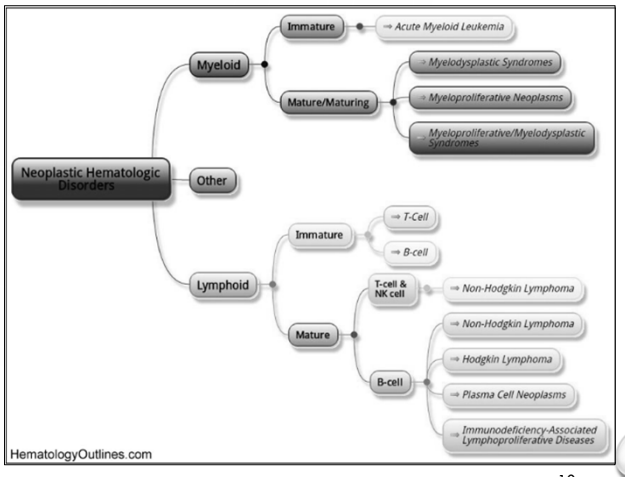


9

Source: NCI SEER

HEMATOPOIESIS AND "BLOOD CANCERS"





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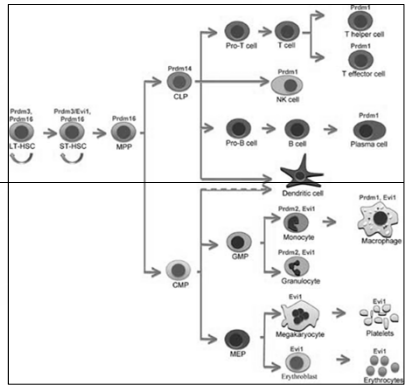
https://www.medicalnewstoday.com/articles/285666.php

https://HematologyOutlines.com

CELLULAR DIFFERENTIATION & REGULATORY FUNCTION

- CELL DIFFERENTIATION
- REGULATION OF PROLIFERATION
- REGULATION OF DIFFERENTIATION
- TURN ON/TURN OFF
  - GROWTH FACTORS
  - GENES (INCLUDING MUTATIONS)
  - PROTEINS
- DYSREGULATION DISRUPTS NORMAL DEVELOPMENT
- ONCOGENESIS – BECOMING MALIGNANT



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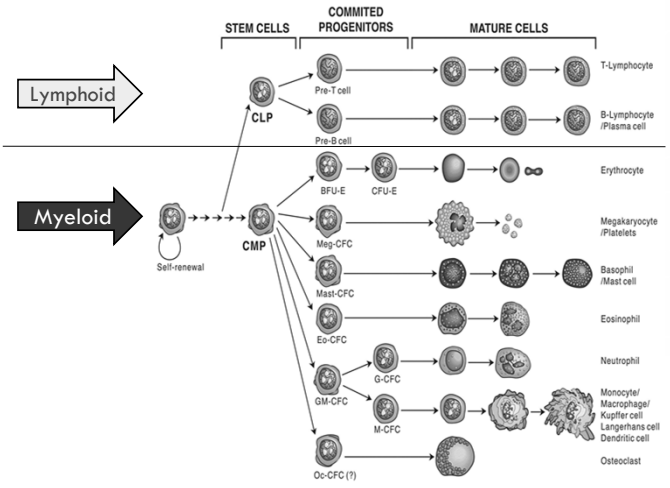
Hematopoietic stem cells give rise to two major progenitor cell lineages, myeloid and lymphoid progenitors
https://www.researchgate.net/figure/51746020_fig3_Figure-3-Illustration-of-hematopoietic-differentiation-from-immature-precursor-cells

CELLULAR DIFFERENTIATION & REGULATORY FUNCTION



- 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
- Too many or too few cells leads to chronic/acute condition

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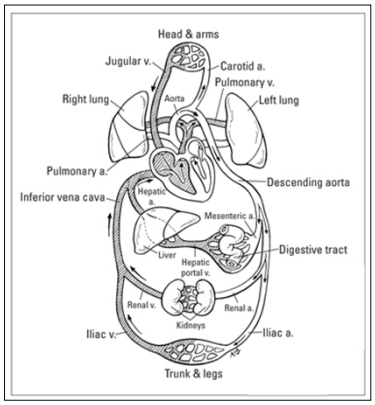
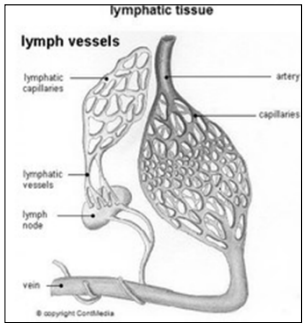
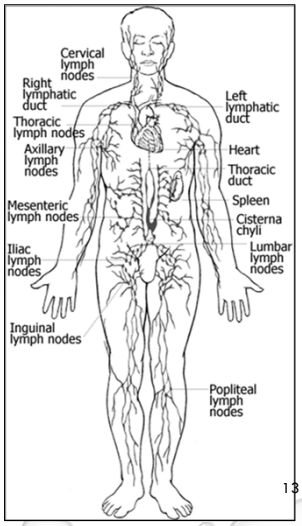
Blood Lines – Donald Metcalf, AlphaMED Press, 2005
Figure 3.2 The eight major hematopoietic lineages generated by self-renewing multipotential stem cellsB

TWO CIRCULATORY SYSTEMS – BLOOD & LYMPHATIC





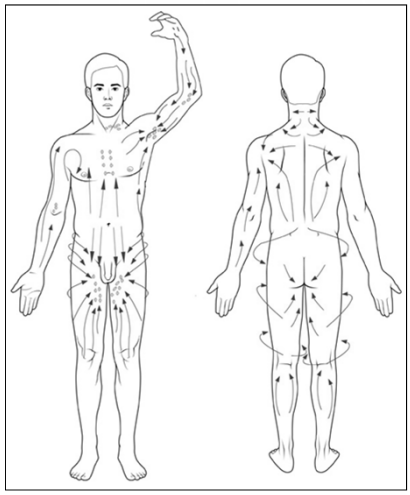


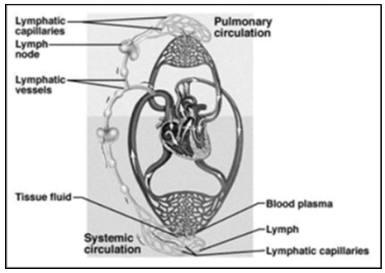
13

http://www.dummies.com/education/science/biology/the-path-of-blood-through-the-human-body

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

LYMPHATIC CIRCULATORY SYSTEM





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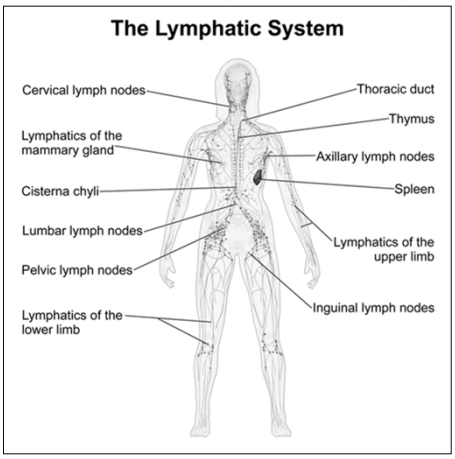
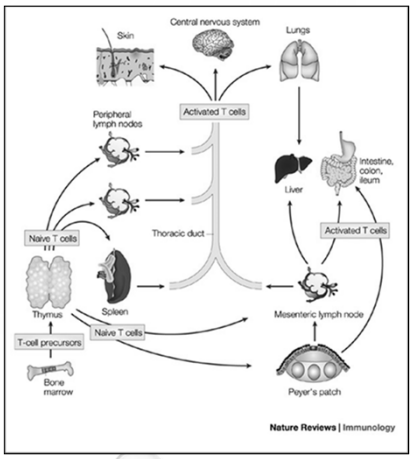
Source: Nature Reviews Immunology http://www.nature.com/nri/journal/v4/n5

THE LYMPHATIC SYSTEM





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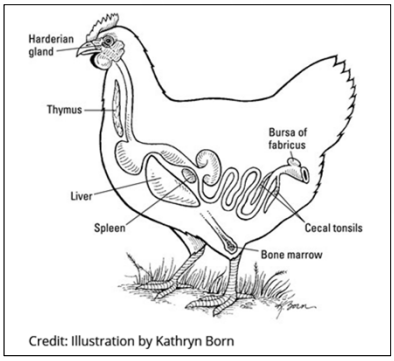
Blausen.com staff (2014). "Medical gallery of Blausen Medical 2014".

LYMPHATIC ORGANS

- **PRIMARY ORGANS**
  - BONE MARROW
  - THYMUS



Credit: Illustration by Kathryn Born

- **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

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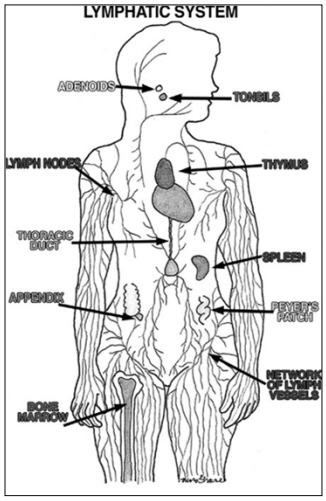
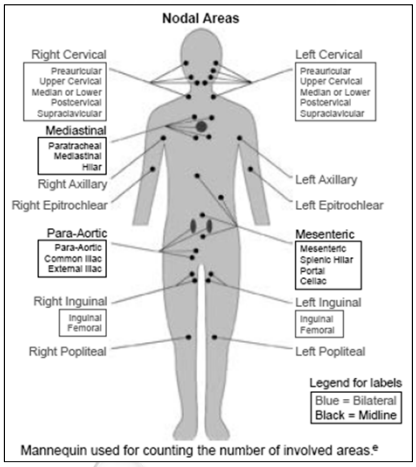
LYMPHATIC ORGANS VS REGIONS



http://commonsensehealth.com



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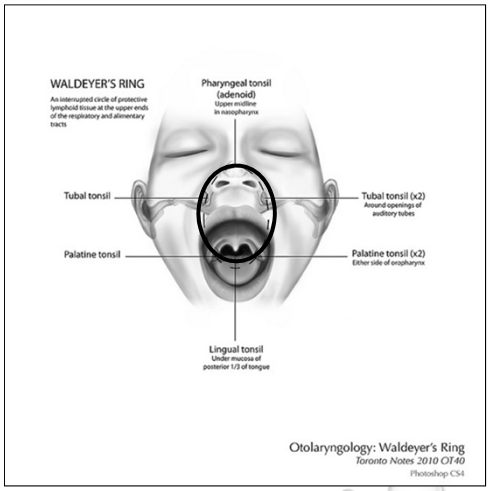
LYMPHATIC ORGANS



http://www.flickr.com/photos

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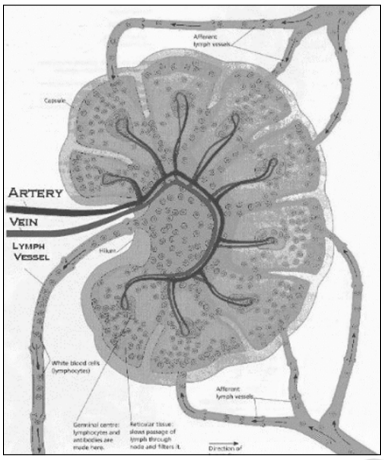
LYMPH NODE



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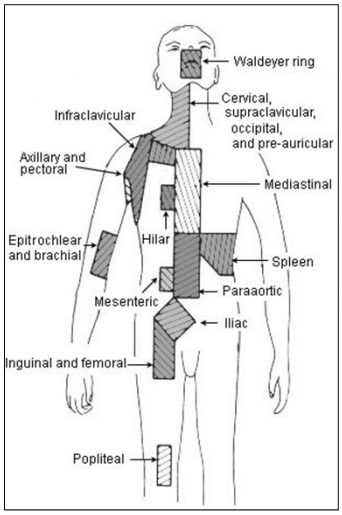
Source: http://www.bcb.uwc.ac.za/SCI_ED/grade10/manphys/plan.htm

LYMPH NODE CHAINS AND REGIONS

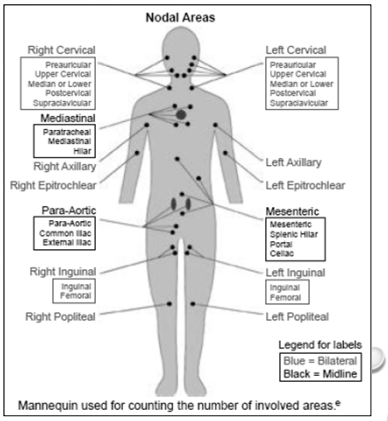


Lymph nodes above the diaphragm

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



Mannequin used for counting the number of involved areas.[6]

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Source: AJCC Cancer Staging Form, 7th edition

Appendix C
Lymph Node/Lymph Node Chain Reference Table

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	C775	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
Aselli'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

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MILESTONES IN THE CLASSIFICATION OF TUMORS OF HEMATOPOIETIC TISSUES

- 1951, WILLIAM DAMESHEK DESCRIBED THE CONCEPT OF 'MYELOPROLIFERATIVE DISORDERS' BY GROUPING TOGETHER CHRONIC MYELOGENOUS LEUKEMIA, POLYCYTHEMIA VERA, ESSENTIAL THROMBOCYTHEMIA, PRIMARY MYELOFIBROSIS AND ERYTHROLEUKEMIA
- 1960, NOWELL AND HUNGERFORD DISCOVERED THE PHILADELPHIA (PH) CHROMOSOME IN CML.
- 1967, FIALKOW AND COLLEAGUES USED X-LINKED POLYMORPHISMS TO ESTABLISH CML AS A CLONAL STEM CELL DISEASE.
- 1967, THE PV STUDY GROUP WAS SUMMONED BY LOUIS WASSERMAN TO STUDY THE NATURAL HISTORY OF POLYCYTHEMIA VERA AND CONDUCT LARGE-SCALE CLINICAL TRIALS.
- 1972, JANET ROWLEY DECIPHERED THE PH CHROMOSOME AS A RECIPROCAL TRANSLOCATION BETWEEN CHROMOSOMES 9 AND 22, THUS PAVING THE WAY FOR ITS SUBSEQUENT CHARACTERIZATION AS AN ONCOGENIC BCR–ABL MUTATION.
- 1996, BRIAN DRUKER DISCOVERED IMATINIB (GLEEVEC) —A SMALL MOLECULE ABL INHIBITOR WITH EXCEPTIONAL THERAPEUTIC ACTIVITY IN CML.
- 2005, A GAIN-OF-FUNCTION JAK2 MUTATION (JAK2V617F) WAS DESCRIBED IN BCR–ABL-NEGATIVE MPDS, RAISING THE PROSPECT OF A CML-LIKE TREATMENT STRATEGY IN PV, ET AND PMF.

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MILESTONES IN THE CLASSIFICATION OF TUMORS OF LYMPHOID TISSUES

- 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
- 1982 – WORKING FORMULATION
- 1994 –REVISED EUROPEAN-AMERICAN CLASSIFICATION OF LYMPHOID NEOPLASMS
- 2001 – WHO CLASSIFICATION OF TUMORS OF HEMATOPOIETIC AND LYMPHOID TISSUES, 3RD EDITION, 2001
- 2008 – WHO CLASSIFICATION OF TUMORS OF HEMATOPOIETIC AND LYMPHOID TISSUES, 4TH EDITION, OCTOBER 2008
- 2016 – REVISION TO 4TH EDITION, 2017

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THE 2010 HEMATOPOIETIC MPH RULES MANUAL AND THE HEMATOPOIETIC DATABASE

- BASED ON THE 2008 WHO CLASSIFICATION OF HEMATOPOIETIC AND LYMPHOID TISSUES
- REPLACED ICD-O-3 FOR ANY HISTOLOGY CODE IN RANGE 9590-9992
- UPDATED IN 2012 – NO MAJOR CHANGES – DETAILS ADDED TO HEME DATABASE
- UPDATED IN 2014 – THE ORIGINAL 43 PRIMARY SITE AND HISTOLOGY CODING RULES WERE REDUCED TO 31 RULES. SOME RULES WERE DELETED, SOME COMBINED AND SOME CLARIFIED. AND, CLARIFIED THAT NO DESIGNATED OBSOLETE CODES ARE TO BE USED AS OF 1/1/2010.
- UPDATED IN 2015 – NO MAJOR CHANGES

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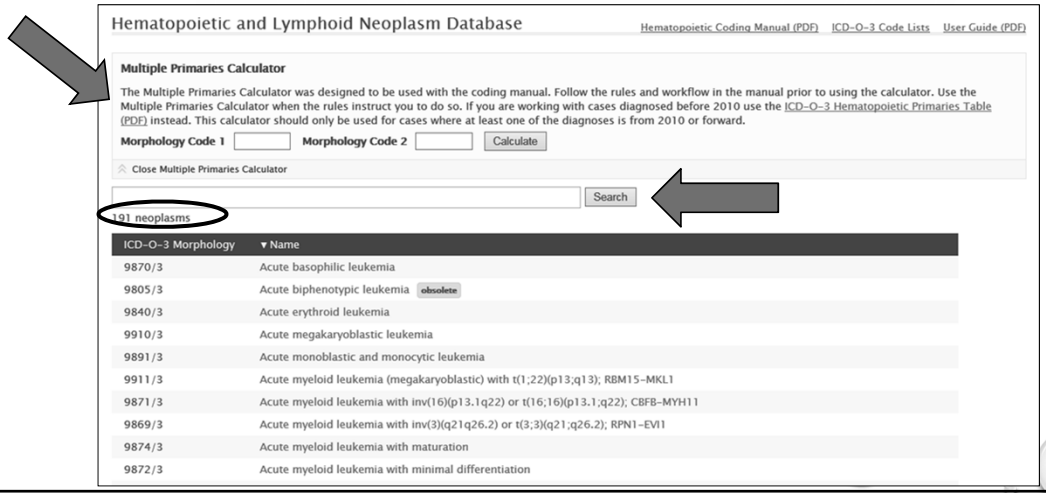
THE 2010 HEMATOPOIETIC MPH RULES MANUAL AND THE HEMATOPOIETIC DATABASE

HTTPS://SEER.CANCER.GOV/SEERTOOLS/HEMELYMPH/



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THE 2010 HEMATOPOIETIC MPH RULES MANUAL AND THE HEMATOPOIETIC DATABASE

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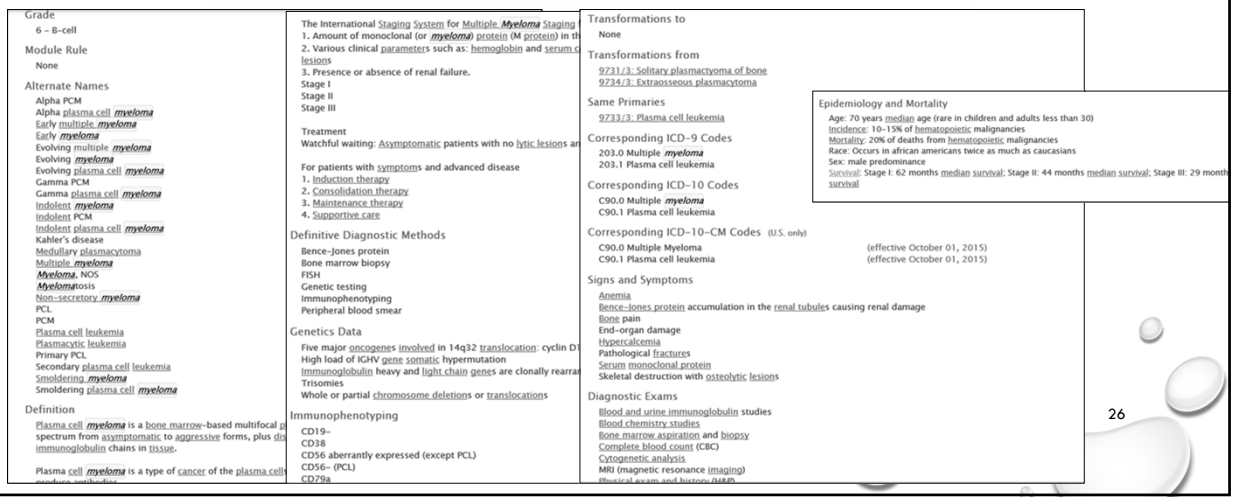

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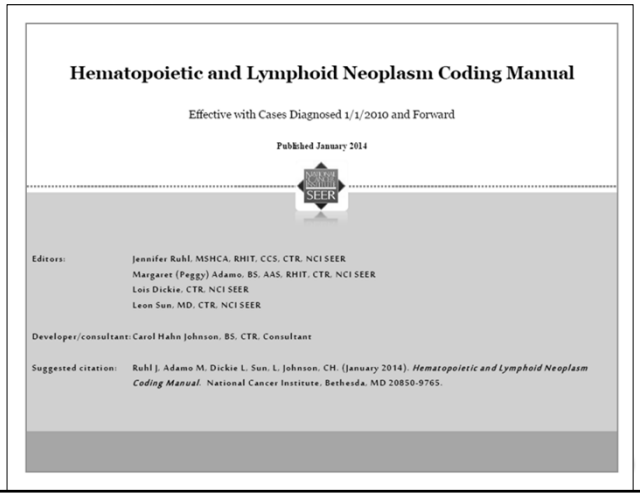

Hematopoietic and Lymphoid Neoplasm Coding Manual

Effective with Cases Diagnosed 1/1/2010 and Forward

Published January 2014

Editors: Jennifer Ruhl, MSHCA, RHIT, CCS, CTR, NCI SEER
Margaret (Peggy) Adamo, BS, AAS, RHIT, CTR, NCI SEER
Lois Dickie, CTR, NCI SEER
Leon Sun, MD, CTR, NCI SEER

Developer/consultant: Carol Hahn Johnson, BS, CTR, Consultant

Suggested citation: Ruhl J, Adamo M, Dickie L, Sun, L, Johnson, CH. (January 2014). *Hematopoietic and Lymphoid Neoplasm Coding Manual*. National Cancer Institute, Bethesda, MD 20850-9765.

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THE 2010 HEMATOPOIETIC MPH RULES MANUAL AND THE HEMATOPOIETIC DATABASE

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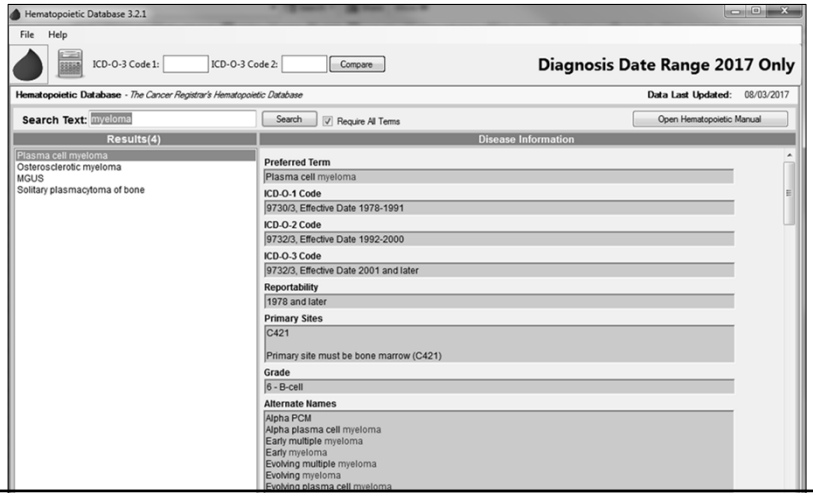

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2016 REVISION OF THE WHO CLASSIFICATION MYELOID NEOPLASMS & ACUTE LEUKEMIA

BLOOD, 19 MAY 2016 X VOLUME 127, NUMBER 20

THE UPDATED WHO CLASSIFICATION OF HEMATOLOGICAL MALIGNANCIES

The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia

Daniel A. Arber,[1] Attilio Orazi,[2] Robert Hasserjian,[3] Jürgen Thiele,[4] Michael J. Borowitz,[5] Michelle M. Le Beau,[6] Clara D. Bloomfield,[7] Mario Cazzola,[8] and James W. Vardiman[9]

[1]Department of Pathology, Stanford University, Stanford, CA; [2]Department of Pathology, Weill Cornell Medical College, New York, NY; [3]Department of Pathology, Massachusetts General Hospital, Boston, MA; [4]Institute of Pathology, University of Cologne, Cologne, Germany; [5]Department of Pathology, John Hopkins Medical Institutions, Baltimore, MD; [6]Section of Hematology/Oncology, University of Chicago, Chicago, IL; [7]Comprehensive Cancer Center, James Cancer Hospital and Solove Research Institute, The Ohio State University, Columbus, OH; [8]Department of Molecular Medicine, University of Pavia, and Department of Hematology Oncology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; and [9]Department of Pathology, University of Chicago, Chicago, IL

The World Health Organization (WHO) classification of tumors of the hematopoietic and lymphoid tissues was last updated in 2008. Since then, there have been numerous advances in the identification of unique biomarkers associated with some myeloid neoplasms and acute leukemias, largely derived from gene expression analysis and next-generation sequencing that can significantly improve the diagnostic criteria as well as the prognostic relevance of entities currently included in the WHO classification and that also suggest new entities that should be added. Therefore, there is a clear need for a revision to the current classification. The revisions to the categories of myeloid neoplasms and acute leukemia will be published in a monograph in 2016 and reflect a consensus of opinion of hematopathologists, hematologists, oncologists, and geneticists. The 2016 edition represents a revision of the prior classification rather than an entirely new classification and attempts to incorporate new clinical, prognostic, morphologic, immunophenotypic, and genetic data that have emerged since the last edition. The major changes in the classification and their rationale are presented here. (*Blood*. 2016; 127(20):2391-2405)

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INTEGRATING GENETIC DATA INTO CLASSIFICATION

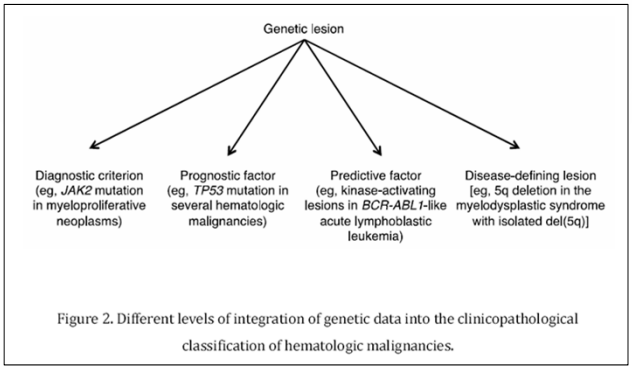

Figure 2. Different levels of integration of genetic data into the clinicopathological classification of hematologic malignancies.

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SUMMARY OF REVISIONS

- WHO SUPPORTS A ROBUST INTEGRATED APPROACH TO DISEASE CLASSIFICATION THAT INCLUDES HEMATOLOGIC, MORPHOLOGIC, CYTOGENETIC, AND MOLECULAR GENETIC FINDINGS
- THIS REVISION PROVIDES FOR A CLOSER INTEGRATION OF MORPHOLOGY AND GENETICS
  - IMPROVED **CHARACTERIZATION AND STANDARDIZATION OF MORPHOLOGICAL FEATURES** AIDING IN THE DIFFERENTIATION OF DISEASE GROUPS
  - DISCOVERY OF UNIQUE BIOMARKERS/MOLECULAR FEATURES THAT SIGNIFICANTLY IMPROVE **DIAGNOSTIC CRITERIA** FOR ENTITIES CURRENTLY INCLUDED IN THE WHO CLASSIFICATION
  - DISCOVERY OF UNIQUE BIOMARKERS/MOLECULAR FEATURES THAT IMPROVE **PROGNOSTIC RELEVANCE** OF ENTITIES CURRENTLY INCLUDED IN THE WHO CLASSIFICATION
  - DISCOVERY OF UNIQUE BIOMARKERS/MOLECULAR FEATURES THAT SUGGEST **NEW ENTITIES** SHOULD BE ADDED.

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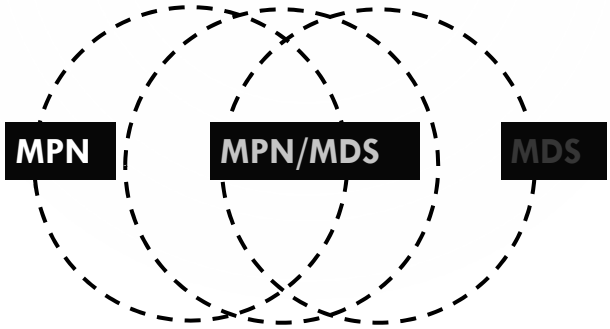
SUMMARY OF REVISIONS

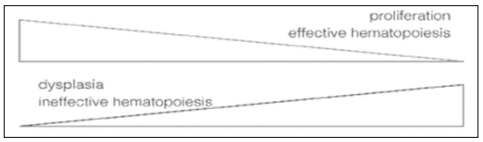
Table. WHO Myeloid Neoplasms and Acute Leukemias

MPN	Myeloid neoplasms with germ line predisposition	**Acute leukemias of ambiguous lineage**
Chronic myeloid leukemia, *BCR-ABL1*+	**AML and related neoplasms**	Acute undifferentiated leukemia
Chronic neutrophilic leukemia	AML with recurrent genetic abnormalities	MPAL with t(9;22)(q34.1;q11.2); *BCR-ABL1*
Polycythemia vera	AML with t(8;21)(q22;q22.1); *RUNX1-RUNX1T1*	MPAL with t(v;11q23.3); *KMT2A* rearranged
PMF	AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*	MPAL, B/myeloid, NOS
PMF, prefibrotic/early stage	Acute promyelocytic leukemia with *PML-RARA*	MPAL, T/myeloid, NOS
PMF, overt fibrotic state	AML with t(9;11)(p21.3;q23.3); *MLLT3-KMT2A*	**B-lymphoblastic leukemia/lymphoma**
Essential thrombocythemia	AML with t(6;9)(p23;q34.1); *DEK-NUP214*	B-lymphoblastic leukemia/lymphoma, NOS
Chronic eosinophilic leukemia, NOS	AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2, MECOM*	B-lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities
Mastocytosis	AML (megakaryoblastic) with t(1;22)(p13.3;q13.3), *RBM15-MKL1*	B-lymphoblastic leukemia/lymphoma with t(9;22)(q34.1;q11.2); *BCR-ABL1*
Myeloid/lymphoid neoplasms with eosinophilia and rearrangement of *PDGFRA, PDGFRB*, or *FGFR1*, or with *PCM1-JAK2*	*Provisional entity: AML with BCR-ABL1*	B-lymphoblastic leukemia/lymphoma with t(v;11q23.3); *KMT2A* rearranged
Myeloid/lymphoid neoplasms with *PDGFRA* rearrangement	AML with mutated *NPM1*	B-lymphoblastic leukemia/lymphoma with t(12;21)(p13.2;q22.1); *ETV6-RUNX1*
Myeloid/lymphoid neoplasms with *PDGFRB* rearrangement	AML with biallelic mutations of *CEBPA*	B-lymphoblastic leukemia/lymphoma with hyperdiploidy
Myeloid/lymphoid neoplasms with *FGFR1* rearrangement	*Provisional entity: AML with mutated RUNX1*	B-lymphoblastic leukemia/lymphoma with hypodiploidy
Provisional entity: myeloid/lymphoid neoplasms with PCM1-JAK2 rearrangement	AML with myelodysplasia-related changes	B-lymphoblastic leukemia/lymphoma with t(5;14)(q31.1;q32.3); *IL3-IGH*
MDS/MPNs	Therapy-related myeloid neoplasms	B-lymphoblastic leukemia/lymphoma with t(1;19)(q23;p13.3); *TCF3-PBX1*
Chronic myelomonocytic leukemia	AML, NOS	*Provisional entity: B-lymphoblastic leukemia/lymphoma, BCR-ABL1–like*
Atypical chronic myeloid leukemia, *BCR-ABL1*	AML with minimal differentiation	*Provisional entity: B-lymphoblastic leukemia/lymphoma with iAMP21*
Juvenile myelomonocytic leukemia	AML without maturation	**T-lymphoblastic leukemia/lymphoma**
MDS/MPN with ring sideroblasts and thrombocytosis	AML with maturation	*Provisional entity: early T-cell precursor lymphoblastic leukemia*
MDS/MPN, unclassifiable	Acute myelomonocytic leukemia	*Provisional entity: natural killer cell lymphoblastic leukemia/lymphoma*
MDS	Acute monoblastic/monocytic leukemia	
MDS with single lineage dysplasia	Pure erythroid leukemia	
MDS-RS	Acute megakaryoblastic leukemia	
MDS-RS with single lineage dysplasia	Acute basophilic leukemia	
MDS-RS with multilineage dysplasia	Acute panmyelosis with myelofibrosis	
MDS with multilineage dysplasia	**Myeloid sarcoma**	
MDS with excess blasts	**Myeloid proliferations related to Down syndrome**	
MDS with isolated del(5q)	Transient abnormal myelopoiesis	
MDS, unclassifiable	Myeloid leukemia associated with Down syndrome	
Provisional entity: refractory cytopenia of childhood	**Blastic plasmacytoid dendritic cell neoplasm**	

Note: Provisional entities are italicized. New or renamed entities are in red. *MLL* has been renamed *KMT2A*. The inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2) does not represent a fusion gene, but repositions *GATA2* to activated *MECOM* expression and confer *GATA2* haploinsufficiency. Abbreviations: AML, acute myeloid leukemia; MDS, myelodysplastic syndromes; MPN, myeloproliferative neoplasms; MDS-RS, MDS with ring sideroblasts; MPAL, mixed phenotype acute leukemia; NOS, not otherwise specified; PMF, primary myelofibrosis.

CHRONIC MYELOID NEOPLASMS





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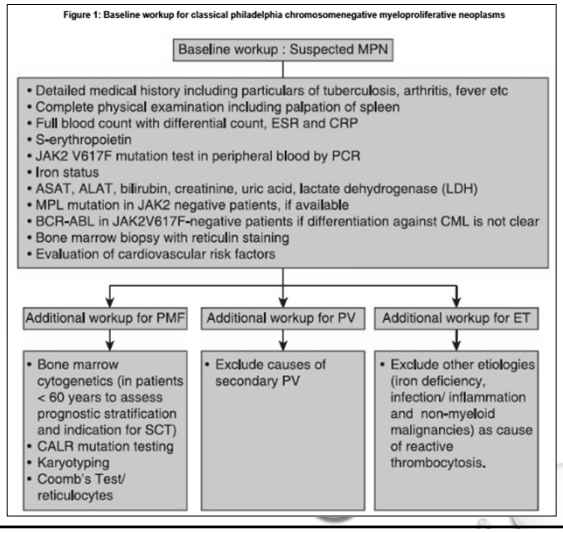
MYELOPROLIFERATIVE NEOPLASMS

Myeloproliferative neoplasms
Chronic myeloid leukaemia, *BCR-ABL1*–positive
Chronic neutrophilic leukaemia
Polycythaemia vera
Primary myelofibrosis
  Prefibrotic/early primary myelofibrosis
  Overt primary myelofibrosis
Essential thrombocythaemia
Chronic eosinophilic leukaemia, not otherwise specified
Myeloproliferative neoplasm, unclassifiable

~~Mastocytosis~~ now has its own group



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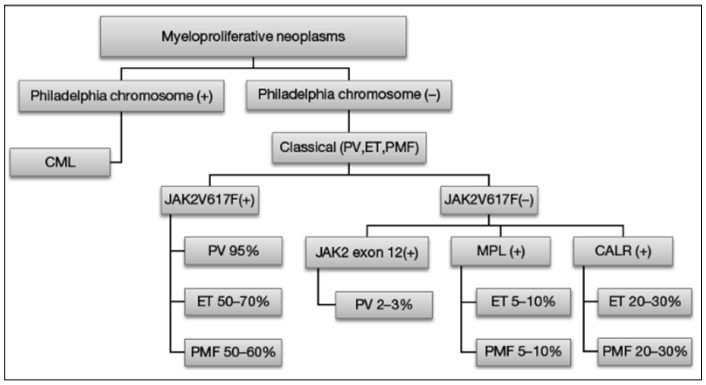
MYELOPROLIFERATIVE NEOPLASMS



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MASTOCYTOSIS

NEW

New WHO Classification Group

Mastocytosis
Cutaneous mastocytosis
Systemic mastocytosis
Mast cell sarcoma

NEW

NEW ICD-10-CM DX CODES FOR MASTOCYTOSIS

- C96.20 - MALIGNANT MAST CELL NEOPLASM, UNSPECIFIED
- C96.22 - AGGRESSIVE SYSTEMIC MASTOCYTOSIS
- C96.22 - MAST CELL SARCOMA

- D47.01 - CUTANEOUS MASTOCYTOSIS
- D47.02 - SYSTEMIC MASTOCYTOSIS
- D47.09 - OTHER MAST CELL NEOPLASMS OF UNCERTAIN BEHAVIOR

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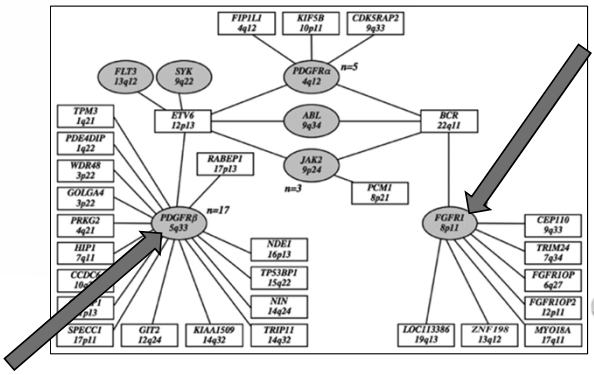
MYELOID/LYMPHOID NEOPLASMS WITH EOSINOPHILIA AND GENE REARRANGEMENT

Myeloid/lymphoid neoplasms with eosinophilia and gene rearrangement
Myeloid/lymphoid neoplasms with *PDGFRA* rearrangement
Myeloid/lymphoid neoplasms with *PDGFRB* rearrangement
Myeloid/lymphoid neoplasms with *FGFR1* rearrangement
Myeloid/lymphoid neoplasms with *PCM1-JAK2*



https://doi.org/10.3324/haematol.10328

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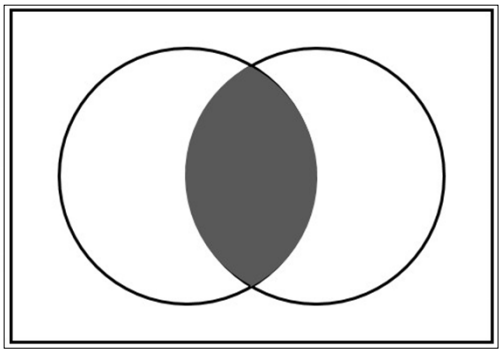
MYELODYSPLASTIC/MYELOPROLIFERATIVE NEOPLASMS

Myelodysplastic/myeloproliferative neoplasms
Chronic myelomonocytic leukaemia
Atypical chronic myeloid leukaemia, *BCR-ABL1*–negative
Juvenile myelomonocytic leukaemia
Myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis
Myelodysplastic/myeloproliferative neoplasm, unclassifiable



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MYELODYSPLASTIC SYNDROMES

Myelodysplastic syndromes
Overview
Myelodysplastic syndrome with single lineage dysplasia
Myelodysplastic syndrome with ring sideroblasts
Myelodysplastic syndrome with multilineage dysplasia
Myelodysplastic syndrome with excess blasts
Myelodysplastic syndrome with excess blasts and erythroid predominance
Myelodysplastic syndrome with excess blasts and fibrosis
Myelodysplastic syndrome with isolated del(5q)
Myelodysplastic syndrome, unclassifiable
Childhood myelodysplastic syndrome
Refractory cytopenia of childhood

NEW

Myelodysplastic syndromes (MDS)

2016
- MDS with single lineage dysplasia
- MDS with multilineage dysplasia
- MDS with ring sideroblasts (MDS-RS)
  - MDS-RS and single lineage dysplasia
  - MDS-RS and multilineage dysplasia
- MDS with isolated del(5q)
- MDS with excess blasts
  - MDS –EB -1
  - MDS -EB- 2
- MDS, unclassifiable
- Provisional entity: Refractory cytopenia of childhood

2008
~~RCUD~~
~~RCMD~~
~~RARS~~
~~RCMD-RS~~
~~RAEB-1~~
~~RAEB-2~~

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MYELOID DISEASE TRANSFORMATION

- PATIENTS WITH MYELOPROLIFERATIVE NEOPLASMS (MPNS), INCLUDING POLYCYTHEMIA VERA, ESSENTIAL THROMBOCYTHEMIA, AND PRIMARY MYELOFIBROSIS, HAVE A PROPENSITY TO DEVELOP ACUTE MYELOID LEUKEMIA (AML) AND MYELODYSPLASTIC SYNDROMES (MDSS).
- BLASTIC TRANSFORMATION REPRESENTS A TRANSFORMATION OF DISEASE FROM INDOLENT AND CHRONIC TO ACUTE AND BLASTIC LIFE THREATENING DISEASE. (EX: CML TRANSFORM TO AML)
- NEW TARGETED DRUGS LIKE GLEEVEK TREAT PRE-ACUTE PHASE HOPING FOR COMPLETE RESPONSE.
- MANY PATIENTS NOW DIAGNOSED AND TREATED AT EARLY PHASE OF DISEASE
- SELDOM SEE INTERMEDIATE/ACCELERATED PHASE
- ACUTE PHASE IS LIFE-THREATENING

A MYELOID DISEASE PROCESS WILL NOT TRANSFORM TO LYMPHOID OR VICE VERSA

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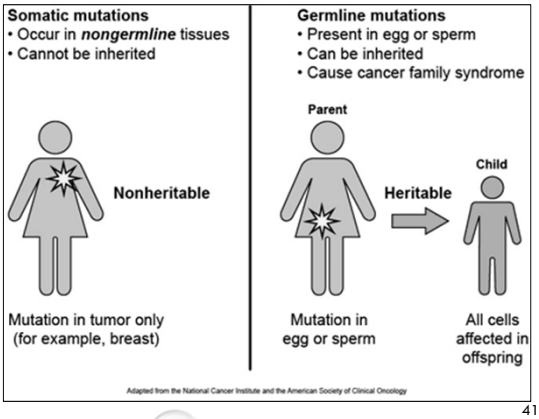
MYELOID NEOPLASMS WITH GERMLINE PREDISPOSITION

NEW

Myeloid neoplasms with germline predisposition
- Myeloid neoplasms with germline predisposition without a pre-existing disorder or organ dysfunction
  - Acute myeloid leukaemia with germline *CEBPA* mutation
  - Myeloid neoplasms with germline *DDX41* mutation
- Myeloid neoplasms with germline predisposition and pre-existing platelet disorders
  - Myeloid neoplasms with germline *RUNX1* mutation
  - Myeloid neoplasms with germline *ANKRD26* mutation
  - Myeloid neoplasms with germline *ETV6* mutation
- Myeloid neoplasms with germline predisposition associated with other organ dysfunction
  - Myeloid neoplasms with germline *GATA2* mutation
- Myeloid neoplasms with germline predisposition associated with inherited bone failure syndromes and telomere biology disorders



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ACUTE MYELOID LEUKEMIA AND RELATED (MYELOID) PRECURSOR NEOPLASMS

NEW

Acute myeloid leukaemia and related precursor neoplasms
- Acute myeloid leukaemia with recurrent genetic abnormalities
  - Introduction
  - Acute myeloid leukaemia with t(8;21)(q22;q22.1); *RUNX1-RUNX1T1*
  - Acute myeloid leukaemia with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*
  - Acute promyelocytic leukaemia with *PML-RARA*
  - Acute myeloid leukaemia with t(9;11)(p21.3;q23.3); *KMT2A-MLLT3*
  - Acute myeloid leukaemia with t(6;9)(p23;q34.1); *DEK-NUP214*
  - Acute myeloid leukaemia with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2, MECOM*
  - Acute myeloid leukaemia (megakaryoblastic) with t(1;22)(p13.3;q13.1); *RBM15-MKL1*
  - Acute myeloid leukaemia with *BCR-ABL1*
  - Acute myeloid leukaemia with gene mutations
    - Acute myeloid leukaemia with mutated *NPM1*
    - Acute myeloid leukaemia with biallelic mutation of *CEBPA*
    - Acute myeloid leukaemia with mutated *RUNX1*

AML, NOS

- Acute myeloid leukaemia with myelodysplasia-related changes
- Therapy-related myeloid neoplasms
- Acute myeloid leukaemia, not otherwise specified
  - Acute myeloid leukaemia with minimal differentiation
  - Acute myeloid leukaemia without maturation
  - Acute myeloid leukaemia with maturation
  - Acute myelomonocytic leukaemia
  - Acute monoblastic and monocytic leukaemia
  - Pure erythroid leukaemia
  - Acute megakaryoblastic leukaemia
  - Acute basophilic leukaemia
  - Acute panmyelosis with myelofibrosis
- Myeloid sarcoma
- Myeloid proliferations associated with Down syndrome
  - Transient abnormal myelopoiesis associated with Down syndrome
  - Myeloid leukaemia associated with Down syndrome

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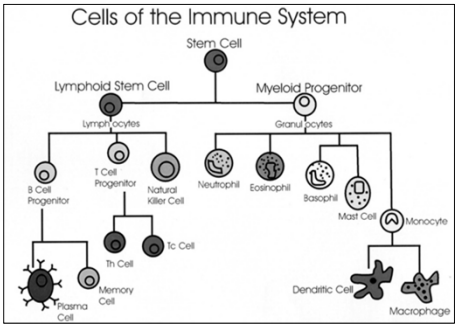
BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM

Blastic plasmacytoid dendritic cell neoplasm

CORRESPONDING LYMPHOID GROUP IS "HISTIOCYTIC AND DENDRITIC CELL NEOPLASMS"

NEW

- "BLASTIC" IS THE KEY – LEUKEMIC PHASE



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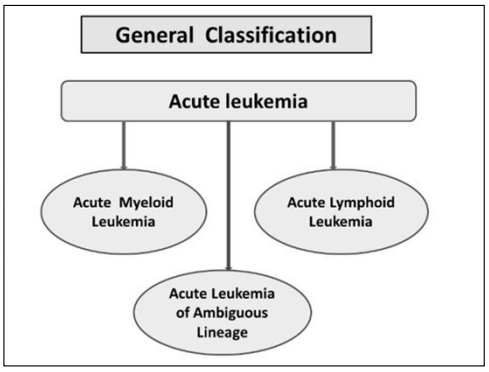
ACUTE LEUKEMIA OF AMBIGUOUS LINEAGE

Acute leukaemias of ambiguous lineage
Acute undifferentiated leukaemia
Mixed-phenotype acute leukaemia with t(9;22)(q34.1;q11.2); *BCR-ABL1*
Mixed-phenotype acute leukaemia with t(v;11q23.3); *KMT2A*-rearranged
Mixed-phenotype acute leukaemia, B/myeloid, not otherwise specified
Mixed-phenotype acute leukaemia, T/myeloid, not otherwise specified
Mixed-phenotype acute leukaemia, not otherwise specified, rare types
Acute leukaemias of ambiguous lineage, not otherwise specified

~~Natural killer (NK) cell lymphoblastic leukemia/lymphoma~~



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2016 REVISION OF THE WHO CLASSIFICATION LYMPHOID NEOPLASMS

BLOOD, 19 MAY 2016 X VOLUME 127, NUMBER 20

THE UPDATED WHO CLASSIFICATION OF HEMATOLOGICAL MALIGNANCIES

The 2016 revision of the World Health Organization classification of lymphoid neoplasms

Steven H. Swerdlow,[1] Elias Campo,[2] Stefano A. Pileri,[3] Nancy Lee Harris,[4] Harald Stein,[5] Reiner Siebert,[6] Ranjana Advani,[7] Michele Ghielmini,[8] Gilles A. Salles,[9] Andrew D. Zelenetz,[10] and Elaine S. Jaffe[11]

[1]Division of Hematopathology, Department of Pathology, University of Pittsburgh School of Medicine, Pittsburgh, PA; [2]Department of Pathology, Hospital Clinic, University of Barcelona, August Pi i Sunyer Biomedical Research Institute, Barcelona, Spain; [3]Haematopathology Unit, European Institute of Oncology, Milan, and Department of Experimental, Diagnostic and Specialty Medicine, Bologna University Medical School, Bologna, Italy; [4]Department of Pathology, Harvard Medical School and Massachusetts General Hospital, Boston, MA; [5]Pathodiagnostik, Berlin, Germany; [6]Institute of Human Genetics, Christian Albrechts University Kiel, Kiel, Germany; [7]Division of Oncology, Department of Medicine, Stanford University, Stanford, CA; [8]Department of Medical Oncology, Oncology Institute of Southern Switzerland, Bellinzona, Switzerland; [9]Department of Hematology, Hospices Civils de Lyon, and Université Claude Bernard Lyon-1, Lyon, France; [10]Department of Medicine, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY; and [11]Hematopathology Section, Laboratory of Pathology, National Cancer Institute, Bethesda, MD

A revision of the nearly 8-year-old World Health Organization classification of the lymphoid neoplasms and the accompanying monograph is being published. It reflects a consensus among hematopathologists, geneticists, and clinicians regarding both updates to current entities as well as the addition of a limited number of new provisional entities. The revision clarifies the diagnosis and management of lesions at the very early stages of lymphomagenesis, refines the diagnostic criteria for some entities, details the expanding genetic/molecular landscape of numerous lymphoid neoplasms and their clinical correlates, and refers to investigations leading to more targeted therapeutic strategies. The major changes are reviewed with an emphasis on the most important advances in our understanding that impact our diagnostic approach, clinical expectations, and therapeutic strategies for the lymphoid neoplasms. (*Blood*. 2016;127(20):2375-2390)

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SUMMARY OF REVISIONS

- CLOSER INTEGRATION OF MORPHOLOGY AND GENETICS
- EXPLOSION OF PATHOLOGICAL AND GENETIC DATA FOR "SMALL B-CELL" LYMPHOMAS – CLL/SLL
- THERE ARE LYMPHOID PROLIFERATIONS THAT WE USED TO DIAGNOSE AS OVERT LYMPHOID NEOPLASMS BUT WHICH ARE NOT CONSIDERED AS SUCH IN 2016 IS FURTHER EMPHASIZED
- THERE ARE MAJOR CHANGES IN AGGRESSIVE B-CELL LYMPHOMAS THAT IMPACT HOW THESE CASES SHOULD BE EVALUATED AND DIAGNOSED THAT HAVE IMPORTANT THERAPEUTIC IMPLICATIONS IN ADDITION TO CHANGES RESULTING FROM BIOLOGICAL INTEREST.
- THE 2008 MONOGRAPH REPORTED THAT "NO CYTOGENETIC ABNORMALITY IS SPECIFIC FOR HAIRY CELL LEUKEMIA", WE NOW KNOW THAT BRAF V600E MUTATIONS ARE FOUND IN ALMOST ALL CASES OF HAIRY CELL LEUKEMIA (HCL) BUT NOT IN HCL-VARIANT (HCL-V) OR OTHER SMALL B-CELL LYMPHOID NEOPLASMS
- THE 2008 MONOGRAPH ALSO NOTED THAT "NO SPECIFIC CHROMOSOMAL OR ONCOGENE ABNORMALITIES ARE RECOGNIZED" IN LYMPHOPLASMACYTIC LYMPHOMA (LPL); HOWEVER, WE NOW KNOW THAT ABOUT 90% OF LPL OR WALDENSTROM MACROGLOBULINEMIA (LPL PLUS AN IMMUNOGLOBULIN M [IGM] PARAPROTEIN) HAVE MYD88 L265P MUTATIONS
- NEW CATEGORY OF HIGH-GRADE B-CELL LYMPHOMA (HGBL), WITH REARRANGEMENTS OF MYC AND BCL2 AND/OR BCL6

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PRECURSOR LYMPHOID NEOPLASMS

Precursor lymphoid neoplasms
B-lymphoblastic leukaemia/lymphoma,
not otherwise specified
B-lymphoblastic leukaemia/lymphoma with recurrent genetic abnormalities
B-lymphoblastic leukaemia/lymphoma with t(9;22)(q34.1;q11.2); *BCR-ABL1*
B-lymphoblastic leukaemia/lymphoma with t(v;11q23.3); *KMT2A*-rearranged
B-lymphoblastic leukaemia/lymphoma with t(12;21)(p13.2;q22.1); *ETV6-RUNX1*
B-lymphoblastic leukaemia/lymphoma with hyperdiploidy
B-lymphoblastic leukaemia/lymphoma with hypodiploidy
B-lymphoblastic leukaemia/lymphoma with t(5;14)(q31.1;q32.1); IGH/*IL3*
B-lymphoblastic leukaemia/lymphoma with t(1;19)(q23;p13.3); *TCF3-PBX1*
B-lymphoblastic leukaemia/lymphoma, *BCR-ABL1*–like
B-lymphoblastic leukaemia/lymphoma with iAMP21
T-lymphoblastic leukaemia/lymphoma
Early T-cell precursor lymphoblastic leukaemia
NK-lymphoblastic leukaemia/lymphoma

NEW

NEW

T-Lymphoblastic leukemia/lymphoma

- Provisional entity: Early T-cell precursor lymphoblastic leukemia
- Provisional entity: Natural killer (NK) cell lymphoblastic leukemia/lymphoma

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MATURE B-CELL NEOPLASMS

Mature B-cell neoplasms
Chronic lymphocytic leukaemia/
small lymphocytic lymphoma
Monoclonal B-cell lymphocytosis
B-cell prolymphocytic leukaemia
Splenic marginal zone lymphoma
Hairy cell leukaemia
Splenic B-cell lymphoma/leukaemia, unclassifiable
Splenic diffuse red pulp small B-cell lymphoma
Hairy cell leukaemia variant
Lymphoplasmacytic lymphoma
IgM Monoclonal gammopathy of undetermined significance

Heavy chain diseases
Mu heavy chain disease
Gamma heavy chain disease
Alpha heavy chain disease
Plasma cell neoplasms
Non-IgM monoclonal gammopathy of undetermined significance
Plasma cell myeloma
Plasma cell myeloma variants
Smouldering (asymptomatic) plasma cell myeloma
Non-secretory myeloma
Plasma cell leukaemia
Plasmacytoma
Solitary plasmacytoma of bone
Extraosseous plasmacytoma
Monoclonal immunoglobulin deposition diseases
Primary amyloidosis
Light chain and heavy chain deposition diseases
Plasma cell neoplasms with associated paraneoplastic syndrome
POEMS syndrome
TEMPI syndrome

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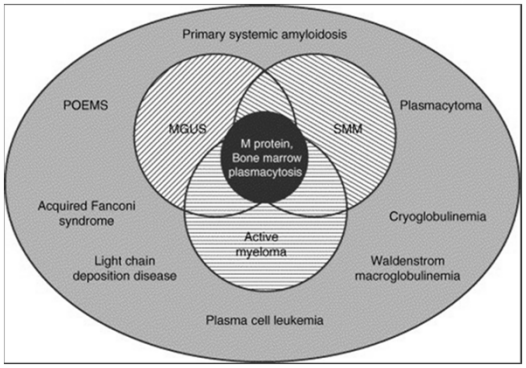
MATURE B-CELL NEOPLASMS



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…MORE…MATURE B-CELL NEOPLASMS

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
Nodal marginal zone lymphoma
Paediatric nodal marginal zone lymphoma
Follicular lymphoma
Testicular follicular lymphoma
In situ follicular neoplasia
Duodenal-type follicular lymphoma
Paediatric-type follicular lymphoma
Large B-cell lymphoma with *IRF4* rearrangement
Primary cutaneous follicle centre lymphoma
Mantle cell lymphoma
Leukaemic non-nodal mantle cell lymphoma
In situ mantle cell neoplasia
Diffuse large B-cell lymphoma (DLBCL), NOS
T-cell/histiocyte-rich large B-cell lymphoma
Primary diffuse large B-cell lymphoma of the CNS
Primary cutaneous diffuse large B-cell lymphoma, leg type

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EBV-positive diffuse large B-cell lymphoma, NOS
EBV-positive mucocutaneous ulcer
Diffuse large B-cell lymphoma associated with chronic inflammation
Fibrin-associated diffuse large B-cell lymphoma
Lymphomatoid granulomatosis
Primary mediastinal (thymic) large B-cell lymphoma
Intravascular large B-cell lymphoma
ALK-positive large B-cell lymphoma
Plasmablastic lymphoma
Primary effusion lymphoma
HHV8-associated lymphoproliferative disorders
Multicentric Castleman disease
HHV8-positive diffuse large B-cell lymphoma, NOS
HHV8-positive germinotropic lymphoproliferative disorder
Burkitt lymphoma
Burkitt-like lymphoma with 11q aberration

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VIRUS-ASSOCIATED LYMPHOID NEOPLASMS

Infectious Agents Associated with the Development of Lymphoid Malignancies

Infectious Agent	Lymphoid Malignancy
Epstein-Barr virus	Burkitt's lymphoma Post–organ transplant lymphoma Primary CNS diffuse large B cell lymphoma Hodgkin's disease Extranodal NK/T cell lymphoma, nasal type
HTLV-I	Adult T cell leukemia/lymphoma
HIV	Diffuse large B cell lymphoma Burkitt's lymphoma
Hepatitis C virus	Lymphoplasmacytic lymphoma
Helicobacter pylori	Gastric MALT lymphoma
HHV 8	Primary effusion lymphoma Multicentric Castleman's disease

Harrison's Principles of Internal Medicine, 17th Edition

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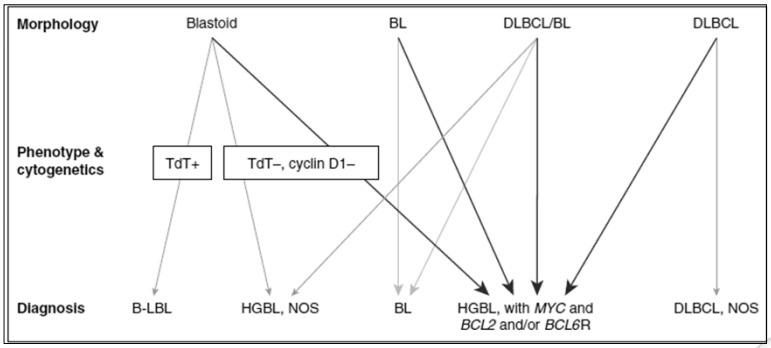
MATURE B-CELL NEOPLASMS

NEW

High-grade B-cell lymphoma
- High-grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* rearrangements
- High-grade B-cell lymphoma, NOS

B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classic Hodgkin lymphoma



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MATURE T- AND NK-CELL NEOPLASMS

Mature T- and NK-cell neoplasms
T-cell prolymphocytic leukaemia
T-cell large granular lymphocytic leukaemia
Chronic lymphoproliferative disorder of NK cells
Aggressive NK-cell leukaemia
EBV–positive T-cell and NK-cell lymphoproliferative diseases of childhood
- Systemic EBV+ T-cell lymphoma of childhood
- Chronic active EBV infection of T- and NK-cell type, systemic form
- Hydroa vacciniforme–like lymphoproliferative disorder
- Severe mosquito bite allergy

Adult T-cell leukaemia/lymphoma
Extranodal NK/T-cell lymphoma, nasal type
Intestinal T-cell lymphoma
- Enteropathy-associated T-cell lymphoma
- Monomorphic epitheliotropic intestinal T-cell lymphoma
- Intestinal T-cell lymphoma, NOS
- Indolent T-cell lymphoproliferative disorder of the gastrointestinal tract

Hepatosplenic T-cell lymphoma

NEW

NEW

Subcutaneous panniculitis-like T-cell lymphoma
Mycosis fungoides
Sézary syndrome
Primary cutaneous CD30-positive T-cell lymphoproliferative disorders
- Lymphomatoid papulosis
- Primary cutaneous anaplastic large cell lymphoma

Primary cutaneous peripheral T-cell lymphomas, rare subtypes
- Introduction
- Primary cutaneous gamma delta T-cell lymphoma
- Primary cutaneous CD8-positive aggressive epidermotropic cytotoxic T-cell lymphoma
- Primary cutaneous acral CD8-positive T-cell lymphoma
- Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder

Peripheral T-cell lymphoma, NOS
Angioimmunoblastic T-cell lymphoma and other nodal lymphomas of T follicular helper (TFH) cell origin
- Angioimmunoblastic T-cell lymphoma
- Follicular T-cell lymphoma
- Nodal peripheral T-cell lymphoma with TFH phenotype

Anaplastic large cell lymphoma, ALK-positive
Anaplastic large cell lymphoma, ALK-negative
Breast implant–associated anaplastic large cell lymphoma

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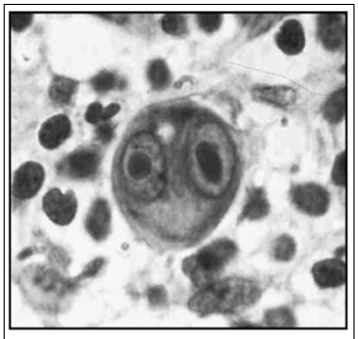
HODGKIN LYMPHOMAS

Hodgkin lymphomas
Introduction
Nodular lymphocyte predominant Hodgkin lymphoma
Classic Hodgkin lymphoma
- Nodular sclerosis classic Hodgkin lymphoma
- Lymphocyte-rich classic Hodgkin lymphoma
- Mixed-cellularity classic Hodgkin lymphoma
- Lymphocyte depleted classic Hodgkin lymphoma



Reed-Sternberg cell

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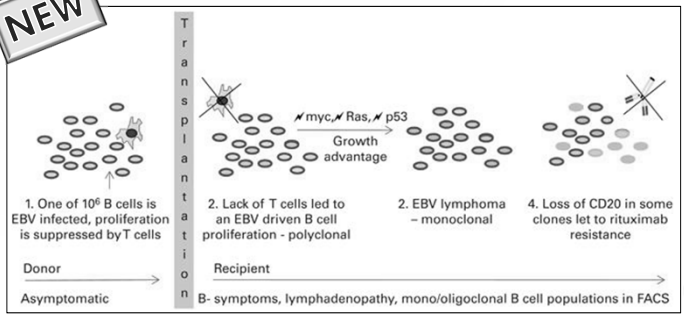
IMMUNODEFICIENCY-ASSOCIATED LYMPHOPROLIFERATIVE DISORDERS

Immunodeficiency-associated lymphoproliferative disorders
- Lymphoproliferative diseases associated with primary immune disorders
- Lymphomas associated with HIV infection
- Post-transplant lymphoproliferative disorders (PTLD)
  - Non-destructive PTLD
  - Polymorphic PTLD
  - Monomorphic PTLD (B- and T/NK-cell types)
    - Monomorphic B-cell PTLD
    - Monomorphic T/NK-cell PTLD
  - Classic Hodgkin lymphoma PTLD
- Other iatrogenic immunodeficiency-associated lymphoproliferative disorders

NEW



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HISTIOCYTIC AND DENDRITIC CELL NEOPLASMS

Histiocytic and dendritic cell neoplasms
- Introduction
- Histiocytic sarcoma
- Tumours derived from Langerhans cells
  - Langerhans cell histiocytosis
  - Langerhans cell sarcoma
- Indeterminate dendritic cell tumour
- Interdigitating dendritic cell sarcoma
- Follicular dendritic cell sarcoma
  - Inflammatory pseudotumour-like follicular/fibroblastic dendritic cell sarcoma
- Fibroblastic reticular cell tumour
- Disseminated juvenile xanthogranuloma
- Erdheim–Chester disease

CORRESPONDING MYELOID/ACUTE LEUKEMIA GROUP IS "BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM"

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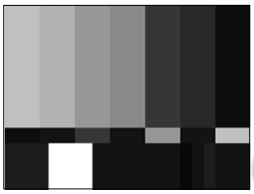
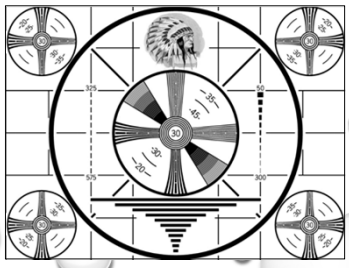
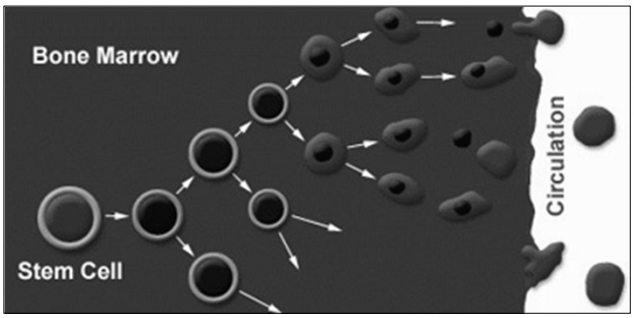
THE **2019** HEMATOPOIETIC MPH RULES & DATABASE

- ICD-O-3 UPDATES WORK GROUP DID NOT HAVE ENOUGH LEAD TIME FOLLOWING 2017 PUBLICATION OF THE REVISION TO THE WHO CLASSIFICATION FOR HEME/LYMPH TO INCORPORATE NEW HISTOLOGY CODES, NEW PREFERRED TERMS, OR NEW MPH OPTIONS.
- DELAYED UNTIL A 2019 RELEASE OF HEMATOPOIETIC MPH RULES & DATABASE
- ONLY A 1 YEAR DELAY WITH UNKNOWN RELEASE DATE IN 2019
- PLEASE STAND BY - CAN STILL PLAN FOR CHANGES
- KEEP EYE ON NEW TERMS
- PATHOLOGIST USE
- CLINICAL TRIALS





STAGING MYELOID NEOPLASMS



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2018 MYELOID NEOPLASMS – REQUIRED SSDI

JAK2	**Chapter 83**	**All Leukemia(C42.1) except CLL/SLL**

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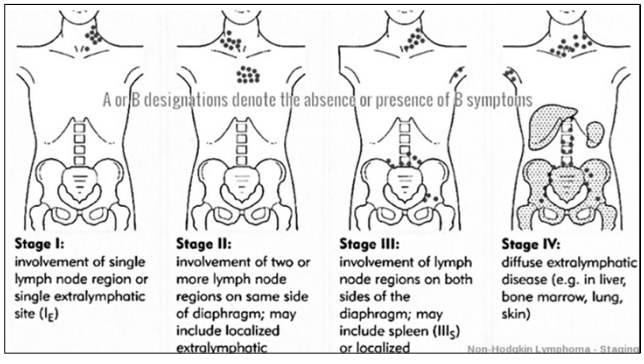
STAGING LYMPHOID NEOPLASMS

- HODGKIN LYMPHOMA
- NON-HODGKIN LYMPHOMA
- EXTRA-NODAL LYMPHOMA
- PLASMA CELL NEOPLASMS
- CLL/SLL
- ALL



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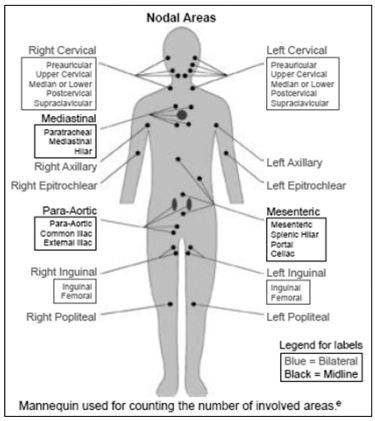
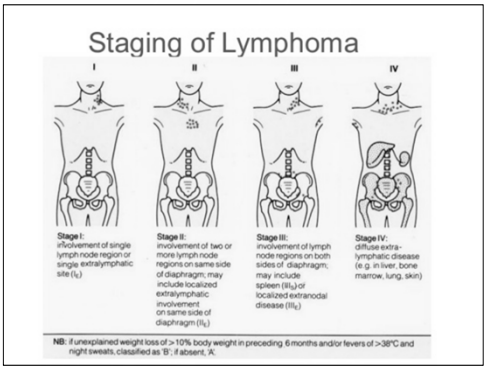
HODGKIN AND NON-HODGKIN LYMPHOMA – MODIFIED ANN ARBOR STAGING





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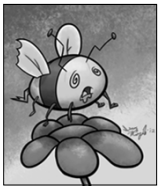
HODGKIN AND NON-HODGKIN LYMPHOMA – MODIFIED ANN ARBOR STAGING

- WHAT ARE "B" SYMPTOMS
  - FEVERS
  - NIGHT SWEATS
  - WEIGHT LOSS > 10% OF BODY WEIGHT



- MINOR SYMPTOMS (NOT "B" SYMPTOMS)
  - MALAISE
  - FATIGUE
  - PRURITIS
  - ALCOHOL INTOLERANCE
  - FREQUENT INFECTIONS

Not a "B"

- **DO NOT CODE MINOR SYMPTOMS AS "B" SYMPTOMS**

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EXTRANODAL LYMPHOMA – MODIFIED ANN ARBOR STAGING

STAGING OF GASTRIC MALT LYMPHOMA: COMPARISON OF DIFFERENT SYSTEMS

Lugano Staging System for Gastrointestinal Lymphomas		Lugano Modification of Ann Arbor Staging System	TNM Staging System Adapted for Gastric Lymphoma	Tumor Extension
Stage I_E	Confined to GI tract[a]			
	I_{E1} = mucosa, submucosa	I_E	T1 N0 M0	Mucosa, submucosa
	I_{E2} = muscularis propria, serosa	I_E	T2 N0 M0	Muscularis propria
		I_E	T3 N0 M0	Serosa
Stage II_E	Extending into abdomen			
	II_{E1} = local nodal involvement	II_E	T1-3 N1 M0	Perigastric lymph nodes
	II_{E2} = distant nodal involvement	II_E	T1-3 N2 M0	More distant regional lymph nodes
Stage II_E	Penetration of serosa to involve adjacent organs or tissues	II_E	T4 N0 M0	Invasion of adjacent structures
Stage IV[b]	Disseminated extranodal involvement or concomitant supradiaphragmatic nodal involvement		T1-4 N3 M0	Lymph nodes on both sides of the diaphragm/ distant metastases (eg, bone marrow or additional extranodal sites)
		IV	T1-4 N0-3 M1	

Zucca E, Bertoni F, Yahalom J, Isaacson P. Extranodal Marginal Zone B-cell Lymphoma of Mucosa-Associated Lymphoid Tissue (MALT lymphoma) in Armitage et al eds. Non-Hodgkin's Lymphomas. Philadelphia: Lippincott, 2010:242. (http://lww.com)

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PLASMA CELL NEOPLASMS – R-ISS STAGING

R-ISS -- THE 2015 **REVISED INTERNATIONAL STAGING SYSTEM** FOR **MULTIPLE MYELOMA**

R-ISS I	✓ serum beta2-microglobulin level < 3.5 mg/L AND ✓ serum albumin level of 3.5 g/dL or greater AND ✓ no high-risk CA [del(17p) and/or t(4;14) and/or t(14;16)] AND ✓ normal LDH level
R-ISS II	includes all other possible combinations
R-ISS III	✓ serum beta2-microglobulin level > 5.5 mg/L and ✓ high-risk CA or ✓ high LDH level

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CLL/SLL – RAI STAGING

RAI STAGING SYSTEM FOR CLL/SLL – 1968

- **Rai stage 0:** Lymphocytosis and no enlargement of the lymph nodes, spleen, or liver, and with near normal red blood cell and platelet counts.
- **Rai stage I:** Lymphocytosis plus enlarged lymph nodes. The spleen and liver are not enlarged and the red blood cell and platelet counts are near normal.
- **Rai stage II:** Lymphocytosis plus an enlarged spleen (and possibly an enlarged liver), with or without enlarged lymph nodes. The red blood cell and platelet counts are near normal.
- **Rai stage III:** Lymphocytosis plus anemia (too few red blood cells), with or without enlarged lymph nodes, spleen, or liver. Platelet counts are near normal.
- **Rai stage IV:** Lymphocytosis plus thrombocytopenia (too few blood platelets), with or without anemia, enlarged lymph nodes, spleen, or liver.

- Stage 0 is considered low risk.
- Stages I and II are considered intermediate risk.
- Stages III and IV are considered high risk.

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2018 LYMPHOID NEOPLASMS – REQUIRED SSDI

1. ADENOPATHY
2. ANEMIA
3. B SYMPTOMS
4. HIGH RISK CYTOGENETICS
5. HIGH RISK HISTOLOGIC FEATURES
6. HIV STATUS
7. **JAK2 – ACUTE LYMPHOID LEUKEMIA (EXCEPT CLL/SLL)**
8. LYMPHOCYTOSIS
9. NCCN INTERNATIONAL PROGNOSTIC INDEX (IPI)
10. ORGANOMEGALY
11. PERIPHERAL BLOOD INVOLVEMENT
12. SERUM ALBUMIN PRETREATMENT LEVEL
13. SERUM BETA-2 MICROGLOBULIN PRETREATMENT LEVEL
14. SERUM LDH (LACTATE DEHYDROGENASE) PRETREATMENT LAB VALUE
15. THROMBOCYTOPENIA

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2018 LYMPHOID NEOPLASMS – REQUIRED SSDI

B Symptoms	Chapters 79, 80	All Lymphoma
HIV Status	Chapters 79, 80	All Lymphoma
NCCN International Prognostic Index (IPI)	Chapters 79, 80	All Lymphoma

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2018 CUTANEOUS LYMPHOMA – REQUIRED SSDI

Peripheral Blood Involvement	Chapter 81: Primary Cutaneous Lymphomas: MF/SS Required for Staging	P Site: C44.*, C51, C60, C63.2 Histology: 9597, 9680, 9700,9701, 9708, 9709, 9712, 9718, 9719, 9726, 9727

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2018 PLASMA CELL NEOPLASMS – REQUIRED SSDI R-ISS STAGING

R-ISS -- THE 2015 **REVISED INTERNATIONAL STAGING SYSTEM** FOR **MULTIPLE MYELOMA**

High Risk Cytogenetics	Chapter 82: Plasma Cell Myeloma Required for Staging (RISS)	9731, 9732, 9734 Only
Serum Albumin Pretreatment Level	Chapter 82: Plasma Cell Myeloma Required for Staging (RISS)	9731, 9732, 9734 Only
Serum Beta-2 Microglobulin Pretreatment Level	Chapter 82: Plasma Cell Myeloma Required for Staging (RISS)	9731, 9732, 9734 Only
Serum LDH (Lactate Dehydrogenase) Pretreatment Lab Value	Chapter 82: Plasma Cell Myeloma Required for Staging (RISS)	9731, 9732, 9734 Only

High Risk Cytogenetics: several cytogenetic abnormalities such as t(4;14), del(17/17p), t(14;16), t(14;20), nonhyperdiploidy, and gain(1q) were identified that confer poor prognosis.

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2018 CLL/SLL – REQUIRED SSDI

RAI STAGING SYSTEM FOR CLL/SLL – 1968

- **Rai stage 0:** Lymphocytosis and no enlargement of the lymph nodes, spleen, or liver, and with near normal red blood cell and platelet counts.
- **Rai stage I:** Lymphocytosis plus enlarged lymph nodes. The spleen and liver are not enlarged and the red blood cell and platelet counts are near normal.
- **Rai stage II:** Lymphocytosis plus an enlarged spleen (and possibly an enlarged liver), with or without enlarged lymph nodes. The red blood cell and platelet counts are near normal.
- **Rai stage III:** Lymphocytosis plus anemia (too few red blood cells), with or without enlarged lymph nodes, spleen, or liver. Platelet counts are near normal.
- **Rai stage IV:** Lymphocytosis plus thrombocytopenia (too few blood platelets), with or without anemia, enlarged lymph nodes, spleen, or liver.

- Stage 0 is considered low risk.
- Stages I and II are considered intermediate risk.
- Stages III and IV are considered high risk.

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2018 CLL/SLL – REQUIRED SSDI RAI STAGING

Thrombocytopenia	Chapter 79: CLL/SLL only (AJCC ID 79.5) Required for staging (RAI)	9823 Only
Adenopathy	Chapter 79: CLL/SLL only (AJCC ID 79.5) Required for staging (RAI)	9823 Only
Adenopathy	Chapter 79: CLL/SLL only (AJCC ID 79.5) Required for staging (RAI)	9823/3 Only
Anemia	Chapter 79: CLL/SLL only (AJCC ID 79.5) Required for staging (RAI)	9823/3 Only
Lymphocytosis	Chapter 79: CLL/SLL only (AJCC ID 79.5) Required for staging (RAI)	9823/3 Only
Organomegaly	Chapter 79: CLL/SLL only (AJCC ID 79.5) Required for staging (RAI)	9823/3 Only

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ADDITIONAL RESOURCES

- WHO CLASSIFICATION OF TUMOURS OF HAEMATOPOIETIC AND LYMPHOID TISSUES, 4TH ED, 1ST REV, 2017
- 2016 REVISION OF THE WHO CLASSIFICATION MYELOID NEOPLASMS & ACUTE LEUKEMIA BLOOD, 19 MAY 2016 X VOLUME 127, NUMBER 20
- 2016 REVISION OF THE WHO CLASSIFICATION LYMPHOID NEOPLASMS BLOOD, 19 MAY 2016 X VOLUME 127, NUMBER 20
- REVISED INTERNATIONAL STAGING SYSTEM FOR MULTIPLE MYELOMA: A REPORT FROM INTERNATIONAL MYELOMA WORKING GROUP; VOLUME 33 NUMBER 26 SEPTEMBER 10 2015
- NCCN CLINICAL PRACTICE GUIDELINES – B-CELL LYMPHOMAS V5.2017
- BLOOD FIRST EDITION PAPER, APRIL 11, 2016; DOI 10.1182/BLOOD-2016-03-657379
- NAACCR 2018 SSDI REQUIRED ITEMS FOR HEME/LYMPH NEOPLASMS BY CHAPTER - AJCC STAGING MANUAL, 8TH ED

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QUESTIONS