“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”.

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.
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

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

WHO CLASSIFICATION OF TUMOURS

- 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)

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
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.

INTRODUCTION

ADULT MYELOID AND LYMPHOID NEOPLASMS
INTRODUCTION
PEDIATRIC MYELOID AND LYMPHOID NEOPLASMS

HEMATOPOIESIS AND “BLOOD CANCERS”
Hematopoietic stem cells give rise to two major progenitor cell lineages, myeloid and lymphoid progenitors. 

- Myeloid: 
  - Stem cells 
  - Committed progenitors: 
    - Meg-CP 
    - CFU 
    - Gr-PC 
    - Meg-PC 
  - Mature cells: 
    - Neutrophil 
    - Monocyte 
    - Macrophage 
    - Eosinophil 
    - Basophil 
    - Megakaryocyte 
    - Platelet 
    - Lymphocyte 
    - Plasma cell 
    - Mast cell 
    - Myeloid 

- Lymphoid: 
  - Stem cells 
  - Committed progenitors: 
    - Pre-B cell 
    - B cell 
    - Pre-T cell 
    - T cell
  - Mature cells: 
    - B cell 
    - T cell 
    - Plasma cell 
    - Macrophage 
    - Neutrophil 


- 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.
THE LYMPHATIC SYSTEM

LYMPHATIC ORGANS

• 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
LYMPH NODE CHAINS AND REGIONS

Lymph nodes above the diaphragm:
1. Waldeyer's ring
2. Cervical, supraclavicular, occipital, and pre-auricular
3. Infracavicular
4. Axillary and pectoral
5. Mediastinal
6. Hilar
7. Epitrochlear and brachial

Lymph nodes below the diaphragm:
8. Splenic
9. Mesenteric
10. Paraaortic
11. Iliac
12. Inguinal and femoral
13. Proprietal

Source: AJCC Cancer Staging Form, 7th edition
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 DECODED THE PH CHROMOSOME AS A RECIPROCAL TRANSLOCATION BETWEEN CHROMOSOMES 9 AND 22, THEREBY 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.
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
- 1982 – WORKING FORMULATION
- 1994 – REVISED EUROPEAN-AMERICAN CLASSIFICATION OF LYMPHOID NEOPLASMS
- 2008 – WHO CLASSIFICATION OF TUMORS OF HEMATOPOIETIC AND LYMPHOID TISSUES, 4TH EDITION, OCTOBER 2008
- 2016 – REVISION TO 4TH EDITION, 2017

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
THE 2010 HEMATOPOIETIC MPH RULES MANUAL AND THE HEMATOPOIETIC DATABASE
HTTPS://SEER.CANCER.GOV/SEERTOOLS/HEMELYMPH/

Hematopoietic and Lymphoid Neoplasm Database

Multiple Primaries Calculator
The Multiple Primaries Calculator was designed to be used with the coding manual. Follow the rules and workflow in the manual prior to using the calculator. Use the Multiple Primaries Calculator when the rules instruct you to do so. If you are working with cases diagnosed before 2010 use the ICD-O-3 Hematopoietic Primaries Table (PDF) instead. This calculator should only be used for cases where at least one of the diagnoses is from 2010 or forward.

Morphology Code 1   Morphology Code 2   Calculate

ICD-O-3 Morphology

9670/3   Acute bازيophilic leukemia
9675/3   Acute biphenotypic leukemia
9680/3   Acute erythroid leukemia
9681/3   Acute megakaryoblastic leukemia
9683/3   Acute monocytic and monocytic leukemia
9684/3   Acute myeloid leukemia with mixed lineage
9685/3   Acute myeloid leukemia with expression of CD34 or CD117
9686/3   Acute myeloid leukemia with maturation
9687/3   Acute myeloid leukemia with minimal differentiation

THE 2010 HEMATOPOIETIC MPH RULES MANUAL AND THE HEMATOPOIETIC DATABASE
HTTPS://SEER.CANCER.GOV/SEERTOOLS/HEMELYMPH/

Epidemiology and Mortality
Age: 70 years and older age in children and adults less than 30.
9092/3: 10% of population in stage II, stage III, and stage IV.
9093/3: 5% of population in stage II, stage III, and stage IV.
9094/3: 20% of population in stage II, stage III, and stage IV.
9095/3: 50% of population in stage II, stage III, and stage IV.
9096/3: 70% of population in stage II, stage III, and stage IV.

Signs and Symptoms
Anemia
Bowel and skin lesions
Cytopenia
Diabetes mellitus
Fatigue
Fever
Hematopoietic malignancies
Infection
Inflammation
Lymphadenopathy
Neutropenia
Nausea
Night sweats
Numbness
Obstructive jaundice
Pallor
Pancytopenia
Pneumonia
Polycythemia
Pruritus
Rash
Retroperitoneal fibrosis
Splenomegaly
Stomatitis
Thrombocytopenia
Tuberculosis
Urticaria
Vomiting
Weight loss
Xerostomia

Diagnostic Exams
Blood and urine chemistries, studies
Bone marrow aspirate and biopsy
Chest x-ray and CT scan
Complete blood count
Diagnosis
Histology
Immunophenotyping
Immunohistochemistry
Magnetic resonance imaging
Medication
Pathology
PET scan
Surgical biopsy
Tissue analysis
Transcranial ultrasound
Ultrasound
USG

The International Staging System for Multiple Myeloma Staging
I. Amount of monoclonal (k or lambda) protein (g/L) protein in serum
2. Various clinical parameters such as hemoglobin and serum calcium.
3. Bone involvement on bone scan.
4. Presence or absence of renal failure.
5. Stage II
6. Stage IV

Treatment
- Treatment of myeloma is based on the disease's aggressiveness.
- For patients with symptoms and advanced disease.
- Induction therapy
- Consolidation therapy
- Maintenance therapy
- Transplantation

Diagnostic Methods
- Bone marrow protein
- Bone marrow biopsy
- Cytogenetics
- Immunophenotyping
- Peripheral blood smear
- Genetics Data

Definition
Myeloma cells are at least 10% of the plasma cells.
2016 REVISION OF THE WHO CLASSIFICATION
MYELOID NEOPLASMS & ACUTE LEUKEMIA

THE UPDATED WHO CLASSIFICATION OF HEMATOLOGICAL MALIGNANCIES

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

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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):2391-2409)

INTEGRATING GENETIC DATA INTO CLASSIFICATION

![Diagram showing different levels of integration of genetic data into the clinicopathological classification of hematologic malignancies.

Figure 2. Different levels of integration of genetic data into the clinicopathological classification of hematologic malignancies.]
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.
CHRONIC MYELOID NEOPLASMS

MPN  MPN/MDS  MDS

proliferation  effective hematopoiesis
cytophilsia  ineffective hematopoiesis

MYELOPROLIFERATIVE NEOPLASMS

Myeloproliferative neoplasms
Chronic myeloid leukaemia, BCR-ABL 1-positive
Chronic neutrophilic leukaemia
Polycythaemia vera
Primary myelofibrosis
Prefibrotic pre-myelofibrosis
Overt primary myelofibrosis
Essential thrombocythaemia
Chronic eosinophilic leukaemia, not otherwise specified
Myeloproliferative neoplasm, unclassifiable

Mastocytosis—now has its own group
MYELOPROLIFERATIVE NEOPLASMS

New WHO Classification Group

Mastocytosis
- Cutaneous mastocytosis
- Systemic mastocytosis
- Mast cell sarcoma

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
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

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
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 fibrosis
Myelodysplastic syndrome with isolated del(5q)
Myelodysplastic syndrome, unclassifiable
Childhood myelodysplastic syndrome
Refractory cytopenia of childhood

Myelodysplastic syndromes (MDS)

NEW

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

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
MYELOID NEOPLASMS WITH
GERMLINE PREDISPOSITION

Myeloid neoplasms with germline predisposition
Myeloid neoplasms with germline predisposition without a
pre-existing disorder or organ dysfunction
Acute myeloid leukaemia with germline
CEBPα mutation
Myeloid neoplasms with germline DDIT4 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

Somatic mutations
• Occur in nongermline tissues
• Cannot be inherited

Germline mutations
• Present in egg or sperm
• Can be inherited
• Cause cancer family syndrome

Nonheritable
Mutation in tumor only
(for example, breast)

Heritable
Mutation in egg or sperm
All cells affected in
offspring

ACUTE MYELOID LEUKEMIA AND
RELATED (MYELOID) PRECURSOR NEOPLASMS

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); CBFβ-AML1
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)(q21.3;q26.2) or
t(3;3)(q21.3;q26.2); GATA2-MECOM
Acute myeloid leukaemia (megakaryoblastic) with
t(1;22)(p13.3;q13.1); RBM15-MLL1
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

Acute myeloid leukaemia with myelodyplasia-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

AML, NOS

Myeloid proliferations not associated with Down syndrome
Transient abnormal myelopoiesis not associated with
Down syndrome
Myeloid leukaemia associated with Down syndrome
BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM

- "BLASTIC" IS THE KEY – LEUKEMIC PHASE

CORRESPONDING LYMPHOID GROUP IS "HISTIOCYTIC AND DENDRITIC CELL NEOPLASMS"

ACUTE LEUKEMIA OF AMBIGUOUS LINEAGE

- Natural killer (NK)-cell lymphoblastic leukemia/lymphoma
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
PRECURSOR LYMPHOID NEOPLASMS

Precursor lymphoid neoplasms
- B-lymphoblastic leukaemia/lymphoma, not otherwise specified
- B-lymphoblastic leukemia/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(11q22.3); 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 hypo diploidy
  - B-lymphoblastic leukaemia/lymphoma with t(16;14)(q31.1;q32.1); IGHV/LJ
  - B-lymphoblastic leukaemia/lymphoma with t(1;19)(q23;p13.3); TOFI-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

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

MATURE B-CELL NEOPLASMS

Mature B-cell neoplasms
- Chronic lymphocytic leukaemia/
  - Small lymphocytic lymphoma
  - Monoclonal B-cell lymphocytosis
- B-cell prolymphocytic leukemia
- 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
- Lymphoplasmacytoid lymphoma
- IgM Monoclonal gammopathy of undetermined significance

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
- Paratrabecular plasmacytoma
- Solitary plasmacytoma of bone
- Extramedullary plasmacytoma
- Monoclonal immunoglobulin deposition diseases
- Primary amyloidosis
- Light chain and heavy chain deposition diseases
- Plasma cell neoplasms with associated paraneoplastic syndrome
- POEMS syndrome
- TEMI syndrome
MATURE B-CELL NEOPLASMS

...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

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 germinotrophic lymphoproliferative disorder
Burkitt lymphoma
Burkitt-like lymphoma with t(11q) aberration
VIRUS-ASSOCIATED LYMPHOID NEOPLASMS

<table>
<thead>
<tr>
<th>Infectious Agent</th>
<th>Lymphoid Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epstein-Barr virus</td>
<td>Burkitt's lymphoma</td>
</tr>
<tr>
<td></td>
<td>Post-organ transplant lymphoma</td>
</tr>
<tr>
<td></td>
<td>Primary CNS diffuse large B cell lymphoma</td>
</tr>
<tr>
<td></td>
<td>Hodgkin's disease</td>
</tr>
<tr>
<td></td>
<td>Extramedullary NK/T cell lymphoma, nasal type</td>
</tr>
<tr>
<td>HTLV-I</td>
<td>Adult T cell leukemia/lymphoma</td>
</tr>
<tr>
<td>HIV</td>
<td>Diffuse large B cell lymphoma</td>
</tr>
<tr>
<td></td>
<td>Burkitt's lymphoma</td>
</tr>
<tr>
<td>Hepatitis C virus</td>
<td>Lymphomatoid papillomatous lymphoma</td>
</tr>
<tr>
<td>Helicobacter pylori</td>
<td>Gastric MALT lymphoma</td>
</tr>
<tr>
<td>HHV 8</td>
<td>Primary effusion lymphoma</td>
</tr>
<tr>
<td></td>
<td>Multicentric Castleman's disease</td>
</tr>
</tbody>
</table>

Harrison's Principles of Internal Medicine, 17th Edition

MATURE B-CELL NEOPLASMS

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

NEW

Morphology

Blasoid  BL  DLBCL/BL  DLBCL

Phenotype & cytogenetics

TdT+  TdT-, cyclin D1+

Diagnosis

B-LBL  HGBL, NOS  BL  HGBL, with MYC and BCL2 and/or BCL6
MATURE T- AND NK-CELL NEOPLASMS

Mature T- and NK-cell neoplasms
- T-cell polymorphic lymphocytic leukemia
- T-cell large granular lymphocytic leukemia
- Chronic lymphoproliferative disorder of NK cells
- Aggressive NK-cell leukemia
- EBV-positive T-cell and NK-cell lymphoproliferative disease 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
- Extramedullary NK/T-cell lymphoma, nasal type
- Intestinal T-cell lymphoma
- Enteropathy-associated T-cell lymphoma
- Monomorphic epitheliod T-cell lymphoma
-estinal T-cell lymphoma, NOS
- Incident T-cell lymphoproliferative disorder of the gastrointestinal tract
- Hepatosplenic T-cell lymphoma

Subcutaneous panniculitis-like T-cell lymphoma
- Mycosis fungoides
- Silitary 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 CDB-positive aggressive epidermotropic cytotoxic T-cell lymphoma
- Primary cutaneous alpha 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

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
IMMUNODEFICIENCY-ASSOCIATED LYMPHOPROLIFERATIVE DISORDERS

HISTIOCYTIC AND DENDRITIC CELL NEOPLASMS

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

Bone Marrow
Circulation
Stem Cell
2018 MYELOID NEOPLASMS – REQUIRED SSDI

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

STAGING LYMPHOID NEOPLASMS

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

• DO NOT CODE MINOR SYMPTOMS AS “B” SYMPTOMS
EXTRANODAL LYMPHOMA – MODIFIED ANN ARBOR STAGING

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
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.

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
### 2018 LYMPHOID NEOPLASMS – REQUIRED SSDI

<table>
<thead>
<tr>
<th>Test</th>
<th>Chapters</th>
<th>All Lymphoma</th>
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<tbody>
<tr>
<td>B Symptoms</td>
<td>75, 80</td>
<td></td>
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<tr>
<td>HIV Status</td>
<td>75, 80</td>
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<tr>
<td>NCCN International Prognostic Index (IPI)</td>
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### 2018 CUTANEOUS LYMPHOMA – REQUIRED SSDI

<table>
<thead>
<tr>
<th>Test</th>
<th>Chapter 81: Primary Cutaneous Lymphomas: MF/SS Required for Staging</th>
<th>P Site: C44.9, C51, C60, C63.2 Histology: 9597, 9680, 9700, 9701, 9708, 9709, 9712, 9718, 9719, 9726, 9727</th>
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<tbody>
<tr>
<td>Peripheral Blood Involvement</td>
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2018 PLASMA CELL NEOPLASMS – REQUIRED SSDI
R-ISS STAGING

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

<table>
<thead>
<tr>
<th>High Risk Cytogenetics</th>
<th>Chapter 82: Plasma Cell Myeloma Required for Staging (R-ISS)</th>
<th>9731, 9732, 9734 Only</th>
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<tbody>
<tr>
<td>Serum Albumin Pretreatment Level</td>
<td>Chapter 82: Plasma Cell Myeloma Required for Staging (R-ISS)</td>
<td>9731, 9732, 9734 Only</td>
</tr>
<tr>
<td>Serum Beta-2 Microglobulin Pretreatment Level</td>
<td>Chapter 82: Plasma Cell Myeloma Required for Staging (R-ISS)</td>
<td>9731, 9732, 9734 Only</td>
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<tr>
<td>Serum LDH (Lactate Dehydrogenase) Pretreatment Lab Value</td>
<td>Chapter 82: Plasma Cell Myeloma Required for Staging (R-ISS)</td>
<td>9731, 9732, 9734 Only</td>
</tr>
</tbody>
</table>

**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.

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.
2018 CLL/SLL – REQUIRED SSDI RAI STAGING

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Chapter 79: CLL/SLL only (AJCC ID 79.5)</th>
<th>5823 Only</th>
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<tr>
<td>Thrombocytopenia</td>
<td>Required for staging (RAI)</td>
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<tr>
<td>Adenopathy</td>
<td>Chapter 79: CLL/SLL only (AJCC ID 79.5)</td>
<td>5823 Only</td>
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<tr>
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<tr>
<td>Anemia</td>
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<td>Lymphocytosis</td>
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<td>Organomegaly</td>
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<td></td>
<td>Required for staging (RAI)</td>
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</table>

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 V.5.2017
- 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
QUESTIONS