Navigating Heme-Lymph Manual & Database

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ICR Video Training Series | Iowa Cancer Registry

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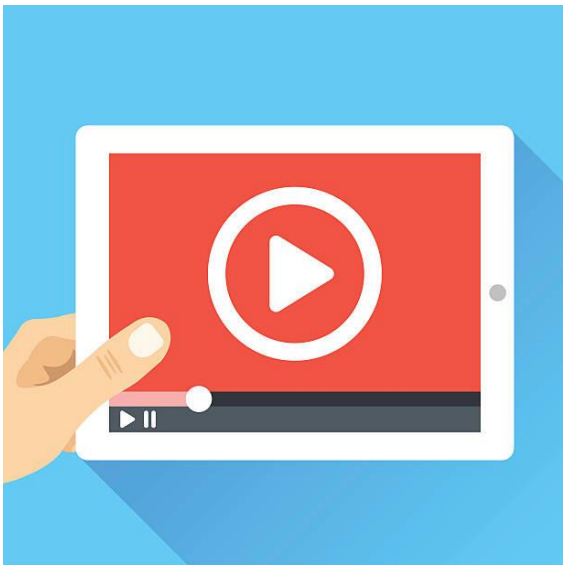


Location:

- Overall Hematopoietic Project:
  https://seer.cancer.gov/tools/heme/
- Heme/Lymph Manual:
  https://seer.cancer.gov/tools/heme/Hematopoietic_Instructions_and_Rules.pdf
- Heme/Lymph Database:
  https://seer.cancer.gov/seertools/hemelymph/
- Change log:
  https://seer.cancer.gov/tools/heme/update.html
  - No changes 2023 or 2024

Steps for Using Heme DB and Manual

1. Identify working (preliminary) histology code(s)
2. Search Heme DB using any of these ways:
   - Unique word
   - Complete name (histology)
   - Mark "Show Alternate Names"
   - Histology code
3. Use MP Rules to determine the number of primaries based on working histology
4. Verify or revise working histology using PH Rules
5. Determine primary site and histology rules

3

3

Step 1:
Identify working histology code

a. Search the Heme DB

b. "Show Alternate Names": This box appears under the Search box. If this box is checked, the results will include an additional column that shows where alternate names include the words being search

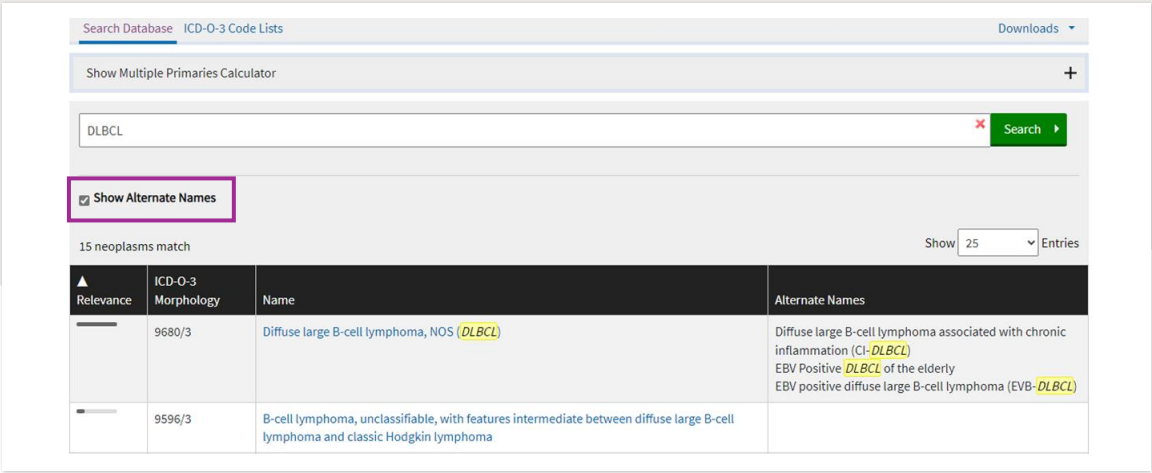
c. Search on histology code if desired, i.e., 9867/3.

d. When multiple results are displayed, click on the desired term (e.g. acute myelomonocytic leukemia) to display the record.

4

4

Heme DB



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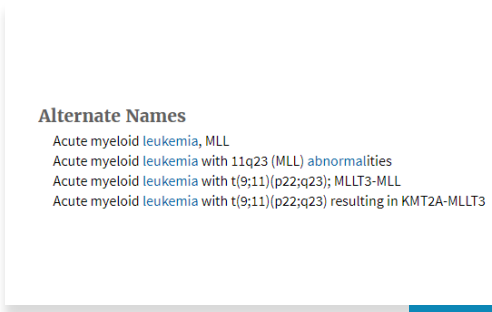
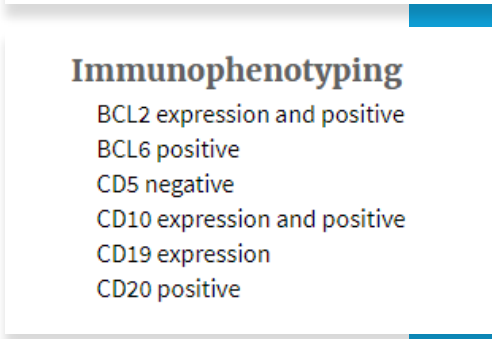
Navigating Database - Search

- Search:
  - Term or code from appendix B
    - Acronyms or Genetics
      - RAEB
      - (p23;q34.1)
  - Alternate names in database
    - Not all parts of genetic string are necessary
      - 9897/3
  - Genetics Data or Immunophenotyping
    - Terms positive or expression mean the same thing per Dr. Nashelsky



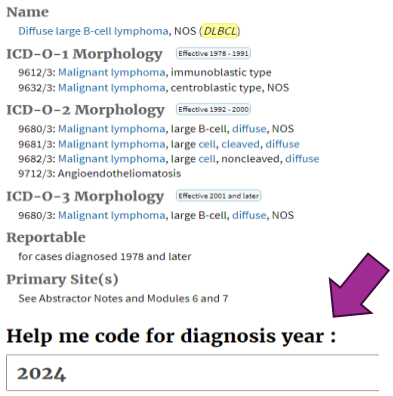


6

6

Heme DB

- Name: preferred term in Heme DB
- Morphology:
  - ICD-O-3 Histology code
    - Many heme histologies have more specific variants that rely on genetic variants
  - ICD-O-1 and ICD-O-2 is for historical reference
- Reportable: whether or not histology is reportable and for what years
- Primary site: assist with determining which module to use to assign site
- Help me code for Dx Year: Provides specific notes based on year of Dx

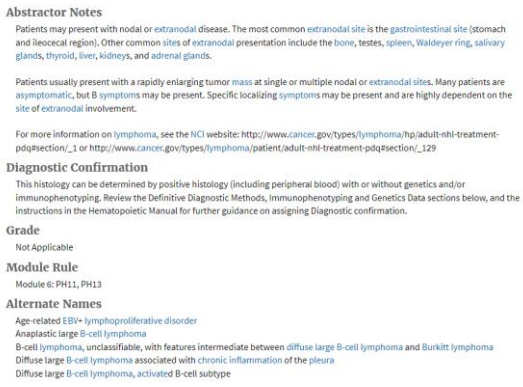


7

7

Heme DB

- Abstractor Notes: Helpful hints for coding
  - More specific histologies to consider
  - Carefully review these notes
- Diagnostic Confirmation: types of tests used to determine histology
- Grade: notes for coding grade; often not applicable
- Module Rule: appropriate module for site/histology
- Alternate Names: terms should be considered the same histology

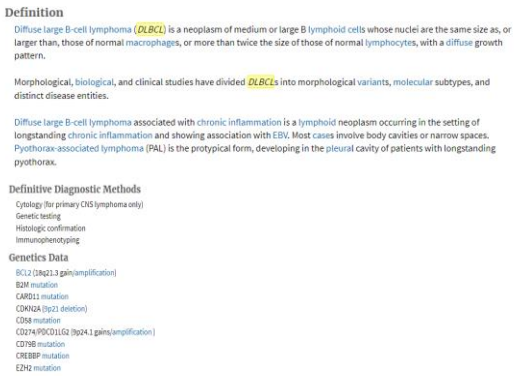


8

8

Heme DB

- Definition: explains what this particular type of neoplasm is
- Definitive Dx Methods: helps with coding dx confirmation
- Genetics Data: list of genetic tests used to assign the specific histology
  - Helps registrars know what to look for in pathology report



Definition

Diffuse large B-cell lymphoma (*DLBCL*) is a neoplasm of medium or large B lymphoid cells whose nuclei are the same size as, or larger than, those of normal macrophages, or more than twice the size of those of normal lymphocytes, with a diffuse growth pattern.

Morphological, biological, and clinical studies have divided *DLBCL*s into morphological variants, molecular subtypes, and distinct disease entities.

Diffuse large B-cell lymphoma associated with chronic inflammation is a lymphoid neoplasm occurring in the setting of longstanding chronic inflammation and showing association with EBV. Most cases involve body cavities or narrow spaces. Pyothorax-associated lymphoma (PAL) is the protypical form, developing in the pleural cavity of patients with longstanding pyothorax.

Definitive Diagnostic Methods

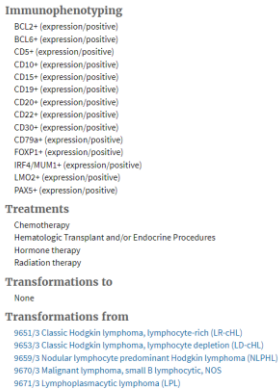
Cytology (for primary CNS lymphoma only)
Genetic testing
Histologic confirmation
Immunophenotyping

Genetics Data

BCL2 (18q21.3 gain/amplification)
B2M mutation
CARD11 mutation
CDKN2A (9p21 deletion)
CD58 mutation
CD274/PDCD1LG2 (9p24.1 gains/amplification)
CD79B mutation
CREBBP mutation
EZH2 mutation

Heme DB

- Immunophenotyping: lists immunophenotyping used to assign specific histology
  - Helps registrars know what to look for
- Treatments: NCCN guidelines, standard of care
- Transformation to: describes more acute histologies/transformations
- Transformation from: describes more chronic histologies/transformations



Immunophenotyping

BCL2+ (expression/positive)
BCL6+ (expression/positive)
CD5+ (expression/positive)
CD10+ (expression/positive)
CD15+ (expression/positive)
CD19+ (expression/positive)
CD20+ (expression/positive)
CD22+ (expression/positive)
CD30+ (expression/positive)
CD79a+ (expression/positive)
FOXP1+ (expression/positive)
IRF4/MUM1+ (expression/positive)
LMO2+ (expression/positive)
PAX5+ (expression/positive)

Treatments

Chemotherapy
Hematologic Transplant and/or Endocrine Procedures
Hormone therapy
Radiation therapy

Transformations to

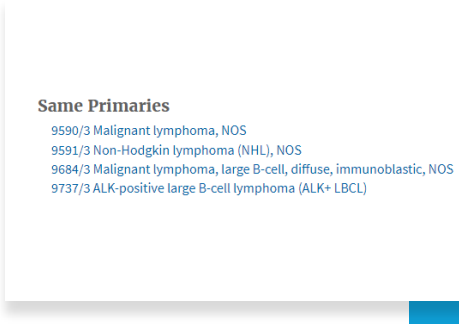
None

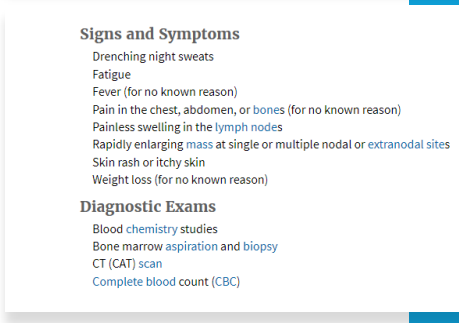
Transformations from

9651/3 Classic Hodgkin lymphoma, lymphocyte-rich (LR-cHL)
9653/3 Classic Hodgkin lymphoma, lymphocyte depletion (LD-cHL)
9659/3 Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL)
9670/3 Malignant lymphoma, small B lymphocytic, NOS
9671/3 Lymphoplasmacytic lymphoma (LPL)

Heme DB

- Same Primaries: suggests alternate names/equivalent histologies
- Signs/Symptoms: details signs and symptoms that are common for this histology
- Diagnostic Exams: typical workup and tests performed for this histology





11

11

Step 2: Use MPH Rules

Start with **rule M1**, move through the rules in consecutive order and **stop at the first rule that applies**. The M rule references in the Heme DB are to be used as a guide only.

Use the Hematopoietic Multiple Primaries Calculator in the Heme DB **only when instructed** by the rules in the Hematopoietic Manual.

12

12

General Instructions for Multiple Primary Rules

1. Start with **M1** for each case, move through rules and stop at the first rule that applies. Use the M rule references in Heme DB as a guide only.
2. Within these rules, the term "chronic neoplasm" means that a neoplasm has the potential to transform into another, more acute neoplasm.
3. Common to have provisional diagnosis or several provisional (differential) NOS diagnoses that lead to more testing and a more specific dx. **These are not multiple primaries, just steps in the diagnostic workup.**
4. The Heme DB Multiple Primaries Calculator is to be used **only** when instructed to do so.

13

13

MP Rules

M1 - SINGLE
- Minimal information (path only; DCO)

M2 – SINGLE
- Single histology (See exceptions/notes in manual)

M3 – SINGLE
- Sarcoma diagnosed simultaneously or after a leukemia of same lineage (See manual)

M4 – SINGLE
- 2+ types of NHL simultaneously present in SAME anatomic location (See manual for notes)

14

14

MP Rules

M5 – SINGLE
- Both HL and NHL SAME time and SAME location

M6 – MULTIPLE
- HL in one location and NHL in another

M7 – SINGLE
- More specific histology **AFTER** an NOS histology when MP Calculator confirms same primary

15

15

MP Rules

M8 – SINGLE
- Chronic & acute diagnosed same time or within 21 days **AND** only ONE positive bx

M9 – SINGLE
- Chronic & acute diagnosed same time or w/in 21 days **AND** not documentation on bx

M10 – MULTIPLE
- Original dx chronic **AND** second dx of acute more than 21 days after chronic

M11 – MULTIPLE
- Chronic & Acute dx same time or w/in 21 days **AND** document 2 bx

16

16

MP Rules

M12 – SINGLE
- Orig dx acute **AND** reverts to chronic more than 21 days after **AND** no confirmation of treatment for acute

M13 – MULTIPLE
- Orig dx acute **AND** reverts to chronic AFTER treatment

M14 – SINGLE
- PTLD same time as any B-cell lymphoma, T-cell lymphoma, HL, or plasmactyome/myeloma

M15 – MP Calculator determines single or multiple
- Rule of last resort – go through rules again to be sure

17

17

Step 3:
Use PH Rules to verify or revise histology

When the PH rules lead you to a different histology code, **enter that code** in the **Heme DB** search box and display the record for that histology

The PH rules referenced in the Heme DB are the most common rule(s) used to code Primary Site and Histology for the selected histology. **More than one Module/PH Rule may be needed** to code Primary Site and Histology.

18

18

PH Coding Rules

1. Rules in 9 modules. Each module covers group of related heme or lymph neoplasms. May find neoplasm in more than one module.
2. Modules are not hierarchical. Rules within each module are in order. Apply rules in each module in order. Stop at the first rule that applies.

19

19

PH Modules

Module	PH Rules	Histology
Module 1	**PH1**	Post-Transplant Lymphoproliferative Disorder (PTLD) for 2010-2020 only.
Module 2	**PH 2-4**	Plasmacytomas (9734/3) (9731/3)
Module 3	**PH 5-6**	CLL/SLL (9823/3)
Module 4	**PH 7-8**	Leukemia/Lymphoma (numerous histologies)
Module 5	**PH 9-10**	Myeloid neoplasms (numerous histologies) Mast Cell Neoplasms (9740/3) (9742/3) (9930/3)
Module 6	**PH 11-17**	NHL (numerous histologies)
Module 7	**PH18-27**	Hodgkin Lymphomas; NHL; Extraosseous plasmacytomas etc (numerous)
Module 8	**PH28-29**	NOS and more specific Histology All heme and lymph neoplasms 9590/3-9993/3
Module 9	**PH30-31**	All. Use only when Modules 1-8 are not applicable

20

20

Step 4: Determine primary site

a. See Primary Site Coding Instructions.

b. For certain histologies, only one primary site code is displayed in the Heme DB

- i. The primary site code displayed under Primary Site(s) is the only site code to be used for that histology

c. When there is no primary site code listed under Primary Site(s) in the Heme DB

- i. Review the Primary Site Text field for common primary sites or other primary site instructions and rules.
- ii. Search the Hematopoietic Manual and/or database to find applicable modules.
- iii. Read the Abstractor Notes to find other information regarding sites of involvement for stages II, III, and IV lymphomas. Use the Abstractor Notes to confirm that the site/histology combination indicated by the involvement documented in the medical record is probable. You may also seek a physician's help in determining the primary site.

21

21

Primary Site Instructions

1. Use these instructions, PH Rules and Heme DB to code primary site.
2. Do not use these primary sites for heme neoplasms:
   a) C423 Reticuloendothelial system, NOS
   b) C424 Hematopoietic system, NOS
3. Heme DB gives primary site:
   a) Use the specific site code listed, when applicable
   b) Primary site text field provides additional info
4. Code primary site using:
   a) Scans
   b) Medical record documentation
   c) Path report
   d) Heme DB

22

22

Primary Site Instructions

5. Secondary involvement of distant LNs (extranodal lymphoma,) bone marrow, liver, spleen or CNS are included in staging fields only. Disregard secondary involvement for purpose of coding primary site.

6. Code primary site as indicated on pages 36-40 for each category of disease.

Primary Site

- Per Jennifer Ruhl: Not all sites of involvement are used to assign primary sites. Some sites of disease may be metastatic.
- Module 7 (PH18-PH27)
- Note 2: **Do not simply code the site of a biopsy**; use the information available from imaging to determine the correct primary site
- Note 3: Secondary involvement of distant lymph nodes (for an extranodal lymphoma), bone marrow, liver, spleen or CNS are included in the stage fields only. This secondary involvement excludes rare primary lymphoid neoplasms of spleen, multifocal lung involvement, liver or CNS (see PH Rules). **Secondary involvement of distant site(s) is disregarded for the purpose of coding primary site.** For lymphoid neoplasms, this secondary or distant involvement is akin to metastasis for solid tumors and does not alter the primary site assigned by the physician or determined using the PH Rules.

Histology Instructions

1. Code histology identified by Definitive Diagnostic Method(s) (may be any of following) and no hierarchy to this list:
   a) Clinical dx
   b) Genetic test
   c) Immunophenotyping
   d) Cytology
   e) Pathology (final dx, comment on final dx, addendum, CAP protocol/synoptic report)
2. When tests or reports defined as DDM are **NOT AVAILABLE** use this hierarchy:
   a) Documentation in med rec referring to original scans, genetic testing, immunophenotyping, or path report
   b) Documentation in med rec that refers to histology

25

25

Histology Instructions

3. When test or report lists a specific histology with ambiguous term and an NOS histology, **code the NOS histology.**

   ***Note 1*:** Ambig used for reportability

   ***Note 2*:** Ambig terms may not be used when specific histology has not been confirmed. If no further info re more specific histology, assign NOS.

   See notes and examples

26

26

Histology Instructions

4. If one histology preceded by ambig term, review abstractor notes in Heme DB, look for other info to confirm dx.

Example: CBC states abnormal lymphocytosis, no histology or provisional diagnosis on the CBC or peripheral blood smear. Flow cytometry states **compatible with CLL**. No other workup done. Per the Abstractor Notes in the database, "abnormal lymphocytosis" is present in CLL. Assign histology CLL (9823/3) since "abnormal lymphocytosis" is part of the CLL/SLL definition.

5. If relevant immunophenotyping or genetics is present in abstractor notes and the only histology preceded by ambig term, code ambig term so case can be reported for incidence.

27

27

Step 5: Determine Grade

Note: Grade is **no longer collected** for cases **diagnosed 1/1/2018+**

Cases diagnosed 2010-2017:

a. See the Grade field in the Heme DB

b. See the Grade rules in the manual when grade cannot be coded using the Heme DB

28

28

Diagnostic Confirmation

Diagnostic Confirmation

Note 1: Microscopic confirmation (codes 1-4) take priority over clinical dx (codes 5-8). There is no other hierarchy for coding Dx confirmation.

Note 2: use code 1 when ONLY tissue, bone marrow, or blood was used to diagnose specific histology.

Note 3: Originally confirmed by histology (code 1) and later has immunophenotyping, genetic testing, or JAK2 which confirms a more specific neoplasm and no evidence of transformation, change histology to more specific and code 3 Dx confirmation

Diagnostic Confirmation

Description	Type of examination	Notes	Code
Positive histology	Tissue from LN, organ(s), or other tissue specimens; Bone marrow; Peripheral blood smear (9590-9993)	**Leukemia ONLY** (9800-9948) includes: • CBC • WBC • Immunophenotyping/JAK2 not done **OR** done but negative	**1**
Positive cytology	Exam of fluid ***Rare for heme/lymph***	Specimen fails to provide enough tissue to do histology exam	2
Positive histology + Immunophenotype/ Genetic testing	Tissue specimen and positive immunophenotyping, genetic testing, of JAK2 confirm	Dx 2010+ **Immuno or genetic test confirm neoplasm or more specific histology** See *Notes* in manual	**3**
Positive microscopic confirmation NOS	Unknown ***Rare for heme/lymph***	Microscopically confirmed but type is unknown	4

31

31

Diagnostic Confirmation

Description	Type of Examination	Notes	Code
Positive lab test/marker study	Definitive dx method: lab test, tumor marker, genetics, immunophenotyping	Do **NOT** assign if there is histologic confirmation	**5**
Direct visualization w/out micro confirm	Op report – no bx or cyto ***Rare for heme/lymph***		6
Radiation/Imaging w/out micro confirm	Imaging diagnosis only ***Rare for heme/lymph***	No microscopic exam Could be **lymphoma** diagnosis	**7**
Clinical diagnosis	Physician statement	**NOT** codes 5-7 No microscopic or immuno/genetic confirmation of diagnosis Based on physician expertise	**8**
Unknown	DCO; unknown if dx microscopically; historical cases	No information on how the histology was diagnosed	9

32

32

Case Reportability Instructions

33

Reportability Instructions

1. Search the Heme DB to determine case reportability.
2. Report all cases with morphology code 9590-9993 with /3 behavior.
3. Report heme and lymph neoplasm with morphology 9590-9993 listed as /1 that are described as malignant by physician. **Note: Do not report in situ (/2) lymphomas.**
4. Report the case when dx is preceded by ambiguous terms
   - Pertains to reportability/casefinding ONLY
   - See histology instructions 3-5 for assigning histology w/ ambiguous term

34

"Consistent With"

- "Consistent with" is historically and currently considered ambiguous terminology
  - Becoming the standard of reporting Heme diagnoses
- For Heme Neoplasms **ONLY**
  - "Consistent with" is a definitive diagnosis
  - This is **NOT** an ambiguous term

35

35

Reportability Instructions

5. Report case when patient is treated for reportable neoplasm
6. Report case when there is a clinical diagnosis (physician's statement) of reportable heme/lymph neoplasm
7. Report case when a reportable diagnosis appears in any text or report described as definitive diagnostic method

36

36

Transformation

Transformations

- Certain hematopoietic neoplasms can “transform” to a more serious/acute histology
- Don’t be fooled by “Chronic” or “Acute” in certain histology names
  - This can refer to indolence vs. aggressiveness of the cancer
- Heme DB will indicate histologies that can transform under “Transform from” or “Transform to”
- Not all “chronic” cells/diseases will transform at once
  - Use appropriate timing MP rules to determine number of primaries
  - Some acute diseases can become chronic over time

Transformations

- **Transformation <u>to</u>**
  Chronic → Acute
- **Transformation <u>from</u>**
  Chronic ← **Acute**

39

Transformations

CLL/SLL - Chronic

Transformations to

9680/3 Diffuse large B-cell lymphoma, NOS (DLBCL)

Transformations from

None

Same Primaries

9590/3 Malignant lymphoma, NOS
9591/3 Non-Hodgkin lymphoma (NHL), NOS
9670/3 Malignant lymphoma, small B lymphocytic, NOS
9761/3 Waldenstrom macroglobulinemia (WM)
9800/3 Leukemia, NOS
9820/3 Lymphoid leukemia, NOS

DLBCL - Acute

Transformations to

None

Transformations from

9651/3 Classic Hodgkin lymphoma, lymphocyte-rich (LR-cHL)
9653/3 Classic Hodgkin lymphoma, lymphocyte depletion (LD-cHL)
9659/3 Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL)
9670/3 Malignant lymphoma, small B lymphocytic, NOS
9671/3 Lymphoplasmacytic lymphoma (LPL)
9675/3 Malignant lymphoma, mixed small and large cell, diffuse
9688/3 T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL)
9689/3 Splenic marginal zone lymphoma (SMZL)
9690/3 Follicular lymphoma (FL), NOS
9691/3 Follicular lymphoma, grade 2
9695/3 Follicular lymphoma, grade 1
9698/3 Follicular lymphoma, grade 3
9699/3 Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
9761/3 Waldenstrom macroglobulinemia (WM)
9762/3 Heavy chain desposition disease
9766/3 Lymphomatoid granulomatosis grade (LYG) 3
9823/3 Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)
9940/3 Hairy cell leukemia (HCL)

40

Appendices A-D

Appendix	
A	History of Hematopoietic and Lymphoid Neoplasm Coding
B	WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues | Histology Lineages
C	Lymph Node/Lymph Node Chain Reference Table
D	Introduction to Genetic Nomenclature

41

41

Table B6: Acute Myeloid Leukemia (AML) and Related Precursor Neoplasms

WHO Preferred Term	ICD-O
Acute myeloid leukemias with recurrent genetic abnormalities	
Acute myeloid leukemia (megakaryoblastic) with t(1;22)(p13.3;q13.1); *RBM15-MKL1*	9911/3
Acute myeloid leukemia with *BCR-ABL1* (2021)+	9912/3*
Acute myeloid leukemia with biallelic mutation of *CEBPA* (2021+)	9878/3*
Acute myeloid leukemia with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2, MECOM*	9869/3
Acute myeloid leukemia with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*	9871/3
Acute myeloid leukemia with mutated *NPM1* (2021+)	9877/3*
Acute myeloid leukemia with mutated *RUNX1* (2021+)	9879/3*

Appendix B – Histology Lineage

42

42

Table C1: Lymph Node/Lymph Node Chain Reference Table
***The right and left are separate regions per AJCC**

Lymph Node/Lymph Node Chain	Use for Multiple Primaries in Heme	ICD-O Lymph Node Region(s)	TNM Staging
Abdominal	C772	Intra-abdominal	Mesenteric
Anorectal (pararectal)	C775	Pelvic	Pelvic, right and left*
Anterior axillary (pectoral)	C773	Axilla or arm	Axillary, right and left*
Anterior cecal (prececal)	C772	Intra-abdominal	Mesenteric
Anterior deep cervical (laterotracheal, recurrent laryngeal, recurrent pharyngeal)	C770	Head, face and neck	Cervical, right and left*
Anterior jugular	C770	Head, face and neck	Cervical, right and left*
Anterior mediastinal	C771	Intrathoracic	Mediastinal
Aortic (ascending, lateral, lumbar, subaortic, NOS)	C772	Intra-abdominal	Para-aortic
Aortico-pulmonary window (subaortic)	C772	Intra-abdominal	Para-aortic
Apical (subclavian)	C770	Head, face and neck	Cervical, right and left*
Appendiceal	C772	Intra-abdominal	Mesenteric
Apical axillary (deep axillary, Level III axillary)	C773	Axilla or arm	Axillary, right and left*
Aselli's glands (nodes near pancreas)	C772	Intra-abdominal	Para-aortic
Auricular (infraauricular, postauricular, preauricalar, retroauricular, NOS)	C770	Head, face and neck	Cervical, right and left*
Axillary (anterior, brachial, deep, lateral, superficial, NOS)	C773	Axilla or arm	Axillary, right and left*
Axillary (Level I [low axillary, superficial axillary], Level II, Level III [apical, deep)	C773	Axilla or arm	Infraclavicular, right and left*
Azygos (lower paratracheal)	C771	Intrathoracic	Mediastinal
Brachial (lateral axillary)	C773	Axilla or arm	Axillary, right and left*
Brachiocephalic	C773	Axilla or arm	Axillary, right and left*

Appendix C: Lymph Node/Lymph Node Chain

43

Selected Types of Abnormalities/Mutations

Mutation Type	Abbreviation(s)	Description	Nomenclature Example(s)
Insertion *	ins	Addition of DNA into a gene.	ins(18;5)(q21.1;q31.2)
Deletion	del	Removal of DNA; may occur in one or more base pairs, entire gene(s), or chromosome arm (p or q).	del(5q); del(6q21)
Duplication *	dup	DNA abnormally copied one or more times.	dup(21); FLT3-ITD (Where ITD = internal tandem duplication)
Inversion	inv	Rearrangement within a single chromosome in which a chromosome segment undergoes breakage and rearrangement within itself.	inv(16); inv(3); inv(16)(p13.1;q22); inv(3)(q21;q26.2) (Sometimes described as a translocation between a single chromosome: t(16;16)(p13.1;q22))
Translocation	t(x;x) **	Rearrangement between two chromosomes in which a chromosome segment breaks off and attaches to a different chromosome.	t(9;22); t(8;21); t(9;22)(q34;q11.2); t(8;21)(q22;q22)
Trisomy	(XY, +x) **	An extra copy (three total copies) of the specified chromosome.	47(XY,+8); Trisomy 21; Gain of chromosome 9 (Sometimes these are referred to as just "Trisomy" or "Gain of" abnormalities without abbreviation or specific karyotype notation.)
Monosomy	(XY,-x) **	The presence of only one chromosome from the specified chromosome pair.	45(XY,-16); Monosomy 7; Loss of chromosome 5 (Sometimes these are referred to as just "Monosomy" or "Loss of" abnormalities without abbreviation or specific karyotype notation.)

* Uncommon as a sole genetic/molecular abnormality documented in heme/lymphoid neoplasms.

** Where lowercase "x" represents the chromosome number involved.

Appendix D Intro to Genetic Nomenclature

Pg 81-84 in Heme-Lymph Manual document

44

One bite at a time…

- Start with a working histology(ies)
- Determine number of primaries
- Primary Site
- Final Histology

45

45

SEER*Educate Cases

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- Training – Coding CEs
  - DX 2018-2025 Heme
    - Heme 2018-2025 Series 1: Cases 1-5

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46

46

Thank You!

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47