Deciphering the Heme Manual and Database

Jennifer Ruhl, MSHCA, RHIT, CCS, ODS-C

NCI-SEER

- Requestor: Can you talk on Hematopoietic?
- Me: Yes, what would you like me to discuss
- Requestor: Primary site
- Me: Anything specific regarding primary site?
- Requestor: No, just primary site

Agenda

- Primary site (focusing on lymphomas)
- Multiple primaries
- Histology
- Diagnostic confirmation (change coming)
- Treatment

Primary Site

Lymphoma Basics

- When determining the primary site/stage for a lymphoma
  - Imaging is CRITICAL
    - CT scans: Chest, Abdomen, Pelvis, Brain, MRI, PET
  - Terms that indicate involvement
    - Fixed, Matted, Palpable, Enlarged, shotty, lymphadenopathy
    - Masses in the hilum, mediastinum, retroperitoneum, and/or mesentery

  - Note: Do <u>not</u> apply these terms to Solid Tumors for staging purposes

Lymphoma Basics

- When assigning primary sites:
  - It's important to know what are the common primary sites for the histology you are looking at
    - Primary site information available in the database
    - Note: This doesn't mean you can't have an uncommon primary site
- Instruction #4, Note 1 (pg. 57 of 2026 manual)
  - Do not simply code the site of a lymph node biopsy, use the information available from scans to determine the correct primary site
  - As a reminder, many times with lymphomas, they will biopsy the most convenient location to get a diagnosis. This does not mean this is the primary site
  - Always check your imaging

Case Scenario from Ask a SEER Registrar: 1

- 2021 case I believe the primary site is skin RT thigh. The path report from the skin states consistent w/ NK T cell lymphoma. Bone marrow biopsy shows a NK T cell lymphoma . The imaging states infiltrative lesion soft tissues RT leg, inguinal , thoracic LN, lingula, RT tonsil, uvula….
  The DR is calling this a cutaneous T cell lymphoma, NK/T cell *origin (which also means, this is a NK-T-cell lymphoma involving the skin)*

  The histology is 9719/3: Extranodal NK-/T-cell lymphoma

  - Per the Hematopoietic Database under “Primary Site(s)”
    - Most common sites of involvement: upper aerodigestive tract (nasal cavity, nasopharynx, paranasal sinuses, palate) with the nasal cavity (C300) being the prototypic site of involvement

Case Scenario, cont., 1

- *Case assessment*
  - *Organs involved: Head and Neck (per imaging: lingula, RT tonsil, uvula), RT leg/Skin?*
  - *Lymph nodes: Inguinal, thoracic, cervical*
  - *Metastatic sites: Skin?*
- *Since two parts of the Head and Neck are confirmed (by imaging) to be involved, and there are regional lymph nodes invovled (cervical) best primary site would be C148: Overlapping sites of head and neck, pharynx*
- *PH25 applies: Code primary site when an organ and its regional lymph nodes are involved*
  - *This primary site would be in line with the primary site information for this histology*
  - *Inguinal and Thoracic LNs would be recorded in Mets at Dx-Distant Lymph Nodes*
  - *The skin involvement would be recorded in Mets at Dx-Other*
  - *This is a Stage IV lymphoma*

Lymphoma Basics

- Do not assume that your primary site is going to be C77-
  - A significant percentage of lymphomas have a primary site of C77-
- Lymphomas do originate in organs
- If there is no evidence of lymph node involvement from a biopsy or scan, then lymph nodes (C77-) cannot be your primary site

Coding Primary Site

- Code the primary site to lymph nodes of multiple regions (C778) (see Rule PH21) when:
  - Multiple lymph node regions, as defined by ICD-O, are involved
    - Imaging, or a physician may describe this as “lymph nodes above and below the diaphragm”
  - No organ involvement (except for common metastatic sites, which would be recorded in stage)

- If multiple lymph nodes are involved AND there is organ involvement
  - If the organ and its regional lymph nodes are involved, go to Rule PH25 and code primary site to the organ (lymph node involvement would be recorded in stage)

Case Scenario from Ask a SEER Registrar, 2

- Bone marrow biopsy: DLBCL
- PET: FDG avid left supraclavicular, mediastinal, and portacaval lymph nodes, as well as FDG avid splenomegaly suspicious for lymphoproliferative disorder

Case Scenario, cont., 2

- *Case Assessment*
  - *Organs: Bone marrow? Spleen?*
  - *Lymph nodes: supraclavicular, mediastinal, and portacaval lymph nodes*
  - *Possible metastatic sites: Bone marrow*

- *PH 21: Multiple lymph node regions involved*
- *Bone Marrow involvement recorded in Stage and Mets at Dx Other*
- *Spleen involvement ignored*

Case Scenario from Ask a SEER Registrar, 3

- PET Scan showed widespread FDG avid retroperitoneal and mesenteric lymphadenopathy suspicious for malignancy
- Patient was diagnosed with Mantle Zone Lymphoma on a bone marrow biopsy. Would I use Rule PH21 and code the primary site to C77.8? Or would I use Rule PH22 and code primary site to C77.9?

Case Scenario, cont. 3

- *Case Assessment:*
  - *Organs: Bone marrow?*
  - *Lymph Nodes: widespread retroperitoneal and mesenteric lymphadenopathy*
  - *Possible metastatic sites: Bone marrow?*

- *PH21 applies, code primary site to C778 due to widespread lymphadenopathy*
- *Bone marrow recorded in stage (Stage IV lymphoma) and Mets at Dx Other*

Case Scenario from Ask a SEER Registrar, 4

- Patient asymptomatic. Found to have enlarged neck nodes. CT scans confirmed diffuse lymph node involvement. Biopsy positive for SLL.
- Wait until patient became symptomatic to do bone marrow bx. Patient placed on Active Surveillance
- Became symptomatic, bone marrow biopsy done, positive for CLL
- Is the primary site C778 or C421 due to + bone marrow biopsy

Case Scenario, cont., 4

- *When patient was placed on active surveillance, the initial clinical work up stopped.*
  - *That means the positive bone marrow biopsy is not part of the clinical work up, so therefore the bone marrow cannot factor into primary site. Primary site stays C778*
- *The bone marrow would be recorded as progression/recurrence*
- *Any treatment given after bone marrow dx is second course*
  - *The 2026 Hematopoietic Manual does not cover this type of scenario. We are adding clarifications for the 2027 Manual, including an example like this question*
  - *This will be listed as an "**exception**" to the rule that all treatment until remission is achieved is first course*
  - *The reason for this exception is that there was NO initial treatment*

Proposed Updates to Module 7

- **Rule PH21: Multiple lymph node regions**
  - *See Rules PH22, PH24, PH25 if organs are involved*
  - *Code the primary site to lymph nodes of multiple regions (C778) when multiple lymph node regions are involved.* ***(Note: This is a DRAFT update, may look different when finalized)***

- Even though multiple lymph nodes may be involved, it isn't necessarily true that primary site would be C778.
  - You could have an organ and its regional nodes involved and remaining lymph nodes recorded in Mets at Dx-Distant Lymph nodes

Case Scenario from Ask a SEER Registrar, 5

- Follicular lymphoma of both fallopian tubes found during laparoscopic bilateral salpingectomy for elective permanent sterilization. Path report states: "Primary lymphoma of the fallopian tube" Staging imaging shows Mediastinal, retrocrural, mesenteric, retroperitoneal and pelvic adenopathy, consistent with lymphoma. Negative bone marrow biopsy.
  11/2024 Excision of right inguinal lymph node and retroperitoneal mass x2: All positive for follicular lymphoma.

- Registrars thinks C778 is applicable due to multiple lymph node regions involved.
- PH21 in its current form supports this, but is that correct?

Case Scenario, cont., 5

- *Case Assessment*
  - *Organ involvement: Fallopian Tube*
  - *Lymph Node Involvement: Mediastinal, retrocrural, mesenteric, retroperitoneal and pelvic*
    - *Retroperitoneal regional for Fallopian Tube*
  - *Possible Metastatic sites: None*

- *PH25 applies. Primary site is C570 (fallopian tube)*
  - *Fallopian tube (organ) and retroperitoneal lymph nodes involved (regional lymph nodes)*
  - *Remaining lymph nodes recorded in Mets at Dx: Distant Lymph Nodes*

Lymphoma Basics

- Code primary site to C779 (see Rule PH22) when
  - Lymph nodes and organ(s) are involved
    - If an organ and its regional lymph nodes are involved, then you would code primary site to that organ. If additional lymph nodes (distant for that organ) are also involved, these would be recorded in stage
  - Multiple organs and regional lymph nodes for all
  - Multiple organs and some combination of regional and distant nodes for the involved organs
  - Use this rule when there is no available information concerning where the lymphoma originated, such as historical cases
- No key words for this primary site

PH22

- Rule PH22: Lymph nodes, NOS *(if a single organ and its regional lymph nodes are involved, see PH25)* ***(Note: This is a DRAFT update, may look different when finalized)***

- **Before using this rule, determine if multiple organs are truly involved. When determining the number of organs, exclude the following: bone marrow, spleen and usual metastatic sites such as bone, brain, liver, lung (*See Primary site coding tips*). If these have been ruled out, apply this rule to….**

Case Scenario from Ask a SEER Registrar, 6

- Imaging shows a 10 cm mass involving the scapula with enlarged axillary lymph nodes, likely malignant. There are no other sites of disease, and no other lymphadenopathy. Biopsy of the scapula is positive for DLBCL. I believe the primary site should be C77.3 and Mets at Dx - Bone should be 1. Is this correct? Thank you very much.

Case scenario, cont. 6

- *Case assessment*
  - *Organ involvement: Scapula*
  - *Lymph nodes: Axillary*
  - *Possible metastatic sites: None*

- *PH22: One organ and lymph nodes involved that are not regional for that organ*
  - *Scapula part of Head and Neck, axillary lymph nodes are not regional for H&N*
  - *Primary site: C779*

Case from Ask a SEER Registrar, 7

- Radical prostatectomy, extranodal marginal zone lymphoma (MZL)
- Bone marrow and peripheral blood neg
- Cervical LN bx showed salivary gland tissue involved by extranodal MZL
- CT Neck: Indeterminate cervical chain lns, mass in parotid glad; mild to moderate rt axillary ALD

Case Scenario, cont., 7

- *Case assessment:*
  - *Organs involved: Prostate, Parotid*
  - *Lymph nodes: Cervical, Axillary*
  - *Possible Metastatic sites: None*

- *PH22: Multiple organs and lymph node regions involved*
  - *Two organs and two lymph node regions involved*
    - *Note: Even though the cervical lymph nodes are regional for parotid, you cannot use Rule PH25 since there is other non-metastatic organ involvement*
  - *Primary Site C779*

Primary Site Coding Instructions

- Spleen involvement
  - Splenomegaly or spleen **infiltration** does not mean that the lymphoma originated in the spleen. Infiltration refers to deposits of lymphoma or leukemia in the spleen because of the spleen filtering the blood.
  - Spleen involvement does NOT factor into primary site unless it is a splenic lymphoma
    - Splenic marginal zone lymphoma (9689/3), Hepatosplenic Lymphoma (9716/3)

- Spleen can factor into stage
  - Spleen involvement WITHOUT metastatic disease is Stage III

Primary Site Coding Instructions

- Bone marrow (BM) involvement
  - If ONLY BM involved, code primary site to bone marrow (C421)
  - If BM involved AND other organs and/or lymph nodes are involved, BM involvement is recorded in stage (always Stage IV)
- Reminder: if you have a BM biopsy that is positive
  - Look to see if the patient has a history of lymphoma
  - Review imaging to see if there is other involvement
  - Do not automatically assign BM as primary site

Bone marrow

- Be VERY CAREFUL with how you handle bone marrow biopsies with lymphomas
- Before determining you have a new primary, check your database to see if you have a previous lymphoma, or check the medical history
  - Bone marrow biopsies may indicate metastatic involvement and not be a new primary
  - For example,
    - 2020: Follicular lymphoma, NOS (LN biopsy) (C778, 9690/3)
    - 2025: NHL, NOS (Bone marrow biopsy) (C421, 9591/3)

Case Scenario from Ask a SEER Registrar, 8

- CTA A/P showed progressive splenomegaly.
- Patient had a bone marrow bx positive for Peripheral T-cell lymphoma, NOS & underwent splenectomy which was positive for Peripheral T-cell lymphoma, NOS.
- No lymphadenopathy observed throughout.
- Should the primary site be C809?

Case Scenario, cont., 8

- *Case assessment:*
  - *Organs involved: Spleen? Bone Marrow?*
  - *Lymph nodes involvement: None*
  - *Possible metastatic sites: Bone marrow?*

  - *PH26: Code to bone marrow when that is the only organ involved.*
    - *Reminder: Spleen involvement is ignored (See primary site coding instructions)*
    - *Note being added to PH26: May, or may not include spleen involvement*

Proposed Updates to Module 7

- **Rule PH18: Nodal Lymphomas described as a "mass"** ***and no other lymph node or organ involvement***
  - *If multiple lymph nodes involved, see Rule PH21 (moving from bullet 3)*
  - *If lymph node(s) AND organs are involved, see Rules PH22, 24, or 25*
    - *For this rule, organs does not apply to the spleen or the common metastatic sites: bone, brain, liver, lung, or bone marrow (see Primary Site Coding Instructions)*

- **Note: These changes are in DRAFT form (wording has not been finalized)**

Case Scenario Ask a SEER Registrar, 9

- 7/2024 Soft tissue mass inv. Right brachial plexus roots and extending into R lateral aspect of the spinal canal
- 8/2024 MRI Mild interval increase in size and volume of the large right neck mass extending from the right lateral aspect of the cervical spinal canal. No cervical or axillary lymphadenopathy.

  Bx of supraclavicular neck mass : marginal zone type lymphoma
- Can you confirm if the primary site is C770?

Case Scenario, cont., 9

- *Case assessment:*
  - *Organs involved: Brachial plexus (spinal canal)*
  - *Lymph nodes: Supraclavicular*
  - *Possible metastatic sites: None*

- *My google search tells me that Supraclavicular lymph nodes are NOT regional for the brachial plexus*
- *So, rule PH22 would apply: Assign C779 when an organ and non-regional lymph nodes are involved*

Coding Mets at Dx fields-NEW section

- Registrars struggle with primary site because they don't recognize the common metastatic sites, which incidentally, are also the most common metastatic sites for solid tumors (except bone marrow)
  - Bone
  - Brain (CNS)
  - Liver
  - Lung
  - Distant lymph nodes
  - Other (Bone Marrow)

  - PLEASE review this section carefully

Rule PH24

- PH24: Organ involvement only *(excludes bone marrow involvement only, see PH26)*
  - To use this rule, there is NO lymph node involvement
  - Organ involvement WITH regional lymph node involvement is Rule PH25
- Rule often overlooked due to involvement of common metastatic sites OR the spleen
  - New note added in 2026: This rule does **not** apply to bone marrow, or metastatic sites. (See Primary site coding tips). These are recorded in stage.

Case Scenario from Ask a SEER Registrar, 10

- I have an Extranodal MALT Lymphoma case involving 2 sites: stomach & lung. Do I need to code to an Unknown Primary? I couldn't find any info in the Heme Manual, unless I overlooked it.

- *Per Rule PH27, this rule does not apply to cases when common metastatic sites are involved. Lung is a common metastatic site.*
- *Rule PH24 applies: Primary site Stomach (which is where most extranodal MALT lymphomas occur).*
- *Lung involvement is recorded in Mets at Dx-Lung*
- *Stage IV lymphoma (due to lung involvement)*

Case Scenario from Ask a SEER Registrar, 11

- Hi, when imaging do not show lymph nodes involvement (only brain), which primary site that I should assign for the DLBCL case below?
- Based on Rule PH24 & Primary Site Coding Tips page 52 number 6 & 7(a), should I assign C80.9 unknown primary? Because PH24 number 1 says that this rule does not apply to metastatic sites, which is in this case brain is the metastasis site.

- *Rule PH24 does not state Brain is always a metastatic site, just a common one. Primary brain lymphomas are actually very common.*
- *With no other evidence of disease (per imaging), this would be coded as a primary CNS lymphoma*

Case Scenario from Ask a SEER Registrar, 12

- There is a lesion on the posterior 7th rib, but imaging also finds a large soft tissue component. The bx was done on the rib confirming the histology 9680/3. The med onc note doesn't clarify, and it is staged as 1E. The imaging states it this way: AGGRESSIVE LYTIC LESION W/IN POSTERIOR ASPECT OF RT SEVENTH RIB W/ MULTIFOCAL CORTICAL FENESTRATION AND FAIRLY LARGE SOFT TISSUE COMPONENT 48MM. Is the rib the primary site(PH24) or C809(PH27)?

- *DLBCL can occur anywhere in the body (most lymphomas cannot)*
- *PH24 applies: Primary site is rib since that is the only site involved*
  - *Physician's stage of IE confirms this is the only site of involvement*

Rule PH25

- When reviewing a case for primary site, look to see if you can find organ and regional lymph node involvement
- Registrars are missing this critical link and applying the wrong rules (PH21, C778, or PH22, C779)

- PH25 is for an organ and its regional lymph nodes involved
- What is tripping up registrars is the involvement of distant lymph nodes and common metastatic sites, or the spleen

- Proposed note: *For the purposes of this rule, "organ" does not apply to spleen, bone marrow or the other common metastatic sites (bone, brain, liver, lung). (See Primary site coding tips). These are recorded in stage.*

Case Scenario from Ask a SEER Registrar, 13

- 2024 bone marrow bx Burkitt Lymphoma, also Brain, Bone (skeletal), bladder, retroperitoneal/iliac LN, Would it be correct to use unknown as the primary site ?

- *Two regions lymph nodes: Retroperitoneal (C772), Iliac (C775); HOWEVER, Rule PH21 does not apply*
- *Assign primary site C679 (PH25: code to an organ when that organ and its regional lymph nodes [iliac] are involved)*
- *Retroperitoneal lymph nodes, bone marrow, brain, and bone would be recorded*
  - *Mets at Dx Bone: 1, Mets at Dx Brain: 1, Mets at Dx Distant Lymph Nodes: 1, Mets at Dx Other: 1*

Case Scenario from Ask a SEER Registrar, 14

CT Abdomen and Pelvis: Large mass in cecum, multiple regional lymph nodes involved.

Right hemicolectomy, DLBCL, non-germinal center lymphoma.

PET CT: nodal mets above and below the diaphragm. Skeletal mets. Bone marrow positive for DLBCL.

Case Scenario, cont. 14

- *Case Assessment:*
  - *Organs involved: Colon, Bone?, Bone Marrow?*
  - *Lymph nodes involved: Per CT scan, multiple regional lymph nodes involved, lymph nodes above and below the diaphragm*
  - *Possible metastatic sites: Bone? Bone Marrow? Lymph nodes?*

  - *Rule PH25: Code the primary site to the organ when an organ and its lymph nodes are involved*
    - *Per CT scan, colon and multiple regional lymph nodes involved*
  - *Bone (skeletal) involvement recorded in Mets at Dx-Bone*
  - *Bone marrow involvement recorded in Mets at Dx-Other*
  - *Distant lymph nodes involvement recorded in Mets at Dx-Distant Lymph Nodes*

Case Scenario from Ask a SEER Registrar, 15

- Patient found to have a large liver mass and no LAD on scans between 8/2025 & 9/2025. On MRI found to have a persistent large liver mass ~7cm & mild periportal, portocaval & retrocaval LAD. Diagnosed on imaging as metastatic cholangiocarcinoma.

  Liver biopsy, DLBCL. MD staged them with SG IV, involvement of liver, extra-nodal DLBCL.

  Is the phrase "mild periportal, portocaval & retrocaval LAD" enough to state the primary site is C772? No LN bx was done. Otherwise, I believe the primary site would be C809, but I wasn't sure that was accurate given there was some statement of LAD on imaging.

Case Scenario, cont., 15

- Case Assessment:
  - Organs involved: Liver?
  - Lymph nodes involvement: mild periportal, portocaval & retrocaval LAD
  - Possible metastatic sites: Liver?

- *Rule PH25: Code the primary site to the organ when an organ and its lymph nodes are involved*
  - *Liver and regional lymph nodes (periportal) and portocaval involved*
  - *Liver is a common metastatic site; however, in this case it's the primary site*
  - *Retrocaval Lymph nodes recorded in Mets at Dx-Other: Distant Lymph nodes*

Case Scenario from Ask a SEER Registrar, 16

- Patient with forehead/ scalp mass. Imaging shows LT Forehead mass INV SUBQ tissues above LT orbit EXT to calvarium W/O EXT to bone or intrathecal space. MULT avid osseous lesion BILAT femora and tibiae corresponds to SFT tissue marrow lesions on CT(Stated to have bone METS).
- Pathology states "integrated DX of AML t(9;11)(p21.3;q23.3); MLLT3-KMT2A Rearrange, manifesting as MYELOID SARCOMA, with unusually EXT monocytic DIFF/histiocytic transDIFF. The final histology is felt to represent Myeloid Sarcoma per MED ONC. A bone marrow biopsy is performed and is negative.

Case Scenario, cont., 16

- *Patient has two diagnoses:*
  - *AML diagnosis confirmed by pathology*
  - *Myeloid Sarcoma per physician*
- *Per Rule M3: Abstract a single primary when a myeloid sarcoma is diagnosed during the initial clinical workup at the same time as the myeloid leukemia OR after a leukemia of the same lineage*
- *Per PH10: The histology is the leukemia*
- *Per the pathology report, your histology is 9897/3: Acute myeloid leukemia with t(9;11)(p21.3;q23.3); KMT2A-MLLT3*
  - *Primary site is C421 (default for this histology), even though the bone marrow is negative*

Histology

Histology

- Remember to review alternate names when you are looking for your histology
- Hundreds of new alternate names were added to the database based on the WHO 5th edition
- Review the Heme Manual's revised "Steps for Using the Heme DB and Hematopoietic Coding Manual" section to help you use the database more effectively

Histology

- **Registrars are NOT to update the histology based on genetics or immunophenotyping without a pathologist's/physician's statement.**
  - Pathologist's/physician statement can be found in the final diagnosis, synoptic report, or in the comments section
  - Registrars have been picking positive genetics out from pathology reports and trying to figure out which code to use, sometimes listing 4-5 different codes (especially for Acute Myeloid Leukemia) based on the genetics
  - This is not how a histology is determined and why registrars are not to assign a more specific histology based on genetics or immunophenotyping **UNLESS** the pathologist/managing physician documents it

Histology Coding Rules: Example

Final diagnosis: Acute myeloid leukemia with monocytic differentiation. Note: The combined morphologic and immunophenotypic findings are consistent with involvement by an acute myeloid leukemia with monocytic differentiation. Cytogenetics: RUNX1, RUNX1T1 POS. NPM1+ FLT3 TKD+. No revised diagnosis available.

Registrar asks which of the AML codes should be used: RUNX1, NPM1, or FLT3.

i. *Pathologist has clearly stated the diagnosis **as acute myeloid leukemia with monocytic differentiation** based on the pathology report. The positive genetics cannot be used to assign histology since there is no statement from the pathologist/managing physician. Diagnostic confirmation would be 1.*

ii. *This is a prime example of how registrars have been misreading the rules. **You take the pathologist's diagnosis. Never use the genetics to determine the appropriate histology code.***

Histology

- Many cases will have multiple positive genetics that have unique ICD-O-3 codes
- There are no combination codes
  - Review of draft ICD-O-4 shows no combination codes either
- There are currently no priority order
- Most of these cases will be coded to 9861/3

Case Scenario from Ask a SEER Registrar

- Per pathology report, and physician documentation, patient has AML (NOS). However, the FISH results of this pericardial fluid was abnormal with a KMT2A(MLL) rearrangement and additional copies of the RUNX1 and RUNX1T1 gene regions. Also, abnormal 11q23(MLL sep). Normal t(8;21) RUNX1T1/RUNX1 fusion.
- My question is if this should instead be coded as 9897/3 (Acute myeloid leukemia with KMT2a rearrangement)? MD's reference these abnormalities, but don't specifically call it anything other than AML NOS, thus according to our rules we should only code the histology as stated by MD's.

- *Based on documentation provided, there is no update to the histology based on the FISH results, so this is 9861/3.*
- *Your histology MUST BE supported by the diagnosis from a physician (including the pathology)*

Case Scenario from Ask a SEER Registrar

- Question: In determining the correct histology code for B-acute lymphoblastic leukemia:
  For example, when cytogenetics state only abnormal chromosome & fish analyses and the results include (ABL1,BCR)x2[200], (KMT2A)x2[200], and (ETV6x2,RUNX1x4)[187/200]. Are we to interpret the correct histology code from the results? In this case, what would the correct histology be?

- *Per the updated instructions, pg. 55*
- *Registrars are NOT to update the diagnosis based on positive immunophenotyping and genetics results only. The updated diagnosis based on positive genetics or immunophenotyping MUST be provided by the pathologist or the managing physician. See Note 6*
- *Assign histology 9811/3 (Acute lymphoblastic leukemia, NOS)*

Case Scenario from Ask a SEER Registrars

- C421, 2024 - Patient with diagnosis of multiple myeloma in 2019 treated and relapsed. On routine BMBX in 2024, path showed residual multiple myeloma, but also B-lymphoblastic leukemia/lymphoma. Oncology said this was therapy related. I know we have a therapy-related code for myeloid neoplasms, which is 9920/3, but this is a lymphoid neoplasm. Would I code this to 9811/3, or would this still fall under 9920/3 to capture the therapy-related element?

- *9920/3 is for myeloid neoplasms only. This is not a myeloid neoplasm. This is a lymphoid neoplasm. Just because the myeloid neoplasms have a treatment related histology does not mean the lymphoid ones do (and they don't).*
- *This is 9811/3.*

Case scenario from Ask a SEER Registrar

- 1/12/26: Lymph node biopsy, primary large B-cell lymphoma of immune-privileged sites
- 2/4/26: Bone marrow biopsy, DLBCL

- Database reveals that both these histologies are 9680/3.
- This is one primary-and you don't have to go through the MP rules

Histology and Ambiguous Terminology

- The following terms are now “definitive diagnoses” **for coding histology ONLY.**
  - Compatible with
  - Comparable with
  - Consistent with
  - Most likely
  - Probable
  - Typical (of)

- **DO NOT APPLY THIS TO REPORTABILITY OR STAGE, HISTOLOGY ONLY**

Multiple Primaries

Multiple Primary Rules

- **M2: Same Primary, Same Histology**
- New section (#5) for 9920/3-COMING SOON (October 2026)
  - This clarification covers the situation where you may have a diagnosis of a specific MDS, MPN, MDS/MPN or leukemia AND a diagnosis of a therapy related neoplasm (or Myeloid neoplasm post cytotoxic therapy)
  - This would be one primary, the therapy related (9920/3)
  - Per the Heme DB for 9920/3: If a specific myeloid neoplasm that is described with a different specific histology term is also stated to be therapy related, code 9920/3 to capture the fact that this disease was therapy related. Document the other specific histology term in the text part of the abstract.
  - See if you have any cases where you have 9920/3 in ADDITION to another myeloid neoplasm
    - These need to be one primary

Case Scenario from Ask a SEER Registrar

- Bone marrow bx: Final dx: consistent with acute myeloid leukemia (blasts about 20% by CD34 stain). ETV6:MECOM identified. in view of the prior cytotoxic therapy this is most consistent with myeloid neoplasm (AML) post cytotoxic therapy Cytogenetic analysis showed a complex karyotype including t(2;12;3), i(5)(p10), del(11)(p15p12), and multiple additional structural abnormalities. FISH confirmed MECOM rearrangement and deletions of chromosomes 5q and 7q. Molecular testing identified a pathogenic TP53 mutation and ETV6::MECOM fusion, consistent with therapy-related acute myeloid leukemia.

- Is this one primary or two?
- If one primary, what is the histology?

Case Scenario, cont.

- Per the Heme DB for 9920/3: If a specific myeloid neoplasm that is described with a different specific histology term is also stated to be therapy related, code 9920/3 to capture the fact that this disease was therapy related. Document the other specific histology term in the text part of the abstract.

- 1 primary
- 9920/3, C421
- Histology text: pathogenic TP53 mutation and ETV6::MECOM fusion

Multiple Primary Rules

- **M4: Two or more non-Hodgkin B-cell lymphomas diagnosed in the same specimen (biopsy, surgical resection)**
  - Received confirmation from expert hematopathologist that M4 only applies to B-cell lymphomas
  - Most common situation we've seen is Follicular lymphoma and DLBLC.
  - If you have a B-cell and a T-cell in the same specimen, M15 applies
    - Two primaries

Case Scenario from Ask a SEER Registrar

- Final Dx:
  Submandibular gland excision:
  - involvement by follicular lymphoma, WHO grades 2-3A w/ focal diffuse areas suggestive of diffuse large B-cell lymphoma (see note)

- M4 tells you this is one primary
- PH11 tells you to code histology to 9680/3

Case Scenario from Ask a SEER Registrar

- Bone marrow: Hypercellular marrow showing lymphomatous involvement by peripheral T-cell lymphoma and large B-cell lymphoma with clonal proliferation of plasma cells, lambda light chain restricted. Comment: The marrow shows lymphomatous involvement by a composite lymphoma featuring PTCL and DLBCL with plasmacytic differentiation. No other information available.

- Per old M4 rule: One primary, DLBCL (PH11)
- Per revised M4 rule: Two primaries
  - C421, 9702/3: Peripheral T-cell lymphoma
  - C421, 9680/3: Diffuse Large B-cell lymphoma

Multiple Primary Rules (M8-M13)

- "21 days" and "simultaneously" have been removed
- Many registrars couldn't understand "simultaneously"
- Short headers have been added to all the M and PH rules, which will hopefully help registrars
  - ***Example:***
  - ***Rule M5: Hodgkin and non-Hodgkin B-cell lymphoma in same biopsy specimen***

Chronic/Acute Rules (M8-M13)

- Reminder added to Manual:
  - The transformations listed in the Hematopoietic Database are from the *WHO Blue Book of Hematolymphoid Tissues, 5th edition*.
  - NCI SEER follows only the WHO Blue Book as the source for transformations.
  - Physician's may state other types of transformations. If that is the case, follow the rules as appropriate.
    - Note: You will likely end up at Rule M15, which is to use the Multiple Primaries Calculator

Chronic/Acute Rules (M8-M13)

- **Initial Clinical Workup**
- Several of the M rules now refer to “initial clinical workup.” This is the timeframe of when patients are first diagnosed. The initial clinical workup may include blood work, imaging, biopsies (including bone marrow), and genetic testing. In some situations, treatment may be started before the full workup is completed.

- This is replacing “21 days” and “simultaneously” in the M8-M13 rules

Case Scenario from Ask a SEER Registrar

- I have a case of a plasmacytoma dx'd on 4/25/25 and PCM Dx'd on 5/12/25. When I go to the Hemat database it states, "The presence of a plasmacytoma and a diagnosis of plasma cell myeloma diagnosed during the initial clinical workup is evidence of advanced disease. One primary is abstracted, the plasma cell myeloma (See Rule M11)". However, when I go to Rule M11 it states, "Rule M11: Chronic and acute diagnosed during initial workup with two biopsies…..

- *Here's a registrar unknowingly pointing out a discrepancy between the Heme DB and the Manual*
- *This is how registrars in the field help us!!! ☺*
- *So, a plasmacytoma (9731 or 9734) and plasma cell myeloma (9732) diagnosed within the same clinical workup, will always be one primary-even if there are two separate biopsies!*

Plasma Cell Myeloma (9732) and Plasmacytoma (9731 or 97344)

- For the 2027 updates (release October 2026), the following has been added to Rules M11, M12, M13

- **Note**: This rule does NOT apply to Plasmacytoma (9731 or 9734) and Plasma Cell Myeloma (9732). See the Hematopoietic database

Plasma Cell Myeloma (9732) and Plasmacytoma (9731 or 97344)

- Plasmacytoma does transform to Plasma cell myeloma HOWEVER
  - If they are diagnosed within the same clinical workup, they are one primary, 9732/3
  - If the plasmacytoma is diagnosed after the plasma cell myeloma, it is one primary, 9732/3
  - The presence of two plasmacytomas is indicative of plasma cell myeloma (9732/3, C421) EVEN if there is a negative bone marrow biopsy or one wasn't performed

- M8, M9 and M10 still apply
  - M10: A plasmacytoma is followed by plasma cell myeloma **AFTER** the initial clinical workup has been completed. See Rule M10, Example 2

Multiple Primaries Calculator

- **Rule M15 is not a "default" rule, it's a rule of <u>LAST RESORT.</u>**
  - You are to start with the database first and then work through the rules in the Heme manual
  - Many registrars are missing the applicable rule
  - READ the rules carefully (use the new "road maps")
- **Do NOT** compare the number of primaries you get from the Multiple Primaries Calculator to what is determined in the manual
- Multiple examples of when M15 applies and when M15 doesn't apply are included-review these to become more familiar with how Rule M15 is applied

Example of Rule M15

- I am having trouble finding the correct histology code for the following combination from a bone marrow biopsy and flow cytometry. I am unsure how to capture the T-LGL component within the MDS primary, which has increased blasts, multilineage dysplasia and a STAT3 mutation.

- *There is no combination code here. The registrar has identified correctly the two histologies*
- *Rule M15 applies in this case, two primaries are abstracted*
  - *1. MDS with increased blasts: 9983/3, C421.*
    2. T-cell large granular lymphocytic leukemia: 9831/3, C421.

Diagnostic Confirmation

Diagnostic Confirmation

- Code 3 will be discontinued and all cases currently with a code 3 will be converted to 1 during the v27 updates
- There are some histologies that currently require a code 3 (edits enforced)
  - *Example:* 9871/3: Acute myeloid leukemia with inv(16)(p13.1q22) or t(16;16) (p13.1;q22), CBFB/MYH11 (genetics are required for this histology)
- **You will need to continue to code a 3 for these histologies until the 2027 updates are implemented into your software and the edits metafile is updated**
- After your software is updated, all cases that had a 3 will have been changed to a 1, and only 1 will be needed.

Diagnostic confirmation

- By eliminating code 3 for diagnostic confirmation, this means that review of immunophenotyping and genetics is no longer needed.
  - The database will continue to have the immunophenotyping and genetics fields; however, they will be limited to the most common ones (per WHO)
- If you have positive histology, assign a 1 and you are done

- Reminder: Registrars cannot use immunophenotyping or genetics to update the histology to a more specific histology. The more specific histology must be documented by the pathologist or a managing physician

Case Scenario from Ask a SEER Registrar

- 3/23, Subhepatic mass. FNA, large b-cell lymphoma
- Immunophenotyping most c/w with DLBCL of non-germinal center cell (activated B-cell). Diffuse and strong expression of CD30+.
- Would this be coded as a 2 in the, diagnostic confirmation field, since the FNA is a cytology?

- *No, this would not be a 2. Although this was a cytology specimen, flow cytometry was done on it. The immunophenotyping confirms this is DLBCL. Diagnostic confirmation would be 1 (previously 3).*

Treatment


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First Course of Treatment

- Added information about induction, consolidation/intensification and maintenance
- Updated coding instructions include:
  - When there is only one neoplasm (one primary), use the documented first course of therapy (treatment plan) from the medical record. **First course of therapy ends when the treatment plan is completed or remission is achieved, no matter how long it takes to complete the plan**

Question from Ask a SEER Registrar

- Patient diagnosed with CLL/SLL, asymptomatic. Active surveillance was recommended. Patient was followed for 2 years when they became symptomatic and then were started on chemotherapy. Is the chemotherapy first course of treatment since the patient has not achieved remission?

- *In this situation, the chemotherapy would be second course treatment. The initial treatment was none (active surveillance). This exception has been added to the Hematopoietic Manual and will be released in October 2026 as part of the v27 updates*

Treatment Section update:

- ***Exception:*** *If a patient is asymptomatic at diagnosis and there is not a great disease burden, patient may be placed on* ***active surveillance*** *until symptoms appear or the disease burden increases. In a situation like this, Active Surveillance is the first course of treatment, and any treatment received due to symptoms or increased disease burden would be second course treatment.*
- ***Example:*** *Patient diagnosed with CLL/SLL, due to low disease burden and no symptoms, placed on Active Surveillance. Two years later, the patient presents with worsening anemia and thrombocytopenia and is put on chemotherapy. Should date of first treatment be the AS date, and treatment status stay AS, because that was the first treatment plan? Or, because remission hasn't been achieved, does the information get updated to the chemo date with treatment status being treatment given?*
  - *In this example, date of first course treatment is the date that Active Surveillance was started. There was a decision to not actively treat the patient at time of diagnosis. The chemotherapy started two years later would be second course therapy due to disease progression.*

Treatment example

- Would the Pola/GDP and CAR-T therapy be included in first course treatment since the patient had not reached remission or would it be second course treatment due to the progression?

  Case scenario - DLBCL diagnosed 2/21/25. Stage IV at diagnosis with positive bone marrow biopsy, lymph nodes above and below diaphragm, pelvic mass and osseous mets

  - 2/28/25 R-CHOP
  - 5/20/25 PET: overall improvement but increase in pelvic sidewall mass.
  - Now 4.7 cm, previously 4.1cm Some osseous lesions with increased activity
  - 6/9/25 Biopsy of pelvic mass: Diffuse large B-cell lymphoma
  - 7/10/25 Med Onc consult: refractory diffuse B-cell lymphoma.
  - 7/16/25 Polatuzumab and Rituxan
  - 8/27/25 PET: Progression with new vertebral and femur lesions
  - 9/3/25 CAR-T therapy (Yescarta)

Other


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Appendix B: Lineage Tables

- These are the updated lineage tables based on the WHO 5th edition Blue Book for Hematolymphoid Tissues. Familiarizing yourself with the lineage tables can be helpful in determining what is an NOS code and a more specific code

- **Do NOT use these lineage tables to determine histology.**
  - **Only use the database and the manual**
  - ***Added to beginning of Appendix B:***
  - ***These are <u>reference tables only</u>. Do NOT use these tables to determine reportability, number of primaries, behavior, or histology. Information on all the terms included in these tables can be found in the Hematopoietic Database.***

Resources

- See the SEER Training Website
- We have two new site-specific modules for Hematopoietic that should help you
- Welcome to SEER Training

- Any questions regarding this presentation, please post to:
- Ask a SEER Registrar - SEER Registrars

Final thoughts

Thank You

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