

Hodgkin Lymphoma

Protocol applies to Hodgkin lymphoma involving any organ system except for the gastrointestinal tract.

*Protocol revision date: January 2004
No AJCC/UICC staging system*

Procedures

- **Cytology** (No Accompanying Checklist)
- **Biopsy**
- **Staging Procedure**

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Surgical Pathology Cancer Case Summary (Checklist)*Protocol revision date: January 2004**Applies to non-gastrointestinal Hodgkin lymphoma only**No AJCC/UICC staging system***HODGKIN LYMPHOMA: Biopsy/Staging Procedure**

Patient name:

Surgical pathology number:

Note: Check 1 response unless otherwise indicated.**MACROSCOPIC****Specimen Type** Lymphadenectomy Staging laparotomy Other (specify): _____ Not specified**Tumor Site (check all that apply)** Lymph node(s), site not specified Lymph node(s)

Specify site(s): _____

 Other tissue(s) or organ(s)

Specify site(s): _____

Tumor Size (largest single mass)

Greatest dimension: ___ cm

*Additional dimensions: ___ x ___ cm

Specify site: _____

 Cannot be determined (see Comment)

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* Data elements **with asterisks** are **not required** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

MICROSCOPIC**Histologic Subtype**

- Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL)
 Classical Hodgkin lymphoma (CHL), nodular sclerosis Hodgkin lymphoma (NSHL)
 CHL, mixed cellularity Hodgkin lymphoma (MCHL)
 CHL, lymphocyte-rich classical Hodgkin lymphoma (LRCHL)
 CHL, lymphocyte-depleted classical Hodgkin lymphoma (LDHL)
 Other (specify): _____
 Hodgkin lymphoma, subtype cannot be determined

***Histologic Grade (NSHL only)**

- Not applicable
 Grade I
 Grade II

Extent of Pathologically Examined Tumor (check all that apply)

- Involvement of a single lymph node region
 Specify site: _____
 Involvement of multiple lymph node regions
 Specify: _____
 Splenic involvement
 Liver involvement
 Bone marrow involvement
 Other organ involvement
 Specify: _____
 Not specified

Immunophenotyping

- Performed
 *Specify results: _____
 Not performed

***Additional Pathologic Findings (check all that apply)**

- Progressive transformation of germinal centers (PTGC)
 Castleman disease
 Other (specify): _____

***Comment(s)**

* Data elements **with asterisks** are **not required** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Background Information

Protocol revision date: January 2004

I. Cytologic Material

A. Clinical Information

1. Patient identification
 - a. Name
 - b. Identification number
 - c. Age (birth date) (Note **A**)
 - d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
 - a. Relevant history
 - (1) previous diagnosis and treatment for lymphoma
 - (2) previous or current Epstein-Barr virus infection
 - (3) history of solid organ or bone marrow transplantation
 - b. Relevant findings (eg, distribution of lymphadenopathy, signs and symptoms, imaging studies) (Note **B**)
 - c. Clinical diagnosis
 - d. Procedure (eg, fine-needle aspiration [FNA])
 - e. Anatomic site(s) of specimen(s) (Note **C**)

B. Macroscopic Examination

1. Specimen
 - a. Unfixed/fixed (specify fixative)
 - b. Number of slides received, if appropriate
 - c. Quantity and appearance of fluid specimen, if appropriate
 - d. Other (eg, cytologic preparation from tissue)
 - e. Results of intraprocedural consultation
2. Material submitted for microscopic evaluation (eg, FNA, cytospin of fluid, cell block)
3. Special studies (specify) (eg, flow cytometry for immunophenotyping, cytochemistry, immunohistochemistry, cytogenetic analysis) (Note **D**)

C. Microscopic Evaluation

1. Adequacy of specimen (if unsatisfactory for evaluation, specify reason)
2. Tumor, if present
 - a. Histologic sub-type, if possible (Note **E**)
 - b. Other characteristics (eg, necrosis, types of non-neoplastic background cells present)
3. Additional pathologic findings, if present
4. Results/status of special studies (specify)
5. Comments
 - a. Correlation with intraprocedural consultation, as appropriate
 - b. Correlation with clinical information, as appropriate
 - c. Correlation with other specimens, as appropriate

II. Incisional Biopsy**A. Clinical Information**

1. Patient identification
 - a. Name
 - b. Identification number
 - c. Age (birth date) (Note **A**)
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
 - a. Relevant history
 - (1) previous diagnosis and treatment for lymphoma
 - (2) previous or current Epstein-Barr virus infection
 - (3) history of solid organ or bone marrow transplantation
 - b. Relevant findings (eg, distribution of lymphadenopathy, signs and symptoms, imaging studies) (Note **B**)
 - c. Clinical diagnosis
 - d. Procedure
 - e. Anatomic site(s) of specimen(s) (Note **C**)

B. Macroscopic Examination

1. Specimen
 - a. Unfixed/fixed (specify fixative) (Note: Fresh frozen tissue should be saved, if possible, for immunophenotyping and molecular genetic studies) (Note **D**)
 - b. Number of pieces
 - c. Largest dimension of each piece
 - d. Results of intraoperative consultation
2. Submit all nonfrozen tissue for microscopic evaluation and special studies
3. Special studies (specify) (eg, flow cytometry for immunophenotyping, cytochemistry, immunohistochemistry, cytogenetic analysis) (Note **D**)

C. Microscopic Evaluation

1. Tumor
 - a. Histologic sub-type (Note **E**)
 - b. Histologic grade, if applicable (Note **F**)
2. Additional pathologic findings, if present (Note **G**)
3. Results/status of special studies (specify)
4. Comments
 - a. Correlation with intraoperative consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

III. Excisional Biopsy**A. Clinical Information**

1. Patient identification
 - a. Name
 - b. Identification number
 - c. Age (birth date) (Note **A**)
 - d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information

- a. Relevant history
 - (1) previous diagnosis and treatment for lymphoma
 - (2) previous or current Epstein-Barr virus infection
 - (3) history of solid organ or bone marrow transplantation
 - b. Relevant findings (eg, distribution of lymphadenopathy, signs and symptoms, imaging studies) (Note **B**)
 - c. Clinical diagnosis
 - d. Procedure (eg, axillary lymph node excision)
 - e. Operative findings
 - f. Anatomic site(s) of specimen(s) (Note **C**)
- B. Macroscopic Examination**
1. Specimen
 - a. Organ(s)/tissue(s) (specify)
 - b. Unfixed/fixed (specify fixative) (Note: Fresh frozen tissue should be saved, if possible, for immunophenotyping and molecular genetic studies) (Note **D**)
 - c. Number of pieces
 - d. Dimensions
 - e. Results of intraoperative consultation
 2. Tumor
 - a. Dimensions
 - b. Configuration
 - c. Descriptive characteristics (eg, color, consistency)
 3. Additional pathologic findings, if present
 4. Tissues submitted for microscopic evaluation
 - a. Tumor
 - b. Other lesions
 - c. Section(s) of tissue uninvolved by tumor
 - d. Frozen section tissue fragment(s) (unless saved for special studies)
 - e. Other tissue(s)/organ(s)
 5. Special studies (specify) (eg, flow cytometry for immunophenotyping [for Hodgkin lymphoma, flow cytometry is useful for differentiation from non-Hodgkin lymphoma], cytochemistry, immunohistochemistry, cytogenetic analysis) (Note **D**)
- C. Microscopic Evaluation**
1. Tumor
 - a. Histologic sub-type (Note **E**)
 - b. Histologic grade, if applicable (Note **F**)
 2. Other organs or tissues
 - a. If distant involvement by tumor, specify site (Note **H**)
 - b. Specify if direct extension of tumor into other organ or tissue (Note **I**)
 3. Additional pathologic findings, if present (Note **G**)
 4. Results/status of special studies (specify)
 5. Comments
 - a. Correlation with intraoperative consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

IV. Staging Laparotomy (Note J)**A. Clinical Information**

1. Patient identification
 - a. Name
 - b. Identification number
 - c. Age (birth date) (Note A)
 - d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
 - a. Relevant history
 - (1) previous diagnosis and treatment for lymphoma
 - (2) previous or current Epstein-Barr virus infection
 - b. Relevant findings (eg, distribution of lymphadenopathy, signs and symptoms, imaging studies) (Note B)
 - c. Clinical diagnosis
 - d. Procedure (eg, staging laparotomy)
 - e. Operative findings
 - f. Anatomic site(s) of specimen(s) (Note C)

B. Macroscopic Examination

1. Specimens
 - a. Organ(s)/tissue(s) included
 - b. Fixed/unfixed (specify fixative)
 - c. Number of pieces
 - d. Dimensions; weight (spleen)
 - e. Orientation of specimens, if indicated by surgeon
 - f. Results of intraoperative consultation(s)
2. Spleen
 - a. Weight (Note: slice at 1-cm intervals and fix 6 to 12 hours, then slice at 5-mm intervals)
 - b. Lesions
 - (1) number (count individual lesions up to 10; if more, state ">10")
 - (2) size range
 - (3) location
 - (4) configuration
 - (5) descriptive characteristics (eg, color, consistency)
 - (6) direct extension to other organ(s) or structure(s) (Note I)
 - c. Additional pathologic findings, if present
3. Lymph nodes
 - a. Number of lesions, if discernible
 - b. Descriptive characteristics (eg, color, consistency)
 - c. Additional pathologic findings, if present
4. Bone marrow biopsy
 - a. Size
 - b. Descriptive characteristics (eg, color, consistency)
5. Other organ(s) or structure(s)
 - a. Size
 - b. Descriptive characteristics (eg, color, consistency)
 - c. Noncontiguous lesions, if discernible (Note H)

- (1) number
- (2) size
- (3) descriptive characteristics
- d. Additional pathologic findings, if present
- 6. Tissues submitted for microscopic evaluation
 - a. Lymph nodes, liver biopsy, bone marrow biopsy
 - b. Spleen (Note J)
 - (1) nodules present: section of each nodule up to 6
 - (2) no nodules present: 6 random sections
 - c. Section of tissue uninvolved by tumor
 - d. Other separately submitted lesions/nodules
 - e. Frozen section tissue fragment(s) (unless saved for special studies)
 - f. Other tissue(s)/organ(s)
- 7. Special studies (specify) (eg, flow cytometry for immunophenotyping, cytochemistry, immunohistochemistry, cytogenetic analysis)

C. Microscopic Evaluation

- 1. Tumor
 - a. Histologic sub-type (Note E)
 - b. Histologic grade, if applicable (Note F)
 - c. Extent of involvement (Note J)
 - d. Direct extension to other organ(s) or structure(s) (Note I)
- 2. Other tissues submitted (specify)
 - a. If distant involvement by lymphoma, specify site (Note J)
- 3. Additional pathologic findings, if present (Note G)
- 4. Results/status of special studies (specify)
- 5. Comments
 - a. Correlation with intraoperative consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

Explanatory Notes

A. Age

In Hodgkin lymphoma, patient age above 40 to 50 years has been shown to be associated with decreased survival compared to younger ages. Several multivariate analyses have shown that age has independent prognostic impact on cause-specific survival.¹⁻⁵

B. Clinical Findings

Although not always provided to the pathologist by the physician submitting the specimen, certain specific clinical findings are known to be of prognostic value in Hodgkin lymphoma (across all stages). Among these are systemic symptoms such as fever (greater than 38.5°C), weight loss (more than 10% body weight), night sweats, tumor burden (including tumor bulk and number of sites), and a large (more than one-third the width of the widest thoracic diameter) mediastinal mass.^{1,6-11} The aforementioned systemic symptoms are used to define 2 categories for each stage of Hodgkin lymphoma: A (symptoms absent), and B (symptoms present). The presence of B symptoms has been regarded as an important prognostic factor for survival in many studies, but multivariate analyses in studies with highly accurate evaluations of extent

of disease have shown that B symptoms correlate with extent of disease but are not always of independent significance.^{1,3,12,13} However, fever and/or weight loss have been shown to be independently associated with worse survival in patients with stage II Hodgkin lymphoma.¹⁴

C. Anatomic Sites

Stages of Hodgkin lymphoma (see Note H) are classified by involvement of lymph node “regions” rather than specific lymph nodes or specific lymph node groups (eg, jugular, tracheal). Single lymph node “regions” are defined as follows¹⁵:

- Lymph nodes of head, neck, and face
- Intrathoracic lymph nodes
- Intra-abdominal lymph nodes
- Lymph nodes of axilla or arm
- Lymph nodes of inguinal region or leg
- Pelvic lymph nodes

Involvement of a given region may include involvement of more than 1 lymph node or lymph node group.

D. Special Studies

Cytogenetic studies, flow cytometry, and HLA typing are not uniformly useful as prognostic indicators in Hodgkin lymphoma.^{1,16} However, special studies may be useful diagnostically. The main differential diagnosis in most cases of Hodgkin lymphoma is non-Hodgkin lymphoma. If necessary, immunohistochemical studies (immunophenotyping) and genetic studies (ie, gene rearrangement) should be performed to confirm the diagnosis and exclude non-Hodgkin lymphoma.¹⁷

E. Histologic Classification

Histologic classification of Hodgkin lymphoma should be based on sections of paraffin-embedded tissue stained with hematoxylin-eosin. Primary diagnosis of Hodgkin lymphoma is rarely made by cytological analysis; however, cytologic examinations may be useful in diagnosing relapse in patients with a history of Hodgkin lymphoma.

Hodgkin lymphoma is traditionally categorized histologically by the Rye Classification, which recognizes 4 major histologic sub-types. This classification has been modified and revised by the World Health Organization (WHO)^{18,19} and is recommended by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC).^{20,21} The original Rye categories are now classified as Classical Hodgkin lymphoma. The “non-classical” category of Hodgkin lymphoma as defined by the WHO is nodular lymphocyte predominant Hodgkin lymphoma. This is a monoclonal B-cell neoplasm characterized by a nodular, or nodular and diffuse, proliferation of large neoplastic cells known as “popcorn” or L&H (lymphocytic and/or histiocytic Reed Sternberg variants) with a background of small non-neoplastic lymphocytes. The WHO classification of Hodgkin lymphoma and the corresponding immunophenotypic and genetic characteristics of each type are shown below.

WHO Classification of Hodgkin Lymphoma¹⁸

Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL)
Classical Hodgkin lymphoma (CHL)

Nodular sclerosis Hodgkin lymphoma (grades 1 and 2) (NSHL)
 Mixed cellularity Hodgkin lymphoma (MCHL)
 Lymphocyte-rich classical Hodgkin lymphoma (LRCHL)
 Lymphocyte-depleted classical Hodgkin lymphoma (LDHL)

Prognosis appears to be more related to stage of disease than histologic subtype. The prognosis of patients with stage I and II disease is very good, whereas advanced staged disease has an unfavorable prognosis.

The immunophenotypic characteristics and the genetic alterations that typify each of the subtypes of Hodgkin lymphoma are as follows.¹⁸

Immunophenotypes and Genetics

Nodular lymphocyte predominant: CD45+, PanB+, CD20+, CD75+, EMA+/-, CD15-, CD30-/+ , J-chain+/-, Ig+/-, numerous CD57+ lymphocytes around lymphocytic and histiocytic (L and H) cells; immunoglobulin and T-cell receptor (TCR) genes germline, tumor cells usually Epstein-Barr virus-

Nodular sclerosis CHL: CD30+, CD15+, CD45- (may be CD45+ on frozen section), usually PanB- and PanT-, CD20-/+ , EMA-; immunoglobulin and TCR genes usually germline, occasional IgH gene rearrangement, occasional *bcl-2* gene rearrangement, Epstein-Barr virus infection of tumor in 40% of cases

Mixed cellularity CHL: CD30+, CD15+/-, CD45- (may be CD45+ on frozen sections), usually PanB- and PanT-, CD20-/+ , EMA-; immunoglobulin and TCR genes usually germline, Epstein-Barr virus infection of tumor cells in 60% to 70% of cases

Lymphocyte-rich CHL: CD30+, CD15+/-, CD45-, usually PanB- and PanT-, EMA-; immunoglobulin and TCR genes germline, Epstein-Barr virus-/+

Lymphocyte depleted CHL: CD30+, CD15+/-, CD45-, PanB-, PanT-, EMA-; immunoglobulin and TCR genes germline

F. Histologic Grade

Histologic grading has been developed only for nodular sclerosis (NS) Hodgkin lymphoma and is not applicable to other histologic sub-types of Hodgkin lymphoma. Nodular sclerosis comprises 75% of all cases of Hodgkin lymphoma. It does not coexist with or transform into other histologic sub-types, but the individual nodules may show a variety of histologic appearances that range from a lymphocyte predominant to a lymphocyte depleted background with scant to plentiful neoplastic cells, respectively. In a large series of pathologic stage I and II Hodgkin lymphoma (see following) reported by the British National Lymphoma Investigation, patients with nodular sclerosis having either extensive and easily recognizable areas of lymphocyte depletion or numerous pleomorphic Hodgkin (Reed-Sternberg) cells had a decreased survival independent of disease stage.²² Thus, a 2-tiered grading system for nodular sclerosis Hodgkin lymphoma based on the proportion of lymphocyte depleted nodules present in histologically examined tissue has been proposed as follows:

Grade I (NSI)

- (1) Less than 25% of nodules show lymphocyte depletion, or
- (2) Less than 25% of nodules show numerous anaplastic Hodgkin cells without depletion of lymphocytes

Grade II (NSII)

- (1) 25% or more of nodules show lymphocyte depletion, or
- (2) 25% or more of nodules show numerous anaplastic Hodgkin cells without depletion of lymphocytes

Reported results from different centers differ as to the prognostic importance of grading, but overall, the most significant correlation appears to be that NSI is more indolent than NSII. With optimal therapy, however, it appears that the difference in natural history can be overcome.⁶

G. Other Pathologic Findings

Of particular importance are the distinctive pathologic findings that are known to be associated with Hodgkin lymphoma. Progressively transformed germinal centers (PTGC), for example, are an unusual type of reactive follicle that are often found at the periphery of a lymph node involved by nodular lymphocyte predominant Hodgkin lymphoma or, less often, other types of Hodgkin lymphoma. However, PTGC may also occur in settings unrelated to Hodgkin lymphoma, such as reactive lymphoid hyperplasia. PTGC appear as germinal centers that are infiltrated and expanded by small lymphocytes of the mantle zone type.¹⁶ Other pathologic lesions that may be seen in association with Hodgkin lymphoma and, therefore, should be specifically reported in patients in whom Hodgkin lymphoma is suspected clinically include granulomatous inflammation and changes reminiscent of Castleman disease (hyaline-vascular follicles, hypervascular interfollicular regions, or numerous interfollicular plasma cells). Diligent search for variant or diagnostic Hodgkin cells is necessary to rule out coexistent Hodgkin lymphoma in the presence of these lesions.

H. Stage

In general, TNM classification has not been used for staging malignant lymphomas because the site of origin of the tumor is often uncertain and there is no way to differentiate among T, N, and M. Thus, a special staging system (Ann Arbor System) is used for both Hodgkin lymphoma and non-Hodgkin lymphoma.^{20,21} The Ann Arbor classification for lymphomas has been applied to Hodgkin lymphoma by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC), as shown below. Staging is based on the well-established knowledge that Hodgkin lymphoma tends to spread in a contiguous fashion from one nodal chain to the next. The prognosis worsens with progressive spread of disease.¹

Pathologic staging depends on biopsy or resection of 1 or more regional lymph nodes, splenectomy, wedge and needle liver biopsies, bone marrow biopsy (optional in stages I and II), and biopsy of multiple lymph nodes on both sides of the diaphragm to assess the distribution of disease. Clinical staging generally involves a combination of clinical, radiologic, and surgical procedures and includes medical history, physical examination, laboratory tests (eg, urinalysis, complete blood examination, and blood chemistry studies), imaging studies (eg, computed tomographic scans, magnetic resonance

imaging studies, and nuclear medicine studies), and biopsy to determine diagnosis and histologic sub-type of tumor (initial diagnosis is almost always made on biopsy).

There is general agreement that staging of Hodgkin lymphoma is prognostically significant.^{1,23}

Staging²³

Stage I	Involvement of a single lymph node region (I) or localized involvement of a single extralymphatic organ or site in the absence of any lymph node involvement (I _E) (rare in Hodgkin lymphoma) [#]
Stage II	Involvement of 2 or more lymph node regions on the same side of the diaphragm (II), or localized involvement of a single extralymphatic organ or site in association with regional lymph node involvement with or without involvement of other lymph node regions on the same side of the diaphragm (II _E) ^{##}
Stage III	Involvement of lymph node regions on both sides of the diaphragm (III), which also may be accompanied by extralymphatic extension in association with adjacent lymph node involvement (III _E), or by involvement of the spleen (III _S), or both (III _{E,S})
Stage IV	Diffuse or disseminated involvement of 1 or more extralymphatic organs, with or without associated lymph node involvement; or isolated extralymphatic organ involvement, but in conjunction with disease in distant site(s); or involvement of the liver or bone marrow, or nodular involvement of the lung(s) ^{###, ###, ^}

[#] Multifocal involvement of a single extralymphatic organ is classified as stage I_E and not stage IV.

^{##} The number of lymph node regions involved may be indicated by a subscript, eg, II₃. For stage I to IIIA disease, involvement of 4 or more nodal regions has been shown to adversely affect rates of disease-free survival and overall survival.¹

^{###} For stage IV disease, involvement of more than 2 extranodal sites has been shown to adversely affect rates of complete response to therapy, disease-free survival, and overall survival.¹

[^] Specific sites involved are designated by letter subscripts. When the involved sites have been documented by biopsy, a plus (+) sign is added following the letter subscript. If a biopsy has been performed but the tissue/organ is uninvolved, a minus (-) sign is added following the letter subscript. If the tissue/organ is involved clinically but a biopsy has not been performed, neither a plus nor a minus sign is added.

Spleen	S
Pulmonary (lung)	L
Bone marrow	M
Hepatic	H
Pericardium	Pcard
Pleura	P
Waldeyer's (tonsil, naso-oropharynx)	W

Osseous (bone)	O
Gastrointestinal	GI
Skin	D
Soft tissue	Softis
Thyroid	Thy

I. Direct Spread Into Adjacent Tissues or Organs

Direct spread of a lymphoma into adjacent tissues or organs does not influence classification of stage.

J. Staging Laparotomy

Staging laparotomy historically has been the gold standard for defining the extent of subclinical disease in the abdomen.²⁴ It includes detailed exploration of the abdomen with sampling of the upper abdominal nodes (celiac, splenic hilar, and porta hepatic), the midabdominal nodes (para-aortic and porta caval), and the pelvic nodes (common, external and internal iliac). In addition, it includes splenectomy and wedge plus needle biopsies of the liver as well as biopsies of any suspicious lesions in the abdomen.²⁴

In the past decade, the use of staging laparotomy for Hodgkin lymphoma has decreased for several reasons: (1) the inherent morbidity of the procedure; (2) the increased accuracy of imaging techniques for predicting positive laparotomy findings; and (3) the use of treatment approaches that do not require knowledge of the extent of subclinical disease.²⁴ Currently, staging laparotomies are rarely performed for staging of Hodgkin lymphoma.

In staging laparotomy, thorough examination of spleen is essential since splenic involvement is common but often is not apparent on macroscopic examination. The outer surface is inspected for nodules, and the parenchyma sliced thinly in transverse fashion to be examined for nodular or suspicious lesions. The pathology report should state the number of macroscopically identifiable nodules as well as the microscopic correlation as to the extent of disease.²⁴ In stage III Hodgkin lymphoma, the amount of tumor in the spleen, specifically 4 or more tumor nodules, has been shown to adversely affect disease-free survival in patient's treated with radiation therapy alone.²⁴ Careful examination of each of the organs and tissues submitted at staging laparotomy and detailed reporting of the extent of involvement by tumor is important to establish the total tumor burden. Measures of tumor burden that combine total extent and volume of tumor in the body have been shown to be highly significant independent prognostic indicators in Hodgkin lymphoma.^{1,4,5,11-13,23-27}

The histologic criteria for involvement by tumor at staging laparotomy are as follows:

Lymph Nodes and Spleen: Same criteria as primary diagnosis

Bone Marrow and Liver: Mononuclear Reed-Sternberg variants in appropriate cellular background

In patients with an established diagnosis of Hodgkin lymphoma, granulomas may be found on staging laparotomy in the absence of diagnostic Hodgkin cells or variants in

lymph nodes, spleen, or bone marrow. The liver may also show nonspecific triaditis. Tissues with these findings are considered free of involvement by Hodgkin lymphoma.

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