Testis

Protocol applies to all malignant germ cell and malignant sex cord-stromal tumors of the testis, exclusive of paratesticular malignancies.

Protocol revision date: January 2004
Based on AJCC/UICC TNM, 6th edition

Procedures
• Radical Orchiectomy
• Retroperitoneal Lymphadenectomy (RPLND)

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Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
Applies to invasive cancers only
Based on AJCC/UICC TNM, 6th edition

TESTIS: Radical Orchiectomy

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

*Serum Tumor Markers (check all that apply)
(see optional Serum Tumor Markers Classification [S] in Microscopic section)
* ___ Unknown
* ___ Serum marker studies within normal limits
* ___ Alpha-fetoprotein (AFP) elevation
* ___ Beta-subunit of human chorionic gonadotropin (b-hCG) elevation
* ___ Lactate dehydrogenase (LDH) elevation

MACROSCOPIC

Laterality
___ Right
___ Left
___ Both
___ Not specified

Focality
___ Unifocal
___ Multifocal

Tumor Size
Greatest dimension of main tumor mass: ___ cm
* Additional dimensions: ___ x ___ cm
Greatest dimensions of additional tumor nodules: ___ cm, ___ cm, etc
___ Cannot be determined (see Comment)

* 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 Type**
- Intratubular germ cell neoplasm, unclassified only
- Seminoma, classic type
- Seminoma with syncytiotrophoblastic cells
- Mixed germ cell tumor (specify components and percentages):
  __________________________________________________
  __________________________________________________
- Embryonal carcinoma
- Yolk sac tumor
- Choriocarcinoma, biphasic
- Choriocarcinoma, monophasic
- Placental site trophoblastic tumor
- Mature teratoma
- Immature teratoma
- Teratoma with a secondary malignant component
  (specify type):
  __________________________________________________
- Monodermal teratoma, carcinoid
- Monodermal teratoma, primitive neuroectodermal tumor
- Monodermal teratoma, other (specify):
  __________________________________________________
- Polyembryoma
- Diffuse embryoma
- Spermatocytic seminoma
- Spermatocytic seminoma with a sarcomatous component
- Testicular scar
- Mixed germ cell-sex cord-stromal tumor, gonadoblastoma
- Mixed germ cell-sex cord-stromal tumor, others
  (specify):
  __________________________________________________
- Other (specify):
  __________________________________________________
- Malignant neoplasm, type cannot be determined

**Pathologic Staging (pTNM)**

**Primary Tumor (pT)**
- pTX: Cannot be assessed
- pT0: No evidence of primary tumor
- pTis: Intratubular germ cell neoplasia only (carcinoma in situ)
- pT1: Tumor limited to the testis and epididymis without vascular/lymphatic invasion (tumor may invade tunica albuginea but not tunica vaginalis)
- pT2: Tumor limited to the testis and epididymis with vascular/lymphatic invasion or tumor extending through tunica albuginea with involvement of tunica vaginalis
- pT3: Tumor invades spermatic cord with or without vascular/lymphatic invasion
- pT4: Tumor invades scrotum with or without vascular/lymphatic invasion

* 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.
### Regional Lymph Nodes (pN)
- **pNX**: Cannot be assessed
- **pN0**: No regional lymph node metastasis
- **pN1**: Metastasis with a lymph node mass less than 2 cm in greatest dimension and 5 or fewer positive nodes, none more than 2 cm in greatest dimension
- **pN2**: Metastasis with a lymph node mass greater than 2 cm but not more than 5 cm in greatest dimension, or more than 5 nodes positive, none greater than 5 cm; or evidence of extranodal extension of tumor
- **pN3**: Metastasis with a lymph node mass greater than 5 cm in greatest dimension

Specify:
- Number examined: ___
- Number involved: ___

### Distant Metastasis (pM)
- **pMX**: Cannot be assessed
- **pM1**: Distant metastasis present
  - **pM1a**: Non-regional lymph nodes or pulmonary metastasis
  - **pM1b**: Distant metastasis other than to non-regional lymph nodes and lungs
    *Specify site(s), if known: ____________________________

### Serum Tumor Markers (S)
- **SX**: Serum marker studies not available or performed
- **S0**: Serum marker study levels within normal limits
  - LDH
  - HCG (mIU/mL)
  - AFP (ng/mL)
  - **S1**: <1.5 x nl and <5,000 and <1,000
  - **S2**: 1.5-10 x nl or 5,000-50,000 or 1,000-10,000
  - **S3**: >10 x nl or >50,000 or >10,000

### Margins (check all that apply)
- **Spermatic Cord Margin**
  - Cannot be assessed
  - Uninvolved by tumor
  - Involved by tumor

### Other Margin(s)
- Cannot be assessed
- Uninvolved by tumor (specify): ____________________________
- Involved by tumor (specify): ____________________________
- Not applicable

### Direct Extension of Invasive Tumor (check all that apply)
- **Rete testis**
- **Epididymis**
- **Peri-hilar fat**
- **Spermatic cord**
- **Tunica vaginalis**
- **Scrotal wall**

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Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)
___ Absent
___ Present
___ Indeterminate

*Additional Pathologic Findings (check all that apply)
*___ None identified
*___ Intratubular germ cell neoplasia
*___ Hemosiderin-laden macrophages
*___ Atrophy
*___ Other (specify): ____________________________

*Comment(s)

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Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
Applies to invasive cancers only
Based on AJCC/UICC TNM, 6th edition

TESTIS: Retroperitoneal Lymphadenectomy

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

*Prelymphadenectomy Treatment
*___ Chemo/radiation therapy
*___ No chemo/radiation therapy
*___ Unknown

*Serum Tumor Markers (check all that apply)
*___ Unknown
*___ Serum marker studies within normal limits
*___ Alpha-fetoprotein (AFP) elevation
*___ Beta subunit of human chorionic gonadotropin (b-hCG) elevation
*___ Lactate dehydrogenase (LDH) elevation

MACROSCOPIC

*Specimen Site(s)
*Specify: ____________________________

*Number of Nodal Groups Present
*Specify: ___
*___ Cannot be determined

Size of Largest Metastasis
Greatest dimension: ___ cm
*Additional dimensions: ___ x ___ cm

MICROSCOPIC

Viability of Tumor (if applicable)
___ Viable tumor present
___ Non viable tumor present

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Testis • Genitourinary

___ No tumor present

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**Histologic Type of Metastatic Tumor**

- Seminoma, classic type
- Seminoma with syncytiotrophoblastic cells
- Mixed germ cell tumor (specify components and percentages):
  - __________________________________________________
  - __________________________________________________
- Embryonal carcinoma
- Yolk sac tumor
- Choriocarcinoma, biphasic
- Choriocarcinoma, monophasic
- Placental site trophoblastic tumor
- Mature teratoma
- Immature teratoma
- Teratoma with a secondary malignant component
  (specify type):
  - __________________________________________________
- Monodermal teratoma, carcinoid
- Monodermal teratoma, primitive neuroectodermal tumor
- Polymembryoma
- Diffuse embryoma
- Spermatocytic seminoma
- Spermatocytic seminoma with a sarcomatous component
- Other (specify):
- Malignant neoplasm, type cannot be determined

**Regional Lymph Nodes (pN)**

- pNX: Cannot be assessed
- pN0: No regional lymph node metastasis
- pN1: Metastasis with a lymph node mass less than 2 cm in greatest dimension and 5 or fewer positive nodes, none greater than 2 cm in greatest dimension
- pN2: Metastasis with a lymph node mass greater than 2 cm but no more than 5 cm in greatest dimension, or more than 5 nodes positive, none greater than 5 cm; or evidence of extranodal extension of tumor
- pN3: Metastasis in a lymph node greater than 5 cm in greatest dimension

Specify:
- Total number examined: ___
- Total number involved: ___

**Nonregional Lymph Node Metastasis (M1a)**

- Not applicable
- Absent
- Present

*Comment(s)*

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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.
I. Radical Orchiectomy

A. Clinical Information
   1. Patient identification
      a. Name
      b. Identification number
      c. Age (birth date)
   2. Responsible physician(s)
   3. Date of procedure
   4. Other clinical information
      a. Relevant history
         (1) previous cryptorchidism treated by orchiopexy
         (2) previous contralateral testicular tumor treated by orchiectomy and lymphadenectomy
         (3) retroperitoneal or paraortic lymphadenopathy
         (4) other
      b. Relevant findings
         (1) testicular enlargement or atrophy
         (2) gynecomastia
         (3) ambiguous genitalia, feminization, or other features of intersex disorders
         (4) serum levels of alpha-fetoprotein (AFP) (Note A)
         (5) serum levels of beta subunit of human chorionic gonadotropin (b-hCG) (Note A)
         (6) imaging studies (eg, ultrasound, abdominal computerized tomograms, chest radiographs)
      c. Clinical diagnosis
      d. Procedure
      e. Operative findings
         (1) laterality of testis
         (2) inguinal or abdominal orchiectomy in cases of cryptorchidism

B. Macroscopic Examination
   1. Specimen
      a. Organ(s)/tissue(s) included
      b. Unfixed/fixed (specify fixative)
      c. Dimensions, including length of spermatic cord
      d. External aspect
      e. Cut surface
      f. Results of intraoperative consultation
   2. Tumor
      a. Location
      b. Number, size, and shapes of distinct tumor nodules
      c. Descriptive characteristics (eg, color, hemorrhage, necrosis)
      d. Borders (circumscribed vs invasive)
      e. Extent of invasion
         (1) description of intertunical fluid
         (2) involvement of tunica vaginalis
         (3) involvement of spermatic cord
(4) involvement of paratesticular soft tissue
3. Additional pathologic findings, if present
   a. Scars
   b. Calcification
   c. Other(s)
4. Tissues submitted for microscopic evaluation (Note B)
5. Special studies (specify) (eg, electron microscopy, cytogenetics, molecular studies)

C. Microscopic Evaluation
1. Tumor
   a. Histologic type (estimate percentage of each component for mixed tumors) (Note C)
   b. Intratubular, invasive, or both
   c. Extent of invasion (Note D)
      (1) invasion beyond tunica albuginea (specify)
      (2) involvement of paratesticular structures (specify)
   d. Venous/lymphatic vessel invasion (specify if in testis or paratestis/spermatic cord) (Note E)
2. Status of resection margin(s), including spermatic cord (Note B)
3. Additional pathologic findings, if present (Note F)
4. Regional lymph nodes (if identified in spermatic cord)
   a. Number present
   b. Number involved by tumor
5. Other tissue(s)
   a. Involved by tumor
   b. Uninvolved by tumor
6. Results/status of special studies (specify)
7. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

II. Retroperitoneal Lymphadenectomy
A. Clinical Information
1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history
      (1) previous cryptorchidism treated by orchiopexy
      (2) previous contralateral testicular tumor treated by orchiectomy and lymphadenectomy
      (3) other
   b. Relevant findings
      (1) testicular enlargement or atrophy
      (2) gynecomastia
(3) ambiguous genitalia, feminization, or other features of intersex disorders
(4) serum levels of alpha-fetoprotein (AFP) (Note A)
(5) serum levels of beta subunit of human chorionic gonadotropin (b-hCG)
   (Note A)
(6) imaging studies (eg, ultrasound, abdominal computerized tomograms,
   chest radiographs)
   c. Clinical diagnosis
d. Procedure (eg, radical, nerve-sparing or other form of retroperitoneal
   lymphadenectomy [RPLND])
e. Operative findings
f. Anatomic site(s) of specimen(s)

B. Macroscopic Examination
1. Specimen
   a. Organ(s)/tissues included
   b. Unfixed/fixed (specify fixative)
   c. Results of intraoperative consultation
2. Regional lymph nodes
   a. Number of lymph node groups and site of each
   b. For each nodal group
      (1) size of nodal group (3 dimensions)
      (2) number of lymph nodes identified
      (3) number of lymph nodes involved by tumor
         i. size ranges of identifiable tumor nodules or dimensions of tumor-
            matted nodes
         ii. descriptive features of tumor, if present (eg, color, hemorrhage,
             necrosis)
3. Spermatic cord structures, if present
   a. Descriptive characteristics
   b. Involvement by tumor
4. Tissues submitted for microscopic evaluation (Note B)
   a. All nodal groups
      (1) number of lymph nodes identified per group
      (2) number lymph nodes submitted for each group
   b. Spermatic cord structures
   c. Frozen section tissue fragment(s) (unless saved for special studies)
5. Special studies (specify)

C. Microscopic Evaluation
1. Regional lymph nodes
   a. Number of lymph nodes in each nodal group
   b. Number involved by tumor in each nodal group
      (1) histologic type(s) (Notes C and G)
      (2) extent of nodal replacement (estimate percentage of nodal involvement)
      (3) involvement of extra-nodal soft tissues, including residual spermatic cord
      (4) necrosis, if present
      (5) associated scar tissue
2. Results/status of special studies (specify)
3. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate
Explanatory Notes

A. Serum Markers
The protocol emphasizes the importance of relevant clinical information in the pathologic evaluation of specimens. Serum marker studies play a key role in the clinical management of patients with testicular germ cell tumors.\(^1\)\(^-\)\(^3\) The occurrence of elevated serum levels of alpha-fetoprotein (AFP) or the beta subunit of human chorionic gonadotropin (b-hCG) may indicate the need for additional sections of certain specimens if the initial findings do not account for such elevations. Information regarding serum marker status (lactate dehydrogenase [LDH], AFP and b-hCG) is also important in the “S” categorization of the tumor for stage groupings.

B. Tissues Submitted for Microscopic Evaluation
The entire testicular tumor may be blocked if it requires 10 blocks or less (tissue may be retained for special studies); 10 blocks of larger tumors may be taken, unless the tumor is greater than 10 cm, in which case 1 block may be submitted for every 1 cm of maximum tumor dimension. Some blocks should contain the interface with non-tumorous testis because lymphatic invasion is best appreciated there. Tissues to be sampled include:

- All of the grossly different types of tumor
- Testicular hilus
- Uninvolved testis
- Epididymis
- Spermatic cord, including cord margin
- Other lesion(s)
- All identifiable lymph nodes\(^#\)
- Other tissue(s) submitted with specimen

\(^#\) For large masses which have obliterated individual nodes, 1 section for every centimeter of maximum tumor dimension, especially fleshy appearing foci, may be taken.

The margins in a specimen resected for a malignant tumor of the testis, depending on the extent of the surgery, includes spermatic cord margin, the parietal layer of tunica vaginalis and scrotal skin.

C. Histologic Type
The protocol applies to malignant tumors of the testis, the vast majority of which are of germ cell origin. It may also be applied to other malignant or potentially malignant tumors of the testis included in the classification shown below.\(^4\)\(^-\)\(^15\) For lymphomas and plasmacytomas of the testis, refer to the non-Hodgkin lymphoma protocol.
Modified Armed Forces Institute of Pathology (AFIP) and World Health Organization (WHO) Histologic Classification of Testicular Tumors

Germ Cell Tumors
Precursor lesion
- Intratubular germ cell neoplasm, unclassified
- Intratubular germ cell neoplasm, specific type

Tumors of 1 histologic type
- Seminoma
  - Variant: Seminoma with syncytiotrophoblastic cells
- Spermatocytic seminoma
  - Variant: Spermatocytic seminoma with a sarcomatous component
- Embryonal carcinoma
- Yolk sac tumor
- Choriocarcinoma
  - Variant: “Monophasic” type
- Placental site trophoblastic tumor
- Trophoblastic tumor, unclassified
- Teratoma
  - Mature
  - Immature
  - With a secondary malignant component
  - Monodermal variants
    - Carcinoid
    - Primitive neuroectodermal tumor
  - Others

Tumors of more than 1 histologic type
- Mixed germ cell tumor (specify components; estimate percentage)
- Polyembryoma
- Diffuse embryoma

Regressed ("burnt out") germ cell tumors
- Scar only
- Scar with intratubular germ cell neoplasia
- Scar with minor residual germ cell tumor

Sex Cord-Stromal Tumors
- Leydig cell tumor
- Sertoli cell tumor
  - Variant: Large cell calcifying Sertoli cell tumor
  - Variant: Sclerosing Sertoli cell tumor
- Granulosa cell tumor
  - Variant: Adult type
  - Variant: Juvenile type
- Mixed and indeterminate (unclassified) sex cord stromal tumor

Mixed Germ Cell- Sex Cord-Stromal Tumors
- Gonadoblastoma
- Unclassified
For Information Only

Genitourinary • Testis

Miscellaneous
Sarcoma (specify type)
Plasmacytoma
Lymphoma (specify type)
Granulocytic sarcoma or leukemic infiltrates
Adenocarcinoma of rete testis
Carcinomas and borderline tumors of ovarian type
Malignant mesothelioma

D. Staging
The protocol recommends staging according to the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) TNM staging system. Additional criteria for staging seminomas according to a modification of the Royal Marsden system are also recommended. Some studies suggest that the staging of patients with seminoma by the TNM system is less meaningful therapeutically than staging by a modification of the Royal Marsden method. The latter staging system subdivides cases with retroperitoneal metastases into several groups according to the total tumor dimension rather than the size of the largest lymph node, as in the TNM system. Also, the data from a large Danish study of seminomas clinically limited to the testis do not support the conclusion that local staging of the primary tumor, as performed in the TNM system, provides useful prognostic information; rather, the most valuable prognostic indicator was the size of the seminoma. This protocol, therefore, encourages the use of the TNM system with optional use of the modified Royal Marsden staging system for patients with seminoma.

AJCC/UICC TNM and Stage Groupings
By AJCC/UICC convention, the designation “T” refers to a primary tumor that has not been previously treated. The symbol “p” refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor is not resected for any reason (eg, when technically unfeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

Primary Tumor (T)
TX Primary tumor cannot be assessed
T0 No evidence of primary tumor (eg, histologic scar in testis)
Tis Intratubular germ cell neoplasia (carcinoma in situ)
T1 Tumor limited to the testis and epididymis without vascular/lymphatic invasion; tumor may invade tunica albuginea but not tunica vaginalis

15
T2  Tumor limited to the testis and epididymis with vascular/lymphatic invasion or tumor extending through tunica albuginea with involvement of tunica vaginalis
T3  Tumor invades spermatic cord with or without vascular/lymphatic invasion
T4  Tumor invades scrotum with or without vascular/lymphatic invasion

Regional Lymph Nodes (N)
NX  Regional nodes cannot be assessed
N0  No regional lymph node metastasis
N1  Metastasis with a lymph node mass 2 cm or less in greatest dimension and 5 or fewer positive nodes, none more than 2 cm in greatest dimension
N2  Metastasis with a lymph node mass greater than 2 cm but no more than 5 cm in greatest dimension, or more than 5 nodes positive, none more than 5 cm; or evidence of extranodal extension of tumor
N3  Metastasis with a lymph node mass greater than 5 cm in greatest dimension

Distant Metastasis (M)
MX  Distant metastasis cannot be assessed
M0  No distant metastasis
M1  Distant metastasis present
M1a  Nonregional lymph node or pulmonary metastasis
M1b  Distant metastasis other than to nonregional lymph nodes and lungs

Serum Tumor Markers (S)
SX  Serum marker studies not available or performed
S0  Serum marker study levels within normal limits
LDH HCG (mIU/mL) AFP (ng/mL)
S1  less than 1.5 x N*  and  less than 5,000  and  less than 1,000
S2  1.5 to 10 x N*  or  5,000 to 50,000  or  1,000 to 10,000
S3  greater than 10 x N*  or  greater than 50,000  or  greater than 10,000

*N indicates the upper limit of normal for the LDH assay.

Stage Groupings
Stage 0  pTis  N0  M0  S0, SX
Stage I  pT1-4  N0  M0  SX
Stage IA  pT1  N0  M0  S0
Stage IB  pT2  N0  M0  S0
    pT3  N0  M0  S0
    pT4  N0  M0  S0
Stage IS  Any pT/TX  N0  M0  S1-3
Stage II  Any pT/TX  N1,N2,N3  M0  SX
Stage IIA  Any pT/TX  N1  M0  S0
    Any pT/TX  N1  M0  S1
Stage IIB  Any pT/TX  N2  M0  S0
    Any pT/TX  N2  M0  S1
Stage IIC  Any pT/TX  N3  M0  S0
    Any pT/TX  N3  M0  S1
Stage III  Any pT/TX  Any N  M1,M1a  SX
Stage IIIA  Any pT/TX Any N M1,M1a S0
Stage IIIB  Any pT/TX Any N M1,M1a S1
Stage IIIC  Any pT/TX N1,N2,N3 M0 S2
Any T Any N M1b Any S

TNM Descriptors
For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y,” “r,” and “a” prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The “m” suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

The “y” prefix indicates those cases in which classification is performed during or following initial multimodality therapy (ie, neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a “y” prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The “y” categorization is not an estimate of tumor prior to multimodality therapy (ie, before initiation of neoadjuvant therapy).

The “r” prefix indicates a recurrent tumor when staged after a documented disease-free interval, and is identified by the “r” prefix: rTNM.

The “a” prefix designates the stage determined at autopsy: aTNM.

Additional Descriptors

Residual Tumor (R)
Tumor remaining in a patient after therapy with curative intent (eg, surgical resection for cure) is categorized by a system known as R classification, shown below.

RX  Presence of residual tumor cannot be assessed
R0  No residual tumor
R1  Microscopic residual tumor
R2  Macroscopic residual tumor

For the surgeon, the R classification may be useful to indicate the known or assumed status of the completeness of a surgical excision. For the pathologist, the R classification is relevant to the status of the margins of a surgical resection specimen. That is, tumor involving the resection margin on pathologic examination may be assumed to correspond to residual tumor in the patient and may be classified as macroscopic or microscopic according to the findings at the specimen margin(s).

Modified Royal Marsden Staging System
Stage I  Tumor confined to the testis
Stage II  Infradiaphragmatic nodal involvement
IIA  greatest dimension of involved nodes less than 2 cm  
IIB  greatest dimension of involved nodes 2 cm or more but less than 5 cm  
IIC  greatest dimension of involved nodes 5 cm or more but less than 10 cm  
IID  greatest dimension of involved nodes 10 cm or more  

Stage III  Supraclavicular or mediastinal involvement  
Stage IV  Extranodal metastases  

E. Venous/Lymphatic Vessel Invasion  
In several studies, the presence of vascular space invasion (usually lymphatic but possibly also capillary or venous invasion) has been correlated with a significantly elevated risk for distant metastasis.\textsuperscript{20-26} This observation, therefore, is most pertinent for patients who have clinical stage I disease, ie, those who have no evidence of spread beyond the testis by clinical examination (including radiographic and serum marker studies). Some clinicians treat patients who have clinical stage I disease and whose testicular germ cell tumors lack evidence of lymphatic or vascular invasion (and possibly have other favorable prognostic features, such as relatively small amounts of embryonal carcinoma) by close follow-up examinations rather than intervention. This practice currently is more accepted for patients who have tumors with 1 or more non-seminomatous components than it is for patients with pure seminoma.  

F. Additional Pathologic Findings  
Important findings include Leydig cell-hyperplasia, which may be correlated with b-hCG elevation; scarring, the presence of hemosiderin-laden macrophages, and intratubular calcification, which may indicate regression of a tumor; testicular atrophy; and abnormal testicular development (eg, dysgenesis or androgen-insensitivity syndrome).\textsuperscript{27,28}  

G. Metastatic Teratoma  
Often the most important distinction in patients with metastatic testicular germ cell tumor, particularly following initial chemotherapy, is the differentiation of metastatic teratoma from nonteratomatous types of germ cell tumor. Pure teratomatous metastasis is generally treated by surgical excision, whereas patients who have metastatic embryonal carcinoma, yolk sac tumor, etc, are usually treated with chemotherapy.  

References  


**Bibliography**
