

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 2005
Based on AJCC/UICC TNM, 6th edition*

Procedures

- **Radical Orchiectomy**
- **Retroperitoneal Lymphadenectomy (RPLND)**

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The College of American Pathologists offers these protocols to assist pathologists in providing clinically useful and relevant information when reporting results of surgical specimen examinations of surgical specimens. The College regards the reporting elements in the "Surgical Pathology Cancer Case Summary (Checklist)" portion of the protocols as essential elements of the pathology report. However, the manner in which these elements are reported is at the discretion of each specific pathologist, taking into account clinician preferences, institutional policies, and individual practice.

The College developed these protocols as an educational tool to assist pathologists in the useful reporting of relevant information. It did not issue the protocols for use in litigation, reimbursement, or other contexts. Nevertheless, the College recognizes that the protocols might be used by hospitals, attorneys, payers, and others. Indeed, effective January 1, 2004, the Commission on Cancer of the American College of Surgeons mandated the use of the checklist elements of the protocols as part of its Cancer Program Standards for Approved Cancer Programs. Therefore, it becomes even more important for pathologists to familiarize themselves with the document. At the same time, the College cautions that use of the protocols other than for their intended educational purpose may involve additional considerations that are beyond the scope of this document.

Summary of Changes to Checklist(s)

Protocol revision date: January 2005

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Surgical Pathology Cancer Case Summary (Checklist)

*Protocol revision date: January 2005
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

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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
- | | <u>LDH</u> | | <u>HCG (mIU/mL)</u> | | <u>AFP (ng/mL)</u> |
|--------------------------------|-------------|-----|---------------------|-----|--------------------|
| * <input type="checkbox"/> S1: | <1.5 x nl | and | <5,000 | and | <1,000 |
| * <input type="checkbox"/> S2: | 1.5-10 x nl | or | 5,000-50,000 | or | 1,000-10,000 |
| * <input type="checkbox"/> 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
- None of the above

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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 2005
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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
- No tumor present

8 * 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.

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
 Polyembryoma
 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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Background Documentation

Protocol revision date: January 2005

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 intertunicular 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
 - c. Correlation with clinical information, 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

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.^{16,17} Additional criteria for staging seminomas according to a modification of the Royal Marsden system are also recommended.¹⁸ 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.¹⁶⁻¹⁸ 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.¹⁹ 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
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
	Any pT/TX	Any N	M1,M1a	S1
Stage IIIB	Any pT/TX	N1,N2,N3	M0	S2
	Any pT/TX	Any N	M1,M1a	S2
Stage IIIC	Any pT/TX	N1,N2,N3	M0	S3
	Any pT/TX	Any N	M1,M1a	S3
	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 DescriptorsResidual 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.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).^{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

1. Chisolm GG. Tumour markers in testicular tumours. *Prog Clin Biol Res.* 1985;203:81-91.
2. Javadpour N. Tumor markers in testicular cancer: an update. *Prog Clin Biol Res.* 1985;203:141-154.
3. Aass N, Klepp O, Cavallin-Stahl E, et al. Prognostic factors in unselected patients with nonseminomatous metastatic testicular cancer: a multicenter experience. *J Clin Oncol.* 1991;9:818-826.
4. Lawrence WD, Young RH, Scully RE. Sex cord - stromal tumors. In: Talerma A, Roth LM, eds. *Pathology of the Testis and Its Adnexa.* New York: Churchill Livingstone; 1986:67-92.
5. Proppe KH, Scully RE. Large-cell calcifying Sertoli cell tumor of the testis. *Am J Clin Pathol.* 1980;74:607-619.
6. Young RH, Talerma A. Testicular tumors other than germ cell tumors. *Semin Diagn Pathol.* 1987; 4:342-360.
7. Kim I, Young RH, Scully RE. Leydig cell tumors of the testis: a clinicopathological analysis of 40 cases and review of the literature. *Am J Surg Pathol.* 1985;9:177-192.
8. Mostofi FK, Price EBJ. *Tumors of the Male Genital System. Atlas of Tumor Pathology.* 2nd series. Fascicle 8. Washington DC: Armed Forces Institute of Pathology; 1973.
9. Mostofi FK, Sobin LH. *Histological Typing of Testicular Tumors (International Histological Classification of Tumors).* No. 16. Geneva: World Health Organization; 1977.
10. Mostofi FK, Spaander P, Grigor K, Parkinson CM, Skakkebaek NE, Oliver RT. Consensus on pathological classifications of testicular tumours. *Prog Clin Biol Res.* 1990;357:267-276.
11. Young RH, Scully RE. *Testicular Tumors.* Chicago, Ill: ASCP Press; 1990.
12. Ulbright TM, Roth LM. Testicular and paratesticular neoplasms. In: Sternberg SS, ed. *Diagnostic Surgical Pathology.* 2nd ed. New York: Raven Press; 1994:1885-1947.

13. Ulbright TM, Amin MB, Young RH. *Tumors of the Testis, Adnexa, Spermatic Cord, and Scrotum*. Third Series. Fascicle 25. Washington, DC: Armed Forces Institute of Pathology; 1999.
14. Ro JY, Dexeus FH, El-Naggar A, Ayala AG. Testicular germ cell tumors: clinically relevant pathologic findings. *Pathol Annu*. 1991;26(pt 2):59-87.
15. Ferry JA, Harris NL, Young RH, Coen J, Zietman A, Scully RE. Malignant lymphoma of the testis, epididymis, and spermatic cord: a clinicopathologic study of 69 cases with immunophenotypic analysis. *Am J Surg Pathol*. 1994;18:376-390.
16. Greene FL, Page DL, Fleming ID, et al, eds. *AJCC Cancer Staging Manual*. 6th ed. New York: Springer; 2002.
17. Sobin LH, Wittekind C. *UICC TNM Classification of Malignant Tumours*. 6th ed. New York: Wiley-Liss; 2002.
18. Thomas G, Jones W, VanOosterom A, Kawai T. Consensus statement on the investigation and management of testicular seminoma 1989. *Prog Clin Biol Res*. 1990;357:285-294.
19. von der Maase H, Specht L, Jacobsen GK, et al. Surveillance following orchidectomy for stage I seminoma of the testis. *Eur J Cancer*. 1993;29A:1931-1934.
20. Jacobsen GK, Rorth M, Osterlind K, et al. Histopathological features in stage I non-seminomatous testicular germ cell tumours correlated to relapse: Danish Testicular Cancer Study Group. *APMIS*. 1990;98:377-382.
21. Marks LB, Rutgers JL, Shipley WU, et al. Testicular seminoma: clinical and pathological features that may predict para-aortic lymph node metastasis. *J Urol*. 1990;143:524-527.
22. Hoeltl W, Pont J, Kosak D, Honetz N, Marberger M. Treatment decision for stage I non-seminomatous germ cell tumours based on the risk factor "vascular invasion." *Br J Urol*. 1992;69:83-87.
23. Sesterhenn IA, Weiss RB, Mostofi FK, et al. Prognosis and other clinical correlates of pathologic review in stage I and II testicular carcinoma: a report from the Testicular Cancer Intergroup Study. *J Clin Oncol*. 1992;10:69-78.
24. Horwich A, Alsanjari N, A'Hern R, Nicholls J, Dearnaley DP, Fisher C. Surveillance following orchidectomy for stage I testicular seminoma. *Br J Cancer*. 1992;65:775-778.
25. Sturgeon JF, Jewett MA, Alison RE, et al. Surveillance after orchidectomy for patients with clinical stage I nonseminomatous testis tumors. *J Clin Oncol*. 1992;10:564-568.
26. Moul JW, McCarthy WF, Fernandez EB, Sesterhenn IA. Percentage of embryonal carcinoma and of vascular invasion predicts pathological stage in clinical stage I nonseminomatous testicular cancer. *Cancer Res*. 1994;54:362-364.
27. Rutgers JL, Scully RE. Pathology of the testis in intersex syndromes. *Semin Diagn Pathol*. 1987;4:275-291.
28. Wallace TM, Levin HS. Mixed gonadal dysgenesis: a review of 15 patients reporting single cases of malignant intratubular germ cell neoplasia of the testis, endometrial adenocarcinoma, and a complex vascular anomaly. *Arch Pathol Lab Med*. 1990;114:679-688.

Bibliography

- Morse MJ, Whitmore WF. Neoplasms of the testis. In: Walsh PC, Gittes RF, Perlmutter AD, Stamey TA, eds. *Campbell's Urology*. Philadelphia, Pa: WB Saunders; 1986:1535-1582.
- Rowland RG, Donohue JP. Scrotum and testis. In: Gillenwater JY, Grayhack JT, Howards SS, Duckett JW, eds. *Adult and Pediatric Urology*. 2nd ed. St. Louis, Mo: Mosby Year Book; 1991:1565-1598.