COLLEGE of AMERICAN PATHOLOGISTS

Protocol for the Examination of Specimens from Patients with Malignant Germ Cell and Sex Cord-Stromal Tumors of the Testis

Protocol applies to all malignant germ cell and sex cord-stromal tumors of the testis. Paratesticular malignancies are excluded.

Version: Testis 3.4.1.0 **Protocol Posting Date:** February 2017
Includes pTNM requirements from the 7th Edition, AJCC Staging Manual

Procedures
• Radical Orchiectomy
• Retroperitoneal Lymphadenectomy (RPLND)

Accreditation Requirements
This protocol can be utilized for a variety of procedures and tumor types for clinical care purposes. For accreditation purposes, only the definitive primary cancer resection specimen is required to have the core and conditional data elements reported in a synoptic format.

- Core data elements are required in reports to adequately describe appropriate malignancies. For accreditation purposes, essential data elements must be reported in all instances, even if the response is "not applicable" or "cannot be determined."
- Conditional data elements are only required to be reported if applicable as delineated in the protocol. For instance, the total number of lymph nodes examined must be reported, but only if nodes are present in the specimen.
- Optional data elements are identified with "+" and although not required for CAP accreditation purposes, may be considered for reporting as determined by local practice standards.

The use of this protocol is not required for recurrent tumors or for metastatic tumors that are resected at a different time than the primary tumor. Use of this protocol is also not required for pathology reviews performed at a second institution (ie, secondary consultation, second opinion, or review of outside case at second institution).

CAP Laboratory Accreditation Program Protocol Required Use Date: November 2017*
** Beginning January 1, 2018, the 8th edition AJCC Staging Manual should be used for reporting pTNM. The CAP will offer a revised 8th edition version of this protocol by mid-year 2017.*

Authors
Satish K. Tickoo MD*, Ming Zhou MD PhD*, Mahul B. Amin MD, Sam S. Chang MD, Peter A. Humphrey MD PhD, James McKiernan MD, Victor E. Reuter MD, John R. Srigley MD, Thomas M. Ulbright MD
With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.
** Denotes primary authors. All other contributing authors are listed alphabetically.*

CAP Testis Protocol Revision History

Summary of Changes
The following changes have been made since the October 2013 release.

Radical Orchiectomy

The following data elements were modified:
- Histologic Type
- (Microscopic) Tumor Extension (all elements now required)
- Additional Pathologic Findings

The following data element was added:
- Regional Lymph Node Involvement

Retroperitoneal Lymphadenectomy

The following data elements were modified:
- Size of Largest Metastatic Deposit in Lymph Node Mass
- Histologic Type of Metastatic Tumor
- Nonregional Lymph Node Metastasis

The following data element was added:
- Regional Lymph Node Involvement

Surgical Pathology Cancer Case Summary

Protocol posting date: February 2017

TESTIS: Radical Orchiectomy

Select a single response unless otherwise indicated.

Specimen Laterality
___ Right
___ Left
___ Not specified

Tumor Focality
___ Unifocal
___ Multifocal

Tumor Size
Greatest dimension of main tumor mass: ___ cm
+ Additional dimensions: ___ x ___ cm

Greatest dimensions of additional tumor nodules (required only if applicable): ___ cm, ___ cm[#]
___ Cannot be determined (explain): _____
[#]*Note: Include additional greatest dimensions for additional nodules as necessary*

Histologic Type (select all that apply) (Notes A, B, and C)
Intratubular germ cell neoplasia
___ Germ cell neoplasia in situ (GCNIS)
___ Intratubular seminoma
___ Intratubular embryonal carcinoma
___ Other intratubular germ cell tumor (specify): _____

Seminoma
___ Seminoma
___ Seminoma with syncytiotrophoblastic cells
___ Seminoma with associated scar

___ Embryonal carcinoma
___ Yolk sac tumor, postpubertal type
___ Choriocarcinoma
___ Mixed germ cell tumor (specify components and approximate percentages): _____

Non-choriocarcinomatous trophoblastic tumor
___ Non-choriocarcinomatous trophoblastic tumor, NOS
___ Placental site trophoblastic tumor
___ Epithelioid trophoblastic tumor
___ Cystic trophoblastic tumor

___ Teratoma, postpubertal type
___ Teratoma with somatic-type malignancy (specify type): _____

Testicular scar/regressed germ cell tumor
___ Scar diagnostic of regressed germ cell tumor
___ Scar suspicious for regressed germ cell tumor

___ Spermatocytic tumor
___ Spermatocytic tumor with a sarcomatous component
+ ___ Prepubertal type teratoma
    + ___ Dermoid cyst
    + ___ Epidermoid cyst
    + ___ Well-differentiated neuroendocrine tumor (monodermal teratoma)
    + ___ Other, (specify): _____
___ Mixed germ cell-sex cord stromal tumor, gonadoblastoma

Sex cord-stromal tumor
___ Leydig cell tumor
___ Malignant Leydig cell tumor
___ Sertoli cell tumor, NOS
___ Sertoli cell tumor, malignant
___ Sertoli cell tumor, large cell calcifying
___ Sertoli cell tumor, intratubular large cell hyalinizing
___ Granulosa cell tumor, adult type
___ Granulosa cell tumor, juvenile type
___ Fibroma-thecoma
___ Sex cord-stromal tumor, mixed type (specify components and approximate percentages): _____
___ Sex cord-stromal tumor type, unclassified

___ Other histologic type, (specify): _____

Tumor Extension (select all that apply) (Note D)
___ Rete testis[#]
___ Tunica vaginalis (perforates mesothelium)
___ Epididymis
___ Hilar fat
___ Scrotal wall
___ Other (specify): _____
___ Cannot be assessed
___ Not identified
[#] *See note D for definition of rete testis invasion*

Margins

Spermatic Cord Margin
___ Cannot be assessed
___ Involved by tumor
___ Uninvolved by tumor

Other Margin(s)
___ Cannot be assessed
___ Involved by tumor (specify): _____
___ Uninvolved by tumor (specify): _____
___ Not applicable

Lymphovascular Invasion (Note E)
___ Not identified
___ Present
___ Cannot be determined

Regional Lymph Nodes

___ No lymph nodes submitted or found

Lymph Node Examination (required only if lymph nodes are present in the specimen)

Number of Lymph Nodes Involved: _____
___ Number cannot be determined (explain): _____

Number of Lymph Nodes Examined: _____
___ Number cannot be determined (explain): _____

Lymph Node Metastasis (required only if lymph nodes are involved)

Site(s) of Involved Lymph Nodes (specify): _____ #
 # Note: Sites may include interaortocaval, paraaortic, paracaval, preaortic, precaval, retroaortic, retrocaval, other lymph nodes, or not specified

Size of Largest Lymph Node (or Nodal Mass) Involved (centimeter): ___ cm
___ Cannot be determined (explain): _____

+ Size of Largest Metastatic Deposit (millimeter): ___ mm
+ Specify Location: _____

Extranodal Extension (required only if lymph nodes involved)
___ Not identified
___ Present
___ Cannot be determined

Histologic subtype of germ cell tumor in involved lymph nodes (If applicable, specify): _____

Pathologic Stage Classification (pTNM, AJCC 7th Edition) (Note F)

TNM Descriptors (required only if applicable) (select all that apply)
___ m (multiple)
___ r (recurrent)
___ y (posttreatment)

Primary Tumor (pT)
___ pTX: Cannot be assessed
___ pT0: No evidence of primary tumor
___ pTis: Intratubular germ cell neoplasia (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 the tunica albuginea with involvement of the tunica vaginalis
___ pT3: Tumor invades the spermatic cord with or without vascular/lymphatic invasion
___ pT4: Tumor invades the scrotum with or without vascular/lymphatic invasion

Regional Lymph Nodes (pN)
___ pNX: Cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis with a lymph node mass 2 cm or less in greatest dimension and less than or equal to 5 nodes positive, none more than 2 cm in greatest dimension
___ pN2: Metastasis with a lymph node mass more than 2 cm but not 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
___ pN3: Metastasis with a lymph node mass more than 5 cm in greatest dimension

Distant Metastasis (pM) (required only if applicable)
___ pM1: Distant metastasis present
___ pM1a: Nonregional nodal or pulmonary metastasis
___ pM1b: Distant metastasis other than to nonregional lymph nodes and lung
Specify site(s), if known: _____

+ Pre-Orchiectomy Serum Tumor Markers (select all that apply) (Notes F and G)
+ ___ Unknown
+ ___ Serum marker studies within normal limits
+ ___ Alpha-fetoprotein (AFP) elevation
+ ___ Beta subunit of human chorionic gonadotropin (b-hCG) elevation
+ ___ Lactate dehydrogenase (LDH) elevation

+ Post-Orchiectomy Serum Tumor Markers (select all that apply) (Notes F and G)
+ ___ Unknown
+ ___ Serum marker studies within normal limits
+ ___ Alpha-fetoprotein (AFP) elevation
+ ___ Beta subunit of human chorionic gonadotropin (b-hCG) elevation
+ ___ Lactate dehydrogenase (LDH) elevation

+ Serum Tumor Markers (S) (Note G)
+ ___ 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 N[#]	and	<5,000	and	<1,000
+ ___ S2:	1.5-10 X N	or	5,000-50,000	or	1,000-10,000
+ ___ S3:	>10 X N	or	>50,000	or	>10,000

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

+ Additional Pathologic Findings (select all that apply) (Note H)
+ ___ None identified
+ ___ Microlith
+ ___ Sertoli cell nodule (Pick's adenoma)
+ ___ Atrophy
+ ___ Other (specify): _____

+ Comment(s)

Surgical Pathology Cancer Case Summary

Protocol posting date: February 2017

TESTIS: Retroperitoneal Lymphadenectomy (Note A)

Note: For patient care the use of this protocol is recommended for reporting retroperitoneal lymphadenectomy specimens but for accreditation purposes the use of case summary for these specimens is not required.

Select a single response unless otherwise indicated.

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

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

+ Specimen Site(s)
+ Specify: _____

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

Histologic Viability of Tumor (if applicable) (select all that apply)
___ Viable teratoma present
___ Viable nonteratomatous tumor present
___ No viable tumor present

Histologic Type of Metastatic Tumor (Note B)
___ Seminoma
___ Seminoma with syncytiotrophoblastic cells
___ Embryonal carcinoma
___ Yolk sac tumor, postpubertal type
___ Choriocarcinoma
___ Mixed germ cell tumor, specify components and approximate percentages: _____
___ Non-choriocarcinomatous trophoblastic tumor, NOS
___ Placental site trophoblastic tumor
___ Epithelioid trophoblastic tumor
___ Cystic trophoblastic tumor
___ Teratoma, postpubertal type
___ Teratoma with somatic-type malignancy (specify type): _____
___ Spermatocytic tumor
___ Spermatocytic tumor with a sarcomatous component
___ Well-differentiated neuroendocrine tumor (monodermal teratoma)
___ Other histologic type, (specify): _____

Regional Lymph Nodes

Number of Lymph Nodes Involved: _____
___ Number cannot be determined (explain): _____

Number of Lymph Nodes Examined: _____
___ Number cannot be determined (explain): _____

Lymph Node Metastasis (required only if lymph nodes are involved)

Site(s) of Involved Lymph Nodes (specify[#]): _____
[#] *Note: Sites may include interaortocaval, paraaortic, paracaval, preaortic, precaval, retroaortic, retrocaval, other lymph nodes, or not specified.*

Size of Largest Lymph Node (or Nodal Mass) Involved (centimeter): ___ cm
___ Cannot be determined (explain): _____

+ Size of Largest Metastatic Deposit (millimeter): ___ mm
+ Specify Location: _____

Extranodal Extension
___ Not identified
___ Present
___ Cannot be determined

Nonregional Lymph Node Metastasis (M1a) (Note I)
___ Not applicable
___ Not identified
___ Present
+ Specify site(s): _____
+ Number of lymph nodes examined (specify): _____
+ Number of lymph nodes involved (specify): _____
+ Number cannot be determined (explain): _____

Regional Lymph Nodes (pN; AJCC 7th Edition) (Note I)
___ pNX: Cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis with a lymph node mass 2 cm or less in greatest dimension and less than or equal to 5 nodes positive, none more than 2 cm in greatest dimension
___ pN2: Metastasis with a lymph node mass more than 2 cm but not 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
___ pN3: Metastasis in a lymph node more than 5 cm in greatest dimension

+ Comment(s):_____

Explanatory Notes

A. 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. Blocks must contain the interface with nontumorous testis, as well as the tunica albuginea, even away from the tumor, because lymphatic invasion is best appreciated in the peritumoral tissue, as well as in the vessels within and under/parallel to the tunica. Tissues to be sampled include:

- Tumor, including interface with surrounding testis, and tunica albuginea
- All of the grossly different appearing areas in the tumor
- Testicular hilum/mediastinum testis
- Uninvolved testis, including tunica albuginea
- 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, one section for every centimeter of maximum tumor dimension, including grossly different looking areas, is recommended.*

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

B. Histologic Type

The protocol mainly 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.[1-12] For hematolymphoid neoplasms involving the testis, refer to the corresponding CAP protocols.

World Health Organization (WHO) Histologic Classification of Testicular Tumors (2016)[13]

Germ Cell Tumors derived from germ cell neoplasia in situ
Noninvasive germ cell neoplasia
- Germ cell neoplasia in situ
- Specific forms of intratubular germ cell neoplasia

Tumors of a single histologic type (pure forms)
- Seminoma
- Seminoma with syncytiotrophoblastic cells

Nonseminomatous germ cell tumors
- Embryonal carcinoma
- Yolk sac tumor, postpubertal type
- Trophoblastic tumors
  - Choriocarcinoma
  - Nonchoriocarcinomatous trophoblastic tumors
  - Placental site trophoblastic tumor
  - Epidermoid trophoblastic tumor
  - Cystic trophoblastic tumor
- Teratoma, postpubertal type
- Teratoma with somatic-type malignancy

Nonseminomatous germ cell tumors of more than one histologic type
- Mixed germ cell tumor

Germ cell tumors of unknown type
- Regressed germ cell tumor

Germ Cell Tumors Unrelated to Germ Cell Neoplasia In Situ
Spermatocytic tumor
Teratoma, prepubertal type
- Dermoid cyst
- Epidermoid cyst
- Well-differentiated neuroendocrine tumor (monodermal teratoma)
- Yolk sac tumor, prepubertal type

Mixed teratoma and yolk sac tumor, prepubertal type
York sac tumor, prepubertal type

Sex Cord-Stromal Tumors
Pure tumors
Leydig cell tumor
- Malignant Leydig cell tumor

Sertoli cell tumor
- Malignant Sertoli cell tumor
- Large cell calcifying Sertoli cell tumor
- Intratubular large cell hyalinizing Sertoli cell neoplasia

Granulosa cell tumor
- Adult granulosa cell tumor
- Juvenile granulosa cell tumor

Tumors in the fibroma-thecoma group
Mixed and unclassified sex cord stromal tumor
- Mixed sex cord-stromal tumor
- Unclassified sex cord-stromal tumor

Tumor Containing Both Germ Cell and Sex Cord-Stromal Elements
Gonadoblastoma

Miscellaneous
Ovarian epithelial-type tumors
- Serous cystadenoma
- Serous tumor of borderline malignancy
- Serous cystadenocarcinoma
- Mucinous cystadenoma
- Mucinous borderline tumor
- Mucinous cuystadenocarcinoma
- Endometrioid adenocarcinoma
- Clear cell adenocarcinoma
- Brenner tumor

Juvenile xanthogranuloma
Hemangioma

Hematolymphoid tumors
Diffuse large B-cell lymphoma
Follicular lymphoma
Extranodal NI/T-cell lymphoma, nasal type
Plasmacytoma
Myeloid sarcoma
Rosai-Dorfman disease

Tumors of Collecting Duct and Rete Testis
Adenoma
Adenocarcinoma

Tumors of Paratesticular Structures

Adenomatoid tumor
Mesothelioma
    Well-differentiated papillary mesothelioma
Epididymal tumors
    Cystadenoma of the epididymis
    Papillary cystadenoma
    Adenocarcinoma of the epididymis
Squamous cell carcinoma
Melanotic neuroectodermal tumor
Nephroblastoma
Paraganglioma

Mesenchymal tumors of the spermatic cord and testicular adnexa
Apipocytic tumors
    Lipoma
    Well-differentiated liposarcoma
    Dedifferentiated liposarcoma
    Myxoid liposarcoma
    Pleomorphic liposarcoma

C. Scar
Testicular scars, particularly in patients presenting with metastatic disease and clinically inapparent testicular primaries, may represent regressed, "burnt-out" testicular germ cell tumors. There are two established criteria to indicate a scar is diagnostic of a regressed germ cell tumor (GCT): a scar with associated germ cell neoplasia in situ (GCNIS) or a scar that contains coarse intratubular calcifications within expanded tubular profiles, which correspond to dystrophic calcifications that occurred in completely necrotic intratubular embryonal carcinoma. Features that are suspicious for, although not diagnostic of, regressed germ cell tumors include testicular atrophy, microlithiasis, and, in the scar, lymphoplasmacytic infiltrates and prominent vascularity.[14] In otherwise pure seminoma, such partial regression may have clinically important implications, since it is possible that some of these scars may represent regression of a nonseminomatous germ cell tumor component of the tumor.

D. Invasion of the Rete Testis, Hilar/Mediastinal Soft Tissue, Epididymis or Tunica Vaginalis
Tumors invading the tunica vaginalis (perforating the mesothelial lining) (Figure 1, Tumor A) are considered as stage pT2 by the American Joint Committee on Cancer (AJCC) TNM staging system. Invasion of rete testis is not assigned a higher pT stage than that for a tumor limited to the testis. Rete testis invasion has been reported by some to be associated with higher risk of relapse in clinical stage I seminoma.[15] Rete testis invasion is that the invasive tumor involves the rete testis stroma, with or without luminal involvement. Pagetoid extension of GCNIS into the rete testis should not be considered rete testis invasion. Hilar soft tissue invasion (Figure 1, Tumor B) is the predominant pathway of extratesticular extension for testicular tumors.[16,17] There is evidence beginning to accumulate that rete testis and hilar soft tissue invasion have predictive value for metastatic disease in patients with nonseminomatous GCTs.[17] *Invasion of epididymis and hilar soft tissue will be staged as pT2 by the 8th edition of AJCC TNM.* [26]

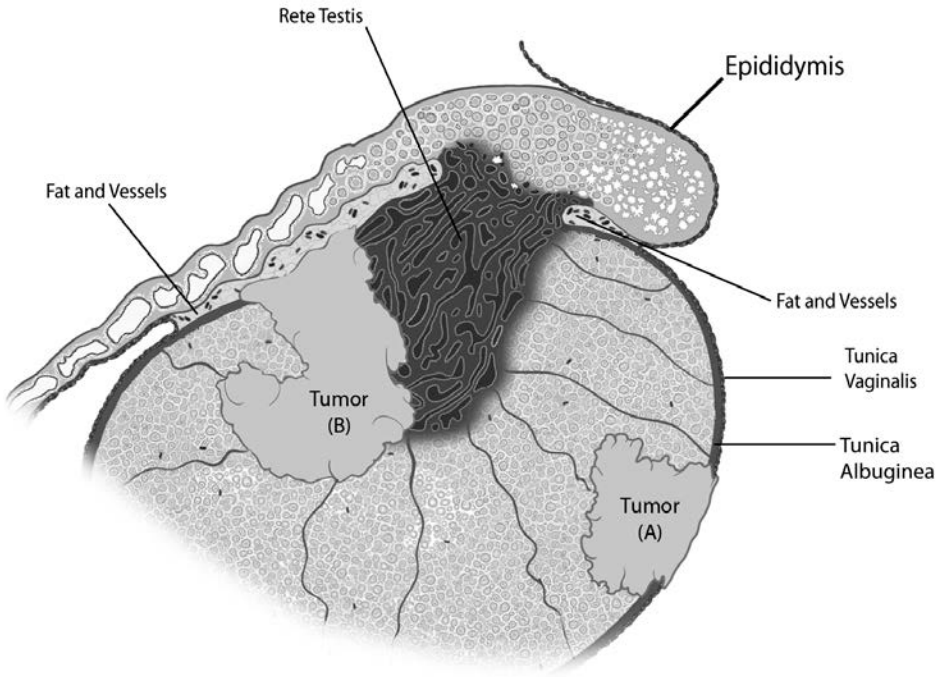

Figure 1. Diagrammatic representation of a tumor (Tumor A) invading tunica vaginalis, perforating through the mesothelium, and another tumor (Tumor B) partly involving the rete testis and invading the hilar soft tissue. Figure courtesy of Satish K. Tickoo, MD.

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.[18-24] 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 manage the patients with clinical stage I disease who lack evidence of lymphatic or vascular invasion in their orchiectomy specimens (with possibly other favorable prognostic features, such as relatively small amounts of embryonal carcinoma) by close follow-up examinations rather than intervention.

F. Staging

The protocol recommends staging according to the American Joint Committee on Cancer (AJCC) TNM staging system.[25] Additional criteria for staging seminomas according to a modification of the Royal Marsden system are also recommended.[27] 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.[25,27] 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.[28] 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 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.

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	

G. 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.[29-31] 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 preorchiectomy serum marker status (lactate dehydrogenase [LDH], AFP, and b-hCG) is also important in the "S" categorization of the tumor for stage groupings. Postorchiectomy serum markers are important for the assignment of stage IS only.

Anatomic Stage/Prognostic Groups

Group	T	N	M	S
Stage 0	pTis	N0	M0	S0
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 (measured post orchiectomy)
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	SX
Stage IIIA	Any pT/TX	Any N	M1a	S0
	Any pT/TX	Any N	M1a	S1
Stage IIIB	Any pT/TX	N1,N2,N3	M0	S2
	Any pT/TX	Any N	M1a	S2
Stage IIIC	Any pT/TX	N1,N2,N3	M0	S3
	Any pT/TX	Any N	M1a	S3
	Any T	Any N	M1b	Any S

Prognostic Factors

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 N[#]	and	<5,000	and	<1,000
S2	1.5-10 X N	or	5,000-50,000	or	1,000-10,000
S3	>10 X N	or	>50,000	or	>10,000

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

The serum tumor markers (S) category comprises the following:

- Alpha fetoprotein (AFP) – half-life 5 to 7 days
- Human chorionic gonadotropin (hCG) – half-life 1 to 3 days
- Lactate dehydrogenase (LDH)

H. 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 coarse intratubular calcifications in expanded tubular profiles (distinct from microlithiasis), which may indicate regression of a tumor; testicular atrophy; sertoli cell nodules (Pick's adenoma), which most often are associated with undescended testes, and abnormal testicular development (eg, dysgenesis or androgen-insensitivity syndrome).[32,33]

I. Metastatic Tumor

Often the most important distinction in patients with metastatic testicular germ cell tumor following initial chemotherapy is the differentiation of metastatic residual teratoma from nonteratomatous types of germ cell tumor.

Pure teratomatous metastasis is generally treated by surgical excision alone, whereas patients who have other residual germ cell tumor components are usually treated with additional chemotherapy.

References

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The CAP 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 CAP 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 required data 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 these documents. At the same time, the CAP 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.

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