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Clinical manifestations, diagnosis, and staging of testicular germ cell tumors

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INTRODUCTION

Testicular cancer is the most common solid malignancy affecting males between the ages of 15 and 35, although it accounts for only 1 percent of all cancers in men [1]. Testicular cancer is also one of the most curable of solid neoplasms because of remarkable treatment advances, with five-year survival rates of approximately 95 percent [1,2].

Germ cell tumors (GCTs) account for 95 percent of testicular cancers (table 1). They may consist of one predominant histologic pattern or represent a mix of multiple histologic types. For treatment purposes, two broad categories of testis tumors are recognized: pure seminoma (no nonseminomatous elements present) and all others, which together are termed nonseminomatous germ cell tumors (NSGCTs). In most series, the ratio of seminoma to NSGCT is approximately one.

The clinical manifestations, diagnosis, and staging of testicular cancer will be presented here. Optimal therapy, which varies with the stage of disease, is discussed separately. (See "Overview of the treatment of testicular germ cell tumors".)

CLINICAL MANIFESTATIONS

Testicular tumors usually present as a nodule or painless swelling of one testicle, which may be noted incidentally by the patient or by his sexual partner [3]. Occasionally, a man with a

previously small atrophic testis will note enlargement. Approximately 30 to 40 percent of patients complain of a dull ache or heavy sensation in the lower abdomen, perianal area, or scrotum, while acute pain is the presenting symptom in 10 percent.

The presenting manifestations of testicular cancer are attributable to metastatic disease in approximately 10 percent of patients. Symptoms vary with the site of metastasis:

- A neck mass (supraclavicular lymph node metastasis)
- Cough or dyspnea (pulmonary metastasis)
- Anorexia, nausea, vomiting, or gastrointestinal hemorrhage (retroduodenal metastasis)
- Lumbar back pain (bulky retroperitoneal disease involving the psoas muscle or nerve roots)
- Bone pain (skeletal metastasis)
- Central or peripheral nervous system symptoms (cerebral, spinal cord, or peripheral root involvement)
- Unilateral or bilateral lower extremity swelling (iliac or caval venous obstruction or thrombosis)

Gynecomastia, which occurs in approximately 5 percent of men with testicular germ cell tumors, is a systemic endocrine manifestation of these neoplasms [4]. It also occurs in 20 to 30 percent of patients with the less common (2 percent of testicular tumors) Leydig cell tumors of the testes [5]. These tumors are found in 6- to 10-year-old boys who present with precocious puberty and in 26- to 35-year-old men who present with a testicular mass, gynecomastia, impotence, and loss of libido. (See "Testicular sex cord stromal tumors".)

Gynecomastia is usually associated with production of human chorionic gonadotropin (hCG) by foci of choriocarcinoma or trophoblastic cells in the tumor. However, the relationship between gynecomastia, testicular tumor morphology, and endocrine abnormalities remains incompletely defined. In individual patients, gynecomastia may or may not be associated with elevated serum concentrations of hCG, human chorionic somatomammotropin, prolactin, estrogens, or androgens. (See "Epidemiology, pathophysiology, and causes of gynecomastia" and "Clinical features, diagnosis, and evaluation of gynecomastia in adults".)

Patients with marked overproduction of hCG can develop another endocrine complication, paraneoplastic hyperthyroidism [6]. Thyroid-stimulating hormone and hCG have a common alpha subunit and a beta subunit with considerable homology. As a result, hCG has weak thyroid-stimulating activity. (See "Overview of thyroid disease and pregnancy", section on 'hCG and thyroid function' and "Disorders that cause hyperthyroidism", section on 'Trophoblastic disease and germ cell tumors'.)

Patients with testicular cancer may rarely develop a paraneoplastic limbic encephalitis. Most of these patients have anti-Ma2 (also called anti-Ta) antibodies [7]. The Ma2 antigen is selectively expressed in the neuronal nucleoli of normal brain tissue and the testicular tumor of the patient. (See "Paraneoplastic and autoimmune encephalitis" and "Paraneoplastic and autoimmune encephalitis", section on 'Ma2-associated encephalitis'.)

Testicular examination — Physical examination of the testes should begin with bimanual examination of the scrotal contents, starting with the normal contralateral testis. This permits the examiner to appreciate the relative size, contour, and consistency of the normal testis as a baseline for comparison with the suspected gonad. The testis should be carefully palpated between the thumb and first two fingers of the examining hand.

The normal gonad is homogeneous in consistency, freely movable, and separable from the epididymis. Any firm, hard, or fixed area within the substance of the tunica albuginea should be considered suspicious until proven otherwise. Further evaluation of the affected side should be directed toward possible involvement of the spermatic cord, scrotal investments, or skin.

Testicular tumors tend to remain ovoid, being limited by the tough investing tunica albuginea. However, spread to the epididymis or spermatic cord occurs in 10 to 15 percent of patients. In general, a seminoma tends to expand within the testis as a painless, rubbery enlargement, while an embryonal carcinoma or teratocarcinoma forms an irregular mass with indiscrete borders. However, this distinction is not always easily appreciated.

A hydrocele may be present and can make evaluation of a suspected testicular tumor more difficult. In such cases, ultrasonography of the scrotum is a rapid, reliable technique to exclude a hydrocele or epididymitis; it is indicated in any man with a suspected testicular tumor. (See 'Scrotal ultrasound' below.)

Physical examination should also include palpation of the abdomen for evidence of nodal disease or visceral involvement. Routine assessment of the supraclavicular lymph nodes may reveal adenopathy in men with advanced disease. Examination of the chest may disclose gynecomastia or raise suspicion for thoracic involvement.

Cryptorchidism — Men with a history of cryptorchidism and prior orchiopexy are at increased risk for testicular cancer in both testes (greater in the undescended one), although the magnitude of increased risk compared with men in the general population is poorly quantified. Regardless, testicular self-examination is an important part of the routine evaluation. Because of the rarity of such tumors, surveillance scrotal ultrasound (in the absence of clinical exam findings) is not indicated. (See "Epidemiology of and risk factors for testicular germ cell tumors",

section on 'Cryptorchidism' and "Undescended testes (cryptorchidism) in children: Management", section on 'Long-term follow-up'.)

DIAGNOSTIC EVALUATION

In any man with a solid, firm mass within the testis, testicular cancer must be the considered diagnosis until proven otherwise. Prompt diagnosis and treatment of testicular cancer provides the best opportunity for cure. Nevertheless, both patient and clinician factors often contribute to a delay in diagnosis. Painless scrotal masses are sometimes ignored, while testicular cancers presenting with scrotal pain are often treated as epididymitis.

The differential diagnosis of a testicular mass includes testicular torsion, epididymitis, or epididymo-orchitis. Less common problems include hydrocele, varicocele, hernia, hematoma, spermatocele, or syphilitic gumma. In patients in whom the diagnosis is unclear or in whom a hydrocele precludes adequate examination, imaging studies are an important second step in determining the cause. (See "Acute scrotal pain in adults".)

The diagnostic evaluation of men with suspected testicular cancer includes scrotal ultrasound followed by radiographic testing, measurement of serum tumor markers, radical inguinal orchiectomy, and in some cases, retroperitoneal lymph node dissection (RPLND). The results are used to determine the histologic type and extent of disease, and to guide therapy. Testicular biopsy is not performed as part of the evaluation due to concern that it may result in tumor seeding into the scrotal sac or metastatic spread of tumor into the inguinal nodes.

In addition, since the vast majority of these patients are young men, consideration should be given to fertility issues and sperm cryopreservation during the initial diagnostic evaluation. If possible, a baseline sperm count and sperm banking should be performed prior to the radiographic diagnostic evaluation in order to avoid radiation exposure of the sperm. (See 'Cryopreservation of sperm' below.)

Scrotal ultrasound — Bilateral scrotal ultrasound can distinguish intrinsic from extrinsic testicular lesions with a high degree of accuracy and can detect intratesticular lesions as small as 1 to 2 mm in diameter. In men with testicular masses, scrotal ultrasound has become an extension of the physical examination, but it should never be considered a substitute for the latter.

A cystic or fluid-filled mass is unlikely to represent malignancy. By comparison, seminomas appear as well-defined hypoechoic lesions without cystic areas, while nonseminomatous germ cell tumors (NSGCTs) are typically inhomogeneous with calcifications, cystic areas, and indistinct

margins [8,9]. However, this distinction is not always apparent; in one series for example, the radiologist's interpretation of the type of tumor was correct in only 70 percent of cases [9]. Even magnetic resonance imaging (MRI) does not improve the specificity [10].

Another limitation is that because the tunica albuginea is difficult to discern by ultrasonography, local tumor staging has proved to be unreliable with this technique [8,9]. In the above report, tumor staging was accurate in 44 percent of seminomas and only 8 percent of nonseminomatous tumors [9]. For these reasons, scrotal ultrasound cannot replace radical inguinal orchiectomy for the determination of histology and stage.

The widespread use of scrotal ultrasound in the evaluation of male infertility occasionally leads to the diagnosis of an incidental nonpalpable testicular mass [11,12]. (See "Approach to the male with infertility".)

In the largest series, 46 asymptomatic lesions smaller than 10 mm were identified in 4418 men evaluated for infertility [11]. The majority of the men did not undergo surgery and were followed with active surveillance and serial ultrasound. Among the eight patients who either chose surgery or who had surgery because of progressive enlargement of the lesion, one seminoma and two Leydig cell tumors were identified. The remaining five patients had benign lesions. The authors concluded that ultrasound surveillance for small, incidentally discovered testicular masses is a safe and appropriate alternative to surgery. For those men with an incidentally detected testicular mass (and normal serum tumor markers) who choose to undergo surgery, less-radical surgery (ie, excisional biopsy), rather than orchiectomy, is appropriate [13,14].

Microlithiasis — Testicular ultrasonography identifies patients with microlithiasis, defined as five or more echogenic 1 to 3 mm foci in a single cross-sectional ultrasound image. Retrospective cohort studies have demonstrated a strong association between microlithiasis and testicular cancer, both in adult and pediatric populations [15,16]. However, a causal link is unlikely as ultrasound surveillance of patients with microlithiasis with no clinical risk factors has not shown an increased incidence of cancer [17]. Consequently, patients with microlithiasis and otherwise normal ultrasound findings do not require further imaging, although they should be instructed in testicular self-examination [18].

Imaging studies

CT scan — A high-resolution computed tomography (CT) scan of the abdomen and pelvis, and a chest radiograph are generally performed [3]. Chest CT is recommended if the chest radiograph is abnormal or if metastatic disease involving the thorax is strongly suspected.

Regional metastases first appear in the retroperitoneal lymph nodes. Although CT is the imaging modality of choice to evaluate the retroperitoneum, false-negative rates as high as 44 percent have been described [19]. Occult micrometastases are responsible for most of these false negatives, as evidenced by a retroperitoneal relapse rate of 20 to 25 percent in men with clinical stage I disease who do not undergo RPLND [20-22].

The utility of the staging CT scan is also dependent on the cutoff value used to define an abnormal node. Most institutions use a 10 mm cutoff (measurement based upon the short axis in the transverse plane) to define pathologic adenopathy. Higher cutoffs (greater than 15 mm) yield higher false-negative rates, while lower cutoffs (less than 5 mm) may result in some patients undergoing unnecessary therapeutic RPLND [23] (see "Retroperitoneal lymph node dissection for early-stage testicular germ cell tumors"). A more exacting method to evaluate lymph node enlargement utilizes craniocaudal measurement of lymph nodes in the suspected landing site. Above 10 mm, for every 3 mm increase in craniocaudal length in patients with nonseminomatous tumors, the risk of relapse increased by 52 percent [24].

MRI — Magnetic resonance imaging (MRI) of the abdomen and pelvis or scrotum usually adds little to the information obtained by CT scan and ultrasound [10]. MRI of the brain is performed if brain metastases are suspected. Bone radionuclide scan is rarely indicated.

Is there a role for PET imaging? — Positron emission tomography (PET) scan is of limited utility in the initial staging of patients with testicular germ cell tumors (GCTs) [25,26] because of the frequent occurrence of false-negative results:

- The utility of PET as compared with CT as an initial staging modality for the retroperitoneum was studied in a German study of 72 men, all of whom underwent subsequent RPLND for clinical stage I or II NSGCT [25]. In this study, correct nodal staging was achieved in more patients by PET compared to CT (83 versus 71 percent), and the positive predictive value was also higher with PET (95 versus 87 percent). However, false-negative results with PET-CT were still a problem, with a negative predictive value that was only modestly higher than that achieved by CT (78 versus 67 percent).

- Similar results were seen in a subsequent study in 111 patients with clinical stage I NSGCT that used the negative results of PET to select patients for surveillance [26]. Of the 87 patients with a negative PET who were managed with surveillance, 33 (38 percent) relapsed within one year.

PET scanning is more commonly used for the evaluation of posttherapy residual masses than for initial diagnostic evaluation. (See "Treatment of stage II seminoma", section on 'Posttherapy residual masses'.)

Serum tumor markers — In a man suspected of having testicular cancer, blood should be obtained for a chemistry profile, a complete blood count, and serum tumor markers. Three serum tumor markers have established roles in testicular cancer: alpha-fetoprotein (AFP), the beta subunit of human chorionic gonadotropin (beta-hCG; since the alpha subunit is common to several pituitary hormones), and lactate dehydrogenase (LDH). Serum levels of AFP and/or beta-hCG are elevated in 80 to 85 percent of men with NSGCTs, even when nonmetastatic. By contrast, serum beta-hCG is elevated in less than 20 percent of testicular seminomas, and AFP is not elevated in pure seminomas. (See "Serum tumor markers in testicular germ cell tumors".)

Neither serum beta-hCG nor AFP, alone or in combination, is sufficiently sensitive or specific to establish the diagnosis of testicular cancer in the absence of histologic confirmation. Marked elevations in these markers are rarely found in men, except in GCTs.

- Serum beta-hCG concentrations above 10,000 milli-international units/mL occur only in GCTs, the rare patient with trophoblastic differentiation of a primary lung or gastric cancer, or in women, pregnancy or gestational trophoblastic disease [27]. (See "Hyperthyroidism during pregnancy: Clinical manifestations, diagnosis, and causes" and "Hydatidiform mole: Epidemiology, clinical features, and diagnosis".)

- Serum AFP concentrations above 10,000 ng/mL occur almost exclusively in GCTs and hepatocellular carcinoma. (See "Clinical features and diagnosis of hepatocellular carcinoma".)

These observations are especially pertinent for the patient with a suspected extragonadal GCT. Elevated serum tumor markers can be used to make the diagnosis if a biopsy is not feasible or will compromise a patient with compatible clinical features or if biopsy reveals poorly differentiated carcinoma. (See "Poorly differentiated cancer from an unknown primary site", section on 'Extragonadal germ cell tumors' and "Poorly differentiated cancer from an unknown primary site", section on 'Clinical evaluation'.)

Although serum tumor markers are helpful at the time of initial diagnosis of testicular cancer and for prognostication, their main utility is for subsequent follow-up of disease status after primary treatment. (See "Serum tumor markers in testicular germ cell tumors".)

Radical inguinal orchiectomy — A radical inguinal orchiectomy should be performed to permit histologic evaluation of the primary tumor and to provide local tumor control. Neither scrotal ultrasound, as mentioned above, nor serum tumor markers are sufficiently accurate to replace radical inguinal orchiectomy. (See "Radical inguinal orchiectomy for testicular germ cell tumors", section on 'Scrotal violation'.)

Contralateral testicular biopsy — The role of contralateral testicular biopsy at the time of radical orchiectomy in a clinically normal testis is controversial. Testicular germ cell neoplasia in situ (GCNIS, formerly called intratubular germ cell neoplasia unclassified [28]), a precursor for GCT, is present in 2 to 5 percent of men with GCTs [29-31]. (See "Testicular germ cell neoplasia in situ".)

In North America, biopsy is not recommended, but instead, careful surveillance of the contralateral testis is advocated. By contrast, many European groups suggest biopsy, particularly in patients considered at increased risk of GCNIS (eg, cryptorchidism) [32].

Retroperitoneal lymph node dissection — RPLND is the only reliable method to identify nodal micrometastases given the high false-negative rate with CT scan (see 'CT scan' above). It is also the gold standard for providing accurate pathologic staging of the retroperitoneum. Both the number and size of involved retroperitoneal lymph nodes have prognostic importance. (See "Retroperitoneal lymph node dissection for early-stage testicular germ cell tumors".)

Following radiographic evaluation of the retroperitoneum and radical inguinal orchiectomy, a subset of patients with low-stage NSGCT (T1-3,N0-2,M0, see below) should be considered candidates for a surgical staging RPLND. By comparison, primary chemotherapy is the treatment of choice for patients with stage III disease or high-volume stage II disease; in such patients, RPLND is reserved for those with postchemotherapy residual disease (see "Initial risk-stratified treatment for advanced testicular germ cell tumors"). Surveillance is an appropriate option for men with clinical stage I testicular cancer, especially those with limited risk factors, such as a minimal embryonal cell component and the absence of lymphovascular invasion. (See "Active surveillance following orchiectomy for stage I testicular germ cell tumors".)

STAGING

The results of clinical and radiographic evaluation are used to assign a clinical stage in order to estimate prognosis and guide therapy. Testicular cancer is staged using the eighth (2017) tumor, node, metastasis (TNM) staging system developed jointly by the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC), which applies to both seminomas and nonseminomatous germ cell tumors (NSGCTs) [33]. In the TNM system, assessments of the primary tumor (T), lymph nodes (N), and distant metastases (M) are combined with serum tumor marker values (S) for the beta subunit of human chorionic gonadotropin (beta-hCG), alpha-fetoprotein (AFP), and lactate dehydrogenase (LDH) to define prognostic stage groups from I to III (table 2A-B).

It is important to note that for the purposes of TNM staging, the serum tumor markers should be assessed as S0 to S3 only **after** orchiectomy has been completed. (See "Radical inguinal orchiectomy for testicular germ cell tumors", section on 'Serum tumor markers'.)

Compared with NSGCTs, pure seminomas are more likely to be localized to the testis at presentation. Approximately 80 percent of men with seminomas present with stage I disease (limited to the testicle), while 15 percent have stage II disease (limited to the retroperitoneal nodes). (See "Treatment of stage I seminoma".)

For men who present with advanced disease, numerous staging and prognostic systems have been proposed to separate different prognostic subgroups, based primarily on single-institution experience [34-38]. In 1997, consensus was reached on a uniform, validated prognostic model by the International Germ Cell Cancer Collaborative Group (IGCCCG). The classification system is discussed separately [39]. (See "Initial risk-stratified treatment for advanced testicular germ cell tumors", section on 'Definition of risk'.)

Because of the availability of serum tumor markers and the predictable metastatic pattern of testicular cancer, most experts do not require a confirmatory biopsy of suspected disease as part of the staging procedure. Biopsies of suspected disease should only be performed in unusual situations, such as in patients who present with imaging-detected masses without elevated tumor markers, or the presence of disease in atypical locations (eg, bone [40]). If patients have evidence of advanced disease suggested by imaging and/or elevated tumor markers, definitive treatment is recommended. (See "Overview of the treatment of testicular germ cell tumors".)

CRYOPRESERVATION OF SPERM

Semen cryopreservation should be made available to all men diagnosed with testicular cancer prior to instituting therapy if they wish to preserve fertility. If possible, a baseline sperm count and sperm banking should be performed prior to the radiographic diagnostic evaluation in order to avoid radiation exposure of the sperm. (See "Effects of cytotoxic agents on gonadal function in adult men".)

However, a number of issues need to be considered:

- Testicular tumors are associated with gonadal dysgenesis, and approximately 50 percent of men have some degree of underlying impairment of spermatogenesis [41-47] (see "Effects of cytotoxic agents on gonadal function in adult men", section on 'Testicular cancer'). Semen quality may further deteriorate following removal of the affected testis

[47], although others have shown no impact of orchiectomy [48]. The cause of gonadal dysgenesis is unknown in these men; it has been suggested that common etiologic factors are responsible for both low semen quality and testicular cancer [49].

- Despite this abnormality, sperm from men with testicular cancer does not appear to be more sensitive to the effects of cryopreservation and thawing than normal donors [45]. Men with seminoma may have better sperm quality both before and after cryopreservation than those with nonseminomatous germ cell tumors [50].

- Newer assisted reproductive techniques and improvements in cryopreservation techniques may permit successful future pregnancy in 30 to 60 percent of men who undergo treatment for testicular cancer [51-53] (see "Treatments for male infertility"). Congenital abnormalities have not been noted in these children.

- Not all men are willing to undergo sperm testing or banking.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Testicular cancer".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Beyond the Basics topic (see "Patient education: Testicular cancer (Beyond the Basics)")

SUMMARY

- **Clinical manifestations**
  - Testicular germ cell tumors (GCTs) are the most common malignancies affecting adult men between the ages 15 and 35 years. Testicular GCTs are highly curable cancers.
  - A majority of patients present with a painless testicular mass. Other less common clinical manifestations include local symptoms (such as pain or a heaviness in the lower abdomen), gynecomastia, or symptoms due to metastases. (See 'Clinical manifestations' above.)
- **Diagnostic evaluation** – The initial diagnostic evaluation of the patient with a suspected testicular tumor should include (see 'Diagnostic evaluation' above):
  - **Physical exam and scrotal ultrasound** – Physical examination of the scrotum supplemented by ultrasound to differentiate tumor from a hydrocele or epididymitis. (See 'Scrotal ultrasound' above.)
  - **Serum tumor markers** – These include the beta subunit of human chorionic gonadotropin [beta-hCG], alpha-fetoprotein [AFP], and lactate dehydrogenase [LDH]). (See 'Serum tumor markers' above.)
  - **Imaging studies** – Imaging studies should include chest radiograph as well as computed tomography (CT) or magnetic resonance imaging (MRI) of the pelvis and abdomen to look for evidence of regional lymph node metastases. (See 'Imaging studies' above.)
  - **Sperm cryopreservation** – Prior to definitive treatment, cryopreservation of sperm should be made available to all males who wish to preserve fertility. (See 'Cryopreservation of sperm' above.)
- **Diagnosis** – Radical inguinal orchiectomy is used both to provide the histologic diagnosis and for local tumor control. Lesser surgical procedures, such as biopsy of the testicle, are generally contraindicated. (See 'Radical inguinal orchiectomy' above.)
- **Staging** – Tumor staging (table 2A-B) is determined from pathology of the primary tumor, lymphatic spread, the presence or absence of metastases, and the levels of serum beta-hCG, AFP, and LDH. (See 'Staging' above.)

- **Risk stratification** – For men with metastatic testicular cancer, men are stratified into separate prognostic groups using the International Germ Cell Cancer Collaborative Group (IGCCCG) stratification system. (See "Initial risk-stratified treatment for advanced testicular germ cell tumors", section on 'Definition of risk'.)

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GRAPHICS

Classification of testicular tumors

Noninvasive germ cell tumors
Germ cell neoplasia in situ (GCNIS)
Intratubular seminoma
Intratubular embryonal carcinoma
Invasive germ cell tumors
Seminoma
Nonseminomatous germ cell tumors
Embryonal carcinoma
Choriocarcinoma
Yolk sac tumor (endodermal sinus tumor)
Teratoma
Teratoma with malignant/somatic transformation
Mixed germ cell tumor
Spermatocytic tumor
Sex cord-stromal tumors
Sertoli cell tumor
Leydig cell tumor
Granulosa cell tumor
Mixed types (eg, Sertoli-Leydig cell tumor)
Unclassified
Mixed germ cell and stromal tumors
Gonadoblastoma
Adnexal and paratesticular tumors
Adenocarcinoma of rete testis
Adenocarcinoma of the epididymis
Mesothelial neoplasms
Malignant mesothelioma
Adenomatoid tumor

Miscellaneous tumors
Carcinoid
Lymphoma
Metastatic tumors (prostate carcinoma is the most common)

Data from: Tumours of the Urinary System and Male Genital Organs. Moch H, Humphrey PA, Ulbright TM, et al (Eds), In: World Health Organization Classification of Tumours. Lyon 2016.

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Testicular cancer TNM staging AJCC UICC 8th edition

Primary tumor (T)	
Clinical T (cT)	
cT category	**cT criteria**
cTX	Primary tumor cannot be assessed
cT0	No evidence of primary tumor
cTis	Germ cell neoplasia *in situ*
cT4	Tumor invades scrotum with or without vascular/lymphatic invasion
NOTE: Except for Tis confirmed by biopsy and T4, the extent of the primary tumor is classified by radical orchiectomy. TX may be used for other categories for clinical staging.	
Pathological T (pT)	
pT category	**pT criteria**
pTX	Primary tumor cannot be assessed
pT0	No evidence of primary tumor
pTis	Germ cell neoplasia *in situ*
pT1	Tumor limited to testis (including rete testis invasion) without lymphovascular invasion
pT1a*	Tumor smaller than 3 cm in size
pT1b*	Tumor 3 cm or larger in size
pT2	Tumor limited to testis (including rete testis invasion) with lymphovascular invasion **or** Tumor invading hilar soft tissue or epididymis or penetrating visceral mesothelial layer covering the external surface of tunica albuginea with or without lymphovascular invasion
pT3	Tumor directly invades spermatic cord soft tissue with or without lymphovascular invasion
pT4	Tumor invades scrotum with or without lymphovascular invasion
* Subclassification of pT1 applies only to pure seminoma.	
Regional lymph nodes (N)	
Clinical N (cN)	
cN category	**cN criteria**
cNX	Regional lymph nodes cannot be assessed

cN0	No regional lymph node metastasis
cN1	Metastasis with a lymph node mass 2 cm or smaller in greatest dimension **or** Multiple lymph nodes, none larger than 2 cm in greatest dimension
cN2	Metastasis with a lymph node mass larger than 2 cm but not larger than 5 cm in greatest dimension **or** Multiple lymph nodes, any one mass larger than 2 cm but not larger than 5 cm in greatest dimension
cN3	Metastasis with a lymph node mass larger than 5 cm in greatest dimension

Pathological N (pN)

pN category	**pN criteria**
pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis with a lymph node mass 2 cm or smaller in greatest dimension and less than or equal to five nodes positive, none larger than 2 cm in greatest dimension
pN2	Metastasis with a lymph node mass larger than 2 cm but not larger than 5 cm in greatest dimension; or more than five nodes positive, none larger than 5 cm; or evidence of extranodal extension of tumor
pN3	Metastasis with a lymph node mass larger than 5 cm in greatest dimension

Distant metastasis (M)

M category	**M criteria**
M0	No distant metastases
M1	Distant metastases
M1a	Nonretroperitoneal nodal or pulmonary metastases
M1b	Nonpulmonary visceral metastases

Serum markers (S)¶

S category	**S criteria**
SX	Marker studies not available or not performed
S0	Marker study levels within normal limits
S1	LDH <1.5 × N$^{\Delta}$ **and** hCG (mIU/mL) <5000 **and** AFP (ng/mL) <1000
S2	LDH 1.5 to 10 × N$^{\Delta}$ **or** hCG (mIU/mL) 5000 to 50,000 **or** AFP (ng/mL) 1000 to 10,000
S3	LDH >10 × N$^{\Delta}$ **or** hCG (mIU/mL) >50,000 **or** AFP (ng/mL) >10,000

¶ Markers used for risk classification are postorchiectomy.
Δ N indicates the upper limit of normal for the LDH assay.

TNM: Tumor, Node, Metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control; LDH: lactate dehydrogenase; hCG: human chorionic gonadotropin; AFP: alpha-fetoprotein.

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Testicular cancer TNM prognostic stage groups AJCC UICC 8th edition

When T is…	And N is…	And M is…	And S is…	Then the stage group is…
pTis	N0	M0	S0	0
pT1-T4	N0	M0	SX	I
pT1	N0	M0	S0	IA
pT2	N0	M0	S0	IB
pT3	N0	M0	S0	IB
pT4	N0	M0	S0	IB
Any pT/TX	N0	M0	S1-3	IS
Any pT/TX	N1-3	M0	SX	II
Any pT/TX	N1	M0	S0	IIA
Any pT/TX	N1	M0	S1	IIA
Any pT/TX	N2	M0	S0	IIB
Any pT/TX	N2	M0	S1	IIB
Any pT/TX	N3	M0	S0	IIC
Any pT/TX	N3	M0	S1	IIC
Any pT/TX	Any N	M1	SX	III
Any pT/TX	Any N	M1a	S0	IIIA
Any pT/TX	Any N	M1a	S1	IIIA
Any pT/TX	N1-3	M0	S2	IIIB
Any pT/TX	Any N	M1a	S2	IIIB
Any pT/TX	N1-3	M0	S3	IIIC
Any pT/TX	Any N	M1a	S3	IIIC
Any pT/TX	Any N	M1b	Any S	IIIC

TNM: Tumor, Node, Metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

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