Table 21-6 Staging of Prostatic Adenocarcinoma Using the TNM System

TNM Designation	Anatomic Findings
Extent of Primary Tumor (T)	
T1	Clinically inapparent lesion (by palpation/imaging studies)
T1a	Involvement of ≤ 5% of resected tissue
T1b	Involvement of > 5% of resected tissue
T1c	Carcinoma present on needle biopsy (following elevated PSA)
T2	Palpable or visible cancer confined to prostate
T2a	Involvement of ≤ 5% of one lobe
T2b	Involvement of > 5% of one lobe, but unilateral
T2c	Involvement of both lobes
T3	Local extraprostatic extension
T3a	Extracapsular extension
T3b	Seminal vesical invasion
T4	Invasion of contiguous organs and/or supporting structures including bladder neck, rectum, external sphincter, levator muscles, or pelvic floor
Status of Regional Lymph Nodes (N)	
N0	No regional nodal metastases
N1	Metastasis in regional lymph nodes
Distant Metastases (M)	
M0	No distant metastases
M1	Distant metastases present
M1a	Metastases to distant lymph nodes
M1b	Bone metastases
M1c	Other distant sites

PSA, Prostate-specific antigen.

commonly, the Gleason score remains stable over a period of several years.

Staging of prostatic cancer is also important in the selection of the appropriate form of therapy (Table 21-6). Stage T1 refers to incidentally found cancer, either on TURP done for BPH symptoms (T1a and T1b depending on the extent and grade) or on needle biopsy typically performed for elevated serum prostate-specific antigen (PSA) levels (stage T1c). Stage T2 is organ-confined cancer. Stage T3a and T3b tumors show extra-prostatic extension, with and without seminal vesicle invasion, respectively. Stage T4 reflects direct invasion of contiguous organs. Any spread of tumor to the lymph nodes regardless of extent is eventually associated with a fatal outcome, such that the staging system merely records the presence or absence of this finding (N0/N1).

Clinical Course. It is generally accepted that most incidentally discovered focal (stage T1a) cancers found on TURP do not progress when followed for 10 or more years. Older patients with stage T1a disease are typically followed, but younger men with a longer life expectancy may undergo needle biopsy to look for additional cancer in the peripheral zone of the prostate. Stage T1b lesions are more ominous and are treated the same as tumors that are found on needle biopsy, since they have a mortality of 20% if left untreated.

Localized prostate cancer is asymptomatic, and is usually discovered by the detection of a suspicious nodule on rectal examination or elevated serum PSA level (discussed later). Most prostatic cancers arise peripherally away from the urethra, and therefore urinary symptoms occur late. Patients with clinically advanced prostatic cancer may present with urinary symptoms, such as difficulty in starting or stopping the stream, dysuria, frequency, or hematuria. Today it is uncommon for patients to come to attention because of back pain caused by vertebral metastases. As already mentioned, **the finding of osteoblastic metastases by skeletal surveys or the much more sensitive radionuclide bone scanning is virtually diagnostic of this form of cancer in men**. These cancers pursue a universally fatal course.

Digital rectal examination may detect some early prostatic carcinomas because of their posterior location, but the test suffers from both low sensitivity and specificity. Likewise, while transrectal ultrasonography and other imaging modalities show characteristic findings in those with cancerous prostates, the poor sensitivity and specificity of these tests also limit their diagnostic utility. Typically a transrectal needle biopsy is required to confirm the diagnosis.

Measurement of serum PSA levels is widely used to assist with the diagnosis and management of prostate cancer. PSA is a product of prostatic epithelium and is normally secreted in the semen. It is an androgen-regulated serine protease whose function is to cleave and liquefy the seminal coagulum formed after ejaculation. In normal men, only minute amounts of PSA circulate in the serum. Elevated blood levels of PSA occur in association with localized as well as advanced cancer. However, as a screening test for prostate cancer, the use of PSA remains controversial in that it lacks both sensitivity and specificity. Importantly, PSA is organ specific, but not cancer specific. Although serum levels of PSA are elevated to a lesser extent in BPH than in prostatic carcinomas, there is considerable overlap. Other factors such as prostatitis, infarction of nodular hyperplasias, instrumentation of the prostate, and ejaculation also increase serum PSA levels. If the cut-off between normal and abnormal PSA levels is too low, this may falsely indicate the need for a prostate biopsy in some men and result in the detection and potentially unnecessary treatment of indolent and non–life-threatening tumors. In most laboratories, a serum level of 4 ng/mL is reported as the cut-off between normal and abnormal; however, this cut-off may be too high because 20% to 40% of patients with organ-confined prostate cancer have a PSA value of 4 ng/mL or less, which is not detected by this simple screening test. Thus, some guidelines consider PSA values above 2.5 ng/mL abnormal.

Several refinements in the estimation and interpretation of PSA values are currently used. These include the ratio between the serum PSA value and volume of prostate gland (*PSA density*), the rate of change in PSA value with time (*PSA velocity*), the use of age-specific reference ranges, and the ratio of free and bound PSA in the serum. Men with enlarged hyperplastic prostate glands have higher total serum PSA levels than men with small glands. The measurement of serum PSA density factors out the