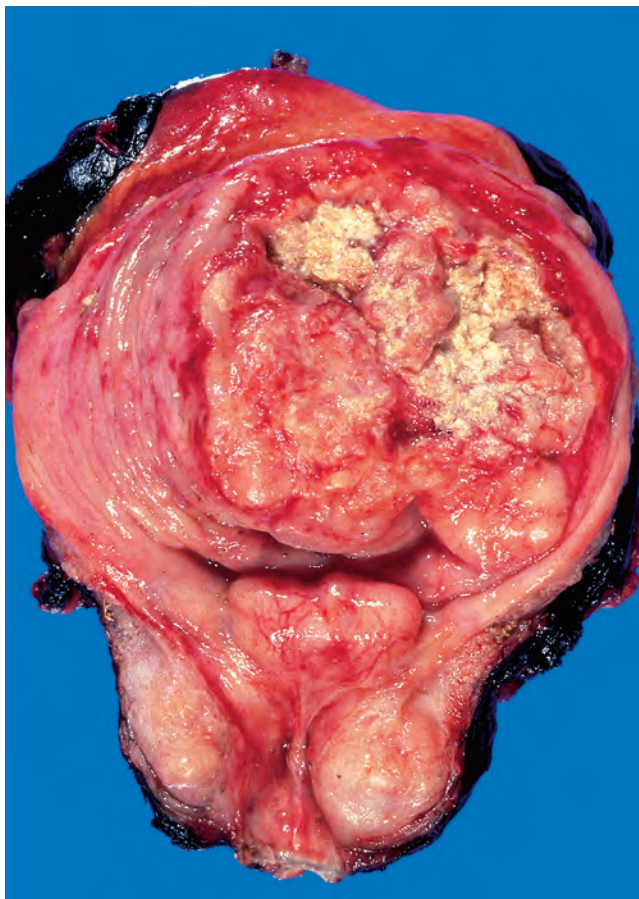


**Figure 21-11** **A**, Normal urothelium with uniform nuclei and well-developed umbrella cell layer (arrow). **B**, Flat carcinoma in situ with numerous cells having enlarged and pleomorphic nuclei.

of initial diagnosis is the most important factor in determining the outlook for a patient (Table 21-4). Almost all infiltrating urothelial carcinomas are high grade, and as a result grading of the infiltrating component is not critical, as opposed to the importance of grading noninvasive papillary urothelial carcinoma.



**Figure 21-12** Opened bladder showing a high-grade invasive transitional cell carcinoma at an advanced stage. The aggressive multinodular neoplasm has fungated into the bladder lumen and spread over a wide area. The yellow areas represent areas of ulceration and necrosis.

**Variants of Urothelial Carcinoma.** Unusual variants of urothelial cancer include a nested variant with deceptively bland cytology, lymphoepithelioma-like carcinoma, and micropapillary carcinoma.

**Other Epithelial Bladder Tumors.** *Squamous cell carcinomas* resembling squamous cancers occurring at other sites make up 3% to 7% of bladder cancers in the United States, but are much more frequent in countries where urinary schistosomiasis is endemic. Pure squamous cell carcinomas are nearly always associated with chronic bladder irritation and infection. *Mixed urothelial carcinomas with areas of squamous carcinoma* are more frequent than pure squamous cell carcinomas. Most are invasive, fungating tumors or are infiltrative and ulcerative. The level of cellular differentiation varies widely, from well differentiated lesions producing abundant keratin to anaplastic tumors with only focal evidence of squamous differentiation.

*Adenocarcinomas* of the bladder are rare and histologically identical to adenocarcinomas seen in the gastrointestinal tract. Some arise from urachal remnants or in association with extensive intestinal metaplasia (discussed earlier).

*Small-cell carcinomas*, indistinguishable from small-cell carcinomas of the lung, arise in the bladder often in association with urothelial, squamous, or adenocarcinoma.

**Clinical Course of Bladder Cancer.** Bladder tumors classically produce *painless hematuria*. This is their dominant and sometimes only clinical manifestation. Frequency, urgency, and dysuria occasionally accompany the hematuria. When the ureteral orifice is involved, pyelonephritis or hydronephrosis may follow. About 60% of neoplasms,

**Table 21-4** Pathologic T (Primary Tumor) Staging of Bladder Carcinoma

Depth of Invasion	AJCC/UICC
Ta	Noninvasive, papillary
Tis	Carcinoma in situ (noninvasive, flat)
T1	Lamina propria invasion
T2	Muscularis propria invasion
T3a	Microscopic extravescicle invasion
T3b	Grossly apparent extravescicle invasion
T4	Invades adjacent structures

AJCC/UICC, American Joint Commission on Cancer/Union Internationale Contre le Cancer.