cases are associated with chronic mucosal ulcers *(Hunner ulcers)*; this is termed the *late (classic, ulcerative) phase*. Increased numbers of mucosal mast cells are characteristic of this disease, but their pathogenic significance and diagnostic utility are uncertain. Late in the course, transmural fibrosis may appear, leading to a contracted bladder. The pathologic findings are nonspecific, and the main role of biopsy is to rule out carcinoma in situ, which may mimic interstitial cystitis clinically.

Malakoplakia. A distinctive chronic inflammatory reaction that appears to stem from acquired defects in phagocyte function, malakoplakia arises in the setting of chronic bacterial infection, mostly by *E. coli* or occasionally *Proteus* species. It occurs with increased frequency in immunosuppressed transplant recipients.

MORPHOLOGY

In the bladder, malakoplakia takes the form of soft, yellow, slightly raised mucosal plaques, 3 to 4 cm in diameter (Fig. 21-4), that are filled with large, foamy macrophages mixed with occasional multinucleate giant cells and lymphocytes. The **macrophages have an abundant granular cytoplasm** due to phagosomes stuffed with particulate and membranous debris of bacterial origin. In addition, laminated mineralized concretions resulting from deposition of calcium in enlarged lysosomes, known as **Michaelis-Gutmann bodies,** are typically present within the macrophages (Fig. 21-5). The unusual-appearing macrophages and giant phagosomes point to defects in the phagocytic function of macrophages, which become overloaded with undigested bacterial products. Similar lesions have been described in the colon, lungs, bones, kidneys, prostate, and epididymis.

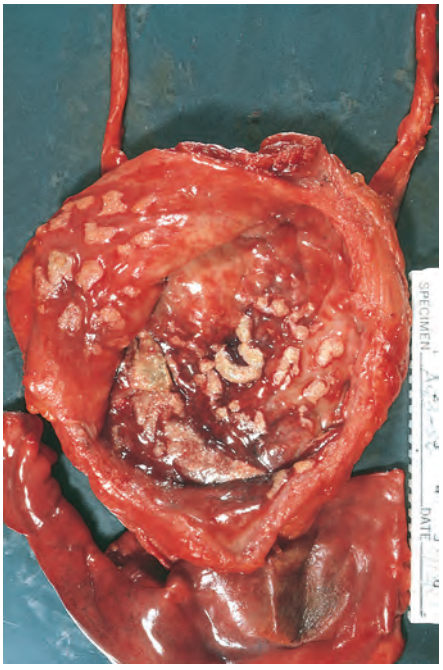

Figure 21-4 Cystitis with malakoplakia showing inflammatory exudate and broad, flat plaques.

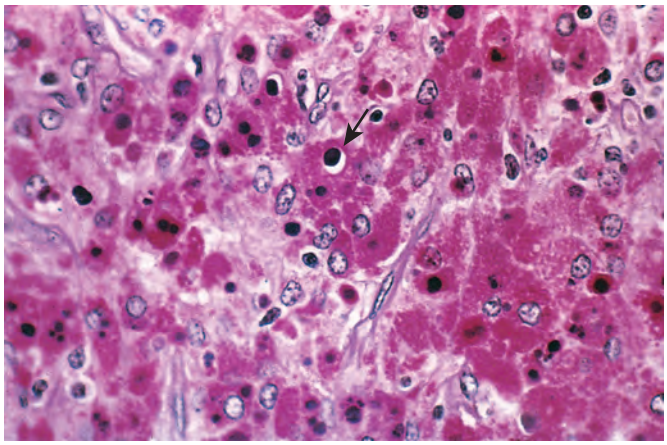

Figure 21-5 Malacoplakia, periodic acid–Schiff (PAS) stain. Note the large macrophages with granular PAS-positive cytoplasm and several dense, round Michaelis-Gutmann bodies surrounded by artifactual cleared holes in the upper middle field *(arrow)*.

Polypoid Cystitis. Polypoid cystitis is an inflammatory lesion resulting from irritation of the bladder mucosa. Although indwelling catheters are the most commonly cited culprits, any injurious agent may give rise to this lesion. The urothelium is thrown into broad bulbous polypoid projections as a result of marked submucosal edema. Polypoid cystitis may be confused with papillary urothelial carcinoma both clinically and histologically.

Metaplastic Lesions

- **Cystitis glandularis and cystitis cystica.** These are common lesions of the urinary bladder in which nests of urothelium (Brunn nests) grow downward into the lamina propria. Here, epithelial cells in the center of the nest undergo metaplasia and take on a cuboidal or columnar appearance *(cystitis glandularis)*, or retract to produce cystic spaces lined by flattened urothelium *(cystitis cystica)*. Because the two processes often coexist, the condition is typically referred to as *cystitis cystica et glandularis*. In a variant of cystitis glandularis goblet cells are present, and the epithelium resembles intestinal mucosa *(intestinal* or *colonic metaplasia)*. Both variants are common incidental findings in normal bladders, but they can also arise in the setting of inflammation and metaplasia.
- **Squamous metaplasia.** As a response to injury, the urothelium is often replaced by nonkeratinizing squamous epithelium, which is a more durable lining. This should be distinguished from glycogenated squamous epithelium that is normally found in women at the trigone.
- **Nephrogenic adenoma.** Nephrogenic adenoma is an unusual lesion that results from implantation of shed renal tubular cells at sites of injured urothelium. The overlying urothelium may be focally replaced by cuboidal epithelium, which can assume a papillary growth pattern. Although the lesions are typically less than a centimeter in size, larger lesions have been reported that can produce signs and symptoms that raise a suspicion of cancer. In addition, the tubular proliferation can