Fine-needle aspiration (FNA) of the kidneys and bladder to obtain cells for cytologic evaluation is a simple, rapid, safe, and relatively inexpensive procedure. The primary indications for cytologic examination of the urinary tract include unilateral or bilateral renomegaly, discrete bladder masses or bladder wall thickening, and urethral masses. Cytologic evaluation of the urinary tract can frequently distinguish between common causes of organomegaly (inflammation, cyst, and neoplasia), direct further diagnostics (e.g., culture or biopsy), or prevent needless surgical intervention (e.g., in cases of metastatic neoplasia).

NORMAL ANATOMY AND HISTOLOGY

The urinary system is composed of kidneys, ureters, urinary bladder, and urethra. The kidney has four basic morphologic components: glomeruli, tubules, interstitium, and blood vessels (Fig. 10-1). The functional unit of the kidney is the nephron. Each nephron is composed of a glomerulus and renal tubule system. The glomerulus is a capillary tuft lined by fenestrated endothelium that is intimately associated with tubule epithelial cells. Components of the glomerulus (Fig. 10-2), including the endothelium, basement membrane, and specialized epithelial cells known as podocytes, make up the filtration barrier of the kidney (Jones et al., 1997).

The renal tubule is divided into distinct functional segments, including the proximal convoluted tubule, loop of Henle (ascending and descending limbs), distal convoluted tubule, and collecting ducts. Reflective of function, the epithelial cells lining the tubules vary from a single layer of cuboidal cells with a brush border in the proximal convoluted tubules to columnar epithelium with no brush border in the distal convoluted segments (Fig. 10-3). Caudate transitional cells line the renal pelvis and calyces. Similarly, the mucosa of the ureters, urinary bladder, and urethra are lined almost exclusively by transitional epithelial cells. Renal interstitial tissue is composed of connective tissue (mesenchymal cells), an extensive capillary network, lymphatic tissue, and smooth muscle cells (Borjesson, 2003; Jones et al., 1997).

SPECIALIZED COLLECTION TECHNIQUES

Sampling method for obtaining cytologic specimens depends on lesion location but may involve either direct mass FNA or traumatic catheterization in the case of a urethral mass or bladder mass in the area of the trigone. Conversely, renal biopsy is frequently indicated in dogs and cats with glomerular disease (and proteinuria) or acute renal failure (Nowicki et al., 2010). Biopsy can be performed under ultrasound guidance or using surgical methods (Debruyne et al., 2012). The increased risks associated with biopsy include the transection of blood vessels or renal pelvis with resultant hemorrhage, hydronephrosis, or hematuria (Borjesson, 2003). A multiinstitutional study found complication rates for renal biopsy of dogs and cats at 13.4% and 18.5%, respectively (Nowicki et al., 2010; Vaden, 2004; Vaden et al., 2005). The most common complication was hemorrhage. There have been a number of recent published reviews comparing renal biopsy methods to optimize specimen procurement and minimize biopsy-induced complications (Rawlings et al., 2003; Rawlings and Howerth, 2004; Vaden, 2004, 2005; Vaden et al., 2005).

For FNA, manual kidney immobilization and blind percutaneous aspiration can be used to obtain samples for cytologic review, especially in cats. However, this technique is best reserved for diffuse lesions that result in renomegaly because focal lesions may be missed and there is an increased risk of inadvertent puncture or laceration of major blood vessels. Ultrasound-guided FNA is recommended as it is minimally invasive and has a low complication rate (Debruyne et al., 2012). The primary potential complication is hemorrhage; as such, a clotting profile may be indicated.

For ultrasound-guided aspiration, the patient is maintained in dorsal recumbency. If changes are bilateral, aspiration of the caudal pole of left kidney is recommended as it decreases the risk of accidental aspiration of bowel and pancreas. The needle is directed from the cortex of the caudal pole, ventral to dorsal. The needle can be angled from medial to lateral to avoid hitting a large renal vessel. Care should be taken to avoid hitting the renal pelvis. Begin with a 25- to 27-gauge, ½-inch needle. If sample of adequate cellularity is not obtained, a larger bore needle can be used. The best results are obtained if multiple preparations are made and one slide is rapidly stained with either a Romanowsky stain or new methylene blue to assess sample adequacy (Borjesson, 2003).

Regardless of the type of mass, aspiration of both the central and peripheral areas is recommended. Frequently the center of a mass may consist solely of necrotic debris or inflammatory cells, resulting in a nondiagnostic sample. Although purulent inflammation and necrosis can be associated with malignancy, abundance of either frequently masks the primary disorder. Thus multiple aspirations in different areas of the mass are almost always recommended to maximize cellular yield and diagnostic potential as well as to differentiate between primary and secondary inflammation (Borjesson, 2003). If fluid is obtained, a
direct smear can be made immediately and the remaining fluid can be placed into EDTA to prevent clotting. Both sediment and cytocentrifuged smears can then be prepared, especially if the sample is of low cellularity. Finally, impression smears can be made from renal biopsy specimens. Cytologic evaluation of impression smears can aid in rapid diagnosis of infectious agents or neoplasia (Borjesson, 2003).

Cells from masses within the bladder can be readily obtained using ultrasound-guided FNA or traumatic urethral catheterization. Occasionally, tumor cells can be noted in urine sediment; however, the submission of urine for cytology rarely results in a definitive diagnosis of neoplasia. Traumatic urethral catheterization can provide adequate and diagnostic samples; however, many of the cells obtained may be superficial and reactive transitional epithelial cells. As such, traumatic catheterization can result in a false negative cytology report due to sample bias with the primary mass not being successfully sampled. Although a few cases of tumor implantation along the ventral abdominal wall following direct FNA of bladder masses have been reported, this complication is infrequent and more frequently associated with surgical invention for tumor removal or debulking (Higuchi et al., 2013; Nyland et al., 2002). Thus ultrasound-guided FNA may remain the best method for obtaining tissue-associated cells and maximizing cellular yield for cytologic review.

NORMAL RENAL CYTOLOGY

Renal aspirates are typically of low cellularity and usually contain small clusters of renal tubular cells admixed with blood. As the kidneys are highly vascular, blood is generally due to iatrogenic hemorrhage at the time of sampling. Tubular cells generally exfoliate singly or in small clusters of round to oval, often eccentrically placed nuclei (Fig. 10-4). Feline tubular cells are cytologically similar except that cats normally have lipid deposition within their renal tubules. Lipid droplets appear as prominent, variably sized, intracytoplasmic, clear, punctate vacuoles (Figs. 10-5 and 10-6). Fully intact renal tubules arranged in cohesive linear structures may also be present (Fig. 10-7). Tubular cells can also contain dark, intracytoplasmic granules that should not be confused with a well-differentiated melanocyte tumor (Fig. 10-8). Glomeruli may exfoliate singly or in dense, deeply basophilic, rounded clusters and have very uniform round to oval nuclei (Fig. 10-9).

NONNEOPLASTIC AND BENIGN LESIONS OF THE URINARY TRACT

Bladder

Polypoid Cystitis, Transitional Cell Polyps, and Papilloma

Hyperplastic and benign mass lesions of the bladder are an uncommon but important subset of bladder diseases that may mimic malignant neoplasia. Polypoid cystitis is characterized by inflammation, epithelial proliferation, and development of
Canine renal tubular epithelial cells. Depicted is a small cluster of renal tubular cells that vary from round to columnar in appearance. The background erythrocytes provide a perspective on cell size. (Wright-Giemsa; HP oil.)

Feline renal tubular epithelial cells. Note the variably sized intracytoplasmic lipid droplets that appear as clear, punctate vacuoles within the renal tubule cells. Free vacuolated cytoplasm from a ruptured cell is also present (long arrow). The size of the tubular cells can be compared to the neutrophils present (short arrows). (Wright-Giemsa; HP oil.)

Tissue section of feline renal tubules. Note the variably sized intracytoplasmic lipid droplets that appear as clear, punctate vacuoles within these proximal renal tubule cells from a feline kidney section (arrows). (H&E; HP oil.)

Intact renal tubule. Cells within the tubule are minimally pleomorphic. Cell nuclei are round and uniform with small regular nucleoli. The large size is suggestive of a collecting duct or distal tubule. Leukocytes provide a perspective of size (arrows). (Wright-Giemsa; HP oil.)

Intact renal tubule. The dark intracytoplasmic granules (arrows) of the cells composing this segment of a tubule indicate the ascending loop of Henle or distal tubules as the site of origin. The possibility of a well-differentiated melanocyte tumor could be an initial misleading impression. (Wright-Giemsa; HP oil.)

a nonneoplastic mass. Similar to most urinary bladder diseases, these dogs present with hematuria or recurrent urinary tract infection. However, unlike transitional cell neoplasia, these masses are most frequently located cranioventrally in the bladder rather than in the trigone region (Martinez et al., 2003).

Transitional cell hyperplasia and benign transitional cell polyps can exfoliate in large cellular sheets with mild pleomorphism (Fig. 10-10). Nuclei are generally uniform with coarse, ragged chromatin patterns (Fig. 10-11). Transitional cell papillomas may also occur; they are characterized by varying size clusters of uniform transitional epithelial cells. These cells are cuboidal to polyhedral and show mild anisokaryosis, with an increased nuclear-to-cytoplasmic ratio (Fig. 10-12). Differentiation between the benign processes of hyperplasia, polyps, and papillomas cannot be made cytologically. Often these processes can be difficult to differentiate from neoplastic processes because close proximity to urine causes mild to marked cellular disruption, making definitive identification problematic (Fig. 10-13).

Renal Cysts
Renal cysts can be acquired or congenital and single or numerous. They are thin walled and generally contain viscous or watery and clear or yellow-tinged fluid. Although readily evaluated cytologically, clinical history and ultrasound examination may be sufficient for a diagnosis, especially in the case of polycystic disease. Cytologic evaluation of cysts is utilized only when necessary to distinguish between abscesses, neoplasia, or primary cystic disease (Borjesson, 2003).

FIGURE 10-10 Transitional cell hyperplasia or benign polyps. Epithelial hyperplasia or polyp formation is distinguished from malignant epithelial neoplasia by the distinctive, regular clustering pattern and uniform appearance of the epithelial cells. (Wright-Giemsa; IP.)

FIGURE 10-11 Transitional cell hyperplasia or benign polyps. The transitional cells within this epithelial cluster have round to oval uniform nuclei. The chromatin is coarse (a common cytomorphologic feature of the urothelial system) without obvious nucleoli. Cell-cell borders are often readily observed, and there is only mild pleomorphism. Contrast the features of this cell cluster to the cells in Figs. 10-20 to 10-24. (Wright-Giemsa; HP oil.)

FIGURE 10-12 Transitional cell papilloma. Epithelial polyp formation or hyperplasia is distinguished from malignant epithelial neoplasia by the uniform appearance of the epithelial cells. These cells show mild anisokaryosis and anisocytosis with a mildly increased nuclear-to-cytoplasmic ratio. Note the cytoplasmic vacuoles that can be seen in cells from the urothelial system. Contrast the features of this cell cluster to the cells in Figs. 10-20 to 10-24. (Wright-Giemsa; HP oil.)

FIGURE 10-13 Degenerate transitional cells. Prolonged exposure to urine causes mild to marked cellular disruption, inhibiting definitive cytologic characterization. Common alterations include coarse chromatin, clear vacuoles within the cytoplasm and/or nucleus, and irregular nuclear margins. (Wright-Giemsa; HP oil.)
Cytologically, cysts have low to moderate cellularity with a dense, stippled background consistent with increased protein. Nucleated cells consist primarily of activated macrophages with many large vacuoles that often contain pink secretory material and heme breakdown products, hemosiderin, and hematoidin if hemorrhage is a component of the disease process (Fig. 10-14). Some neoplastic processes have a cystic component; however, the neoplastic cells may or may not exfoliate into the fluid. Therefore aspiration of the wall or more solid components of a cystic structure should be performed.

**Crystals**

Crystals are rarely noted in cytologic preparations from renal aspirates. However, their presence can be very useful to diagnose nephrotoxicosis. Oxalic acid, a metabolite of ethylene glycol, can precipitate in renal tubules as calcium oxalate crystals (Fig. 10-15A&B). Cytologically, these crystals will appear clear, with barely perceptible ragged to linear borders (Fig. 10-16A). These crystals are readily visualized under polarized light (Fig. 10-16B).

Acute renal disease and intratubular crystals have also been associated with outbreaks of nephrotoxicosis due to ingestion of contaminated pet food (Puschner and Reimschuessel, 2011). Pale green to yellow-golden, round to dumbbell-shaped crystals have been identified on renal histology (Fig. 10-17A&B) and in urine sediment cytology. These crystals are suggestive of those formed from the combined precipitation of melamine and cyanuric acid and may be readily misclassified as green-tinged calcium carbonate crystals or smooth ammonium biurate crystals.

**Inflammation**

Pyelonephritis is an infectious tubulointerstitial disease that generally results from an ascending infection of the lower urinary tract. Marked suppurative inflammation is easily diagnosed cytologically and is characterized by increased numbers of neutrophils with scattered activated macrophages (Fig. 10-18). Often, nuclear morphology is degenerate. When the underlying etiology is bacterial infection, intracytoplasmic bacteria can be noted such as *Mycobacterium* sp. (Fig. 10-19). Bacterial culture and sensitivity is recommended regardless of the presence of bacteria. Similarly, systemic algal (e.g., *Prototheca zopfii*), fungal (e.g., *Cryptococcus neoformans*, *Aspergillus* spp., and phaeohyphomycosis) (Giri et al., 2011), protozoal (e.g., *Leishmania*) (Zatelli et al., 2003), and amebic (e.g., *Balamuthia mandrillaris*) (Foreman et al., 2004) infections can localize in the kidneys and be readily diagnosed cytologically. Cytology is characterized by mixed inflammation, clusters of renal tubular cells, and the presence of organisms. Samples obtained by FNA can also be submitted for fungal culture or other diagnostic techniques (e.g., polymerase chain reaction). Finally, feline infectious peritonitis is uncommonly diagnosed using cytology (Giodano et al., 2005). Aspirates have a mixed pyogranulomatous inflammation with a basophilic, proteinaceous background. Findings should be interpreted in light of clinical signs and other laboratory tests.
**FIGURE 10-16** Ethylene glycol toxicosis. Cat. Same case A-B. **A, Tissue aspirate.** Irregularly shaped crystals were present within renal tubular epithelium from an animal diagnosed histologically with oxalate crystals at necropsy. (Wright-Giemsa; HP oil.) **B, Tissue aspirate. Polarized.** A polarizing filter demonstrates that the irregularly shaped crystals present within renal tubular epithelium were refractive as expected for calcium oxalate. (Wright-Giemsa; HP oil.) (A and B, Courtesy of Rose Raskin, University of Florida.)

**FIGURE 10-17** Tissue section of canine renal tubules with intratubular crystals. Same case A-B. **A, Pet food toxicosis.** Note the large, yellow to golden, round to oval crystals filling this renal tubule and compressing renal tubule epithelial cells. These crystals are presumed to form secondary to melamine and cyanuric acid precipitation associated with consumption of tainted dog food in 2007. Acute tubular necrosis is present but not depicted here. **B, Polarized.** Polarized light demonstrates a colorful refractivity of crystals within the tubules. (A and B, Courtesy of Jessica Hoane, Michigan State University.)

**FIGURE 10-18** Pyelonephritis. Note the small, cohesive cluster of basophilic renal tubular cells (big arrow) admixed with a population of nondegenerate neutrophils (arrow heads). Large, foamy macrophages (small arrows) containing smooth, blue cellular debris are also present. (Wright-Giemsa; HP oil.)

**FIGURE 10-19** Mycobacterial nephritis. Aspirate. Cat. One intact macrophage contains *Mycobacterium* sp. as demonstrated by negative-staining streaks within the cytoplasm. Also present is a renal epithelial cell shown with multiple discrete vacuoles along with a neutrophil and a small lymphocyte. This animal had a systemic infection. (Wright-Giemsa; HP oil.) (Courtesy of Rose Raskin, University of Florida.)
NEOPLASIA

Renal

Primary renal tumors are rare in dogs and cats (Bryan et al., 2006; Henry et al., 1999). Tumors can arise from epithelial tissue, mesenchymal tissue, or embryonal tissue of mixed origin. Several paraneoplastic syndromes, including polycythemia, leukocytosis, hypertrophic osteopathy, and hypercalcemia, have been described secondary to renal tumors (Chiang et al., 2007; Durno et al., 2011; Gajanayake et al., 2010; Johnson and Lenz, 2011; Petterino et al., 2011; Peeters et al., 2001). Most primary renal tumors in both dogs and cats consist of malignant epithelial tumors (renal cell carcinomas, transitional cell carcinomas [TCCs], and adenocarcinomas) (Bryan et al., 2006; Gil da Costa et al., 2011; Henry et al., 1999; Ramos-Vara et al., 2003). Other tumors include fibromas, sarcomas—including hemangiosarcoma, fibrosarcoma, leiomyosarcoma (Sato et al., 2003), and osteosarcoma—and nephroblastoma. Renal lymphoma, a common entity in cats, may represent primary renal disease or be a manifestation of multicentric disease (Breshears et al., 2011; Snead, 2005).

Malignant renal epithelial neoplasms often exfoliate well for cytologic evaluation. In general, renal carcinomas are characterized by high cellularity with many cells observed in variably sized, loose aggregates to poorly cohesive clusters (Figs. 10-20 to 10-22). Due to the number of single, occasionally round cells present in renal cell carcinomas, they can be mistaken for nephroblastomas, round cell tumors, or neuroendocrine tumors. Individual cells are generally cuboidal with mild to occasionally marked anisocytosis and anisokaryosis (Fig. 10-21). The cells in general have variable nuclear-to-cytoplasmic ratios with a moderate amount of often deep blue cytoplasm and round to polygonal nuclei. Hyaline globules were demonstrated in a canine case of renal carcinoma that appeared as magenta amorphous hyalinized material (2012 ASVCP slide set presented by Nancy Collicutt).

TCCs may exfoliate in small sheets, loose aggregates, or as individual cells. Single cells are large and can be cuboidal, polygonal, or even spindle-shaped. Transitional cells have a variable to low nucleocytoplasmic ratio (with abundant cytoplasm); however, they are often markedly pleomorphic with numerous and strong criteria of malignancy, including marked anisocytosis and anisokaryosis, pleomorphic nuclei, and prominent and multiple nucleoli (Fig. 10-23A&B). Characteristic pink homogenous to granular cytoplasmic inclusions are often noted in TCC (Fig. 10-23A, arrow).

Renal nephroblastomas are composed of mixed cell populations, including blastemal, epithelial, and mesenchymal elements (Henry et al., 1999; Michael et al., 2013). Cytologically,
the predominant cell types are usually the blastemal or epithelial components as cells tend to exfoliate singly or in loose aggregates and sheets. Similar to renal cell carcinomas, cells from this tumor can mimic round cell neoplasia (e.g., lymphoma or tumors of neuroendocrine origin). Cells are generally polygonal to cuboidal with a high nuclear-to-cytoplasmic ratio, a scant amount of pale blue cytoplasm, and mild anisokaryosis and anisocytosis. Nucleolar criteria of malignancy are generally absent (Fig. 10-24). Histopathology and immunohistochemistry are often necessary for definitive characterization. Nephroblastomas are characterized by positive vimentin staining of the mesenchymal cells and positive cytokeratin staining of the epithelial cells present within the tumor.

Renal lymphoma aspirates generally contain a homogeneous population of discrete cells with cytomorphologic features consistent with large, immature lymphocytes. There can be numerous lysed cells with “smudge cells” in the background. Neoplastic lymphocytes often show moderate to marked pleomorphism, have nuclei composed of homogeneous smooth chromatin, and have a small to moderate amount of basophilic cytoplasm (Fig. 10-25). Occasionally, prominent nucleoli can be

![FIGURE 10-23](image1.png)
**Transitional cell carcinoma.** A, This cluster of transitional cells contains numerous criteria of malignancy, including marked anisocytosis and anisokaryosis, variable nuclear-to-cytoplasmic ratio, pleomorphic and multiple nuclei, and micronuclei (arrowhead). Note the characteristic pink cytoplasmic inclusions (arrow). Contrast the features of these cells with the features of the cells in Figs. 10-10 to 10-12. (Wright-Giemsa; HP oil.) B, Urinary bladder. Dog. This group of transitional epithelial cells appeared individualized with marked anisocytosis and anisokaryosis, variable nucleocytoplasmic ratio, and pleomorphic nuclei. Contrast the features of these cells with the features of the cells in Figs. 10-10 to 10-12. (Wright-Giemsa; HP oil.) (B, Courtesy of Rick Alleman, University of Florida.)

![FIGURE 10-24](image2.png)
**Nephroblastoma.** This cluster of polygonal to cuboidal cells shows high nucleocytoplasmic ratios with mild anisocytosis and anisokaryosis. Note the pink extracellular matrix material (stroma or basement membrane) coursing through the cluster (arrow). Nuclei are round to polygonal, chromatin is stippled, and nucleoli are not obvious. (Wright-Giemsa; HP oil.)

![FIGURE 10-25](image3.png)
**Renal lymphoma.** This sample contains a dense population of discrete cells with cytomorphologic features consistent with large immature lymphocytes. Note the marked pleomorphism; smooth, homogeneous nuclear chromatin; and relatively abundant basophilic cytoplasm as compared to a small, mature lymphocyte (long arrow). The presence of pink cytoplasmic granules is a less common feature of lymphoma. These cells are differentiated from renal tubular cells by their abundance and high nuclear-to-cytoplasmic ratio. An activated macrophage (short arrow) and a mitotic figure (double arrow) are also seen. (Wright-Giemsa; HP oil.)
seen; and rarely, the neoplastic lymphocytes may contain bright pink cytoplasmic granules (Fig. 10-26).

Renal sarcomas often exfoliate poorly. They are composed of spindle cells observed individually or in variably sized aggregates. Nuclear-to-cytoplasmic ratios are high, with small amounts of moderate to deep blue, often wispy cytoplasm and round to oval to polygonal nuclei with prominent nucleoli.

Anisocytosis and anisokaryosis are often marked (Fig. 10-27). Cytology alone cannot distinguish between metastatic sarcomas and sarcomas arising from renal vessels or smooth muscle.

Ureters

Primary ureteral neoplasia is very rare, with ureteral invasion by neoplastic processes originating from the bladder (especially TCC) being far more common. Rigas et al (2012) describe cytologic features of an anaplastic sarcoma with giant cells. Documented cases of primary ureter neoplasia in dogs have been reported, composed mainly of benign neoplasms, primarily fibroepithelial polyps (Deschamps et al., 2007). Figs. 10-28A&B demonstrate the cytologic and histologic features of a fibroepithelial polyp in a dog that produced unilateral renomegaly and hematuria.

**FIGURE 10-26 Renal lymphoma.** A relatively normal, small, mature lymphocyte (arrow) accentuates the immature features of the neoplastic lymphocytes. In addition to the features described in Fig. 10-25, prominent nucleoli can be seen in some of the malignant cells, and the pink cytoplasmic granules are more readily observed. Five or six lacy, pink, ovoid formations, sometimes referred to as “basket cells” or “smudge cells,” represent free nuclear chromatin from lysed cells (long arrow). It is a frequent finding in aspirates from tissues composed of fragile cells such as lymphoma. (Wright-Giemsa; HP oil.)

**FIGURE 10-27 Renal sarcoma.** Cells of mesenchymal neoplasia tend to exfoliate singly or in small aggregates rather than cohesive clusters. Cell shape may vary from round to oval to spindle shaped. A cytologic impression of mesenchymal cells is endorsed by finding cells with wispy tails (arrow). Cytologically, malignancy is characterized by variable, often high nuclear-to-cytoplasmic ratios; moderate to deep blue, wispy cytoplasm that often contains numerous uniform punctate vacuoles; cellular pleomorphism and moderate anisokaryosis and anisocytosis; and variable staining intensity. (Wright-Giemsa; HP oil.)

**FIGURE 10-28 Fibroepithelial polyp. Ureter. Dog.** Same case A and B. A, Mass imprint. Cytologic features include benign transitional cell epithelium surrounding a blood vessel (left) and eosinophilic proliferative mucinous spindle cells (right). (Modified Wright; HP oil.) B, Tissue section. Shown is a marked proliferation of benign fibrovascular and myxomatous elements, the latter being Alcian blue positive. Uniform transitional epithelium surrounds blood vessels and the surface of the mass (not shown). (H&E, LP) (A and B, Courtesy of Athena Etzioni, Purdue University.)
Bladder and Urethra

Tumors of the urinary bladder are infrequent in dogs and cats. However, the most common bladder tumor in both dogs and cats is TCC (Mutsaers et al., 2003; Norris et al., 1992; Wilson et al., 2007). Squamous cell carcinomas, malignant tumors of muscle origin (Alleman et al., 1991) such as leiomyosarcoma and rhabdomyosarcoma (Fig. 10-29A&B), lymphoma (Fig. 10-30), and metastatic disease are less frequently encountered. TCC is of urothelial origin. In the dog, it is most commonly associated with the trigone region of the bladder, whereas the opposite is true in the cat (Mutsaers et al., 2003; Wilson et al., 2007). Neutered male dogs have a significantly increased risk of developing TCCs of the bladder compared to unneutered male dogs (Bryan et al., 2007). TCCs appear cytologically similar (Fig. 10-23A&B) whether they originate in the kidneys or bladder (see full cytologic description in renal section above). The diagnosis of canine TCC can frequently be made cytologically as the majority of patients present with high-grade disease and large masses (Mutsaers et al., 2003). However, in addition to cytology, the veterinary bladder tumor antigen test (V-BTA; Alidex Inc., subsidiary of Polymedco, Redmond, WA, United States) can be used to noninvasively detect tumor antigens present in urine. This test is suitable to screen for TCC in dogs in the absence of moderate to marked hematuria, pyuria, glucosuria, or proteinuria (Borjesson et al., 1999). However, the specificity of the test declines rapidly if dogs have non-TCC urinary tract disease (Borjesson et al., 1999; Henry et al., 2003). Finally, cyclooxygenase-2 (COX-2), uroplakin III, and cytokeratin 7 show promise as useful immunohistochemical stains to verify tumors of urothelial origin in histology sections if needed (Khan et al., 2000; Knottenbelt et al., 2006; Ramos-Vara et al., 2003).

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