Acute Postrenal Azotemia: Etiology, Clinicopathology, and Pathophysiology

**Abstract:** When rupture or obstruction of the urinary tract prevents the normal collection and expulsion of urine from the body, the resulting azotemia is termed postrenal. Postrenal azotemia can coexist with prerenal and/or renal azotemia. Detection of postrenal azotemia requires attentiveness to the history and physical examination findings and to the results of specifically directed diagnostic tests. Prompt correction of postrenal causes of azotemia limits the potential for intrinsic renal damage and can contribute to a positive clinical outcome; therefore, postrenal azotemia should be investigated in all azotemic patients.

Prompt and accurate assessment of the origins of azotemia—prerenal, renal, and/or postrenal—is essential to the proper management of azotemic patients. Prerenal azotemia occurs when decreased renal perfusion results in a diminished glomerular filtration rate (GFR); common causes of prerenal azotemia include volume depletion, vascular collapse, thrombotic diseases, and shock (cardiogenic, hemorrhagic, hypovolemic, or septic). Renal azotemia occurs when nephrons are directly damaged, most frequently by toxic, infectious, inflammatory, ischemic, or neoplastic processes. Postrenal azotemia is caused by urinary tract breach or obstruction. Any process distal to the renal tubules that interferes with the collection, containment, or excretion of urine can result in azotemia by preventing elimination of waste material in the urine, which can rapidly result in life-threatening fluid, electrolyte, and acid–base imbalances. Conditions causing prerenal and postrenal azotemia can also result in intrinsic renal damage if not identified and corrected.

Postrenal azotemia can be acute or chronic; this article addresses acute azotemia. Because causes of postrenal azotemia interfere with normal urine collection and elimination from the body, their identification is critical not only to determining definitive therapeutic strategies but also to developing appropriate stabilization and treatment plans.

**Etiologies**

**Urinary Tract Obstruction**

Obstruction of the lower urinary tract (LUT) is a common urologic emergency that results in significant azotemia in cats more often than in dogs. LUT obstruction can usually be diagnosed based on the history and palpation of a turgid, painful urinary bladder during physical examination. Most owners report that the pet has made unproductive attempts to urinate, often associated with discomfort. In cats, stranguria is sometimes mistaken for a sign of constipation. Most LUT obstruction in dogs is caused by urolithiasis or neoplasia; most LUT obstruction in cats is caused by urolithiasis or urethral mucocystic plugs.¹ ²

Urethral obstruction by uroliths is more common in male dogs than in female dogs because of several anatomic characteristics:
a smaller relative urethral diameter and longer urethral length, the curving course of the urethra around the ischium, and the presence of the os penis along the distal urethra, limiting expansion of the urethral diameter. Uroliths most often lodge at the ischial arch or just proximal to the os penis. Calcium oxalate and ammonium urate stones are most frequently implicated in urethral obstruction; their relatively small size and tendency to occur as multiple stones, along with the increased incidence of oxalates and urates in male dogs, likely factor into this predilection (FIGURE 1).

Transitional cell carcinoma is the most common neoplasm of the canine LUT. Most transitional cell carcinomas occur at the trigone of the bladder or at the prostatic urethra; a tumor at either location can lead to LUT obstruction. Prostatic carcinoma should be ruled out in any male dog with LUT obstruction and is the primary differential in a castrated dog with prostatomegaly. Proliferative urethritis is an infiltrative chronic inflammatory disease that can mimic urethral neoplasia and cause LUT obstruction. It is more common in female dogs than in males. Proliferative urethritis may cause a valve-like urethral obstruction that allows passage of a urinary catheter but precludes normal antegrade urine flow. Although proliferative diseases of the urethra and bladder outlet frequently lead to LUT obstruction, they rarely cause acute azotemia, unless the proliferative tissue suddenly obstructs the ureterovesicular junctions. The slow progression of proliferative disease generally produces recognizable clinical signs before obstruction is complete.

Obstruction of the upper urinary tract (UUT) is an increasingly common cause of azotemia, particularly in cats, and one that can only be definitively diagnosed by specific imaging of the kidneys and ureters. Congenital obstruction of the UUT, usually stenosis of the ureteropelvic junction or ureterovesicular junction, is very rare in dogs and cats, as it is in people. Acquired obstruction can be due to intraluminal, extraluminal, or intramural causes, including uroliths, nonmineralized material, trauma, neoplasia, proliferative disease, ureteroceles, inflammation, fibrosis, stricture, and inadvertent surgical trauma or ligation. For UUT obstruction to produce azotemia, bilateral kidney disease—either bilateral obstruction or unilateral obstruction with dysfunction or absence of the contralateral kidney—must be present. The obstruction may be partial or complete; azotemia can be acute and profound or chronic and mild/progressive.
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The most common cause of UUT obstruction is urolithiasis, and the most common component of UUT stones in dogs and cats is calcium oxalate (CaOx).1–10 Presentation of cats for management of ureterolithiasis increased steadily over the 18 years of a recent study by Kyles et al,6 leveling to a relatively stable rate during the last 3 years studied and paralleling trends in cats presenting for hemodialysis.11 The incidence of CaOx urolithiasis has increased dramatically in the past 10 years, to the point that >90% of analyzed nephroliths and ureteroliths are composed of this mineral.8–10 CaOx stones are formed in the parenchyma of the kidneys and may remain there or pass into the ureters and bladder. The formation of CaOx stones is influenced by many factors, including the degree of urine saturation with calculogenic minerals, urinary inhibitors of crystallization and crystal aggregation and growth, and urinary promoters of crystal aggregation and growth.8,12

UUT obstruction with uroliths is chiefly diagnosed in cats and small dogs. The ureters of medium-sized and larger dogs can accommodate the passage of stones up to several millimeters in diameter; the feline ureteral lumen measures approximately 0.4 mm and may be obstructed by much smaller objects.7 Some patients that present with acute, severe postrenal azotemia due to UUT obstruction have simultaneous, acute bilateral obstruction; however, many present with acute obstruction of a single functional kidney. These animals usually have permanent partial or complete dysfunction of one kidney, either from clinically silent or subtle unilateral obstruction or from another cause. In these patients, the contralateral kidney has hypertrophied to compensate for the functional decrement, and obstruction of this single functional kidney has resulted in acute azotemia. Physical examination of these patients may find renal asymmetry: the smaller kidney is firm, atrophied, and nonpainful; the larger kidney is resilient, obstructed, and often painful. In Kyles’ study,6 56% of the cats that presented with unilateral ureteral obstruction were found to have a small contralateral kidney on ultrasonography. Some astute owners detect subtle behavioral signs accompanying initial unilateral UUT obstruction, including antisocial behavior, flank licking, and back or abdominal pain, leading to earlier diagnosis of nephrolithiasis or ureterolithiasis.

The UUT may also be obstructed by nonmineralized material. A retrospective study13 evaluated 49 cats with urinary calculi composed entirely of dried, solidified blood (DSB; Figure 2). DSB calculi may occur as one or many small to medium-sized calculi anywhere in the urinary tract. Most often, DSB calculi are not the result of a known urinary tract bleed but are discovered during evaluation of the urinary tract for obstructive or other clinical signs. However, moderate to marked microscopic hematuria was present on all urinalyses evaluated in this retrospec-
tive study. The median age of the 49 affected cats was 9 years (range: 1 to 15 years), and the male:female ratio was 2.5:1. Approximately 40% of DSB stones were recovered from the UUT; it was unknown whether DSB stones found in the LUT formed there or passed from the UUT into the bladder. No causative factors for DSB calculi were identified in the study, although investigation of possible systemic and local infectious, inflammatory, ischemic, or traumatic factors that could contribute to hematuria seems warranted in these cases. The growing detection of DSB calculi also highlights questions surrounding management of microscopic renal hematuria in cats.

UUT obstruction with clotted blood may occur secondary to trauma, renal biopsy that penetrates into the renal pelvis, or renal hematuria. Accumulated debris (e.g., exudate from inflammation or ureteral trauma, fungal granuloma, sloughed renal papillary tissue from infection or ischemic insult) may also result in a soft, nonmineralized UUT obstruction (Figure 3). Sloughed, necrotic renal papillary tissue secondary to NSAID administration has been documented to occasionally result in ureteral obstruction in humans. There is little literature-based information regarding this type of obstruction in dogs and cats, but in our experience, such obstruction may occur due to acute pyelonephritis, acute renal tubular necrosis from a toxic insult (e.g., lily toxicosis), or intraluminal trauma from the presence or passage of stones. Experientially, these obstructions often occur proximally in the UUT, may be acutely bilateral, and can often be milked to a dilated region of the ureter or to the ureteropelvic junction for removal. Recurrence seems uncommon with appropriate management of the underlying disease.

Ureteral damage (inflammation, mineralization, fibrosis, stricture) can also cause progressive complete or partial obstruction. Iatrogenic ureteral damage, including ligation, transection, crushing, or devascularization, is an infrequently reported risk of abdominal surgery. Such damage occurs most often in the course of uterine body ligation during ovariohysterectomy in dogs and cats, particularly when the bladder is distended and the ureters are slackened by cranial displacement of the trigone, but it is possible in the course of any abdominal, particularly caudal abdominal, surgery. Ureteral entrapment during ovariohysterectomy is best avoided by visualization of the isolated uterine body before ligation. We have observed bilateral ureteral occlusion caused by direct ureteral entrapment during closure of caudal cystotomy incisions and by pressure of overzealous closure on the ureterovesicular junction (Figure 4). Often, iatrogenic ureteral trauma is not detected during surgery but becomes apparent in the postoperative period, requiring surgical revision. If ureteral entrapment, compression, or other nonpenetrating damage is noted and corrected during the initial surgery, ureteral patency and serum biochemistry can be monitored postoperatively. Many of these injuries do not require surgical revision if immediately addressed. Postoperative progressive ascites, azotemia, and/or dilation of the ureter or renal pelvis mandate prompt and aggressive evaluation, potentially including cytologic and biochemical assessment of ascites, excretory urography/antegrade pyelography, retrograde cystography, and exploratory laparotomy.

Primary ureteral neoplasia is rare in dogs,
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Blunt trauma and urethral catheterization are the most common causes of urinary tract rupture.

although transitional cell carcinoma, leiomyoma, leiomyosarcoma, fibropapilloma, and other primary ureteral tumors have been reported, as has metastasis to the ureter.7 Primary ureteral neoplasia is even less common in cats. More commonly, prostatic and trigonal neoplasia, usually adenocarcinoma or transitional cell carcinoma, can spread to encompass and obstruct the ureter(s), as can retroperitoneal neoplasia.

Urinary Tract Rupture

Rupture of the UUT or LUT results in partial or complete inability to void urine. Depending on the site of the rupture, urine may collect in the retroperitoneal space, peritoneum, or subcutaneous tissues, and presenting clinical signs may be associated with the inciting trauma, uremia, chemical irritation of the tissues where urine collects (e.g., cellulitis, urine peritonitis), or, if the urine is infected, septic complications. Causes of ureteral rupture include blunt or penetrating trauma, inadvertent damage during laparoscopy or laparotomy, damage from calculi, and neoplasia or infection.7 Ureteral damage from blunt or penetrating trauma is relatively uncommon because the retroperitoneal space is protected by the spine and lumbar musculature, although unilateral and bilateral ureteral ruptures due to vehicular trauma have been reported.18 The incidence of ureteral injury in dogs sustaining blunt pelvic trauma has been reported at 4%.19 Rupture of the proximal ureter results in uroretroperitoneum if the peritoneal membrane partitioning the retroperitoneum is intact. If the retroperitoneal membrane or distal ureter is also ruptured, uroabdomen results (FIGURE 5).

Rupture of the bladder or urethra is most commonly secondary to caudal abdominal trauma (often associated with pelvic fractures), instrumentation (usually catheterization) of the urethra, or application of excessive pressure during manual expression of urine.1,20,21 Preexisting urinary tract pathology, such as urethral or bladder tumors or bladder wall damage due to prolonged urethral obstruction, can cause LUT rupture directly or can compromise structural integrity and predispose the affected area to rupture with instrumentation or compression. Spontaneous rupture of a necrotic or damaged bladder wall is uncommon.20 In dogs, the most common cause of urethral rupture is vehicular trauma; in cats, it is trauma secondary to urethral catheterization.21

History and Physical Examination

Once azotemia is documented, the history and physical examination frequently provide initial evidence supporting a postrenal component. The history should include the owner’s observations of urination behavior, including frequency, amounts voided, and any clinical signs associated with voiding (e.g., anuria, dysuria, hematuria, stranguria, pollakiuria). Any prior UUT or LUT disease (e.g., urinary tract infection, incontinence, polyuria, vaginal discharge) should be detailed, including any diagnoses and therapies instituted. Known trauma and potential for trauma should be investigated. Mild azotemia may be clinically silent, and the patient may present for signs associated with the causative factor (e.g., trauma with multiple fractures and bladder rupture) rather than for signs associated with uremia. Patients with severe postrenal azotemia, however, are more likely to present with uremic signs, including hyporexia, weight loss, vomiting, lethargy, mild to moderate obtundation, and uremic or fetid breath.

Significantly uremic patients are usually hypothermic from interference of uremic toxins
with normal thermoregulation, unless a cause of systemic inflammation (e.g., pyelonephritis, neoplasia) is present. Uremic or fetid breath, xerostomia, or oral ulcerations (particularly on the ventrolateral tongue margins) may be present on oropharyngeal examination. Abdominal palpation may detect renal or bladder pain or suggest ascites. The physical examination should include surveillance for excoriations, lacerations, fractures, sheared claws, or other evidence of trauma. Examination of the urinary and genital tracts must be systematic and thorough. Renal size, shape, symmetry, and consistency should be assessed as possible, as should pain associated with renal or paralumbar palpation. More than half of cats with ureteral obstruction have renal asymmetry.\(^6\)\(^{,}\)\(^{22}\) Characteristics of the urinary bladder, including size, turgidity, pain on palpation, and ability to be expressed (if full), should be noted. Most patients with postrenal azotemia due to urethral obstruction resent abdominal palpation and present with a hard, painful urinary bladder that cannot be expressed, while approximately half of patients with bladder rupture present with no palpable bladder.\(^3\) Digital vaginal examination may detect neoplasia affecting the distal urethra or urethral orifice. Digital rectal examination in dogs permits evaluation of the size and consistency of the pelvic urethra, which should be smooth and mobile; uroliths may be palpable in the pelvic urethra, and some fractures of the pelvic outlet are palpable per rectum. In most male dogs, the prostate is accessible per rectum; in intact dogs, prostatic size, consistency, symmetry, and pain should be evaluated.\(^3\) In larger dogs, use of the nondominant hand on the caudal abdomen to caudally displace the bladder during digital rectal examination may permit easier and more complete prostate palpation. In peripubertally castrated dogs, a subtle thickening in the prostatic region may be palpable; the presence of an easily palpated, distinct prostate should raise a strong suspicion of neoplasia. The penis should be extruded in male dogs (and, if possible, cats) and examined for patency and the presence of stone or crystalline material at the orifice.

Clinicopathology
The clinicopathologic sequelae associated with postrenal azotemia may range from mild to life-threatening. Because the kidneys are the chief organs of elimination for nitrogenous waste products, as well as for phosphate, potassium, and many other dissolved solutes, the earliest derangements seen are usually elevations in the concentrations of blood urea nitrogen (BUN), creatinine, phosphorus, and, with complete obstructions, potassium. With complete obstruction, normal hydrogen ion excretion is prevented, resulting in metabolic acidosis, which manifests on the biochemical profile as decreased serum bicarbonate concentration and on blood gas analysis as a decreased bicarbonate concentration, negative base excess, and decreased pH.

Biochemical Changes
The biochemistry of acute postrenal azotemia has been best characterized in cats with UUT or LUT obstruction. In a retrospective study\(^6\) of 163 cats presented for ureteral calculi, only 83% of the cats were azotemic. At presentation, 48% were anemic (median packed cell volume: 29%, range: 11% to 51%) and 35% were hyperkalemic (median potassium concentration: 4.4 mmol/L; range: 2.8 to 9.4 mmol/L); BUN concentrations ranged from 19 to 456 mg/dL (median: 71 mg/dL); and creatinine concentrations ranged from 1 to 32.9 mg/dL (median: 4.4 mg/dL). In another review of 11 cats with ureteral obstruction,\(^3\) the median BUN concentration was 149 mg/dL and the median creatinine level was 10.2 mg/dL. In a review of 50 cats presented for hemodialysis because of azotemia due to ureteral obstruction,\(^2\) the median BUN concentration was 238 mg/dL (range: 68 to 456 mg/dL), median creatinine concentration was 17.4 mg/dL (range: 8.4 to 34.4 mg/dL), median potassium concentration was 6.8 mmol/L (range: 2.1 to 10.9 mmol/L), and median phosphorus concentration was 15.6 mg/dL (range: 1.1 to 27.6 mg/dL).

In an evaluation of 223 male cats with urethral obstruction,\(^2\) 69% of the cats were azotemic (defined as a BUN concentration greater than the reference range) at the time of presentation. The BUN concentration ranged from 10 to 100 mg/dL (100 mg/dL was the upper detection limit of the analyzer used). Of these cats, 40% were acidemic (median venous pH: 7.29, range: 7.02 to 7.45) and 41% were hyperkalemic (median potassium concentration: 5.2 mmol/L, range: 3.4 to 10.5 mmol/L). Ionized calcium (iCa\(^{2+}\)) levels were...
Although hematuria is commonly observed with urinary tract rupture, lack of hematuria does not rule out this possibility.

Urinalysis
Urinalysis findings in dogs and cats with post-renal azotemia vary. Because intrinsic renal damage is not necessarily present, urine may be dilute or concentrated, and the urinary pH can vary through the range of physiologic possibility. Hematuria, often grossly apparent, is a common finding in animals with LUT obstruction. Although hematuria is commonly observed with urinary tract rupture, lack of hematuria does not rule out this possibility. Microscopic hematuria may be present with UUT obstruction; gross hematuria is uncommon. Crystalluria may be associated with the underlying etiology (e.g., struvite crystalluria in a cat with a mucocrystalline urethral plug) or incidental to it (e.g., calcium oxalate crystalluria in a dog with prostatic adenocarcinoma). For some causes, such as ureteral obstruction, early detection and correction can limit the impact on the kidney and prevent or minimize the development of secondary renal azotemia.

Pathophysiology of Urinary Tract Obstruction
Upper Urinary Tract Obstruction
The current understanding of obstructive nephropathy is largely based on rat, dog, and other laboratory models. The type and degree of kidney damage that result from ureteral obstruction depend on a complex interplay of physical and cytochemical factors, the duration and completeness of obstruction, pre-existing renal pathology, patient species, and function of the contralateral kidney. In models of complete ureteral obstruction, duration of obstruction is the most significant variable influencing functional recovery after relief of obstruction. Mechanical obstruction of urine flow initiates a rapid, dramatic reduction in GFR, development of interstitial inflammation and edema, and, if unchecked, tubular atrophy, fibrosis, and apoptotic renal cell death.

Hemodynamic Effects
Acute obstruction causes ureteral peristalsis to increase and intraluminal ureteral and tubular pressures to rise rapidly. The rise in proximal tubular pressures induces production of prostaglandin E2 and prostacyclin and renal capillary endothelial release of nitric oxide (NO). Collectively, these substances cause afferent arteriolar dilation and increased renal blood flow. Glomerular capillary hydraulic pressure (Pge) increases in response, but the increase in proximal tubular pressure and Bowman’s capsule pressure exceeds the increase in Pge, resulting in decreased net ultrafiltration pressure. GFR declines rapidly once renal pelvic pressure exceeds 20 mm Hg and may be only 20% to 50% of normal after 24 hours of complete obstruction.

Acute UUT obstruction initiates a series of renal events that collectively increase vascular resistance. Within 5 hours of complete obstruction, sodium delivery to the distal tubules is decreased, juxtaglomerular renin release is stimulated, and local and peripheral angiotensin II (Ang II) production is increased, causing increasing peripheral arterial as well as renal arterial resistance. The effect of Ang II on the efferent arterioles exacerbates the increased Pge but has no functional effect on net ultrafiltration pressure because of the increased Bowman’s capsule pressures. Ang II also generates oxidative stress, increasing

Ionized hypocalcemia and edema, and, if unchecked, tubular atrophy, fibrosis, and apoptotic renal cell death.
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NO catabolism and thus decreasing local NO levels. Tubular epithelial cells and infiltrating macrophages release thromboxane A₂ (TXA₂), which augments renal arteriolar vasoconstriction. Because NO levels are substantially decreased, Ang II and TXA₂ exert an unopposed constrictive effect on the afferent renal arterioles, and renal plasma flow declines. Reabsorption of sodium and water through the renal tubules into the perirenal vasculature and lymphatics causes proximal tubular pressure to decrease toward normal at this point, and successive decreases in GFR are chiefly due to increased afferent vascular resistance. Preferential constriction of afferent renal arterioles results in reduced renal plasma flow and reduced glomerular capillary pressure, markedly decreasing GFR and filtration fraction.

Inflammatory Effects

The near-immediate consequence of complete UUT obstruction is reversible functional failure of the associated kidney(s), but complete obstruction also initiates inflammatory cascades that rapidly initiate the development of interstitial fibrosis and tubular cell apoptosis. Ang II has been identified as a key factor influencing induction and progression of interstitial fibrosis in obstructed kidneys. The release of Ang II, along with other chemokines and cytokines, attracts classically activated macrophages and activated cytotoxic T lymphocytes into renal tissue. Infiltrating macrophages produce a variety of proinflammatory cytokines and growth factors, including tumor necrosis factor α (TNF-α), transforming growth factor β1 (TGF-β1), interleukin 1, interleukin 6, and fibroblast growth factor. Leukocyte infiltration is mediated in part by Ang II–induced upregulation of the transcription factor nuclear factor κB (NF-κB), as well as other profibrotic cytokines such as TGF-β1 and TNF-α. Activation of NF-κB stimulates two known autocrine positive feedback loops, the amplification of Ang II and the formation of TNF-α, additionally fueling the inflammatory cascade. Infiltrating macrophages also generate reactive oxygen species, inducing oxidative damage that exacerbates matrix expansion and apoptosis.

The renal interstitium consists of resident fibroblasts in a matrix of collagen, proteoglycans, and fluid. Matrix metalloproteinases (MMPs) and other enzymes such as collagenase maintain the interstitial equilibrium between collagen bundle deposition and dismantling by countering the actions of profibrotic factors. The interstitial effects of MMPs are checked by tissue inhibitors of metalloproteinases (TIMPs). Increased local concentrations of profibrotic cytokines, such as NF-κB, TGF-β1, and TNF-α, shift the interstitial balance toward extracellular matrix deposition; TGF-β1 has a directly inhibitory effect on col-
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These kidneys, photographed at necropsy, demonstrate the marked renal asymmetry that can be present in sequential bilateral UUT obstruction. The smaller kidney most likely became obstructed without clinical signs and progressed to end-stage atrophy and fibrosis. The larger kidney hypertrophied to compensate for the functional decrement. The marker at the bottom of the photo is 1 cm long.

This transformation is accompanied by increased expression of MMPs that specifically target type IV collagen and laminin, principal proteins found in the tubular basement membrane. Consequent structural and functional disruption of the basement membrane allows the transformed cells to migrate from the tubular lumen into the interstitium. Ang II, TGF-β1, and many other growth factors, hormones, and cytokines also contribute to the process of epithelial to mesenchymal transition. This process is a recently elucidated mechanism of renal fibrogenesis in which renal tubular cells lose their epithelial phenotype and acquire mesenchymal characteristics. Tubular dilation resulting from UUT obstruction induces loss of the epithelial property of adhesion and acquisition of mesenchymal properties such as expression of α-smooth muscle actin. This transformation is accompanied by increased expression of MMPs that specifically target type IV collagen and laminin, principal proteins found in the tubular basement membrane. Consequent structural and functional disruption of the basement membrane allows the transformed cells to migrate from the tubular lumen into the interstitium. Loss of tubular epithelial cells, basement membrane disruption, and increasing interstitial fibroblast populations all contribute to initiation and propagation of interstitial fibrosis. Epithelial to mesenchymal transition probably plays a role in the pathogenesis of a wide range of fibrotic kidney diseases. Use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers to interfere with Ang II results in decreased local levels of Ang II–induced profibrotic cytokines, which significantly diminishes macrophage recruitment, collagen expression, and interstitial fibrosis in rats and mice.

Apoptotic Effects
Mechanical stretch from tubular distention has been shown to directly stimulate apoptosis of tubular epithelial cells in humans, rats, and mice as early as 4 days after obstruction; tubular cell loss leads eventually to tubular atrophy and obsolescence and thus to loss of functional renal mass. Apoptosis in renal tissues is effected by caspases (cysteinyll aspartate–specific proteinases), a family of cytosolic and nuclear enzymes. Caspases are activated by two distinct pathways: one involves TNF ligand binding, and the other involves intrinsic cell stress signals. Caspase levels increase markedly and rapidly in obstructed kidneys, and the degree of tubular cell apoptosis in an obstructed kidney mirrors the rise and fall of caspase expression. TGF-β1 has proapoptotic effects in obstructed kidneys, and administration of TGF-β1 inhibitors or monoclonal antibodies to TGF-β1 reduces obstruction-induced apoptosis and increases renal tubular cell proliferation. Increased concentrations of reactive oxygen species present in UUT obstruction also promote apoptosis, and administration of exogenous antioxidants attenuates apoptosis in mouse models. The role of Ang II in apoptotic renal cell death remains controversial.

Role of the Contralateral Kidney
The rate and degree of renal damage, as well as the capacity for repair, in an obstructed kidney are significantly affected by the presence of a functional contralateral kidney.

QuickNotes
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syndrome). In this scenario, clinically subtle unilateral UUT obstruction initiates the profibrotic processes described above. The presence of a contralateral functioning kidney subverts repair mechanisms, even if patency is restored to the obstructed kidney (which frequently does occur over time), and instead promotes progression of renal fibrosis to an end-stage state (FIGURE 6). The patent kidney simultaneously undergoes compensatory hypertrophy, resulting in potentially dramatic asymmetry.

**Lower Urinary Tract Obstruction**

Obstruction of the LUT produces increased pressure in the bladder and urethra proximal to the obstruction. If prolonged or severe, this pressure may be transmitted to the UUT. Urethral or trigonal mucosal damage, swelling, and/or denudation may occur at the site of obstruction. Such damage induces infiltration by inflammatory leukocytes. Urethral damage and inflammation from obstruction or instrumentation may cause urethral spasm that manifests as functional obstruction after relief of a mechanical obstruction. Submucosal hemorrhage, perivascular aggregations of inflammatory cells, and urothelial necrosis in the bladder can occur with obstruction of as little as 10 hours’ duration. Overdistention damages the bladder wall, likely through hypoxic damage caused by pressure-induced reduction in blood flow, and is postulated to disrupt tight junctions between detrusor myocytes. Axonal degeneration and Schwann cell edema may be detected by electron microscopy, and severe or prolonged overdistention may result in fundamental reorganization of the detrusor muscle electrical syncytium and thus in irreversible suppression of detrusor cell-to-cell electrical transfer.

Frequently, this neuromuscular damage manifests clinically as postobstructive detrusor atony. In most patients, this is transient and resolves clinically if the bladder is kept empty with the use of an indwelling catheter, but if overdistention is prolonged, the described changes may result in permanent detrusor dysfunction. If markedly elevated intravesicular pressures are transmitted to the UUT due to chronicity or ureterovesicular valve dysfunction, intrinsic renal damage may occur, as described above.

**Summary**

Acute postrenal azotemia is a common urologic emergency, particularly in cats, and may be fatal if not rapidly diagnosed and corrected. The most common causes of postrenal azotemia in small animals are urethral obstruction, ureteral obstruction, and traumatic urinary tract rupture. Azotemia from postrenal causes can be reversed because it results from urinary tract obstruction or rupture, rather than intrinsic damage to the kidneys; thus, the presence and significance of postrenal causes of disease should be identified in every azotemic patient. Historical and physical examination findings, coupled with diagnostic imaging, usually identify postrenal azotemia and localize its origin within the urinary tract. In some cases (such as acute ureteral obstruction), promptly addressing the cause of postrenal azotemia may forestall or mitigate the development of intrinsic renal damage and hasten clinical recovery.

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**References**


**REFERENCES CONTINUE ON PAGE 533**
1. Which statement(s) regarding urinary tract obstruction is/are true?
   a. Calcium oxalate stones and urate stones are frequently implicated in canine LUT obstruction.
   b. UUT obstruction rarely results in significant postrenal azotemia.
   c. UUT obstruction in cats is most frequently caused by calcium oxalate urolithiasis.
   d. a and c

2. In a severely azotemic cat, significant renal asymmetry is most consistent with
   a. sequential bilateral ureteral obstruction.
   b. chronic interstitial nephritis.
   c. simultaneous bilateral ureteral obstruction.
   d. blunt unilateral renal trauma.

3. In acute ureteral obstruction, GFR decreases precipitously because of
   a. increased intratubular pressure.
   b. Ang II and TxA2-mediated afferent arteriolar constriction.
   c. prostacyclin and NO-mediated afferent arteriolar dilation.
   d. a and b

4. The most common cause of urethral rupture in cats is
   a. firm palpation of the bladder in a cat with urethral obstruction.
   b. vehicular trauma.
   c. urethral trauma from catheterization.
   d. inadvertent surgical trauma.

5. Which substance has direct vasodilatory effects on the glomerular afferent arterioles?
   a. Ang II
   b. prostaglandin E2
   c. NF-κB
   d. TIMPs

6. The most common neoplasm of the canine LUT is
   a. transitional cell carcinoma.
   b. squamous cell carcinoma.
   c. prostatic adenocarcinoma.
   d. lymphoma.

7. Which statement regarding UUT obstruction is true?
   a. UUT obstruction with DSB occurs only in the presence of gross hematuria.
   b. UUT obstruction from neoplasia is common in cats.
   c. Microscopic hematuria is a common finding in cats with UUT obstruction from DSB.
   d. UUT obstruction can be definitively diagnosed based on physical examination findings.

8. Which clinicopathologic findings are most consistent with acute postrenal azotemia?
   a. metabolic acidosis and hyperkalemia
   b. metabolic alkalosis and hypokalemia
   c. metabolic acidosis and hypokalemia
   d. metabolic alkalosis and hyperkalemia

9. Which statement regarding urinary tract rupture in trauma patients is true?
   a. A palpable bladder on physical examination of a trauma patient rules out bladder rupture.
   b. The ability to urinate rules out bladder rupture in a trauma patient.
   c. Ureteral rupture is relatively common in trauma patients.
   d. Vehicular trauma is the most common cause of urethral rupture in dogs.

10. Which mechanism does not contribute to loss of functional renal mass consequent to UUT obstruction?
    a. epithelial to mesenchymal transition
    b. caspase-mediated apoptosis of renal tubular epithelial cells
    c. TGF-β1-mediated renal tubular aplasia
    d. disruption of the interstitial equilibrium to favor matrix deposition
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