Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Acute Kidney Injury

Cathy Langston and Adam Eatroff

ETIOLOGY AND PATHOPHYSIOLOGY

Acute kidney injury (AKI) has traditionally been classified into hemodynamic (prerenal), renal parenchymal (intrinsic), and postrenal etiologies. Although conceptually these categories provide a framework for understanding the pathophysiology of various renal insults, the clinical relevance of this taxonomy is questionable, because AKI is often the culmination of systemic, extra-renal disease, and renal-specific insults. Recent work has questioned whether azotemia secondary to volume depletion truly results in kidney injury *per se* or whether it represents an appropriate, physiologic renal response (i.e., marked reduction in glomerular filtration) to the need for extracellular fluid conservation.[1] Furthermore, the diagnosis of hemodynamic (prerenal) azotemia is often made in retrospect, limiting its clinical utility. Nonetheless, in people, hemodynamic azotemia (referred to as *transient azotemia*) is associated with a higher odds ratio for mortality, similar to persistent azotemia.[2] Although postrenal etiologies of AKI are typically recognized as structural or functional alterations in the urinary tract that prevent urine outflow, the pathophysiologic processes that result in uremia may be unrelated to renal excretory function (e.g., lower urinary tract rupture) or may be comprised of multiple components of this classification scheme. For example, in the case of a ureteral obstruction, azotemia may be the result not only of blockade of urine outflow from the renal pelvis, but also the maladaptive renal response to such obstruction, consisting of intense arteriolar vasoconstriction and influx of inflammatory cells.[3] The inflammatory response to ureteral obstruction may in itself produce significant, intrinsic renal parenchymal injury sufficiently severe to affect renal excretory function.

Classically, the clinical course of AKI proceeds through four phases: the initiation phase, the extension phase, the maintenance phase, and the recovery phase. These phases are defined by experimental models of AKI and may not be representative of the multifactorial nature of the disease. In clinical cases of AKI, the pathophysiologic process resulting in renal dysfunction is often multifactorial, with overlapping ischemic, inflammatory, toxic, and septic components in many cases; partitioning of AKI into these phases has little clinical utility.

There are a myriad of possible etiologies of feline AKI (Box 50-1). The most frequently encountered, diagnosed, or discussed etiologies in feline medicine are discussed in the following sections.

Ureteral Obstruction

Obstruction of the upper urinary tract has become a common cause of feline AKI in the last 20 years. The inner diameter of the feline ureter is approximately 0.4 mm (0.016 inches), making this structure highly prone to obstruction due to stricture, intraluminal concretion, mural inflammation or edema, muscular spasm, or extramural compression.[4,5] Although calcium oxalate nephroliths and ureteroliths are most frequently implicated as obstructive lesions,[6] the emergence of blood stones,[7] inflammation and fibrosis with smooth muscle hypertrophy of the ureteral wall (strictures),[8] and circumcaval ureters[9] have made advanced imaging techniques paramount for accurate presurgical identification of the cause of ureteral obstruction. This information can inform whether referral to select institutions for specific interventions (e.g., subcutaneous [SC] ureteral bypass) is indicated. The pathophysiology of AKI secondary to ureteral obstruction is complex, and most of the available information has been obtained from species other than the cat.[3,10] Pathophysiologic processes shared among various species include vasoconstriction, an influx of inflammatory cells and the release of proteolytic enzymes, and fibroblast recruitments with resultant fibroplasia.

Lily Intoxication

Species from the genera *Lilium* and *Hemerocallis* have been implicated in feline AKI of varying severity. Although neither the toxic principle nor a toxic dose has been clearly established, a report suggests that the aqueous fraction of the flowers and leaves of these plants is toxic and that ingestion of a single flower can cause clinically apparent AKI.[11] Pancreatitis has been implicated as a complicating factor in experimental models, as well as clinically and at the time of necropsy,[12] but whether pancreatitis precedes, is a consequence of, or occurs independently of AKI has yet to be determined. Early reports of lily intoxication portrayed a poor prognosis.[12,13] However, more recent studies suggest that azotemia develops infrequently secondary to lily exposure.[14,15] In the authors' experience, AKI secondary to lily intoxication that results in anuria carries a poor prognosis.

Pyelonephritis

In the authors' experience, the most commonly cited differential diagnosis for AKI (alone or superimposed on

BOX 50-1 List of Etiologies for Feline Acute Kidney Injury

Nephrotoxins

Antimicrobial Agents
Aminoglycosides
Aztreonam
Carbapenems
Cephalosporins
Penicillins
Polymyxins
Quinolones
Rifampin
Sulfonamides
Tetracyclines
Vancomycin

Antifungal Agents
Amphotericin B

Antineoplastic Drugs
Cisplatin and carboplatin
Doxorubicin
Methotrexate

Antiviral Agents
Acyclovir
Foscarnet

Antiprotozoal Agents
Dapsone
Pentamidine
Sulfadiazine
Thiacetarsamide
Trimethoprim-sulfamethoxazole

Immunosuppressive Drugs
Azathioprine
Calcineurin inhibitors (e.g. cyclosporine, tacrolimus)
Interleukin-2

Miscellaneous Therapeutic Agents
Acetaminophen
Allopurinol
Angiotensin-enzyme converting inhibitors
Antidepressants
Apomorphine
Cimetidine
Deferoxamine
Dextran-40
Diuretics
e-Aminocaproic acid
Ethylenediaminetetraacetic acid
Lipid-lowering drugs
Lithium
Methoxyflurane

Nonsteroidal anti-inflammatory drugs
Penicillamine
Phosphorus-containing urinary acidifiers
Streptokinase
Tricyclic antidepressants
Vitamin D analogs

Endogenous compounds
Hemoglobin
Myoglobin (e.g. trauma/rhabdomyolysis)

Heavy Metals
Antimony
Arsenic
Bismuth salts
Cadmium
Chromium
Copper
Gold
Lead
Mercury
Nickel
Silver
Thallium
Uranium

Organic Compounds
Carbon tetrachloride and other chlorinated hydrocarbons
Chloroform
Ethylene glycol
Herbicides
Pesticides
Solvents

Miscellaneous Nontherapeutic Agents
Bee venom
Diphosphonate
Calcium antagonists
Gallium nitrate
Illicit drugs
Lilies
Mushrooms
Radiocontrast agents
Snake venom
Sodium fluoride
Superphosphate fertilizer
Vitamin D-containing rodenticides

Continued

BOX 50-1 List of Etiologies for Feline Acute Kidney Injury—cont'd

Non-Nephrotoxic Insults

Decreased Cardiac Output/Ischemia
Volume depletion
Congestive heart failure
Arrhythmia
Cardiac arrest
Cardiac tamponade
Fluid overload
Deep anesthesia
Extensive surgery
Renal vessel thrombosis
Hyperviscosity/polycythemia
Hepatorenal syndrome

Infectious
Bacterial/fungal pyelonephritis
Leptospirosis
Feline infectious peritonitis
Bacterial endocarditis

Immune-Mediated/Inflammatory
Acute glomerulonephritis
Systemic lupus erythematosus
Renal transplant rejection
Vasculitis
Systemic inflammatory response syndrome
Sepsis
Disseminated intravascular coagulation

Obstructive
Ureteral obstruction
Urethral obstruction

Miscellaneous
Lymphoma
Blood transfusion reaction
Heatstroke/hyperthermia
Malignant hypertension
Neoplasia
Hypercalcemia

---

pre-existing chronic kidney disease [CKD]) is pyelonephritis. A definitive diagnosis of pyelonephritis requires identification of bacteria within the urine collected by pyelocentesis, but this procedure is rarely performed due to the associated risks of uroretroperitoneum, uroperitoneum, or urosepsis. Therefore, this diagnosis is frequently made based on the ultrasonographic appearance of the renal pelves with or without a positive bacterial culture of urine obtained by cystocentesis. The use of renal pelvic dimensions for the diagnosis of pyelonephritis is problematic for several reasons. First, there appears to be a large overlap in renal pelvic dimensions among healthy cats and cats with a variety of renal diseases, including pyelonephritis.[16] Second, the association between renal pelvic dilation and pyelonephritis was largely shaped by an experimental study in which pyelonephritis was induced in cats by ligation of the ureter and intravenous injection of *Escherichia coli*.[17] Finally, in other species (particularly humans), imaging criteria for pyelonephritis do not typically include the degree of renal pelvic dilation that is accepted as supportive for this disorder in veterinary medicine.[18] For these reasons, despite its ubiquity as a presumptive diagnosis for AKI, the true incidence and importance of this disease in the feline population are currently unknown.

Leptospirosis

Although feline AKI is not frequently associated with leptospirosis, there have been reports of acute azotemia associated with positive microscopic agglutination titers for specific *Leptospira* spp. serogroups.[19] Furthermore, serologic surveys have demonstrated exposure among a significant proportion of domestic cats.[20,21] This data, along with the fact that cats frequently prey on rodents which serve as reservoirs for many pathogenic leptospires, suggest the role of leptospirosis as an emerging cause of feline AKI should be re-examined.[22]

EPIDEMIOLOGY

Epidemiologic data characterizing feline AKI is lacking. The information available is limited to case series and anecdotal reports from referral centers with high caseloads. Furthermore, epidemiologic data likely varies, depending on the underlying etiology of AKI. For example, the patient population susceptible to unilateral ureteral obstructions resulting in uremic complications (i.e., typically middle-aged to older cats with underlying CKD) is likely different from the population at greatest risk for AKI secondary to lily exposure (i.e., young, curious cats). Lastly, the limited data that is available characterizing feline AKI has been generated from single institutions with limited patient and client demographics and geographic range. Therefore, generalizations regarding epidemiologic characteristics of feline AKI should be interpreted with caution.

In addition to the difficulties inherent in characterization of a syndrome with broad etiologic and epidemiologic characteristics, the lack of a standard definition for AKI and the wide spectrum of injury (ranging from clinically undetectable, subcellular damage to fulminant, excretory failure) has

Table 50-1	**International Renal Interest Society Grading Scheme for Acute Kidney Injury**	
Grade[†]	**Creatinine**	**Clinical Description**
Stage I	<1.6 mg/dL (<140 μmol/L)	Nonazotemic AKI Documented AKI: Historical, clinical, laboratory, or imaging evidence of AKI; clinical oliguria/anuria; volume responsiveness[*] *and/or* Progressive *nonazotemic* increase in serum creatinine ≥0.3 mg/dL (≥26.4 μmol/L) within 48 hours Measured oliguria (<1 mL/kg/hr) or anuria over 6 hours
Stage II	1.7-2.5 mg/dL (141-220 μmol/L)	Mild AKI Documented AKI and static or progressive azotemia Progressive azotemic increase in serum creatinine ≥0.3 mg/dL (≥26.4 μmol/L) within 48 hours, or volume responsiveness[*] Measured oliguria (<1 mL/kg/hr) or anuria over 6 hours
Stage III Stage IV Stage V	2.6-5.0 mg/dL (221-439 μmol/L) 5.1-10.0 mg/dL (440-880 μmol/L) >10.0 mg/dL (>880 μmol/L)	Moderate to severe AKI Documented AKI and increasing severities of azotemia and functional failure

AKI, Acute kidney injury.
*Volume responsive is an increase in urine production to >1 mL/kg/hr over 6 hours and/or decrease in serum creatinine to baseline over 48 hours.
[†]Each stage of AKI is further substaged on the basis of current urine production as oliguric or nonoliguric and on the requirement for renal replacement therapy.

hindered progress in understanding the scope of this disease. Recent standardization of the definition and stratification of severity of AKI in human medicine has not only allowed for more applicable epidemiologic studies but has allowed for the extraction of more clinically meaningful results from various clinical trials. The two most widely accepted schemes for defining and classifying human AKI are the Risk Injury Failure End-Stage Kidney Disease (RIFLE) scheme and the Acute Kidney Injury Network (AKIN), the latter of which was developed by modification of the former, with the intent to improve the sensitivity of detection of AKI.[23,24] Both sets of criteria appear to perform equally well when both sensitivity for detection of AKI and predictive ability for adverse outcomes are evaluated; therefore, these schemes have become accepted within the human nephrology community as the standard means of defining AKI for epidemiologic characterization. Based on several obstacles preventing application of these schemes to the feline population, Cowgill recently proposed a veterinary staging scheme designed for application to the veterinary population (Table 50-1).[25] This proposed scheme has yet to be validated for clinical utility in cats.

HISTORY, CLINICAL SIGNS, AND PHYSICAL EXAMINATION

Common historical findings include lethargy, vomiting, diarrhea, and anorexia, but these signs are nonspecific and may be the result of a variety of extra-renal diseases. Oliguria, anuria, or polyuria may be reported. When a patient is polyuric, compensatory polydipsia may be present, or water intake may be reduced due to anorexia. When patients are severely affected, reports of seizures, syncope, and dyspnea may overshadow more classic presenting signs associated with AKI.

Physical examination yields few findings specific to AKI, aside from enlarged, painful kidneys. Renomegaly and renal angina are inconsistently present, however, and for some cases in which underlying CKD is present concurrently, the kidneys are small. Dehydration is a common finding at the time of initial presentation, especially in those cats with AKI superimposed on CKD. However, inaccurate assessment of hydration status by physical examination parameters is common, and many euhydrated and overhydrated patients are erroneously categorized as dehydrated. Other findings may include halitosis, scleral injection, bradycardia, cutaneous bruising, peripheral edema, melena, and diarrhea. Oral mucosa ulceration and necrosis are common in patients with severe uremia. These findings may be due to the phenomenon of either uremic calciphylaxis or uremic stomatitis. Although the anatomic distribution and histologic lesions vary between these two processes, the gross appearance may be similar (i.e., ulceration).[26,27] Further work is warranted to better characterize these lesions because appropriate treatment may vary. Many of the aforementioned physical examination findings may be secondary to uremia, the primary disease process resulting in AKI (e.g., disseminated intravascular coagulation, vasculitis), or concurrent extra-renal organ injury (e.g., pancreatitis). Hypothermia is a frequent finding, and in the absence of circulatory shock, is thought to be associated with alteration of the hypothalamic thermoregulatory set point

secondary to the influence of uremia.[28] Normothermia or hyperthermia may be suggestive of an infectious, inflammatory, or immune-mediated etiology.

A diagnostic dilemma often associated with the initial evaluation of the feline patient is the determination whether there is an underlying chronic component to AKI. The presence of underlying CKD can have serious implications in determining a patient's prognosis and potential for renal recovery and can influence a cat owner's willingness to pursue the intensive treatment often necessary to maximize the likelihood of a positive outcome. Clinicopathologic data characterizing prior renal function is frequently not available, however, making subtle historical and physical examination findings vital in assessing the likelihood of underlying CKD. Body fat and muscle condition can provide insight into the chronicity of renal or extra-renal disease. Careful palpation of the kidneys can aid in assessment of renal size and shape (e.g., small size or irregular contours of kidneys are often detected in association with CKD). A more sensitive means of assessing these characteristics is visualization with radiography or ultrasonography. Although the use of imaging, clinicopathologic techniques, and (rarely) renal histopathology can be helpful for cases in which underlying CKD is not readily apparent, many feline AKI cases with an underlying chronic component can be identified by a thorough questioning of the owner and physical examination.

DIAGNOSIS

Because most cases of feline AKI are manifested as a severe decline in renal excretory function, diagnosis is typically made based on a single evaluation or serial evaluations of creatinine and/or urea concentration in whole blood, serum, or plasma. Therefore, the diagnostic techniques discussed in the following sections are employed to determine the etiology, appropriate treatment options, and prognosis of the already identified AKI.

Laboratory Tests

Although changes in the complete blood count are often nonspecific in AKI, subtle changes in various components of the erythron and leukon can be useful for gaining insight into the chronicity, etiology, and prognosis. Although the presence of anemia can be due to a multitude of causes, this abnormality has important implications for both determination of chronicity and planning for treatment options, such as hemodialysis. Although anemia can be a complication of both acute and CKD, it is more frequently encountered and is more frequently severe (i.e., hematocrit less than 20%) in cases with an underlying chronic component. A moderate to severely anemic cat will almost assuredly require a red blood cell (RBC) transfusion during an extended course of treatment, given the need for serial blood sampling. Therefore, the availability of donor blood products, as well as blood typing and crossmatching capabilities, should be determined near

the time of initial presentation. Although the leukon frequently displays abnormalities consistent with a stress or inflammatory response, changes such as the presence of a left shift (circulating band neutrophils) may indicate more clinically significant inflammation, such as systemic inflammatory response syndrome (with or without concurrent sepsis).

The serum or plasma biochemistry panel may provide insight into extra-renal manifestations or consequences of AKI, as well as the presence of multisystemic disease. The severity of azotemia depends on the etiology and duration of AKI. The ratio of blood urea nitrogen to creatinine can be high from gastrointestinal (GI) bleeding or dehydration, or it can be low in early stages of AKI. The degree of hyperphosphatemia typically mirrors that of hypercreatinemia with few exceptions (e.g., acute ethylene glycol intoxication, juvenile growing animal, refeeding syndrome). Ionized calcium concentrations are normal or low, provided that hypercalcemia is not the cause of the AKI. Ethylene glycol intoxication causes a profound ionized hypocalcemia, due to both severe hyperphosphatemia and chelation of calcium by oxalate. The anion gap is usually high secondary to retained organic and inorganic acids, but it can be normal early in the course of disease, or if hypoalbuminemia is present. A high anion gap without (or prior to) the presence of azotemia is supportive of intoxication in cases of suspected ethylene glycol exposure. The anion gap is calculated by the formula*:

$$\text{Anion gap} = (Na^+ + K^+) - (HCO_3^- + Cl^-)$$

The normal anion gap is approximately 13 to 27 mEq/L.

The urinalysis can provide information regarding the etiology and severity of AKI. Care must be taken, however, to examine urine shortly after collection to avoid artifactual changes in biochemical and cellular composition. The urine specific gravity is frequently isosthenuric (1.007 to 1.015) in cases of intrinsic failure. A urine dipstick may reveal any combination of glucosuria (without hyperglycemia), proteinuria, bilirubinuria, and hemoglobinuria, depending on the underlying etiology. Care must be taken to obtain a thorough history, however, as administration of various medications (e.g., ascorbic acid, cephalexin, enrofloxacin) can interfere with the results of certain assays aimed at detecting glucosuria.[29,30] Proteinuria is frequently present, but qualitative (dipstick) and quantitative (urine protein : creatinine ratio) severity can vary within a specific etiology. Dipstick assessment of proteinuria has limited value in cats, due to discordance with urine protein : creatinine ratios.[31] The urine pH is usually acidic, unless there is a concurrent bacterial urinary tract infection (UTI). Careful microscopic assessment of urine sediment may disclose pyuria (suggestive of nephritis), dysmorphic RBCs (suggestive of glomerular disease, an uncommon diagnosis in the cat), or casts (most frequently granular, but red and white blood cell casts are uncommonly observed). In human medicine, eosinouria has historically

---

*Na^+, Sodium; K^+, potassium; HCO_3^-, bicarbonate; Cl^-, chloride.

been associated with acute interstitial nephritis (secondary to a drug reaction). However, more recent publications have shown that this finding lacks the satisfactory test characteristics to make it useful in the identification of this specific etiology.[32] Calcium oxalate crystals present in large numbers are supportive of ethylene glycol intoxication, although a few oxalate crystals may be present in the urine of healthy patients. Crystalluria is a common *in vitro* artifact that is secondary to prolonged storage of urine prior to analysis.[33] An in-house variation of a Romanowsky stain is frequently useful for detailed assessment of red and white blood cell morphology, as well as for the identification of bacteria. A bacterial urine culture is important to confirm the presence of a UTI and to guide antimicrobial therapy.

Imaging

Survey abdominal radiographs may show a normal renal silhouette or renomegaly, but hydronephrosis cannot be detected by radiography. Uroliths may be apparent, provided their size is above the limit of detection (typically 3 to 4 mm in diameter). Although radiography and ultrasonography are typically complementary (ureteral calculi that may be obscured by gas or ingesta during ultrasonography frequently can be detected by radiography), ultrasonography often provides more information.

In cases of AKI without an underlying chronic component, abdominal ultrasonography usually shows normal or enlarged kidneys with normal parenchymal architecture. Because many (especially geriatric) patients with AKI have underlying CKD, ultrasonographic changes (such as decreased corticomedullary definition, cysts, infarcts, small size, and irregular renal contour) are significant, and they should be considered important factors in formulating a long-term prognosis. The presence of ultrasonographic changes consistent with CKD does not preclude the possibility of a superimposed acute injury and, thus, the potential for at least partial renal recovery. Likewise, normal ultrasonographic renal architecture does not rule out the possibility of CKD. Perirenal fluid is commonly seen with a variety of etiologies of AKI and can also be seen secondary to volume overload. Aspiration and analysis of the perirenal fluid is typically unrewarding, because the fluid can be viscous, resulting in an inability to collect a sufficient volume for analysis.[34] A renal ultrasonographic finding described as subcapsular hypoechoic thickening has been described in cats undergoing fine-needle aspiration (FNA) or needle biopsy of the kidney. The presence of renal subcapsular hypoechoic thickening has a reasonably high positive predictive value for the identification of renal lymphoma (80.9%), but the negative predictive value (66.7%) does not allow for lymphoma to be ruled out in the absence of this finding.[35]

Ultrasonography of the renal pelves and ureters is the most practical tool for diagnosing ureteral obstructions. The renal pelvic diameter should always be measured in the transverse plane from the tip of the renal papilla to the most proximal aspect of the ureter (Figure 50-1A), because this
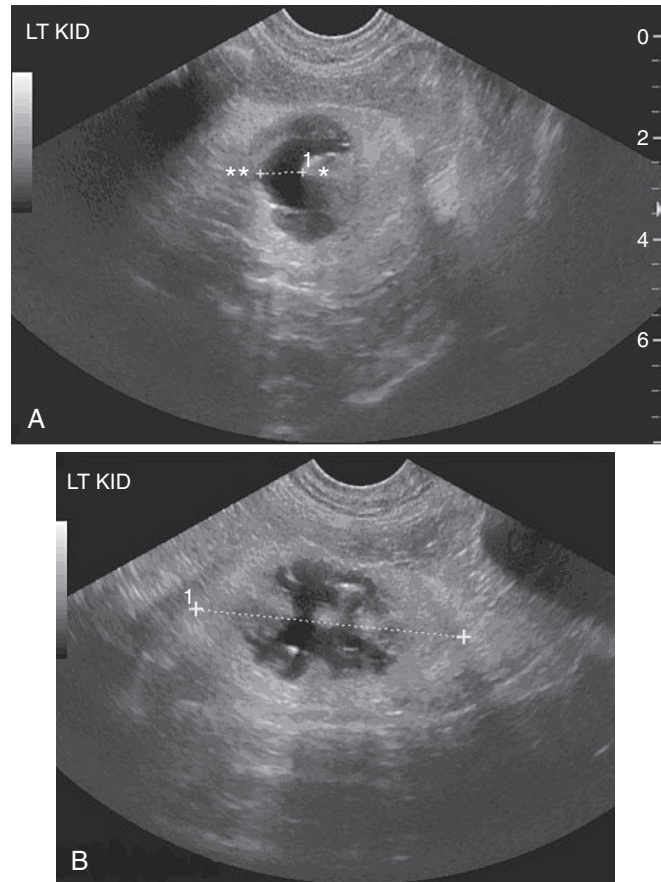

Figure 50-1: **A,** The renal pelvic diameter measured in the transverse plane. The calipers measure a renal pelvic diameter of 0.83 cm from the tip of the renal papilla *(*)* to the most proximal portion of the ureter *(**)*. **B,** The same kidney viewed in the sagittal plane. Note the irregularity of the renal pelvic margin.

convention allows consistent methodology in evaluation of serial ultrasound studies. Measurement of the renal pelvic diameter in the sagittal plane can be problematic because the periphery of the renal pelvis can be uneven when evaluated from this view (see Figure 50-1B). In a recent study of both dogs and cats, a renal pelvic width equal to or exceeding 13 mm (0.5 inches) had 100% specificity for identification of renal outflow obstruction.[16] Serial examinations are occasionally necessary in patients where a ureteral obstruction is strongly suspected, but the initial renal pelvic diameter is not supportive of obstruction. The documentation of an increasing renal pelvic width over hours to days is strongly supportive of an acute ureteral obstruction.

Occasionally, an intravenous (IV) pyelogram can aid in the identification of pelvic, ureteral, and cystic disease processes, especially obstructive renal lesions that are not readily apparent with survey radiography or ultrasound. In addition, it can provide information regarding renal function in the contralateral kidney. For example, if uptake of radiocontrast is not detectable in the renal parenchyma or collecting system, the likelihood of a substantial glomerular filtration rate

(GFR) in that kidney is low. If the GFR in an obstructed kidney is below a certain threshold, historically identified with a serum creatinine concentration greater than 3.5 mg/dL (267 μmmol/L),[36] an IV pyelogram will result in inadequate study quality due to poor uptake of contrast. Antegrade pyelography may be a better choice for detection of obstructive ureteral lesions, because this technique does not rely on an adequate GFR for proper distribution of contrast material.[37] Computed tomography (CT) or magnetic resonance imaging can add information about renal architecture and better characterize obstruction. These techniques also eliminate the problems associated with superimposition of soft tissue and bone, as well as shadowing artifact encountered when the overlying GI tract is filled with gas. With the recently increased availability of high-speed image acquisition on many CT platforms, this technique is likely to become the standard means of acquiring images from contrast studies.

Other Diagnostic Modalities

Measurement of GFR (e.g., via iohexol clearance, endogenous creatinine clearance, or scintigraphy) has limited applicability in the initial identification of clinical AKI, because the degree of impairment in GFR is almost always detectable by surrogate markers, such as serum or plasma creatinine concentration. Typically, following a diagnosis of AKI with serum or plasma creatinine and urea concentrations, no additional tests are useful in confirming that renal impairment is present or further characterizing the degree of impairment. Although more advanced procedures (e.g., nuclear scintigraphy, contrast-enhanced CT) may provide information characterizing the GFR of each individual kidney, these techniques can be expensive and are not readily available.

Cytology of tissue acquired by FNA has limited utility in cases of AKI but can aid in detection of an infiltrative etiology. Cases of feline lymphosarcoma are frequently diagnosed based on percutaneous FNA of the kidney. Occasionally, false-negative results are obtained from cytologic analysis, and histopathology is necessary to confirm the diagnosis. Diagnosis of glomerular amyloidosis and feline infectious peritonitis requires special cytologic techniques (e.g., Congo red staining or coronavirus immunocytochemistry, respectively), and these diagnostic techniques have not been rigorously assessed. The risk of bleeding secondary to FNA of the kidneys is low, but possible, especially when platelet dysfunction is present.

Histopathologic samples can be obtained by percutaneous, ultrasonographically-guided needle biopsy, laparoscopy, or surgical wedge biopsy. Histopathology may confirm a suspected etiology (e.g., ethylene glycol intoxication, renal lymphosarcoma) or it may disclose nonspecific findings. When AKI cannot be distinguished from end-stage CKD clinically, histopathology (particularly Masson's trichrome stain) can aid in assessment of the severity of fibrosis and provide insight into the potential for renal recovery. The risk of significant hemorrhage secondary to percutaneous renal biopsy

is high in cats due to the small size of their kidneys. This risk is intensified when uremia is severe and platelet dysfunction in present.[38]

THERAPY

Treatment of AKI is primarily aimed at addressing the underlying cause (if it can be identified and treated) and supportive measures to minimize the clinical sequelae of uremia (Table 50-2). There are no pharmacologic options available that reliably result in improvement of renal excretory and regulatory function. When treatable causes of AKI have been addressed and conventional medical therapy is insufficient for controlling the consequences of uremia, renal replacement therapy (e.g., intermittent hemodialysis, continuous renal replacement therapy, peritoneal dialysis, or renal transplantation) should be considered.

Addressing the Underlying Cause

There are few etiologies of AKI that can be addressed with a specific maneuver that directly results in improved excretory renal function. Fortunately, one of the most common causes of feline AKI, ureteral obstruction, can be addressed surgically or (in select cases) endoscopically. Restoration of ureteral patency can be achieved with the surgical removal of ureteroliths (ureterotomy) or, in cases in which concern for reobstruction exists, the placement of ureteral stents specifically sized for the feline patient. Potential exists, however, for stent encrustation, obstruction, and/or migration. Additionally, in some cases, the presence of a ureteral stricture prevents stent placement. An alternative to ureteral stents is placement of a SC ureteral bypass device.[39] This device consists of a nephrostomy tube and a cystostomy tube, both of which are tunneled SC and connected to a SC port (Figure 50-2). This device allows for aspiration of urine, as well as flushing of the entire device to maintain patency and perform positive contrast radiographic studies.

Traditionally, ureteral obstructions have been addressed surgically, but a recent study describing treatment of AKI with intermittent hemodialysis documented spontaneous resolution of ureteral obstruction in cats supported with hemodialysis alone. In this study, eight of 13 cats with ureteral obstructions that were not treated surgically survived longer than 365 days following hospital discharge.[40] This data is in contrast to a previous study that documented a lower success rate for medical management of cats with ureteral obstruction. The latter study, however, described cats with ureteral obstructions secondary to ureteral calculi, whereas the former study did not differentiate between obstructive disease caused by calculi versus alternative causes (e.g., stricture, spasm, edema, etc.).[41] Based on the results of these two studies, the authors do not recommend withholding surgery from cats with severe AKI secondary to ureteral calculi but consider supportive care (either with conventional methods or with renal replacement therapy) an option when

Table 50-2	Indications, Doses, Adverse Effects, and Comments for Drugs Frequently Used in Cases of Acute Kidney Injury			
Drug	**Indication**	**Dosage**	**Adverse Effects**	**Comments**
Furosemide	Fluid overload, oliguria/anuria, hyperkalemia	2 to 5 mg/kg IV bolus, may be repeated three to five times; 0.5 to 1 mg/kg/hr CRI if urine production increased following bolus	Ototoxicity; volume depletion (unlikely if patient is monitored)	Results are frequently not satisfactory in cases of severe AKI but adverse effects minimal, so use in anuric AKI
Regular insulin	Hyperkalemia	0.5 units/kg IV or IM, may be repeated every 4 to 6 hours, provided hypoglycemia is avoided	Hypoglycemia	Hypokalemic effect modest and transient; IV dextrose must be administered concurrent with and following insulin administration
Dextrose	Hyperkalemia; avoidance of hypoglycemia following insulin administration	IV bolus of 2 g/unit of insulin administered; bolus followed by CRI (the dextrose concentration and administration rate is dependent on serial blood glucose concentrations, patient's fluid status, and accessibility of central line)	Hyperglycemia, hyperosmolarity, hyponatremia, phlebitis with high dextrose concentrations	Dextrose should be diluted to avoid phlebitis; frequent changes in dextrose CRI frequently necessary based on serial blood glucose measurements
Calcium gluconate (10%)	Hyperkalemia; symptomatic hypocalcemia	0.5 to 1.5 mL/kg of 10% solution or 50 to 150 mg/kg IV slowly, to effect, while monitoring ECG; may be repeated	Worsening bradycardia and ECG changes; hypercalcemia; soft tissue mineralization	ECG should be monitored during administration; will not affect extracellular potassium concentration; effective in rapidly normalizing ECG but results transient; administration of large volumes may contribute to soft tissue mineralization
Sodium bicarbonate	Severe acidemia	$\frac{1}{4}$ to $\frac{1}{3}$ of the base deficit over 30 to 60 minutes, followed by an additional $\frac{1}{4}$ over the next 4 to 6 hours; additional dosing based on serial blood gas analyses	Paradoxical central nervous system acidosis, hypernatremia, fluid overload, hypochloremia; may cause or exacerbate hypokalemia if patient is polyuric; may exacerbate hypocalcemia	Requires close monitoring of blood gases and electrolytes for effective treatment and avoidance of adverse effects
Albuterol (inhaled)	Hyperkalemia	Four puffs; 90 microgram actuation via Aerokat device; repeated every 1 to 4 hours as necessary	Tachycardia, tremors, hyperexcitability	Adverse effects are uncommon at this dose; effects observed within 1 to 2 hours but may require multiple doses; effects can be sustained (several hours); only recommended for peracute hyperkalemia
Sodium polystyrene sulfonate	Hyperkalemia	2 g/kg per day PO or via feeding tube, divided into three to four doses per day; dose can be adjusted to effect	Hypernatremia, constipation, colonic necrosis	Rarely used except in chronic dialysis patients

AKI, Acute kidney injury; *CRI,* continuous rate infusion; *ECG,* electrocardiogram; *IM,* intramuscularly; *IV,* intravenously; *PO, per os* (orally).
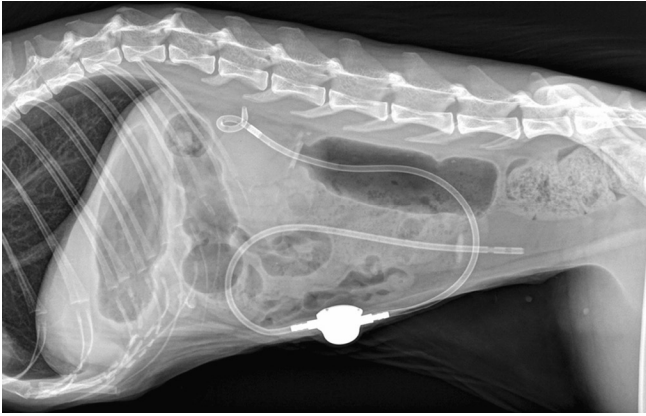
Figure 50-2: This lateral radiograph depicts proper placement of a subcutaneous ureteral bypass device. The locking loop pigtail catheter is secured in the right renal pelvis and the cuffed, fenestrated catheter allows urine drainage through the apex of the bladder. The two catheters are connected by a titanium access port.

ureteral calculi are not documented by radiography or ultrasonography.

Fluid Therapy

The goal of parenteral fluid therapy is to restore (the resuscitative phase) and maintain normal fluid balance among all body compartments. To ensure adequate tissue perfusion, extracellular fluid deficits should be corrected with a balanced polyionic solution. Colloidal support may also be considered to reduce the total amount of fluid administered if oliguria or anuria is suspected to be secondary to severe deficits in renal perfusion, although no benefit over crystalloid therapy has been documented in human or veterinary medicine.[42] Historically, synthetic colloids have been considered to have a volumetric equivalence ratio of 1:4 compared to crystalloids.[43] However, evidence suggests that the true, overall volume-sparing benefit of colloids is far less.[44] Furthermore, evidence compiled in multiple meta-analyses in humans suggests that synthetic colloidal solutions may have a deleterious effect not only on renal function, but overall survival, especially in septic patients.[45,46] For these reasons, it is the authors' opinion that colloids should be used with caution and only be considered in the resuscitative phase of fluid therapy. In the resuscitative phase, goal-directed therapy to restore surrogate markers of perfusion (e.g., blood pressure, venous lactate concentration, venous oxygen saturation) should be employed with endpoints set to be reached within 24 hours. If oliguria or anuria is present and persists despite achievement of normal surrogate markers of perfusion, additional fluid administration should be withheld to avoid fluid overload. Avoidance of fluid overload (typically defined as fluid accumulation greater than 10% of baseline body weight) is essential, because there is ample evidence documenting the association between fluid overload and worse clinical outcomes in both humans[47-50] and, more recently, dogs.[51]

The benefits of a restrictive fluid administration plan are becoming evident not only in AKI, but in a variety of disease states. In humans with AKI, avoidance of fluid overload is associated with a reduced risk of mortality. Furthermore, in disease states frequently encountered concurrently with AKI, such as acute lung injury, a restrictive fluid plan was associated with improved oxygenation parameters and increased numbers of ventilator-free and intensive care unit–free days.[52] In patients undergoing various abdominal surgeries, complications were significantly reduced with restrictive fluid regimens.[53]

Aggressive fluid therapy resulting in volume loading frequently has the effect of decreasing serum or plasma creatinine concentrations. Although historically, aggressive fluid therapy has been lauded as an effective means of diuresing uremic toxins, the relationship between this treatment strategy and effect is more complex. A recent human study demonstrates that changes in serum creatinine concentrations were directly proportional to the degree of fluid accumulation in patients with AKI, suggesting that changes in serum creatinine concentrations are directly related to changes in the volume of distribution of creatinine.[54] Therefore, changes in serum creatinine concentration associated with administration of fluid products beyond that which is necessary to restore normal renal perfusion (when affected by volume deficits) is likely a result of dilution of this creatinine, rather than increased renal excretion.

Maintenance fluid administration (both the volume and composition) should be guided by the volume and composition of urine produced, as well as ongoing sensible losses (e.g., from vomitus, diarrhea, and yield from gastric suction) and insensible loss (e.g., from respiration, formed stools). Many oliguric or anuric patients require no parenteral fluid therapy, because the obligatory fluid load that accompanies such treatments as parenteral or enteral nutrition administration (canned foods are typically composed of 80% to 90% water), IV antibiotics (frequently diluted), and IV catheter flushes sufficiently replace that which is lost from sensible and insensible routes. Insensible losses have been estimated to range between 12 and 29 mL/kg/day[55,56] and are dependent on a variety of factors, such as patient activity level, underlying disease process, and body temperature. Careful attention must be given to serial changes in the patient's body weight, because peracute fluctuations in weight are most likely due to changes in fluid balance rather than changes in lean muscle or fat content. High maintenance fluid rates have been historically advocated for patients producing urine, based on the rationale that high volume fluid administration beyond that which is necessary to restore normal volume status will improve GFR. However, there is no evidence supporting this claim and, in the author's experience, this practice is often futile in restoring GFR and frequently results in fluid overload. Fluid overload with concurrent oliguria or anuria is a clear indication for dialysis.

Monitoring fluid status to avoid volume overload is an ongoing process that must be repeated frequently. Efforts should be made to adhere to objective monitoring parameters

(e.g., body weight, venous lactate concentration, urine production) of fluid status, because subjective parameters (e.g., skin turgor, saliva production) are inaccurate and often affected by variables other than hydration status. Body weight should be measured two to six times daily to assess for trends in fluid accumulation or deficit. Central venous pressure measurement has traditionally been recommended as a surrogate marker of cardiac preload and, thus, fluid status. However, a thorough understanding of the limitations of this technique is necessary for appropriate interpretation, because the correlation between central venous pressure and blood volume (as well as the clinical manifestations of fluid overload) is poor.[57,58]

Diuretics

The use of diuretics in the treatment of AKI is a controversial topic in both human and veterinary medicine.[59,60] Many of the benefits of the most commonly used diuretics in veterinary AKI, furosemide and mannitol, have only been theorized or demonstrated in experimental models of AKI. In fact, there is little or no clinical evidence in human or veterinary medicine that diuretics improve outcome in established AKI. It has been postulated that the ability to respond to diuretics is a marker of less severe renal injury associated with a better prognosis. However, an increase in urine output after diuretic administration does not necessarily coincide with an increase in uremic solute excretion and, therefore, does not preclude the need for renal replacement therapy if severe uremia or acid-base and electrolyte abnormalities persist. In veterinary medicine, because renal replacement therapies are not readily available, diuretic administration plays a large role in volume management. Conversion from an oliguric or anuric state to normal urine production or polyuria may enhance the clinician's ability to prevent or manage fluid overload and thus allow administration of necessary medications and nutrition that would otherwise contribute to fluid overload.

No class of diuretics has been proven to be superior to another. However, the use of loop diuretics predominates in both human and veterinary AKI patients due to the relatively high efficacy and safety margin of these drugs, compared to the osmotic diuretics. There are several potential adverse effects associated with the administration of mannitol. Mannitol is typically administered in concentrations ranging from 20% to 25%, which correspond to osmolalities of 1100 to 1373 mOsm/L, and this high osmolality can contribute to fluid overload by promoting water movement from the intracellular to extracellular space. Furthermore, administration of mannitol has been associated with the development of a renal tubular morphologic lesion called *osmotic nephrosis*.[61] This lesion is characterized by swelling and vacuolization of the renal tubules and resultant renal tubular dysfunction and obstruction. Cumulative doses of approximately 200 g/person/day have been associated with this lesion, but when baseline renal function is normal, the toxic dose appears to be significantly higher.[62] When extrapolating a dose of 200 g

for a 70 kg (154 lb) human to that for a 5 kg (11 lb) feline patient, the g/kg cumulative dosage frequently found in many veterinary textbooks (0.25 to 1 g/kg bolus a variable number of times, followed by 1 to 2 mg/kg/min as a constant rate infusion) reaches the human nephrotoxic dose. For these reasons, the author does not recommend the use of mannitol as a diuretic for AKI.

Acid-Base Balance

Metabolic acidosis is a frequent complication in AKI of varying severity and is due to the damaged nephron's inability to excrete hydrogen ions and reabsorb bicarbonate ions, as well as lactic acidosis secondary to compromised tissue perfusion (i.e., either volume deficit or excess). Once perfusion has been restored, provision of supplemental alkali, usually in the form of parenteral sodium bicarbonate, should be considered if severe acidemia (pH less than 7.2; bicarbonate less than 12 mmol/L) persists. The bicarbonate dosage can be calculated from the formula:

$$0.3 \times body\ weight\ (kg) \times base\ deficit = bicarbonate\ (mEq),$$

where the base deficit = 24 mEq/L − patient bicarbonate concentration.

One-fourth to one-third of the dose is typically given IV as a slow bolus, and an additional one-fourth is typically given over the next 4 to 6 hours. Although the preceding formula provides a framework for estimating appropriate bicarbonate dosing, the osmolality of readily available formulations of bicarbonate must be taken into account when formulating and dosing this drug. For example, the most commonly used concentration of sodium bicarbonate is 8.4% (2000 mOsm/L). The osmole load administered with this formulation is considerable, and volumes necessary to correct acid-base derangements may easily result in hypernatremia. Therefore, an alternative strategy for administration of this medication is dilution with sterile water and IV administration at the desired maintenance parenteral fluid rate (provided the patient is not anuric or severely polyuric). In the authors' experience, this practice allows for gradual (over 24 hours) correction of acidemia and avoidance of rapid administration of a large solute load. In cases of oliguria or anuria, it is difficult to provide supplementary, parenteral alkali without provoking solute and fluid perturbations. In these cases, hemodialysis is indicated to correct acid-base derangements. With this treatment modality, provision of bicarbonate is accomplished by diffusion of the anion across the dialysis membrane, without concurrent administration of a sodium or fluid load.

Whether provided by IV injection or by hemodialysis, administration of bicarbonate to a hypoventilating patient or rapid administration of large loads of bicarbonate can further increase the partial pressure of carbon dioxide and can lead to paradoxical central nervous system acidosis.[63,64] This phenomenon is due to the ability of carbon dioxide to diffuse across the blood-brain barrier, whereas the

charged bicarbonate molecule diffuses across this barrier less readily.

Despite the potential benefits, multiple routes, and relative ease of bicarbonate administration, it is important to note that, as with diuretic therapy, there is no evidence in the form of randomized controlled trials supporting supplementation of alkali in human AKI.[65]

Electrolyte Balance

Hyperkalemia can be an immediately life-threatening complication of AKI and is secondary to a decline in renal excretory function. Excitable cells become refractory to repolarization, thus resulting in decreased conduction of both cardiac and neuromuscular tissue. Typical electrocardiographic changes include bradycardia; tall T waves; shortened QT intervals; wide QRS complexes; and small, wide, or absent P waves. However, electrocardiographic abnormalities are variable and difficult to predict based on the degree of hyperkalemia. Concurrent acidemia and hypocalcemia likely potentiate the effect of hyperkalemia on cardiac conduction. Therefore, addressing these abnormalities may mitigate the adverse effects of hyperkalemia. Severe hyperkalemia can lead to a ventricular fibrillation or standstill. There are a variety of pharmacologic treatments available for severe hyperkalemia, but these therapies act to translocate potassium to the intracellular space or increase the resting membrane potential to allow repolarization of excitable cells, rather than enhance excretion of potassium. The efficacy of these treatments is typically modest and transient. Only provision of renal replacement therapy or restoration of native renal excretory function can significantly reduce the potassium burden in fulminant AKI.

Expansion of the extracellular space with a non-potassium containing fluid (e.g., 0.9% sodium chloride) may be sufficient to at least partially correct hyperkalemia. This maneuver should be implemented in cases of suspected volume depletion, but should be used with caution or not at all if a patient is anuric or has volume overload. Despite recent evidence supporting the use of balanced (potassium-containing) crystalloids for the treatment of feline urethral obstruction, this practice is not recommended in the case of intrinsic parenchymal injury (renal azotemia). Drobatz and Cole were unable to demonstrate a difference in the rate of decline of blood potassium concentrations among cats treated with 0.9% sodium chloride and Normosol-R following restoration of urethral patency.[66] Results of this study should not be extrapolated to feline patients with intrinsic AKI, because these patients are not provided with an excretory route for potassium. Therefore, provision of a fluid with potassium of 5 mEq/L is far less effective at diluting the extracellular potassium concentration than a fluid that contains no potassium.

Administration of regular insulin is a common pharmacologic treatment for hyperkalemia. Insulin upregulates synthesis of subunits of the sodium/potassium adenosine triphosphatase (Na^+/K^+-ATPase) pump, recruits the pump to the plasma cell membrane, and activates those pumps already located in the plasma membrane to stimulate intracellular translocation of potassium.[67] The potassium lowering effect of regular insulin may be observed as early as 15 minutes following administration,[68-70] but the effect is typically modest (decline of 1 to 2 mmol/L) and transient (redosing is frequently necessary within 3 to 4 hours). A potentially catastrophic adverse effect associated with regular insulin administration is hypoglycemia, so dextrose must be administered concurrently with regular insulin. If fluid overload is not present, the administration of a continuous rate infusion of dextrose following the initial bolus is recommended. Frequent assessment of blood glucose concentration is imperative, as dextrose is metabolized more rapidly than insulin, and redosing of dextrose is often required.

Calcium salts are frequently administered IV to increase the threshold potential of polarized cells,[71] thus allowing depolarization at high extracellular potassium concentrations. The membrane stabilizing effects of calcium salts are rapid and dramatic; however, the beneficial effects are even more transient than those of regular insulin. Readministration is typically necessary within 1 hour.[72] The patient should be monitored with an electrocardiogram during administration to identify worsening bradycardia, a shortened QT interval, a widened T wave, or alterations in the ST amplitude. If any of these changes are recognized, the calcium infusion should be discontinued. Calcium gluconate is favored over calcium chloride due to the severe extravasation injuries that can occur with calcium chloride administration. Calcium gluconate can also cause extravasation injuries (albeit less severe), so care must be taken to ensure IV catheter patency prior to administration. Lastly, theoretical concerns regarding promotion of calcium-phosphorus/phosphate precipitation and soft tissue mineralization exist with repeated administration of calcium salts.

The beta-2 agonist drug, albuterol, which is administered by the inhalant route, is frequently used by the authors as a first-line treatment for emergent hyperkalemia, having an effect within 15 to 30 minutes and lasting 2 to 3 hours. Beta-2 agonists exert a hypokalemic effect by activating membrane bound Na^+/K^+-ATPase pumps. Nebulized albuterol, in combination with IV insulin with or without IV calcium gluconate, is considered the treatment of choice in human medicine;[73] and with the development of masks and spacers designed specifically for cats, controlled drug delivery via the inhalant route is possible. The use of inhaled albuterol eliminates many of the adverse effects associated with systemic administration of beta-agonist drugs and experimental studies have demonstrated a large margin of safety[74,75] with doses that have been anecdotally recognized as effective. Inhaled albuterol does not contribute to the volume loading that many other medications entail.

Sodium polystyrene sulfonate is a cation exchange resin that is administered orally through an enteral feeding tube, or by colonic enema, and is the one treatment other than renal replacement therapy that removes potassium from the body. Within the GI lumen, sodium polystyrene sulfonate exchanges sodium ions for potassium ions. Administration

via enema or use of formulations containing sorbitol increases the risk of colonic necrosis and perforation in human patients. In cases where hyperkalemia cannot be controlled with the most aggressive therapy (i.e., renal replacement therapy), the use of sodium polystyrene sulfonate can be beneficial, especially in the interdialytic period. A lag period of 1 to 3 days following initiation of therapy should be allowed before the maximum effect of a particular dose can be determined.

Historically, sodium bicarbonate was thought to promote intracellular translocation of potassium via exchange of hydrogen ions. However, recent evidence suggests that the hypokalemic effects of sodium bicarbonate may be a result of the promotion of kaliuresis,[76] and is likely independent of a change in blood pH.[77] Kaliuresis, however, may be difficult to achieve in a patient with injured or compromised function of the majority of nephrons. Nonetheless, correction of acidemia may mitigate the deleterious effects of hyperkalemia on cardiac conduction. Loop diuretics can promote kaliuresis in the distal nephron by promoting tubular flow. Although conversion from an oliguric state to one of increased urine production assists in management of electrolyte excesses (such as hyperkalemia), the authors have treated several patients whose hyperkalemia persisted despite resumption of urine production. Furthermore, loop diuretics are not a reliable means of increasing urine production in cases of anuric AKI. For these reasons, sodium bicarbonate and furosemide are not recommended as stand-alone treatments for emergent hyperkalemic AKI.

Although ionized hypocalcemia occurs frequently in AKI, clinical signs (e.g., tetany) associated with this problem are rare. Ionized calcium concentrations should be assessed and continuously monitored however, regardless of whether supplemental calcium salts are being administered, because ionized calcium concentrations may influence the tendency for cardiac arrhythmias. When manifestations of hypocalcemia (e.g., neurologic complications, arrhythmias) do occur, the minimum dose of supplemental calcium that controls clinical signs should be used to minimize precipitation with phosphorus. As with the treatment of hyperkalemia, the electrocardiogram should be monitored closely during infusion.

Additional electrolyte abnormalities may be present or develop during the course of disease, the most common of which are hyponatremia and hyperphosphatemia. Hyponatremia may be the result of GI or urinary losses, with or without the contribution of decreased excretion of free water. Hyponatremia, if severe (less than 120 mmol/L), may result in neurologic sequelae. In critically ill human patients, hyponatremia has been identified as a poor prognostic indicator.[78,79] However, this association has not been made in cats. Hyponatremia is frequently encountered in the authors' practices and is putatively associated with the profound natriuresis that typically accompanies recovery phase polyuria (especially in cases in which ureteral patency is re-established following an obstruction) or aggressive water supplementation via enteral feeding tubes. This phenomenon has been documented in a cat administered both enteral water via

esophagostomy tube and a cat administered 5% dextrose in water SC.[80] If fluid is being lost in sufficient volumes to require enteral or parenteral replacement, care should be taken to either investigate the electrolyte composition of the lost fluid or to closely monitor the patient's blood electrolyte concentrations so that the appropriate replacement fluid composition is administered.

Hyperphosphatemia contributes to acidosis and renal secondary hyperparathyroidism.[81] However, the use of phosphate-binding drugs has not been shown to improve outcome in human or feline cases of AKI. Furthermore, administration of aluminum hydroxide (the most commonly used phosphate-binding drug in veterinary medicine) may result in acute aluminum intoxication, which manifests as encephalopathy, a condition which may not be readily recognizable in a patient severely affected with AKI.[82] Therefore, aluminum-containing phosphate-binding drugs should be used with caution in AKI. The authors recommend withholding phosphate-binding drugs during the initial phase of diagnostic investigation and therapy and considering administration of these drugs only when the patient's overall status is stable.

Nutritional Support

Nutritional support is an important but often overlooked component of supportive care for AKI. Nutritional support may be precluded by the need to restrict nonessential potassium loading and administration of enteral or parenteral fluids (e.g., anuria). Enteral feeding is the preferred method of nutrient delivery but is often limited by vomiting and ileus. For those patients that are not vomiting, esophageal, gastric, and jejunal feeding devices can be used. If vomiting cannot be controlled, partial or total parenteral nutrition should be considered. Administration of parenteral nutrition can pose difficult challenges in regulating plasma osmolality and electrolyte concentrations. Furthermore, this route of nutritional provision necessitates a dedicated central line and increases the risk of septic complications.[83,84] In patients that are anuric or oliguric, total or partial parenteral nutrition may constitute a relative contraindication unless there is a method of excess fluid and solute removal (e.g., renal replacement therapies).

The optimal dietary composition for veterinary AKI patients has not been determined. The authors are unaware of any particular diet that is appropriate in all scenarios of AKI. Rather, individual patients should be evaluated for the following factors, because each may influence the choice of diet to be fed: the requirement of a liquid diet for tube delivery, the availability of renal replacement to assist in mitigating the obligatory volume load, the electrolyte balance, and the availability of assisted feeding (e.g., esophagostomy or gastrostomy tube). Human guidelines do not support protein restriction for patients with AKI.[85,86] Furthermore, some disease states associated with AKI promote a hypercatabolic state and, therefore, may result in greater protein requirements than the established maintenance requirements.

Patients treated with dialysis may actually require more protein than patients with extra-renal disease, due to loss of amino acids in dialysate/filtrate. Protein restriction for the purpose of restricting the generation of uremic solutes has traditionally been advocated in veterinary medicine. However, a negative protein balance may hinder renal repair/recovery. Therefore, prescription diets marketed for feline patients with CKD may not be appropriate for feline patients with AKI.

Patients that are prone to volume overload and have feeding tubes in place should be fed the most calorically dense diet that will pass through the tube to minimize the amount of fluid administered. Some commercially-available recovery diets have caloric contents of approximately 2 kcal/mL and easily pass through most 14 French feeding tubes. Most other commercial diets (including prescription renal diets) must be diluted and blended with water in order to achieve a consistency that will pass through a feeding tube. Many patients with AKI are hyponatremic due to GI and renal losses; administration of large volumes of hypotonic enteral fluid in the form of a diluted renal diet may exacerbate hyponatremia and cause severe neurologic sequelae. Recovery diets typically have a high protein and potassium content, the latter of which may be problematic in hyperkalemic patients. The same problem exists for most feline prescription renal diets as well.

Based on the complexity associated with choosing a proper commercial diet and ensuring adequate provision of appropriate amounts of minerals, vitamins, and essential amino and fatty acids, as well as the difficulty in formulating and preparing custom home- or hospital-cooked diets, the authors typically administer recovery diets through feeding tubes as a first-line option for nutritional management. Hyperkalemia, if present, is addressed with polystyrene sodium sulfonate and renal replacement therapy, if the latter is available.

Renal Replacement Therapy/Dialysis

Extracorporeal renal replacement therapy (intermittent hemodialysis and continuous renal replacement therapy) is being used with increasing frequency for control of acid-base, electrolyte, and fluid imbalances, as well as the uremic manifestations of AKI. Because details regarding the use of this treatment modality are beyond the scope of this chapter, the reader is referred to publications describing the technical aspects, although a few factors particular to treating cats are mentioned later.[87-90] Extracorporeal renal replacement therapy is the most efficient means of managing uremic, acid-base, electrolyte, and fluid-related sequelae of AKI. In fulminant cases, available pharmacologic therapies are, at best, incompletely effective at reversing the aforementioned complications, and their effects are transient.

One of the greatest determinants of the ease of application of extracorporeal renal replacement therapy is the size and associated blood volume of the patient. Therefore, treatment of the feline patient poses some important problems regarding blood volume regulation and RBC transfusion requirements. First, the size of the extracorporeal circuit determines the amount of blood that must circulate outside of the patient's body during the treatment. The smallest circuits currently used in veterinary medicine are approximately 60 mL. In a typical 5 kg (11 lb) cat with a normal RBC concentration, removal of this volume of RBCs should not contribute greatly to overall cardiovascular instability. However, removal of this volume of blood can be catastrophic in a smaller patient (e.g., 2.5 kg [5.5 lb]) that is anemic. Second, the chemical composition of some of the available hollow fiber membranes affects the tendency for blood to clot or to adhere to the fibers. If a large volume of the patient's blood remains within the fibers following attempts to return blood to the patient at the end of the treatment, significant blood loss accompanies each treatment. For these reasons, the authors recommend that any institution providing extracorporeal renal replacement therapies for cats have access to a plentiful donor RBC supply. Lastly, the extracorporeal circuits must be primed with either a crystalloid, colloid, or blood product prior to treatment. The priming solution represents a volume load obligatory to commencement of treatment. Therefore, ultrafiltration (plasma water removal) of *at least* the extracorporeal circuit must be achieved to maintain a neutral fluid balance throughout the treatment, unless the clinician plans to discard the blood present in the circuit following completion of the treatment. Ultrafiltration of any volume of plasma water may be difficult in patients that are hemodynamically unstable.

Additional Treatment Considerations

Antiemetic therapy is recommended for all patients with severe AKI, regardless of whether they are vomiting. It is beyond the scope of this chapter to discuss antiemetic options in detail, but the authors prefer the use of 5-HT3 antagonists or neurokinin-1 antagonists, because the former was found to be superior to metoclopramide in prevention of vomiting and nausea in uremic human patients.[91]

The use of antisecretory drugs (e.g., histamine-2 (H2) receptor antagonists, proton pump inhibitors) has historically been recommended for patients with AKI. Although uremic gastritis and stress-related mucosal disease are concerns in human AKI patients, gastric acid output and intragastric pH are not compatible with a hypersecretory state.[92] Nonetheless, due to the high incidence of hemorrhage from the GI tract in human AKI patients (presumably related to a combination of uremic injury and stress-related mucosal disease) and its association with mortality,[93] antisecretory drugs should be considered in high-risk patients. A recent meta-analysis showed superiority of proton pump inhibitors versus H2 receptor antagonists in the prevention of stress-related mucosal bleeding.[94] These results, in combination with the potential for accumulation of H2 receptor antagonists in patients with diminished renal function, favor the use of proton pump inhibitors. Sucralfate is frequently used for gastroprotection, but human data shows that even short-term administration of this drug to patients with AKI can result in toxic aluminum concentrations.[95,96]

Dopamine is a pharmacologic treatment for AKI that has fallen out of favor with both human and veterinary nephrologists. Dopamine was initially advocated for its perceived augmentation of renal blood flow. Its benefit in cats, however, was doubted as it was originally thought that cats did not possess renal dopamine receptors, a concept supported by the absence of changes in urine output, sodium excretion, or GFR in cats administered a low-dose dopamine infusion.[97] However, a putative dopamine receptor (DA-1) has been identified in the feline renal cortex.[98] Regardless of this recent discovery, the evidence available assessing the effect of dopamine on the feline kidney, when infused via the IV and intra-arterial routes, suggests that an increase in renal blood flow is not due to the renal effects of dopamine, but rather to the systemic cardiovascular effects.[99] Furthermore, the observed increase in urine flow is likely due to a combination of these systemic effects and an alteration in renal tubular function.[99] Fenoldopam is a drug that has received recent interest as a pharmacologic treatment option for feline AKI, because the feline DA-1 receptors show higher affinity for this drug versus dopamine.[98] Although a prolonged infusion of fenoldopam increased creatinine clearance and urine output in healthy cats,[100] the authors are unaware of any evidence of efficacy in conversion from an oliguric or anuric state in clinical cases of feline AKI. The authors do not recommend this drug as a first-line treatment, because the expense, undetermined efficacy, and unknown pharmacokinetic properties in feline AKI are major drawbacks to its use.

PROGNOSIS

There is sparse information available regarding the prognosis for feline AKI. One study of 32 cats documented a 53% survival rate, with approximately 50% of survivors left with CKD, although obstructive etiologies of AKI were excluded from analysis.[101] Another study assessed survival in cats with AKI treated with intermittent hemodialysis, documenting a 50% survival rate at the time of discharge, a 48% survival rate at 30 days following discharge, and a 38% survival rate at 365 days following discharge.[40] Considering that patients treated with dialysis are more likely to have a greater severity of renal dysfunction and more complications associated with AKI, it can be deduced that dialysis offers a survival benefit in these cases.

References

1. Payen D, Legrand M: Can we identify prerenal physiology and does it matter? *Contrib Nephrol* 174:22–32, 2011.
2. Uchino S, Bellomo R, Bagshaw SM, et al: Transient azotaemia is associated with a high risk of death in hospitalized patients. *Nephrol Dial Transplant* 25:1833–1839, 2010.
3. Capelouto CC, Saltzman B: The pathophysiology of ureteral obstruction. *J Endourol* 7:93–103, 1993.
4. Kochin EJ, Gregory CR, Wisner ER, et al: Evaluation of a method of ureteroneocystostomy in cats. *J Am Vet Med Assoc* 202:257–260, 1993.
5. Mathews K: Ureters. In Tobias KM, Johnston SA, editors: *Veterinary surgery small animal*, ed 1, Philadelphia, 2012, Saunders, pp 1962–1977.
6. Kyles AE, Hardie EM, Wooden BG, et al: Clinical, clinicopathologic, radiographic, and ultrasonographic abnormalities in cats with ureteral calculi: 163 cases (1984-2002). *J Am Vet Med Assoc* 226:932–936, 2005.
7. Westropp JL, Ruby AL, Bailiff NL, et al: Dried solidified blood calculi in the urinary tract of cats. *J Vet Intern Med* 20:828–834, 2006.
8. Zaid MS, Berent AC, Weisse C, et al: Feline ureteral strictures: 10 cases (2007-2009). *J Vet Intern Med* 25:222–229, 2011.
9. Steinhaus J, Berent A, Weiss C, et al: Circumcaval ureters in twenty-one cats. *J Vet Intern Med* 27:731, 2013.
10. Vaughan ED, Jr, Marion D, Poppas DP, et al: Pathophysiology of unilateral ureteral obstruction: studies from Charlottesville to New York. *J Urol* 172:2563–2569, 2004.
11. Rumbeiha WK, Francis JA, Fitzgerald SD, et al: A comprehensive study of Easter lily poisoning in cats. *J Vet Diagn Invest* 16:527–541, 2004.
12. Langston CE: Acute renal failure caused by lily ingestion in six cats. *J Am Vet Med Assoc* 220:49–52, 2002.
13. Hall JO: Nephrotoxicity of Easter lily (*Lilium longiflorum*) when ingested by the cat. *J Vet Intern Med* 6:121, 1992. (Abstract).
14. Bennett AJ, Reineke EL: Outcome following gastrointestinal tract decontamination and intravenous fluid diuresis in cats with known lily ingestion: 25 cases (2001-2010). *J Am Vet Med Assoc* 242:1110–1116, 2013.
15. Slater MR, Gwaltney-Brant S: Exposure circumstances and outcomes of 48 households with 57 cats exposed to toxic lily species. *J Am Anim Hosp Assoc* 47:386–390, 2011.
16. D'Anjou MA, Bedard A, Dunn ME: Clinical significance of renal pelvic dilatation on ultrasound in dogs and cats. *Vet Radiol Ultrasound* 52:88–94, 2011.
17. Kelly DF, Lucke VM, McCullagh KG: Experimental pyelonephritis in the cat. 1. Gross and histological changes. *J Comp Pathol* 89:125–139, 1979.
18. Rollino C, Beltrame G, Ferro M, et al: Acute pyelonephritis in adults: a case series of 223 patients. *Nephrol Dial Transplant* 27:3488–3493, 2012.
19. Arbour J, Blais MC, Carioto L, et al: Clinical leptospirosis in three cats (2001-2009). *J Am Anim Hosp Assoc* 48:256–260, 2012.
20. Lapointe C, Plamondon I, Dunn M: Feline leptospirosis serosurvey from a Quebec referral hospital. *Can Vet J* 54:497–499, 2013.
21. Markovich JE, Ross L, McCobb E: The prevalence of leptospiral antibodies in free roaming cats in Worcester County, Massachusetts. *J Vet Intern Med* 26:688–689, 2012.
22. Hartmann K, Egberink H, Pennisi MG, et al: Leptospira species infection in cats: ABCD guidelines on prevention and management. *J Feline Med Surg* 15:576–581, 2013.
23. Bellomo R, Ronco C, Kellum JA, et al: Acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care* 8:R204–R212, 2004.
24. Mehta RL, Kellum JA, Shah SV, et al: Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care* 11:R31, 2007.
25. Cowgill LD, Langston CE: Acute kidney disease. In Bartges JW, Polzin DJ, editors: *Nephrology and urology of small animals*, Ames, IA, 2011, Wiley-Blackwell, pp 472–523.
26. Sowers KM, Hayden MR: Calcific uremic arteriolopathy: pathophysiology, reactive

oxygen species and therapeutic approaches. *Oxid Med Cell Longev* 3:109–121, 2010.

27. Antoniades DZ, Markopoulos AK, Andreadis D, et al: Ulcerative uremic stomatitis associated with untreated chronic renal failure: report of a case and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 101:608–613, 2006.

28. Ash SR: An explanation for uremic hypothermia. *Int J Artif Organs* 14:67–69, 1991.

29. Rotblatt MD, Koda-Kimble MA: Review of drug interference with urine glucose tests. *Diabetes Care* 10:103–110, 1987.

30. Rees CA, Boothe DM: Evaluation of the effect of cephalexin and enrofloxacin on clinical laboratory measurements of urine glucose in dogs. *J Am Vet Med Assoc* 224:1455–1458, 2004.

31. Syme HM: Proteinuria in cats. Prognostic marker or mediator? *J Feline Med Surg* 11:211–218, 2009.

32. Perazella MA, Markowitz GS: Drug-induced acute interstitial nephritis. *Nat Rev Nephrol* 6:461–470, 2010.

33. Sturgess C, Hesford A, Owen H, et al: An investigation into the effects of storage on the diagnosis of crystalluria in cats. *J Feline Med Surg* 3:81–85, 2001.

34. Holloway A, O'Brien R: Perirenal effusion in dogs and cats with acute renal failure. *Vet Radiol Ultrasound* 48:574–579, 2007.

35. Valdes-Martinez A, Cianciolo R, Mai W: Association between renal hypoechoic subcapsular thickening and lymphosarcoma in cats. *Vet Radiol Ultrasound* 48:357–360, 2007.

36. Biery DN: Upper urinary tract. In O'Brien TR, editor: *Radiographic diagnosis of abdominal disorders in dogs and cats*, Davis, 1981, Covell Park Vet, pp 481–542.

37. Adin CA, Herrgesell EJ, Nyland TG, et al: Antegrade pyelography for suspected ureteral obstruction in cats: 11 cases (1995-2001). *J Am Vet Med Assoc* 222:1576–1581, 2003.

38. Vaden SL, Levine JF, Lees GE, et al: Renal biopsy: a retrospective study of methods and complications in 283 dogs and 65 cats. *J Vet Intern Med* 19:794–801, 2005.

39. Berent A, Weisse C, Wright M, et al: The use of a subcutaneous ureteral bypass device for ureteral obstructions in cats. *Vet Surg* 39:E30, 2010.

40. Eatroff AE, Langston CE, Chalhoub S, et al: Long-term outcome of cats and dogs with acute kidney injury treated with intermittent hemodialysis: 135 cases (1997-2010). *J Am Vet Med Assoc* 241:1471–1478, 2012.

41. Kyles AE, Hardie EM, Wooden BG, et al: Management and outcome of cats with ureteral calculi: 153 cases (1984-2002). *J Am Vet Med Assoc* 226:937–944, 2005.

42. Finfer S, Bellomo R, Boyce N, et al: A comparison of albumin and saline for fluid resuscitation in the intensive care unit. *N Engl J Med* 350:2247–2256, 2004.

43. Hughes D, Boag A: Fluid therapy with macromolecular plasma volume expanders. In Dibartola S, editor: *Fluid, electrolyte, and acid–base disorders in small animal practice*, ed 4, St Louis, 2012, Elsevier, pp 647–664.

44. Hartog CS, Bauer M, Reinhart K: The efficacy and safety of colloid resuscitation in the critically ill. *Anesth Analg* 112:156–164, 2011.

45. Zarychanski R, Abou-Setta AM, Turgeon AF, et al: Association of hydroxyethyl starch administration with mortality and acute kidney injury in critically ill patients requiring volume resuscitation: a systematic review and meta-analysis. *JAMA* 309:678–688, 2013.

46. Serpa Neto A, Veelo DP, Peireira VG, et al: Fluid resuscitation with hydroxyethyl starches in patients with sepsis is associated with an increased incidence of acute kidney injury and use of renal replacement therapy: a systematic review and meta-analysis of the literature. *J Crit Care* 29(1):185.e1–7, 2013.

47. Modem V, Thompson M, Gollhofer D, et al: Timing of continuous renal replacement therapy and mortality in critically ill children. *Crit Care Med* 42(4):943–953, 2014.

48. Sutherland SM, Zappitelli M, Alexander SR, et al: Fluid overload and mortality in children receiving continuous renal replacement therapy: the prospective pediatric continuous renal replacement therapy registry. *Am J Kidney Dis* 55:316–325, 2010.

49. Bouchard J, Soroko SB, Chertow GM, et al: Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. *Kidney Int* 76:422–427, 2009.

50. Heung M, Wolfgram DF, Kommareddi M, et al: Fluid overload at initiation of renal replacement therapy is associated with lack of renal recovery in patients with acute kidney injury. *Nephrol Dial Transplant* 27:956–961, 2012.

51. Mobley A, Sullivan L: Retrospective determination of fluid overload in critically ill dogs. *J Vet Emerg Crit Care* 22:2012.

52. Wiedemann HP, Wheeler AP, Bernard GR, et al: Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med* 354:2564–2575, 2006.

53. Bundgaard-Nielsen M, Secher NH, Kehlet H: "Liberal" vs. "restrictive" perioperative fluid therapy—a critical assessment of the evidence. *Acta Anaesthesiol Scand* 53:843–851, 2009.

54. Macedo E, Bouchard J, Soroko SH, et al: Fluid accumulation, recognition and staging of acute kidney injury in critically-ill patients. *J Crit Care* 14:R82, 2010.

55. Hamlin R, Tashjian R: Water and electrolyte intake and output of feces in healthy cats. *Vet Med Small Anim Clin* 59:746, 1964.

56. Thrall B, Miller L: Water turnover in cats fed dry rations. *Feline Pract* 6:10, 1976.

57. Marik P, Barram M, Vahid B: Does central venous pressure predict fluid responsiveness? A systemic review of the literature and the tale of seven mares. *Chest* 134:172–178, 2008.

58. Reems MM, Aumann M: Central venous pressure: principles, measurement, and interpretation. *Compend Contin Educ Vet* 34:E1, 2012.

59. Bagshaw SM, Bellomo R, Kellum JA: Oliguria, volume overload, and loop diuretics. *Crit Care Med* 36:S172–S178, 2008.

60. Bagshaw SM, Delaney A, Haase M, et al: Loop diuretics in the management of acute renal failure: a systematic review and meta-analysis. *Crit Care Resusc* 9:60–68, 2007.

61. Dickenmann M, Oettl T, Mihatsch MJ: Osmotic nephrosis: acute kidney injury with accumulation of proximal tubular lysosomes due to administration of exogenous solutes. *Am J Kidney Dis* 51:491–503, 2008.

62. Dorman HR, Sondheimer JH, Cadnapaphornchai P: Mannitol-induced acute renal failure. *Medicine (Baltimore)* 69:153–159, 1990.

63. Kindig NB, Sherrill DS, Shapiro JI, et al: Extracorporeal bicarbonate space after bicarbonate or a bicarbonate-carbonate mixture in acidotic dogs. *J Appl Physiol (1985)* 67:2331–2334, 1989.

64. Shapiro JI, Whalen M, Kucera R, et al: Brain pH responses to sodium bicarbonate and Carbicarb during systemic acidosis. *Am J Physiol* 256:H1316–H1321, 1989.

65. Hewitt J, Uniacke M, Hansi NK, et al: Sodium bicarbonate supplements for treating acute kidney injury. *Cochrane Database Syst Rev* (6):CD009204, 2012.

66. Drobatz K, Cole S: The influence of crystalloid type on acid-base and electrolyte status of cats with urethral obstruction. *J Vet Emerg Crit Care* 18:355–361, 2008.

67. Sweeney G, Klip A: Regulation of the Na^+/K^+-ATPase by insulin: why and how? *Mol Cell Biochem* 182:121–133, 1998.

68. Li Q, Zhou MT, Wang Y, et al: Effect of insulin on hyperkalemia during anhepatic stage of liver transplantation. *World J Gastroenterol* 10:2427–2429, 2004.

69. Allon M, Copkney C: Albuterol and insulin for treatment of hyperkalemia in hemodialysis patients. *Kidney Int* 38:869–872, 1990.

70. Allon M, Shanklin N: Effect of bicarbonate administration on plasma potassium in dialysis patients: interactions with insulin and albuterol. *Am J Kidney Dis* 28:508–514, 1996.

71. Bisogno JL, Langley A, Von Dreele MM: Effect of calcium to reverse the electrocardiographic effects of hyperkalemia in the isolated rat heart: a prospective, dose-response study. *Crit Care Med* 22:697–704, 1994.

72. Weisberg LS: Management of severe hyperkalemia. *Crit Care Med* 36:3246–3251, 2008.

73. Mahoney BA, Smith WA, Lo DS, et al: Emergency interventions for hyperkalemia. *Cochrane Database Syst Rev* (2):CD003235, 2005.

74. Leemans J, Kirschvink N, Bernaerts F, et al: A pilot study comparing the antispasmodic effects of inhaled salmeterol, salbutamol and ipratropium bromide using different aerosol devices on muscarinic bronchoconstriction in healthy cats. *Vet J* 180:236–245, 2009.

75. Reinero CR, Delgado C, Spinka C, et al: Enantiomer-specific effects of albuterol on airway inflammation in healthy and asthmatic cats. *Int Arch Allergy Immunol* 150:43–50, 2009.

76. Carlisle EJ, Donnelly SM, Ethier JH, et al: Modulation of the secretion of potassium by

accompanying anions in humans. *Kidney Int* 39:1206–1212, 1991.

77. Fraley DS, Adler S: Correction of hyperkalemia by bicarbonate despite constant blood pH. *Kidney Int* 12:354–360, 1977.

78. Funk GC, Lindner G, Druml W, et al: Incidence and prognosis of dysnatremias present on ICU admission. *Intensive Care Med* 36:304–311, 2010.

79. Stelfox HT, Ahmed SB, Khandwala F, et al: The epidemiology of intensive care unit-acquired hyponatraemia and hypernatraemia in medical-surgical intensive care units. *Crit Care* 12:R162, 2008.

80. Lee JY, Rozanski E, Anastasio M, et al: Iatrogenic water intoxication in two cats. *J Vet Emerg Crit Care* 23:53–57, 2013.

81. Druml W, Schwarzenhofer M, Apsner R, et al: Fat soluble vitamins in patients with acute renal failure. *Miner Electrolyte Metab* 24:220–226, 1998.

82. Segev G, Bandt C, Francey T, et al: Aluminum toxicity following administration of aluminum-based phosphate binders in two dogs with renal failure. *J Vet Intern Med* 22:1432–1435, 2008.

83. Wylie MC, Graham DA, Potter-Bynoe G, et al: Risk factors for central line-associated bloodstream infection in pediatric intensive care units. *Infect Control Hosp Epidemiol* 31:1049–1056, 2010.

84. Peter JV, Moran JL, Phillips-Hughes J: A metaanalysis of treatment outcomes of early enteral versus early parenteral nutrition in hospitalized patients. *Crit Care Med* 33:213–220, discussion 260–261, 2005.

85. Fiaccadori E, Cremaschi E: Nutritional assessment and support in acute kidney injury. *Curr Opin Crit Care* 15:474–480, 2009.

86. Gervasio JM, Garmon WP, Holowatyj M: Nutrition support in acute kidney injury. *Nutr Clin Pract* 26:374–381, 2011.

87. Langston C: Hemodialysis. In Bartges J, Polzin D, editors: *Nephrology and urology of small animals*, Ames, IA, 2011, Blackwell, pp 354–400.

88. Bloom CA, Labato MA: Intermittent hemodialysis for small animals. *Vet Clin North Am Small Anim Pract* 41:115–133, 2011.

89. Acierno MJ: Continuous renal replacement therapy. In Bartges JW, Polzin DJ, editors: *Nephrology and urology of small animals*, Ames, IA, 2011, Wiley-Blackwell, pp 286–292.

90. Acierno MJ: Continuous renal replacement therapy in dogs and cats. *Vet Clin North Am Small Anim Pract* 41:135–146, 2011.

91. Ljutic D, Perkovic D, Rumboldt Z, et al: Comparison of ondansetron with metoclopramide in the symptomatic relief of uremia-induced nausea and vomiting. *Kidney Blood Press Res* 25:61–64, 2002.

92. Wesdorp RI, Falcao HA, Banks PB, et al: Gastrin and gastric acid secretion in renal failure. *Am J Surg* 141:334–338, 1981.

93. Fiaccadori E, Maggiore U, Clima B, et al: Incidence, risk factors, and prognosis of gastrointestinal hemorrhage complicating acute renal failure. *Kidney Int* 59:1510–1519, 2001.

94. Barkun AN, Bardou M, Pham CQ, et al: Proton pump inhibitors vs. histamine 2 receptor antagonists for stress-related mucosal bleeding prophylaxis in critically ill patients: a meta-analysis. *Am J Gastroenterol* 107:507–520, quiz 521, 2012.

95. Thorburn K, Samuel M, Smith EA, et al: Aluminum accumulation in critically ill children on sucralfate therapy. *Pediatr Crit Care Med* 2:247–249, 2001.

96. Mulla H, Peek G, Upton D, et al: Plasma aluminum levels during sucralfate prophylaxis for stress ulceration in critically ill patients on continuous venovenous hemofiltraiton: a randomized, controlled trial. *Crit Care Med* 29:267–271, 2001.

97. Wohl JS, Schwartz DD, Flournoy WS, et al: Renal hemodynamic and diuretic effects of low-dose dopamine in the cat. *Seventh International Veterinary Emergency and Critical Care Symposium* 14–24, 2000.

98. Flournoy WS, Wohl JS, Albrecht-Schmitt TJ, et al: Pharmacologic identification of putative D1 dopamine receptors in feline kidneys. *J Vet Pharmacol Ther* 26:283–290, 2003.

99. Wassermann K, Huss R, Kullmann R: Dopamine-induced diuresis in the cat without changes in renal hemodynamics. *Naunyn Schmiedebergs Arch Pharmacol* 312:77–83, 1980.

100. Simmons JP, Wohl JS, Schwartz DD, et al: Diuretic effects of fenoldopam in healthy cats. *J Vet Emerg Crit Care* 16:96–103, 2006.

101. Worwag S, Langston CE: Acute intrinsic renal failure in cats: 32 cats (1997-2004). *J Am Vet Med Assoc* 232:728–732, 2008.