

Acute Kidney Injury

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In acute kidney injury (AKI), renal function declines rapidly over hours to days, and affected dogs and cats become acutely ill. Prompt diagnosis and treatment can prevent or minimize permanent renal damage. If affected renal tissue is not irreversibly damaged, patients maintained with supportive care may regain sufficient renal function to sustain normal life.

Risk factors for AKI include:

- Increasing age
- Preexisting/subclinical chronic kidney disease (CKD)
- Adverse drug combinations (eg, gentamicin/furosemide¹; amphotericin/furosemide²)
- Sepsis
- Prolonged anesthesia (especially with concurrent NSAIDs)³
- Dehydration, hypovolemia, hypotension



Phases

Two phases of AKI are recognized: oliguric and polyuric.

Oliguric AKI is the sudden onset and rapid development of azotemia with reduced urine flow (ie, <0.27 mL/kg/h). Typically in oliguric AKI, renal blood flow, glomerular filtration rate (GFR), and urine production are diminished, and affected dogs and cats demonstrate sudden onset of depression, vomiting, anorexia, and polydipsia. Seizures and muscle fasciculations may be observed, and terminal patients can become comatose.

Laboratory studies may show hyperkalemia and severe metabolic acidosis with a wide anion gap. Blood glucose concentrations may be mildly increased. Urine specific gravity (USG) is usually low (ie, <1.017) despite dehydration. Proteinuria, hematuria, and glucosuria in the absence of severe hyperglycemia are commonly found.

Other clinical signs associated with the underlying cause of AKI may also be present (eg, leptospirosis patients often have a fever).

Some patients present initially with **polyuric AKI** (eg, aminoglycoside toxicity), the sudden onset and rapid development of azotemia with increased urine flow (ie, dogs: >45 mL/kg/d; cats: >40 mL/kg/d). Renal damage is generally less severe than with oliguric AKI. GFR is reduced, but glomerular and tubular damage are insufficient to cause oliguria.

During recovery from the oliguric phase of AKI,

patients can develop polyuria, which typically lasts 24 to 72 hours, and normokalemia or hypokalemia can ensue. Possible causes of polyuria include excretion of accumulated solutes, excretion of fluid volume overload from overzealous treatment, and poor modification of the glomerular filtrate by damaged tubular cells.⁴

Causes & Signs

AKI causes can be categorized as prerenal, primary renal, or postrenal in origin. (See **Table 1**.) Certain findings are common to all causes of AKI, whereas others are specific to the origin of the injury.^{5,6} (See **Table 2**.)

TABLE
1 Acute Kidney Injury Causes

Prerenal	Primary Renal	Postrenal
Hypovolemia <ul style="list-style-type: none"> • Dehydration • Hemorrhage • Hypoadrenocorticism • Hypoalbuminemia • Diuretic use Reduced “Effective” Blood Volume <ul style="list-style-type: none"> • Prolonged anesthesia • Congestive heart failure • Antihypertensive agents • Sepsis Renal Hemodynamic Changes <ul style="list-style-type: none"> • Epinephrine • NSAIDs • ACE inhibitors • Hemolytic-uremic syndrome Thromboembolic Events <ul style="list-style-type: none"> • Disseminated intravascular coagulation 	Nephrotoxic <ul style="list-style-type: none"> • Ethylene glycol • Aminoglycoside antibiotics • Heavy metals • Radiographic contrast agents • Cisplatin • Doxorubicin • Masitinib • Amphotericin B • Methoxyflurane • Tetracyclines • Sulfonamides • Easter lily ingestion • Grape/raisin ingestion Infectious <ul style="list-style-type: none"> • Leptospirosis • Ehrlichiosis • Lyme disease • Sepsis Other <ul style="list-style-type: none"> • Hypercalcemia (lymphosarcoma, cholecalciferol rodenticide) • Heat stroke 	Obstruction <ul style="list-style-type: none"> • Urethral plugs (mucoid/cellular/crystalline) • Urethral urolithiasis • Urethral stricture (neoplasia, granulomatous inflammation, fibrosis, or trauma) • Bladder neoplasia with bilateral ureteral obstruction

Diagnosis

AKI is characterized by rapidly rising or sudden onset of azotemia. Primary renal azotemia must be differentiated from both prerenal and postrenal causes.

In most patients with prerenal azotemia, USG is high and fractional excretion of sodium (FE_{Na^+}) is less than 1. Treatment of prerenal signs (eg, dehydration) corrects azotemia.

Postrenal azotemia occurs with urethral obstruction, and extreme bladder distention or urinary tract rupture is diagnostic.

Hyponatremia is seen in dogs following bladder rupture, and ascitic fluid creatinine and potassium concentrations are higher than serum concentrations.⁷

Once primary renal azotemia is confirmed, AKI must be differentiated from CKD to guide both treatment and prognosis. (See **Table 3**, page 38.)

TAKE ACTION

- 1 Encourage clients with patients that have some forms of AKI (eg, leptospirosis, NSAID-induced) to persist in treatment because, with time, kidney function is often restorable to near-normal levels.
- 2 Be thoroughly familiar with toxin-induced AKI signs and causes because prompt diagnosis and treatment are key to preventing or minimizing permanent renal damage.
- 3 Never persist with rapid IV fluid administration in fully hydrated patients in the oliguric phase because overhydration can be fatal.

TABLE

2 Findings Associated with Acute Kidney Injury

Clinical Signs

- Dehydration
- Uremic breath odor
- Hypothermia (except in the presence of infections [eg, leptospirosis])
- Increased kidney size, painful palpation (except when AKI is superimposed on CKD)
- Large, distended bladder (with urinary tract obstruction)
- Fluid in peritoneal cavity, retroperitoneal space, or subcutaneous perineal tissue (depending on location of obstruction and/or rupture)
- Lingual, palatine, and gingival necrosis
- Hypertension (systolic pressure >160 mm Hg)^b

Laboratory Test Results

- Rapid increase in serum creatinine, urea nitrogen, and phosphate concentrations (if renal damage is severe, concentrations may continue to rise until death ensues or dialysis is started)
- Hyperphosphatemia ± hypocalcemia
- Hyperkalemia^a
- Severe metabolic acidosis with wide anion gap (especially in ethylene glycol poisoning)
- Lymphopenia
- Active urine sediment (contains epithelial cells, erythrocytes, neutrophils, lymphocytes, and hyaline, granular, and cellular casts)

^a Leptospirosis can also induce kaliuresis (ie, increased urinary potassium excretion) and severe hypokalemia in dogs.⁵

^b Reported in more than 50% of AKI patients.⁶

Treatment

Treatment includes recognition and anticipation of predisposing factors with early correction or avoidance to prevent AKI; early diagnosis, treatment, and correction of the primary cause(s) of AKI; and correction of

life-threatening disturbances of extracellular fluid (ECF) volume and composition.

Recognition and prompt correction of potential initiating causes of AKI can minimize or prevent renal damage⁸ (see **Table 1**, page 36); however, AKI often is recognized well after renal damage has occurred. Life-threatening aberrations in ECF volume and composition must be corrected for a sufficient period to allow return of adequate renal function.⁹ Time must be allowed for tubular regeneration, nephron compensation, and restoration of renal function.

Treatment options include the following.

Renal Replacement Therapy

Hemodialysis, both continuous and intermittent, is the most reliable treatment for eliminating nephrotoxins, reducing azotemia, and correcting life-threatening disturbances of ECF volume and composition, which include hyperkalemia, acidemia, and volume overload.⁹ Renal replacement therapy (RRT) is not available or affordable for all patients.

Fluid & Electrolyte Correction

Prerenal factors that negatively affect renal blood flow (eg, hypovolemia) should be corrected with appropriate IV fluid administration. Balanced isotonic electrolyte solutions (ie, sodium 130-154 mEq/L [mmol/L]) typically are chosen based on the hematologic, colloidal, electrolyte, and acid-base status of the patient.

Anemia should be corrected with whole blood or packed red blood cells to achieve a PCV at least at the low end of the normal range (ie, dogs: 30%-35%; cats: 20%-24%).

Hypoalbuminemia should be treated with

TABLE 3 | Differentiation of Acute Kidney Injury & Chronic Kidney Disease

Acute Kidney Injury	Chronic Kidney Disease
History	
<ul style="list-style-type: none"> • Sudden onset • No previous problems • Toxin and risk factor exposure • Depression • Vomiting • Anorexia 	<ul style="list-style-type: none"> • Chronic weight loss • Poor appetite • Chronic vomiting • Chronic polyuria/polydipsia
Physical Examination	
<ul style="list-style-type: none"> • Dehydration • Normal or large kidney size • Lingual palatine and gingival necrosis (rare) • Hypothermia (except in the presence of infections [eg, leptospirosis]) • Large, distended bladder 	<ul style="list-style-type: none"> • Poor body condition score • Poor hair coat • Distinctive uremic breath odor • Oral ulcers • Small or irregular kidneys^a • Pale mucous membranes
Clinical Pathology	
<ul style="list-style-type: none"> • PCV normal • Hyperkalemia • Urine sediment active <ul style="list-style-type: none"> – Many granular casts – Many inflammatory cells 	<ul style="list-style-type: none"> • PCV often low • Hypokalemia (in cats) • Urine sediment inactive <ul style="list-style-type: none"> – Few casts (wide) – Few cells
Imaging (Radiography, Ultrasound)	
<ul style="list-style-type: none"> • Normal or large kidney size 	<ul style="list-style-type: none"> • Small kidneys^a • Increased cortical echogenicity • Loss of corticomedullary distinction, cortical infarcts, irregular kidney borders

^a Not in amyloidosis in dogs; many young cats with CKD have large kidneys.

replacement plasma or alternative colloidal solutions (starches should be avoided).^{10,11}

Hyperkalemia (ie, potassium >7.5 mEq/L [mmol/L]) should be corrected with specific treatment, including calcium gluconate, which counteracts the cardiotoxic effects of hyperkalemia but does not reduce plasma potassium, and sodium bicarbonate, which decreases plasma potassium. These treatments reduce or ameliorate the effects of hyperkalemia only transiently, and RRT may be necessary if hyperkalemia persists.

Most dogs and cats with AKI develop metabolic acidosis with a wide anion gap,⁹ but patients may be acidemic or alkalemic depending on respiratory compensation and vomiting extent. Replacement bicarbonate can be given if the deficit is known. Frequent reevaluation of bicarbonate deficit may be necessary in patients with severe azotemia.

Once dehydration is corrected, patients may demonstrate oliguria or polyuria.

If oliguria persists, rapid fluid and electrolyte administration must be curtailed to avoid excessive volume overload with pulmonary edema, respiratory distress, and respiratory failure. In persistent oliguria, IV fluid administration rate should be calculated as follows:

$$\begin{aligned} &\text{Daily fluid volume} \\ &= \text{insensible losses (10-15 mL/kg/d)} \\ &+ \text{measured urine loss} + \text{extraordinary losses} \\ &\quad (\text{eg, vomiting, diarrhea, fever}) \end{aligned}$$

Body weight should be measured at least daily to assess fluid volume administration adequacy. Insensible losses during oliguria must be replaced by fluids low in sodium (65.5-77 mEq/L [mmol/L]) or 5% dextrose in water.

Careful attention to fluid and electrolyte status is essential during the polyuric phase because patients can become dehydrated and develop hypokalemia. Frequent assessment of clinical fluid status and measurement of both urine output and body weight are essential, and regular measurement of serum sodium and potassium concentrations may be necessary. The rate of fluid administration should be based on and match urine volume, with careful attention to the patient's body weight and clinical signs indicating the level of hydration.

Balanced electrolyte solutions are appropriate for the polyuric phase of AKI. Potassium supplementation may be necessary, but the IV administration rate should not exceed 0.5 mEq/kg/h (mmol/kg/h). To avoid unnecessary prolongation of diuresis with excessive IV fluid administration, replacement volume should be judiciously reduced with careful monitoring of hydration status.¹²

Diuretic Administration

Renal function and prognosis are not improved when osmotic diuretics, loop diuretics, calcium channel blockers, and dopamine agonists are given after oliguric AKI is established. However, after appropriate rehydration and correction of renal underperfusion, diuretics have been recommended to induce increased urine production because establishing adequate urine output simplifies fluid management of AKI patients.⁹

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The osmotic diuretic mannitol should not be given to patients who are already hyperosmolar (eg, from ethylene glycol intoxication) because patients with a high risk for congestive heart failure can develop volume overload, pulmonary edema, and respiratory failure.⁹ Furosemide can be administered IV, and treatment can be repeated if diuresis is not induced in 30 minutes. If a brisk diuresis is established, diuresis can be maintained with furosemide at the appropriate dosage. Furosemide may be contraindicated if the AKI is associated with aminoglycoside administration.

Vomiting Control

Control of persistent vomiting is often necessary in AKI and can be accomplished with these medications:

- Maropitant, a neurokinin-1 receptor antagonist
- Omeprazole, a proton-pump inhibitor
- Famotidine or ranitidine, H₂ blockers
- Metoclopramide—may be less effective but can control abnormal motility and promote normal gastric emptying

Hypertension Reduction

In a recent study, hypertension was observed in 52% of canine AKI patients, and amlodipine was effective in reducing systolic blood pressure. Treatment with amlodipine was not associated with increased survival.⁶

Acute kidney injury is characterized by rapidly rising or sudden onset of azotemia.

Prognosis

AKI reversibility varies with the cause. AKI induced by NSAID intoxication, lily poisoning, and leptospiral infections tends to be reversible, whereas patients with ethylene glycol poisoning and aminoglycoside-induced AKI often fail to regain sufficient renal function to support long-term survival, even with long-term RRT, which can be cost-prohibitive.

Conservative treatment (ie, without RRT) of patients with AKI is also expensive, but supportive care for 2 weeks usually provides sufficient time for improved renal function. Renal tubular damage in all AKI forms impairs sodium reabsorption. Patients with decreased FE_{Na^+} during the recovery phase have an encouraging prognosis, whereas failure to decrease FE_{Na^+} suggests a poor prognosis.¹³

Conclusion

Iatrogenic AKI can be prevented by avoiding successive and additive insults to renal hemodynamics (eg, dehydration, hypovolemia, hypotension, prolonged anesthesia [especially with concurrent NSAID administration]). Nephrotoxic drugs (eg, aminoglycosides) should be avoided, and patients who must receive nephrotoxic drugs should be monitored appropriately for toxicity signs (eg, reduced USG, granular casts in urine sediment). At the first signs of AKI, initiating causes should be identified and addressed and then treated and managed by:

- Correcting prerenal influences that negatively affect renal blood flow (eg, hypovolemia, hypotension)
- Regularly monitoring and addressing electrolyte and acid-base disturbances

- Avoiding overhydration during the oliguric phase
- Avoiding dehydration during the polyuric phase

AKI recovery can take at least several weeks, and 2 weeks of supportive care may be needed before renal function improves. Patients must be given time to convalesce. ■

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FUN FACT: David loves to spend time with his 5 grandchildren and considers it an honor that they consider him their “fun grandpa.”

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