

# Management of acute kidney injury in the dog and cat

**Acute kidney injury (AKI) is a serious and potentially life-threatening disease that affects all species; in this article, Laura Cole MA VetMB PgCert VPS CertAVP (ECC) MRCVS veterinary specialist-in-training, Department of Clinical Science and Services, Queen Mother Hospital for Animals, Royal Veterinary College, UK, discusses the classification and diagnosis of AKI in dogs and cats and highlights the causes of AKI based on their effect on renal function**

This article will highlight the cornerstones of management of AKI including the management of life-threatening electrolyte and acid base abnormalities, careful fluid therapy alongside gastroprotectants and supportive nutrition, as well as any aetiology-specific treatment. AKI has a diverse presentation and prognosis is dependent primarily on underlying cause. AKI is a potentially life-threatening disease, with mortality rates between 23.8-78.3% of cases in dogs and cats. (Behrend et al, 1996; Worwag and Langston, 2008). Prompt recognition, aggressive management and careful monitoring is required for a successful outcome for a patient with AKI.

## CLASSIFICATION OF ACUTE KIDNEY INJURY

AKI is defined as an acute and abrupt decrease in kidney function resulting in abnormal glomerular filtration rate (GFR) tubular function and/or urine output. It can be graded

AKI grade	Creatinine (umol/L)	Clinical description
Grade I	<140	<b>Non-azotaemic AKI:</b> <ul style="list-style-type: none"> <li>Documented AKI (history, clinical or imaging evidence of AKI);</li> <li>Progressive non-azotaemic increase in creatinine &gt;28.4umol/L within 48 hours; and/or</li> <li>Measured oliguria (&lt;1ml/kg/hr) or anuria over six hours</li> </ul>
Grade II	141-220	<b>Mild AKI:</b> <ul style="list-style-type: none"> <li>Documented AKI and static or progressive azotaemia</li> <li>Progressive azotaemic increase in blood creatinine; <math>\geq 26.4 \mu\text{mol/l}</math> within 48 hours, or volume responsiveness</li> <li>Measured oliguria (&lt;1ml/kg/hr) or anuria over six hours</li> </ul>
Grade III	221-439	<b>Moderate to severe AKI:</b> <ul style="list-style-type: none"> <li>Documented AKI and increasing severities of azotaemia and functional renal failure</li> </ul>
Grade IV	440-880	
Grade V	>880	

Table 1: IRIS AKI grading system adapted from IRIS-AKI grading criteria (2013) Available from <http://iris-kidney.com>.

to encompass a continuum of functional and parenchymal damage.

There are various classification schemes of acute kidney injury in man and animals. All the systems highlight the potential for AKI in non-azotaemic animals. A useful grading system for daily use is the IRIS-AKI grading system (see Table 1). Identification of acute kidney injury should be based on a rising creatinine value as well as an absolute value alongside evidence of tubular damage on urine analysis and/or changes in urine output.

## CAUSES OF AKI

There are numerous possible causes of AKI. Causes of AKI can be divided up into how they affect renal function;

<b>Pre-renal</b>	<ul style="list-style-type: none"> <li>Dehydration</li> <li>Hypovolaemia</li> <li>Cardiac disease</li> <li>Thromboembolic disease</li> <li>Hypertension</li> <li>Systemic inflammation</li> <li>Pancreatitis</li> </ul>
<b>Renal (Glomerular and tubulointerstitial)</b>	<ul style="list-style-type: none"> <li>Exogenous toxins</li> <li>Food stuff; grapes and raisins</li> <li>Plants; Lilies and mushrooms</li> <li>Organic compounds: Ethylene glycol</li> <li>Heavy metals</li> <li>Veterinary medication: NSAIDS, antibiotics, diuretics, vitamin D analogues</li> </ul> <p><b>Endogenous toxins:</b></p> <ul style="list-style-type: none"> <li>Haemoglobin</li> <li>Myoglobin</li> </ul> <p><b>Infectious causes:</b></p> <ul style="list-style-type: none"> <li>Pyelonephritis</li> <li>Leptospirosis</li> <li>Borrelia</li> <li>Erichia</li> <li>Babesia</li> </ul> <p><b>Immune mediated diseases:</b></p> <ul style="list-style-type: none"> <li>Amyloidosis</li> <li>Vasculitis</li> <li>Systemic lupus erythematosus</li> </ul> <p><b>Neoplasia</b> Lymphoma Adenocarcinoma</p> <p><b>CRVG</b></p>
<b>Post-renal</b>	<ul style="list-style-type: none"> <li>Ureteral obstruction</li> <li>Urethral obstruction</li> </ul> <p><b>Bladder rupture</b></p>

Table 2: Causes of AKI.



**Figure 1: CVRG.**

haemodynamic (pre-renal), parenchymal (intrinsic) renal injury and post-renal causes (see Table 2).

Haemodynamic causes result from reduced renal perfusion and post-renal causes from the result of obstruction of renal flow. It is important to recognise the continuum of these three major categories as both pre-renal and post-renal causes can lead to intrinsic renal damage. Prompt recognition and subsequent correction of these factors can minimise or prevent intrinsic AKI.

Ethylene glycol is a highly-nephrotoxic substance found in anti-freeze and other solvents. On ingestion, ethylene glycol is rapidly metabolised to glycoaldehyde and subsequently, to glyoxylic acid and this metabolite is more dangerous than ethylene glycol itself. Cats have a lower minimum-toxic dose than dogs but dogs can still develop AKI with ingestion of larger quantities. Any animal presenting with anuric renal failure with accompanying hypocalcaemia and hyperlactaemia should alert the clinician to the possibility of ethylene-glycol toxicity.

Pyelonephritis is a common cause of AKI in patients with an acute deterioration of previously-diagnosed chronic kidney disease. Conversely, leptospirosis is a widely-recognised cause of AKI, in a previously healthy patient. Any dog presenting with AKI with no known inciting cause should have serum and urine submitted for microscopic agglutination testing (MAT), polymerase chain reaction (PCR) and culture. PCR of blood and urine is most useful in detecting leptospirosis early in infection before antibiotic treatment, while MAT is more useful later in infection. Therefore, both tests should be performed in all suspected cases (Shuller et al, 2015). Barrier nursing and antibiotics should be commenced if there is suspicion of leptospirosis due to its zoonotic potential.

Cutaneous vascular renal glomerulopathy (CVRG) or 'Alabama rot' is an emerging cause of AKI in predominantly middle-to-large breed dogs in the UK. Patients with the disease usually have necrotic or ischaemic skin lesion, thrombocytopenia and anemia alongside AKI (see Figure 1). The underlying cause is unknown, but there is some suggestion of a winter/spring seasonality to the disease. This condition progresses rapidly to anuria with a high-mortality



**Figure 2: Pyelogram.**

rate and therefore, any case suspected to have this should be referred to a specialist institution.

Post-renal causes of AKI include ureteral and urethral obstruction. Ureteral obstruction with calcium-oxalate stones is usually an under-recognised condition in cats. Patients with unilateral obstruction may have minimal-biochemical parameters and urine output, whereas patients with bilateral ureteral obstruction can present anuric. It is important to be aware that the presence of both ureteral and urethral obstruction can lead to intrinsic renal disease resulting in a persistent azotaemia post-surgical management of the obstruction.

**DIAGNOSING AKI**

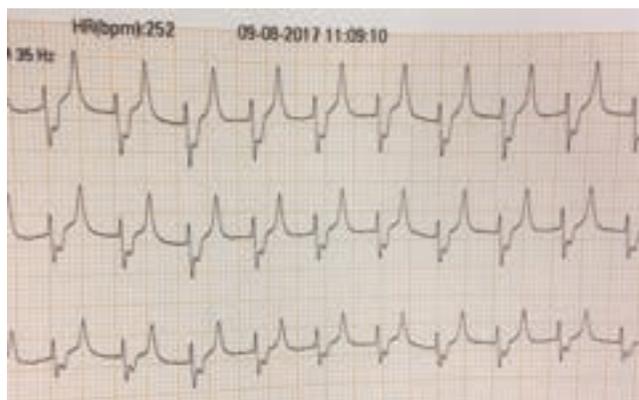
**HISTORY AND PHYSICAL EXAMINATION**

A good history and physical examination are important in distinguishing AKI and chronic kidney disease (CKD). Usually the former, has a shorter non-specific history, such as vomiting and anorexia, with possible known access to toxins and the latter has a longer course with associated weight loss and polyuria and polydipsia. However, patients with chronic kidney disease can also develop 'acute on chronic disease'; an acute exacerbation of their chronic disease. Risks factors for AKI include: recent general anesthesia, administration of anti-inflammatories and ingestion of toxic foodstuff, such as grapes and raisins.

**BLOOD BIOCHEMISTRY. ELECTROLYTES AND HAEMATOLOGY**

AKI results in the retention of uraemic solutes, namely urea and creatinine. The presence of hyperkalaemia alongside azotaemia should alert the clinician to the possibility of anuric AKI and prompt emergency management.

**Urine assessment:** Urine analysis should be performed on all patients with a concern of AKI. This should ideally be performed prior to the start of fluid therapy. The urine sediment can provide evidence of renal disease before significant changes in serum creatinine. The presence of glucosuria, renal tubular casts and proteinuria are all potential indicators of an AKI. Detection of calcium-oxalate crystalluria may help in diagnosis of ethylene-glycol toxicity with



**Figure 3: T-waves from ECG.**

compatible clinical history. However, the absence of these crystals in the urine does not preclude a diagnosis of ethylene glycol toxicity. Culture of urine should be performed in all cases of AKI.

**Urine biomarkers:** The commercial renal biomarker symmetric dimethylarginine (SMDA) has been shown to be useful in the diagnosis of AKI but cannot be used to discriminate between AKI and CKD in affected animals (Dahlem et al, 2017).

**Imaging:** Ultrasound may be a useful adjuvant test to assess the renal size and architecture, such as evidence of chronic disease, presence of renal infarcts and evidence of renal pelvis and ureteral dilation suggestive of ureteral obstruction. Injection of water-soluble contrast agent into the renal pelvis (a pyelogram) may be necessary to confirm obstructive disease (see Figure 2). The presence of ureteral obstruction is a surgical emergency with improved short-term survival when compared to other causes of anuric renal disease and, therefore, it is important to rule out this disease early in your diagnostics.

**Urine output:** It is important to determine the urine output of patients presenting with acute kidney injury as this will effect their management and prognosis. Patients' urine production can be classified as anuric (no urine production), oliguric (<0.5-2ml/kg/hr) and polyuric (>2ml/kg/hr). Assessment of urine output should only be performed once the patient is adequately hydrated.

Initial assessment can involve bladder palpation and assessing the tray with appropriate non-absorbent litter. However, if there is a concern that the patient is failing to produce urine, a urinary catheter should be placed to correctly detect the presence of anuria and oliguria. Measurement of urine output is also important in polyuric patients in order to quantify losses.

### MANAGEMENT OF AKI

Specific therapy for the management of patients with AKI are limited. The administration of ethanol or fomepizole, competitive inhibitors of alcohol dehydrogenase, are antidotes for ethylene glycol toxicity. These antidotes act to prevent the formation of the toxic metabolites of ethylene glycol metabolism and are only useful if given within three hours post-ingestion, normally when the patient is non-

azotaemic (Connally et al, 2010). Misoprostol, a prostaglandin analogue, is indicated in cases of non-steroidal toxicity and antibiotic therapy, based on culture and sensitivity results, should be instituted in cases with a documented urinary tract infection or in cases of suspected leptospirosis. Potentiated amoxicillin should be considered first-line therapy in these cases and changed based on culture and sensitivity and MAT-testing results.

Medical management of AKI is, therefore, fundamentally based on supportive care, management of life-threatening electrolyte and acid-base abnormalities, fluid therapy and supportive treatment.

### MANAGEMENT OF ELECTROLYTE AND ACID BASE ABNORMALITIES

In cases of obstruction or anuric intrinsic renal failure, the most common electrolyte abnormality is hyperkalaemia and less commonly hypocalcaemia and acidaemia. Bradycardia is not a reliable finding for diagnosis of hyperkalaemia and ECG abnormalities secondary to hyperkalaemia are variable and are not specific to a given potassium concentration (Tag, Day 2008). Peaked T waves however, are often seen with hyperkalaemia (see Figure 3).

Management of hyperkalaemia consists mainly of calcium gluconate, glucose-insulin bolus and subsequent glucose continuous rate infusion to prevent hypoglycaemia. Bicarbonate is usually reserved for patients with a severe acidaemia (pH <7; see Table 3). Continuous electrocardiogram (ECG) and regular monitoring of electrolytes and glucose is important when starting patients on this treatment.

Fluid therapy in patients with AKI is a balance between too much and too little. Traditionally, crystalloid is administered at a high rate in attempt to maximise excretion of metabolic wastes. However, increasing fluid administration does not equate to elevated urine production and has been associated with increased mortality in humans (Legrand and Payne, 2011). The current recommendation is to correct the dehydration deficit, usually over a six to eight-hour period and, if the patient's bladder is not filling and the patient is continuing to gain weight then the patient should be considered to be anuric or oliguric. At this point, a urinary

Drug	Action	Dose
Calcium gluconate 5%	Stabilisation of myocardial conduction whilst attempting to restore urine flow	0.5-1ml/kg over 5-15 minutes with continual ECG monitoring
Glucose-insulin bolus and then continuous rate infusion (CRI) of 50% dextrose	Movement of potassium intracellularly	0.25-0.5IU/kg and 0.5ml/kg 50% dextrose and then supplement with 2.5-5% glucose supplementation
Bicarbonate	Improves extracellular acidosis and promotes intracellular shift of potassium	1-2mEq/kg IV slowly over 15 minutes

**Table 3: Drug management of hyperkalaemia.**



**Figure 4: Continuous renal replacement therapy**

catheter should be placed to carefully monitor urine output to tailor the fluid therapy. Fluid therapy should match the urine output and correct any deficit from other sensible losses (vomiting, diarrhoea) alongside replacement of insensible losses, estimated at 0.6-1ml/kg/hr. In a patient that is considered anuric, they should only receive fluid to replace insensible losses. During the recovery phase of AKI the patient can be polyuric. Urine output, alongside the patient’s weight, needs to be monitored to ensure the fluid management plan is balanced with the losses.

**SPECIFIC THERAPY FOR THE MANAGEMENT OF OLIGURIA AND ANURIA**

Furosemide is the mainstay of medical management of anuric AKI. It has a role in diuresis and naturesis. Continuous rate infusions of furosemide have proven to be more beneficial than bolus injections (Adin et al, 2003). Dopamine, and the more selective dopamine receptor-agonist fenoldopam, have been suggested to have a role increasing renal blood flow. However, currently there is no evidence for their use in management of AKI (Wohl et al, 2007, Nielsen et al, 2015, Kelly et al, 2016).

The current recommendation for patients that are persistently anuric is referral to a specialist institution for continuous renal replacement therapy (CRRT) in larger patients (see Figure 4) or peritoneal dialysis in smaller patients (see Figure 5). Indications for CRRT and peritoneal dialysis are anuria, fluid

overload and hyperkalaemia. Both of these therapies are costly and labour-intensive but can be successful depending on the underlying cause of the AKI.

**MANAGEMENT OF URAEMIC GASTRITIS AND NUTRITIONAL CARE**

Patients with marked azotaemia invariably have a degree of uraemic gastritis. Gastroprotectants, anti-nausea and supportive nutrition are, therefore, important when managing these patients. Patients with AKI can be in hospital for days-weeks. A naso-oesophageal feeding tube is a relatively easy to place and allows trickle feeding of specialised renal diet whilst the patient is in hospital.

**MONITORING AND MANAGEMENT OF HYPERTENSION**

Systemic hypertension has been reported in dogs and cats with AKI. Therefore, daily blood-pressure monitoring and initiation of anti-hypertensives, such as amlodipine, may be warranted in cases of hypertension.

**OUTCOME AND PROGNOSIS**

Prognosis is variable dependent on the underlying cause; ethylene glycol toxicity is associated with a 93% mortality rate and once azotaemic, mortality rate of lily intoxication is between 50-100%, compared to survival of least two thirds of cats with ureteral obstruction and pyelonephritis (Hadley et al, 2003; Segev et al, 2013). These figures highlight the importance of attempting to determine the underlying cause of AKI, as well as highlighting the importance in prophylactic therapy, such as fluids in patients with history of exposure to nephrotoxins like lilies and raisins. Certain biochemical findings have been suggested as prognostic indicators. However, the initial degree of azotaemia has not been consistently shown as a negative prognostic indicator and should not be used as a sole factor to decide whether to pursue treatment or not (Lee et al, 2011, Segev et al, 2013).

**CONCLUSIONS**

AKI is a severe, potentially life-threatening injury with multiple possible aetiologies with different prognoses. Prompt recognition and aggressive medical management with close monitoring of fluid balance and supportive care is required as well as prompt referral and management of a patient if it is persistently anuric despite medical management.

**REFERENCES**

Bates N et al. Common questions in veterinary toxicology. *Journal of Small Animal Practice* 2015; 56: 298-306  
 Legran, Payen (2011) Understanding urine output in critically ill animals. *Annals of Intensive Care* 2011; 1: 1-13  
 Worwag S, Langston C. Acute intrinsic renal failure in cats: 32 cases (1997-2004). *Journal of the American Veterinary Medical Association* 2008; 232: 728-732  
 Tart KM, Powell LL. 4 methylpyrazole as a treatment for naturally occurring ethylene glycol intoxication in cats. *Journal of Veterinary Emergency Medicine and Critical Care* 2011; 20: 191-206



**Figure 5: Peritoneal dialysis.**

Acierno M.J et al. Preliminary validation of a point-of-care ethylene glycol test for cats. *Journal of Veterinary Emergency Medicine and Critical Care* 2008; 18: 477-479

Schuller S et al. European consensus statement on leptospirosis in dogs and cats. *Journal of Small Animal Practice* 2015; 56: 159-179

Dahlem DP. Plasma symmetric dimethylarginine concentration in dogs with acute kidney injury and chronic kidney disease. *Journal of Veterinary Internal Medicine* 2017; 31: 799-804

Tag TL, Day TK. Electrocardiographic assessment of hyperkalaemia in dogs and cats. *Journal of Veterinary Emergency and Critical Care* 2008; 18: 61-67

Connally HE et al. Safety and efficacy of high-dose fomepizole compared with ethanol as therapy for ethylene glycol intoxication in cats. *Journal of Veterinary Emergency Medicine and Critical Care* 2010; 1: 191-206

Adin DB et al. Intermittent bolus injection versus continuous infusion of furosemide in normal adult greyhound dogs. *Journal of Veterinary Internal Medicine* 2003; 17: 632-636

Nielsen LK et al. Administration of fenoldopam in critically ill small animal patients with acute kidney injury: 28 dogs and 34 cats (2008-2012). *Journal of Veterinary Emergency Medicine and Critical Care* 2015; 25: 396-404

Kelly KL et al. Effect of fenoldopam continuous infusion on glomerular filtration rate and fractional excretion of sodium in healthy dogs. *Journal of Veterinary Internal Medicine* 2016; 30: 1655-1660

Hadley RM et al. A retrospective study of daylily toxicosis in cats. *Veterinary and Human Toxicology* 2003; 45: 38-39

Lee Y-J et al. Prognosis of acute kidney injury in dogs using RIFLE-like criteria. *Veterinary Record* 2011; 168,264, doi: 10.1136/vr/c6234

Segev G et al. A retrospective study of acute kidney injury in cats and development of a novel clinical scoring system for predicting outcome for cats managed with haemodialysis. *Journal of Veterinary Internal Medicine* 2013; 27: 830-839

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## READER QUESTIONS AND ANSWERS

**1. WHAT ACID BASE AND ELECTROLYTE CHANGES WOULD YOU ASSOCIATE WITH ETHYLENE-GLYCOL TOXICITY?**

- A Hypokalaemia, hypercalcaemia and acidaemia
- B Hyperkalaemia, hypocalcaemia and acidaemia
- C Hyperkalaemia hypercalcaemia and alkalosis
- D Hypokalaemia, hypocalcaemia and alkalosis

**2. WHAT TESTS ARE RECOMMENDED FOR DIAGNOSIS OF LEPTOSPIROSIS?**

- A Urine culture
- B MAT only
- C MAT + PCR of blood and urine
- D PCR of blood and urine only

**3. WHAT THREE FINDINGS ON URINE DIPSTICK AND SEDIMENT EXAM ARE INDICATIVE OF AKI?**

- A Renal casts, bilirubinuria, proteinuria
- B White blood cells, proteinuria, renal casts
- C Glucosuria, proteinuria, renal casts
- D White blood cells, glucosuria, proteinuria

**4. IN WHAT TIMEFRAME IS THE ADMINISTRATION OF FOMEPIZOLE USEFUL FOR MANAGEMENT OF ETHYLENE GLYCOL TOXICITY?**

- A 1-3 hours
- B 4-6 hours
- C 7-10 hours
- D Within 12 hours

**5. WHAT THERAPIES SHOULD BE USED ALONGSIDE EACH OTHER FOR FIRST-LINE MANAGEMENT OF HYPERKALAEMIA?**

- A Calcium gluconate and insulin-glucose
- B Calcium gluconate and sodium bicarbonate
- C Insulin glucose and sodium bicarbonate
- D Beta antagonist and sodium bicarbonate

**6. WHAT ARE THE THREE INDICATIONS FOR CONTINUOUS RENAL REPLACEMENT THERAPY (RRT) OR PERITONEAL DIALYSIS?**

- A Azotaemia, hypernatraemia, fluid overload
- B Hyperkalaemia, anuria, fluid overload
- C Acute history, azotaemia, hyperkalaemia
- D Anuria, azotaemia, fluid overload

ANSWERS: 1: B; 2: C; 3: C; 4: A; 5: A; 6: B