Pathophysiology
In dogs and cats, acute renal failure is primarily due to acute tubular damage. This results in necrosis and sloughing of tubular cells into the tubular lumen, causing tubular obstruction and in loss of tight junctions between tubular cells, leading to tubular fluid leaking out of the tubule and into renal interstitial space. Renal arteriolar vasoconstriction is another component of acute renal failure. This leads to decreased GFR and renal ischemia with secondary tubular damage. As a result of acute renal injury, GFR is decreased and tubular function is abnormal.

Since nephrons rapidly become dysfunctional, there is no time for compensation. Although fewer nephrons may be dysfunctional than in chronic disease, the signs are as severe. Animals with acute renal failure usually appear more ill at a given level of azotemia than animals with chronic renal failure. Because of the potential for repair and compensation, animals with acute disease have the potential to recover (depending on the severity of injury). Two to three months are required for maximal compensation and repair to occur.

Common causes include toxins (acute nephrosis). Ethylene glycol is the most common cause of acute renal failure in small animals; it requires only small amounts. Animals are generally oliguric due to tubular obstruction with crystals and renal tubular cell injury. The first signs are CNS (ataxia) plus severe metabolic acidosis; renal failure usually develops in 24–48 hours. A presumptive diagnosis is based on history of CNS signs (ataxia) plus severe acidemia plus markedly increased anion gap plus renal failure; serum calcium may be decreased; on ultrasonography kidneys are mildly, symmetrically enlarged and markedly hyperechoic. Confirmation of diagnosis is by finding large numbers of oxalate crystals in urine or in renal biopsy specimen or by blood test for ethylene glycol in the first 24–48 hours.

Aminoglycoside antibiotics (all except streptomycin) are a too common cause of nephrotoxicity. These are proximal tubular toxins that cause mild proteinuria, isosthenuria, occasionally glucosuria, cylindruria, and progressive azotemia, particularly if administration continues. These animals are initially polyuric but terminally oliguric. In individual animals, risk factors include fever, dehydration, old age, preexisting renal disease, hypokalemia, overdosage, sepsis, some cephalosporins, prior use of aminoglycosides, furosemide, and frequency of administration. The median onset of toxicity is 9 days (range 5–17), and maximal toxicity does not occur until at least 4 days after the drug is stopped. Recommended monitoring includes daily urinalysis (waiting until BUN or creatinine increases is too late).

Other causes of acute renal failure include amphotericin B, NSAIDs, hemoglobinuria and myoglobinuria (impair renal function in the presence of hypotension), dehydration or acidosis; plant toxicities (e.g., lily toxicity in cats), food toxicities (raisins and grapes in dogs; chocolate in dogs; melamine in dogs and cats); prolonged ischemia (decreased perfusion); and infectious causes of acute nephritis such as leptospirosis, bacterial sepsis, and Rocky Mountain Spotted Fever.

Diagnosis (Differentiation of Acute from Chronic Is Important Prognostically)
The history typically shows an acute onset with no previous problems related to the urinary system. Physical findings include symmetrical, normal, or mildly enlarged kidney, and occasionally there is evidence of renal pain due to swelling and stretching of renal capsule (uncommonly recognized). Clinicopathologic evaluation may demonstrate leukocytosis, nonspecific azotemia, and hyperphosphatemia; urinalysis may demonstrate casts, low USG, pyuria, glucosuria (uncommon), crystals (ethylene glycol, melamine). In acute renal failure the kidneys are symmetrical, either normal in size or mildly enlarged on radiographs. Ultrasonography may reveal normal or increased echogenicity.

Treatment
As the clinical signs of uremia are due to fluid, acid-base, and electrolyte abnormalities and retention of metabolic wastes, the basis of treatment is to manage identified abnormalities and keep the animal alive until the kidney can reestablish adequate function. Problems to address include acidosis, hyperphosphatemia, hyperkalemia (associated with oliguria), hypokalemia (associated with polyuria and diuresis), and volume overload.
It is important to avoid giving any medications unnecessarily, as drugs eliminated by the kidneys can accumulate; for required medications eliminated by the kidney with toxic potential, one can adjust the interval between doses by multiplying the usual interval by the patient’s serum creatinine concentration. Key to supportive care is maintenance of fluid, electrolyte, acid-base, and caloric balance as much as possible; specific requirements for therapy will depend on the severity of the renal failure. If possible, avoid catheterization of vascular and urinary systems. Monitor the animal’s physical condition often to determine whether it is improving or worsening; monitor body weight to help determine hydration status/appetite; and monitor BUN, creatinine, calcium, phosphorus, acid/base, and electrolytes to evaluate response to and efficacy of therapy.

Hypokalemia is a common problem in polyuric animals and those receiving aggressive fluid therapy or diuresis. In general, if a patient is polyuric (producing > 2.2 ml/kg/hr) or is undergoing osmotic diuresis, she will become hypokalemic if not supplemented; one can supplement orally (if the patient is not vomiting) 1–3 mEq/kg/day or subQ with 40 mEq KCl/L in Lactated Ringers or IV KCl, 20 mEq KCl/L Lactated Ringers. The IV and subQ dosages are added KCl and are calculated to provide adequate K, assuming 1–2x maintenance fluid rates (60 mL/kg/day).

If oliguric (producing < 0.5 ml/kg/hr), insert an intravenous catheter (jugular vein) and an indwelling urinary catheter and correct fluid deficit over a few hours, usually with lactated Ringer’s solution (LRS) or similar solution. One must monitor for signs of overhydration such as increasing body weight, pulmonary edema, increasing central venous pressure, clear nasal discharge, and peripheral edema. After rehydration, if the animal remains oliguric, consider osmotic diuresis with mannitol or 10% dextrose (5 ml/kg for 20 minutes). An alternate or next line of approach would be a natriuretic diuretic (generally furosemide IV in increasing doses beginning at 2.2 mg/kg; can be increased to 10 mg/kg if no response; diuresis should begin within 15 minutes of an IV dose; will be maximal at 30–45 minutes and persist for 2 hours; often used with dopamine as described below). Always bear in mind that the most common precipitating cause of death in oliguric acute renal failure is fluid overload.

If associated with renal vasoconstriction (certain toxins, anesthesia), one can try dopamine (3 microg/kg/min) with or without furosemide; this low dose causes renal arterial vasodilation. If too high a dose or too fast a rate is given, renal arterial vasoconstriction can occur; if the dose is too high, respiratory and heart rate increase. At the appropriate rate and dose, respiratory and heart rates are stable. One can also try amlodipine (0.1–0.25 mg/kg orally once) or diltiazem.

Prevention
The keys to prevention are to evaluate renal function by measuring BUN/serum creatinine/urinalysis before major surgical procedures in all animals with a history of PU/PD (this should be a standard question before any anesthetic episode) and in all older dogs and cats (> 5 years), to rapidly correct dehydration and electrolyte abnormalities, and to utilize adequate fluid therapy before, during, and after any anesthetic episode.

Resource