Acute azotemia occurs due to rapid hemodynamic, filtration, tubulointerstitial, or excretory damage to the upper and/or lower urinary tract. The abrupt decrease in glomerular filtration rate that results from any of these forces leads to accumulation of uremic toxins and dysregulation of fluid, electrolyte, and acid-base balance. Dogs and cats that develop acute azotemia usually show clinical signs of uremia; however, signs may be more subtle in cases with an acute but mild increase in urea and creatinine. For example, a sudden increase in plasma creatinine of only 0.5 mg/dl or twofold is considered significant in human patients.

Acute uremia can develop due to prerenal, intrinsic renal, or postrenal disease; intrinsic renal causes (acute kidney injury) are usually toxicant-induced, ischemia-induced, or infectious in nature. These core concepts structure the diagnostic and therapeutic plan. Establishing the cause of acute uremia can help predict prognosis and determine if specific therapy is indicated in addition to standard supportive care.

Diagnostic and therapeutic steps

**Step 1. Determine contribution of prerenal forces on azotemia and initiate fluid support.**
- Assess patient for evidence of dehydration or hypotension, history or other signs of hypoadrenocorticism.
- Review urinalysis. Pretreatment Urine Specific Gravity > 1.030 (dogs) or >1.035 (cats supports prerenal azotemia.
- Other urinary indices (Urine sodium, FE Na) can be useful in determining prerenal versus renal azotemia (sodium should be preserved in prerenal azotemia, so the fractional excretion should be very low), but are not routinely measured in small animals.
- Regardless of likely cause, initiate fluid therapy early to correct deficits, provide for ongoing losses, and promote diuresis. Deficits are usually replaced in 6 – 8 hours but more rapid replacement, up to shock fluid doses, may be needed in some cases.
- During rehydration phase, monitor hydration and urine output carefully. Be prepared to significantly scale back or curtail fluid infusion at any sign of overhydration.
- Reevaluate the plasma creatinine after replacing fluid deficits. Prerenal azotemia should resolve with volume replacement, so the degree of reduction in the creatinine at this stage will give you a general idea of how much of the presenting azotemia was prerenal. Note that urea is more easily “washed out” during diuresis; changes in creatinine are more useful in determining progress.

**Step 2. Determine contribution of postrenal forces on azotemia and their reversibility.**
- Review the patient history for trauma, urethral obstruction or urolithiasis.
- Attempt to pass a urinary catheter if there is any suspicion of urethral obstruction.
- Proceed to imaging studies that will rule in or rule out ureteral obstruction, bladder neck obstruction, or uroabdomen.
- After appropriate medical stabilization, proceed to correct reversible disorders to alleviate postrenal contribution.

**Step 3. Investigate intrinsic renal disease as cause of uremia.**
- Is it acute or chronic? Although chronic kidney disease can present as an acute crisis (“acute on chronic” disease), historical, clinical and imaging findings are usually significant to make a determination of chronicity (Table 1)
- For acute toxicoses (or suspected toxicosis): Proceed with gastrointestinal decontamination as soon as possible (e.g. lily ingestion, medications, etc)
- For acute azotemia due to acute kidney injury, proceed with a diagnostic plan tailored to the most likely diagnoses (Table 2).

<table>
<thead>
<tr>
<th>Feature</th>
<th>Acute Renal Failure</th>
<th>Chronic Renal Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor body condition or weight loss</td>
<td>Absent or infrequent</td>
<td>Common</td>
</tr>
<tr>
<td>History of PU/PD</td>
<td>Absent</td>
<td>Common</td>
</tr>
<tr>
<td>Renal size</td>
<td>Normal to small</td>
<td>Normal to large</td>
</tr>
<tr>
<td>CBC Findings</td>
<td>Anemia absent initially</td>
<td>Common if advanced</td>
</tr>
<tr>
<td>Serum potassium</td>
<td>Normal to increased</td>
<td>Normal to decreased</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>Moderate to severe</td>
<td>Mild to moderate</td>
</tr>
<tr>
<td>Urinalysis Findings</td>
<td>“Active” - cellular or granular casts, proteinuria, variable USG</td>
<td>No casts, isosthenuria</td>
</tr>
<tr>
<td>-----------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Urine volume</td>
<td>Normal to oliguria</td>
<td>Polyuria</td>
</tr>
</tbody>
</table>

**Table 2. Causes of acute kidney injury in dogs and cats**

**Ischemia/vascular:**
- Thrombosis/infarction
- Hypovolemia
- Anesthesia
- Vasculitis
- DIC, hyperviscosity
- Systemic hypertension

**Nephrotoxicant-induced:**
- Ethylene glycol
- Aminoglycosides
- Cisplatin
- ACE Inhibitors
- NSAIDs
- Radiocontrast agents
- Amphotericin B

**Infectious:**
- Cholecalciferol
- Lily toxicosis
- Grape/Raisin toxicosis
- Hypercalcemia (also vascular)
- Melanine (food products)
- Chicken jerky treats
- Leishmania
  - Other Disorders Associated with ARF:
  - Pre-existing renal disease

**Miscellaneous:**
- Trauma, Burns
- Sepsis
- Pancreatitis
- Diabetes Mellitus
- Snakebite

**Common diagnostic tests to perform in acutely azotemic patient include**

- Drug, food, toxicant and vaccination history
- Indirect blood pressure measurement
- Urine culture
- Total and ionized calcium (ideally prior to fluid administration)
- Electrolytes (Na, K, Cl)
- Coagulation panel
- Leptospirosis serology or PCR
- Ethylene glycol tests
- +/- Renal aspirate (most helpful for infiltrative disease)
- Additional tests based on patient characteristics and geographic region
  - Borrelia PCR
  - Rickettsial titers
  - Contrast urography or CT
  - Vitamin D measurement
  - ACTH stimulation test
  - FeLV/FIV (cats)
- Renal biopsy may or may not shed light on the original diagnosis but will give valuable information about extent of injury and prognosis. Histologic evidence of intact renal tubular epithelial basement membranes and regenerating epithelial cells indicates that recovery may be able to occur. Biopsies are indicated in cases in which diagnosis cannot be determined by other means, highly proteinuric patients, suspected neoplasia, and prior to extensive and costly advanced treatments (dialysis).
- Urinary biomarkers, including various proteins and enzymatic markers of glomerular or tubular injury, have been examined in small animals, may eventually be clinically helpful for detecting early insults and for establishing a prognosis for recovery.

**Step 4. Continue tailored medical management**

- Continue fluid support based on hydration, maintenance needs and losses (consider CVP measurements or “ins and outs.”) Shift to maintenance fluid type as deficits are corrected.
- Manage acid base and electrolyte needs according to needs
• Monitor blood pressure and manage hypertension if needed
• Address vomiting and uremic gastropathy with antiemetics and gastroprotectants
• Ensure caloric intake as early as possible (consider esophageal feeding tube)
• Pain management if needed
• Blood products if needed
• Aggressive monitoring
• Enhance urine output in oliguric to anuric patients
  o Appropriate fluid replacement
  o Mannitol

Step 5. Consider referral for undiagnosed or unresponsive patients. Indications for advanced treatment modes (dialysis or CRRT) include
• Severe hyperkalemia
• Ethylene glycol or other dialyzable toxicant
• Failure of medical management
• Severe azotemia unresponsive to fluid therapy
• Peri-operative support of ureteral obstruction

Key prognostic points
• Prognosis for prerenal azotemia and some infectious renal diseases is good
• If postrenal problem can be corrected early (urethrolith or uroabdomen), prognosis is excellent; prognosis declines as the duration of urinary obstruction (urethral or ureteral) increases
• Prognosis is good for hospital acquired AKI when caught early (defined by small increase in SCr)
• Even with dialytic support, overall mortality for initial episode of AKI is still about 50/50, with about one-third of affected patients achieving one-year survival.
• Prognosis declines when intrinsic renal function has been chronically affected
• Prognosis for established ethylene glycol induced renal failure, and for persistent oliguric renal failure is poor.
• Signs associated with negative outcome in cats include older age, lower body temperature, hypoalbuminemia and hypocalcemia.
• Prognostic data and schema are available that may help provide a more objective prediction:
  o NGAL levels are higher in more severely affected dogs with AKI
  o Dogs: More advanced azotemia and age are associated with less favorable outcomes
  o Cats: Mathematical index including body temperature (C), albumin in (g/dl) and LDH (IU/L) was accurate in predicting mortality.
  o RIFLE: Dogs in the F=Failure category (> 3x increase in baseline creatinine and oligoanuria) had a high mortality rate