Chronic renal disease (CRD) or failure is a common condition in cats. The incidence approaches 15% in cats older than 15 years, but CRD is not limited to the geriatric population. The chronic lymphoplasmacytic interstitial nephritis that is commonly seen in older cats is probably not a single entity but rather the end result of any kind of renal insult. Because each nephron works as a unit, if the glomerulus is irreversibly damaged, the associated tubule will degenerate and vice versa. As nephrons are lost, the remaining nephrons hypertrophy. Although initially adaptive, glomerular hypertension damages the nephron, which leads to further nephron loss. After a certain amount of damage has been sustained, renal failure may be progressive despite resolution of the initiating cause(s).

Just as there are many causes of CRD, there are many levels of renal dysfunction. In some patients, mild asymptomatic azotemia is discovered incidentally, perhaps in conjunction with geriatric or preanesthesia (e.g., for dental work) screening. Other patients are presented for evaluation because of early signs of renal failure, and some present in uremic crisis. The asymptomatic pet with very mild elevations in blood urea nitrogen (BUN) or creatinine that is maintaining body weight and appropriate hydration may not need specific treatment other than dietary therapy, although routine monitoring is indicated. A markedly dehydrated pet with severe uremic syndrome that has decompensated is likely to need hospitalization for intensive therapy, including IV fluid administration. Once the uremic crisis is controlled, however, continued treatment at home can help delay another crisis. For pets that fall in the middle ground, outpatient management is sufficient without the need for a hospital stay. Many drugs and therapies are available for management of CRD, but they do not stop the progression of renal failure or reverse structural lesions already present. The goals of therapy are to slow progression, minimize hospitalization time, and improve the pet’s sense of well-being (quality of life).

**DIAGNOSTIC CRITERIA**

**Historical Information**

**Gender Predisposition**
- None.

**Age Predisposition**
- CRD can affect cats of any age but is more common in older cats.
- Mean age of symptomatic cats: 12.5 to 14.5 years.
- Asymptomatic cats may be younger.

**Breed Predisposition**
- One report lists Maine coon cats, Abyssinians, Siamese, and Russian blues as predisposed.
- Other studies report no breed disposition.

**Owner Observations**
- Polyuria and polydipsia.
- Weight loss.
- Anorexia.
- Vomiting.

**Also in this issue:**

9 Colitis and Large Bowel Diarrhea
• Lethargy or depression.
• Halitosis (uremic breath odor), dysphagia, or oral discomfort.
• Weakness.

Other Historical Considerations/Predispositions
• Mild clinical signs (especially polyuria, polydipsia, and/or weight loss) may be present for months to years before presentation.
• CRD may be discovered as part of preanesthesia or geriatric screening in apparently healthy cats.

Physical Examination Findings
• Asymptomatic cats may have no abnormal physical examination findings.
• Symptomatic cats:
  — Thin body condition.
  — Dehydration.
  — Abnormal kidney size or shape.
  — Heart murmur.
  — Oral ulceration, gingivitis, and/or uremic breath odor.
  — Hypothermia.
  — Pale mucous membranes.
• Severely affected cats may present with altered consciousness, seizures, and/or bleeding problems (particularly in association with oral ulceration) or may be moribund.

Laboratory Findings
• Azotemia.
• Poorly concentrated urine (urine specific gravity < 1.035).
• Hyperphosphatemia.
• Hypokalemia.
• Metabolic acidosis.
• Nonregenerative anemia: Lack of erythropoietin, a hematopoietic hormone, leads to nonregenerative anemia. Chronic inflammation or iron deficiency from chronic gastrointestinal (GI) blood loss may contribute. Some cats present with acute anemia (which may be partially regenerative) due to acute blood loss from a GI ulcer.
• Hypercalcemia or hypocalcemia; ionized calcium is usually normal.
• Active urine sediment (leukocytes, erythrocytes, bacteria) may indicate a urinary tract infection (UTI) as the cause (i.e., pyelonephritis) or a consequence of CRD.
• Hematuria may indicate nephroliths, ureteroliths, or UTI.
• Positive urine culture: Cats with CRD may have silent UTI (no clinical signs and inactive urine sediment). Routine urine cultures are recommended.
• Urine protein: creatinine ratio: Usually normal (<0.4) in cats.

KEY TO COSTS
$ indicates relative costs of any diagnostic and treatment regimens listed.
$ costs under $250
$$ costs between $250 and $500
$$$ costs between $500 and $1,000
$$$$ costs over $1,000
Microalbuminuria indicates renal damage but is not specific for the cause, whether primary or secondary. The role of microalbuminuria in monitoring or treating cats with CRD is not established.

Platelet count is usually normal, although platelet function may be decreased with uremia. Buccal mucosal bleeding time may be prolonged, but coagulation panel (prothrombin time and partial thromboplastin time) results are expected to be normal.

### Other Diagnostic Findings

#### Abdominal Radiography

- Abnormal kidney size or shape: Approximately 33% of affected cats have small kidneys, 33% have normal-sized kidneys, and 33% have large kidneys.
- Nephroliths or ureteroliths may be seen, although some uroliths are too small to be detected radiographically.

#### Abdominal Ultrasonography

- Affected cats frequently have diminished renal architecture as a result of renal tissue being replaced with fibrosis.
- Other changes that may be identified include:
  - Renal mineralization or nephroliths.
  - Renal pelvic dilation and ureteral dilation from obstruction or pyelonephritis.
  - Polycystic kidney disease.
  - Perinephric pseudocysts.

#### Blood Pressure Measurement

- Twenty percent of cats with CRD have a systolic blood pressure exceeding 175 mm Hg.
- Risk of end organ damage (systolic/diastolic):
  - Minimal risk: <150/95.
  - Low risk: 150/95 to 160/100.
  - Moderate risk: 160/100 to 180/120.
  - High risk: >180/120.
- Artfactually high blood pressure ("white-coat hypertension") may be minimized by:
  - Measuring blood pressure before performing the physical examination or other procedures.
  - Measuring blood pressure in a calm environment with the owner present.
- The presence of retinal changes consistent with hypertension (e.g., tortuous retinal vessels, retinal edema, retinal hemorrhage) supports a diagnosis of hypertension (as opposed to white-coat effect).

#### Renal Biopsy

- Indicated primarily in patients with renomegaly to evaluate for lymphoma and feline infectious peritonitis.
- The risk of bleeding is increased in uremic patients because of platelet dysfunction.

#### Other

- Measurement of glomerular filtraton rate is rarely used when azotemia is present.
- Parathyroid hormone concentration may be elevated if renal secondary hyperparathyroidism is present.

### Summary of Diagnostic Criteria

- Azotemia with poorly concentrated urine in absence of urinary obstruction defines renal failure.
- Evidence of clinical (i.e., polyuria, polydipsia, partial anorexia, weight loss) or laboratory signs for over 3 months.
- Abnormalities of kidney size, shape, or architecture usually present but not necessary for diagnosis.

### Diagnostic Differentials

#### Symptomatic Cats

- Polyuria/polydipsia with weight loss: Hyperthyroidism, diabetes mellitus.
- Poor appetite, weight loss, and poor haircoat: Inflammatory bowel disease, neoplasia, hyperthyroidism.

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**ON THE NEWS FRONT**

A low dose of calcitriol (0.75–5 ng/kg/day) has been shown to decrease mortality in dogs with CRD and is postulated to help by decreasing parathyroid hormone production. Studies evaluating low-dose calcitriol in cats are under way. If calcitriol is eventually proven to be of benefit in cats, caveats concerning treatment in dogs are likely to be relevant to cats:

- Administration is contraindicated in patients with hyperphosphatemia because of the risk of soft tissue mineralization.
- Serum calcium level should be monitored closely; calcitriol may cause hypercalcemia.
- Careful attention to the dose is necessary: Doses are in ng/kg, but calcitriol is supplied in micrograms (µg); the amount to be given must be accurately calculated to avoid overdosing.
• Chronic intermittent vomiting and weight loss: Inflammatory bowel disease, pancreatitis, liver disease, hyperthyroidism.

Specific Differentials for Chronic Renal Disease
• Tubulointerstitial nephritis is most common (70% of cases).
• Nephrolithiasis or ureterolithiasis.
• Polycystic kidney disease (in Persians and other long-haired cats; less frequent in domestic short-haired cats).
• Chronic pyelonephritis.
• Renal dysplasia (young cats).
• Infarction.
• Lymphoma.
• Incomplete resolution of acute renal failure.
• Amyloidosis (genetic predisposition in Abyssinians).
• Glomerulonephritis.

TREATMENT RECOMMENDATIONS

Decompensated cats (e.g., animals that are dehydrated, anorectic, and/or vomiting) may benefit from hospitalization for more aggressive therapy. Outpatient therapy is appropriate for cats that are compensated, which includes cats that are eating and drinking with minimal vomiting and those that have been stabilized after hospitalization for a uremic crisis.

Initial Treatment
• IV crystalloid fluid therapy (i.e., lactated Ringer’s solution, Plasmalyte, 0.9% saline): $ 
  — Rehydration over 24 hours is usually appropriate if the patient is well perfused. If the patient is hypoperfused (“shocky”), fluid boluses should be administered until a response is noted. On the other hand, rapid fluid administration may lead to symptomatic cardiovascular compromise.
  — Fluid rate: Maintenance (66 ml/kg/day) plus replacement of dehydration (% dehydration × body weight in kilograms = liters deficit) plus ongoing losses (estimated volume of polyuria and vomiting).
  — If patient is adequately hydrated, administration of fluids at the maintenance rate plus 5% to 6% of body weight per 24 hours to promote diuresis is indicated.
  — Profound polyuria (sometimes >10 ml/kg/hr) necessitates a much higher rate of fluid administration to match the ongoing losses.

Potassium Supplementation of IV Fluids

<table>
<thead>
<tr>
<th>Serum Potassium (mEq/L)</th>
<th>mEq Potassium Chloride/L Fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5–4.5</td>
<td>20</td>
</tr>
<tr>
<td>3.0–3.5</td>
<td>30</td>
</tr>
<tr>
<td>2.5–3.0</td>
<td>40</td>
</tr>
<tr>
<td>2.0–2.5</td>
<td>60</td>
</tr>
<tr>
<td>&lt;2.0</td>
<td>80</td>
</tr>
</tbody>
</table>

$May need to be adjusted in patients receiving aggressive fluid administration.

• Potassium supplementation of IV fluids: Rate based on potassium measurement (Table 1), but do not exceed 0.5 mEq/kg/hr (potassium supplementation may need to be adjusted in patients receiving aggressive fluid administration). $
• Other treatments described for chronic therapy may be applicable (e.g., H₂ blockers, antiemetics), but injectable forms should be used until oral medications can be tolerated.
• Diet changes may not be accepted in anorectic or nauseated cats. To avoid food aversion, attempts to change the diet should be delayed until anorexia is resolving. Diet changes should be gradual, never abrupt, and should occur only after complete resolution of GI signs.

Outpatient Therapy$ 

Dietary Therapy $ 
• A restricted (but high-quality) protein and restricted phosphorus diet (“renal diet”) slows disease progression, prolongs survival, and decreases clinical signs of uremia. Many brands of renal diets are available, and palatability varies with the individual patient. Homemade diets may also be used. Dietary therapy should be recommended for all cats (symptomatic and asymptomatic) with CRD.
  — Available diets include Hill’s Prescription Diet Feline k/d, Eukanuba Multi-Stage Renal Formula, Royal Canin Renal L/P, Purina Veterinary Diets NF Kidney Function, Royal Canin/IVD Modified Formula.
  — Acidifying diets should be avoided.
  — Acceptance of diet changes can be problematic, particularly in severely affected patients. Renal diets should be gradually introduced when uremia is minimized.

$Cost estimate based on 3 months of therapy.
meals. Dose is titrated based on serum phosphorus concentration. Liquid forms are more effective than tablets. Aluminum carbonate capsules (opened and mixed with food) may be more palatable.

- Calcium acetate: 60–90 mg/kg/day. Hypercalcemia is a possible side effect.

- New phosphate binders (sevelamer hydrochloride, lanthanum carbonate) are available for use in humans. Veterinary experience with these agents is limited.

Elevated Gastrin Levels
Cats with CRD have elevated gastrin levels; histamine blockers are commonly used to decrease gastric acidity, which may be associated with anorexia, nausea, or vomiting.

- Famotidine (H$_2$ blocker): 2.5 mg/cat PO once daily.

- Omeprazole (proton pump blocker): 0.5–1 mg/kg/day PO.

Persistent Vomiting
Antiemetics may be useful in persistently vomiting cats.

- Metoclopramide: 0.2–0.4 mg/kg PO q6–8h. Acts as a motility modifier and central antiemetic.

- Limited information is available regarding 5-hydroxytryptamine (5-HT) serotonin antagonists (ondansetron, 0.22–1.0 mg/kg PO q8–12h), but anecdotally they seem to help in cases of intractable vomiting.

GI Ulceration
GI ulceration should be suspected in patients with hematemesis, melena, anemia, and an elevated BUN:creatinine ratio.

- Sucralfate: 0.25–0.5 g PO q8–12h for 1–2 weeks or until signs resolve.

Hypokalemia
Cats with low serum potassium should be supplemented with potassium (see Table 1 and Initial Treatment for IV supplementation guidelines).

- Potassium gluconate: 2–6 mEq/4.5 kg/day. 

- Potassium citrate: 50–75 mg/kg PO q12h; also treats acidosis.

Metabolic Acidosis
Treatment should be considered if total carbon dioxide is less than 15 to 16 mEq/L or pH is less than 7.2.

- Potassium citrate: 50–75 mg/kg PO q12h; also treats hypokalemia.

- Sodium bicarbonate: 8–12 mg/kg PO q8–12h. Many cats do not tolerate this therapy well.
Hypertension

- Amlodipine: 0.625–1.25 mg q12–24h. Start at low end and titrate upward as needed. First choice for most cases, effective as a single agent in about 60% of cases. $

- If amlodipine is ineffective as a single agent or if proteinuria is present, add an angiotensin-converting enzyme (ACE) inhibitor. BUN, creatinine, and electrolytes should be measured 1 week after starting therapy or increasing the dose. If creatinine continues to increase, ACE inhibitor therapy should be discontinued.
  - Benazepril: 0.25–0.5 mg/kg PO q12–24h. $
  - Enalapril: 0.25–0.5 mg/kg PO q12–24h. $

- If other classes of drugs or combinations are ineffective and tachycardia is present, β-blockers may be used as an adjunctive therapy:
  - Atenolol: 6.25–12.5 mg/day PO. $

Anemia of CRD

- Transfusion (whole blood or packed erythrocytes) for patients with severe clinical signs of anemia. Transfused cells are usually destroyed within 2 to 3 weeks. $$

- Human recombinant erythropoietin (epoetin alfa, Epogen [Amgen] and Procrit [Ortho Biotech Products]) should be restricted to use in cats that are symptomatic for anemia (weakness, anorexia, exercise intolerance, tachycardia, heart murmur, and the like) and used only in cats in which the potential benefit outweighs the potential risk; I generally reserve it for treatment of cats with a packed cell volume (PCV) of less than 20%. Up to 25% of cats treated will develop antibodies, which creates a transfusion-dependent state. $$
  - Starting dose: 100 U/kg SC three times/week.
  - Administration is decreased to twice/week when the cat’s PCV reaches the bottom of the target range (25%–30%).
  - Maintenance dose: 50–100 U/kg SC once or twice a week.
  - PCV should be monitored weekly during the initial treatment period and the dose adjusted as needed.

- Ensure adequate iron stores in cats receiving epoetin alfa (usually requires iron administration during initial treatment period). Oral iron is poorly absorbed and may cause GI upset. Injectable iron is preferred. $
  - Iron dextran: 50 mg/cat via deep IM injection once monthly.
  - Ferrous sulfate: 50–100 mg/cat PO once daily.
  - Iron proteinate (Pet Tinic, Pfizer Animal Health): 10–20 mg (3.5–7 ml) PO daily. (Note: This dose is higher than usual and may be less effective than other forms of iron).

Proteinuria

Significant proteinuria is uncommon in cats with CRD. A urine protein:creatinine ratio above 1.0 is considered abnormal, but some suggest that a level above 0.43 should prompt intervention. The small percentage of cats with significant proteinuria does seem to benefit from ACE inhibition, whereas ACE inhibition has no statistical effect on survival times in cats without proteinuria.

- Benazepril: 0.25–0.5 mg/kg PO q12–24h. $
- Enalapril: 0.25–0.5 mg/kg PO q12–24h. $

Alternative/Optional Treatments/Therapy

- Renal transplantation may be appropriate for some animals and/or owners. The greatest chance of success is in mildly to moderately azotemic cats without concurrent illness or infection. Transplantation should be considered at the point of early decomposition (i.e., when the cat can no longer maintain weight and signs of uremia cannot be controlled by treatments). $$$$$

- Dialysis: $$$$$
  - Hemodialysis is available in a limited number of places. Because of the ongoing need for dialysis (two to three times/week for the life of the patient) and the high cost, long-term hemodialysis is not commonly used.
  - Complications associated with peritoneal dialysis (especially catheter occlusion and peritonitis) have limited its use to acute settings.

Supportive Treatment

- Dietary therapy decreases the number of uremic crises and mortality. All cats with CRD should be encouraged to eat a renal diet if there are no contraindications (e.g., dietary allergies).

- ACE inhibitors may slow disease progression in the small subset of proteinuric cats.

- All other therapies listed in the Initial Treatment section are also supportive treatments to alleviate the signs associated with CRD.

Patient Monitoring

The frequency of monitoring depends on the clinical situation of the patient. Any change in the patient’s clinical condition should prompt a recheck evaluation. General guidelines are listed in Table 2. Clinical signs of
hypokalemia, hyperphosphatemia, anemia, and hypertension may not occur until the problem is severe; early interventions (before devastating clinical effects occur) can be implemented when abnormalities are detected on routine screenings.

- In cats receiving erythropoietin therapy, PCV and blood pressure should be measured weekly during the initial phase of therapy (i.e., while the cat is receiving the drug three times/week). As the PCV and the erythropoietin dose stabilize, the frequency of monitoring can be decreased to monthly.

- Cats with CRD are predisposed to UTIs, which may be asymptomatic. Routine urine culture is recommended even in the absence of clinical signs.

- Cats with proteinuria have shorter survival times. The need for or frequency of monitoring for proteinuria after initial diagnosis has not been determined.

- The effect of most antihypertensive medications can be assessed about 1 week after dose adjustments.

**Home Management**

- As uremia progresses and the number of uremic complications increases, the number of medications to control complications increases. The nursing care involved may require a substantial time commitment from the owner.

- The cost of treatment (including monitoring and medications) can be substantial, especially for cats with severe uremia (comparatively speaking, 1 year of treatment may exceed the cost of 1 year of the standard chemotherapy protocol for lymphoma in a cat).

**Milestones/Recovery Time Frames**

- **Hospitalized cats on IV fluids:** Once the prerenal component of the azotemia has resolved, the serum creatinine concentration usually decreases by at least 1 mg/dl/day (generally monitored q48h). When the creatinine concentration reaches a baseline value (i.e., no longer decreasing despite IV fluid therapy), fluid therapy should be tapered in preparation for patient discharge. Patients should be monitored for recurrence of dehydration during this time, and patients should be as well hydrated as possible at discharge. Aggressive fluid diuresis should be gradually tapered over approximately 2 to 3 days.

- **Cats receiving erythropoietin therapy will generally respond** (increased hematocrit, reticulocytosis) after 2 weeks of treatment, unless extraneous factors causing resistance (such as GI hemorrhage, infection, or chronic inflammation) are present.

**TREATMENT CONTRAINDICATIONS**

- **Potential drug interactions:**
  - Aluminum-containing phosphate binders may interfere with absorption of other medications, such as antibiotics.
  - Sucralfate is most effective in an acid environment and should be administered before histamine blockers or other antacids.

- **Potentially nephrotoxic drugs** (e.g., aminoglycoside antibiotics) or drug combinations (e.g., NSAIDs with ACE inhibitors) should be avoided. If use of these drugs is necessary, adequate hydration must be ensured and the patient monitored carefully for deterioration in renal function.

- Although anesthesia and associated hypotension are risk factors for worsening renal function, if anesthe-
sia cannot be avoided, ensuring adequate hydration before anesthesia, providing intraoperative fluids, and careful monitoring of intraoperative blood pressure (along with appropriate measures to correct hypotension) can minimize the risk.

PROGNOSIS

Favorable Criteria
CRD is a progressive disease, but the rate of progression is highly variable. There are no known predictors of impending decompensation. Most cats will die of CRD or related complications, although some maintain stable renal function and die of unrelated causes (such as neoplasia). Cats with mild to moderate renal disease commonly survive 1 to 3 years.

Unfavorable Criteria
An elevated urine protein:creatinine ratio (>0.43) predicts a shorter survival time. ACE inhibitor treatment (e.g., benazepril) prolongs survival in cats with a protein:creatinine ratio above 1.

RECOMMENDED READING


