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Graduado en la Universidad de Melbourne, pasó un año como interno clínico en la misma institución después de su graduación. Trabajó en la práctica veterinaria de bovinos de carne y leche en Alberta, Canadá. Concluyó su residencia de Medicina Interna en Animales de Compañía en la Universidad de Pennsylvania. Después de varios años como profesor en la Universidad de Florida, donde se especializó y estudió enfermedades de las vías urinarias, en 1992 llegó a ser profesor y jefe del Departamento de Ciencias Clínicas Veterinarias en la Universidad del Estado de Louisiana, Facultad de Medicina Veterinaria. El Dr. Senior es Diplomado del Colegio Americano de Medicina Interna Veterinaria (ACVIM) y del Colegio Europeo de Medicina Interna Veterinaria (Animales de Compañía). Es coordinador de la Conferencia Norteamericana de Veterinaria. Participó en el rescate de animales después del huracán Katrina.
Progression of CRF: Renal function usually declines progressively in patients with CRF irrespective of the primary cause and even if the cause is no longer apparent. Factors that may contribute to spontaneous progression of CRF in mammals are shown in Table 1. Although glomerular hypertension has been documented in dogs with CRF, its role in causing progression of CRF in dogs is not clear. In addition, moderate dietary protein restriction does not appear to reduce progression of renal disease in dogs and cats as it does in other species. Dietary phosphate restriction has been reported to limit progressive loss of renal function in dogs and to prevent renal mineralization in cats. The effect of systemic hypertension and renal ammoniagenesis on progression of CRF has not been studied in dogs and cats.

Table 1. Factors that may contribute to progression of CRF in mammals

<table>
<thead>
<tr>
<th>Factor</th>
<th>Clinical Association</th>
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<tr>
<td>Glomerular hypertension</td>
<td>High protein diet</td>
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<td></td>
<td>High calorie diet</td>
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<td></td>
<td>High n-6 fatty acid diet</td>
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<td>Renal mineralization</td>
<td>Dietary phosphorus</td>
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<td></td>
<td>Renal secondary hyperparathyroidism</td>
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<td>Systemic hypertension</td>
<td>High sodium intake</td>
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<td>Renal ammoniagenesis</td>
<td>Metabolic acidosis, hypokalemia</td>
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DIAGNOSIS:

The presence of CRF is established based on clinical history, physical examination and laboratory test results. Typical test results include normocytic normochromic anemia, lymphopenia, azotemia, hyperphosphatemia, and metabolic acidosis with increased anion gap. Both lipase and amylase may be increased 2.5–3 times normal without the presence of pancreatitis. Urinalysis shows isosthenuria, mild proteinuria (unless the disease process specifically involves the glomerulus), and a benign urine sediment. On those occasions when tubular casts are observed, they tend to have a wide diameter. Renal size, shape, and density may be abnormal on radiographic and ultrasonographic evaluation. Renal biopsy shows glomerular and tubular atrophy with variable degrees of glomerulosclerosis and mononuclear interstitial infiltrate with fibrosis. Tremendous variation exists with presenting signs and the degree of azotemia at the time of presentation.

MANAGEMENT:

Many animals first presented with CRF require stabilization of an acute crisis with appropriate fluid and electrolyte treatment. Causes of both renal damage and progression of renal failure must be identified and eliminated, if possible. Owners should be advised of their pet’s limited adaptability to sudden changes in environment and diet.

Appetite enhancers and antiemetics: Food may be more palatable if it is warmed or if the texture is familiar to the patient. The low-protein, low-sodium diets recommended for management of CRF patients are intrinsically unpalatable to dogs and cats. To avoid the possibility of the animal associating the introduction of a special diet with the adverse environment of the clinic, dietary modification may best be reserved for when the patient has returned home. Patients usually eat more each day if they are fed small frequent meals rather than larger less frequent meals. Low-dose calcitriol treatment and administration of erythropoietics also seem to increase appetite (see below). Improved appetite and decreased vomition can be achieved in some patients with H$_2$-histamine receptor antagonists such as cimetidine hydrochloride (5 mg/kg p/o q8–6h in dogs, 2.5–5 mg/kg q24–12h in cats) or ranitidine hydrochloride (0.5 mg/kg p/o q12h in dogs and cats). For gastric motility disturbances, metoclopramide (0.2–0.4 mg/kg p/o q8h) has also proven effective in controlling vomiting in dogs and cats. For refractory vomiting, centrally acting anti-emetics...
can be used as a choice of last resort, e.g. trimetho-benzamide (3 mg/kg p/o q8h (dogs only); prochlor-perazine (0.13 mg/kg p/o q8–6h in dogs and cats); and chlorpromazine (0.5–2 mg/kg p/o q24–6h in dogs and cats). Long-term use of centrally-acting antiemetics is not recommended because they cause drowsiness.

**Dietary adjustment:** Nutrition is the basis of management of CRF. Fresh, clean water must be available at all times and the diet should provide 70–110 kcal ME/kg/day. Actual amounts need to be adjusted based on each animal’s body condition and response to feeding.

Protein restriction In regulating protein intake in dogs with CRF, a useful clinical goal is the reduction of BUN levels to <80 mg/dl (urea 13.3 mmol/l). Low-protein diets cause dogs with CRF to appear stronger, act more lively, and have healthier hair coats. In addition, urine volume is decreased. Because uremic dogs tend to be in a catabolic state, the minimum dietary protein requirement may be higher than in a normal dog. Dogs in CRF do not tolerate diets providing less than 2.2 g protein/kg body weight/day and in cats the lower limit is 4.25 g/kg body weight/day. When dietary protein restriction is too severe in dogs with CRF, hypoalbuninemia, anemia, and metabolic acidosis have been reported, and regular tests should be performed to assess these values.

**Renal secondary hyperparathyroidism:** Renal secondary hyperparathyroidism can be controlled by low-phosphate diet, phosphate binding agents given orally and low-dose calcitriol. When dietary phosphate intake is reduced commensurate with reduced GFR, renal secondary hyperparathyroidism can be controlled. Dietary levels of phosphate can be reduced to 30–60 mg/100 kcal ME in dogs and 100 mg/100 kcal ME in cats. The goal should be to reduce serum phosphorus levels to <6 mg/dl (1.9 mmol/l).

When dietary phosphate restriction alone fails to reduce serum phosphate to below this level, phosphate binding agents can assist in achieving this goal. Suitable phosphate binders include aluminum hydroxide gel and aluminum carbonate. Although the liquid forms may be more effective, tablet or capsule forms are more easily given and better accepted by dogs. The suggested dose for aluminum hydroxide or aluminum carbonate is 10–30 mg/kg p/o q8h in both dogs and cats. Phosphate binders are more effective in lowering serum phosphate when given in conjunction with a low-phosphate diet. Calcium salts given to normalize serum phosphate levels should be given with meals to minimize their hypercalcemic effect. Hypercalcemia with persistent hyperphosphatemia causes soft tissue mineralization and rapid progression of renal failure.

Serum PTH levels often remain abnormally high in CRF even in animals fed a low-phosphate diet and treated with phosphate binders. If serum phosphate levels are < 6 mg/dl, direct inhibition of PTH production can be provided by calcitriol given at 1.2–3.5 ng/kg p/o q24h, a dose that minimally affects intestinal calcium absorption. Serum calcium and phosphorus levels must be monitored at regular intervals throughout calcitriol treatment and PTH levels should be measured to determine effectiveness of treatment. Hyperparathyroidism is known to be detrimental but the precise benefits of reducing PTH levels using calcitriol in patients with CRF are yet to be determined.

**Sodium restriction:** Moderate dietary sodium restriction is recommended in dogs and cats with CRF: 50–60 mg/100 kcal ME. Even in advanced CRF, renal sodium excretion can accommodate a wide range of sodium intake provided dietary adjustment is made gradually over several days. However, high sodium intake should be avoided because it can exacerbate hypertension and cause retinal detachment and blindness.

**Alkali treatment:** Alkali treatment should be given to maintain a serum bicarbonate level of >17 mEq/l (mmol/l) in both dogs and cats. Doses required are variable but should start at 0.1 mEq (mmol/l)/kg p/o q12–8h. For sodium bicarbonate this corresponds to 10 mg/kg p/o q12–8h. To avoid excessive sodium supplementation when correcting metabolic acidosis, nonsodium alkalinizers such as potassium citrate and potassium gluconate may be used.

**Potassium supplementation:** Potassium supplementation is often required in cats in CRF to maintain the serum potassium level >4 mEq/l (mmol/l). Potassium gluconate can be given at 2–6 mEq (mmol/l)/day p/o with higher doses to begin with and lower doses for subsequent daily maintenance. Serum potassium levels should be closely monitored during the initial treatment of cats with severe potassium depletion and polymyopathy.

**Vitamin supplementation:** Dietary supplementation with B-complex and C vitamins is used in human uremic patients because they tend to become deficient in folate, pyridoxine, and ascorbate. Similar
recommendations are made for dogs and cats but definitive data regarding requirements in these species are not available.

**Lipid supplementation:** High N:3 to N:6 polyunsaturated fatty acid diets (1:5) may prevent progression of CRF in dogs. All commercial CRF diets have been adjusted accordingly.

**Correction of anemia:** The anemia of CRF in dogs is best treated with epoetin alfa (50–100 U/kg s/c twice weekly). Many patients with anemia of CRF are iron depleted. Appropriate replacement is provided by giving ferrous sulfate (100–200 mg p/o q24h in dogs; 50–100 mg p/o q24h in cats). Treatment with epoetin alfa can begin once serum iron concentration, total iron binding capacity, and transferrin saturation are normal. The patient’s PCV should be measured regularly to determine the effectiveness of treatment and to prevent polycythemia caused by overdosage. Once the anemia is corrected, epoetin alfa can be given in lower doses and less often. Treatment with epoetin alfa is usually only reserved for CRF patients with severe anemia (e.g. PCV <25%) because the drug tends to be immunogenic in about 60% of dogs and cats. Fortunately the antibody response is often not extreme; however, in the 39% of dogs that develop a high antibody titer, epoetin alfa becomes ineffective and anemia returns.

Prior to the development of epoetin alfa, anabolic steroids (e.g. nandrolone decanoate, 1–1.5 mg/kg i/m weekly) were recommended to correct the anemia of CRF. This therapy is only minimally effective at correcting anemia in human patients and the efficacy of anabolic steroids as hematopoietics in dogs and cats has not been demonstrated.

**Antihypertensives:** Antihypertensives should be reserved for those patients with documented severe hypertension (systolic: >180 mmHg [24 kPa], diastolic: >120 mmHg [16 kPa], and mean: >140 mmHg [18.7 kPa]) bearing in mind that even severe hypertension can be clinically silent. The most obvious clinical consequences of hypertension are retinal detachment and acute blindness which only become apparent when blood pressure values are extremely high. Consequently, it is usually not necessary, advisable, or even possible to reduce pressures all the way down to the normal range. Pressures of <160 mmHg (21.3 kPa) systolic, 110 mmHg (14.7 kPa) diastolic, and 130 mmHg (17.3 kPa) mean most likely will prevent ocular complications.

Treatment for hypertension should be instituted in a step-wise manner, with re-evaluation of blood pressure after 2–4 weeks of treatment before adding the next level of treatment. The first step is to feed a low-sodium diet. The second step calls for treatment with an angiotensin-converting enzyme (ACE) inhibitor, e.g. enalapril or benazapril (0.5 mg/kg p/o q24–12h) in dogs and amlodipine (0.625–1.25 mg/kg p/o q24h) in cats. A third step can include the beta-blocker atenolol given at 2 mg/kg p/o q24h in both dogs and cats. Calcium channel blockers such as diltiazem may also be used for vasodilation. When multiple drug regimens are required, the potential for drug interactions becomes more likely, particularly in CRF when drug retention and enhanced drug effects may occur.

**Hemodialysis and transplantation:** Hemodialysis delivered 2–3 times weekly for maintenance of dogs and cats in CRF is offered at a few referral centers in the US, and the procedure is technically feasible in all but the smallest of dogs. However, reliable long-term vascular access and the expense of equipment, supplies, and trained technician support remain major obstacles to widespread use.

Renal transplantation has yielded some success in cats but limited success in dogs because of problems with tissue rejection. Immunosuppressive agents and antilymphocyte serum have been used to control rejection and results at the few centers performing the procedure offer some encouragement that survival time can be increased. The procedure is expensive.

**Drug dose adjustment in CRF:** Adverse drug side-effects are more common in animals with CRF. Drugs excreted primarily by the kidneys tend to accumulate to higher than desired plasma levels when normal doses are given. Also, drug distribution and protein binding are altered in azotemia so that side-effects are enhanced.

Drugs primarily excreted by nonrenal systems are less likely to cause a problem. Drugs primarily excreted by the kidneys may be: 1. innocuous even at very high blood concentration; 2. toxic at high plasma concentration; or, even worse, 3. nephrotoxic at high plasma concentration.

For drugs excreted primarily by the kidneys, dose adjustment ideally should be based on measured drug blood levels or by using an accurate measurement of the patient’s GFR to estimate the dose fraction (Kf).
Kf = patient GFR/normal GFR

Dose modification can be made in two ways:
• Dose reduction: multiply the normal dose by Kf.
• Interval adjustment: divide the normal dose interval by Kf.

As GFR estimations are not available in most clinical situations, the ratio of the patient’s serum creatinine value to the middle range of normal for serum creatinine for dogs in the clinician’s own laboratory can be used as a rough estimate of Kf. Aminoglycoside antimicrobials require precise dose adjustment calculated from Kf. Increased interval, fixed dose adjustment appears to be less nephrotoxic than reduced dose, fixed interval adjustment.

**Prevention of progression:** Current recommendations call for a low phosphate diet with a high N:3 to N:5 polyunsaturated fatty acid ratio (1:5) and further treatment with an angiotensin-converting enzyme (ACE) inhibitor, e.g. enalopril or benazapril (0.5 mg/kg p/o q24–12h).