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Feline Chronic Renal Failure: Long-Term Medical Management

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ABSTRACT: Chronic renal failure (CRF) is one of the most common illnesses of geriatric cats. Common clinical signs include polydipsia, polyuria, decreased appetite, weight loss, and vomiting. Although CRF is incurable, it may be possible to delay the progression of the disorder by feeding an appropriate diet and by monitoring and normalizing (if possible) several parameters, including blood pressure, serum phosphorus and potassium levels, parathyroid hormone levels, and proteinuria.

Chronic renal failure (CRF) is one of the most common illnesses of geriatric cats. In 1990, there were 45 cases of CRF for every 1,000 cats admitted to veterinary teaching hospitals. In 2000, the number increased to 96 cases per 1,000 cats. Clearly, the incidence of CRF is increasing.¹

Unless the underlying cause of the initial renal injury can be discovered and treated, CRF invariably progresses. In many cases, even after identification of the initial cause of the renal injury, a threshold or “trigger” point has already been reached, and self-perpetuating mechanisms of kidney destruction have been activated. In most cases of CRF, an underlying cause of the initial renal insult cannot be found.

In the past, most practitioners have qualitatively classified CRF as mild, moderate, or severe, based on laboratory findings and clinical signs. A less arbitrary classification system has been developed by the International Renal Interest Society (IRIS; Table 1).² In this system, stages are based on degree of kidney function:

- clinical signs have not developed. Renal disease is rarely detected in this stage.
- In **stage 2**, renal disease has progressed, glomerular filtration has decreased, and mild azotemia has been detected. Clinical signs may not be detected. The earliest clinical signs attributable to renal dysfunction are polyuria and polydipsia, which occur when approximately 66% of nephron function is lost. This happens in late stage 2 or early stage 3.
- In **stages 3 and 4**, at least 75% of nephron function has been lost. Azotemia is present, and most cats have overt clinical signs of renal dysfunction. Cats are particularly adept at urine concentration: some cats with primary glomerular disease may become azotemic while retaining the ability to concentrate their urine above a specific gravity of 1.035.

The IRIS classification system should be used as a guideline and not necessarily as a strict prognostic indicator because a significant prerenal component is often superimposed on the azotemia. Correction of acute dehydration may reveal a different “picture” regarding the true level of renal azotemia.



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Table 1. IRIS Classification of Stages of Kidney Disease²

Stage	Renal Azotemia	Creatinine Concentration (mg/dl)
1	Nonazotemic	<1.6
2	Mild	1.6–2.8
3	Moderate	2.9–5.0
4	Severe	>5.0

CRF is incurable. With the exception of a kidney transplant, it is difficult or impossible to improve kidney function in cats with CRF. However, recent developments (i.e., a variety of dietary and drug interventions) have made it possible to delay the progression of renal failure, extend a cat's survival time, and improve the quality of life.

Therapy for cats presenting with CRF and clinical signs can include simple dietary changes to a hospital stay of several days, depending on disease severity and how early the disease has been detected. Fluid therapy remains the cornerstone of treatment for hospitalized cats with CRF. Fluid administration corrects dehydration and increases urine production, reducing azotemia. Fluid therapy can also correct acid–base imbalances and help restore normal phosphorus and potassium levels. This is crucial because increased phosphorus levels and decreased potassium levels can accelerate progression of the renal damage.^{3,4} Cats with CRF may have trouble conserving water-soluble vitamins (the B vitamins and vitamin C) because of excessive loss through urine,^{5,6} and some of these vitamins can be replaced through fluid therapy as well.

Nutrition is an essential part of the therapy for CRF. Most cats hospitalized with CRF have a decreased appetite or no appetite. During hospitalization, nutritional support can be achieved through force feeding, tube (nasogastric or esophagostomy) feeding, or intravenous feeding, depending on the severity of the inappetence, the degree of malnutrition, and the cat's demeanor.

Nausea often accompanies anorexia and is a common finding in cats with CRF. Because the kidneys are responsible for excreting the hormone gastrin, many cats with CRF are hypergastrinemic and produce excessive amounts of gastric acid.⁷ This may contribute to anorexia and vomiting in many cats with CRF. Administration of

H₂-receptor antagonists such as famotidine, either subcutaneously or orally, may be beneficial in this regard.

A major objective of acute therapy is to significantly decrease the level of azotemia. Reducing the blood urea nitrogen and creatinine to normal levels is rarely possible, however, and should not necessarily be the practitioner's goal. During hospitalization, blood urea nitrogen and creatinine levels should be measured every 2 or 3 days until a plateau is reached. After several days, many cats improve clinically (e.g., their appetite returns, vomiting decreases or ceases, hydration is restored) and can be released to the owner. A typical hospital stay is 3 to 6 days.

It should be made clear to the owners of cats with CRF that the treatment the cat received while hospitalized does not return the kidneys to normal and that a conscientious home maintenance program will be necessary for the remainder of the cat's life.

DIETARY MANAGEMENT

Protein, when metabolized, results in uremic toxins that failing kidneys cannot properly excrete. Reducing the amount of protein in the diet lessens azotemia, thereby helping ameliorate clinical signs, such as weight loss, poor appetite, vomiting, and lethargy. In the past, choices of protein-reduced diets for cats were very limited. Fortunately, several companies now manufacture palatable feline kidney-failure diets that are restricted in protein as well as phosphorus and sodium.

Much controversy has been generated as to whether dietary protein restriction can actually slow the progression of kidney disease in cats. However, several recent studies have confirmed that dietary modification can have a significant impact on the mortality rate of affected cats. Cats with naturally occurring renal failure that were fed a veterinary renal diet lived considerably longer (median survival: 633 days) than cats that did not receive (or refused to eat) this diet (median survival: 264 days).⁴ Another study⁸ compared 23 cats fed a maintenance food with 22 cats fed a prescription renal failure diet. Cats fed the maintenance food had a significantly greater number of uremic episodes than did cats fed the renal diet. Throughout the 2-year study, none of the cats fed the renal diet died from kidney-related causes, whereas five cats in the maintenance group died from renal causes.⁸ These data led the authors to recommend feeding a renal diet to cats with CRF early in the course of disease (i.e., when the patient's serum creatinine level exceeds 2 mg/dl). More recently, a retrospective study⁹ compared 175 cats with CRF fed maintenance diets

with 146 cats fed special renal failure diets. The survival time of cats that received the conventional diets was 7 months compared with 16 months for cats fed a prescription diet.⁹ These studies confirm that cats that consume a prescription kidney-failure diet have increased survival times and a good quality of life compared with cats that do not (or will not) eat this type of diet. Many manufacturers (i.e., Hill's Pet Nutrition, Iams, Nestlé Purina PetCare, Royal Canin) now offer prescription kidney-failure diets.

Because of the finicky nature of cats, compliance can be a problem after a prescription diet has been prescribed. If a client is sent home with a large (4 to 8 lb) bag of a dry renal diet and discovers that his or her cat will not eat it, the client may mistakenly assume that the cat will dislike all renal diets, and the client may not want to purchase a different brand of dry renal food. Rather than prescribing an entire bag of one type of dry food or an entire case of canned renal diets, I advocate creating a sampler pack (*Veterinary Economics*, "Samplers

and hypokalemia in cats with CRF may result from inadequate consumption of potassium, dietary issues, enhanced renal loss of potassium, or a combination of these factors.¹¹

Hypokalemia contributes to the progression of kidney failure.³ In many cats with CRF and hypokalemia, kidney function improves when low potassium levels are restored to normal using oral or parenteral potassium therapy, suggesting that hypokalemia may induce a reversible reduction in the glomerular filtration rate (GFR).^{10,11} Potassium supplements (usually in the form of potassium gluconate) are currently available in a variety of palatable forms (tablets, liquids, granules or powder to add to food, flavored ointments), increasing the likelihood of successful administration in cats that tend to be finicky or difficult to medicate. Potassium citrate can also be used to supplement potassium and is an ideal choice for cats with metabolic acidosis because citrate is an effective alkalinizing agent.¹² The serum potassium concentration should be monitored 7 to 14

Chronic renal failure, although incurable, can be successfully managed through a variety of nutritional, pharmaceutical, and nutraceutical interventions.

Boost Dietary Compliance," December 2006, p. 24) consisting of one can and one small sandwich bag of dry kibble of each company's renal failure diet. Clients can then offer their cat a variety, maximizing the chances of finding a palatable choice. Whether one brand offers more benefit than another has not been determined; however, the importance of diet in managing CRF should not be underestimated.

MONITORING POTASSIUM

Hypokalemia is a common finding in feline CRF. Approximately 20% to 30% of cats with CRF are hypokalemic.¹⁰ Total body potassium depletion is likely to be even higher. It is unclear whether hypokalemia is a cause or consequence of CRF or both.¹ Most instances of hypokalemia are mild, with no apparent clinical signs. Marked hypokalemia, however, can lead to general muscle weakness. In more severe cases, cats can develop hypokalemic polymyopathy, which, if misdiagnosed, can lead to paralysis of the respiratory muscles and death by respiratory arrest if aggressive potassium supplementation is not initiated. Potassium depletion

days after supplementation has been initiated, and the dose should be adjusted accordingly.

VITAMINS AND OMEGA-3 FATTY ACIDS

Cats with CRF are often polyuric and may have difficulty conserving water-soluble vitamins. Therefore, a daily multivitamin should be given to all cats with CRF.⁵

In humans with CRF, increased free radical production and antioxidant depletion may play roles in progression of the disease,¹³ and supplementation of the diet with antioxidants (e.g., vitamins A, C, and E) has been shown to reduce oxidative stress in humans with chronic kidney disease.¹⁴ A recent study, in which cats with CRF were fed a prescription renal failure diet that was supplemented with additional vitamin E (742 mg/kg), vitamin C (84 mg/kg), and β -carotene (2.1 mg/kg), showed a significant reduction of oxidative DNA damage.¹⁵

Prescription diets designed for cats with renal failure are restricted in protein, phosphorus, and sodium. Recently, manufacturers have been adding a larger proportion of omega-3 fatty acids to these diets based on studies showing evidence of the beneficial effects of

these fatty acids in dogs¹⁶ and, presumably, cats with CRF. While it has been shown that cats fed prescription renal failure diets live longer and have an improved quality of life compared with cats fed conventional diets,^{4,8,9} it is impossible to say which single nutrient alteration (or combination of alterations) is responsible for the improvement. In a retrospective study that evaluated the median survival time of cats fed a variety of renal failure diets versus maintenance diets, not only did the cats fed the modified diets live longer (median survival: 16 months versus 7 months), but the diet associated with the longest survival time (23 months) had particularly high levels of eicosapentaenoic acid.⁹ The ideal ratio of omega-6:omega-3 fatty acids in renal failure diets has not been determined. For cats unwilling to eat a prescription renal diet, it seems reasonable to consider daily supplementation with omega-3 fatty acids.

CONTROLLING EXCESSIVE URINARY PROTEIN LOSS

Proteinuria is a risk factor for the progression of CRF in humans, and controlling proteinuria has been shown to increase survival times in humans with CRF. A recent study has shown that the severity of proteinuria in cats with naturally occurring CRF has prognostic significance regarding survival time.¹⁷

increased production of mesangial matrix (i.e., glomerulosclerosis), resulting in further kidney damage.

Measuring the intraglomerular pressure is impossible in a clinical setting; however, proteinuria is a reasonable indicator of elevated glomerular pressure. Proteinuria can be detected and quantified through a simple urine test—the urine protein:creatinine ratio (UPC). In cats, a UPC of 0.5 or higher is indicative of persistent renal proteinuria.¹⁹ In a study that examined the relationship between survival time and proteinuria in cats with CRF, the UPC was shown to be a significant predictor of survival time. The median survival time of cats with a UPC lower than 0.43 was 766 days compared with only 281 days for cats with a UPC higher than 0.43.¹⁷ Although cats with CRF typically have low protein concentrations in their urine, the degree of proteinuria is of prognostic importance.

ACE inhibitors are ideally suited to treat elevated intraglomerular pressure because they selectively dilate the efferent arteriole of the glomerulus. The ACE inhibitor benazepril has been shown to prolong survival time and reduce proteinuria in a large clinical trial in humans²⁰ and to have beneficial hemodynamic effects (normalization of glomerular hypertension with a maintained or an increased GFR) in a model of CRF in cats.²¹ Benazepril has been studied in cats with naturally occurring CRF.^{22,23} In a double-blind, prospective, randomized clinical trial involving 192 cats with CRF,

Hypokalemia and hyperphosphatemia, if not corrected, can accelerate the progression of chronic renal failure.

As the kidneys start to fail and nephrons are lost, hemodynamic adaptations occur in some of the remaining nephrons, causing increased single nephron GFR, glomerular plasma flow, and hydraulic pressure across the glomerulus.¹⁸ Angiotensin-converting enzyme (ACE) catalyzes the generation of angiotensin II from angiotensin I within the kidneys, causing vasoconstriction of glomerular arterioles. The efferent arteriole is preferentially constricted, leading to increased intraglomerular capillary pressure. Initially, this is adaptive, allowing maintenance of excretory function and total kidney GFR. However, ongoing intraglomerular hypertension is ultimately maladaptive, leading to increased trafficking of macromolecules into the mesangium, resulting in proliferation of mesangial cells and

benazepril produced a significant reduction in proteinuria in all cats that received it, including those with minimal proteinuria (UPC <0.2), although the effect was largest in cats with higher UPCs. There was no difference in survival times between cats receiving benazepril or a placebo when all 192 cats were compared. However, there was a trend ($P = .27$) toward longer survival times in the 13 cats with more marked proteinuria (UPC >1.0; 402 days) compared with cats that received a placebo (149 days).²² A beneficial effect of benazepril on appetite was observed in cats with more pronounced proteinuria (UPC >1.0). Benazepril was well tolerated in all cats. In another study of 61 cats with CRF, several nonsignificant trends were observed, including lower plasma urea and creatinine concentra-

tions, improved quality of life, and a delay in the progression of stage 2 or 3 CRF to stage 4 in cats that were given benazepril compared with those that received a placebo.²³ In summary, benazepril appears to decrease proteinuria in all cats, thereby increasing survival times of those with marked proteinuria and apparently slowing the progression of renal disease in cats diagnosed with CRF.

PHOSPHORUS RESTRICTION, RENAL SECONDARY HYPERPARATHYROIDISM, AND CALCITRIOL

Renal secondary hyperparathyroidism occurs when the parathyroid glands secrete excessive parathyroid hormone (PTH) as a result of CRF. This is due to several factors, the primary one being an impaired ability to synthesize calcitriol, the natural, biologically active form of vitamin D.

The kidneys are responsible for the final step in the synthesis of calcitriol from its precursor, 25-hydroxyvitamin D. As the kidneys fail, there are fewer healthy proximal tubule cells with the enzyme system necessary to catalyze this synthesis.

Phosphorus is filtered from the bloodstream by the kidneys. When the kidneys begin to fail, the phosphorus levels begin to rise. When serum phosphorus levels are high, phosphorus can combine with calcium in the bloodstream. This is known as *the law of mass action*. The formation and deposition of calcium phosphate in the soft tissues, including the kidneys, can cause further renal damage. A serum phosphorus level greater than 7 or 8 mg/dl decreases the serum ionized calcium level approximately 0.1 mg/dl, which is enough to stimulate PTH secretion. Also, phosphorus inhibits the enzyme system involved in calcitriol synthesis. As the phosphorus level begins to rise in cats with CRF, calcitriol synthesis is further inhibited. This is another way in which hyperphosphatemia promotes the development of renal secondary hyperparathyroidism.

Calcitriol is necessary for the intestines to properly absorb dietary calcium; thus calcitriol plays a role in maintaining a normal calcium level in the bloodstream. As the kidneys fail and become incapable of producing an adequate amount of calcitriol, the serum calcium level begins to fall. To maintain an adequate calcium level in the bloodstream, the parathyroid glands release PTH, restoring and maintaining a normal calcium level.

In summary, the parathyroid glands secrete excessive PTH as a result of an elevated phosphorus level, an

inadequate calcitriol level, or both. Therefore, the PTH level can be reduced by administration of calcitriol or control of dietary phosphorus.

Controlling PTH levels is beneficial in patients with CRF. Although PTH production is physiologically appropriate, excessive amounts of PTH are toxic to the kidneys and other organs. Toxic effects of PTH on the brain likely contribute to depression and stupor in cats with renal failure.²⁴ In experimental animals, excessive PTH also slows nerve conduction, contributes to the anemia that often occurs with CRF, and enhances the progression of kidney failure.²⁴ This likely occurs in cats as well.

When administered to animals with renal secondary hyperparathyroidism, calcitriol causes a reduction in PTH production by the parathyroid glands.²⁰ Calcitriol has been used in managing renal secondary hyperparathyroidism in humans with end-stage renal disease for its ability to decrease PTH secretion and inhibit parathyroid gland hypertrophy. Although calcitriol would be expected to normalize elevated PTH levels in cats with CRF, a recent study in which calcitriol was administered daily (2.5 ng/kg PO q24h) or intermittently (8.75 ng/kg PO q84h) failed to reduce the PTH level in 10 cats with CRF.²⁵ However, a dose titration study was not conducted, and it is possible that the calcitriol dose, which was based on clinical recommendations made for dogs,²⁴ could have been too low. Calcitriol has many direct beneficial effects in uremic animals independent of its PTH-lowering properties²⁴ and may still have a place in treating renal secondary hyperparathyroidism in cats with CRF.

Prescription kidney-failure diets for cats are phosphorus restricted. Limiting phosphorus consumption appears to slow the progression of CRF in humans and dogs, and there is evidence that dietary phosphorus restriction also limits renal injury in cats with CRF.⁴

Orally administered phosphorus binders, such as aluminum salts (e.g., aluminum hydroxide) and calcium salts (e.g., calcium carbonate), are most commonly administered. Aluminum salts have been removed from the human market because of concerns regarding aluminum toxicity. Many clients (and some practitioners) mistakenly believe that the commonly used phosphorus binders work by directly lowering the serum phosphate level. Phosphate binders work by binding with phosphate in food, thereby preventing the absorption of phosphate. Administering a phosphate binder independent of feeding has no effect on the serum phosphate level.

Sevelamer hydrochloride (Renagel, Geltex Pharmaceuticals), an organic polymer that does not contain calcium or aluminum, binds phosphorus in the intestinal tract. This drug has been used safely in cats but can also bind vitamins in the intestinal tract. Animals receiving this drug should be given a vitamin supplement as a precaution. Lanthanum carbonate (Fosrenol, Shire) is a new intestinal phosphate binder for humans that does not contain calcium or aluminum. Reports of its clinical use in dogs or cats are lacking. Epakitin (Vétoquinol USA) is a phosphate binder consisting of calcium carbonate and chitosan. Most cats dislike the taste of liquid phosphorus binders, and the tablets are often difficult to administer because of their large size. Epakitin is a palatable powder that can be mixed into canned food. Phosphorus binders are most effective when given at, or shortly after (within 2 hours), a meal.

I use intestinal phosphate binders based on a recently published roundtable discussion on the topic.²⁶ The degree of phosphate restriction depends on the IRIS stage of CRF. At 2 months after treatment, the target serum phosphate level for cats in stage 2 is 2.5 to 4.5 mg/dl. As the renal disease progresses to stage 3, the high end of the target range increases to 5.0 mg/dl; as the disease progresses to stage 4, the target range increases to 6.0 mg/dl.²⁶ Phosphorus restriction may initially be achieved through a phosphorus-restricted diet alone. However, if the serum phosphate concentration is greater than 6 mg/dl 4 weeks after dietary therapy, phosphate binders should be administered.²⁶

Phosphorus restriction was traditionally initiated when a high phosphorus level was detected on a blood test. However, phosphorus restriction may be beneficial when initiated before the onset of an overtly high phosphorus level because renal secondary hyperparathyroidism occurs before the serum phosphorus concentration exceeds the normal range and because the fasting serum phosphorus concentration may not accurately reflect overall phosphorus metabolism.^{11,26} More research is necessary before specific recommendations can be made; however, phosphorus should probably not be restricted in a patient with a serum phosphate level less than 4.5 mg/dl unless the serum PTH level is elevated.²⁶ The return of serum phosphorus to a normal level does not guarantee that the PTH levels will return to normal because phosphorus restriction is effective only in animals with an adequate number of healthy proximal tubule cells to synthesize calcitriol once the inhibitory effects of excessive phosphorus are controlled. For patients with PTH levels that remain

high despite a seemingly well-controlled phosphorus level, administration of calcitriol may be necessary to control the PTH level. Because the effective dose of calcitriol necessary to reduce the PTH level in cats with CRF and renal secondary hyperparathyroidism has not been determined and because reduction of the PTH level through control of dietary phosphorus intake has been shown to improve survival in cats^{4,27} with CRF, dietary phosphorus restriction should be the initial approach to control elevated PTH levels in these cats. If the PTH level remains elevated after hyperphosphatemia has been controlled, administration of calcitriol should be considered. Calcitriol should not be given to cats until hyperphosphatemia has been controlled. If the calcium \times phosphorus product exceeds 70 or the serum phosphorus level remains higher than 6.0 mg/dl, calcitriol should not be administered because mineralization of soft tissue, including renal tissue, is a risk.

CRF-management diets are already phosphorus restricted, and feeding this type of diet alone may be sufficient to prevent hyperphosphatemia. If a cat with CRF refuses to eat a prescription renal diet, the use of a phosphate binder becomes even more important. It has been shown that administration of a phosphate binder to cats eating a maintenance diet with a standard amount of phosphorus decreases the serum phosphate level.²⁶

FLUID THERAPY

Fluid therapy is the cornerstone of treating acutely ill cats with CRF and an important factor in the long-term management of cats with CRF. Cats with CRF are usually polyuric and have higher fluid requirements than other patients. If water losses exceed water consumption, dehydration and volume depletion may occur. Dehydration decreases renal perfusion and may lead to a rapid, severe decline in renal function. While there are ways to encourage water intake at home (e.g., feeding canned rather than dry food; adding water or broth to food), the fluid intake of cats with CRF is often inadequate, and some cats require subcutaneous fluid administration. Most cats tolerate this well, and clients can easily be taught how to do this. Fluids should initially be administered every day and may be tapered to every other day or even less frequently, depending on how the cat is feeling at home. There is apparently no consensus among veterinarians regarding whether or when subcutaneous fluid therapy should be initiated in a cat. In my experience, acutely ill cats with CRF that require hospitalization and intravenous fluid therapy usually require subcutaneous

fluid therapy at home to maintain adequate diuresis. However, many cats that are incidentally discovered to be in stage 2 (or even stage 3) through routine blood work are often managed well at home without the need for subcutaneous fluids. In general, cats seem to be clinically more sensitive to changes in hydration status than are dogs and sometimes show dramatic improvement in appetite and activity when given subcutaneous fluids, with no clear correlation to their level of azotemia. The decision to initiate subcutaneous fluid therapy at home should be made on a per case basis.

CONTROLLING HIGH BLOOD PRESSURE

High blood pressure occurs in almost 20% of cats with CRF that present to primary care facilities.²⁸ In referral practices, the incidence has reportedly been as high as 65%. In CRF, perfusion pressure in remnant glomeruli tends to be increased. Increased systemic blood pressure may be transmitted to the glomeruli, causing further damage. If left uncontrolled, hypertension can also cause damage to the brain, eyes, and heart.

recommended for cats and dogs with CRF on the supposition that this would promote urinary excretion of nitrogenous wastes, thereby lessening the clinical signs of azotemia. As the relationship between CRF and hypertension later became apparent, it became standard practice to recommend sodium restriction for patients with CRF based on the concern that salt would increase intraglomerular pressure, injure the kidneys, and increase the risk for progression of CRF. However, studies of dogs and cats with induced CRF have failed to show a consistent relationship between increased sodium intake and an elevation in the systemic blood pressure.^{33,34} Cats with CRF are less flexible in terms of handling changes in dietary sodium content, and many maintenance diets contain more sodium than is needed (approximately 1%). Prescription renal failure diets for cats provide approximately 0.2% to 0.3% sodium.

When fed a high-sodium diet, cats with impaired renal function showed an increase in serum urea nitrogen, phosphorus, and creatinine concentrations, suggesting

Excessive proteinuria is a negative prognostic indicator in cats with chronic renal failure. Administration of the angiotensin-converting enzyme inhibitor benazepril decreases proteinuria and may improve survival times in proteinuric cats with chronic renal failure.

Hypertension may occur at any stage of CRF, and the presence of hypertension is unrelated to the serum creatinine concentration.²⁹

High blood pressure is a major risk factor for the progression of CRF in humans and rats, and evidence has shown this to be true for dogs³⁰; this is presumably true for cats as well. Cats with CRF should have their blood pressure evaluated, preferably with the owner present. Hypertension in cats is defined as an indirect systolic pressure greater than 160 or 170 mm Hg and a diastolic pressure greater than 100 mm Hg.^{31,32}

Amlodipine besylate is currently the preferred treatment to control hypertension in cats. If amlodipine is ineffective, an ACE inhibitor such as enalapril or benazepril may also be administered. Hypertensive cats need lifelong therapy to control their blood pressure.

SODIUM RESTRICTION

The relationship between sodium and CRF remains nebulous. Many years ago, salt supplementation was

progressive deterioration of renal function.³⁵ Interestingly, hypertension was not a factor in this deterioration. Dietary treatment did not affect mean arterial, systolic, or diastolic blood pressure. However, feeding a diet with too little sodium may cause a reduction in the GFR, resulting in excessive urinary loss of potassium and activation of the renin-angiotensin-aldosterone system with no beneficial effect on systemic blood pressure.³³ It is becoming clear that excessive amounts of dietary sodium may be harmful in cats with renal insufficiency, but there are insufficient data to confirm or refute benefits or disadvantages of dietary sodium restriction. Commonly used subcutaneous fluids (i.e., saline or lactated Ringer's solution) contain substantial amounts of sodium. It is unknown whether the sodium in subcutaneous fluids affects hypertension and progression of CRF.

URINARY TRACT INFECTIONS

The normally high osmolality of feline urine provides an inhospitable environment for bacterial colonization.

As the ability to concentrate urine gradually wanes, cats with CRF become more susceptible to bacterial urinary tract infections. Urine culture should be conducted if urinalysis results are suggestive of infection or if clinical signs of bacterial urinary tract infection develop.

METABOLIC ACIDOSIS

Cats with CRF have a decreased ability to excrete hydrogen ions. The resulting metabolic acidosis may contribute to the other common signs of CRF, including anorexia, nausea, vomiting, lethargy, and generalized muscle weakness. Fortunately, prescription renal diets are alkalinizing and help control metabolic acidosis in most cats with CRF. However, if acidosis persists (the serum bicarbonate level is consistently <15 mmol/L) several weeks after dietary change, alkalinization therapy should be considered.¹² Although sodium bicarbonate is the most common alkalinizing agent, potassium citrate may be a better choice in cats with low or borderline potassium levels because it can simultaneously address acidosis and hypokalemia. Regardless of the alkalinizing agent chosen, the serum bicarbonate level should be monitored for 10 to 14 days after therapy and the dose adjusted accordingly.

NAUSEA, VOMITING, AND POOR APPETITE

Gastrin is a digestive hormone that causes the stomach to produce acid. The kidneys are responsible for excreting much of the gastrin produced in the body. As the kidneys fail, the gastrin level begins to rise, and the degree of hypergastrinemia increases with the severity of renal insufficiency.⁷ This results in increased gastric acidity, nausea, vomiting, poor appetite, and possible gastric ulceration and justifies the use of appropriate treatments (e.g., H_2 -receptor antagonists, proton pump inhibitors) to suppress gastric acid secretion. Cimetidine, ranitidine, and famotidine are effective at decreasing gastric acidity in cats. Famotidine may offer an advantage in that it may be administered only once daily. Proton pump inhibitors, such as omeprazole, are also effective in controlling gastric acidity and are effective in cats when given once daily. Cats that continue to vomit despite administration of H_2 -receptor antagonists or proton pump inhibitors may benefit from a centrally acting antiemetic, such as metoclopramide. For cats suspected of having gastric ulcers, sucralfate can help form a protective coating over the ulcer, reducing signs such as pain, nausea, and vomiting. The use of a compound-

ing pharmacy may be necessary because sucralfate tablets cannot be divided accurately for proper dosing in most cats. Sucralfate is most effective in an acid environment and should be given 30 to 60 minutes before H_2 -blockers or phosphate binders.

Although cats with severe azotemia are frequently anorectic, many cats with CRF experience poor appetite despite relatively mild degrees of azotemia. In some instances, the appetite can be stimulated using drugs that affect serotonin and dopamine receptors in the central nervous system. Cyproheptadine, an antihistamine with antiserotonin effects, is commonly used for this purpose. Benzodiazepines, such as diazepam and oxazepam, have been used but often cause an unacceptable degree of sedation. Mirtazapine, a tetracyclic antidepressant, is newly recognized as an appetite stimulant for cats and, in small doses (3 to 4 mg PO q72h), appears to act in a fashion similar to cyproheptadine in increasing appetite. Few data are available about the use of this drug in cats, so caution should be advised.

ANEMIA

As the kidneys fail, they produce inadequate amounts of erythropoietin, and many cats with CRF become progressively anemic. Anemia contributes to lethargy and poor appetite in cats with CRF. When given to cats, recombinant human erythropoietin (r-HuEPO) dramatically reverses anemia. Therapy should be considered only if anemia is severe (packed cell volume [PCV] $<20\%$) and the patient is symptomatic. r-HuEPO should be administered subcutaneously three times per week until the PCV exceeds 30% and should then be decreased to once or twice per week to maintain an adequate PCV. Iron supplementation should be administered concurrently, and blood pressure should be evaluated before and throughout treatment.

r-HuEPO is not of feline origin, and approximately 25% to 30% of cats develop antibodies against it. These antibodies bind not only the r-HuEPO being administered but also the remaining endogenous feline erythropoietin. As a result, cats can develop sudden, severe anemia and become transfusion dependent. At this point, owners usually elect euthanasia. For clients who choose not to euthanize their cat at this point, it may take several months before the anti-erythropoietin antibodies dissipate. The anemia will eventually return to pretreatment values, and the cat will remain transfusion dependent. After this, further use of r-HuEPO is no longer an option.

INTRAINTESTINAL BACTERIOTHERAPY (“ENTERIC DIALYSIS”)

The concept of enteric dialysis is based on the premise that the intestinal wall functions as a semipermeable membrane: solutes that are in high concentration in the blood readily diffuse from plasma into the intestinal lumen. Thus the ingestion of live bacteria that catabolize uremic solutes in the gut would create a gradient favorable for the uremic toxins to diffuse from the plasma into the gut. Azodyl (Vétoquinol USA) is a recently introduced nutritional supplement for this purpose that contains *Enterococcus thermophilus*, *Bifidobacterium longum*, and *Lactobacillus acidophilus* in capsule form. However, no controlled clinical trials have been conducted regarding the use of these probiotics to treat azotemia and CRF in cats. In my experience, there has been a favorable response—decreased azotemia and increased appetite—in the limited number of cases in which it has been prescribed.

CONCLUSION

There have been many advances regarding the treatment of CRF. Although CRF is incurable, with appropriate management, cats can live for many years after the diagnosis. Cats are remarkable because they can often survive for long periods with a seemingly minute fraction of functional renal tissue.

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ARTICLE #1 CE TEST



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1. Which is not a common clinical sign of CRF?

- a. polydipsia
- b. polyphagia
- c. weight loss
- d. anorexia

2. ACE inhibitors may be beneficial in treating cats with CRF because these drugs

- a. dilate the afferent arteriole, thereby increasing glomerular blood flow.
- b. cause vasoconstriction of glomerular vessels by inhibiting the conversion of angiotensin I to angiotensin II.
- c. are preferred in treating systemic hypertension in cats.
- d. dilate the efferent arteriole, thereby decreasing glomerular hypertension.

3. Cats with CRF are not at increased risk of developing

- a. hyperphosphatemia.
- b. hypercalcemia.
- c. hyperkalemia.
- d. hypertension.

4. Proteinuria

- a. is not associated with intraglomerular pressure.
- b. can be quantified by urinalysis.
- c. has no prognostic significance in cats with CRF.
- d. is best quantified by determining the UPC.

5. Which statement regarding calcitriol and renal secondary hyperparathyroidism is incorrect?

- a. In cats with CRF, increased PTH production occurs partly because of inhibition of calcitriol synthesis due to a high phosphorus level.
- b. In cats with CRF, increased PTH production occurs partly because of a decreased number of functional proximal tubule cells.
- c. Calcitriol impairs the ability of the intestine to absorb dietary calcium.
- d. In cats with CRF, increased PTH production results in a decrease in serum calcium because of an increase in the serum phosphorus level (law of mass action).

6. Which condition associated with CRF has not been shown to contribute to the progression of CRF in cats?

- a. hypergastrinemia
- b. hyperphosphatemia
- c. hypokalemia
- d. proteinuria

7. Which treatment is not likely to be safe and effective?

- a. famotidine for uremic gastritis
- b. amlodipine for hypertension
- c. benazepril for proteinuria
- d. calcitriol for hyperphosphatemia

8. Calcitriol, the biologically active form of vitamin D₃,

- a. should not be administered if the serum phosphorus level is elevated.
- b. is derived from a precursor molecule, 1,25-dihydroxyvitamin D₃.
- c. restores the serum calcium level to normal, enhancing PTH synthesis.
- d. restores the serum phosphorus level to normal, inhibiting PTH synthesis.

9. Possible consequences of CRF in cats include

- a. hypokalemic polymyopathy.
- b. uremic gastritis.
- c. hypertensive eye damage.
- d. all of the above

10. A _____-restricted diet is inappropriate for cats with CRF.

- a. protein
- b. phosphorus
- c. sodium
- d. potassium