Chronic Kidney Disease in Dogs and Cats

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KEYWORDS
- Chronic kidney disease
- Geriatric
- Nutrition
- Treatment
- International Renal Interest Society

KEY POINTS
- Chronic kidney disease occurs commonly in dogs and cats.
- Chronic kidney disease is progressive; however, management utilizing dietary modification and pharmacologic agents may improve quality of life and survival.
- Management of dogs and cats with chronic kidney disease is directed at minimizing the excesses and deficiencies that occur.
- Specifically, management is directed at providing nutritional support, treating hypokalemia and metabolic acidosis, decreasing the degree of proteinuria, maintaining hydration, decreasing retention of wastes such as nitrogen containing compounds, avoiding other renal insults, improving anemia, minimizing renal secondary hyperparathyroidism and hyperphosphatemia, and decreasing blood pressure if systemic arterial hypertension is present.
- Serial monitoring of dogs and cats with chronic kidney disease is essential because of the progressive nature of the disease.

Chronic kidney disease (CKD) occurs commonly in older dogs and cats and is the most common renal disease occurring in elderly patients. It is defined as structural and/or functional impairment of one or both kidneys that has been present for more than approximately 3 months. In most patients, there is loss of function and structure with CKD; however, degree of functional impairment does not always mirror loss of structure. CKD implies irreversible loss of renal function and/or structure that remains stable for some period of time but is ultimately progressive. In some patients, CKD may be complicated by concurrent prerenal and/or postrenal problems that may worsen the condition, but if managed, they may improve the situation.

CKD is considered a disease of older animals, although it occurs at all ages. The estimated incidence of CKD in the general population of dogs and cats is 0.5% to

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At the University of Minnesota Veterinary Medical Center, more than 10% of dogs and 30% of cats over 15 years of age are diagnosed with CKD. One retrospective study reported that 53% of cats with CKD were over 7 years old, but animals ranged in age from 9 months to 22 years. In a study on age distribution of kidney disease in cats based on data submitted from 1980 to 1990 to the Veterinary Medical Data Base at Purdue University, 37% of cats with the diagnosis of “renal failure” were less than 10 years old, 31% of cats were between the ages of 10 and 15, and 32% of cats were older than 15 years. Similarly, in a study of cats with CKD reported in 1988, the mean age was 12.6 years with a range of 1 to 26 years. Mean age among 45 control cats in this study was 10.0 years. During 1990, the prevalence of kidney disease was reportedly 16 cases for every 1000 cats of all ages, 77 cases per 1000 cats over age 10 years, and 153 per 1000 among cats older than 15 years. Maine coon, Abyssinian, Siamese, Russian blue, and Burmese cats were disproportionately reported as affected.

The kidneys are involved with whole body homeostasis; therefore, CKD affects many organ systems, is associated with many metabolic derangements, and affects general well-being. Glomerular filtration results in formation of urine in Bowman’s space except for cells and protein-bound compounds; a small amount of albumin is filtered. Bulk reabsorption of the filtrate occurs in the proximal tubule with additional secretion or reabsorption of anionic and cationic compounds. The loop of Henle concentrates then dilutes the filtrate through selective reabsorption of water and sodium. The distal convoluted tubule and collecting ducts fine-tune the solute and moisture content of urine. In addition to these processes, the kidneys are intimately involved in metabolic regulation of acid-base status, have endocrine function (eg, erythropoietin and vitamin D), and have a role in blood pressure regulation (eg, renin production and adrenal secretion of aldosterone). Therefore, when renal function declines there is disruption of these normal processes resulting in retention of compounds that should be excreted (eg, phosphorous and creatinine) and loss of compounds that should be retained (eg, water and protein).

CLINICAL, BIOCHEMICAL, AND IMAGING FINDINGS WITH CKD

It is the retention or loss of compounds that results in clinical manifestations of CKD. Many, but not all, patients show clinical signs of chronic disease such as loss of body condition, BW, and muscle mass, and an unkempt appearance. Polyuria and polydipsia occur because of an inability of the kidneys to regulate water balance. Hyporexia/anorexia, vomiting, halitosis, and ulcerative stomatitis and gastroenteritis may be present (Fig. 1). With CKD, the kidneys often palpate small and irregular, and this is confirmed with abdominal radiography and ultrasonography. Occasionally, renomegaly is present with CKD when there is renal neoplasia, pyelonephritis, or ureteral obstruction present. Biochemically, azotemia with inappropriately dilute urine (urine specific gravity <1.030 in dogs and <1.035 in cats), metabolic acidosis, and hyperphosphatemia are present. Additionally, some patients may have hypokalemia (seen more commonly in cats than in dogs), nonregenerative anemia, hypoalbuminemia, dyslipidemia, and bacterial urinary tract infection. Arterial systemic hypertension occurs in 40% to 80% of patients. Proteinuria may also occur and has been associated with a poorer prognosis and more rapid progression of CKD than in patients without proteinuria.

TREATMENT OF CKD

Treatment of CKD is directed at correcting these imbalances and in slowing down progression; it is lifelong because CKD is irreversible. Additionally, treatment is
directed at ameliorating clinical signs of CKD and at correcting or controlling nonrenal
disease that may affect a patient with CKD. We developed an acronym to assist in
treating CKD based on excesses and deficiencies that occur: NEPHRONS.

- **N** nutrition
- **E** electrolytes
- **P** pH of blood (acid-base status); proteinuria
- **H** hydration
- **R** retention of wastes
- **O** other renal insults — avoid
- **N** neuroendocrine function — hyperparathyroidism, hypoproliferative anemia,
  and hypertension
- **S** serial monitoring — CKD is irreversible and progressive

**Key Therapeutic Points**

The kidneys are involved with homeostasis through filtration, reabsorption, secretion,
and metabolism of compounds. A conservative medical treatment of CKD consists of
supportive and symptomatic treatment designed to correct excesses and deficiencies
that occur (NEPHRONS). Guidelines for managing dogs and cats with CKD have
been established by the International Renal Insufficiency Society (http://www.IRIS-
kidney.com). This staging system is designed for use with dogs and cats with CKD
(Table 1).7

A diagnosis of CKD is made first and staging is accomplished by evaluating (1) 2
serum creatinine concentrations when patient is well hydrated, (2) 2 or 3 urine
protein–to–urine creatinine ratios (UPCs), and (3) 2 to 3 indirect arterial blood pressure
determinations.1 CKD is staged by magnitude of renal dysfunction and further
modified (substaged) by presence or absence of proteinuria and/or hypertension.
Proteinuria ONLY refers to renal proteinuria and not prerenal (eg, hyperglobulinemia)
or postrenal (eg, urinary tract infection, hematuria, etc), and is based on UPC.8 Blood
pressure determination should be performed several times with an nonsedated and
calm patient that has acclimated to a quiet area using a standard protocol.9
<table>
<thead>
<tr>
<th>Stage</th>
<th>Dogs</th>
<th>Cats</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;125</td>
<td>&lt;140</td>
<td>Nonazotemic</td>
</tr>
<tr>
<td></td>
<td>&lt;1.4</td>
<td>&lt;1.6</td>
<td>Some other renal abnormality present such as inadequate concentrating ability without identifiable nonrenal cause; abnormal renal palpation and/or abnormal renal imaging findings; proteinuria of renal origin; abnormal renal biopsy results</td>
</tr>
<tr>
<td>2</td>
<td>125–179</td>
<td>140–249</td>
<td>Mild renal azotemia [lower end of the range lies within the reference range for many labs but the insensitivity of creatinine as a screening test means that animals with creatinine values close to the upper limit of normality often have excretory failure] Clinical signs usually mild or absent</td>
</tr>
<tr>
<td></td>
<td>1.4–2.0</td>
<td>1.6–2.8</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>180–439</td>
<td>250–439</td>
<td>Moderate renal azotemia</td>
</tr>
<tr>
<td></td>
<td>2.1–5.0</td>
<td>2.9–5.0</td>
<td>Many systemic clinical signs may be present</td>
</tr>
<tr>
<td>4</td>
<td>&gt;440</td>
<td>&gt;440</td>
<td>Severe renal azotemia</td>
</tr>
<tr>
<td></td>
<td>&gt;5.0</td>
<td>&gt;5.0</td>
<td>Many extrarenal clinical signs present</td>
</tr>
</tbody>
</table>

### Substage of CKD based on presence or absence of proteinuria determined by a UPC

#### UPC Value

<table>
<thead>
<tr>
<th>Dogs</th>
<th>Cats</th>
<th>Substage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.2</td>
<td>&lt;0.2</td>
<td>Nonproteinuric</td>
</tr>
<tr>
<td>0.2–0.5</td>
<td>0.2–0.4</td>
<td>Borderline proteinuric</td>
</tr>
<tr>
<td>&gt;0.5</td>
<td>&gt;0.4</td>
<td>Proteinuric</td>
</tr>
</tbody>
</table>

### Substage of CKD based on presence or absence of systemic arterial hypertension and risk of systemic arterial hypertension-related complications

<table>
<thead>
<tr>
<th>Systolic Blood Pressure, mm Hg</th>
<th>Diastolic Blood Pressure, mm Hg</th>
<th>Adaptation When Breed-Specific Reference Range Is Available*</th>
<th>Substage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;150</td>
<td>&lt;95</td>
<td>&lt;10 mm Hg above reference range</td>
<td>AP0: Minimal Risk (N)</td>
</tr>
<tr>
<td>150–159</td>
<td>95–99</td>
<td>10–20 mm Hg above reference range</td>
<td>AP1: Low Risk (L)</td>
</tr>
<tr>
<td>160–179</td>
<td>100–119</td>
<td>20–40 mm Hg above reference range</td>
<td>AP2: Moderate Risk (M)</td>
</tr>
<tr>
<td>&gt;180</td>
<td>&gt;120</td>
<td>&gt;40 mm Hg above reference range</td>
<td>AP3: High Risk (H)</td>
</tr>
</tbody>
</table>

*Courtesy of Novartis Animal Health, Inc, Basel, Switzerland, sponsor of the International Renal Interest Society (IRIS), with permission.*
The main goal of nutritional support of any patient with a chronic disease is maintenance of lean muscle mass and optimal body condition, and this is true of patients with CKD. A thorough physical examination is performed and a body condition score (BCS) and muscle condition score (MCS) are assigned. Assigning a BCS (Table 2) provides more information than BW alone and estimates body fat content. The goal for most pets is a BCS of 2.5 to 3 of 5 or 4 to 5 of 9.

An MCS may also be assigned and is an assessment of muscle mass and tone. Evaluation of muscle mass includes visual examination and palpation of muscles over temporal bones, scapulae, lumbar vertebrae, and pelvic bones. Muscle condition is an assessment of lean mass and loss of muscle mass may adversely affect strength, immune function, wound healing, and ability to compensate for chronic conditions such as CKD. A simple MCS has been suggested using a 0-to-3 scale where 0 = normal muscle mass and tone, 1 = slightly decreased muscle mass and tone,
2 = moderately decreased muscle mass and tone, and 3 = markedly decreased muscle mass and tone.\textsuperscript{14}

Daily caloric requirements are determined by estimating resting energy requirement (RER) using 1 of 2 equations\textsuperscript{15}:

\begin{align*}
\text{Exponential} & : 70 \, \text{BW}_{\text{kg}}^{0.75} \\
\text{Linear} & : 30\left(\text{BW}_{\text{kg}}\right) + 70
\end{align*}

The exponential equation is more accurate because energy requirements relate to body weight (BW) in a parabolic fashion rather than a linear one. Once the RER is estimated, the result is multiplied by an activity or life stage factor (Table 3) to estimate the maintenance energy requirement (MER).\textsuperscript{15} These equations give only estimates of daily energy requirements and energy intake should be adjusted based on response to estimated energy requirements and through serial monitoring of BW, BCS, and MCS.

Patients with CKD may exhibit some degree of anorexia depending on stage of CKD. Causes of anorexia and nausea include retention of uremic toxins, dehydration, biochemical alterations (azotemia, metabolic acidosis, electrolyte imbalances, and mineral imbalances), anemia, renal secondary hyperparathyroidism, and uremic gastroenteritis.\textsuperscript{16} Gastric ulcers occur less commonly in dogs and cats than in human beings; however, many dogs and cats with CKD have gastric pathology including vascular changes and edema\textsuperscript{17} and probable gastric hyperacidity associated with hypergastrinemia from decreased renal excretion.

Feed a highly palatable diet or increase the palatability of diet by adding water to dog food, using flavoring agents, and warming food to near body temperature.\textsuperscript{18} Consuming diets that are more calorically dense than maintenance adult foods promotes adequate energy intake with less volume intake resulting in less gastric distention and nausea. Because dietary fat is more calorically dense than dietary protein and carbohydrates, diets formulated for patients with CKD are typically higher

<table>
<thead>
<tr>
<th>Life Stage</th>
<th>Canine Factor</th>
<th>Feline Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation</td>
<td>1.0–3.0</td>
<td>1.6–2.0</td>
</tr>
<tr>
<td>Dogs: first $\frac{1}{2}$–$\frac{3}{4}$</td>
<td>1.0–2.0</td>
<td></td>
</tr>
<tr>
<td>Dogs: last $\frac{1}{2}$</td>
<td>2.0–3.0</td>
<td></td>
</tr>
<tr>
<td>Lactation</td>
<td>2.0–8.0</td>
<td>1.0–2.0</td>
</tr>
<tr>
<td>Growth</td>
<td>2.0–3.0</td>
<td>2.0–5.0</td>
</tr>
<tr>
<td>Adult intact</td>
<td>1.8</td>
<td>1.4</td>
</tr>
<tr>
<td>Adult neutered</td>
<td>1.6</td>
<td>1.2</td>
</tr>
<tr>
<td>Senior</td>
<td>1.4</td>
<td>1.1</td>
</tr>
<tr>
<td>Work: light</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>Work: moderate</td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>Work: heavy</td>
<td>4.0–8.0</td>
<td></td>
</tr>
<tr>
<td>Obese prone</td>
<td>1.4</td>
<td>1.0</td>
</tr>
<tr>
<td>Weight loss</td>
<td>1.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Weight gain</td>
<td>1.2–1.4 ideal</td>
<td>0.8–1.0 ideal</td>
</tr>
<tr>
<td>Critical care (usually)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>
in fat compared with maintenance adult foods. Available diets contain 12% to 30% crude fat (dry matter basis).

Nausea and anorexia associated with chronic renal failure may also occur because of hypergastrinemia and gastric hyperacidity. Dietary protein stimulates gastric acid secretion; therefore, dietary protein restriction may decrease gastric hyperacidity. Administration of histamine$_2$-receptor antagonists (famotidine: dogs and cats, 1.1 mg/kg po q 12–24 hours; ranitidine: dogs and cats, 1–2 mg/kg po q 8–12 hours) or other antacids are beneficial in dogs and cats with CKD; many phosphate binders also bind gastric acid and act as antacids. Sucralfate (dogs, 0.5–2.0 g po q 6–12 hours; cats, 0.25–0.5 g po q 6–12 hours) is an aluminum-containing compound that binds to exposed submucosal collagen in an acidic environment and may have cytoprotectant effects via prostaglandin E$_2$. It is used to treat active gastric ulcers, but may also act as an antacid and phosphate binder. Maropitant (dogs and cats: 2–8 mg/kg po q24h; although not recommended for more than 5 days) is an anti-emetic that inhibits neurokinin-1; it is used for motion sickness but is effective with many other causes of vomiting including uremic gastroenteritis. Mirtazapine (dogs, 15–30 mg po q 24 hours; cats, 1.875–3.75 mg po q 48–72 hours) is a noradrenergic and serotonergic antidepressant that stimulates appetite and has antiemetic properties. In cats with CKD, it should be administered every 48 hours. Metoclopramide (dogs and cats, 0.1–0.5 mg/kg po q 6–24 hours), an intestinal prokinetic agent that has central antiemetic effects via dopamine receptor antagonism, may also be used although it is less effective than serotonin receptor antagonists in uremic human beings.

In patients that are unwilling or unable to eat, nutrition may be provided by feeding tubes including nasogastric, esophagostomy, and gastrostomy feeding tubes. A study of 56 dogs with renal failure were managed with gastrostomy feeding tubes; 10 were low profile and 46 were standard mushroom-tipped tubes. Gastrostomy tubes were used for 65 ± 91 days (range, 1–438 days). Eight dogs gained weight, 11 did not have a change in BW, and 17 lost weight; information was not available for 20 dogs. Mild stoma-site complications included discharge, swelling, erythema, and pain in 26 (46%) of dogs. Twenty-six gastrostomy tubes were replaced in 15 dogs; 11 were replaced because of patient removal, 6 were replaced because of tube wear, and 3 were replaced for other reasons. Three dogs were euthanatized because they removed their gastrostomy tubes, 2 were euthanatized because of evidence of tube migration, and 1 died of peritonitis. Based on this report, gastrostomy tubes appear to be safe and effective for improving nutritional status of dogs with renal failure. In another report, 96% of owners of dogs or cats managed with gastrostomy feeding tubes had a positive experience and would use a gastrostomy feeding tube again in their pet if necessary.

In addition to providing calories (energy), there are specific nutrients that may alter progression of CKD in dogs and cats. With a decrease in numbers of functioning nephrons, pressure inside remaining nephrons increased; this is termed intraglomerular hypertension. The intraglomerular hypertension increases the filtration rate in the remaining nephrons. The tradeoff of intraglomerular hypertension is damage to these nephrons over time. In dogs with induced CKD, feeding diets containing omega-3 fatty acids has been shown to decrease intraglomerular hypertension, maintain glomerular filtration rate, and increase survival. In dogs fed omega-3 long chain fatty acids, renal function actually increased and remained above baseline over 20 months of the study. Glomerulosclerosis, tubulointerstitial fibrosis, and interstitial inflammatory cell infiltrates were less in dogs fed an omega-3 fatty acid–supplemented diet compared with
dogs fed an omega-6 fatty acid–supplemented diet. Omega-3 fatty acids reduce hypercholesterolemia, suppress inflammation and coagulation, lower blood pressure, and improve renal hemodynamics. An omega-6–to–omega-3 fatty acid ratio of 3:1 to 5:1 appears to be beneficial and is present in many renal failure diets.

B vitamins are water-soluble vitamins and may be decreased with CKD due to the polyuric state. B vitamin deficiency may be associated, in part, with hyporexia/anorexia, which occurs commonly with CKD. A recent study showed that B vitamin deficiency is not common in patients with CKD. Nonetheless, diets formulated for CKD in dogs and cats are supplemented with B vitamins.

Oxidative stress may be an important component of CKD. Renal cells, particularly renal tubular cells, are among the most metabolically active cells. The kidneys maintain persistently high levels of mitochondrial oxidative phosphorylation and arterial blood flow, making them an environment in which reactive oxygen species formation occurs. Important factors in generation of reactive oxygen species include angiotensin II, glomerular hypertension, hyperfiltration, tubular hypermetabolism, systemic arterial hypertension, anemia, regional hypoxia, and renal inflammation. The result of reactive oxygen species formation may be glomerulosclerosis and interstitial fibrosis, thereby promoting progression of CKD. Renal oxidative stress may be decreased by treating systemic arterial hypertension, correcting anemia, providing omega-3 fatty acids, and treating with angiotensin-converting enzyme inhibitors. In a study of cats with induced CKD, feeding a diet with vitamins C and E and beta-carotene for 4 weeks decreased evidence of oxidative stress as measured by serum levels of 8-hydroxy-2'-deoxyguanosine and comet assay parameters.

Supplementation with omega-3 fatty acids and antioxidants has not been adequately evaluated in cats. A retrospective study on the effects of several renal diets did find that survival was greatest among cats fed the diet with the highest omega-3 fatty acid content. The study, however, was retrospective and it is not possible to accurately assess effects of dietary omega-3 fatty acids from these data.

Recently, an extract of medicinal rhubarb (Rheum officinale) has become available for dogs and cats with CKD. Experimentally, it decreases renal fibrosis in an induced CKD model in rats. One study of cats with CKD showed no benefit when administered alone or in combination with benazepril.

E Electrolytes

The kidneys are involved with regulation of electrolyte balance. Electrolytes are filtered at the glomerulus, most of the filtered electrolytes are reabsorbed in the proximal convoluted tubule, and the remainder of the nephron reabsorbs or secretes electrolytes depending on status. A common electrolyte disturbance in cats and occasionally in dogs with CKD is hypokalemia, which has been reported to occur in 20% to 30% of cats with stage 2 or 3 CKD. Hypokalemia may occur because of hyporexia or anorexia, excessive renal losses, transcellular shift due to chronic metabolic acidosis, and activation of the renin-angiotensin-aldosterone system due to dietary sodium restriction. Hypokalemia often manifests as polymyopathy. Clinical signs include decreased activity and muscle weakness or classically as an inability for the patient to lift its head while sitting sternally (Fig. 2). Additionally, hypokalemia may result in hyporexia or anorexia and progression of CKD. The target for plasma or serum potassium concentration should be in the middle to upper half of reference range for the laboratory. Once hypokalemia is present, whole body potassium content is low and it is difficult to replete in patients with CKD.

Diets formulated for use in patients with CKD are supplemented with potassium, typically using potassium citrate as it is a source of potassium and an alkalinizing
agent. This is based, in part, on diets low in potassium and high in acid content being implicated in impairing renal function and promoting development of lymphoplasmacytic tubulointerstitial lesions in cats.\textsuperscript{47–51} Potassium may be supplemented orally using potassium gluconate or potassium citrate. If patients are receiving subcutaneously administered fluids, potassium may be added to the fluids up to 30 mEq/L as potassium chloride.\textsuperscript{7} Irritation at injection site may occur with concentrations above this. Potassium chloride may also be added to fluids administered intravenously depending on blood potassium concentration (\textbf{Table 4}). Rate of administration should not exceed 0.5 mEq/kg/h because cardiotoxicity may occur. Potassium may be supplemented orally as well as gluconate or citrate salts; potassium citrate is used more often as it provides alkalization as well. Potassium gluconate (dogs and cats, 2 mEq/kg po q 12 hours)\textsuperscript{19} or potassium citrate (dogs and cats, 75 mg/kg po q 12 hours)\textsuperscript{19} may be administered; dosage is adjusted to achieve a serum or plasma potassium concentration in the middle to upper half of the reference range. If hypokalemic polymyopathy is present, it usually resolves within 1 to 5 days after initiating parenteral or oral potassium supplementation. Typical commercial modified diets for CKD in dogs and cats contain 0.4% to 0.8% potassium on a dry matter basis for dogs and 0.7% to 1.2% potassium on a dry matter basis for cats.\textsuperscript{52}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|}
\hline
Serum Potassium (mEq/L) & Amount of Potassium to Add to Lactated Ringer’s Solution (mEq/L) & Maximum Fluid Rate (mL/kg/h) \\
\hline
<2.0 & 80 & 6 \\
2.1–2.5 & 60 & 8 \\
2.6–3.0 & 40 & 12 \\
3.1–3.5 & 28 & 18 \\
3.6–5.0 & 20 & 25 \\
\hline
\end{tabular}
\caption{Suggested guidelines for intravenous potassium supplementation}
\end{table}
Blood sodium concentrations are typically normal in patients with CKD. Sodium retention may occur with CKD because of intravascular volume contraction. This may promote systemic arterial hypertension, in part; therefore, dietary sodium restriction may be beneficial in patients with CKD. Furthermore, there is evidence that excessive sodium intake may be harmful to the kidneys and excessive salt intake may impair effectiveness of antihypertensive therapy.\textsuperscript{53} Excessive dietary sodium restriction may be detrimental, however. In one study of experimentally induced CKD in cats, dietary sodium restriction to 50 mg sodium/kg of diet promoted hypokalemia due to activation of the renin-angiotensin-aldosterone system.\textsuperscript{46} Additionally, in one study, dietary intake of sodium at 1.1% as fed was associated with increased azotemia in cats with CKD\textsuperscript{54}; however, other studies did not find this.\textsuperscript{55} Typical commercial modified diets for CKD in dogs and cats contain 0.3% sodium or less on a dry matter basis for dogs and 0.4% sodium or less on a dry matter basis for cats.\textsuperscript{52}

\textbf{P pH of Blood (Acid-Base Status)}

Metabolic acidosis occurs commonly with CKD due to retention of acids that are excreted normally by the kidneys. It has been reported that metabolic acidosis occurs in less than 10% of cats with stage 2 or 3 CKD but in nearly 50% of cats with uremia.\textsuperscript{56,57} With CKD, there is increased retention of metabolic acids, increased production of ammonia, and decreased bicarbonate reclamation with CKD. Metabolic acidosis is associated with hyporexia/anorexia, hypokalemia, and muscle weakness. Bicarbonate therapy in human beings with CKD has been reported to slow progression and improve nutritional status.\textsuperscript{58} Transcellular shifting of potassium occurs with metabolic acidosis because the increased hydrogen ion concentration in blood results in movement of hydrogen ions into cells in exchange for potassium ions that leave the cell and enter the circulation. Potassium is then excreted resulting, in part, a propensity for hypokalemia. Acid-base status may be assessed by measuring blood pH and bicarbonate concentration on an arterial or venous blood gas analysis. Measurement of plasma or serum bicarbonate, also called total carbon dioxide, gives a measure of acid-base status. The goal of treatment is to maintain a normal concentration; in human beings with stage 3 or 4 CKD, a low or high serum bicarbonate concentration is associated with increased mortality.\textsuperscript{59} There are several treatments for metabolic acidosis. Many renal failure diets are formulated to contain an alkalinizing agent usually potassium citrate, which is also a source of potassium. Because metabolism of dietary protein results in production of organic acids, dietary protein restriction decreases amount of organic acid that must be excreted by kidneys. Supplemental alkalinizing agents may be administered including potassium citrate or sodium bicarbonate. Potassium citrate (dogs and cats, 75 mg/kg po q 12 hours initially)\textsuperscript{19} is preferred because it provides potassium in addition to its alkalinizing properties. Sodium bicarbonate (dogs and cats, 8–12 mg/kg po q 8–12 hours)\textsuperscript{19} administration provides alkalinization but may worsen systemic arterial hypertension and fluid retention due to the sodium load.

\textbf{P Proteinuria}

Proteinuria occurring in association with CKD in dogs and cats is associated with progression.\textsuperscript{5,6,60} Proteinuria is considered a hallmark of glomerular disease; however, proteinuria appears to be nephrotoxic even without overt primary glomerular disease.\textsuperscript{61} In humans with CKD, reducing proteinuria slows progression; however, no such evidence exists for dogs and cats with CKD.\textsuperscript{62–65} Proteinuria may promote progressive renal injury by several mechanisms including mesangial toxicity, tubular overload and hyperplasia, toxicity from specific filtered proteins (eg, transferrin), and
induction of proinflammatory molecules (eg, monocyte chemoattractant protein-1). Excessive proteinuria may injure renal tubules via toxic or receptor-mediated pathways or an overload of lysosomal degradative mechanisms. The abnormally excessive filtered proteins accumulate in proximal tubular lumens, are endocytosed into proximal tubular cells, and contribute to tubulointerstitial injury through upregulation of vasoactive and inflammatory genes and by secretion into peritubular tissue where they incite inflammation. Additionally, components of complements may enter filtrate and initiate interstitial injury, and filtered proteins may form casts obstructing tubular flow.

Proteinuria is often detected by a positive semiquantitative test on routine urine dipsticks. It is further localized to pre-renal, renal, or postrenal causes. The most common causes of proteinuria are postrenal including urinary tract infection or inflammation (exudation of plasma proteins into the urine) and hematuria (loss of plasma proteins with red blood cells). Prerenal causes of proteinuria include hemolysis (hemoglobinuria) and hyperglobulinemia (eg, plasma cell myeloma). Proteinuria is localized to renal causes after prerenal and postrenal causes have been ruled out. Renal proteinuria is often considered glomerular in nature; however, tubular disorders (eg, Fanconi syndrome) and interstitial disorders result in proteinuria as well albeit to a lesser degree. Once prerenal and postrenal causes have been excluded, verification and quantitation of renal proteinuria are made by determining a UPC. Healthy dogs and cats have a UPC less than 0.2; between 0.2 and 0.4 in cats and 0.5 in dogs is borderline proteinuria, and greater than 0.4 in cats and 0.5 in dogs is abnormal. In dogs and cats with CKD, treatment is indicated when the UPC is greater than 2.0 in stage 1 CKD and when the UPC is greater than 0.4 in cats and greater than 0.5 in dogs in stages 2 through 4 CKD. In humans with CKD, reducing proteinuria slows progression; however, no such evidence exists for dogs and cats with CKD.

Treatment of renal proteinuria involves decreasing filtration and loss of proteins, principally albumin. Feeding a protein-restricted diet decreases the degree of renal proteinuria. Angiotensin-converting enzyme inhibitors (enalapril and benazepril: dogs and cats, 0.25–0.1.0 mg/kg po q 12–24 hours) have also been shown to decrease proteinuria in dogs and cats. Benazepril has been advocated over enalapril because benazepril’s biliary excretion may compensate for reduced renal clearance in patients with CKD. Serum/plasma creatinine concentration should be evaluated approximately 7 days after initiating therapy with angiotensin-converting enzyme inhibitors. An increase of greater than 0.2 mg/dL indicates a decrease in glomerular filtration rate secondary to therapy and the dosage should be adjusted. Omega-3 fatty acids, specifically eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are also beneficial with renal proteinuria. An omega-6-to–omega-3 fatty acid ratio of 3:1 to 5:1 appears to be beneficial and is present in many renal failure diets. Omega-3 fatty acids may also be supplemented to dogs and cats, if necessary (300 mg of EPA + DHA per 10–22 kg po q 24 hours). Immunosuppressive therapy may be considered for dogs with primary glomerular proteinuria as approximately 50% of evaluated renal biopsies from dogs with glomerular proteinuria have an immune-mediated basis.

**H Hydration**

Patients with CKD are polyuric due to decreased ability to concentrate urine from decreased nephron mass. Polyuria is offset by polydipsia. Because of polyuria, dehydration may occur if water loss exceeds water intake. This occurs more often in cats than in dogs with CKD. In patients that are dehydrated, parenteral fluid is administered. Intravenous administration is preferred over other parenteral routes.
Intravenous fluid therapy is composed of 3 components: amount necessary for rehydration, maintenance fluid requirements, and amount to treat additional losses (eg, vomitus, diarrhea, etc).

- Amount needed for rehydration in milliliters is estimated by multiplying estimated percentage of dehydration by BW in kilograms and multiplying the resultant product by 1000.
- Maintenance fluid requirements are estimated to be 2.2 mL/BWkg/h.
- Amount necessary to replace fluid lost by other routes can be measured or estimated to be 1.1 mL/BWkg/h.

Dehydration may be prevented by increasing oral water intake by having clean and fresh water available at all times, by feeding canned formulated diets, or by adding water to dry formulated diets. Cats may drink more if circulating water fountains are used. In some patients, particularly cats, supplemental fluid may be provided by subcutaneous route as they are unable to maintain hydration by oral intake. Subcutaneously administered fluids are administered using a syringe or bag of fluids with an extension set and a 20- or 22-gauge needle. The easiest site to administer fluids subcutaneously is to insert the hypodermic needle in the loose skin located along the dorsal aspect of the body between the scapulae. Cats that require supplemental subcutaneously administered fluids often require 75 to 150 mL administered every 12 to 72 hours. Lactated Ringer’s solution is used most often; however, other types of fluids may be used. Potassium as potassium chloride may be added to fluids administered subcutaneously up to a concentration of 20 mEq/L; above this concentration, administration of the fluid results in discomfort. Some patients do not tolerate subcutaneously administered fluids. Feeding tubes, such as nasogastric or more preferred esophagostomy or gastrostomy, may be placed and used. Esophagostomy and gastrostomy feeding tubes include may also be used for diet delivery and medication administration if the oral route is unavailable.

**R Retention of Substances**

With CKD, substances that are eliminated normally in urine are retained. These substances include nitrogenous compounds (blood urea nitrogen and creatinine) among others. Elimination of nitrogenous compounds is a major function of the kidneys and retained nitrogenous compounds are associated with clinical signs of CKD. Azotemia is a hallmark of CKD. Thus, restriction of dietary protein is logical. Results of studies are contradictory concerning the influence of dietary protein restriction on progression of CKD.69–72 Restricting dietary protein may be associated with a decreased degree of azotemia, decreased dietary phosphorous as meat-based protein is also high in phosphorous, decreased metabolic acids generated from dietary protein, and decreased stimulus for gastric hydrochloric acid production and may reduce dosage of antihypertensive agents and decrease requirement for erythropoietin.73 Modified diets for managing CKD in dogs and cats typically contain 14% to 20% protein on a dry matter basis for dogs and 28% to 35% protein on a dry matter basis for cats.52

There are 3 studies of dietary intervention in dogs and cats with spontaneously occurring CKD: 2 in cats and 1 in dogs.74–77 In these studies, a diet formulated to contain lower quantities of protein, phosphorous, and sodium and higher quantities of potassium, B vitamins, calories, alkalization potential, and omega-3 fatty acids were compared with a diet that was formulated to be similar to maintenance over-the-counter adult dog or cat foods. Results of these studies showed benefit in dogs and cats with CKD: patients lived longer, had fewer episodes of uremia, time to onset of
first uremic episode was longer, and owners perceived quality of life was better. Although diets formulated for renal failure are lower in protein than over-the-counter maintenance adult foods, they are still adequate and typically contain higher biologic value protein.

Prebiotics and probiotics have been suggested to redistribute a small amount of nitrogen into the gastrointestinal tract for elimination, thus decreasing the degree of azotemia. Prebiotics are dietary fiber, typically soluble fiber that promotes proliferation of beneficial bacteria in the colon that metabolizes nitrogen and urea intraluminal. The proliferation of bacteria also promotes uptake and utilization of intraluminal nitrogen by the bacteria resulting in less absorption from the colon. Probiotics are live, nonpathogenic bacteria that are presumed to populate the gastrointestinal tract, providing the same benefit. One such probiotic (Azodyl; Vetoquinol, Lure Cedex, France) is commercially available and marketed as “enteric dialysis.” A small uncontrolled study showed decreased degree of azotemia; however, a controlled study evaluating administration of the probiotic with and without food failed to show a benefit.78

O Other Renal Insults—Avoid

Circumstances, drugs, toxins, and infections may compound CKD by inducing a prerenal azotemia (dehydration) or by affecting remaining nephrons. Dehydration due to any cause not only is associated with worsening azotemia (prerenal) but may also precipitate acute kidney injury resulting in progression of CKD. Patients in CKD are less tolerant of dehydration. Drugs, such as aminoglycosides, urinary acidifiers, amphotericin, nonsteroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, and catabolic drugs (eg, glucocorticoids and immunosuppressive drugs) may be nephrotoxic. These should be used cautiously or not at all in patients with CKD. Patients with CKD have a higher incidence of bacterial urinary tract infections, which has been reported to be 20%. There are several reasons for increased risk of bacterial urinary tract infections with CKD including dilute urine, premature apoptosis of white blood cells, decreased white blood cell recruitment and function, and decreased immunoglobulin concentration in urine. Clinical signs of bacterial urinary tract infection may be absent. If the infection ascends from the urinary bladder to the kidneys, it may promote progression of CKD. Prophylactic antimicrobial therapy should be avoided, if possible, as it may select for multidrug resistant microorganisms. Some antimicrobial agents (eg, aminoglycosides) may be nephrotoxic and many are excreted renally; therefore, pharmacokinetic parameters may be altered. Additionally, some antimicrobial agents may cause hyporexia/anorexia, vomiting, and/or diarrhea that can induce dehydration. Many active bacterial urinary tract infections in patients with CKD are not associated with pyuria or hematuria; therefore, aerobic microbial culture of urine collected by cystocentesis may be necessary to document an active bacterial urinary tract infection.

N Neuroendocrine Function

There are 3 abnormalities of neuroendocrine function that may occur with CKD: renal secondary hyperparathyroidism, hypoproliferative anemia, and systemic arterial hypertension.

Renal secondary hyperparathyroidism

Renal secondary hyperparathyroidism occurs commonly with CKD, and the more advanced the CKD, the more advanced is the renal secondary hyperparathyroidism.76,79–84 In extreme cases, renal secondary hyperparathyroidism results in fibrous
osteodystrophy, particularly of the mandible and maxilla; this occurs more commonly in dogs with congenital or juvenile-onset CKD but may occur in adult patients. Fig. 3. It occurs, in part, because of phosphorous retention and decreased calcitriol (1,25-dihydroxy vitamin D3) metabolism. Renal tubular cells contain 1α-hydroxylase, which is the enzyme that converts 25-hydroxyvitamin D to the active 1,25-dihydroxyvitamin D3. Calcitriol stimulates gastrointestinal absorption of calcium and phosphorous and inhibits parathyroid hormone production. Parathyroid hormone stimulates renal reabsorption of calcium and excretion of phosphorous, stimulates calcium and phosphorous release from bone, and stimulates calcitriol production. With CKD, there is decreased enzyme activation of calcitriol. In response to decreased calcitriol, parathyroid hormone production and secretion are increased. Parathyroid hormone may be considered a uremic toxin. With decreased glomerular filtration rate, hyperphosphatemia occurs, which may result in dystrophic mineralization and progression of CKD and further inhibits calcitriol production. Hyperphosphatemia is associated with progression of CKD and shortened survival.
Treatment of renal secondary hyperparathyroidism is aimed at decreasing serum phosphorous concentrations and possibly parathyroid hormone concentrations. The goal is to achieve a serum phosphorous concentration of less than 4.5 mg/dL with stage 2, less than 5.0 mg/dL with stage 3, and less than 6.0 mg/dL with stage 4. Serum phosphorous concentration may be decreased by feeding a low phosphorous diet, administering phosphate binders, and possibly administering calcitriol. Typical commercial modified diets for CKD in dogs and cats contain 0.2% to 0.5% phosphorous on a dry matter basis for dogs and 0.3% to 0.6% phosphorous on a dry matter basis for cats.52

There are several phosphate binders that may be used. Conventionally, aluminum hydroxide (dogs and cats, 30–100 mg/kg po q 24 hours divided and administered with meals)19 has been used. Primary side effects are constipation and anorexia, although aluminum toxicity has been reported with very high dosage. Calcium-containing phosphate binders, such as calcium acetate (PhosLo; Nabi Biopharmaceuticals, Rockville, MD; dogs and cats, 60–90 mg/kg po q 24 hours divided and administered with meals)19 and chitosan with calcium carbonate (Epakitan; Vetoquinol; dogs and cats: 200 mg/kg po mixed with meals)19 may be used. The chitosan with calcium carbonate phosphate binder has been shown to decrease serum phosphorous concentrations in cats with spontaneously occurring CKD.85 In addition to the aforementioned side effects, hypercalcemia may occur particularly if used in association with calcitriol. Non–calcium- and non–aluminum-containing phosphate binders include sevelamer hydrochloride (Renalgel; Genzyme, Cambridge, MA, USA; dogs and cats, 400–1600 mg po q 8–12 hours)19 and lanthanum carbonate (Fosrenal; Shire, Wayne, PA, USA, and Renalzin; Bayer, Newbury, UK; dogs and cats, 30–90 mg/kg po divided and administered with meals).19 Both of these appear to have minimal side effects in dogs and cats; however, they have not been evaluated in a controlled fashion.

Hypovitaminosis D occurs in dogs and cats with CKD, but not until an advanced stage (stages 3 and 4).80 Benefits of calcitriol therapy in patients with CKD has been thought to be mediated by its effects on parathyroid hormone and mineral metabolism86; however, other beneficial renal effects have been recognized including suppression of activity of the renin-angiotensin-aldosterone system, systematic activation of vitamin D receptors, and reducing podocytes loss associated with glomerular hypertrophy.87–90 Calcitriol supplementation (dogs and cats: initial dose of 2.0–2.5 ng/kg po q 24 hours, increase if parathyroid hormone concentrations do not normalize and decrease if hypercalcemia occurs; do not exceed 5 ng/kg po q 24 hours)7,19 may help decrease serum phosphorous concentration and parathyroid hormone concentration. Because calcitriol enhances intestinal absorption of calcium and phosphorous, it should not be given with meals; administration in the evening on an empty stomach reduces the risk of hypercalcemia.7 When calcitriol therapy is associated with hypercalcemia, the daily dose may be doubled and given every other day reducing calcitriol-induced intestinal absorption.91 Calcitriol supplementation may increase appetite, activity, and quality of life.86 To date, it has been shown to improve survival in dogs with stage 3 or 4 CKD, but not in stages 1 and 2, and it has not been shown to be beneficial in cats with any stage CKD.7

Hypoproliferative anemia. A normocytic, normochromic, nonregenerative anemia often occurs in patients with CKD. Causes of the anemia include decreased renal production of erythropoietin, nutritional imbalances because of hyporexia/anorexia, reduced red blood cell life span, and blood loss due to uremic gastroenteritis.92,93 There is evidence that anemia may be associated with progression of CKD due to decreased blood flow and oxygen delivery, oxidative stress, and induction of
It has been shown that patients with CKD have increased survival if the hematocrit is above 35%. Treatment includes maintaining good nutritional status, minimizing gastrointestinal blood loss, and stimulating red blood cell production.

Patients with CKD may have blood loss due to uremic gastroenteritis. Hypergastrinemia occurs with CKD and gastrin stimulates hydrochloric acid production by gastric parietal cells resulting in gastric hyperacidity. Histamine2-receptor-blocking agents may be beneficial in decreasing gastric acid production, although they are not potent and the effect may be transient. Proton pump inhibitors (dogs and cats, omeprazole: 0.7–2.0 mg/kg po q 12–24 hours; esomeprazole: 0.7 mg/kg po q 12 hours) decrease gastric acid secretion by inhibiting the potassium-hydrogen pump located in the cell membrane; they are the most potent antisclads. Sucralfate is also an antacid that has phosphate binding properties and is used to treat active gastric ulcer disease.

Red blood cell production by bone marrow may be stimulated pharmacologically. Anabolic steroids have been used to stimulate red blood cell production and to stimulate appetite. While they may stimulate appetite and increase lean muscle mass, they have minimal effect in promoting red blood cell production and may induce hepatopathy. In addition to anabolic steroids, other hormones may be supplemented including erythropoietin (dogs and cats, initial dose of 100 IU/kg subcutaneously 3 times per week and adjust based on hematocrit) and darbepoetin, a longer-acting form of erythropoietin (induction phase: 1.5 μg/kg subcutaneously q 7 days and when desired target hematocrit is reached the dosage is decreased to q 14 days; frequency or amount of dosage is adjusted depending on response). Studies with erythropoietin have shown that dogs and cats with CKD feel better even before hematocrit is increased. The main limitation of erythropoietin administration is development of anterythropoietin antibodies, which occurs in 20% to 70% of patients. There have been no controlled studies with darbepoetin. Because of antibody production, it has been recommended to begin erythropoietin therapy when the hematocrit is less than 20% or in patients that do not feel well that are anemic but not to that degree. Darbepoetin may be started at a lesser degree of anemia because of the decreased risk of antibody production. Because uremic gastroenteritis is common, iron should be supplemented to offset the iron deficiency associated with blood loss (ferrous sulfate: dogs, 100–300 mg po q 24 hours; cats, 50–100 mg po q 24 hours; iron dextran: dogs, 10–20 mg IM q 3–4 weeks; cats, 50 mg intramuscularly q 3–4 weeks). Additionally, infections should be treated to minimize iron sequestration that may result in decreased effectiveness of erythropoietin and darbepoetin administration. It is the author’s opinion that a hematocrit of 35% to 40% is the goal. This is based on results of a study in cats with CKD where the median packed cell volume in the group with progressive disease was 32% (interquartile range of 29%–36%) compared with the group with nonprogressive disease where the median packed cell volume was 36% (interquartile range of 34%–41%). Once the target is reached, the dosage can be slowly decreased to find the lowest amount necessary to control anemia. Complications of administration may include irritation at injection site, systemic arterial hypertension, and polycythemia. In patients that initially respond but in whom the hematocrit begins to decline, suspect antibody production against the recombinant human erythropoietin. Additionally, ensure iron deficiency has not occurred, which would result in decreased red blood cell production.

Systemic arterial hypertension. Systemic arterial hypertension has been reported to occur in up to 65% to 75% of dogs and cats with CKD. It occurs, in part, because of activation of the renin-angiotensin-aldosterone system, increased vasopressin (antidiuretic hormone) levels, and increased sympathetic tone. Indirect determination
of systemic arterial blood pressure is indicated in all patients diagnosed with CKD and is used to substage CKD. Systemic arterial hypertension may promote progression of CKD and proteinuria; result in left ventricular hypertrophy and possibly left-sided heart failure; neurologic signs such as ischemic encephalopathy, seizures, and death; and ocular disease such as retinal vascular tortuosity and hemorrhage, hyphema, and blindness (Fig. 4). The risk is moderate to high with a systolic blood pressure greater

Fig. 4. Hypertensive retinopathy and blindness in a 14-year-old, spayed female domestic shorthair cat with CKD. (A) The right pupil is dilated due to retinal detachment and hyphema is present in the left eye. (B) Fundic examination of the right eye shows retinal detachment and retinal hemorrhage.
than 160 mm Hg. Diagnosis is made by indirect measurement of systemic arterial blood pressure, although direct measurement can be performed by cannulation of the femoral artery. Arterial blood pressure can be determined indirectly using Doppler or oscillometric instruments. Doppler monitors use the Doppler effect to determine systolic blood pressure. Although mean and diastolic blood pressures may be determined using Doppler instruments, they are difficult and inaccurate. Oscillometric instruments measure systolic, mean, and diastolic blood pressures by detecting vibrations of the vascular wall. They are easy to use but require good technique. Indirect blood pressure is usually determined from the palmar, plantar, or coccygeal arteries.

Unless there is evidence of retinal lesions, neurologic signs, unexplained progression of CKD, or systolic blood pressure is greater than 180 mm Hg, the decision to begin antihypertensive therapy is not an emergency. Patients with CKD stages 2 to 4 having arterial systolic blood pressures persistently above 160 mm Hg (AP2; see Table 1) or patients with CKD stage 1 with arterial systolic blood pressures persistently exceeding 180 mm Hg (AP3; see Table 1) are candidates for treatment. The goal of treatment is to achieve a systolic blood pressure less than 150 mm Hg. Dietary sodium restriction may aid in decreasing systemic arterial blood pressure and may potentiate effects of antihypertensive medications. Calcium channel blockers (amlodipine: dogs, 0.25–0.5 mg/kg po q 12–24 hours; cats, 0.625–1.25 mg po q 12–24 hours) are the most effective antihypertensive drugs used in dogs and cats with CKD. They decrease systemic arterial blood pressure by inducing arterial vasodilation and on average decrease arterial systolic blood pressure by 50 mm Hg. Additionally, they may help to decrease degree of proteinuria, but are not as effective as angiotensin-converting enzyme inhibitors for this. Amlodipine appears safe with few side effects. Angiotensin-converting enzyme inhibitors (enalapril: dogs and cats, 0.25–1.0 mg/kg po q 12–24 hours; benazepril: dogs and cats, 0.25–0.5 mg/kg po q 12–24 hours) decrease enzymatic metabolism of angiotensin I to angiotensin II, resulting in vasodilation and decreased aldosterone production. They are more effective to decrease degree of proteinuria but on average reduce arterial systolic blood pressure by 10 mm Hg. Administration of angiotensin-converting enzyme inhibitors may be associated with an increase in the degree of azotemia and potassium. Laboratory evaluation should be performed 7 to 10 days after initiation or adjustment of angiotensin-converting enzyme therapy. Angiotensin-converting enzyme inhibitors have not been shown to slow down progression of CKD in cats except in patients with UPC greater than 1.0. Calcium channel blockers and angiotensin-converting enzyme inhibitors may be used together. Other treatments for systemic arterial hypertension that may be used include angiotensin receptor blockers (ARBs; irbesartan: dogs, 5 mg/kg PO q 12–24 hours; or losartan: dogs: 1–5 mg/kg PO q 12–24 hours), beta-blockers (atenolol: dogs, 0.25–1.0 mg/kg po q 12–24 hours; cats, 0.5–3.0 mg/kg po q 12–24 hours), alpha-blockers (prazosin: dogs, 1 mg/15 kg po q 12–24 hours; cats: 0.25–0.5 mg po q 12–24 hours), direct arteriolar vasodilators (hydralazine: dogs, 0.5–2.0 mg/kg po q 12 hours; cats, 2.5 mg po q 12–24 hours), and aldosterone receptor antagonists (spironolactone: dogs and cats, 1–2 mg/kg po q 12 hours).

### Serial Monitoring

Because CKD is dynamic and progressive, serial monitoring should be performed on all patients with CKD in order to adjust treatment. Monitoring should include body condition, BW, muscle condition, thoracic auscultation, assessment of hydration status, indirect measurement of systemic arterial blood pressure, complete blood
count, biochemical analysis, urinalysis, and possibly aerobic microbial culture of urine collected by cystocentesis. Frequency and extent of monitoring depend on how rapidly CKD is progressing, any nonrenal influences that may affect renal function, and owner satisfaction and finances.

**HOW CAN TREATMENT OF CKD BE IMPROVED?**

Early detection of CKD in patients may be an important factor on response to treatment. It may be worthwhile to determine serum creatinine concentration and urine specific gravity at 1 to 2 years of age and yearly beginning at 5 to 10 years of age. This may provide detection of CKD at an early stage and intervention at this point may provide better quality of life and longer quantity of life. It is important to keep in mind that the diagnosis of azotemia using the International Renal Insufficiency Society system may be different than the normal reference ranges used by your laboratory. It is recommended to use the values in the International Renal Insufficiency Society staging system where a serum creatinine greater than 1.6 mg/dL in cats and greater than 1.4 mg/dL in dogs is considered azotemic. Analytical techniques used to measure creatinine are consistent across laboratories; therefore, a change in 0.2 mg/dL is considered significant. Also, significant renal disease may be present without azotemia being present (stage 1). Whenever measuring serum creatinine concentration, a urine specific gravity must be determined at the same time in order to interpret the serum creatinine concentration. A complete urinalysis provides much information concerning urinary tract health and should be collected as part of a minimum database. Use of the International Renal Insufficiency Society staging system is important to guide therapy and monitoring and to permit comparison of a patient’s disease with others. However, treatment should be individualized to the patient and owners but avoid overtreatment. Minimize or eliminate nonrenal influences that may affect renal function.

Despite appropriate treatment and monitoring, CKD is ultimately a progressive disease. Early identification and treatment may modify the rate of progression and provide for a better quality and longer quantity of life for the patient. Owners can be educated to evaluate disease by observing changes in water intake, urine volume, food intake, BW, body and muscle condition, activity, and behavior.

**WHEN SHOULD DIET BE CHANGED IN A PATIENT DIAGNOSED WITH CKD?**

Dietary modification is an important component of treating patients with CKD. Dietary modification can be used to offset many deficiencies and excesses that occur with CKD. It is more than protein restriction as diets formulated for use in patients with CKD are calorically dense, phosphorous and sodium restricted, have increased potassium and B vitamins, contain omega 3 fatty acids, contain soluble fiber, and are alkalinizing. Dietary modification has been shown to increase quality and quantity of life in dogs and cats with azotemic CKD (stage 2 or higher), but there are no studies evaluating dietary modification in patients with stage 1, non-proteinuric CKD. Nonetheless, in most patients the diet should be changed at the time of diagnosis of CKD. Furthermore, it is easier to introduce a therapeutic diet when the patient feels good rather than waiting until the disease process has progressed and introduction of a therapeutic diet is not possible.

**SUMMARY**

Many strides have been made in diagnosing and treating dogs and cats with CKD including dietary modification and pharmacologic therapy. Use of the International
Renal Insufficiency Society staging system provides a basis for diagnosis and management and for assessing response to treatment as well as comparison of results of studies for application to patients.

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