

# The Silent Killer

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*It is the leading cause of death of cats. It is one of the top causes of death of dogs. And yet many pet owners - dog owners in particular - are unaware of chronic renal failure. What is it? What are the symptoms and how is it diagnosed? Is there any treatment? Perhaps even more important, what can be done to reduce its effect and prolong a pet's life?*

**NB: Information within is believed to be accurate but is not provided as medical or veterinarian advice; please consult with your vet to determine the best treatment options for your pet.**

## What is CRF?

The primary function of the kidneys is to filter out of the blood waste products left behind from the body's metabolism. Excess water is also removed and the combination becomes urine. In addition to cleansing the blood, the kidneys help regulate blood pressure and blood composition (pH, red cells, sugar, volume, water). Renal failure comes in two primary forms: acute (ARF) and chronic (CRF). In both ARF and CRF, renal function is impaired. CRF can also be called chronic kidney disease (CKD).



Acute renal failure may occur quickly when a pet consumes something poisonous - antifreeze, raisins, lily plants (cats) - or from a severe bacterial infection. If caught quickly, ARF is usually treatable. If not, impairment can be significant, putting the pet's life at grave risk.

Chronic renal failure takes place over a protracted period of time (typically many months or years). While it can sometimes occur in young animals, CRF is most commonly seen in older dogs and cats. CRF generally does not have an attributable cause, has no cure and the resulting kidney impairment is not reversible.

## What are the symptoms?

CRF is a silent killer primarily because the symptoms are not manifest until the kidneys have lost most of their function and are significantly impaired. This "silence" is in part because the kidneys are able to perform acceptably well even while they are losing their capacity to work. Some of the early symptoms may also be difficult for a pet owner to pick up upon as a decisive indication of medical troubles in their pet.

One of the first signs of problems is increased thirst. Unfortunately, the increase may not be noticeable to the owner until it becomes significant. In warmer climates it can also be difficult to separate abnormal water consumption from normal variability caused by temperature and humidity swings.

Another symptom that may show before others is an increase in the frequency and quantity of urination. Again, this may happen gradually over time so as not to stand out as a large departure from normal until considered against conditions many months, not days, prior.



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Additional symptoms arise as the impairment becomes more significant and the kidneys can only function at a greatly reduced level. Most noticeable will be a loss in the pet's weight and decreased appetite. Lethargy may also be apparent. Unfortunately, by this point kidney function is usually greatly reduced and it may no longer be possible to take counter measures to slow the impairment process.

Other symptoms, often at the latest stages, are nausea, vomiting, blindness and seizures.

## Clinical Diagnosis

To properly diagnose either ARF or CRF, blood and urine samples are analyzed. Standard testing includes a complete blood count, a biochemical profile and urinalysis. The vet may also check the pet's blood pressure, protein to creatinine ratio and the amount of parathyroid hormone. Many vets are able to do these tests in-house so results are available the same day.



The three items the vet will be most interested in are BUN (blood urine nitrogen), creatinine and phosphorus levels. All are likely to show significant elevation as CRF progresses and will be very high in late stage CRF. Sodium, potassium and magnesium (electrolytes) may also be checked for irregularity.

"Staging" is just a clinical term that means 'to identify to what point a disease has progressed'. Diseases are often split into different stages (or levels) to indicate changes in the types of symptoms seen and severity of damage to the body over time. Low numbers indicate the onset of the disease, the fewest symptoms and least damage with the numbers increasing to the final, worst case. The table below defines the four accepted stages of CRF per the International Renal Interest Society (IRIS).

CRF Staging

Stage	Serum Creatinine (mg/dl)	Serum Creatinine (µmol/L)
1	<1.4 (dog)	<125 (dog)
	<1.6 (cat)	<140 (cat)
2	1.4-2.0 (dog)	125-179 (dog)
	1.6-2.8 (cat)	140-249 (cat)
3	2.1-5.0 (dog)	180-439 (dog)
	2.9-5.0 (cat)	250-439 (cat)
4	>5.0 (dog/cat)	>440 (dog/cat)

Stage	Additional Notes
1	Shows a mild renal abnormality such as an increase in proteins in the urine or decreased concentrating ability
2	Some signs of excess urea, creatinine and/or proteins in the urine. May show signs of increased dilute urine
3	Excess urea, creatinine and/or proteins in the urine. Many systemic signs of CRF present
4	Very high urea levels, excess proteins may be present, decreased urinary concentrating ability. Systemic clinical signs are severe.

Excess protein levels ("proteinuria") occur at a protein/creatinine ratio > 0.4 (cats) or 0.5 (dogs). Levels below 0.2 are normal and in between is considered borderline. However, testing with basic urine dipsticks may sometimes give rise to false positives so additional screening is appropriate in those cases.

Blood pressure over 160/100 is indicative of moderate risk, 180/120 is high risk of organ damage when persistent and seen in conjunction with other CRF indicators. Existing hypertension will increase complications. To be useful, readings should be taken multiple times over multiple days. Proteinuria and blood pressure results are then used to "sub-stage" the dog or cat's condition.

A valuable test that can give indications of CRF at an earlier stage measures the amount of SDMA (Symmetric dimethylarginine). Meta-analysis in human studies indicate SDMA exhibits some properties of a reliable marker of renal function.<sup>1</sup> Studies in pets show knowledge of irregular SDMA levels can provide nearly 18 months earlier warning of CRF in cats and 9 months in dogs.

As with cancer, the earlier CRF is detected the better the chance the disease can be slowed and the pet's quality of life extended. Another potential early warning indicator in dogs is periodontal disease. A study in 2011 showed an association between increasingly severe periodontal disease with high serum creatinine and blood urea nitrogen levels (this does not mean to say dental disease is the cause of CRF).

The stage and sub-stage will, in consideration of any other health conditions, indicate what course of treatment is likely to best reduce the symptoms and damage from CRF in order to extend a pet's quality of life and expected life span.

As mentioned previously, there is no cure for CRF. But if caught at a relatively early stage, modification of diet can extend the life of a pet many months, with studies showing an average of around 13 months.

## Treatment

Treatment for CRF is primarily focused upon diet and fluids. Additional treatment and medicines will be prescribed on a case by case basis to deal with other complications of CRF.

A vet will usually prescribe a specially formulated canned food for the pet that is very low in phosphorous and contains proteins that are easy to digest and produce less waste products. These formulations are also often low in sodium (in case of age related heart issues) and high in omega-3 fatty acids. Unfortunately, dogs and cats do not always find low protein wet (or dry) foods to be appetizing. Pet parents may also find the cost of special foods to be outside of their budget. Hills, Purina and Royal Canin all make prescription formulations. Royal Canin has a [website](#) just for their renal products, Purina has a [page](#) as well.

In some cases, pet owners may be able to find a suitable *non-prescription* low phosphorous food at their local pet store or via one of the many online retailers. As an example, Hill's Science Diet "Mature adult gourmet beef entree" is very low in phosphorous (0.5% dry matter basis) and approaches that of the prescription lines (note: there is a variation of this food without "mature" with the same low phosphorous content but about 6% points more protein). It is very hard to find a dry (and less costly), non-prescription formula that is low in phosphorous. Hill's does have Hill's Science Diet "Adult Oral Care" (0.6% dry matter basis) but it may higher in protein content (24.0% dry matter) than is suitable for a CRF patient.

As a reference, the prescription diets have phosphorus levels of 0.4 - 0.5%. Protein levels vary, with kibbles in the 10-18% range and wet as low as 3%. Keep in mind that it is not just the quantity of protein that is important but the ease with which it is digested and the amount of metabolic by products left behind. If you are unable to afford long term care using a prescription diet you *must* review carefully with your pet's vet the alternatives that are available to you. With some time and the correct choices,

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<sup>1</sup> Symmetric dimethylarginine (SDMA) as endogenous marker of renal function—a meta-analysis



home cooking for your pet may be a good option. The pet parent must do whatever it takes to keep their pet eating enough to maintain body weight. Home cooking may even become a requirement for finicky eaters or during later stages of CRF as appetite declines.

[A note on measurements: it can be very difficult for a pet parent to evaluate pet food nutritional content. Most bags only report "guaranteed analysis" which is a measure of *minimum* levels on an "as fed" basis. As different foods have wildly different moisture content "as fed" is pretty much useless. A better measure is "dry matter" basis which tries to account for differences in moisture content and is probably good for comparison of foods within a single manufacturer. The absolute best measure, however, is given in milligrams per 100 kilo calories. Unfortunately, no pet food manufacturers publish data on their packaging or websites with mg/100 kCal measurements. However, the major brands usually will be able to provide these figures by phone or email. ]

As noted earlier, studies have shown the positive effects of a "renal" diet can be dramatic, in particular for cats. As blood phosphorus levels continue to elevate during later stages of CRF, diet alone may not be sufficient. To help lower phosphorous levels, a binder is usually prescribed. One example is flavorless aluminum carbonate in water solution given orally after eating. The binder attaches to the phosphorus so that it can be eliminated from the body through the digestive tract.

It is very important that CRF pets stay hydrated. In addition to having plenty of fresh water available, supplementation with other fluids may be necessary. Broths that are very low in sodium are one way to encourage additional hydration. In some cases, intravenous fluids may be necessary. Your pet's vet may administer these at this office on a one off basis or may recommend that the pet parent begin regular subcutaneous fluid injections. Not every pet parent will feel comfortable giving these injections (or may feel they lack the skill or a cooperative patient). However, it is usually possible to hire a local veterinary technician to come to the home periodically to administer the fluids.

Other complications that may arise include unstable sodium levels, low potassium, elevated parathyroid hormone (PTH), hypertension and anemia. Sodium levels are generally controlled with diet and are important to watch, more so for CRF pets that also have heart health issues. Sodium is important in regulating both blood pressure and volume.

Potassium is one of the most important electrolytes in the body and low levels can contribute to lethargy and reduced appetite. A sure sign of dangerously low levels of potassium is a pet that is unable to lift its head upright in a normal fashion. This symptom is more common to feline CRF patients. Potassium levels may become low as a result of increased urination and are easily supplemented. However, potassium supplementation should only be done at the direction of a vet as it may cause dangerous complications if heart disease is also present.

PTH maintains proper phosphorous and calcium levels but becomes elevated in CRF pets and Vitamin D, which works with PTH, is reduced. There are indications that elevated PTH levels may also contribute to CRF. *Research has shown that supplementation with low doses of a type of vitamin D, calcitriol, can reduce elevated PTH levels and in some cases help slow the progression of CRF.*

Just as in humans, hypertension in pets can be controlled with medication. Unlike humans, it can be very difficult to get an accurate assessment of a dog or cat's resting blood pressure. This makes both the initial diagnosis and amount of medication to dispense challenging. Medications used for treating high blood pressure are also effective in treating another complication, excess protein in the urine.

A pet with CRF may make less of the hormones necessary for red blood cell production and become anemic. One treatment for anemia is to give human erythropoietin. Unfortunately, there are differences between the human and the canine and feline variants of erythropoietin. Over time this can lead to a pet developing antibodies that cause the human erythropoietin to be rejected.



Because the potential complications are so numerous, regular monitoring of blood composition and other symptoms is crucial so that additional actions can be taken in the most timely and effective manner as necessary. Pets that also suffer from heart disease pose a significant challenge as medications used to treat many heart problems can be contra indicated for treatment of kidney disease.

As you can see, there is no magic bullet in the treatment of CRF. By catching the disease early, diet modifications offer the best chance to slow its progression.

The most important thing to understand is that CKD is a progressive disease with no single known cause and is increasingly likely as a pet ages. What pet parents can do is try to mitigate risk factors and be proactive in analyzing their pet's health so as to catch the onset of CKD at the earliest possible moment.

## Diet

As you now know, protein and phosphorus are problematic for pets that already have CKD. But what about healthy pets?

Begin with phosphorus. It is rare that a diet is too low in phosphorus. The need for phosphorus in the diet grows through the adolescent years and then declines, leveling off at roughly 75% of its peak value. But can a diet be too high in phosphorus?

Perhaps so, though there is no definitive red line for pets or humans and no direct link to CKD. However, elevated phosphorus levels can hinder the effective usage of calcium, iron, magnesium and zinc by the body.

The amount of phosphorus in pet foods is broadly proportional to the amount of protein. Recently, some pet advocates have pushed to have pet food manufacturers increase both the amount of protein and the percentage derived from animal sources in their products.

Like phosphorus, there is no definitive evidence that a high protein diet in otherwise healthy pets will increase the chances of developing CKD. Human studies focus on two areas:

- increased volume and size of kidney glomeruli
- an increase in the glomerular filtration rate (GFR hyperfiltration).

Studies in the mid 2000's were conflicting. One, in *The American Journal of Kidney Disease*, cautioned that "high protein HP consumption has been found, under various conditions, to lead to glomerular hyperfiltration and hyperemia; acceleration of chronic kidney disease (CKD); increased proteinuria; diuresis, natriuresis, and kaliuresis with associated blood pressure changes; increased risk for nephrolithiasis; and various metabolic alterations." <sup>2</sup>

Another study, published in *Nutrition & Metabolism*, states "...some studies suggest that hyperfiltration, the purported mechanism for renal damage, is a normal adaptive mechanism that occurs in response to several physiological conditions." And continues "...we find no significant evidence for a detrimental effect of high protein intakes on kidney function in healthy persons after centuries of a high protein Western diet." <sup>3</sup>



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2. [Am J Kidney Dis](#). 2004 Dec;44(6):950-62 *High-protein diets: potential effects on the kidney in renal health and disease* Friedman AN.

3 Nutr Metab (Lond). 2005; 2: 25. *Dietary protein intake and renal function* William F Martin, Lawrence E Armstrong and Nancy R Rodriguez

A more recent study from 2012 found that rats fed a diet of 45% over 12 weeks (said to be equivalent to 9 human years) had significant changes in both the composition and size of their kidneys. Of particular concern was significant drop (88%) in urinary citrate compared to the control group. Hypocitraturia is commonly found in patients with nephrolithiasis - kidney stones.

In addition to the amount of protein, there really is a concern over the move away from mixed sources (i.e., grain and animal proteins) to foods that are all or mostly animal protein. Those foods are higher in phosphorus, sometimes excessively so. Television commercials trumpeting “our food is made from real meat!” sound so appealing and reasonable to pet parents they then refuse to consider better balanced alternatives, often having years of research and testing behind them.

As CKD is ‘the silent killer,’ pet parents must recognize that their pet may already have developed CKD many months, even years, before any formal diagnosis. During that time, the excessive phosphorus found in high protein formulations is accelerating the death of their pet.

## Recommendations

The common sense take away from these studies is that excessive protein should be avoided and in the case of dogs, tailored to reflect activity levels. Working breeds (doing work and not watching TV) will require more than more sedentary breeds. There may also be limits to the usable uptake of protein; the figure most often suggested is 35%.

As pets age, pet parents need to be much more focused on phosphorus levels and strive to feed a balanced diet that provides sufficient protein with reduced phosphorus. Because there are so many opportunities for manufacturers to game the ingredient label, I recommend that owners pick up the phone and contact the company to request information about the phosphorus content on a dry or mg/Kcal basis.

Be sure to ask for each variant you may feed your pet - nutritional content for chicken based foods are often *dramatically* different from those using fish. I also recommend that you ask for sodium content (seeing you are making the call).. As your pet ages, heart related issues may also develop and it is a good idea to avoid products high in sodium (or mix them with others that are low sodium).

**By proactively keeping phosphorus uptake under control, the progression of undiagnosed CKD can be mitigated with no harm to pets that never develop the disease.**

## Testing & Observation

While diet modifications are very important, owners have additional tools to help them fight against CKD. One of the most important is to begin annual blood testing as your pet nears breed based old age. For instance, if your line of Golden Retrievers has a life expectancy of 11 years, you might begin regular blood and urine work at age 7 or 8.

Of course, this will mean additional expense and every pet owner will have a different ability and willingness to pay for testing. It may be possible to begin with just blood or urine and your vet can assist in determining exactly what analysis will be done. Also keep in mind that some vets may be reluctant to ever suggest blood or urine testing be performed unless you indicate your pet has a specific problem. It is up to the pet parent to suggest (or demand) that screening be done. Even a 100% healthy, normal result is valuable as it establishes a baseline against which future tests may be compared.

Owners should also pay regular attention to the frequency and quality of their pet’s urine. If the frequency increases with no obvious reason or the color becomes consistently lighter, seek out your vet. When judging frequency, try to compare not just to recent days or weeks but also prior years. This will



help when trying to determine if the increase is due to seasonal variation or may be indicative of a problem.

Ditto for water consumption. If you wake up one morning and say to yourself, 'hmm.. I'm filling her water dish more often...' and can't point to any clear change like a heat wave or change in diet, that too is a reason to contact your vet for examination and additional testing.

Finally, do monitor your pets activity level for signs of lethargy. All too often pet parents (and humans too) attribute a slow down to 'just old age'. Certainly, a dramatic change is a big red flag. But this is another case where, while you may notice your pet is slowing down and think it normal, one day you realize 'boy, he's really slowed down a lot this year.' Again, get in touch with your vet and express your concerns.

Be proactive!

