

# Chronic Kidney Disease Staging in Dogs & Cats

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## Overview

To promulgate standards of care for small animals, the International Renal Interest Society (IRIS) has established guidelines to diagnose, assess, and manage chronic kidney disease (CKD) in dogs and cats. The most recent versions can be found on the IRIS website ([iris-kidney.com](http://iris-kidney.com); see **Resources**).

Diagnosing and staging CKD requires serum (from fasting blood) creatinine, a readily available diagnostic test, to infer glomerular filtration rate (GFR; see **CKD Toolkit**, page 87). GFR should be assessed on at least 2 occasions in a stable patient. Of note, alternative assessments of GFR (eg, symmetric dimethylarginine [SDMA]) may add to or supplant blood creatinine in the future.<sup>1</sup> Important additional supportive information includes assessment of urinary concentrating ability (ie, urine specific gravity) without identifiable nonrenal cause, abnormal renal palpation or renal imaging findings, proteinuria of renal origin, and abnormal renal biopsy results.

SDMA, now available on commercial serum chemistry profiles, appears to enter the plasma at a constant rate, independent of muscle mass and dietary protein intake. SDMA is cleared by glomerular filtration alone, independent of urine volume. These characteristics suggest that SDMA may offer a more consistent indicator of GFR, less affected by confounding factors that impact both serum creatinine and blood urea nitrogen as indicators of kidney function and could allow earlier detection of CKD than traditional tests.<sup>2</sup>

The **magnitude of proteinuria and degree of hypertension** can provide further insight regarding the nature and likelihood of CKD progression

### CKD TOOLKIT

Find detailed figures on CKD staging and substaging by proteinuria or blood pressure on page 87.

and are incorporated as substages (see *CKD Toolkit*, page 87). Some breeds (eg, greyhounds) tend to have a higher normal range for blood pressure as compared with most other breeds.<sup>3</sup>

Staging can facilitate appropriate patient monitoring and treatment. IRIS has developed additional guidelines to address these elements (see *Resources*). These guidelines reinforce the value of repeating tests to make sure they accurately reflect patient status and regular patient reassessment to determine response to treatment, rate of CKD progression, and the need to adjust management strategies.

### Diagnosis & Staging

IRIS has established algorithms for diagnosis and staging to accompany the staging criteria for dogs and cats (see *Resources*). The algorithms use standard, readily available test results to establish initial staging; however, substaging requires collection of urine for estimation of the urine protein:creatinine ratio and measurement of blood pressure. Blood pressure measurements can be inconsistent because of the requirement for special equipment and, most importantly, a standard technique.<sup>4</sup>

### Treatment

IRIS staging can assist with development of empirical recommendations regarding appropriate, logical treatment for each CKD stage (see *Resources*). Predictions based on clinical experience might be made about the likely response to treatment.

Management strategies may include:

- ▶ Discontinuing all potentially nephrotoxic drugs, if possible
- ▶ Identifying and treating any pre- or postrenal abnormalities
- ▶ Ruling out any treatable conditions (eg, pyelonephritis, renal urolithiasis)
- ▶ Correcting dehydration
- ▶ Reducing proteinuria (eg, low-protein diet,

## RESOURCES

Several resources are available from IRIS to help diagnose, stage, and treat dogs and cats with CKD:

- ▶ Staging of CKD: [iris-kidney.com/pdf/staging-of-ckd.pdf](http://iris-kidney.com/pdf/staging-of-ckd.pdf)
- ▶ Treatment Recommendations for CKD in Dogs: [iris-kidney.com/pdf/treatment-recommendation-dogs.pdf](http://iris-kidney.com/pdf/treatment-recommendation-dogs.pdf)

ACE inhibitors, angiotensin-receptor blockers)

- ▶ Addressing systemic hypertension (eg, calcium channel blockers, ACE inhibitors)
- ▶ Reducing dietary intake and GI absorption of phosphate
- ▶ Correcting metabolic acidosis (usually only encountered in advanced Stage 3 and Stage 4)
- ▶ Treating anemia (usually only encountered in advanced Stage 3 and Stage 4)

Reduced phosphate intake<sup>4</sup> and reduction of proteinuria<sup>5-9</sup> are the most important treatment strategies for reducing CKD progression. Patients in Stage 1 represent the best opportunity for intervention with these strategies to prevent or ameliorate CKD's rate of progression.<sup>5-10</sup> Correction of systemic hypertension, if present, is also important.<sup>11-14</sup>

Dogs and cats in Stages 1 through 3 often respond to appropriate management with improved longevity and slowing of progression,<sup>15</sup> whereas those in Stage 4 tend to be fragile and much more prone to repeated episodes of uremic crises that require IV fluid support and renal replacement therapy (ie, dialysis) for restabilization.

### IRIS Staging for the Medical Record

IRIS staging allows characterization of patient status in the medical record in a shorthand format that facilitates rapid recognition of status, disease progression, and response to treatment. For example\*:

CKD = chronic kidney disease  
GFR = glomerular filtration rate  
IRIS = International Renal Interest Society  
SDMA = symmetric dimethylarginine

A feline CKD patient before treatment with a blood creatinine of 1.6 mg/dL (283 µmol/L), UP/C of 1.5, and systolic blood pressure of 230 mm Hg would be classified as:

**IRIS CKD Stage 1, P (proteinuric), SH (severely hypertensive)**

On follow-up after treatment with antihypertensive agents and strategies to reduce proteinuria, the cat returns with a blood creatinine of 2 mg/dL (353 µmol/L), UP/C of 0.4, and systolic blood pressure of 155 mm Hg and would be reclassified as:

**IRIS CKD Stage 2, BP(T) (borderline proteinuric on treatment)**

A canine CKD patient presented with a blood creatinine of 2.5 mg/dL (220 µmol/L), UP/C of 0.4, and systolic blood pressure of 165 mm Hg would be classified as:

**IRIS CKD Stage 3, BP (borderline proteinuric), H (hypertensive)**

On follow-up during administration of treatment to address both proteinuria and hypertension, the dog returns with a blood creatinine of 3.8 mg/dL (336 µmol/L), UP/C of <0.2, and systolic blood pressure of 145 mm Hg and would be reclassified as:

**IRIS CKD Stage 3, NP(T) (nonproteinuric on treatment), NH(T) (nonhypertensive on treatment)**

**Conclusion**

IRIS staging CKD patients can help improve patient assessment and outcome, promote timely implementation of treatment strategies, facilitate assessment of treatment effectiveness, and standardize the terminology of CKD patient status. Although adoption is likely far from universal, implementation in practice is encouraged. ■■■

\*Examples are based on similar examples found on the IRIS website.

See page 90 for references.



**CHEWABLES**

**CAUTION:** Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

**INDICATIONS:** For use in dogs to prevent canine heartworm disease by eliminating the tissue stage of heartworm larvae (*Dirofilaria immitis*) for a month (30 days) after infection and for the treatment and control of ascarids (*Toxocara canis*, *Toxascaris leonina*) and hookworms (*Ancylostoma caninum*, *Uncinaria stenocephala*, *Ancylostoma braziliense*).

**DOSAGE:** HEARTGARD® Plus (ivermectin/pyrantel) should be administered orally at monthly intervals at the recommended minimum dose level of 6 mcg of ivermectin per kilogram (2.72 mcg/lb) and 5 mg of pyrantel (as pamoate salt) per kg (2.27 mg/lb) of body weight. The recommended dosing schedule for prevention of canine heartworm disease and for the treatment and control of ascarids and hookworms is as follows:

Dog Weight	Cheewables Per Month	Ivermectin Content	Pyrantel Content	Color Coding On Foil Backing and Carton
Up to 25 lb	1	68 mcg	57 mg	Blue
26 to 50 lb	1	136 mcg	114 mg	Green
51 to 100 lb	1	272 mcg	227 mg	Brown

HEARTGARD Plus is recommended for dogs 6 weeks of age and older. For dogs over 100 lb use the appropriate combination of these chewables.

**ADMINISTRATION:** Remove only one chewable at a time from the foil-backed blister card. Return the card with the remaining chewables to its box to protect the product from light. Because most dogs find HEARTGARD Plus palatable, the product can be offered to the dog by hand. Alternatively, it may be added intact to a small amount of dog food. The chewable should be administered in a manner that encourages the dog to chew, rather than to swallow without chewing. Chewables may be broken into pieces and fed to dogs that normally swallow treats whole.

Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes after administration to ensure that part of the dose is not lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

HEARTGARD Plus should be given at monthly intervals during the period of the year when mosquitoes (vectors), potentially carrying infective heartworm larvae, are active. The initial dose must be given within a month (30 days) after the dog's first exposure to mosquitoes. The final dose must be given within a month (30 days) after the dog's last exposure to mosquitoes.

When replacing another heartworm preventive product in a heartworm disease preventive program, the first dose of HEARTGARD Plus must be given within a month (30 days) of the last dose of the former medication.

If the interval between doses exceeds a month (30 days), the efficacy of ivermectin can be reduced. Therefore, for optimal performance, the chewable must be given once a month on or about the same day of the month. If treatment is delayed, whether by a few days or many, immediate treatment with HEARTGARD Plus and resumption of the recommended dosing regimen will minimize the opportunity for the development of adult heartworms.

Monthly treatment with HEARTGARD Plus also provides effective treatment and control of ascarids (*T. canis*, *T. leonina*) and hookworms (*A. caninum*, *U. stenocephala*, *A. braziliense*). Clients should be advised of measures to be taken to prevent reinfection with intestinal parasites.

**EFFICACY:** HEARTGARD Plus Chewables, given orally using the recommended dose and regimen, are effective against the tissue larval stage of *D. immitis* for a month (30 days) after infection and, as a result, prevent the development of the adult stage. HEARTGARD Plus Chewables are also effective against canine ascarids (*T. canis*, *T. leonina*) and hookworms (*A. caninum*, *U. stenocephala*, *A. braziliense*).

**ACCEPTABILITY:** In acceptability and field trials, HEARTGARD Plus was shown to be an acceptable oral dosage form that was consumed at first offering by the majority of dogs.

**PRECAUTIONS:** All dogs should be tested for existing heartworm infection before starting treatment with HEARTGARD Plus which is not effective against adult *D. immitis*. Infected dogs must be treated to remove adult heartworms and microfilariae before initiating a program with HEARTGARD Plus.

While some microfilariae may be killed by the ivermectin in HEARTGARD Plus at the recommended dose level, HEARTGARD Plus is not effective for microfilariae clearance. A mild hypersensitivity-type reaction, presumably due to dead or dying microfilariae and particularly involving a transient diarrhea, has been observed in clinical trials with ivermectin alone after treatment of some dogs that have circulating microfilariae.

**Keep this and all drugs out of the reach of children.**

In case of ingestion by humans, clients should be advised to contact a physician immediately. Physicians may contact a Poison Control Center for advice concerning cases of ingestion by humans.

Store between 68°F - 77°F (20°C - 25°C). Excursions between 59°F - 86°F (15°C - 30°C) are permitted. Protect product from light.

**ADVERSE REACTIONS:** In clinical field trials with HEARTGARD Plus, vomiting or diarrhea within 24 hours of dosing was rarely observed (1.1% of administered doses). The following adverse reactions have been reported following the use of HEARTGARD Plus: Depression/lethargy, vomiting, anorexia, diarrhea, mydriasis, ataxia, staggering, convulsions and hypersalivation.

**SAFETY:** HEARTGARD Plus has been shown to be bioequivalent to HEARTGARD, with respect to the bioavailability of ivermectin. The dose regimens of HEARTGARD Plus and HEARTGARD are the same with regard to ivermectin (6 mcg/kg). Studies with ivermectin indicate that certain dogs of the Collie breed are more sensitive to the effects of ivermectin administered at elevated dose levels (more than 16 times the target use level) than dogs of other breeds. At elevated doses, sensitive dogs showed adverse reactions which included mydriasis, depression, ataxia, tremors, drooling, paresis, recumbency, excitability, stupor, coma and death. HEARTGARD demonstrated no signs of toxicity at 10 times the recommended dose (60 mcg/kg) in sensitive Collies. Results of these trials and bioequivalency studies, support the safety of HEARTGARD products in dogs, including Collies, when used as recommended.

HEARTGARD Plus has shown a wide margin of safety at the recommended dose level in dogs, including pregnant or breeding bitches, stud dogs and puppies aged 6 or more weeks. In clinical trials, many commonly used flea collars, dips, shampoos, anthelmintics, antibiotics, vaccines and steroid preparations have been administered with HEARTGARD Plus in a heartworm disease prevention program.

In one trial, where some pups had parvovirus, there was a marginal reduction in efficacy against intestinal nematodes, possibly due to a change in intestinal transit time.

**HOW SUPPLIED:** HEARTGARD Plus is available in three dosage strengths (See DOSAGE section) for dogs of different weights. Each strength comes in convenient cartons of 6 and 12 chewables.

For customer service, please contact Merial at 1-888-637-4251.



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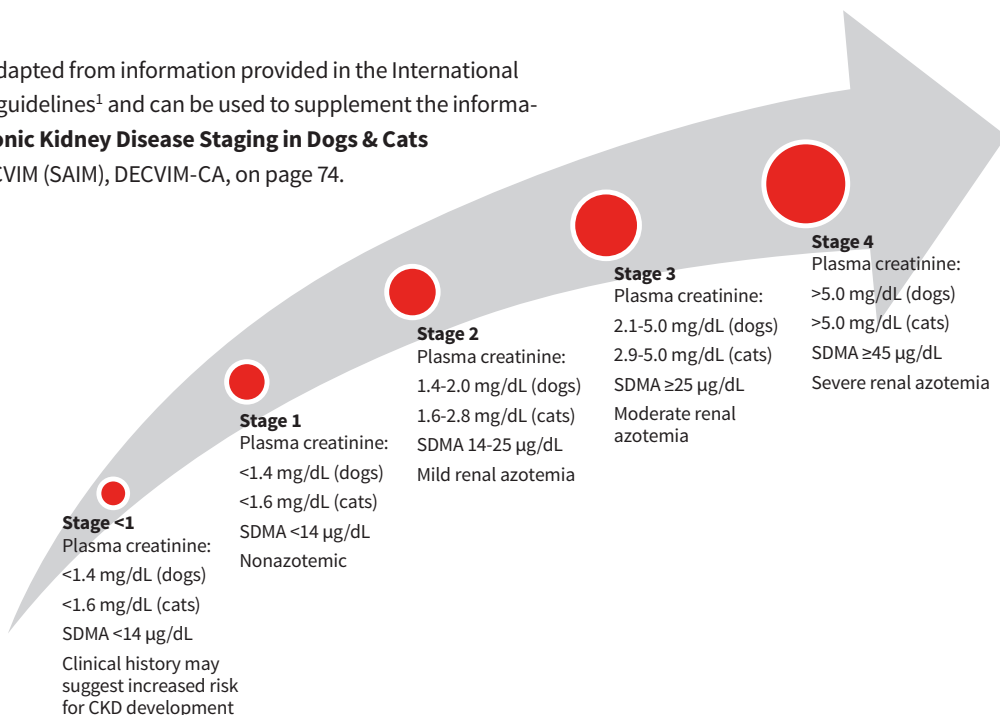
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# CKD Toolkit: Staging in Dogs & Cats

The following figures were adapted from information provided in the International Renal Interest Society (IRIS) guidelines<sup>1</sup> and can be used to supplement the information found in the article **Chronic Kidney Disease Staging in Dogs & Cats** by David F. Senior, BVSc, DACVIM (SAIM), DECVIM-CA, on page 74.

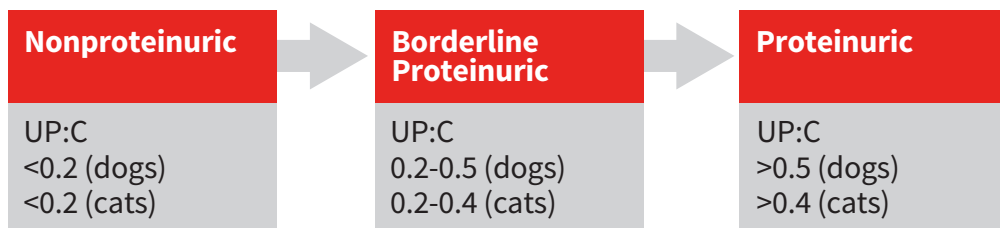
## CHRONIC KIDNEY DISEASE STAGING IN DOGS & CATS

SDMA = symmetric dimethylarginine



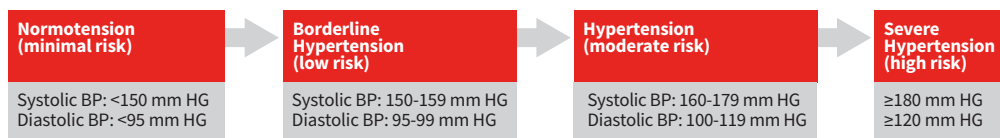
## SUBSTAGING BASED ON PROTEINURIA

UP:C = urine protein:creatinine ratio



## SUBSTAGING BASED ON BLOOD PRESSURE\*

\*Adjustments should be made for breeds with typically higher blood pressure.



### Reference

1. International Renal Interest Society. IRIS Staging of CKD. <http://www.iris-kidney.com/pdf/staging-of-ckd.pdf>. Modified 2015. Accessed May 11, 2017.

**References**

- Hall JA, Yerramilli M, Obare E, Yerramilli M, Almes K, Jewell DE. Serum concentrations of symmetric dimethylarginine and creatinine in dogs with naturally occurring chronic kidney disease. *J Vet Intern Med.* 2016;30(3):794-802.
- Nabity MB, Lees GE, Boggess MM, et al. Symmetric dimethylarginine assay validation, stability, and evaluation as a marker for the early detection of chronic kidney disease in dogs. *J Vet Intern Med.* 2015;29(4):1036-1044.
- Cox RH, Peterson LH, Detweiler DK. Comparison of arterial hemodynamics in the mongrel dog and the racing Greyhound. *Am J Physiol.* 1976;230(1):211-218.
- Brown S, Atkins C, Bagley R, et al. Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats. *J Vet Intern Med.* 2007;21(3):542-558.
- Brown SA, Crowell WA, Barsanti JA, White JV, Finco DR. Beneficial effects of dietary mineral restriction in dogs with marked reduction of functional renal mass. *J Am Soc Nephrol.* 1991;1(10):1169-1179.
- Vaden SL, Elliott J. Management of proteinuria in dogs and cats with chronic kidney disease. *Vet Clin North Am Small Anim Pract.* 2016;46(6):1115-1130.
- Zatelli A, Roura X, D'Ippolito P, Bertanda M, Zini E. The effect of renal diet in association with enalapril or benazepril on proteinuria in dogs with proteinuric chronic kidney disease. *Open Vet J.* 2016;6(2):121-127.
- Cortadellas O, Talavera J, Fernández del Palacio MJ. Evaluation of the effects of a therapeutic renal diet to control proteinuria in proteinuric non-azotemic dogs treated with benazepril. *J Vet Intern Med.* 2014;28(1):30-37.
- King JN, Gunn-Moore DA, Tasker S, Gleadhill A, Strehlau G. Benazepril in Renal Insufficiency in Cats Study Group. Tolerability and efficacy of benazepril in cats with chronic kidney disease. *J Vet Intern Med.* 2006;20(5):1054-1064.
- Mizutani H, Koyama H, Watanabe T, et al. Evaluation of the clinical efficacy of benazepril in the treatment of chronic renal insufficiency in cats. *J Vet Intern Med.* 2006;20(5):1074-1079.
- Finco DR. Association of systemic hypertension with renal injury in dogs with induced renal failure. *J Vet Intern Med.* 2004;18(3):289-294.
- Elliott J, Barber PJ, Syme HM, Rawlings JM, Markwell PJ. Feline hypertension: clinical findings and response to antihypertensive treatment in 30 cases. *J Small Anim Pract.* 2001;42(3):122-129.
- Jepson RE, Elliott J, Brodbelt D, Syme HM. Effect of control of systolic blood pressure on survival in cats with systemic hypertension. *J Vet Intern Med.* 2007;21(3):402-409.
- Braga ET, Leite JH, Rosa FA, et al. Hypertension and its correlation with renal lesions in dogs with leishmaniosis. *Rev Bras Parasitol Vet.* 2015;24(1):45-51.
- Jacob F, Polzin DJ, Osborne CA, et al. Clinical evaluation of dietary modification for treatment of spontaneous chronic renal failure in dogs. *J Am Vet Med Assoc.* 2002;220(8):1163-1170.

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