Chronic Kidney Disease Staging in Dogs & Cats

David F. Senior, BVSc, DACVIM (SAIM), DECVIM-CA
Professor Emeritus, Louisiana State University

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; 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. 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.

1 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.

2 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.3

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.4

**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, 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^4^ and reduction of proteinuria^5–9^ 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.5–10 Correction of systemic hypertension, if present, is also important.11–14

Dogs and cats in Stages 1 through 3 often respond to appropriate management with improved longevity and slowing of progression,15 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*:

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**RESOURCES**

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

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.*

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**HEARTGARD Plus** (ivermectin/pyrantel)

**CHEWABLES**

<table>
<thead>
<tr>
<th>Dog Weight Per Month</th>
<th>Dewormer Content</th>
<th>Pyrantel Content</th>
<th>Color Coding On Foil Backing and Carton</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 25 lb</td>
<td>1 68 mcg</td>
<td>27 mg</td>
<td>Blue</td>
</tr>
<tr>
<td>26 to 50 lb</td>
<td>1 136 mcg</td>
<td>54 mg</td>
<td>Green</td>
</tr>
<tr>
<td>51 to 100 lb</td>
<td>1 272 mcg</td>
<td>227 mg</td>
<td>Brown</td>
</tr>
</tbody>
</table>

**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, A. braziliense***) (see INDICATIONS section).

**DOSEAGE:** **HEARTGARD Plus** is recommended orally at monthly intervals at the recommended minimum dose level of 6 mcg of ivermectin per kilogram (2.7 mcg/kg) and 5 mg of pyrantel (as pamoate salt) per kg (2.7 mg/kg) 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:

- Administer the chewable 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 maximize the opportunity for the development of adult heartworms.

**Administration:** **HEARTGARD Plus** also provides effective treatment and control of ascariasis (**T. canis, T. leonina**) and hookworms (**A. caninum, 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, A. braziliense**). One dose of **HEARTGARD Plus** per month provides adequate intestinal anthelmintic coverage.

**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**.

**Dosage:** A majority of dogs swallowed their entire **HEARTGARD Plus** chewable within minutes after administration. 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, re-administration is recommended.

**Dosing Schedule:** **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 last dose’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.

**Store and Disposal:** Store at room temperature, protected from light and moisture. Keep out of reach of children and pets. **HEARTGARD Plus** Chewables are available in cartons of 6 and 12 chewables.

**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**: Depression/lethargy, vomiting, anorexia, diarrhea, mydriasis, ataxia, staggering, convulsions and hypersalivation.

**Patient Information:** **HEARTGARD Plus** has been shown to be biocompatible and well-tolerated in animals. In field trials, dogs receiving **HEARTGARD Plus** have experienced minimal adverse effects such as vomiting, anorexia, diarrhea, mydriasis, ataxia, staggering, convulsions and hypersalivation. No deaths have been reported in dogs receiving **HEARTGARD Plus**.

**SAFETY:** **HEARTGARD Plus** may cause death in sensitive dogs. A wide hyperexcitability reaction, presumably due to death or dying microfilariae and particularly involving a transient diaphoresis, has been observed in clinical trials with **HEARTGARD Plus** after treatment of some dogs that have circulating microfilariae. Keep and all dogs 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.

**CONTRAINDICATIONS:** **HEARTGARD Plus** should not be administered to dogs that were exposed to HEARTGARD products in dogs, including Collies, when used as recommended. **HEARTGARD Plus** must be given within a month (30 days) of the last dose of the former medication.

**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**.

**INDICATIONS:** **HEARTGARD Plus** is recommended orally at monthly intervals at the recommended dose level of 6 mcg of ivermectin per kilogram (2.7 mcg/kg). Studies with ivermectin indicate that certain dogs of the Collie breed are more sensitive to the effects of ivermectin alone after treatment of some dogs that have circulating microfilariae.

**Adverse Reaction Reporting:** 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 155 mm Hg and would be reclassified 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.
CKD Toolkit: Staging in Dogs & Cats

The following figures were adapted from information provided in the International Renal Interest Society (IRIS) guidelines¹ 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.

**Stage <1**
Plasma creatinine: <1.4 mg/dL (dogs) <1.6 mg/dL (cats)
SDMA <14 μg/dL
Clinical history may suggest increased risk for CKD development

**Stage 1**
Plasma creatinine: 1.4-2.0 mg/dL (dogs) 1.6-2.8 mg/dL (cats)
SDMA 14-25 μg/dL
Mild renal azotemia

**Stage 2**
Plasma creatinine: 1.4-2.0 mg/dL (dogs) 1.6-2.8 mg/dL (cats)
SDMA 14-25 μg/dL
Mild renal azotemia

**Stage 3**
Plasma creatinine: 2.1-5.0 mg/dL (dogs) 2.9-5.0 mg/dL (cats)
SDMA ≥25 μg/dL
Moderate renal azotemia

**Stage 4**
Plasma creatinine: >5.0 mg/dL (dogs) >5.0 mg/dL (cats)
SDMA >45 μg/dL
Severe renal azotemia

**Nonproteinuric**
UP:C <0.2 (dogs) <0.2 (cats)

**Borderline Proteinuric**
UP:C 0.2-0.5 (dogs) 0.2-0.4 (cats)

**Proteinuric**
UP:C >0.5 (dogs) >0.4 (cats)

**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.

**Nonproteinuric**

**Borderline Hypertension (low risk)**
Systolic BP: 150-159 mm HG
Diastolic BP: 95-99 mm HG

**Hypertension (moderate risk)**
Systolic BP: 160-179 mm HG
Diastolic BP: 100-119 mm HG

**Severe Hypertension (high risk)**
Systolic BP: ≥180 mm HG
Diastolic BP: ≥120 mm HG

**Normotension (minimal risk)**
Systolic BP: <150 mm HG
Diastolic BP: <95 mm HG

**Borderline Hypertension (low risk)**
Systolic BP: 150-159 mm HG
Diastolic BP: 95-99 mm HG

**Reference**
References


