CHRONIC REANAL DISEASE & IRIS STAGING

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Decline in kidney function can result from a variety of causes including pyelonephritis, amyloidosis, polycystic kidney disease, neoplasia, nephrotoxicosis, hydronephrosis and chronic glomerulonephritis (Scherk, 2011). Although acute insult can lead to chronic kidney disease (CKD), age seems to be the only major, consistent risk factor associated with chronic renal insufficiency (White, 2011).

Mature cat visits ideally include a complete physical examination/consultation as well as data collection in the form of a minimum database (MDB) every 4 to 6 months. A minimum database for mature cats includes a full clinical chemistry, a total thyroid test (TT4), a complete blood count, a urinalysis and a blood pressure (BP) series. Blood urea nitrogen (BUN) and creatinine have traditionally been the go-to serum values for diagnosis of kidney disease. Early diagnosis can be challenging utilizing only these values, as azotemia does not develop until there is 75% loss of nephron function. The BUN can be influenced by factors other than renal disease, including dehydration, dietary protein content, gastrointestinal bleeding and hepatic insufficiency. Creatinine is a more reliable indicator of glomerular filtration rate (GFR). However, creatinine can be influenced by muscle wasting and by dehydration. Routine screening of these values can assist the clinician in documenting upward trends in these values. Symmetrical dimethylarginine (SDMA) measures the methylated form of the amino acid arginine. This is a by-product of protein degradation excreted by the kidneys. SDMA increases with about 40% loss of kidney function. It can be impacted by dehydration. Symmetrical dimethylarginine is not a stand-alone test and should always be interpreted in light of patient status as well as other laboratory findings. Elevated SDMA in the absence of any other evidence of renal disease should be re-evaluated.

Table 1 Urine Specific Gravity Varies with Age & Diet (Scherk, 2011)

Age or condition	Expected USG	Comments
4-8 weeks of age	1.020-1.038	
8+ weeks of age	Up to 1.080	Denotes age at which full concentrating ability is reached
Dehydrates/normal renal function	>1.040	Diet dependent (wet vs dry)
Canned food only	>1.025	
Dry food only	>1.035	
Inability to concentrate urine	1.008-1.012	Nephrons no longer able to modify glomerular filtrate
Dehydrated/unknown renal function	1.007-1.039	Suggestive of renal insufficiency with or without azotemia

It is recommended that urine samples be collected by cystocentesis and tested immediately in the clinic laboratory. Urine testing should include chemistry testing using testing strips, measurement of urine specific gravity (USG) by refractometer and sediment analysis. Urine specific gravity can be impacted by age, diet and hydration status. Urine specific gravity varies throughout the day, such that a single low USG is not reliable evidence of a loss of concentrating ability (Scherk, 2011). Samples with a low urine specific gravity (USG; less than 1.035) should be submitted for culture.

International Renal Interest Society (IRIS)

For cats that are diagnosed with CKD, it is critical for practitioners to develop and promote a relationship with clients that will allow continued monitoring of the disease, including disease staging. The application of human IRIS staging guidelines to the study of feline renal disease has dramatically advanced our ability to tailor our patient therapy, thereby improving quantity and quality of life. In addition to the MDB as discussed above, imaging is likely to be beneficial.

Table 2. IRIS Staging Guidelines

Stage	Renal Azotemia	Creatinine	Clinical signs
1	Non-azotemic	<140 µmol/L	Absent
2	Mild	140-249 µmol/L	Mild or absent
3	Moderate	250-439 µmol/L	Moderate
4	severe	>440 µmol/L	Severe

Adapted from AAFP 2015 Dru Forrester, DVM, MS, DACVIM & Jane Robertson, DVM, DACVIM ***Chronic Kidney Disease: Making the most of early diagnosis***

Table 3. Subclassifications of IRIS staging: Proteinuria

Urine Protein:Creatinine Ratio (UPC)	Substage
<0.2	Non-proteinuric (NP)
0.2-0.4	Borderline proteinuric (BP)
>0.4	Proteinuric (P)

Taken from AAFP 2015 Dru Forrester, DVM, MS, DACVIM & Jane Robertson, DVM, DACVIM **Chronic Kidney Disease: Making the most of early diagnosis**

Table 4. Subclassifications of IRIS staging: Blood pressure

Systolic BP (mmHg)	Diastolic BP (mmHg)	Substage
<150	<95	Minimal risk (N)
150-159	95-99	Low Risk (L)
160-179	100-119	Moderate Risk (M)
>180	>120	High Risk (H)

Taken from AAFP 2015 Dru Forrester, DVM, MS, DACVIM & Jane Robertson, DVM, DACVIM ***Chronic Kidney Disease: Making the most of early diagnosis***

True proteinuria in cats is a known marker of poor prognosis in renal disease (Syme, H.M. et al, 2006; Syme, H.M., 2009). If proteinuria is established on the chemistry stick in the absence of active sediment, the sample will need to be submitted for a urine protein creatinine ratio (UPCR). The result should be used to direct therapy with medications to reduce the loss of protein into the urine. Ratios over 0.4 are significant and therapy is needed. If there is active sediment in the presence of proteinuria on the chemistry stick, and the UPCR is very high (>0.5), then the value may be significant and therapy may be indicated.

Blood pressure changes can be impacted by and/or impact the renal state of health (Brown, 2011). Sixty-five to 100% of cats with hypertension have evidence of reduced renal function (Jepson, 2011). The gold standard for blood pressure assessment in any species is central venous catheter assessment. Blood pressures can be measured non-invasively either by Doppler or oscillometric methods.
Patient stress can be a limiting factor. Proper use of pain management in advance, as well as following cat friendly practice and handling guidelines will significantly reduce stress.

Therapeutics, Monitoring and Maintenance

With the utilization of IRIS staging, the clinician gains significant ground in combatting chronic renal disease in cats. The data collected for the purpose of IRIS staging allows a tailored, individual approach to patient therapy.

Table 5: Survival time by IRIS Stage

IRIS Stage	2b*	3	4
Median Survival (days)	1151	778	103
Range (days)	2-3107	22-2100	1-1920

*2b Creatinine of 203-249 µmol/L
Taken from AAFP 2015 Dru Forrester, DVM, MS, DACVIM & Jane Robertson, DVM, DACVIM ***Chronic Kidney Disease: Making the most of early diagnosis***

Treatment for pain is essential. Medications such as gabapentin should be prescribed at a dosage of 15-20 mg/kg PO q12h. In debilitated cats, a dosage of 10 mg/kg POq12h is the initial chosen dosage. This medication is safe for use in all diseased states and the only initial side effect is sedation. After 1-2 weeks, any sedation will wear off and the cat will continue to be more comfortable. Injectable products such as cartrophen or adequan are also beneficial. Additional pain medications such as buprenorphine, amantadine and non-steroidal anti-inflammatory drugs (NSAIDs) may also require consideration. Elevated stages of CKD may preclude safe use of NSAIDs.

Dietary changes recommended for cats with renal disease will vary depending on the IRIS staging results. Many renal specific diets are formulated with reduced phosphorus and protein. These diets are not necessarily considered ideal in early disease states (Scherk and Laflamme, 2016). Increasing water intake may be a key

factor in improving renal function and overall patient hydration status. Indirectly this can reduce pain from dehydration and constipation.

Identification of BP values over 160-180, with or without retinal changes indicate the need for BP-controlling drugs. Calcium channel blockers such as amlodipine are the most effective at controlling blood pressure in the feline species. Some patients will have partially or uncontrollable hypertension with amlodipine and may require additional medications. Benazepril (Fortekor) is **not** effective in the control of hypertension. The newly available drug telmisartran (Semintra) may be effective at controlling hypertension at higher doses, but has yet to be evaluated for further benefit to hypertension cats.

The indiscriminate use of antibiotics in the absence of evidence of urinary tract infection is not recommended. Antibiotics should be selected based on urine culture and sensitivity patterns. A repeat urine culture 7 days following cessation of therapy is critical. In cases where urine culture is negative, but a low USG exists in the face of renal disease, ultrasound is recommended.

Patients who exhibit even mild decreases in potassium levels in their serum require supplementation with potassium gluconate. The majority of body potassium is held in the intracellular or interstitial space. The serum potassium represents only 2% of body potassium. Therefore any decrease noted in the serum is significant of a major decrease in the overall body stores.

Elevated UPCR indicates abnormalities with the renin angiotensin aldosterone system (RAAS). These changes alter intraglomerular pressures and result in protein loss into the filtrate/urine. The use of benazepril has been recommended in the past. However, this drug is not targeted to the particular pathway of RAAS that is affected and impacting the glomerulus. Over time, the RAAS can escape the control that benazepril exerts, resulting in resumed proteinuria. Telmisartran is a newer alternative that is more targeted and not likely to lead to escape mechanisms over time.

Improving hydration status in renal patients is generally considered to be beneficial to renal function and overall patient health. Addition of 20-40 mEq/L of potassium chloride to the fluids should be considered in the case of hypokalemia and/or where regular subcutaneous fluids will be administered.

Patients identified with elevated total calcium, elevated ionized calcium and/or elevated phosphorus may require phosphorus-binding agents to reduce phosphorus levels. The use of agents such as aluminum hydroxide can be challenging, as palatability is less than optimal. The use of phosphorus binding agents containing calcium should be minimized unless serial monitoring of ionized calcium can be pursued.

Calcitriol is a drug that is recommended frequently in renal patients. It's primary indication for use is following diagnosis of renal secondary hyperparathyroidism. In these cases, the use of calcitriol, with regulated serum phophporus levels, may benefit the patient in the short and long term. Calcitriol supplementation at low doses may be recommended by some experts as a means of improving quality of life. More detailed studies on this mode of utilization are warranted (Sparkes et al, 2016).

Chronic kidney disease can lead to a reduced production of erythropoietin. The result is a reduced production of new red blood cells from the bone marrow. Some patients will also have iron deficiencies reducing production of new RBC. Evaluation of iron levels with consideration for supplementation is needed. These patients may also require injectable erythropoietin or darbopoietin to stimulate bone marrow production of RBC.

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