SDMA: A New Test for Early Detection of Chronic Kidney Disease

Phoenix Lab recently added the symmetric dimethylarginine (SDMA) (IDEXX) test to our sendouts catalogue. This is a new commercial test and we have much to learn about its use. The following summarizes some basic concepts; please see other side for references and test submission information.

**Summary:** SDMA is a methylated arginine amino acid. It is a byproduct of L-arginine metabolism and released into the circulation during protein metabolism. SDMA is almost exclusively eliminated by renal filtration and therefore correlates with glomerular filtration rate (GFR). The GFR clearance test is the gold standard for measuring GFR but not practical for private practice. Thus, we use creatinine, BUN and urinalysis to evaluate kidney function. Preliminary studies indicate that the addition of SDMA testing to our current methods for evaluating kidney function will help us detect chronic kidney disease (CKD).

**Reference Interval:** SDMA has long been established as a kidney biomarker but this commercial assay, an immunoassay performed on the chemistry analyzer, is the first of its kind and currently only available through IDEXX. Their established reference range for both dogs and cats is 0-14ug/dl. Any increase in SDMA above this range may be abnormal. A borderline SDMA concentration, along with at least BUN and creatinine, might benefit from being rechecked in two weeks in order to determine its significance and need for additional testing. Most animals with early kidney disease have values of 15-20ug/dl. Values greater than 20ug/dl usually occur with increases in creatinine and indicate more advanced disease. The linearity of the assay is up to 100ug/dl. Initial studies suggest that in puppies and kittens and greyhounds, SDMA concentration may run slightly higher and values at or above the reference range may be normal in these patients.

**Advantages of SDMA:** SDMA increases earlier than creatinine and can be used to detect early kidney disease at an average of 40% loss of kidney function vs. 75% loss of function with creatinine. SDMA has drawn particular interest in identifying CKD before creatinine is increased above the reference range, i.e., International Renal Interest Society (IRIS) Stage 1 in our small animal patients. In these patients, creatinine is within the reference range (for IRIS Staging <1.4 mg/dl in dogs, <1.6 mg/dl in cats) and urine is inappropriately dilute (<1.030 in dogs, <1.035 in cats). IRIS Stage 2 CKD (creatinine 1.6-2.8mg/dl in cats, 1.4-2.0 mg/dl in dogs), again with inappropriately dilute urine, is usually when we first identify the patient as having CKD. Another advantage to SDMA is that loss of lean muscle mass associated with aging and chronic disease, particularly in cats, will decrease creatinine but does not affect SDMA. Therefore, it may be better at monitoring progression of CKD over time. It should be noted that SDMA, like creatinine and GFR, has an intrinsic biologic variability of 15-20%. A change greater than 20% would be needed to indicate a true progression of CKD. SDMA is not affected by dietary protein levels or gastrointestinal hemorrhage, factors that may increase BUN.

**Dehydration impacts SDMA:** Both dehydration and CKD affect GFR and increase SDMA concentration. Evaluation of urine specific gravity, and other parameters including clinical signs, is important when evaluating increases in SDMA. SDMA will also increase in other disease conditions that decrease GFR. An increased SDMA concentration does not determine the cause of renal disease.
SDMA and Proteinuria: SDMA is a marker of GFR. In tubulointerstitial disease, the most common cause of CKD in older dogs and cats, patients may have only mild proteinuria or no proteinuria and SDMA will be the best indicator for early CKD. In glomerular disease, patients often develop proteinuria long before GFR decreases. Assessment of proteinuria through urine protein:creatinine testing (UPC) will detect early glomerular disease before SDMA rises. Pre-renal and post-renal causes of proteinuria should be ruled-out before running a UPC. Microalbuminuria, a urine test for small amounts of protein, does not correlate with GFR and is rarely used.

Use of SDMA: SDMA testing could be considered on any patient where assessment of GFR is desired. This would include acute and chronic kidney disease and proteinuric renal disease.

What do we do with an increased SDMA concentration so that we balance being proactive without excessive testing? In some cases SDMA may detect CKD before urine is dilute. In patients with normal history, physical exam findings, and normal urinalysis including concentrated urine and normal creatinine, we may want to simply monitor the SDMA and recheck in 4-6 months or sooner depending on the clinical impression and veterinarian’s discussion with the owner. In those patients where early chronic kidney disease is suspected, i.e., IRIS Stage 1, the next step would be to identify concurrent conditions and contributing factors that could be treated with the goal of slowing disease progression. These steps could include measurement of UPC, systolic blood pressure and urine culture and sensitivity. Additional testing may include assessing for regional infectious disease and renal imaging.

How do we treat early CKD? According to IRIS guidelines, it is appropriate to start the dog or cat on a renal protective diet when the patient is in IRIS Stage 1 CKD with proteinuria (UPC > 2.0) or IRIS Stage 2 CKD. Also, renal protective diets should be fed to maintain serum phosphorus in the range between 2.7 mg/dl and 4.6 mg/dl. With patients in IRIS Stage 1 CKD without proteinuria, we may want to evaluate the current diet to make sure calories are adequate and the diet is neither excessive in phosphorus nor acidifying. Treatment of proteinuria and/or hypertension would be warranted. In addition, we would want to avoid further insults to the kidneys by carefully considering our choices in prescription drugs and anesthetic agents.

Our new Sendout Test Code is SO513. Specimen requirement is 1 ml serum from SST. Turnaround time is 1-4 days.

For additional information on SDMA, please go to www.idexx.com/SDMA
For additional information on IRIS staging of renal disease, please go to www.iris-kidney.com