Dear Colleague,

For several years, IDEXX has been collaborating with leading veterinary nephrologists to study symmetric dimethylarginine (SDMA). Studies have confirmed that SDMA is a biomarker of kidney function and correlates extremely well with glomerular filtration rate (GFR) in both dogs and cats. These features make SDMA a sensitive indicator of kidney function:

- SDMA identifies chronic kidney disease earlier than creatinine.
- SDMA is not impacted by lean body mass, making it a more sensitive indicator of kidney function in animals with poor body condition.

In preparation for a 2016 launch of the SDMA assay in Australia we are seeking to collaborate with specialists to build a local SDMA knowledge base as we prepare to launch to the wider veterinary community.

Because you are a leader in your field, we recognise that practitioners may reach out to you for insight into this test. The links to the right provide quick and easy access to a number of available resources on SDMA. We hope you find the information in these resources helpful for understanding the value of SDMA and the clinical studies that have been completed to support its key attributes.

If you have questions about SDMA, please feel free to contact us directly.

Regards,

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Resources

Click the links below.

**Webinar**
Introduction to SDMA - The Science  >  >

**White paper**
Introduction to a New Kidney Test: SDMA  >  >

**Algorithm**
Diagnosing Early Kidney Disease with SDMA and What to Do Next  >  >

**Publications**
Relationship between Serum Symmetric Dimethylarginine Concentration and Glomerular Filtration Rate in Cats  >  >
Comparison of Serum Concentrations of Symmetric Dimethylarginine and Creatinine as Kidney Function Biomarkers in Cats with Chronic Kidney Disease  >  >
2014 ACVIM Small-Animal Nephrology/Urology Abstracts NU-41 and NU-42  >  >
2013 ACVIM Small-Animal Nutrition/Metabolism Abstract NM-10  >  >

For more information, please visit www.idexx.com/sdma
Q: How does storage affect symmetric dimethylarginine (SDMA)? How stable is SDMA?
A: SDMA was found to be stable in specimens that were freeze-thawed three times and then stored at 4°C (tested at days 1, 3, 7, 10 and 14) as well as stored at room temperature (tested at days 1, 3 and 7). SDMA is stable for years in frozen specimens.

Q: If SDMA is measured repeatedly in the same day, on the same patient, how stable will it be?
A: The intraday (within same day) and interday (over several days) variability on the same specimen of SDMA, which was measured by the liquid chromatography-mass spectrometry (LC-MS) SDMA assay used in the studies, was under 3%. The precision requirements of the commercial assay will be tight. Biologic variability of SDMA for repeated specimens on the same animal over time appears similar to creatinine and glomerular filtration rate (GFR), with a 15%–20% change seen in one study, where specimens were collected over a 3-week period. Biologic variability of SDMA on different specimens on the same animal in the same day has not been specifically evaluated but likely much less than those seen over a 3-week period.

Q: Is SDMA impacted by preanalytic factors, including haemolysis, icterus and lipaemia?
A: There is no impact of lipaemia, haemolysis and icterus on the SDMA assay.

Q: Have the reference intervals for puppies of various ages been determined?
A: Not at this time, but it appears likely that the SDMA reference interval for puppies will be similar to adult dogs based on results from the unaffected male dogs from the X-linked hereditary nephropathy colony.

Q: In all studies with IDEXX, was GFR measured via iohexol as the gold standard?
A: Yes, GFR was determined by iohexol clearance.

Q: Does SDMA increase prior to development of isosthenuria? Would SDMA also be helpful in diagnosing causes of PU/PD in nonazotemic patients without another apparent diagnosis?
A: SDMA increases when there is on average a 40% loss of GFR. Isosthenuria typically develops when there is on average a 67% loss of GFR. Therefore, if an animal were assessed when there was on average a 40% – 67% loss of GFR, the SDMA could be increased and there would likely be inappropriate urine specific gravity (i.e., <1.030) but not isosthenuria. The cases that have been seen with increased SDMA and creatinine results within the reference interval have had a range of urine specific gravity values from isosthenuria up to just under 1.030. It is possible that SDMA will be able to help diagnose or rule out early CKD in dogs with PU/PD of unknown origin.

Q: Do endocrinopathies, including Cushing’s and diabetes, affect SDMA?
A: SDMA correlates strongly with GFR. Therefore, if GFR is normal in an animal with an endocrinopathy, the SDMA will also be normal. IDEXX has evaluated SDMA in several dogs with confirmed Cushing’s and hypo- or isosthenuria, and SDMA was well within the reference interval. In animals evaluated with confirmed diabetes and no evidence of kidney disease, SDMA results have also been normal.
Q: Has there been any correlation between SDMA and different types of kidney disease, based on histologic diagnosis (e.g., glomerular vs. tubular disease, membranoproliferative glomerulonephritis vs. other)?
A: SDMA does not help localise kidney disease. It increases as GFR decreases, regardless of lesion localisation.

Q: How is SDMA handled by the renal tubules? Is there any secretion/reabsorption?
A: SDMA is freely filtered from the kidneys and there is no reabsorption.

Q: Will SDMA help us determine which hyperthyroid cats will develop azotaemia with treatment, especially after I-131 therapy?
A: Maybe in some cases, and it will depend on how decreased the GFR is from normal pretreatment. SDMA increases when there is on average a 40% decrease in GFR. Untreated cats often have an increased GFR secondary to their hyperthyroidism. If their GFR prior to treatment is on average 60% normal or better, then the SDMA will likely be normal. If the GFR decreases beyond this level during treatment, then the SDMA would increase above normal; as GFR loss approaches 75%, azotaemia would develop. So, the short answer is that SDMA might be helpful in some cases if pretreatment GFR is decreased by about 40% or more, but it will not be if the GFR is higher than this because of the hyperthyroidism. A normal pretreatment SDMA definitely does not rule out the possibility of the cat developing azotaemia with treatment, and routine precautions should still be taken. In a study evaluating hyperthyroid cats on Hill's® Prescription Diet® y/d® Feline, SDMA better correlated with GFR than did creatinine, but none of the cats became azotaemic.

Q: Is the SDMA too sensitive? This seems to have the same potential pitfalls as the microalbuminuria test.
A: The microalbuminuria test detects very small amounts of protein in the urine, which can be from anywhere in the urinary tract, therefore false positives are common, especially with urinary tract infections. It can be an early indicator of kidney disease but only when there is glomerular damage either from primary glomerular diseases or increased intraglomerular filtration pressure in CKD. False negatives can occur if the primary disease is elsewhere and intraglomerular filtration pressure is not sufficient to cause protein leakage. SDMA, on the other hand, is a serum test and a good marker of GFR; it increases as kidney function decreases, regardless of underlying cause.

Q: Is SDMA influenced by the amount of arginine in the diet?
A: This has not been studied specifically in animals, but it has been confirmed that there was no correlation in dogs and cats between SDMA and serum arginine concentrations. In addition, in pregnant women with pre-eclampsia who received prolonged supplementation with L-arginine, there was no impact on serum SDMA concentrations.

Q: Does SDMA accumulate in inflammatory diseases, such as pancreatitis or IBD, etc.?
A: No correlation between SDMA and Spec cP and Spec fP has been seen. In well-characterised cats with IBD, SDMA only correlated with GFR. In human studies, when kidney function is not compromised, SDMA has been shown to not be impacted by acute inflammatory response, hepatic disease, stroke or cardiovascular disease.