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### Symmetric Dimethylarginine: Improving the Diagnosis and Staging of Chronic Kidney Disease in Small Animals

Roberta Relford, Jane Robertson, and Celeste Clements

Chronic kidney disease (CKD) is a common condition in cats and dogs, traditionally diagnosed after substantial loss of kidney function when serum creatinine concentrations increase. Symmetric dimethylarginine (SDMA) is a sensitive circulating kidney biomarker whose concentrations increase earlier than creatinine as glomerular filtration rate decreases. Unlike creatinine, SDMA is unaffected by lean body mass. The IDEXX SDMA test introduces a clinically relevant and reliable tool for the diagnosis and management of kidney disease. SDMA has been provisionally incorporated into the International Renal Interest Society guidelines for CKD to aid staging and targeted treatment of early and advanced disease.

### Kidney Disease and the Nexus of Chronic Kidney Disease and Acute Kidney Injury: The Role of Novel Biomarkers as Early and Accurate Diagnostics

Murthy Yerramilli, Giosi Farace, John Quinn, and Maha Yerramilli

Chronic kidney disease (CKD) and acute kidney injury (AKI) are interconnected and the presence of one is a risk for the other. CKD is an important predictor of AKI after exposure to nephrotoxic drugs or major surgery, whereas persistent or repetitive injury could result in the progression of CKD. This brings new perspectives to the diagnosis and monitoring of kidney diseases highlighting the need for a panel of kidney-specific biomarkers that reflect functional as well as structural damage and recovery, predict potential risk and provide prognosis. This article discusses the kidney-specific biomarkers, symmetric dimethylarginine (SDMA), clusterin, cystatin B, and inosine.

### Is Progressive Chronic Kidney Disease a Slow Acute Kidney Injury?

Larry D. Cowgill, David J. Polzin, Jonathan Elliott, Mary B. Nabity, Gilad Segev, Gregory F. Grauer, Scott Brown, Cathy Langston, and Astrid M. van Dongen

International Renal Interest Society chronic kidney disease Stage 1 and acute kidney injury Grade I categorizations of kidney disease are often confused or ignored because patients are nonazotemic and generally asymptomatic. Recent evidence suggests these seemingly disparate conditions may be mechanistically linked and interrelated. Active kidney injury...
biomarkers have the potential to establish a new understanding for traditional views of chronic kidney disease, including its early identification and possible mediators of its progression, which, if validated, would establish a new and sophisticated paradigm for the understanding and approach to the diagnostic evaluation, and treatment of urinary disease in dogs and cats.

Current Understanding of the Pathogenesis of Progressive Chronic Kidney Disease in Cats 1015
Rosanne E. Jepson

In cats with chronic kidney disease (CKD), the most common histopathologic finding is tubulointerstitial inflammation and fibrosis; however, these changes reflect a nonspecific response of the kidney to any inciting injury. The risk of developing CKD is likely to reflect the composite effects of genetic predisposition, aging, and environmental and individual factors that affect renal function over the course of a cat’s life. There is still little information available to determine exactly which individual risk factors predispose a cat to develop CKD. Although many cats diagnosed with CKD have stable disease for years, some cats show overtly progressive disease.

Controversies in Veterinary Nephrology: Renal Diets Are Indicated for Cats with International Renal Interest Society Chronic Kidney Disease Stages 2 to 4: The Pro View 1049
David J. Polzin and Julie A. Churchill

Renal diets have been the mainstay of therapy for cats with chronic kidney disease (CKD) for many decades. Clinical trials in cats with CKD have shown them to be effective in improving survival, reducing uremic crises, and improving serum urea nitrogen and phosphorous concentrations. It has shown that, when food intake is adequate, renal diets can maintain body weight and body condition scores for up to 2 years. Although some have questioned whether renal diets provide adequate protein and have advocated feeding higher-protein diets to cats with CKD, there is currently no convincing evidence in support of this proposal.

Controversies in Veterinary Nephrology: Renal Diets Are Indicated for Cats with International Renal Interest Society Chronic Kidney Disease Stages 2 to 4: The Con View 1067
Margie A. Scherk and Dottie P. Laflamme

Renal diets typically incorporate protein and phosphorus restriction, supplement with potassium and Omega-3 fatty acids, and address metabolic acidosis. Compared to “maintenance” diets, these modifications appear to benefit cats with chronic kidney disease (CKD); however, there is limited data in cats justifying the specific amounts of the nutrients used in these diets, and there is little evidence supporting protein restriction in cats with CKD. Energy intake, maintenance of body weight, and muscle and body condition need to be addressed, and may take precedence over special diets. Further research is needed to better define optimum diets for cats with CKD.
The role of diet in management of chronic kidney disease (CKD) is important. There are different interpretations of the current knowledge on this topic. Neither clinical trials involving product testing, nor prospective research investigating dietary influences on cats with induced kidney disease provide guidance on the utility of specific nutritional strategies. Likewise, data derived from other species also has limitations. More research is needed to further our understanding of this topic; however, practical guidance from current knowledge for the management of individual patients can be utilized with success.

Esophagostomy feeding tubes are useful, and, in many cases essential, for the comprehensive management of cats with moderate to advanced chronic kidney disease (CKD). They should be considered a lifelong therapeutic appliance to facilitate the global management of cats with CKD thus providing improved therapeutic efficacy and quality of life. Esophagostomy tubes facilitate the maintenance of adequate hydration and increase owner compliance by facilitating the administration of medications. Finally, feeding tubes provide a means to deliver a stage-appropriate dietary prescription for cats with CKD and maintain an adequate nutritional plane in a patient that otherwise would be subject to chronic wasting.

Proteinuria is a negative prognostic indicator for dogs and cats with chronic kidney disease. A normal dog or cat should excrete very little protein and have a urine protein:creatinine ratio that is less than 0.4, or less than 0.2, respectively; persistent proteinuria above this magnitude warrants attention. Administration of angiotensin converting enzyme inhibitors and/or angiotensin receptor blockers, blood pressure control and nutritional modification are considered a standard of care for renal proteinuria. Renal biopsy and administration of immunosuppressive agents should be considered in animals with glomerular proteinuria that have not responded to standard therapy. Targeted patient monitoring is essential when instituting management of proteinuria.

The inappropriate phosphorus retention observed in chronic kidney disease is central to the pathophysiology of mineral and bone disorders observed in these patients. Subsequent derangements in serum fibroblast growth
factor 23, parathyroid hormone, and calcitriol concentrations play contributory roles. Therapeutic intervention involves dietary phosphorus restriction and intestinal phosphate binders in order to correct phosphorus retention and maintain normocalcemia. Additional therapies may be considered to normalize serum fibroblast growth factor 23 and parathyroid hormone.

Does Secondary Renal Osteopathy Exist in Companion Animals? 1151
Gilad Segev, Hagar Meltzer, and Anna Shipov
Secondary renal hyperparathyroidism is an inevitable consequence of chronic kidney disease. In human patients, the disease is associated with decreased bone quality and increased fracture risk. Recent evidence suggests that bone quality is also decreased in companion animals, more pronouncedly in cats compared with dogs, likely because of a longer disease course. The clinical significance of these findings is yet to be determined. Clinicians should keep in mind that animals with chronic kidney disease have decreased bone quality and increased fracture risk.

Update on Medical Management of Clinical Manifestations of Chronic Kidney Disease 1163
Jessica M. Quimby
Dysregulation of normal kidney functions in chronic kidney disease (CKD) leads to several pathophysiologic abnormalities that have the potential to significantly clinically affect the CKD patient. This article discusses the clinical impact of hypertension, hypokalemia, anemia, dysrexia, nausea/vomiting, and constipation in the CKD patient and therapies for these conditions. These clinical manifestations of disease may not occur in every patient and may also develop later during the progression of disease. Therefore, monitoring for, identifying, and addressing these factors is considered an important part of the medical management of CKD.

Nephroureteral Obstructions: The Use of Stents and Ureteral Bypass Systems for Renal Decompression 1183
Carrie A. Palm and William T.N. Culp
Canine and feline nephroureteral obstruction is a complex disease process that can be challenging to treat. Although the availability of various imaging modalities allows for a straightforward diagnosis to be made in most cases, the decision-making process for when a case should be taken to surgery and the optimal treatment modality that should be used for renal decompression remains controversial. In the following discussion, an overview of the perioperative management of cases with nephroureterolithiasis and nephroureteral obstruction is reviewed, with particular focus on the use of renal decompressive procedures, such as ureteral stenting and subcutaneous ureteral bypass system placement.

Update on the Current Status of Kidney Transplantation for Chronic Kidney Disease in Animals 1193
Lillian R. Aronson
Kidney transplantation is a novel treatment option for cats suffering from chronic renal failure or acute irreversible renal injury. Improvement in
quality of life as well as survival times of cats that have undergone transplan
tation has helped the technique to gain acceptance as a viable treat-
ment option for this fatal disease. This article reviews information
regarding the optimal time for intervention, congenital and acquired condi-
tions that have been successfully treated with transplantation, recipient
and donor screening, immunosuppressive therapy, recent advances in
anesthetic and surgical management, postoperative monitoring and
long-term management, and troubleshooting perioperative and long-
term complications.