

GUT-KIDNEY AXIS AND CHRONIC KIDNEY DISEASE MANAGEMENT IN CATS

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INTRODUCTION

Chronic kidney disease (CKD) is one of the most common and impactful chronic diseases of aging cats. While traditional approaches have centered on managing azotemia, electrolyte abnormalities, anemia, and proteinuria, recent research has brought attention to the gut-kidney axis—highlighting the gastrointestinal tract as a novel therapeutic target. Disruptions in the gut microbiome and intestinal barrier function in cats with CKD can lead to the increased production and systemic accumulation of microbial-derived uremic toxins, which in turn exacerbate renal damage, promote inflammation, and compromise patient well-being. This proceedings document outlines therapeutic strategies designed to reduce the burden of gut-derived uremic toxins, notably indoxyl sulfate (IS) and p-cresol sulfate (pCS) and ultimately improve outcomes for cats with CKD. These strategies are grounded in the published literature and emphasize the practical application of diet, adsorbents, and constipation management in clinical feline practice.¹

THE GUT-KIDNEY AXIS IN CKD

The gut-kidney axis refers to the bidirectional interactions between the gastrointestinal tract and renal physiology. In CKD, uremia disrupts the gut microbiome, increases intestinal permeability, and shifts microbial metabolism toward proteolytic fermentation. These alterations result in:

- Increased production of protein-bound uremic toxins (IS, pCS)
- Reduced generation of beneficial short-chain fatty acids
- Altered bile acid profiles
- Systemic inflammation and renal fibrosis

In cats with CKD, functional gut dysbiosis has been documented as reduced microbial richness (ie, fewer microbial taxa) and alterations in the production of microbial metabolites. Most notably, IS concentrations are consistently elevated and associated with disease progression. Cats with CKD can have higher serum IS concentrations prior to the detection of azotemia, emphasizing the importance of early initiation of therapies aimed at reducing uremic toxins.²

Interventions targeting the gut-kidney axis—such as diet, adsorbents, and treatment of constipation—aim to restore microbial balance, improve intestinal barrier function, and reduce the systemic accumulation of uremic toxins.

DIETARY STRATEGIES: BALANCING PROTEIN AND FIBER

Protein

Protein restriction is a long-standing strategy in the management of CKD in both human and veterinary medicine, with studies showing improved survival in cats fed renal therapeutic diets. Since the gut-derived uremic toxins IS and pCS are produced through microbial fermentation of dietary amino acids, reducing dietary protein—especially in relation to fiber—can lower toxin concentrations. Diets with a low protein concentration (60-70 g/1000 kcal) have shown to reduce IS levels in healthy cats and those with early CKD when compared to diets with higher protein concentration (>80 g/1000 kcal).^{3,4}

While protein restriction helps reduce uremic toxins, the extent of restriction in cats remains debated due to their obligate carnivore status and high protein requirements. Older cats may need more protein than younger cats, and CKD often leads to progressive loss of body weight, condition, and muscle mass. Therefore, dietary strategies should prioritize highly digestible, complete protein sources and adequate caloric intake to minimize muscle loss while modulating toxin generation. Protein intake should be adjusted based on the stage of CKD and the cat's current dietary intake. According to the European Pet Food

Industry Federation (FEDIAF), the minimum recommended level of protein for complete cat food is 83.3 g/1000 kcal (based on minimum energy requirement of 75 kcal/kg^{0.67}), but there is notable variation in the protein content of both renal and over the counter (OTC) feline diets. While renal diets are generally formulated to control protein intake to some degree, the protein concentration in OTC diets can vary widely. Some senior diets have moderate protein (70-90 g/1000 kcal) and phosphate concentration (1.4-2.0 g/1000 kcal) and may be appropriate for some cats with early-stage CKD.

Dietary management should be individualized, considering the stage of disease, nutritional status, and comorbidities. For cats with Stage 1 and 2 CKD, the author avoids high protein diets (>100 g/1000 kcal) and strives for a moderate protein intake of approximately 70–90 g/1000 kcal. To make individualized dietary recommendations, it is beneficial to assess the cat's current intake. Some cats with Stage 1 or 2 CKD may already be consuming a diet with moderate protein concentration and need further reduction in protein intake; for example, a cat exhibiting signs of uremia or a cat with significant proteinuria. In these cases, consider a reduction by 25–50% from baseline protein intake.

For cats with Stage 3 and 4 CKD, dietary management becomes more critical due to the increased risk of phosphorus overload and the clinical consequences of uremia. At this stage, feeding a renal therapeutic diet is strongly recommended, as endorsed by the International Renal Interest Society (IRIS). These diets are specifically formulated to provide restricted phosphorus, moderate to low protein, and enhanced caloric density to address anorexia, protein-energy wasting, and toxin accumulation. Controlling dietary phosphorus is especially important, as hyperphosphatemia contributes to disease progression and mineral-bone disorders. Ensuring adequate caloric intake is crucial. Prescribing medications to augment appetite, such as transdermal mirtazapine, and alleviating nausea is often necessary at this stage. In some cases, caregivers may opt for placement of an esophagostomy tube to provide adequate nutrition and calories.

Fiber

Dietary fibers differ in their physical and functional properties, including solubility, fermentability, and viscosity. Solubility refers to fiber's ability to dissolve in water, while fermentability describes how easily gut microbes can break down the fiber to produce beneficial metabolites. Most soluble fibers are fermentable to varying degrees, contributing to gut health and microbial balance. Viscosity reflects the fiber's ability to form a gel-like consistency when mixed with water. A prebiotic is a soluble/fermentable fiber that promotes growth of gut microbes that ferment fiber rather than protein. The fermentation of fiber results in the production of beneficial metabolites, such as short-chain fatty acids, and fermentation of protein results in production of gut-derived uremic toxins. Therefore, increasing dietary fermentable fiber, either through a fiber-enhanced commercial diet or a fiber supplement, could lower systemic uremic toxin burden. Some renal therapeutic diets are enhanced with fiber and have been shown to increase total body mass, lean body mass (ie, muscle) and reduce uremic toxin burden.^{5,6}

ADSORBENTS

Adsorbents are used in human medicine to reduce intestinal absorption of gut-derived uremic toxins such as IS and pCS and have been shown to slow CKD progression. In veterinary medicine, a commercial carbon-based oral adsorbent is available for cats. This adsorbent consists of tiny black carbon spheres measuring 0.1–0.3 mm in diameter. Their electrical charge facilitates the binding of small molecules, allowing them to capture uremic toxin precursors in the gut and prevent their absorption into systemic circulation. The adsorbent is added to the cat's food or a liquid cat treat daily. This product has proven to reduce deleterious gut-derived uremic toxins in senior cats and those with Stage 2–3 CKD after eight weeks of use. Giving the product twice a day could lead to more significant reductions in IS and pCS than with once daily dosing.⁷

CONSTIPATION

Constipation is a common gastrointestinal complication in people with end-stage CKD and is increasingly recognized in veterinary patients as well. Studies have shown that cats with CKD tend to have less frequent bowel movements and are at increased risk of presenting for constipation. The condition is likely driven by chronic dehydration from impaired urine-concentrating ability, altered gastrointestinal motility, and contributing factors such as hypokalemia and phosphate binder use.

Beyond its clinical implications, constipation exemplifies the gut-kidney axis. Prolonged fecal retention increases microbial fermentation of aromatic amino acids, leading to greater production of uremic toxin

precursors and systemic accumulation of uremic toxins. In people, constipation is associated with higher serum concentrations of the uremic toxins pCS and indole acetic acid. Improving bowel motility may reduce gut-derived uremic toxins.

Management strategies include correcting dehydration and electrolyte imbalances, dietary adjustments, supplementation with soluble fibers, stool softeners, and promotility agents. Utilizing fiber-enhanced diets that are also moderately restricted in protein and phosphorus may be an option for some cats with Stage 1 or 2 CKD. Fiber can also be supplemented to a diet using a commercial product. Psyllium husk powder is a soluble, partially fermentable, viscous fiber commonly used in the treatment of constipation. Utilizing diets or supplements containing this fiber can be beneficial to lubricate the stool for easier evacuation of feces. Using an osmotic stool softener, such as polyethylene glycol 3350, and the promotility agent cisapride can also be used in the treatment of constipation in cats.

CONCLUSION

Gut-derived uremic toxins represent an important and modifiable contributor to the progression and clinical impact of CKD. Early intervention targeting the gut microbiome offers a promising avenue to reduce toxin burden and support overall health in cats with CKD. Therapeutic strategies should be implemented proactively and tailored to the individual needs of each patient—especially in the context of dietary management—to balance toxin reduction with the preservation of nutritional status and quality of life.

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