

clinician's update™

SUPPLEMENT TO NAVC CLINICIAN'S BRIEF®

Chronic Kidney Disease & the Role of Phosphorus Binders



NAVC

clinician's brief®

THE OFFICIAL PUBLICATION OF THE NORTH AMERICAN VETERINARY CONFERENCE

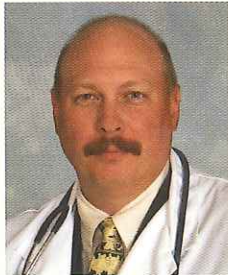
NOVEMBER 2005 SUPPLEMENT

www.cliniciansbrief.com

Chronic Kidney Disease

& THE ROLE OF PHOSPHORUS BINDERS

Gregory F. Grauer and Scott Brown



Gregory F. Grauer
DVM, MS, DACVIM
Department of Clinical
Sciences
Kansas State University
Manhattan, Kansas



Scott Brown
VMD, PhD, DACVIM
Department of Physiology
& Pharmacology
University of Georgia
Athens, Georgia

Chronic kidney disease (CKD) is one of the leading causes of death in dogs and cats. In North America it is estimated that 8% of cats aged 10 years or older and approximately 2.4% of dogs aged 10 years or older suffer from CKD.¹

Renal failure results when more than three quarters of nephrons in both kidneys are not functioning. Nephron damage associated with CKD is usually irreversible and the cause is often difficult to determine. Because of the interdependence of the vascular and tubular components of the nephron, the end point of irreversible glomerular or tubular damage is the same. The histologic changes are not process-specific, frequently making an etiologic diagnosis impossible. Progressive disease that destroys nephrons at a slow rate allows intact nephrons to undergo compensatory hypertrophy; but when renal failure finally occurs, hypertrophic nephrons can no longer maintain adequate renal function.

DIAGNOSIS OF CKD

A diagnosis of renal failure is confirmed when persistent azotemia with concurrent isosthenuria or minimally concentrated urine is documented. Early stages of kidney disease may be difficult to confirm because there are usually no overt clinical signs. Sequential monitoring of blood pressure, serum creatinine, urine specific gravity, and proteinuria may aid in the recognition of early kidney disease. Serum creatinine levels are commonly used to measure kidney dysfunction and are the basis of the IRIS staging system. Serum creatinine concentrations should always be interpreted in light of urine specific gravity. For example, azotemia concurrent with hypersthenuria (unusually high specific gravity and solute concentration in urine) suggests decreased renal perfusion rather than renal disease. Serial evaluation of serum creatinine concentrations on an annual or semi-annual basis may allow clinicians to detect renal disease prior to the onset of persistent azotemia. For example, an increase in serum creatinine concentration from 0.6 to 1.2 mg/dl over

Renal Diseases & CKD

- Glomerulonephritis
- Amyloidosis
- Pyelonephritis
- Feline infectious peritonitis
- Lymphosarcoma
- Polycystic kidney disease
- Nephroliths
- Tubulointerstitial disease

CKD Terms

Kidney disease	Renal lesions present
Renal insufficiency	Renal reserve lost
Renal failure	Indicates level of organ function, not specific disease
Azotemia	Increased blood concentration of urea nitrogen, creatinine, and other nonproteinaceous nitrogenous waste products
Isosthenuria	Urine concentration similar to plasma
Proteinuria	Protein in urine

IRIS* CKD Staging System**

Canine

Stage	Azotemia	Creatinine	Comments ¹
1	None	< 1.4	Hyperphosphatemia unlikely Hypertension possible Proteinuria possible
2	Mild renal	1.4 to 2.0	Hyperphosphatemia possible Hypertension possible Proteinuria possible
3	Moderate renal	2.1 to 5.0	Hyperphosphatemia probable Hypertension possible Proteinuria possible
4	Severe renal	> 5.0	Hyperphosphatemia probable Hypertension possible Proteinuria possible

Feline

Stage	Azotemia	Creatinine	Comments ¹
1	None	< 1.6	Hyperphosphatemia unlikely Hypertension possible Proteinuria possible
2	Mild renal	1.6 to 2.8	Hyperphosphatemia possible Hypertension possible Proteinuria possible
3	Moderate renal	2.9 to 5.0	Hyperphosphatemia probable Hypertension possible Proteinuria possible
4	Severe renal	> 5.0	Hyperphosphatemia probable Hypertension possible Proteinuria possible

*The International Renal Interest Society (IRIS) was created to advance the scientific understanding of kidney disease in small animals at the 8th Annual Congress of the European Society of Veterinary Internal Medicine in Vienna, Austria, in 1998. Seventeen independent veterinary experts from eight different countries are on the board. The mission of IRIS is to help veterinary practitioners better diagnose, understand, and treat renal disease in cats and dogs.

** Can be further classified by presence or absence of proteinuria (P or Non-P) and presence or absence of systemic hypertension (H or Non-H); see comments.

¹Renal proteinuria defined as urine protein:creatinine ratio (dog > 0.5, cat > 0.4)

Case Study – Max

Hx

- 6-year-old beagle
- Intact male
- BCS 2.5/5
- Presented for dental work
- No clinical signs

Dx

- Routine screen – azotemia, proteinuria
- Stage II; proteinuria, no hypertension

Rx

- Renal failure food (low phosphorus, low protein, high omega-3 polyunsaturated fatty acids)
- Phosphorus binder
- ACE inhibition (ACE-I)
- Low-dose aspirin

Follow-up

- Serial urine protein: creatinine (UP/C), BUN; phosphorus and urine protein assessment Q 1 to 3 mo and 7 to 14 days after any adjustment in ACE-I dosage
- Urine culture Q 6 to 12 mo
- Serial biochemistry profiles Q 6 mo
- Blood pressure Q 6 mo



Results

BUN	26 mg/dl
Creatinine	2.0 mg/dl
K	4.3 mEq/L
TCO ₂	19.3 mmol/L
Ca	10.1 mg/dl
Phos	6.0 mg/dl
Urine SG	1.025
Protein	+4
Albumin	High +
UP/C	4.3
Bacteria	Negative
Systolic BP	147 mmHg

Case Study – Sarah

Hx

- 13-year-old domestic shorthair
- Spayed female
- BCS 1.5 to 2/5
- Ongoing weight loss, inactivity
- Anorexic and vomiting
- Kidneys shrunken and firm
- 10% Dehydrated

Dx

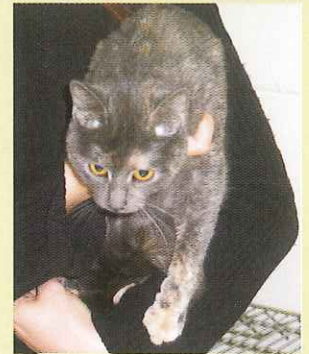
- Urine culture – *E. coli*
- Renal ultrasound (U/S) – mild pyelectasia
- Stage III, proteinuria, hypertension

Rx

- Fluid therapy
- Long-term antibiotics
- Potassium supplementation
- GI protectant
- Renal failure food
- Phosphorus binder
- ACE inhibitor/calcium channel antagonist
- Feeding tube?

Follow-up

- Serial UP/C
 - Urine culture Q 1 to 2 mo
- Serial biochemistry profiles
 - Blood pressure Q 1 to 2 mo



Results

BUN	86 mg/dl
Creatinine	4.4 mg/dl
K	2.4 mEq/L
TCO ₂	12.8 mmol/L
Ca	10.2 mg/dl
Phos	8.6 mg/dl
Urine SG	1.015
Protein	+2
Albumin	Med/High +
UP/C	1.1
Bacteria	Negative
Systolic BP	177 mmHg

time can indicate a 50% or greater reduction in glomerular filtration rate even though a value of 1.2 mg/dl is within the normal range.

Vomiting and anorexia are also common in dogs and cats with CKD. Causes include stimulation of chemoreceptors by uremic toxins, decreased gastrin excretion and uremic vasculitis, increased gastric acid secretion, and gastrointestinal irritation secondary to uremic toxicity.

ROLE OF PHOSPHORUS IN CKD

Plasma phosphorus concentrations increase in CKD because of decreased renal excretion, causing hyperphosphatemia. At the same

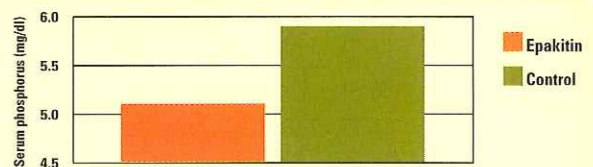
Serum creatinine levels are commonly used to measure kidney dysfunction and are the basis of the IRIS staging system

time, there is a decrease in the active form of vitamin D₃ that reduces intestinal absorption of calcium. This process, combined with impaired ability to reabsorb calcium in the kidney,

causes ionized calcium concentrations to decrease. In response to decreased vitamin D₃ and plasma calcium concentrations, parathyroid hormone (PTH) levels increase. This functional hyperparathyroidism

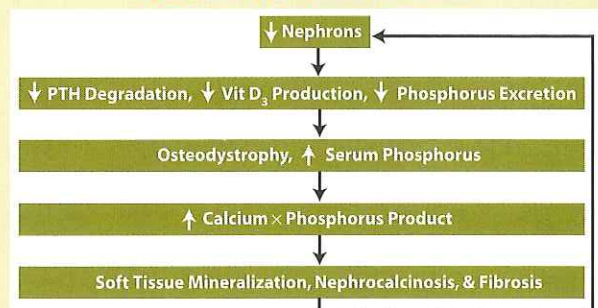
Phosphatemia in Cats with CKD

Serum phosphorus*



* Effects of phosphorus binder (Day 28) in cats with IRIS stage II chronic renal insufficiency (P<0.05 Epakitin vs control)

Cycle of Hyperphosphatemia



can cause osteodystrophy, neuropathy, bone marrow suppression, and soft tissue mineralization. It has been shown that by adding enteric phosphorus binders and reducing phosphorus in the diet, hyperphosphatemia can be reduced.

MANAGEMENT

Even though CKD is usually irreversible from a histologic and functional viewpoint, with proper treatment, the severity of clinical signs can generally be reduced. Longevity may even be increased by decreasing phosphatemia.² It is important that water be available ad libitum so that dehydration does not occur, that fluids be

Epakitin Highlights

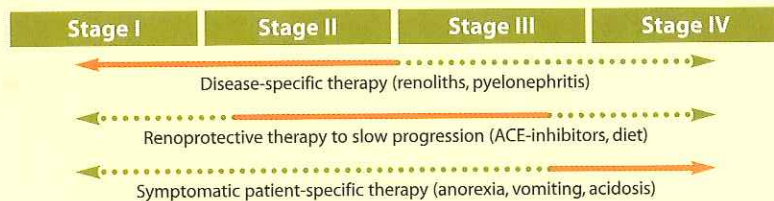
It is possible to slow down the destructive cycle of CKD and increase life expectancy by limiting phosphatemia with the help of a low phosphorus diet and/or by adding a phosphorus binder to the diet.² Epakitin is a chitosan-based nutritional supplement (chitosan is a natural polysaccharide, extracted from crab and shrimp shells).

- Binds phosphorus
- Reduces uremia
- Improves general health of animals with CKD
- Demonstrated clinical efficacy
- Highly palatable

replaced parenterally if necessary, and that any infection be managed.

Therapy to slow progression of disease should be started as soon as diagnosis is conclusive. Dietary sodium levels can remain normal or if hypertension is present sodium can be gradually decreased. Dietary protein should be reduced but should never go below the patient's protein requirement.

Therapeutic Approaches



REFERENCES

1. *Textbook of Veterinary Internal Medicine, 4th Edition*. Ettinger SJ, Feldman EC (eds). WB Saunders, 1995.
2. *Survival of cats with naturally occurring chronic renal failure: effect of dietary management*. Elliott J, Rawlings JM, Markwell PJ, Barber PJ. *J Sm Anim Pract* 41:235-242, 2000.

Management of CKD

Dogs & Cats

- Fresh water ad libitum
- Disease-specific therapy
 - Control infection
 - Remove urolith obstructions
- Therapy to control progression
 - Sodium levels normalized or gradually decreased
 - Protein levels reduced but within protein requirements
 - Canine 2.0 to 2.2 g protein/kg/day
 - Feline 3.3 to 3.5 g protein/kg/day
 - Dietary phosphorus levels reduced
 - Phosphorus binder (Epakitin) added to diet**
 - ACE inhibitors & calcium channel blockers if needed
- Patient-specific therapy
 - Control uremia
 - Control acidosis
 - Control vomiting

Management Challenges

- **Calorie malnutrition** may be caused by vomiting and anorexia. Controlling uremia may improve appetite and remove some of the causes of vomiting. Palatable enteric phosphorus binders will also help increase caloric intake.
- **Hypokalemia & potassium depletion** may occur in cats. Anorexia, high protein diets or acidifying diets, polyuria/polydipsia, and vomiting all contribute to potassium depletion. Oral potassium should begin early.
- **Pyelonephritis & renoliths** may occur in cats. Urinary tract infections are rare in healthy cats but may increase in older cats, especially those with CKD. Calcium oxalate uroliths are the most common type of renoliths in older cats.
- **Hyperthyroidism** is a common endocrinopathy in cats. Many hyperthyroid cats are more than 10 years old and often have concurrent renal insufficiency or CKD. Coexistence of these conditions can complicate diagnosis and treatment.



This summary is based on presentations to the veterinary profession by Dr. Gregory F. Grauer and Dr. Scott Brown, research cited, and information from www.epakitine.com and on file at Vétoquinol USA, Inc., Buena, NJ. Supported by an educational grant from Vétoquinol USA, Inc.