Diagnosing chronic renal disease in cats

Going beyond basic testing can give you a more accurate picture.

By David Julien, DVM
Contributing Author

One in three cats and one in five dogs will develop kidney disease within their lifetimes.[1] While it is extremely prevalent, renal disease can be difficult to diagnose in its early stages. All cats, especially aging cats, are predisposed to renal disease, and identifying any underlying cause will allow you to develop the best treatment plan to medically manage the condition and hopefully extend the Pet's life.

A thorough assessment of a cat with suspected renal disease is best achieved through diagnostic testing since cats may not present with physical signs until the condition has progressed to the later stages. By the time blood chemistry abnormalities are apparent, significant kidney function has been lost. While blood chemistry results are usually unremarkable in stages 1 and 2 of renal disease, urine protein concentrations are often elevated earlier and can be beneficial in diagnosing and monitoring early renal disease in Pets (see *Managing feline renal disease*, page 32). As the disease progresses to stage 3 and then stage 4, clinical signs become more apparent. The cat presents with obvious polyuria and polydipsia (PU-PD), weight loss and decreased appetite or vomiting. Laboratory abnormalities also become more definitive as kidney function declines.

During the last several years, advancements in diagnostic testing have allowed for earlier detection. This article discusses how a comprehensive assessment will help practitioners fully evaluate renal disease in cats—or any Pet—which may help extend Pets' lives.

Defining renal conditions

First it may be helpful to distinguish between chronic renal disease and chronic renal failure. *Chronic renal disease* is defined as renal damage that has existed for at least three months, with or without a reduction in the glomerular filtration rate.

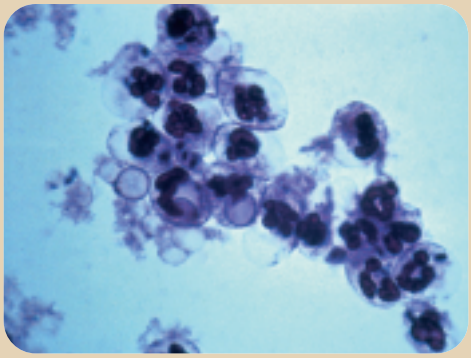
Chronic renal failure is a subset of patients with renal disease and is usually defined as persisent azotemia with a concurrent isothenuria. Common clinical signs include lethargy, PU-PD, vomiting and

Table 1: Diagnostic Testing Plan

Primary Testing	Secondary Testing	Tertiary Testing
■ Thorough history and physical examination	■ Urine protein test ◆ Urine protein-creatinine ratio ◆ Microalbuminuria	■ Serum titer testing
■ Serum biochemistry profile with electrolytes	■ Urine culture	■ Renal biopsy or aspiration
■ CBC	■ Abdominal ultrasonography	
■ FeLV-FIV test	■ Blood pressure determination	
■ Abdominal radiographs		
■ Urinalysis		
■ T_4 determination		
■ Iohexol clearance test*		

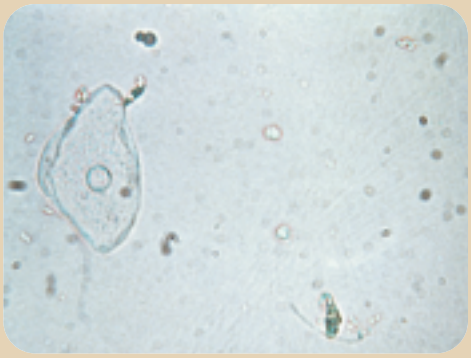
*Test is not usually performed as part of primary diagnostics but is used to determine kidney function.

Figure 1



Neutrophils present in urine sediment: Substantial numbers indicate active inflammation in response to many infectious and noninfectious conditions. Neutrophils can enter the urinary tract at various sites, so the source must be determined based on clinical signs and further diagnostic testing.

Figure 2



Squamous epithelial cells originate from the genital tract and though they are a normal finding, they indicate contamination of the urine sample.

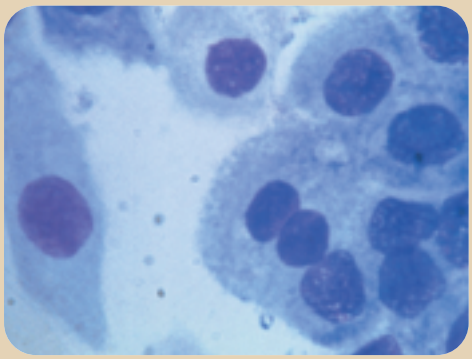
Photos: Banfield Lab Atlas

anorexia. Physical examination findings may include nonregenerative anemia, dehydration, weight loss and small, irregularly shaped kidneys. Possible underlying causes of chronic renal disease and failure include glomerulonephritis, leptospirosis, toxicosis, feline infectious peritonitis, nephrolithiasis, pyelonephritis, neoplasia and hereditary or congenital disorders.

Primary diagnostic plan

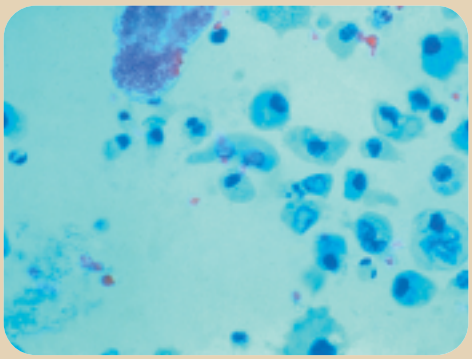
When a cat presents with signs consistent with chronic renal disease, a full diagnostic workup is indicated (*Table 1*). After obtaining the history, practitioners should carefully examine the Pet and then perform a serum biochemistry profile with electrolyte profile, complete blood cell count (CBC), complete urinalysis (*Figures 1-7,* pages 19-20), FeLV-

Figure 3



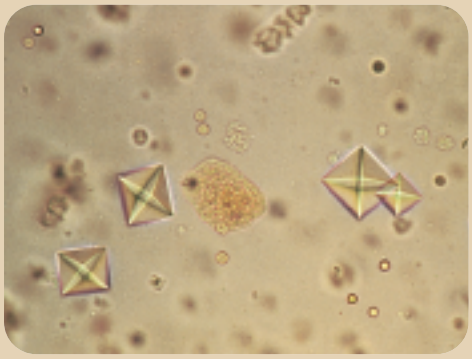
Transitional epithelial cells originate from the mucosal lining of the kidney, ureters, bladder and urethra, and they are normal when found in small numbers.

Figure 4



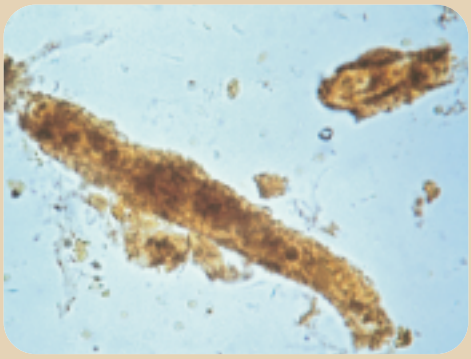
Renal epithelial cells originate from the renal tubules and are normal when found in small numbers. They are not a reliable indicator of kidney disease because it's difficult to distinguish them from other epithelial cell types.

Figure 5



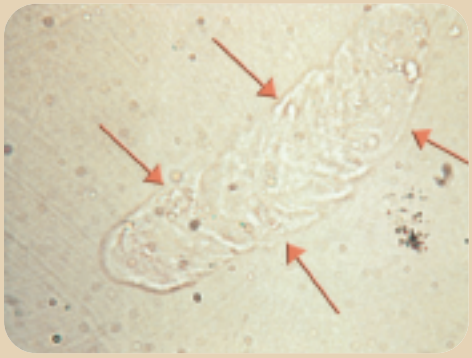
Dihydrate calcium oxalate crystals are found in normal Pets and in Pets with calcium oxalate urolithiasis. (Most nephroliths in cats are composed of calcium oxalate.)

Figure 6



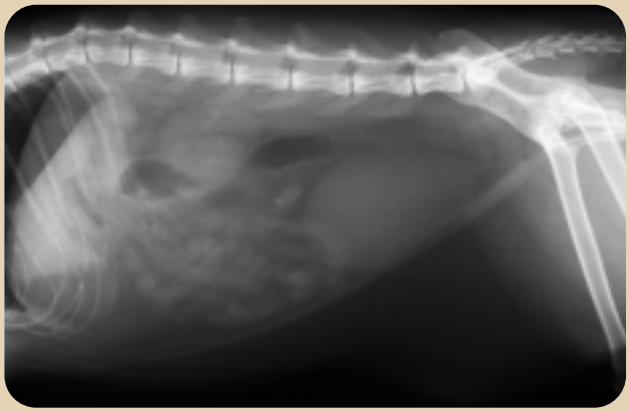
Granular casts are usually associated with diseases causing degeneration and necrosis of tubular epithelial cells, including infarction, ischemia and nephrotoxicosis.

Figure 7



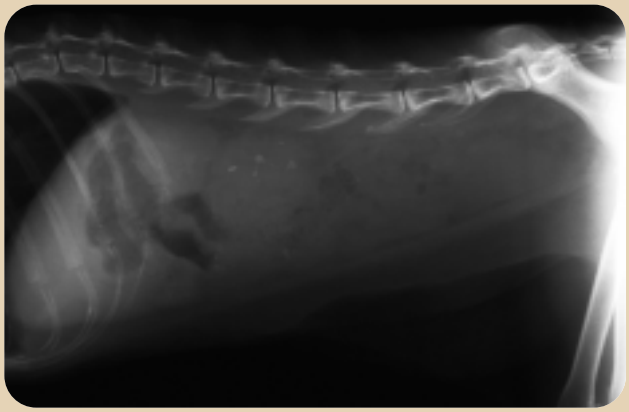
Hyaline casts are commonly associated with renal and extrarenal causes of proteinuria and can suggest mild or severe disease.

Figure 8



Healthy kidney: A 10-year-old spayed female Sealpoint Siamese cat with a normal-sized kidney.

Figure 9



Diseased kidney: A 12-year-old neutered male domestic shorthair cat in the later stages of renal disease. The silhouette of the kidney no longer retains its identifiable shape and smoothness. It is round and the surface is irregular. Renal opacities are also observable.

FIV test, T_4 determination and survey abdominal radiography (*Figures 8-9*). Note that urine specific gravity is needed to diagnose renal failure no matter how significant the azotemia, since azotemia can be caused by prerenal, renal or postrenal issues.

Other serum biochemistry changes may include hypoalbuminemia, hyperphosphatemia and elevations in amylase and lipase. CBC results may reveal a nonregenerative anemia. Kidneys usually appear small and irregular on radiographs, but they can be enlarged in cases of lymphoma, pyelonephritis or polycystic kidney disease.

In order to identify chronic vs. acute renal failure, practitioners need to look at all factors–historical signs, examination findings and laboratory data. In a case of chronic renal failure, an owner may notice changes occurring in the cat over a lengthy period of time (weeks to months). The cat may be anemic, and the kidneys are usually small and irregular in shape. The body condition score and coat condition tend to be more compromised with chronic disease.

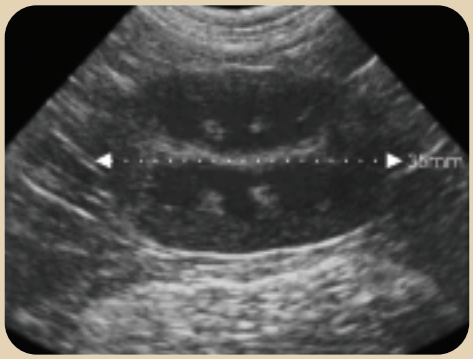
Renal insufficiency can be difficult to detect early in the disease process. The kidneys don't lose their ability to concentrate urine until 66 percent of total kidney function has been lost. BUN and creatinine concentrations do not increase until 75 percent of total function has been lost.

An iohexol clearance test, which estimates glomerular filtration rate, helps detect the early stages of renal insufficiency before a cat becomes azotemic. The test is not commonly performed as part of an initial primary diagnostic plan but will help determine kidney function (see *Using an Iohexol Clearance Test*, page 28).

Secondary diagnostic testing

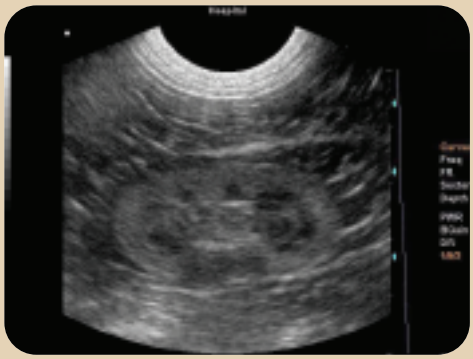
After the primary diagnostic workup, additional testing can help identify the underlying causes of renal dysfunction and help practitioners develop a treatment plan. The second tier of diagnostic evaluation should include urine protein testing; an abdominal ultrasound examination to help rule out neoplasia, pyelonephritis and radiolucent nephrolithiasis (*Figures 10-12,* page 24);

Figure 10



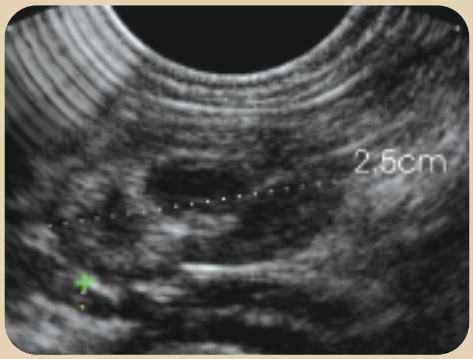
Normal kidney: A normal feline kidney should be about 3.5 to 4.5 cm in a normal-size cat. The capsule should be smooth and regular and there should be discrete definition between the cortex and medulla, which gives it a "ladybug" appearance. The spleen should generally be brighter than the cortex of the kidney when comparing echogenicity.

Figure 11



Midstage failure: Here, the size is close to the normal range, but the kidney has become hyperechoic as the tissue becomes fibrous and denser than normal tissue.

Figure 12



End stage failure: The kidneys are small, the capsule is irregular and there is a loss of definition between the cortex and medulla.

and a urine culture to aid in the diagnosis of pyelonephritis. Blood pressure should also be assessed since hypertension can result in further renal damage.

Urine protein testing. As renal glomeruli become damaged, protein is lost in the urine. Urine dipsticks provide a semiquantitative evaluation of proteinuria but are not always definitive.

A test to determine the urine protein-creatinine (UPC) ratio (VetTest® Urine P:C Ratio, IDEXX Laboratories) is an easy and inexpensive way to quantify urine protein and identify persistent renal proteinuria.[2] Because it is fully quantitative, the UPC ratio can be used to monitor renal disease patients and evaluate their response to therapy.

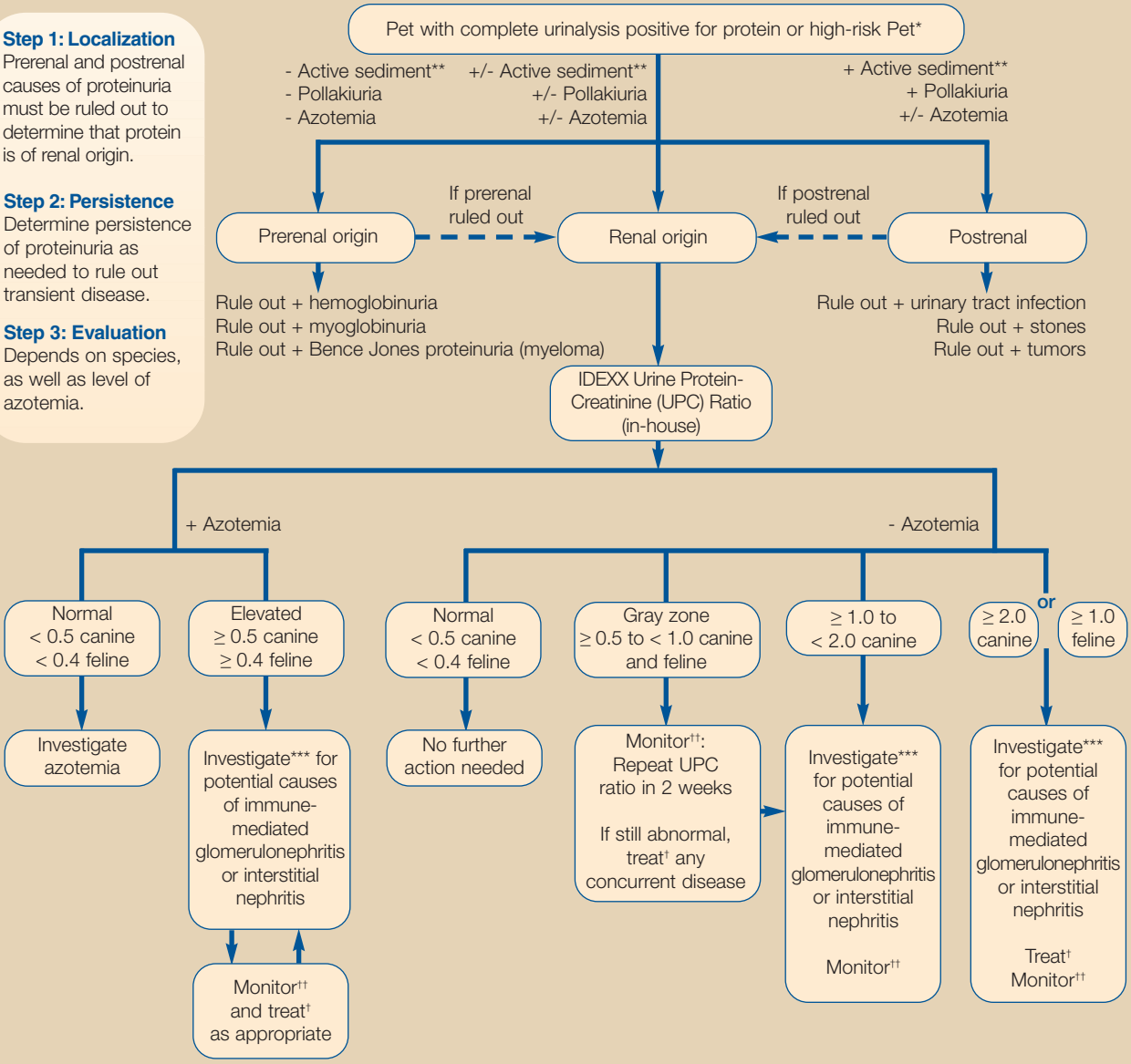
The UPC ratio is run on urine samples

Diagnostic Protocol for Urine Protein-Creatinine Ratio: Canine and Feline

Step 1: Localization
Prerenal and postrenal causes of proteinuria must be ruled out to determine that protein is of renal origin.

Step 2: Persistence
Determine persistence of proteinuria as needed to rule out transient disease.

Step 3: Evaluation
Depends on species, as well as level of azotemia.



* High-risk Pet = predisposed breed, prior history of renal concerns or geriatric Pet

** Active sediment = cells, casts and bacteria

*** Investigate = determine underlying cause, if any; consider ancillary testing as needed (thoracic and abdominal radiography to rule out neoplasia, ultrasonography, blood pressure evaluation, heartworm testing, vector-borne disease profile [SNAP 3Dx®], fungal titers, FeLV-FIV testing, other infectious disease testing, endocrine testing including ACTH stimulation test or low-dose dexamethasone testing, autoimmune panel and T_4 panel)

† Treat = consider the following treatment options when appropriate: renal diet (medium protein renal diet, etc.), ACE inhibitor drug therapy, phosphorus binders, fluid therapy

†† Monitor = recheck to determine trends; recheck should include internal organ function screen, IDEXX UPC ratio, CBC, electrolytes and urinalysis.

and measures both urine protein and urine creatinine. Urine creatinine excretion is very stable and is used in the ratio to adjust the urine protein concentration, which can fluctuate according to urine volume and concentration. This makes the test robust and provides valid results regardless of the patient's hydration status or urine concentration ability. In order to properly assess UPC results, the proteinuria must first be localized to the kidneys and then determined to be persistent.[2]

To localize proteinuria to the kidneys, prerenal and postrenal causes must be eliminated. This can easily be done by performing a serum biochemistry profile, a CBC and a complete urinalysis including a urine sediment exam, all of which are included in your primary diagnostic plan. It is worth noting that the most common cause of proteinuria in dogs and cats is a bacterial urinary tract infection. While the UPC ratio is very specific for urine protein, it cannot determine the origin of that protein. The UPC ratio is also extremely sensitive for urine protein and therefore may detect minute levels that correspond with an increase in blood pressure and glomerular filtration rate associated with stress, exercise, fever and extreme fluctuations in temperature. Repeat testing will establish that the proteinuria is persistent. Lastly, the level of proteinuria should be evaluated for each patient to determine how to proceed with diagnosis and treatment (see *Diagnostic Protocol for Urine Protein-Creatinine Ratio*, page 26).

Microalbuminuria. The microalbuminuria test (E.R.D.-HealthScreen,® Heska) has been used as a screening test for geriatric patients, and it can also be used as a screening test before running the UPC ratio. If the microalbuminuria test is negative, you can assume the UPC ratio will be less than 0.2. If the test is positive, a UPC ratio should be run to quantify the proteinuria.

Tertiary diagnostics

Other tests can be performed to help rule out less common diseases. Serum titer tests can be performed to check for infectious diseases (leptospirosis is often overlooked and can cause both liver and renal disease in dogs but is rarely a problem in cats). Renal biopsies and aspirations are not routine but may be beneficial when neoplasia is suspected.

Using an Ioxehol Clearance Test

Although the iohexol clearance test is not performed on a regular basis, it is a good diagnostic tool to measure kidney function. The clearance of iohexol from the blood by the kidneys is due to filtration and is not substantially altered by the kidney tubules once filtered by the glomerulus. Therefore, iohexol clearance is related to the glomerular filtration rate and allows for determination of kidney function.

PU-PD due to renal disease may be noted before azotemia is evident, so renal disease must be considered in patients that present with PU-PD but are not azotemic. In these patients, all common causes of PU-PD should be ruled out and then renal function tests can be performed.

Clinical reasons to perform an iohexol clearance test to determine kidney function include:

- PU-PD due to possible renal insufficiency
- Small or irregularly shaped kidneys found on ultrasound examination, radiographs or palpation
- An upcoming surgical or medical procedure in a patient with questionable renal function.

Following are the criteria for performing an iohexol clearance test:

- The cat must be nonazotemic.
- The cat is well-hydrated.
- Food is withheld for 12 hours before testing.

The ioxehol clearance test requires advance planning, and samples are shipped to a commercial laboratory the same day collection occurs. For best results, the Pet should stay at the hospital for five or six hours while testing is performed. At our practice, we always recommend a client drop the cat off early in the morning and arrange pickup in the early evening.

Educating clients

The most important step in addressing any Pet health issue is explaining to owners the benefits of diagnostic testing (see *Timely testing*, page 14). To do so, we need to be confident in the care we provide our patients and convey this to their owners. I like to review my list of rule-outs with clients and then briefly explain each test. The key is to provide a detailed explanation so clients can comprehend each test's value–but be careful not to overwhelm them with too much information.

I also have the PetNurse review the diagnostic plan with the client. The PetNurse is in a unique position to reinforce the need for diagnostics. Owners view PetNurses as unbiased advisors. A well-trained PetNurse can educate clients who are having a difficult time deciding whether to proceed with a test. They provide clients with additional information to make their decision and often put clients at ease.

Owners often want to proceed with just one or two tests to see if a diagnosis can be made from those results. The veterinary team needs to explain to clients that this approach markedly compromises the care we provide and will result in more questions regarding the Pet's condition. As a veterinarian, you need to collect all the information on your patients in order to provide high-quality care. Without a complete picture, you may misdiagnose the Pet. With a very ill cat, there may be multiple abnormalities. For example, of what diagnostic value is a serum biochemistry profile without a complete urinalysis? If azotemia is revealed, we need the results of the urinalysis to determine if it is due to severe dehydration or renal failure. This will help direct appropriate treatment and care of the Pet. It is our job to advocate for the Pet, and educating the client properly makes diagnosing and treating the Pet easier.

Chronic renal disease is seen commonly in veterinary practice, especially in older cats. The diagnosis of chronic renal disease is often considered routine. However, we sometimes forget the limitations of baseline diagnostic testing. Since azotemia is apparent only after severe kidney damage has occurred, an attempt should be made to diagnose renal disease much earlier. It is also important to remember that there are underlying causes of chronic renal failure and this disease is not just a normal aging process. If an underlying cause is identified, we have a better opportunity to make an impact on our patients' lives.

References

1. Proteinuria and renal disease: A roundtable discussion. Advanstar Veterinary Healthcare Communications, Lenexa, Kan, 2005:1-15. In *Vet Med* 100(4). Sponsored insert.

2. Kahn, Michelle. Urine P:C Ratio Testing using IDEXX VetTest® Chemistry Analyzer, Banfield Education Symposium, 2005.

Selected Reading

1. Ettinger SJ, Feldman EC. *Textbook of Internal Veterinary Medicine*. 4th ed. Philadelphia, Pa: WB Saunders Co, 1995;1734-1758.

2. Nelson RW, Couto CG. *Small Animal Internal Medicine*. 3rd ed. St Louis, Mo: Mosby, 2003;584-617.

3. Thrall DE. *Textbook of Veterinary Diagnostic Radiology*. 3rd ed. Philadelphia, Pa: WB Saunders Co, 1998;466-472.

David Julien, DVM, is a 2000 graduate of the University of Prince Edward Island. After graduating, he moved to Phoenix, where he now lives with his wife, Meghan; their three dogs, Kona, Kai and Midge; three cats, Star, Murrey and Dylan; and a chinchilla, Finnigan. They are expecting a baby in January.