

Glossary of
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Chronic renal failure causes difficult to pinpoint

The top 13 questions addressed



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Q: What causes chronic renal failure (CRF)?

A: Unlike acute renal failure, the cause of CRF usually is difficult to determine. Because of the interdependence of the vascular and tubular components of the nephron, the endpoint of irreversible glomerular or tubular damage is the same. A morphologic heterogeneity among nephrons exists in the chronically diseased kidney with the changes ranging from severe atrophy and fibrous scar tissue replacement to marked hypertrophy. The histopathologic changes are not process-specific, and therefore the cause is usually unknown.

Q: What are the clinical signs of CRF?

A: CRF develops over a period of weeks, months or years, and its clinical signs are often relatively mild for the magnitude of the azotemia. Unique signs of CRF include a long-standing history of weight loss, polydipsia/polyuria and poor body condition. A non-regenerative anemia is

often documented on a CBC, and small and irregularly shaped kidneys can be palpated on physical examination. Renal ultrasonography usually will show diffusely hyperechoic renal cortices with loss of the normal corticomedullary boundary. The increased cortical echogenicity results from replacement of the irreversibly damaged nephrons with fibrous scar tissue. Radiographic studies and ultrasonography also can help identify or rule out potentially treatable causes of CRF, such as bacterial pyelonephritis and renal urolithiasis.

Q: How do the treatment strategies for acute and chronic renal failure differ?

A: The tubular lesions and dysfunction caused by toxic, ischemic and infectious insults can be reversible. The goals of treatment of established acute renal failure (ARF) are to eliminate renal hemodynamic disorders and alleviate water and solute imbalances to “buy time” for nephron repair and compensatory hypertrophy. Conversely, because the nephron damage in CRF usually is irreversible, the goal of treatment is to reduce the renal workload and the clinical signs associated with the decreased

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renal function. It is also important to attempt to slow down the progressive loss of nephrons in CRF patients.

Q: Why is CRF usually irreversible?

A: Progressive diseases that slowly destroy nephrons allow time for repair of reversibly damaged nephrons as well as hypertrophy of intact nephrons. When renal failure finally occurs, the repaired and hypertrophied nephrons can no longer maintain adequate renal function. Because new nephrons cannot be produced, the functional abnormalities of CRF usually are irreversible and often progressive.

What mechanisms contribute to the progressive decline of renal function observed in many CRF patients?

Proteinuria and systemic hypertension have been associated with increased risk of uremic crises and death, although a direct link to progressive nephron loss has not been established. The soft-tissue mineralization that can occur when the serum calcium x phosphorus product exceeds 50-70 mg/dl has been linked to progressive loss of nephrons in dogs and cats. Ascending urinary tract infections (bacterial pyelonephritis) and renoliths (most commonly calcium oxalate) are additional causes of progressive nephron loss.

Q: Is dietary therapy effective in slowing the progression of CRF?

A: In a controlled, prospective study, dietary modifications were beneficial in minimizing extra-renal manifestations of uremia and mortality rates in dogs with mild/moderate spontaneous CRF. Results were consistent with the hypothesis that the delay in mortality rate was associated, at least in part, with a reduction in disease progression. Similarly, feeding a specifically formulated feline CRF diet, alone or in combination with an en-

teric phosphate binder, to cats with spontaneous CRF resulted in lower concentrations of parathyroid hormone and phosphorus, as well as increased survival time. These results suggest that dietary therapy and enteric phosphate binders, if appropriate, can improve the quality and quantity of life for our patients.

Q: Is calcitriol indicated as a treatment for CRF?

A: This remains a controversial issue in veterinary medicine. The primary benefit of ultra-low dose calcitriol treatment is lower parathyroid hormone concentrations. Much of the controversy stems from a study in which parathyroidectomized dogs with experimental CRF fared no better than parathyroid-intact CRF dogs.

Loss of nephrons in CRF results in afferent glomerular arteriole vasodilatation causing intraglomerular pressure to increase.

Most experts agree that calcitriol should be supplemented only if parathyroid hormone and phosphorus concentrations remain increased after dietary and enteric phosphate binder treatment has been initiated.

Q: Are angiotensin-converting enzyme inhibitors (ACEIs) indicated for the treatment of CRF? What about calcium channel antagonists (CCAs)?

A: Loss of nephrons in CRF results in afferent glomerular arteriole vasodilatation, which causes intraglomerular pressure to increase. This "hyperfiltration" can lead to progressive loss of nephrons. Treatment with ACEIs result in efferent arteriolar vasodilatation, which reduces intraglomerular hypertension. In a study of dogs with surgically-induced CRF, enalapril was associated with a reduction of glomerular and systemic hypertension and proteinuria, prompting investigators to conclude that ACEIs might be effective in modulating progressive renal injury in dogs with CRF. Similarly, in cats with the remnant kidney model of CRF, treatment with benazepril sustained single nephron GFR and was associated with a significant reduction in systemic hypertension and an increase in whole kidney GFR. The conclusion of this study was that ACEIs might slow the rate of disease progression in cats with CRF.

Amlodipine had an antihypertensive effect in cats with coexistent systemic hypertension and remnant kidney-induced renal insufficiency. Therefore, treatment with CCAs can improve the prognosis for cats with hypertension by decreasing the risk of ocular and/or neurologic injury. In many feline cases, CCAs are more effective in reducing systemic hypertension than ACEIs. Inasmuch as ACEIs normalize intraglomerular pressures to a greater extent than CCAs, combination treatment may be indicated in cats when ACEIs alone fail to control systemic hypertension.

Q: When should I treat anemia in CRF patients?

A: After initiation of the previously discussed treatments, the anemia of CRF should be treated if it appears to be contributing to the patient's poor quality of life. Studies assessing the effects of recombinant human erythropoietin (r-HuEPO)

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treatment on anemia in dogs and cats with CRF have generally shown it to be successful. The cost of treatment for medium-sized and large-breed dogs is high, however. Recombinant erythropoietin treatment also often results in heightened appetite, weight gain, increased strength and an improved sense of well-being. It's important to keep in mind that there is a potential for antibodies to form in

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up to 30-40 percent of dogs and cats treated with r-HuEPO. If antibodies are produced against r-HuEPO, then they also can react with endogenous erythropoietin, making the animal transfusion-dependent. Because of the potential for antibody formation, many clinicians reserve the use of r-HuEPO for patients whose anemia is moderate to severe and contributing to poor quality of life. Commercially available canine and feline recombinant erythropoietin would improve our ability to treat the anemia of CRF significantly.

Q: How do I stimulate appetite in a CRF patient?

A: The most important aspect of stimulating appetite is control of metabolic deficits and excesses associated with CRF (e.g., dehydration, acidosis, anemia, hypertension). Second, gastrointestinal tract dysfunction (e.g., motility, acidity, constipation, oral disease) should be addressed. Third, feeding management

problems (force feeding, sudden dietary change, not recognizing social and antisocial eaters, and giving pills and injections associated with feeding) should be addressed. In general, tricks designed to increase diet palatability and use of appetite stimulants are less effective. Vomiting can be treated with metoclopramide, which blocks the chemoreceptor trigger zone and increases gastric motility and emptying without increasing gastric acid secretion. H₂-receptor blockers (e.g., ranitidine) and proton pump blockers (e.g., omeprazole) have been shown to effectively decrease gastric acid secretion, which can attenuate vomiting in dogs and cats with CRF.

Q: Are feedings tubes helpful?

A: If vomiting can be controlled, but the animal still will not eat enough to meet its daily caloric requirements, then a feeding tube might be indicated. Cats tend to tolerate gastrostomy tubes especially well, and they can remain in place for months. Esophagostomy and gastrostomy tubes not only facilitate provision of potentially unpalatable, and appropriate, calories but also provide a relatively stress-free route for fluid therapy and medications.

Q: When should I initiate subcutaneous fluid therapy?

A: Daily maintenance fluid requirements in animals with CRF are higher than those of normal animals because of polyuria. If the patient with CRF is not able to drink enough to keep up with its urine output, then daily subcutaneous fluids might be indicated. In some cases, owners are able to perform this treatment at home. If in doubt, a trial of subcutaneous fluid therapy may be indicated. If the patient seems energized by the fluids and BUN and creatinine concentrations are decreased, then continued therapy is warranted.

Q: How do I diagnose CRF early or in its most treatable stages?

A: Annual or semi-annual health examinations that include clinicopathologic evaluations in middle-aged and older patients are an excellent way to document trends compatible with declining renal function. Data flow charts facilitate observation of trends and are recommended. Decreases in body weight, packed cell volume, and urine-specific gravity over time, for example, can occur in patients with subclinical renal dysfunction. Conversely, increases in serum urea nitrogen, creatinine, phosphorus and microalbuminuria/proteinuria (even when these increases remain within the laboratory normal range) might be early indicators of declining renal function. In patients with diminished urine concentrating ability, urine should be cultured periodically due to the diminished antibacterial properties of minimally concentrated urine. An ultrasound examination of the kidneys is indicated if trends in the above data are compatible with developing renal insufficiency failure.

Dr. Grauer earned his DVM degree from Iowa State University in 1978. He then completed his postgraduate training (internship, residency and MS degree) at Colorado State University between 1978 and 1982. Dr. Grauer obtained his specialty board certification in internal medicine in 1983. After his postgraduate training, Dr. Grauer was a member of the faculty at the School of Veterinary Medicine, University of Wisconsin for seven years and then returned to the Department of Clinical Sciences at Colorado State University where he served as professor and section chief of small animal medicine until 2000. Dr. Grauer also has served as president and chairman of the Board of Regents of the American College of Veterinary Internal Medicine. Currently, Dr. Grauer is professor and head of the Department of Clinical Sciences at the College of Veterinary Medicine, Kansas State University. His interests in clinical medicine and research involve the small animal urinary system. **DVM**