Comparison of Multistix PRO dipsticks with other biochemical assays for determining urine protein (UP), urine creatinine (UC) and UP:UC ratio in dogs and cats.

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BACKGROUND: Urine protein: urine creatinine (UP:UC) ratio determined from the quantitative measurement of protein and creatinine in a single urine sample is the best feasible assessment of clinically significant proteinuria in dogs and cats. A dipstick that measures urine protein, urine creatinine, and UP:UC ratio has been used in human medicine and could have application for veterinary practice. OBJECTIVE: The objective of this study was to compare the Multistix PRO dipstick (Bayer Corporation, Elkhart, IN, USA) to other biochemical methods for determination of urine protein and creatinine, and UP:UC ratio in canine and feline urine. METHODS: A complete urinalysis, including sulfosalicylic acid (SSA) precipitation, was performed on urine samples submitted to our laboratory between February and April 2003 from 100 dogs and 49 cats. Urine protein and creatinine concentrations were determined by the Multistix PRO dipstick using a Clinitek 50 analyzer (Bayer) and compared with the results of SSA precipitation and quantitative biochemical analysis. The UP:UC ratios from the dipstick results (calculated by the Clinitek 50 and also manually) were compared with those calculated from quantitative values. Pearson product-moment correlation analysis and diagnostic sensitivity and specificity (using quantitative results as the gold standard) were determined. RESULTS: For both canine and feline urine, protein and creatinine concentrations determined by the Multistix PRO correlated closely with quantitative concentrations for protein (dogs $r = .78$, $P = .0001$; cats $r = .87$, $P = .0001$) and creatinine (dogs $r = .78$, $P = .0001$; cats $r = .76$, $P = .0001$). The Multistix PRO was more sensitive and less specific than SSA precipitation for diagnosing clinically significant proteinuria. UP:UC ratios obtained by manual calculation of dipstick results correlated best with quantitative UP:UC ratios in dogs, and had higher specificity but lower sensitivity for the diagnosis of proteinuria. In cats, UP:UC ratios determined by the dipstick method did not correlate ($r = -.24$, $P = .0974$) with quantitative values. CONCLUSIONS: The Multistix PRO, with manual calculation of UP:UC, may be a good alternative for the diagnosis of clinically significant proteinuria in dogs, but not cats. Dipstick creatinine concentration should be considered as an estimate.
Survival of cats with naturally occurring chronic renal failure is related to severity of proteinuria.

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BACKGROUND: Tubulointerstitial kidney disease is a common cause of illness and death in pet cats and is typically not associated with overt proteinuria.

HYPOTHESIS: Proteinuria would be independently related to survival in cats with renal failure, with or without hypertension.

ANIMALS: The study included 136 client-owned cats; 28 apparently normal, 14 hypertensive but not azotemic, 66 azotemic but not hypertensive, and 28 both hypertensive and azotemic.

METHODS: Cox's proportional hazards model was used to determine the influence of initial plasma creatinine concentration, proteinuria (urine protein-to-creatinine ratio or albumin-to-creatinine ratio), age, and systemic hypertension on the risk of death or euthanasia during the follow-up period. Multivariable linear regression was used to determine the relation between severity of proteinuria and predictive variables, including age, plasma creatinine concentration, systolic blood pressure, sex, and urine specific gravity.

RESULTS: Plasma creatinine concentration and proteinuria were very highly related to survival. The hazard ratio (95% confidence intervals) for death or euthanasia was 2.9 (1.4-6.3) and 4.0 (2.0-8.0) for urine protein-to-creatinine ratio 0.2-0.4 and >0.4, respectively, compared with the baseline group with a urine protein-to-creatinine ratio of <0.2 and were 2.4 (1.2-4.8) and 4.9 (2.3-10.2) for an albumin-to-creatinine ratio of 30-82 mg/g and <82 mg/g, respectively, compared with a baseline group with albumin-to-creatinine ratio of <30 mg/g. Treated hypertensive cats did not have reduced survival, although systolic blood pressure, together with plasma creatinine concentration was positively related to the magnitude of proteinuria.

CONCLUSIONS AND CLINICAL IMPORTANCE: Despite the relatively low concentrations of proteinuria typical of chronic renal disease in cats, this measurement is of prognostic significance.
Glomerular disease in the dog is not only a common form of renal disease but also an important cause of chronic renal failure. The presence of immune complexes in glomerular capillary walls is a major cause of canine glomerular disease and is commonly referred to as glomerulonephritis. Leakage of plasma proteins, principally albumin, across the damaged glomerular capillary walls results in persistent proteinuria—the clinicopathological hallmark of glomerulonephritis. Recent evidence suggests that, in addition to being a marker of disease, persistent proteinuria is associated with progressive glomerular and tubulointerstitial lesions and loss of additional nephrons. Perhaps the best treatment for glomerulonephritis is the identification and correction of any underlying inflammatory, immune-mediated or neoplastic disease that results in the deposition or formation of glomerular immune complexes. In cases of idiopathic glomerulonephritis, angiotensin-converting enzyme inhibitors have been shown to decrease proteinuria and potentially slow disease progression.

Publication Types:

Review

**Vet Rec. 2005 Sep 24;157(13):378-82.**

**Proteinuria and immunoglobulinuria in neonatal dogs.**

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Samples of urine and serum from 45 newborn rottweiler puppies from six litters, and milk from their mothers, were taken 24, 48 and 72 hours and seven and 14 days after birth. Urine total protein and creatinine concentrations were determined and the ratios calculated. The immunoglobulin (Ig) concentrations of IgG, IgM and IgA in urine, serum and milk were determined with a commercially available elisa kit. The concentration of total protein in urine decreased from 1.64 to 0.29 mg/ml, and it and the ratio of total protein to creatinine in the urine of the neonatal puppies exceeded the normal values for adult dogs, but all the puppies developed normally. The average concentration of IgG in urine decreased from 0.0035 to 0.0003 mg/ml, that of IgA from 0.0035 to 0.0002 mg/ml and that of IgM from 0.0006 mg/ml to undetectable levels after two weeks. After two weeks, 47 per cent of the puppies had measurable levels of IgA and 70.6 per cent had measurable levels of IgG, but none of them had measurable levels of IgM.

Publication Types:
Assessment and management of proteinuria in dogs and cats: 2004 ACVIM Forum Consensus Statement (small animal).


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Emerging data indicate that more attention should be given to the detection, evaluation, monitoring, and treatment of dogs and cats with proteinuria. The purposes of this consensus statement are to describe an appropriate approach for accomplishing these tasks and to provide specific recommendations for assessing and managing dogs and cats with proteinuria based on data that are currently available. Because proteinuria and albuminuria have numerous possible causes, they must be assessed appropriately to determine their implications for the patient. This assessment involves localization of the origin of the proteinuria as well as determination of its persistence and magnitude. Because persistent renal proteinuria usually indicates presence of chronic kidney disease, which sometimes is a progressive disorder, its detection identifies dogs and cats that have increased risk for adverse health outcomes. Thus, urine testing that will detect proteinuria should be a component of the clinical evaluations of dogs and cats under all circumstances that prompt their veterinarians to also perform comprehensive hematologic and serum biochemical evaluations. At a minimum, this testing should consist of a complete urinalysis that includes a satisfactorily accurate semiquantitative test for protein, and positive reactions should be properly followed with further testing. The appropriate response to persistent renal proteinuria depends on the magnitude of proteinuria and the status of the patient. The recommended response generally involves continued monitoring, further investigation, and therapeutic intervention, which should be implemented as an escalating series of inclusive, stepwise responses.

Publication Types:
- Consensus Development Conference
- Guideline
- Practice Guideline
- Review
Validation of a human immunoturbidimetric assay to measure canine albumin in urine and cerebrospinal fluid.

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The aim of this study was to validate an automated immunoturbidimetric assay used to quantify human albumin in urine and to accurately measure canine albumin concentrations in both urine and cerebrospinal fluid. The partial homology existing between human and canine albumin limited the accuracy of the human assays in measuring canine albumin without method modifications. Thus, the assay was modified by calibrating the analyzer with calibrators made in the laboratory containing known concentrations of canine albumin. To prepare the set of calibrators, the albumin concentration of pooled sera of healthy dogs was assessed in 5 replicates using the BromocresolGreen assay. Pooled samples were aliquoted and serially diluted to obtain the expected concentrations of albumin (0.5, 1, 5, 13, and 30 mg/dl) for establishing the canine calibration curve. Thereafter, the performance was assessed by analyzing canine urine and CSE. The modified assay accurately quantified canine albumin in both specimens, as indicated by the following. Intra- and interassay variability was 0.92% and 2.74%, respectively; recovery was 99.66% and 99.07% in urine and 105.02% in CSE. No interference was detected when hemolysate and glucose were added to urine. The test was linear within the verified range (0-225 mg/dl). These results demonstrate that the modified human albumin immunoturbidimetric assay can be a useful tool in the veterinary diagnostic laboratory. It is accurate and tends itself to automatization on chemistry analyzers.

Publication Types:
• Validation Studies

Urinalysis interpretation: how to squeeze out the maximum information from a small sample.

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The urinalysis is an essential part of the diagnostic evaluation for all urinary and many metabolic diseases. Its assessment includes evaluation of physical
characteristics (color, clarity, and volume), biochemical parameters (urine pH, blood, glucose, ketones, bilirubin, urobilinogen, and protein) and microscopic sediment evaluation (RBC, WBC, organisms, epithelial cells, crystals, and casts). Many of these parameters are influenced by collection method and therefore, it is essential to interpret accordingly. Knowledge of factors that can interfere with the accuracy of some test results can decrease improper interpretation. When all of these parameters are evaluated in combination with clinical signs, physical examination, thorough history and other laboratory tests, a diagnosis will often be attained.

**Publication Types:**
- Review

**J Am Vet Med Assoc. 2005 Feb 1;226(3):393-400.**

**Evaluation of the association between initial proteinuria and morbidity rate or death in dogs with naturally occurring chronic renal failure.**

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**OBJECTIVE:** To determine whether urine protein-to-creatinine ratio (UP:C) > or = 1.0 at initial diagnosis of chronic renal failure (CRF) is associated with greater risk of development of uremic crises, death, and progression of renal failure in dogs. **DESIGN:** Prospective cohort study. **ANIMALS:** 45 dogs with CRF. **PROCEDURE:** Dogs were prospectively assigned to 2 groups on the basis of initial UP:C < 1.0 or 2 > or = 1.0. The association between magnitude of proteinuria and development of uremic crises and death was determined before and after dogs with initial UP:C > or =1.0 were assigned to 3 subgroups and compared with dogs with initial UP:C < 1.0. Changes in reciprocal serum creatinine concentration were used to estimate decrease in renal function. **RESULTS:** Initially, dogs had similar clinical characteristics with the exception of systolic blood pressure and UP:C. Relative risks of development of uremic crises and death were approximately 3 times higher in dogs with UP:C > or =1.0, compared with dogs with UP:C < 1.0. Relative risk of adverse outcome was approximately 1.5 times higher for every 1-unit increment in UP:C. The decrease in renal function was of greater magnitude in dogs with UP:C > or =1.0, compared with dogs with UP:C < 1.0. **CONCLUSIONS AND CLINICAL RELEVANCE:** Initial UP:C > or =1.0 in dogs with CRF was associated with greater risk of development of uremic crises and death, compared with dogs with UP:C < 1.0. Initial determinations of UP:C in dogs with naturally occurring CRF may be of value in refining prognoses.
Free light-chain proteinuria and normal renal histopathology and function in 11 dogs exposed to Leishmania infantum, Ehrlichia canis, and Babesia canis.

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The purpose of this retrospective study was to investigate the relationship among proteinuria consisting of immunoglobulin free light chains (FLCs), renal histopathologic findings, and routine markers of renal function in 11 dogs exposed to Leishmania infantum (n = 8), Ehrlichia canis (n = 2), and Babesia canis (n = 1). FLC proteinuria was suspected based on identification of a 22- to 27-kDa band by sodium dodecyl sulfate-agarose gel electrophoresis (SDS-AGE) and later confirmed by immunofixation electrophoresis. SDS-AGE identified an isolated band of 22-27 kDa in 8 dogs, whereas the remaining 3 had a 22- to 27-kDa band and an additional band of 67-72 kDa. The median urine protein-to-urine creatinine ratio was 0.37 (range, 0.11-2.24) and increased ratios were found in 6 dogs (54.5%) (reference value, <0.7). All dogs underwent histologic examination of renal percutaneous biopsy specimens and determination of serum creatinine and urea concentrations. Tissue samples for light microscopy were stained with hematoxylin-eosin, periodic acid-Schiff, Goldners trichrome, and methenamine silver. In the study group, the glomerular tufts, mesangium, tubulointerstitium, and vessels appeared unaffected. The median serum creatinine concentration in these 11 dogs was 1.3 mg/dL (range, 0.8-1.5 mg/dL; reference range, 0.6-1.5 mg/dL), whereas the concentration for urea was 28 mg/dL (range, 22-52 mg/dL; reference range, 20-50 mg/dL). All dogs had normal renal morphology and had normal serum creatinine and urea concentrations, suggesting that immunoglobulin FLC may be detected in the urine of dogs exposed to L. infantum, E. canis, and B. canis without any apparent structural or functional renal derangement.

Angiotensin-converting enzyme inhibitors in the therapy of renal diseases.

Lefebvre HP, Toutain PL.
Renal diseases, especially chronic renal failure (CRF), are common in canine and feline medicine. The renin-angiotensin-aldosterone system (RAAS) plays a pivotal role in these conditions in the development of renal lesions and the progression of kidney dysfunction. Angiotensin-converting enzyme inhibitors (ACEI) are currently considered as the most efficient agents in therapeutic strategies. The benefit of an ACEI treatment can be explained by at least three mechanisms: ACEI limit systemic and glomerular capillary hypertension, have an antiproteinuric effect, and retard the development of glomerulosclerosis and tubulointerstitial lesions. These effects have been studied in dogs and cats, and there is now some evidence to support the recommendation of ACEI therapy in dogs and cats with CRF. Nevertheless the prescription of ACEI in such patients should take into account the potential influence of renal impairment on ACEI disposition, and adverse effects on the renal function itself (especially hypotension and acute reductions in glomerular filtration rate). The risk of drug interaction with diuretics, nonsteroidal anti-inflammatory drugs and anesthetics, should not be overestimated. Furthermore, hypotension may occur in patients on a low sodium diet.

Protein profiling of urine from dogs with renal disease using ProteinChip analysis.

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Measurement of total urinary proteins in individuals that tested positive by urinary dipstick is a typical method for assessing the presence of potentially serious renal disorders. In the absence of such overt proteinuria, however, measurement of specific urinary proteins may be useful in the diagnosis of nephropathies and may provide greater insight into the pathogenesis. The urine of 28 dogs (16 with renal disease and 12 healthy) was evaluated to determine whether specific low-molecular-weight proteins or the pattern of protein excretion could also be used as a marker of tubular dysfunction in dogs. Specific proteins were assessed by immunological methods, whereas protein profiles were determined by surface-enhanced laser desorption/ionization time-of-flight mass spectrometry (MS). In particular, changes in the excretion of retinol-binding protein (RBP) and Tamm-Horsfall protein (THP) appear to be of clinical relevance in the diagnosis of canine kidney diseases. The pattern of urinary protein and peptides revealed specific
changes in abundance in dogs with renal disease at molecular masses (kD) of 11.58, 12.41, 12.60, 14.58, 20.95 (RBP), 27.85, and 65.69 (albumin). In conclusion, comparable proteins as in humans might be used as urinary markers for proximal (RBP) and distal (THP) tubular dysfunction in dogs. Surface-enhanced laser desorption/ionization time-of-flight MS is a promising tool for the study of kidney physiology and pathophysiology and might aid in the discovery of new biomarkers of renal disease.

Publication Types:
• Evaluation Studies


Diagnostic relevance of qualitative proteinuria evaluated by use of sodium dodecyl sulfate-agarose gel electrophoresis and comparison with renal histologic findings in dogs.

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OBJECTIVE: To evaluate results of SDS-agarose gel electrophoresis (AGE) of urinary proteins for use in defining glomerular and tubulointerstitial derangements, investigate patterns of high-molecular-weight (HMW) proteins for differentiating among glomerular disorders, and assess low-molecular-weight (LMW) proteins as markers of severity of tubulointerstitial disease in dogs. ANIMALS: 49 dogs with increased serum creatinine concentrations or abnormal renal protein loss. PROCEDURE: Urinary proteins were examined by use of SDS-AGE and differentiated on the basis of molecular weight. The HMW proteins (> or = 69 kd) were considered indicative of glomerular origin, whereas LMW proteins (< 69 kd) were of tubular origin. Renal specimens were examined by use of light microscopy. Glomerular and tubulointerstitial lesions were differentiated by use of the classification for the World Health Organization and semiquantitative grading, respectively. RESULTS: Sensitivity of SDS-AGE was 100% for detection of glomerular lesions and 92.6% for tubulointerstitial lesions; specificity was 40% and 62.5%, respectively. Although HMW urinary proteins were not significantly associated with the type of glomerular lesion, LMW urinary proteins were significantly associated with the grade of tubulointerstitial damage. Detection of 12- or 15-kd proteins or both was highly indicative of a severe tubulointerstitial lesion. CONCLUSIONS AND CLINICAL RELEVANCE: SDS-AGE of urinary proteins in dogs represents a noninvasive test with high sensitivity for identifying glomerular and tubulointerstitial damage, but low specificity limits its validity as a stand-alone test to differentiate between glomerular and tubulointerstitial lesions. The test is particularly useful for identifying dogs with advanced tubulointerstitial disease but cannot be used to characterize glomerular disorders.
Early diagnosis of renal disease and renal failure.

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The main goal of early diagnosis of renal disease and renal failure in dogs and cats is to enable timely application of therapeutic interventions that may slow or halt disease progression. Strategies for early diagnosis of renal disease use urine tests that detect proteinuria that is a manifestation of altered glomerular permselectivity or impaired urine-concentrating ability as well blood tests to evaluate plasma creatinine concentration. Animals with progressive renal disease should be carefully investigated and treated appropriately. Animals with mild, possibly nonprogressive, renal disease should be monitored adequately to detect any worsening trends, which should lead to further investigation and treatment even if the increments of change are small.

Publication Types:
• Review

Sodium dodecyl sulfate polyacrylamide gel electrophoresis of canine urinary proteins for the analysis and differentiation of tubular and glomerular diseases.

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A preliminary investigation was performed to evaluate the use of a new, noninvasive technique for the localization of canine renal lesions by electrophoresis of urinary proteins. Urine specimens from six clinically healthy, nonproteinuric dogs and 12 dogs with persistent proteinuria were examined by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS PAGE). Urine electrophoretic patterns of proteinuric dogs were classified as glomerular (n = 4), tubular (n = 2), or mixed (glomerular and tubular) (n = 6), based on the number and molecular weight of the silver-stained protein bands. Renal tissues from biopsies or necropsies were obtained from eight of the dogs with proteinuric disease. Interpretation of seven of eight electrophoretograms agreed with the histologic interpretation of renal lesions. We concluded SDS
PAGE is a potentially valuable technique for detection and localization of renal lesions in dogs with proteinuric disease.


*Transient proximal renal tubular acidosis and Fanconi syndrome in a dog.*

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A 9-year-old spayed female Labrador Retriever was evaluated for anorexia, lethargy, and vomiting of 5 days' duration. Laboratory abnormalities included azotemia, high liver enzyme activities, hyperchloremic metabolic acidosis, glucosuria, ketonuria, proteinuria, and aminoaciduria. These laboratory abnormalities were diagnostic of proximal renal tubular acidosis and Fanconi syndrome. Results of initial and convalescent serologic tests for leptospirosis were negative. The dog was treated with amoxicillin, sodium bicarbonate, and potassium citrate at discharge. Repeated evaluations revealed resolution of the acidosis, azotemia, proteinuria, glucosuria, ketonuria, and high liver enzyme activities. Alkali administration was gradually discontinued, and the dog was clinically normal 8 months after discharge. The dog's clinical condition appeared to have been transient in nature, a phenomenon that is rarely seen in human or veterinary medicine.

**Publication Types:**
• Case Reports


*Diet modulates proteinuria in heterozygous female dogs with X-linked hereditary nephropathy.*

*Burkholder WJ, Lees GE, LeBlanc AK, Slater MR, Bauer JE, Kashtan CE, McCracken BA, Hannah SS.*

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Young adult heterozygous (carrier) female dogs with X-linked hereditary nephropathy (XLHN) have glomerular proteinuria but are otherwise healthy. Because data regarding dietary influences on the magnitude of proteinuria in
dogs with spontaneous glomerular disease are not available, 12 such dogs were studied in a double crossover experiment intended to determine effects of altering dietary protein intake for up to 6 weeks. Dogs were blocked by urine protein : creatinine ratio (UPC) and randomly assigned to receive 2 diets: high protein (34.6% dry matter [DM], HP) or low protein (14.1% DM, LP) fed in HP-LP-HP or LP-HP-LP sequence. Food intake was measured daily, body weight (BW) was measured twice weekly, and UPC, plasma creatinine, blood urea nitrogen, phosphorus, albumin, and protein concentrations were measured at 2-week intervals. Nutrient digestibility was measured during the third treatment period. Diet had a significant effect (P < .0001) on all measured variables except plasma phosphorus (P > .5), but unintended differences in digestibility of protein and energy (P < or = .01) prevented assignment of the diet effect exclusively to protein. Proteinuria was greater (UPC 4.7 +/- 2.2 versus 1.8 +/- 1.1, P < .0001) when the HP diet was fed, but the LP diet did not maintain starting BW or plasma albumin concentration within the normal reference range. Diet greatly affects the magnitude of proteinuria in XLHN carrier females. Dietary protein restriction can reduce proteinuria in dogs with glomerular disease, but BW and blood protein concentrations may not be maintained if the restriction is too severe.

Publication Types:
- Clinical Trial
- Randomized Controlled Trial


Effects of urinary tract inflammation and sample blood contamination on urine albumin and total protein concentrations in canine urine samples.

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BACKGROUND: Urinary tract inflammation and hemorrhage are believed to be common causes of proteinuria in dogs based on results of studies that measured total urine protein concentration. A method to quantify urine albumin (UAib) concentration in dogs recently has become available; however, the effect of inflammation on albuminuria is unknown. OBJECTIVES: The goals of this study were to determine the effects of urinary tract inflammation, as indicated by pyuria and sample blood contamination, on UAib concentration and on urine protein:creatinine (UPC) ratio in dogs. METHODS: Urine samples were obtained from dogs with pyuria that were presented to a veterinary teaching hospital or were part of a laboratory colony. To mimic the effects of hematuria, canine whole blood was added to a microscopically normal canine
urine sample that had baseline albumin and total protein concentrations below the limits of detection. UAlb concentration was measured using a canine albumin-specific competitive ELISA. UPC ratio was determined using routine methods. RESULTS: Of 70 samples with pyuria, 67% had negligible UAlb concentrations and 81% had normal UPC ratios. UAlb concentration but not UPC ratio was significantly higher (P < 0.05) in samples with concurrent hematuria or bacteriuria. When whole blood was added to normal urine, UAlb concentration did not exceed 1 mg/dL until the sample became visibly pink; the UPC did not exceed 0.4 at any dilution. CONCLUSIONS: Many dogs with pyuria do not have albuminuria or proteinuria; however, albuminuria may be more likely in dogs with pyuria and concurrent hematuria or bacteriuria. Hematuria may not cause an increase in UAlb concentration until it becomes macroscopic and even then may not increase the UPC ratio.


Canine pyometra: a study of the urinary proteins by SDS-PAGE and Western blot.

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Canine pyometra often causes glomerulonephritis by immune complex deposition in the glomeruli. Proteinuria, ranging from moderate to severe, may be present secondary to renal damage. To determine urinary protein excretion due to pyometra, sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) was conducted on urine from 15 bitches with pyometra and 10 healthy bitches. To characterize urinary immunoglobin excretion, Western blot analysis of the urine samples using antibodies to canine IgG and IgA was also performed. Nine bands were detected by electrophoresis in bitches with pyometra, while only four were detected in the healthy animals. The urinary proteins from bitches with pyometra were primarily of glomerular origin; 58% were of medium-high molecular weight (MW), and the remainder were low MW. None of the healthy dogs had IgG or IgA in their urine, whereas three bitches with pyometra had IgG in their urine and another bitch with pyometra had both IgG and IgA. The low proportion of bitches with urinary immunoglobulins was probably due to early diagnosis of the disease. Although only a limited number of dogs was used, this study is apparently the first to characterize the electrophoretic pattern of urinary proteins and to quantify urinary excretion of IgG and IgA in bitches with pyometra.
The effects of exercise on urinary albumin excretion in dogs.

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Persistent microalbuminuria has been shown to be an indicator of glomerular damage associated with early progressive renal disease in people and dogs. In people, transient or reversible microalbuminuria has been shown to occur with exercise. A semi-quantitative test to measure microalbuminuria in the dog recently has become available. The purpose of this study was to determine if mild-to-moderate exercise induced microalbuminuria in the dog. Twenty-six dogs were included in the study after undergoing tests to rule out hyperglycemia, urinary tract infection, azotemia, and a urine protein:creatinine ratio >1. Exercise consisted of 20 minutes of flat treadmill running. Urine samples were collected on 2 separate days before exercise, the morning of exercise, 3 hours postexercise, 7-9 hours postexercise, and each of the 2 mornings after exercise. For 24 of 26 dogs, this procedure was repeated after a minimum 7-day interval between exercise sessions. The canine E.R.D. (early renal disease)-Screen Urine Test (E.R.D.-Screen test) was used to determine semiquantitative urine albumin concentrations. Microalbuminuria-positive samples, as determined by the E.R.D.-Screen test, were further analyzed to determine quantitative albumin concentrations. Four (15%) dogs were microalbuminuria positive. In each of these dogs, microalbuminuria was present both before and after exercise with no quantitative increase in urine albumin concentration postexercise. Twenty-two (85%) dogs were microalbuminuria negative throughout the study and did not develop microalbuminuria at any time after exercise. On a 95% confidence interval, the proportion of dogs that might be expected to develop microalbuminuria after exercise is between 0 and 15%.

Characterization of renal damage in canine leptospirosis by sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) and Western blotting of the urinary proteins.

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Canine leptospirosis is a zoonotic disease that can cause interstitial nephritis.
As a consequence of the renal damage, proteinuria may occur. To determine the urine protein pattern in the disease we performed sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) on the urine from 10 dogs with leptospirosis and 20 healthy dogs. Western blotting analysis of the urine samples with antibodies against canine IgG and IgA was also performed to identify these immunoglobulins in the urine. Urine electrophoresis showed three new bands in the dogs suffering from leptospirosis. Only two of the dogs with leptospirosis showed detectable concentrations of IgG and IgA in urine, while a third animal showed IgG alone. The study showed a 36.7% increase in the excretion of low molecular weight proteins in dogs with leptospirosis but almost no change in the high molecular weight protein pattern. These results, together with the low number of animal with detectable concentrations of IgG and IgA in the urine, support the view that canine leptospirosis is characterized by interstitial nephritis.


Qualitative urinalyses in puppies 0 to 24 weeks of age.

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Suggestions for interpreting qualitative urinalyses from puppies have been based on limited results obtained in the laboratory setting. Proteinuria, glucosuria, and decreased concentration of urine have been considered normal in puppies <8 weeks of age due to immature renal function. In this study, the authors reviewed 149 voided urine samples from 118 different, apparently healthy, random-source puppies. The primary finding was that mean urine specific gravity (USG) was significantly lower in 0- to 3-week-old puppies when compared to puppies 4 to 24 weeks old. Mean USG in all other age groups was >1.030. There was no difference in the frequency of positive protein or occult blood dipstick results among age groups, and there were no positive glucose, ketone, bilirubin, or urobilinogen reactions in any samples analyzed. Urine sediment results are reported for 41 samples. Epithelial cells and white blood cells were the most common sediment findings in these 41 voided samples, observed in 34 (83%) and 18 (44%) samples, respectively. Crystals were observed in 15 (37%) samples, whereas casts, bacteria, and red blood cells were observed less commonly.
Evaluation of the effects of inhibition of angiotensin converting enzyme with enalapril in dogs with induced chronic renal insufficiency.


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OBJECTIVE: To determine whether the angiotensin converting enzyme inhibitor enalapril would lower systemic arterial and glomerular capillary pressure and reduce the magnitude of renal injury in a canine model of renal insufficiency.

ANIMALS: 18 adult dogs that had renal mass reduced by partial nephrectomy.

PROCEDURE: After surgical reduction of renal mass and baseline measurements, dogs in 2 equal groups received either placebo (group 1) or enalapril (0.5 mg/kg, PO, q 12 h; group 2) for 6 months. RESULTS: Values for systemic mean arterial blood pressure determined by indirect and direct measurement after 3 and 6 months of treatment, respectively, were significantly lower in group 2 than in group 1. During treatment, monthly urine protein-to-creatinine ratios were consistently lower in group 2 than in group 1, although values were significantly different only at 3 months. At 6 months, significant reduction in glomerular capillary pressure in group 2 was detected, compared with group 1, but glomerular filtration rate in group 2 was not compromised. Glomerular hypertrophy, assessed by measurement of planar surface area of glomeruli, was similar in both groups. Glomerular and tubulointerstitial lesions were significantly less in group 2, compared with group 1.

CONCLUSIONS AND CLINICAL RELEVANCE: Data suggest that inhibition of angiotensin converting enzyme was effective in modulating progressive renal injury, which was associated with reduction of glomerular and systemic hypertension and proteinuria but not glomerular hypertrophy. Inhibition of angiotensin converting enzyme may be effective for modulating progression of renal disease in dogs.

Publication Types:
- Clinical Trial
- Controlled Clinical Trial

Cyclosporine a slows the progressive renal disease of alport syndrome (X-linked hereditary nephritis): results from a canine model.

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Alport syndrome refers to a hereditary disorder characterized by progressive renal disease and a multilaminar appearance to the glomerular basement membrane (GBM). In a small group of patients with Alport syndrome, cyclosporine A was reported to decrease proteinuria and maintain stable renal function over 7 to 10 yr of follow-up. The present study examined the effect of cyclosporine A on GBM structure and the progression to renal failure in a canine model of X-linked Alport syndrome. Affected male dogs and normal male dogs treated with cyclosporine A underwent serial renal biopsies. Body weight, serum concentrations of creatinine and albumin, and GFR were sequentially determined. Controls consisted of untreated dogs that developed end-stage renal failure by 8 mo of age. Renal biopsies were assessed for glomerulosclerosis and the percent of multilaminar GBM as measured by image analysis. Significant differences were found between treated and untreated affected dogs for weight, serum creatinine, and GFR. There was a significant delay in the progression of multilaminar change to the GBM, although treated affected dogs at termination had attained approximately 100% split GBM as did untreated affected dogs. A significant difference in the number of sclerotic glomeruli was also noted; treated dogs rarely developed obsolete glomeruli during the period studied. Interstitial fibrosis was not significantly affected by cyclosporine A treatment. These findings indicate that cyclosporine A is beneficial in slowing, but not stopping, the clinical and pathologic progression of Alport syndrome. At least part of this beneficial effect comes from a delayed deterioration of GBM structure, which in turn may be related to glomerular hemodynamics altered by cyclosporine A.


 Detection of canine microalbuminuria using semiquantitative test strips designed for use with human urine.

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BACKGROUND: Commercial testing for microalbuminuria in human urine is often performed with point-of-care semiquantitative test strips followed by quantitative testing when indicated. An ELISA that quantifies canine urine albumin concentration has been developed, but semiquantitative test strips for use in the dog are not available. OBJECTIVE: The purpose of this study was to prospectively determine the concordance of canine urine albumin concentrations measured by a commercial human test strip and by ELISA. METHODS: Urine samples were obtained from 67 dogs evaluated for a variety
of clinical conditions. Dipstick urinalyses were performed on all samples; clinician discretion determined method of urine collection and performance of urine sediment examination and/or urine culture. Urine albumin concentration was determined using test strips (Clinitek Microalbumin, Bayer Corporation, Elkhart, Ind, USA), and results were compared with those obtained by ELISA. RESULTS: The Clinitek strips correctly determined albumin concentration in 42 of 67 (63%) urine samples tested. Concordance was lowest (48%) for dogs with microalbuminuria (10-300 microg/mL by ELISA). Clinitek strip sensitivity and specificity for correct identification of microalbuminuria were 48% and 75%, respectively. Concordance was lower in dogs with urinary tract infection or hematuria and in samples collected by catheterization. Sensitivity and specificity for correct identification of microalbuminuria after exclusion of dogs with urinary tract infection or hematuria were 59% and 83%, respectively. CONCLUSIONS: These results suggest that the Clinitek strips lack sufficient concordance with results obtained by ELISA to be a reliable screening for test microalbuminuria in the dog. A reliable semiquantitative point-of-care test for canine urine albumin concentrations below those detected by standard urine dipsticks is still needed.


Renal involvement in dogs with babesiosis.

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Proteinuria, and renal tubular casts and epithelial cells in urine sediment, are commonly observed in both complicated and uncomplicated babesiosis, but do not necessarily reflect or predict renal failure. This study investigated the presence and degree of renal damage in canine babesiosis. Renal function and integrity were evaluated using serum urea and creatinine, serum electrolytes (sodium and potassium), fractional clearance of sodium (FcNa) and potassium (FcK), urine enzyme activity of gamma-glutamyl transpeptidase and alkaline phosphatase, urine protein:creatinine ratio, and urinalysis. One control group (n = 10) and 3 groups of babesiosis cases were studied: mild uncomplicated (n = 10), severe uncomplicated (n = 11), and complicated (n = 9). All babesiosis groups showed well-concentrated urine. Mean serum urea was elevated in the severe and complicated groups, and was significantly different from the control group. There was no statistically significant difference between the groups for creatinine, although the complicated group had a mean value above the normal reference range. Hypokalaemia was uncommon in all the groups. Hyperkalaemia was present in only 2 dogs in the complicated group. Marginal hyponatraemia was present in a minority of dogs in all groups. The serum electrolytes were not significantly different between groups. There was no overall elevation, nor any statistically significant difference in both the FcNa
and FcK between the groups. Only 1 dog, in the complicated group, showed marked enzymuria. Proteinuria was a common finding and was significantly different between the severe and complicated groups and the control group. Some dogs in all groups had renal tubular epithelial cells in the urinary sediment, which increased in severity from the mild to the complicated groups and was significantly different from the control group. This study demonstrated that minimal renal damage occurs more often in canine babesiosis than significant damage or acute renal failure.


Effects of dietary protein on glomerular mesangial area and basement membrane thickness in aged uninephrectomized dogs.


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The primary objective of this study was to determine the effects of diets containing 18% or 34% protein on glomerular mesangial area (GMA) and basement membrane thickness (GBMT) in uninephrectomized aged dogs. A secondary objective was to determine the combined effects of aging and uninephrectomy on GMA and GBMT in dogs. Ten clinically healthy, pure-bred dogs were unilaterally nephrectomized at about 8 y of age. After 2 mo, 5 dogs were fed an 18% protein diet and 5 dogs were fed a 34% protein diet for 48 mo. At month 48, the dogs were euthanized and the remaining kidney was collected. Samples of kidney from both times of collection were used to measure GMA and GBMT using electron microscopy. The effects of diet on GMA and GBMT were analyzed (student's t-test) using necropsy/nephrectomy score ratios. The effects of time-nephrectomy were determined by comparing nephrectomy values for GMA and GBMT with necropsy values (paired t-test). Dogs fed 34% dietary protein did not have a significant increase in GMA and GBM thickness when compared to dogs fed the 18% protein diet. A significant increase in GMA and GBMT occurred with time-nephrectomy (P = 0.011 and 0.018, respectively). Although dietary protein intake was not a significant factor in causing structural changes to glomeruli in uninephrectomized aged dogs, the power to detect a difference was low. However, significant effects of aging and nephrectomy were detected despite the low power of the study. These results suggest that the increases in GMA and GBMT that occur over time are not markedly influenced by dietary protein intake. However, subtle protein effects cannot be eliminated as a possibility based on this study.
Effects of enalapril versus placebo as a treatment for canine idiopathic glomerulonephritis.

Grauer GF, Greco DS, Getzy DM, Cowgill LD, Vaden SL, Chew DJ, Polzin DJ, Barsanti JA.

A blinded, multicenter, prospective clinical trial assessed the effects of enalapril (EN) versus standard care in dogs with naturally occurring, idiopathic glomerulonephritis (GN). Twenty-nine adult dogs with membranous (n = 16) and membranoproliferative (n = 13) GN were studied. Dogs were randomly assigned to receive either EN (0.5 mg/kg PO q12-24h; n = 16) or placebo (n = 14) for 6 months (1 dog was treated first with the placebo and then with EN). All dogs were treated with low-dose aspirin (0.5-5 mg/kg PO q12-24h) and fed a commercial diet. At baseline, serum creatinine (SrCr), systolic blood pressure (SBP), and glomerular histologic grade were not different between groups, but the urine protein/creatinine ratio (UP/C) was greater in the EN group compared with the placebo group (8.7 +/- 4.4 versus 4.7 +/- 2.3). After 6 months of treatment, the change in UP/C from baseline was significantly different between groups (EN = -4.2 +/- 1.4 versus 1.9 +/- 0.9 in the placebo group). When data were adjusted for changes in SrCr (SrCr X UP/C) a similar significant reduction was noted (2.2 +/- 15.2 versus 8.4 +/- 10.1). The change in SBP after 6 months of treatment also was significantly different between groups (EN = -12.8 +/- 27.3 versus 5.9 +/- 21.5 mm Hg in the placebo group). Response to treatment was categorized as improvement (assigned a value of 2), no progression (assigned a value of 1), and progression (assigned a value of 0). Response was significantly better in the EN group (1.4 +/- 0.8) compared with the placebo group (0.3 +/- 0.5). These results suggest that EN treatment is beneficial in dogs with naturally occurring idiopathic GN.
Progressive loss of nephron function may be caused by persistence of factors that initiated renal disease. However, newer studies suggest that nephron damage is self-perpetuating once renal mass is reduced to some critical level. Original theories on mechanisms of self-perpetuated nephron injury focused on intraglomerular hypertension and glomerular hypertrophy, but several other factors have now been incriminated, including tubulointerstitial responses, proteinuria, and oxidative stress. Studies of dogs with surgically reduced renal mass (remnant kidney model of chronic renal disease) have allowed investigation of the self-progression theory in this species. Use of this model eliminates pre-existing renal disease as a confounding factor. Data from these studies indicate that self-perpetuated renal injury is initiated when mild azotemia is induced (plasma creatinine concentration = 2 to 4 mg/dL). Thus, with naturally occurring renal disease(s), it is likely that self-perpetuated nephron damage is occurring before or at the time when most cases of chronic renal disease are diagnosed. In dogs with remnant kidneys, loss of renal function often occurs at a linear rate over time, but non-linear patterns are common as well. The reciprocal of plasma creatinine concentration, which has been used to monitor rate of progression, is only a fair marker of renal function when compared to GFR. Thus, clinical results from creatinine measurements on cases of naturally occurring disease should not be interpreted too stringently. In remnant kidney dogs, the magnitude of proteinuria (UPC ratio) was not predictive of the rate in decline of GFR, casting doubt on importance of proteinuria in causing progression of renal disease. However, progressive increases in UPC may be a marker of an accelerated rate of renal injury. Self-perpetuation of renal injury in dogs could be the sole mechanism by which naturally occurring renal diseases progress. When more information is available on the rate of progression of naturally occurring diseases, it may become apparent whether factors initially inciting renal damage have an additive effect on rate of progression.

Publication Types:
- Review


Protein and calorie effects on progression of induced chronic renal failure in cats.

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OBJECTIVE: To determine effects of dietary protein and calories on progression of induced chronic renal failure in cats. ANIMALS: 28 young adult female cats. PROCEDURE: Renal mass was reduced surgically, and glomerular filtration rate (GFR) was determined. Cats were allotted to 4 groups of 7 with similar mean GFR (1.52 to 1.55 ml/min/kg of body weight). Diets were formulated to provide: low protein and calorie (diet A), low protein and high calorie (diet B), high protein and low calorie (diet C), and high protein and calorie (diet D) intakes. Cats were fed their prescribed diet for 12 months, then blood and urine biochemical variables were measured, after which kidney specimens were examined microscopically. RESULTS: Protein intake by cats of groups C and D (9.0 g/d/kg) was substantially greater than that by cats of groups A and B (5.3 and 5.2 g/d/kg, respectively). Caloric intake by cats of groups B and D (73 and 71 calories/d/kg, respectively) was greater than that by cats of groups A and C (58 and 55 calories/d/kg, respectively). Renal glomerular lesions were mild and not affected by protein, calories or their interactions. Nonglomerular lesions, though mild, were significantly influenced by calorie intake, but not by protein or calorie-protein interactions. The GFR did not decrease in any group. Urine protein-to-creatinine ratio increased significantly in all groups after reduction of renal mass, but values from all groups remained within the reference range (0 to 0.3). CONCLUSIONS AND CLINICAL RELEVANCE: Diets replete in protein were not associated with increased severity of glomerular or nonglomerular renal lesions, increased proteinuria, or decreased GFR. Diets replete in calories were not associated with increased severity of glomerular lesions, but were associated with mild increase of nonglomerular lesions. Factors other than protein and calorie intake must be considered potential causes of progression of renal failure in cats. Results raise questions about the practice of restricting quantity of protein in the diet of cats with chronic renal failure, with the intention of ameliorating development of further renal damage.


Systemic hypertension and proteinuria in dogs with diabetes mellitus.

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OBJECTIVE: To determine prevalence and severity of systemic arterial hypertension and proteinuria in dogs with naturally developing diabetes mellitus (DM) and to determine whether these abnormalities were related to age, sex, duration of DM, or degree of control of glycemia. DESIGN: Case series and cohort study. ANIMALS: Fifty dogs with naturally developing DM. PROCEDURES: Blood pressure was measured in all 50 dogs. Thirty-eight dogs were evaluated once, and 12 were evaluated sequentially. Thirty-five were
evaluated for proteinuria by determining protein-to-creatinine ratio in urine (n = 35) or by electrophoresis of urine (33). RESULTS: Hypertension was detected in 23 on the basis of a systolic pressure > 160 mm HG (12 dogs), a diastolic pressure > 100 mm HG (21), or a mean pressure > 120 mm HG (23). All dogs with systolic hypertension had concurrent diastolic and mean hypertension, and 19 of 21 dogs with diastolic hypertension had concurrent high mean pressure. Ten of 12 dogs reevaluated at subsequent visits had no change in blood pressure. Blood pressure remained consistent in 3 dogs tested at different times during the day on a single visit. Duration of DM and presence of proteinuria were significant predictors of hypertension. Seven of 35 (20%) dogs had an increased protein-to-creatinine ratio in their urine. Albumin concentration and albumin-to-creatinine ratio were significantly higher in urine from diabetic dogs, compared with healthy, nondiabetic dogs. Hypertension was associated with an increased albumin-to-creatinine ratio. CLINICAL IMPLICATIONS: Systemic hypertension and proteinuria may be common in diabetic dogs, but the clinical importance of these findings are, as yet, unknown.


Composition of protein in urine from dogs with pyoderma.

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The protein fractions in urine from proteinuric dogs with and without pyoderma were estimated. Fifteen dogs with pyoderma (five with superficial and 10 with deep pyoderma) were compared with 10 dogs with glomerulopathy and 27 dogs with diseases other than pyoderma or urinary tract problems. Agarose gel electrophoresis was used to fractionate the proteins. Three types of electrophoretogram were obtained with albuminuria, globulinuria and serum-like profiles. An albuminuria profile was found in eight of the 27 dogs with other diseases, in three of the five dogs with superficial pyoderma, in eight of the 10 dogs with deep pyoderma and in all 10 dogs with glomerulopathy. The albuminuria profile (mean [sem] albumin/globulin ratio 1.98 [0.10]) was also characterised by alpha 1b, alpha 2a and beta 2 globulin peaks in all 29 dogs with this profile, which was therefore thought to indicate that albuminuria (glomerular proteinuria) was a result of glomerular damage and inflammation because alpha 1b, alpha 2a, and beta 2 globulins are considered to be acute phase proteins. The serum-like profile (mean [sem] albumin/globulin ratio 0.72 [0.01]) was observed in 13 per cent of the proteinuric dogs examined and contained all the protein fractions normally detected by electrophoresis of serum. The profile was considered to be a variant from of the albuminuria profile, probably indicating advanced glomerular lesions and inflammation. The
globulinuria profile (mean [sem] albumin/globulin ratio 0.33 [0.08]) was significantly different from the other two in that it was characterised by a low albumin peak and the presence of globulin fractions not clearly distinguishable from each other because of their confluency and absence of individual peaks. This profile could indicate severe glomerulotubular lesions and degradation of certain protein fractions. It could also be a result of increased secretion of tissue and other proteins by damaged tubules. It was concluded that glomerular damage leads to glomerular proteinuria characterised by high proportions of albumin together with alpha 1b, alpha 2a and beta 2 globulins in lower but significantly diagnostic proportions.


Beneficial effects of chronic administration of dietary omega-3 polyunsaturated fatty acids in dogs with renal insufficiency.


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Dietary supplementation with polyunsaturated fatty acids (PUFA) alters the course of experimental renal disease in rats. However, chronic renal disease in other laboratory animals and in human beings frequently responds differently to experimental manipulations. We investigated the effects of variations in dietary PUFA composition on the chronic course of induced renal disease in dogs. Two months after 15/16 nephrectomy, dogs were randomly divided into three groups of seven animals each. For the next 20 months, each group of dogs was fed a low-fat basal diet supplemented with one of three sources of lipid to achieve a final concentration of 15% added fat. Fat sources provided omega-3 PUFA (menhaden fish oil, group FO), omega-6 PUFA (safflower oil, group SO), or saturated fatty acids (beef tallow, group BT). Throughout the dietary trial, the magnitude of proteinuria and the plasma concentrations of creatinine, cholesterol, and triglyceride were lower in group FO. The mean overall glomerular filtration rate was 0.89 +/- 0.18 ml/min per kilogram of body weight in group SO, a value that was significantly less (p < 0.05) than the corresponding values for groups BT and FO (1.21 +/- 0.18 and 1.43 +/- 0.20 ml/min/kg, respectively). Renal interstitial fibrosis also was significantly elevated in group SO. The extents of mesangial matrix expansion, glomerulosclerosis, and renal interstitial cellular infiltrate were similar in groups BT and SO, but lower (p < 0.05) in group FO. We conclude that supplementation with omega-6 PUFA enhanced renal injury; supplementation with omega-3 PUFA was renoprotective.
Early diagnosis of familial nephropathy in English cocker spaniels.

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Two litters of English cocker spaniels (ECSs) produced by familial nephropathy (FN) carriers were evaluated to characterize the early features of this disease. Three puppies developed FN. Proteinuria, which began when these puppies were five-to-eight months old, was the first abnormality detected. Proteinuria persisted while each puppy's growth rate slowed, and renal function gradually deteriorated. The interval from onset of proteinuria to development of azotemia was two-to-nine months. Characteristic glomerular capillary basement membrane (GCBM) lesions were seen with transmission electron microscopy (TEM) of renal biopsy specimens obtained during this interval. Ultrastructural GCBM lesions progressed substantially during the interval from biopsy to necropsy. However, routine light microscopic findings did not allow definitive diagnosis of FN in either biopsy or necropsy specimens. Detection of FN can be accomplished by screening at-risk ECSs for proteinuria. Renal biopsies are required to confirm the diagnosis in dogs for which proteinuria cannot be explained otherwise. Percutaneous needle biopsy specimens sufficient for TEM must be used to examine the GCBM to make a definitive diagnosis.

Publication Types:
• Case Reports
to-creatinine (UPC) ratios and 24-hour urine protein excretion (24-hour UPE) values were measured before beginning treatment with mitotane and after establishing appropriate maintenance treatment. RESULTS: Before treatment, UPC ratios ranged from 0.03 to 4.16 (16 dogs, median, 0.695; reference range value, UPC ratio < 0.5; questionable value, UPC ratio > 0.5 but < 1.0; high value, UPC ratio > 1.0). Seven dogs had proteinuria with UPC ratios > 1.0. Twenty-four-hour UPE values ranged from 0.67 to 61.7 mg/kg of body weight/d (0.30 to 28.0 mg/lb/d; 13 dogs, median, 9.7 mg/kg/d [4.4 mg/lb/d]; reference value, 24-hour UPE value, < 20 mg/kg/d [9.1 mg/lb/d]). Five dogs with high UPC ratios also had high values for 24-hour UPE. After establishment of maintenance treatment with mitotane (median, 7 weeks; mean, 7.3 weeks), UPC ratios ranged from 0.02 to 6.5 (16 dogs, median, 0.36). Five dogs continued to have high UPC ratios. Values of 24-hour UPE ranged from 0.47 to 122 mg/kg/d (0.21 to 55.5 mg/lb/d; 13 dogs, median, 5.1 mg/kg/d [2.3 mg/lb/d]). Three dogs continued to have high 24-hour UPE values. Significant differences were not found between dogs before and after treatment with mitotane in terms of UPC ratios or 24-hour UPE values. CLINICAL IMPLICATIONS: In dogs with PDHAC and proteinuria, UPC ratios should be monitored closely. Some dogs with PDHAC may have a decrease in urine protein content following treatment with mitotane. We suggest that renal biopsies be considered in those dogs with progressive increases in UPC ratios.


[Urine protein analysis with the sodium-dodecyl-sulfate-polyacrylamide gel-electrophoresis (SDS-PAGE) in healthy cats and cats with kidney diseases]


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In this investigation, the value of urine protein analysis by means of molecular-weight related sodium dodecyl-polyacryl gradient gel electrophoresis (SDS-PAGE) was examined with regard to its applicability and diagnostic significance in nephropathy in the cat. A total of 87 cats was included in the study, 30 of them that were clinically healthy served as the control group. The urine protein pattern of this group had, besides the band representing the market albumin, and additional broad band within the size of the marker transferrin. In some cases, weak bands were present within the range of the Tamm-Horsfall-protein and immunoglobulin G. Micromolecular protein bands were not demonstrable. The remaining 57 animals had a histologically proven nephropathy. Thirty-eight cats had elevated urea and/or creatinine values in the plasma (group 1), and 19 animals had values within the reference range (group 2). The urine protein pattern as evidenced by SDS-urine electrophoresis was altered in all cats with histologically proven nephropathy, and it is thus
concluded that with this technique a nephropathy can be diagnosed very early and prior to changes of plasma urea and creatinine (group 2). Moreover, in most of the cases, the nephrological changes can be classified as glomerular or tubulo-interstitial (group 1 and group 2). However, it is not possible to draw exact conclusions concerning the underlying morphological changes, nor can the severity of the disease be correctly assessed.


**Thrombocytopenia and light-chain proteinuria in a dog naturally infected with Ehrlichia canis.**

**Varela F, Font X, Valladares JE, Alberola J.**

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A 6-year-old dog was presented for evaluation of recurrent epistaxis. Platelet counts, biochemical tests, and coagulation tests were within the normal range, but a mucosal bleeding time was prolonged; there was hyperproteinemia and a monoclonal gammopathy. Heterogeneity of light chains appeared in urine, however, thus suggesting that the gammopathy was polyclonal. Platelet aggregation tests showed decreased responsiveness to collagen. An *Ehrlichia canis* indirect fluorescent-antibody titer was positive (1:40). Treatment with tetracycline, melphalan, and prednisone resulted in a rapid clinical improvement that persisted for at least 3 years.

Publication Types:
- Case Reports


**Related Articles, Links**

**Treatment of X-linked hereditary nephritis in Samoyed dogs with angiotensin converting enzyme (ACE) inhibitor.**

**Grodecki KM, Gains MJ, Baumal R, Osmond DH, Cotter B, Valli VE, Jacobs RM.**

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X-linked hereditary nephritis (HN) in Samoyed dogs is a model for human HN (Alport's syndrome). Angiotensin converting enzyme (ACE) inhibitors have been shown to slow the progression of renal disease in animal models and human patients. To determine the effect of ACE inhibitor treatment on X-linked
HN in Samoyed dogs, a group of affected and a group of normal males were each randomly divided into two subgroups, which were either treated with an ACE inhibitor or left untreated. ACE inhibitor treatment caused significant increases (P < 0.05) in plasma renin activity in normal and affected dogs, confirming its effectiveness, but did not lower systemic blood pressure. Three of four affected treated dogs had improved weight gains and, overall, treated dogs survived 1.36 times longer than affected untreated dogs (P < 0.05). ACE inhibitor treatment of affected dogs significantly delayed (P < 0.05) the onset of an increase in serum creatinine concentration, tended to delay the decline of glomerular filtration rate and effective renal plasma flow (ERPF), significantly improved (P < 0.05) the ERPF at 110-154 days of age, and significantly slowed (P < 0.01) the rate of increase of proteinuria. Affected treated dogs showed a significant (P < 0.05) transient reduction in glomerular basement membrane splitting. Thus, ACE inhibitor treatment of Samoyed dogs with X-linked HN produced beneficial effects with respect to renal function, renal structure, and survival.


Effects of glucocorticoid therapy on urine protein-to-creatinine ratios and renal morphology in dogs.

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Glomerulonephritis has been associated with exogenous glucocorticoid administration and spontaneous hyperadrenocorticism in the dog. The purpose of this study was to determine the effects of long-term glucocorticoid therapy on urine protein:creatinine ratios (UP/Cs) and renal morphology. Nine young-adult male dogs were determined to be healthy and have normal renal function as assessed by physical examination, CBC, serum biochemistry analysis, Knott's test for Dirofilaria immitis, urinalysis, urine culture, urine protein electrophoresis, endogenous creatinine clearance, 24-hour urinary protein excretion, and UP/C. Prednisone was administered to each dog at a dosage of 2.2 mg/kg PO bid for 42 days. Urinalysis and UP/C were performed on days 0, 7, 14, 21, 28, and 42 of treatment. Mean UP/C on day 0 was 0.29 +/- 0.10. Mean UP/C increased progressively to a maximum of 1.27 +/- 1.02 on day 28. Mean UP/C on day 42 decreased slightly (0.92 +/- 0.56) but remained significantly increased above baseline. The most consistent renal light microscopic finding on necropsy examination was generalized hypercellular glomerular tufts, suggestive of mesangial cell proliferation. Four dogs also had occasional adhesions of glomerular tufts to Bowman's capsule, accompanied by thickening of the capsule. Direct immunofluorescence for immunoglobulin
deposition was negative in all dogs. Electron microscopy, evaluated in 7 dogs, was characterized by occasional mild segmental thickening of basement membranes, fusion of visceral cell foot processes, and glomerular adhesions. The results of this study indicate that long-term administration of glucocorticoids results in significant proteinuria and glomerular changes in the dog.


Systemic arterial blood pressure and urine protein/creatinine ratio in dogs with hyperadrenocorticism.

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OBJECTIVE: To determine prevalence and severity of systemic arterial hypertension and proteinuria in dogs with naturally developing hyperadrenocorticism and to determine whether these abnormalities resolve with adequate management of the disease. DESIGN: Case series and cohort study. ANIMALS: 77 dogs with naturally developing hyperadrenocorticism examined once; 15 dogs examined before and after treatment. RESULTS: Among dogs examined only once, hypertension was diagnosed in 21 of 26 dogs with untreated pituitary-dependent hyperadrenocorticism (PDH), 17 of 21 with inadequately controlled PDH, 8 of 16 with well-controlled PDH, 10 of 10 with an untreated adrenocortical tumor, and 0 of 4 that had undergone adrenalectomy because of an adrenocortical tumor. Untreated dogs and dogs with inadequately controlled PDH had significantly higher blood pressures than did other dogs. Proteinuria was documented in 12 of 26 dogs with untreated PDH, 5 of 16 with inadequately controlled PDH, 3 of 14 with well-controlled PDH, 5 of 8 with an untreated adrenocortical tumor, and 1 of 3 that had undergone adrenalectomy. Dogs with untreated PDH and dogs with an untreated adrenocortical tumor had higher urine protein/creatinine ratios than did dogs with well-controlled PDH. Among dogs evaluated before and after treatment, blood pressure and urine protein/creatinine ratio did not change in 8 dogs with inadequately controlled hyperadrenocorticism, but decreased in 7 dogs with well-controlled disease. CLINICAL IMPLICATIONS: Results suggest that systemic hypertension and proteinuria are common in dogs with untreated hyperadrenocorticism and that successful treatment of hyperadrenocorticism will result in resolution of these abnormalities in many, but not all, dogs.
Diagnosis and long-term management of protein-losing glomerulonephropathy. A 5-year case-based approach.

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Protein-losing glomerulonephropathy can be a challenging disease for veterinarians to manage. This case-based article illustrates long-term management of protein-losing glomerulonephritis in a dog. Prolonged survival of this patient was attributed to early diagnosis and carefully planned therapeutic intervention consisting of dietary protein reduction and modulation of blood pressure with angiotensin converting enzyme inhibition.

Publication Types:
- Case Reports
- Review

Alterations in glomerular anionic sites in the autologous phase of canine anti-glomerular basement membrane nephritis.

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There have been a few studies on canine nephrotoxic glomerulonephritis produced by anti-glomerular basement membrane serum (AGBM), but these reports have not focused on an alteration in the charge properties of glomerular basement membrane (GBM). In this study, rabbit AGBM or normal rabbit serum (NRS) was given intravenously (2 ml/kg body weight) to 16 male beagle dogs. An alteration of anionic sites (ASs) of GBM was studied quantitatively using polyethyleneimine as a cationic probe by electron microscopy at weeks 1, 2, 4, and 8 postinjection. In AGBM-treated dogs, severe or mild proteinuria continued until week 2. At weeks 4 and 8, there was no significant difference in the intensity of proteinuria between AGBM- and NRS-treated groups. Until week 2 postinjection, there were significantly fewer ASs of GBM in AGBM-treated dogs than in NRS-treated dogs. At week 8, however, there was no difference in ASs of GBM between AGBM- and NRS-treated dogs. The fact that a reduction of glomerular AS occurred in AGBM-treated dogs with severe or mild proteinuria and the recovery of AS in the GBM coincided with an improvement of proteinuria suggested that alteration of the
glomerular ASs might play an important role in the pathogenesis of proteinuria in canine anti-GBM nephritis.


**Clinical and pathological features of protein-losing glomerular disease in the dog: a review of 137 cases (1985-1992).**

**Cook AK, Cowgill LD.**

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Medical records of 137 dogs with protein-losing glomerular disease (PLGD) were evaluated. Cases with amyloidosis (23%) were more likely to be azotemic at presentation, with significantly greater proteinuria and hypoalbuminemia than those cases with glomerulonephritis (GN; 77%). The prognosis for all cases was poor, with a median survival time of just 28 days. The most common causes of death in cases with idiopathic disease were chronic renal failure (69.5%) or thromboembolic complications (22.2%). Progression of glomerular disease was unpredictable, with no apparent correlation between survival time and biochemical parameters at presentation.

**Aust Vet J.** **1996 Feb;73(2):52-4.**

**Glomerulopathy in dogs with congenital portosystemic shunts.**

**Tisdall PL, Rothwell TL, Hunt GB, Malik R.**

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Kidney specimens from 12 dogs with congenital portosystemic shunts were examined histologically. Glomerulopathy of variable severity was present in the kidney sections of all 12. Marked irregular thickening of the glomerular capillary wall was the most prominent pathological change, the renal interstitium being largely unaffected. The severity of lesions was not correlated with the age of dogs at the time of necropsy. An immunoperoxidase technique failed to demonstrate significant IgA or IgG deposition in affected glomeruli. Proteinuria was generally mild or absent despite significant glomerular lesions, except in dogs with concurrent urinary tract infection.
Urinary alpha-amylase and serum macroamylase activities in dogs with proteinuria.

Corazza M, Tognetti R, Guidi G, Buonaccorsi A.

Facolta di Medicina Veterinaria, Istituto di Patologia, Speciale e Clinica Medica, Pisa, Italy.

Activities of urinary alpha-amylase and serum macroamylase; concentrations of serum creatinine, immunocomplexes, and urinary protein; and patterns of proteinuria were determined in 35 dogs with proteinuria. Urinary alpha-amylase activity ranged from 37 to 4,031 U/L. Macroamylasemia was detected in 77.14% of dogs and the percentage of alpha-amylase precipitated ranged from 4.68 to 61.63. Serum alpha-amylase activity after immunoglobulin precipitation ranged from 654 to 6,390 U/L in 51.42% of the dogs; the values were higher than the reference limits. Concentrations of serum creatinine and immunocomplexes were higher than reference limits for 25.71 and 60% of dogs, respectively. Urinary protein concentrations ranged from 0.1 to 8.9 g/L. All the patterns of proteinuria were represented. Linear regression indicated correlations between urinary alpha-amylase activities, serum creatinine concentrations (P < 0.01), and concentration of immunocomplexes (P < 0.05). Mann-Whitney test indicated significantly higher urinary alpha-amylase activity (P < 0.01) and percentage of alpha-amylase precipitated (P < 0.05) in dogs with renal insufficiency.

Allergic- and immune-associated diseases of the urinary tract.

Nichols R.

College of Veterinary Medicine, Mississippi State University, Mississippi State.

Glomerular injury has a decided immunologic basis. Any infectious, inflammatory, neoplastic, or degenerative processes capable of sustained antigenic stimulation can induce immune-mediated glomerular injury. A variety of conditions and antigens, both endogenous and exogenous, are known to initiate immunologic glomerular damage. In many clinical situations, however, the precise antigenic source is occult and unrecognizable, and the glomerular disease is referred to as idiopathic.

Publication Types:
• Review

Effects of different antihypertensive treatments on morphologic progression of diabetic nephropathy in uninephrectomized dogs.

Gaber L, Walton C, Brown S, Bakris G.

Department of Pathology, University of Tennessee Medical Center, Memphis.

We previously reported the renal hemodynamic effects of different antihypertensive regimens in uninephrectomized, alloxan-induced, diabetic (DM) beagle dogs following one year of treatment. Dogs were prospectively randomized to one of five groups (N = 26): nondiabetic controls, Group I; dogs with DM on no antihypertensive drugs, Group II; dogs on a converting enzyme inhibitor, lisinopril (L), Group III; dogs on a calcium antagonist, TA3090 (diltiazem-like), Group IV; and dogs on a combination of each drug, in reduced doses, Group V. The current paper extends our previous studies by describing the morphologic changes that occurred within each group of dogs studied. More than 100 glomeruli from the renal cortex of each dog were evaluated for increases in mesangial volume fraction (Vv), glomerulosclerosis (GS) and arteriolar hyalinosis. The interstitium was also evaluated for associated changes. Increases in Vv were attenuated in all treated groups (0.28 +/- 0.04, DM alone versus 0.16 +/- 0.05 L; 0.21 +/- 0.07, TA-3090; 0.19 +/- 0.06 micron 2/micron 2, L+TA 3090; P < 0.05) compared to untreated DM. An attenuated increase in Vv also correlated with a blunted rise in proteinuria in Groups III (r = 0.79) and V (r = 0.81) but not Group IV (r = 0.29). Development of focal GS was blunted in all treated groups; however, global GS was fourfold greater in Group IV compared to untreated DM. The degree of interstitial fibrosis also correlated with the degree of global GS. These data support the concept that both a converting enzyme inhibitor and heart rate lowering calcium antagonist attenuate morphologic progression of diabetic renal disease. (ABSTRACT TRUNCATED AT 250 WORDS)


Proteinuria associated with glomerulosclerosis and glomerular collagen formation in three Newfoundland dog littermates.

Koeman JP, Biewenga WJ, Gruys E.

Department of Pathology, Faculty of Veterinary Medicine, University of Utrecht, The Netherlands.

Three dogs out of a litter of eight Newfoundland dogs developed a progressive fatal glomerulopathy. The affected dogs were a 2-month-old male, a 2.5-month-old female, and a 1-year-old male. The disease in all three animals was
characterized by growth retardation, anorexia, proteinuria (14-16 g/liter), hypoalbuminemia (15-21 g/liter, elevated plasma urea (13-28 mmol/liter), and creatinine (83-296 mumol/liter) concentrations. Because of a bad prognosis the dogs were euthanatized. On postmortem examination, the animals had enlarged, slightly pale kidneys, which revealed glomerulosclerosis and glomerulofibrosis on histologic and electron microscopic examination. The lesions consisted of subendothelial and mesangial collagen fibrils and an increase of mesangial matrix. The fibrosis may result from endothelial or mesangial collagen formation as the manifestation of a metabolic disease.

Publication Types:
• Case Reports


[Urine characteristics in dogs with diabetes mellitus. Is there a diabetic nephropathy in the dog?]

Kirsch M, Reusch C.

I. Medizinischen Tierklinik, Tierarztlichen Fakultat, Ludwig-Maximilians-Universitat Munchen.

Dogs with spontaneous Diabetes mellitus were checked at regular intervals for protein excretion in the urine. A large number of dogs developed a proteinuria, very marked in some cases, with excretion of primarily macroproteins.


Evaluation of the Clinitek 200 urinary test-strip reader in the analysis of dog and rat urines in pre-clinical toxicology studies.

Paquignon A, Tran G, Provost JP.

Department of Biochemistry, Pfizer, Amboise, France.

The performance of a clinical urinary test-strip reader Clinitek 200 was evaluated for dog and rat urines, in the context of pre-clinical toxicology studies. No major discrepancies were found between data generated by visual estimation or automatic measurement. Analysis of spiked samples showed good agreement between actual concentrations and Clinitek 200 responses for ketone bodies and glucose although a lack of sensitivity was found for the latter. Results for proteins showed over- or underestimation in dog and rat
urines respectively at low concentrations, and overestimation at high concentrations in both species. Reproducibility of responses was excellent for ketone bodies, glucose and proteins but was weaker for haemoglobin and bilirubin. High bilirubin concentrations were found to interfere with the haemoglobin reaction. The pH measurements were found to be accurate only around pH 7. Specific gravity measurements were unreliable. Overall, the Clinitek 200 as a screening tool proved sufficiently reliable in the measurement of all parameters tested, with the exception of specific gravity.


Long-term effects of antihypertensive regimens on renal hemodynamics and proteinuria.

Brown SA, Walton CL, Crawford P, Bakris GL.

Department of Physiology and Pharmacology, College of Veterinary Medicine, University of Georgia, Athens.

The long-term effects of different antihypertensive regimens were studied in uninephrectomized beagles with alloxan-induced diabetes mellitus. Mean arterial pressure (MAP) was elevated (P < 0.05) in untreated diabetic dogs. Treatment of diabetic dogs with an angiotensin converting enzyme inhibitor (ACEI; lisinopril), a calcium antagonist (CA; TA-3090), or both lowered MAP. At one year, the RBF, GFR, and SNGFR were similarly elevated (P < 0.05) in all groups of diabetic dogs. The increase in SNGFR present in untreated diabetic dogs was primarily attributable to an increased (P < 0.05) glomerular capillary pressure (PGC). Treatment with lisinopril lowered the PGC to a mean value that was indistinguishable from that for nondiabetic dogs. In contrast, diabetic dogs treated with TA-3090 had an elevated PGC. While untreated diabetic dogs exhibited marked increases in glomerular volume (P < 0.05 vs. nondiabetic dogs), treatment with lisinopril and TA-3090, either alone or in combination, blunted the extent of glomerular hypertrophy observed in diabetic dogs (P < 0.05 vs. untreated diabetic dogs). Proteinuria was similarly reduced (P < 0.05 vs. untreated diabetic dogs) in dogs treated with lisinopril and TA-3090. Combination therapy of diabetic dogs produced a further significant (P < 0.05) decrement in proteinuria. We conclude that although treatment of diabetic dogs with either lisinopril or TA-3090 results in differential effects on PGC; each produces a similar decrement in proteinuria. Further, combination therapy has a greater effect on proteinuria than either agent alone. (ABSTRACT TRUNCATED AT 250 WORDS)


Correlation of urine protein/creatinine ratio and twenty-four-hour
urinary protein excretion in normal cats and cats with surgically induced chronic renal failure.

**Adams LG, Polzin DJ, Osborne CA, O'Brien TD.**

Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Minnesota, St. Paul.

Urine protein/creatinine (UP/C) ratios and 24-hour urinary protein excretion were compared in clinically normal cats and cats with surgically induced chronic renal failure (CRF). Mean 24-hour urinary protein excretion in 30 clinically normal cats fed a 28% protein diet (dry weight basis) was 4.93 mg/kg/24-hour (SD = 1.34) with a range of 2.99 to 8.88. Mean UP/C ratio in these cats was 0.134 (SD = 0.037) with a range of 0.073 to 0.239. Mean 24-hour urinary protein excretion in CRF cats was 10.49 mg/kg/24-hour (SD = 11.28) with a range of 2.16 to 62.93. Mean UP/C ratio in the CRF cats was 0.359 (SD = 0.374) with a range of 0.061 to 1.916. Linear regression showed high correlation (R^2 = 0.973, P less than 0.001) between 24-hour urinary protein excretion and UP/C ratio in clinically normal cats and cats with surgically induced chronic renal failure. The regression equation for 24-hour urinary protein excretion versus UP/C ratio was: 24-hour urinary protein excretion = 29.39 (UP/C) + 0.18. Results of this study indicate that UP/C ratios are a valid estimate of 24-hour urinary protein excretion in clinically normal and CRF cats. Dietary protein intake significantly affected UP/C ratios in clinically normal cats and cats with surgically induced CRF. Therefore, the influence of dietary protein should be considered when interpreting UP/C ratios.

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Characterization of the renal response to protein ingestion in dogs with experimentally induced renal failure.

**Brown SA, Finco DR.**

Department of Physiology and Pharmacology, College of Veterinary Medicine, University of Georgia, Athens 30602.

Effects of a protein meal (2.7 g of casein/kg of body weight) on glomerular filtration rate (GFR) and renal plasma flow (RPF) were assessed in dogs after 15/16 nephrectomy (n = 10), and were compared with observations in dogs with intact kidneys (n = 5). Increase in GFR and RPF was observed in both groups of dogs between 1.5 and 8 hours after protein ingestion. A maximal value for GFR was observed between 4 and 5 hours after protein ingestion in dogs of both groups. Enhancement of urinary protein excretion was evident in partially nephrectomized dogs after protein ingestion (P less than 0.05), a
result that was confirmed by 24-hour total urine collection from partially nephrectomized dogs fed a balanced ration. A qualitatively similar vasodilatory response was observed in partially nephrectomized dogs and in dogs with intact kidneys, and the mean maximal increase of GFR and RPF expressed as a percentage of baseline values in the latter dogs (47.0 +/- 8.1 and 43.6 +/- 10.3%, respectively) exceeded that observed in partially nephrectomized dogs (20.8 +/- 2.2 and 22.7 +/- 6.3%, respectively; P less than 0.01). The incremental response of the kidneys to protein ingestion was directly related to the degree of renal function, as reflected in the linear regression relationship between the incremental increase in GFR and the baseline value for GFR (P less than 0.01, R2 = 0.721).


Investigation of renal protein loss in dogs with acute experimentally induced Ehrlichia canis infection.

Codner EC, Maslin WR.

Department of Small Animal Clinical Sciences, Virginia-Maryland Regional College of Veterinary Medicine, Virginia Polytechnic Institute and State University, Blacksburg 24061.

Urinary protein-to-creatinine ratios and serum albumin concentrations were measured in 8 adult male dogs experimentally inoculated with Ehrlichia canis. Urinary protein concentration increased significantly, but transiently, during the acute phase of infection. Urinary protein-to-creatinine ratios were highest (mean, 8.6) during the third and fourth weeks after infection, and decreased to less than 0.5 by 6 weeks after infection. Correspondingly, albumin concentration decreased significantly during the acute phase. Serum albumin concentrations were lowest (mean, 2.1 g/dl) the fourth week after infection and increased to greater than 3.0 g/dl by 11 weeks after infection. There was an inverse linear correlation between urinary protein-to-creatinine ratio and serum albumin concentration. The magnitude of proteinuria and its inverse relationship with serum albumin concentration suggested that hypoalbuminemia associated with acute E canis infection may be attributable primarily to increased renal loss of protein, rather than decreased hepatic synthesis as previously suggested. Another dog was subsequently inoculated with E canis from 1 of the experimentally infected dogs and a renal biopsy was performed during peak proteinuria (urinary protein-to-creatinine ratio = 22 and serum albumin = 1.1 g/dl). Immunofluorescent staining revealed mild to moderate deposits of anti-canine IgM, and to a lesser extent, anti-canine IgG and complement factor C3 in the glomerular tufts and mesangium. Ultrastructural evaluation revealed distortion and fusion of podocyte foot processes and increased microvilli on podocytes. These morphologic changes were consistent with transient glomerular leakage of protein of a magnitude
that would significantly contribute to hypoalbuminemia during acute *E canis* infection. An underlying immunologic mechanism was suggested by positive glomerular immunofluorescence and previously described histologic findings.


**Treatment of membranoproliferative glomerulonephritis and nephrotic syndrome in a dog with a thromboxane synthetase inhibitor.**

**Grauer GF, Frisbie DD, Snyder PS, Dubielzig RR, Panciera DL.**

Department of Medical Sciences, Veterinary Medical Teaching Hospital, School of Veterinary Medicine, University of Wisconsin, Madison.

A 2-year-old spayed female Whippet with membranoproliferative glomerulonephritis and nephrotic syndrome was treated with a specific thromboxane synthetase inhibitor (3-methyl-2[3-pyridyl]-1-indoleoctanoic acid), resulting in decreased proteinuria and resolution of ascites and edema. Glomerular histology, however, appeared unaffected by treatment. Discontinuation of treatment for 10 weeks resulted in increased proteinuria and decreased serum albumin concentrations that were again attenuated when treatment was reinitiated. Thromboxane synthetase inhibitors have been used successfully to treat experimentally induced glomerulonephritis in several species and this treatment appears to hold promise for naturally occurring glomerulonephritis in dogs.

Publication Types:
- Case Reports


**Urine protein determination in dogs and cats: comparison of dipstick and sulfasalicylic acid procedures.**

**Moore FM, Brum SL, Brown L.**

Department of Pathology, Angell Memorial Animal Hospital, 350 South Huntington Ave, Boston MA 02130.

Protein levels in urine specimens from 91 dogs and 65 cats were evaluated by sulfasalicylic acid precipitation (SSA) and dipstick methods. The dipstick frequently yielded reactions for protein that were greater than the level of protein indicated by SSA (i.e., false positive reactions), although no false negative reactions for protein were noted. All urine specimens with protein levels equal to or greater than 100 mg/dl by SSA had dipstick results of 3 +.
Results of this study suggest that dipstick analysis for urine protein is an adequate screening procedure for the selection of urines for quantitative analysis of protein and creatinine to assess proteinuria.


[The diagnostic significance of the protein-creatinine ratio in urine for the differentiation of feline nephropathies]

Horauf A, Reusch C, Minkus G.


The normal U-P/C-range in cats was established with urine samples of 19 cats. The upper limiting value was fixed at 0.33 (mean +/- 2s). U-P/C is a reliable parameter for diagnosing proteinuria in the uremic cat. However, only very high U-P/C-values allow a conclusion on the type of nephropathy, whereas with moderately increased U-P/C values, do not allow any distinction between feline nephropathies.


Fettman MJ.

Department of Pathology, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins 80523.

The clinical problems and results of urinalyses of 500 dogs were reviewed and summarized to compare the sensitivities for detection of abnormalities indicative of urinary system disease among qualitative (sulfosalicylic acid [SSA]), quantitative (Coomassie brilliant blue [CBB]), and indexed (urinary protein/creatinine ratio [U(P/C)]) determinations of urinary protein loss vs microscopic examination of urine sediment. False-negative rates for the detection of microscopically abnormal urine specimens were 5.4% for SSA greater than or equal to 1+, 8.5% for CBB greater than or equal to 1.0 mg/ml, 9.7% for U(P/C) greater than or equal to 1.0, and 7.7% for CBB + U(P/C). A discriminatory U(P/C) value of 2.0 would have excluded dogs with clinically relevant proteinuria in the lower ranges. Proteinuria was not detected in 4.4% (22/500) of the specimens in which important numbers of leukocytes or
bacteria were observed. False-negative rates for combined interpretation of quantitative protein concentration and U(P/C) were not significantly different (P greater than 0.10) from SSA alone. Degrees of azotemia were higher (high serum creatinine concentration, P greater than 0.10 and high serum urea nitrogen concentration, P less than 0.05) and prevalence of chronically diseased dogs was greater (P less than 0.005) in dog categories with higher U(P/C) values. More quantitative determinations of urinary protein loss as a screening test offer potential labor-saving and diagnostic advantages in the identification of urinary disease over more qualitative routine screening methods.

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**Twenty-four hour urinary protein loss in healthy cats and the urinary protein-creatinine ratio as an estimate.**

**Monroe WE, Davenport DJ, Saunders GK.**

Department of Small Animal Clinical Sciences, Virginia-Maryland Regional College of Veterinary Medicine, Virginia Polytechnic Institute and State University, Blacksburg 24061.

Urinary protein loss was determined in 12 healthy cats. Voided urine was collected and protein quantitated by the Coomassie blue method. Mean protein loss for all cats was 12.65 mg/kg/24 h (5.45 SD). Protein loss for male cats (n = 6) was 16.62 mg/kg/24 h (3.3 SD), which was significantly different (P less than 0.01) from 8.69 mg/kg/24 h (4.09 SD) for females (n = 6). A single urine protein-creatinine ratio correlated well with the total urinary protein loss in mg/kg/24 h. The correlation coefficient for the protein-creatinine ratio in voided urine (UPCV) vs 24-hour urinary protein (UP-24) loss was 0.968, and that for the protein-creatinine ratio in urine obtained by cystocentesis (UPCC) vs UP-24 was 0.945. The regression equations were UPCV = 0.02145 + 0.02338 x UP-24 (mg/kg), and UPCC = 0.02667 + 0.02133 x UP-24 (mg/kg). Using the mean value plus 3 SD of urinary protein loss from the healthy cats in this study, a healthy cat would be expected to have a urinary protein loss of less than 29 mg/kg/24 h. A protein-creatinine ratio from a single urine sample provides an accurate estimate of urinary protein loss in healthy cats.

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**Diabetologia. 1988 Dec;31(12):928-32.**

**Urinary protein excretion rates in experimentally diabetic dogs and experimentally galactosaemic dogs.**

**Kern TS, Engerman RL.**
The relationship between urinary protein excretion and control of diabetes was evaluated in alloxan-diabetic dogs prospectively assigned to poor, moderate, or good glycaemic control. Protein excretion rate increased with the duration of insulin deficiency, and was significantly greater than normal in the poor control group by the fourth year of diabetes. Appreciable differences in the severity of the proteinuria were observed among animals of the poor and moderate glycaemic control groups; some of the animals excreted in excess of 500 mg protein/24 h while others excreted no more than normal throughout the 5 years of study. Differences in glycaemic control among these insulin-deficient animals seem not sufficient to account for the observed differences in protein excretion. Immunoassay for albumin indicated that the defect resulting in supranormal protein excretion was at least partly glomerular in origin. Good glycaemic control prevented the protein loss from exceeding normal. A potential role of hyperglycaemia in the development of proteinuria was examined in nondiabetic dogs made experimentally hyperglycaemic with galactose. Consumption of a 30% galactose diet for up to 5 years duration had little influence on protein excretion.


**Proteinuria in the dog: a pathomorphological study of 51 proteinuric dogs.**

Koeman JP, Biewenga WJ, Gruys E.

Institute of Veterinary Pathology, University of Utrecht, The Netherlands.

Renal cortical biopsies of 51 dogs with spontaneous proteinuria were examined by histology, electron microscopy and immunofluorescence. Glomerular lesions were classified in four groups: mesangioproliferative, membranoproliferative and membranous glomerulonephritis and amyloidosis. The glomerular and the tubulointerstitial lesions were graded, using a semiquantitative system. The results were used for the calculation of correlation coefficients between several parameters. A positive correlation was found between the severity of glomerular and tubulointerstitial lesions. Fibrin detection by immunofluorescence and histochemical methods appeared not to be correlated. The presence of electron dense deposits correlated only with the fluorescence for IgG and C3. Fluorescence for IgA and IgM was frequently observed in cases with or without dense deposits.
Samoyed hereditary glomerulopathy: serial, clinical and laboratory (urine, serum biochemistry and hematology) studies.

Jansen B, Valli VE, Thorner P, Baumal R, Lumsden JH.

Department of Pathology, Ontario Veterinary College, University of Guelph.

Human hereditary nephritis refers to familial glomerular diseases which may progress to renal failure. Samoyed hereditary glomerulopathy has been shown previously to be a model for hereditary nephritis. Clinical and laboratory studies were performed to follow progression to renal failure in 44 dogs in a family with Samoyed hereditary glomerulopathy. Affected males appeared healthy for their first three months but then became progressively wasted. Proteinuria was detected between two to three months of age; after five months, urine protein electrophoresis showed pre-albumin, albumin and alpha and beta globulin peaks. From three months onward, a reduced glomerular filtration rate was detected. Serum albumin decreased while amylase, urea, creatinine and phosphate increased from four to five months of age. Death from renal failure occurred by 15 months. Carrier females also became thinner and developed proteinuria between two and three months of age, but neither renal failure nor death ensued. Hence, SHG progressed rapidly in affected males but not in carrier females.

Effects of collection time and food consumption on the urine protein/creatinine ratio in the dog.

Jergens AE, McCaw DL, Hewett JE.

Effects of collection time and food consumption on the variability of the urine protein/creatinine ratio were determined in 10 healthy dogs. In trial 1, dogs were fasted for 12 hours, and urine specimens were obtained by bladder catheterization every 2 hours over an 8-hour collection period during the day. After a 1-week rest, the dogs were entered into trial 2. Dogs were fed at least 60 kcal of a high protein meal/kg of body weight, and urine specimens were obtained every 2 hours over an 8-hour period during the day. Urine total protein and urine creatinine concentrations and the urine protein/creatinine ratio were determined for each urine specimen obtained. Friedman's 2-way analysis by ranks was used to determine the constancy of this ratio over the 4 periods in the 2 trials (fasted and fed). There was no significant variability (P greater than 0.05) in ratios over the 8-hour collection periods in the fasted or fed trial. Feeding did not significantly alter this ratio, because there was no
significant difference (P greater than 0.05) in the urine protein/creatinine ratios of the dogs when they were fasted, compared with those of the dogs when they were fed. Seemingly, urine specimens obtained anytime during the day from dogs in both trials (fasted and fed) reflected the urine protein/creatinine ratio.


Proteinuria in the dog: a clinicopathological study in 51 proteinuric dogs.

Biewenga WJ, Gruys E.

In 51 dogs with predominantly massive urinary protein loss, the daily loss was quantified and glomerular and tubulointerstitial lesions from renal biopsies were characterised and graded using histology, immune fluorescence and electron microscopy. The highest median daily urinary protein loss occurred in dogs with membranous glomerulonephritis (median 380 mg kg⁻¹ d⁻¹) and renal amyloidosis (median 257 mg kg⁻¹ d⁻¹). Although in nine febrile dogs the urinary protein loss was transient, both glomerular and tubular lesions were diagnosed in five and seven of these dogs, respectively. The pattern of urinary proteins was determined using sodium dodecyl-sulphate polyacrylamide gel electrophoresis. The albumin fractional clearance (FC) was raised in 46 dogs, whereas the FCS of the low molecular weight (MW) protein fraction (MW less than 66,000) and high molecular weight protein fraction (MW more than 66,000) were raised in 42 and 28 dogs, respectively. Both the high molecular weight protein FC and albumin FC significantly correlated to the grade of glomerular lesions, whereas the low molecular weight protein FC only moderately significantly correlated to the grade of tubular lesions. The selectivity index, calculated as (formula; see text) did not differentiate between the various forms of glomerulopathies. The urinary lysozyme concentration was significantly correlated to the grade of tubular lesions. It is concluded that although quantitative and qualitative measurements of urinary proteins can provide additional clinical information, they do not have a reliable predictive value and histopathological examination of renal tissue is still necessary for the final diagnosis.


Long-term renal responses to high dietary protein in dogs with 75% nephrectomy.

Robertson JL, Goldschmidt M, Kronfeld DS, Tomaszewski JE, Hill GS, Bovee KC.
It has been proposed that ingestion of large amounts of dietary protein leads to sustained renal hyperperfusion and progressive glomerulosclerosis in rats. This hypothesis was tested in dogs, with 75% reduction in renal mass, maintained for 4 years on either 56, 27, or 19% dietary protein. Twelve of 21 dogs survived 4 years, and death due to renal failure was not correlated to diet. Dogs fed 56 and 27% protein had increased GFR and CPAH before and after reduction of renal mass compared to the 19% group. A pattern of deterioration of renal function, including proteinuria, was not found in any diet group. Nine of 11 dogs, fed 56, 27, or 19% protein had minimal glomerular lesions, including mesangial proliferation, GBM irregularities, adhesions, and sclerosis. Two other dogs, fed 56% protein, had more severe glomerular lesions. No significant ultrastructural differences were found in glomeruli among the three diet groups. These results do not support the hypothesis that high protein feeding had a significant adverse effect on either renal function or morphology in dogs with 75% nephrectomy.

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24-Hour urine protein/creatinine ratio in dogs with protein-losing nephropathies.

**Center SA, Wilkinson E, Smith CA, Erb H, Lewis RM.**

The 24-hour urine protein/creatinine (U[P/C]) ratio was examined in 19 healthy dogs and in 38 dogs with protein-losing nephropathies. A positive correlation existed between the U(P/C) ratio and the 24-hour urine protein output per kilogram of body weight. The U(P/C) ratio in 18 of 19 healthy dogs was less than 0.2; one dog had a ratio of 0.38. The median U(P/C) ratio in dogs with glomerulonephritis (n = 26) and amyloidosis (n = 6) was 5.73 and 22.50, respectively. The median U(P/C) ratio in dogs with chronic interstitial nephritis (n = 6) was 2.89. In the presence of hypoalbuminemia (albumin less than or equal to 1.5 g/dl), a U/(P/C) ratio greater than 1 indicated a nephrotic syndrome. Severe protein-losing nephropathies (ie, severe glomerulonephritis and amyloidosis) were characterized by U(P/C) ratios greater than 10 and urine protein values exceeding 159 mg/kg/day. The 24-hour U/(P/C) may be more sensitive than the 24-hour urine protein output per kilogram of body weight in the detection of mild glomerular disease. Abnormal U(P/C) ratios were present in 5 dogs, 2 with glomerulonephritis and 3 with chronic interstitial nephritis; that had normal or mildly increased 24-hour urine protein output.

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Estimation of quantitative proteinuria in the dog, using the urine
protein-to-creatinine ratio from a random, voided sample.

**Grauer GF, Thomas CB, Eicker SW.**

The correlation between 24-hour urine protein excretion and the protein-to-creatinine ratio (U-P/C) from random, voided urine specimens was assessed in 16 healthy Beagles (9 to 11 months old) and in 14 dogs with suspected renal proteinuria. Initially, a voided urine specimen was obtained from each dog, and the U-P/C was determined. An attempt was not made to standardize the time of collection of the voided urine. Subsequently, each dog was placed in a metabolism cage, and 24-hour urine specimens were collected for quantitative protein analysis. The Coomassie blue technique was used to measure urine protein. The correlation between the U-P/C and the 24-hour urine protein excretion (mg/kg/24 hr), evaluated by linear-regression analysis, was found to be significant ($r = 0.975$, $P$ less than 0.01). These results substantiate previous findings and indicate that random, voided urine specimens may be used to compute the ratio and to accurately reflect 24-hour urinary protein loss in the dog.

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**Effect of collection time and exercise restriction on the prediction of urine protein excretion, using urine protein/creatinine ratio in dogs.**

**McCaw DL, Knapp DW, Hewett JE.**

Nonproteinuric and proteinuric dogs were studied to determine whether the urine protein/creatinine ratio from a 24-hour urine sample could be used to predict urine protein excretion. Urine protein/creatinine ratios estimated from urine produced during daylight hours and from that produced during nighttime hours were compared to determine whether time of sample collection influenced the prediction of the urine protein excretion value. Urine protein/creatinine ratios in urine from male dogs were compared with those from female dogs to determine whether sex had an influence on the value. Hospitalized and nonhospitalized dogs were used to determine the effect of exercise restriction. The urine protein/creatinine ratio varied significantly between healthy and proteinuric dogs ($P = 0.0001$). It was not influenced by collection period or sex. Animals not confined to hospital cages had a significantly lower urine protein/creatinine ratio than did hospitalized animals confined to a cage ($P = 0.003$).

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**Use of protein-to-creatinine ratio in a single urine specimen for**
quantitative estimation of canine proteinuria.

White JV, Olivier NB, Reimann K, Johnson C.

The daily excretion of urinary protein was evaluated in 8 conditioned research dogs and in 10 hospitalized, proteinuric dogs, using 24-hour urine collections. Concurrent with each 24-hour urine collection, a 5- to 10-ml urine specimen was obtained during midday. The ratio of urine protein to urine creatinine concentration was determined from the single urine specimen for each dog. Linear regression analysis was used to calculate the correlation between that ratio and the 24-hour urinary protein loss (mg/kg of body weight). The coefficient of determination was significant ($r^2 = 0.95$, $P$ less than 0.0001). Determination of the protein-to-creatinine ratio in a single urine specimen was found to be a sensitive, rapid, and dependable diagnostic technique for detection and quantitative estimation of proteinuria.


Urinary protein loss in the dog: nephrological study of 29 dogs without signs of renal disease.

Biewenga WJ, Gruys E, Hendriks HJ.

In 29 dogs without any sign of renal disease, the total daily urinary protein loss was measured and related to renal morphology. The daily urinary protein loss was less than 10 mg/kg bodyweight in most dogs (24 out of 29). The median value of the protein loss in dogs with and without lesions differed significantly, as well as the median values of the ages of dogs with and without lesions. Polyacrylamide gel electrophoresis of urinary protein revealed the presence of albumin, high molecular weight and low molecular weight proteins. With immunofluorescence, especially, the presence of IgA (21 out of 28) and IgM (17 out of 28) was shown. In 12 out of 14 dogs with glomerular lesions IgA deposits were demonstrated (graded as +/- in two dogs and as + in 10 dogs), whereas in nine out of 14 dogs without glomerular lesions IgA deposits were demonstrated (graded as +/- in four dogs and as + in five dogs). The presence of IgA was significantly related to the presence of glomerular lesions ($P$ less than 0.05). Fibrinogen degradation products were not detectable in urine from 15 of 23 dogs.


Urinary protein excretion and immunopathologic findings in dogs with glomerular disease.
DiBartola SP, Spaulding GL, Chew DJ, Lewis RM.

Clinical and histopathologic findings in 21 dogs with glomerular disease were reviewed. Diagnoses included amyloidosis, glomerulonephritis, and secondary glomerular atrophy. Dogs with amyloidosis excreted the largest amount of urinary protein per day, and 5 of 6 so affected had clinical signs of advanced renal disease at the time of examination. Dogs with glomerulonephritis excreted significantly less urinary protein per day, and none had clinical signs of advanced renal disease at the time of examination. The magnitude of proteinuria was correlated more with the nature of the glomerular lesion than with the stage of renal disease.