Accuracy of an oscillometric blood pressure monitor during phenylephrine-induced hypertension in dogs.

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Objective-To examine the agreement between direct arterial blood pressure measurements obtained from 2 arteries and indirect blood pressure measurements obtained with an oscillometric blood pressure monitor (OBPM) during normotension and phenylephrine-induced hypertension in dogs. Animals-16 male Beagles. Procedures-In anesthetized dogs, arterial catheters were placed in the lingual and dorsal pedal arteries for measurement of arterial blood pressure. A blood pressure cuff was placed on either the dog's fore- or hind limb and connected to an OBPM. Systolic, diastolic, and mean arterial blood pressures (SAP, DAP, and MAP, respectively) were recorded from both arteries and the OBPM every 5 minutes for 30 minutes (baseline), during a 30-minute period in which dogs received a phenylephrine infusion IV to induce hypertension, and for 30 minutes after discontinuation of the infusion. Mean differences in blood pressure values and confidence intervals were calculated to compare the indirect and direct measurement techniques. Results-In dogs, oscillometry underestimated SAP during normotension, and the difference between oscillometric and direct measurements increased during hypertension. Oscillometry underestimated DAP, but the difference between oscillometric and direct measurements decreased during hypertension. There was close agreement among techniques for MAP determinations. Biases between direct measurements and OPBM blood pressure values measured from dogs' forelimbs or hind limbs were not significantly different. Conclusions and Clinical Relevance-In normotensive dogs, oscillometric measurements of MAP and SAP agreed more closely with direct arterial pressure measurements than oscillometric estimates of DAP. Oscillometric measurement of MAP was accurate during both normotension and hypertension in dogs.

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.


Pharmacokinetic and pharmacodynamic parameters of ramipril and ramiprilat in healthy dogs and dogs with reduced glomerular filtration rate.

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Ramipril, an angiotensin-converting enzyme (ACE) inhibitor for use in dogs, is converted in vivo to its active form, ramiprilat, which is eliminated in the bile and urine in the dog. The objective of this study was to assess the effect of renal impairment on the pharmacokinetics (PKs) and pharmacodynamics (PDs) of ramipril and ramiprilat. Ten adult Beagle dogs were used. PK/PD studies were performed before and after the induction of subclinical renal impairment. Ramiprilat was given at 0.25 mg/kg by a single IV bolus. After a 2-week washout period, ramipril was administered PO at 0.25 mg/kg once daily for 8 days. Ramipril and ramiprilat PKs were studied by using a physiologically based
model. The relationship between free plasma ramiprilat concentration and ACE activity was described by using the fractional Hill model. Glomerular filtration rate was decreased by 58%. No biologically relevant changes in usual plasma variables were observed between the 1st and the 8th day of oral treatment with ramipril under either condition. After an IV bolus of ramiprilat, the only changes in renal-impaired dogs were a 14 and 49% decrease in clearance of the free fraction of ramiprilat (P < .01) and free plasma concentration required to produce 50% of the maximal effect (P < .05), respectively. After repeated PO administration of ramipril, there were no alterations in any of the PK and PD parameters in healthy or renal-impaired dogs. No adjustment of the recommended PO dosage of ramipril is needed in dogs with moderate renal impairment.

Publication Types:
- Clinical Trial


Quantitative estimation of renal blood flow by power Doppler ultrasonography in renovascular hypertensive dogs.

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BACKGROUND: We estimated the value of power Doppler (PD) imaging analysis for the quantitative assessment of renal cortical blood flow (RCBF) in chronic two-kidney, one-clip (2K-1C) hypertensive dogs. METHODS: To evaluate the correlation between RCBF and PD signals, RCBF and the mean pixel intensity (MPI) of PD signals were simultaneously obtained at same region in renal cortex under progressive constriction of left main renal artery in five mongrel dogs. RCBF was measured by electrolytic hydrogen gas clearance method, and PD images were transferred to computer and analyzed by the image-analysis software Openlab. To assess the value of quantitative PD imaging analysis on RCBF in renovascular hypertension, in six mongrel dogs with chronic 2K-1C hypertension, PD images in both of clipped kidneys (CK) and non-clipped kidneys (NK) were obtained and analyzed before and 60 minutes after the intravenous infusion of captopril or sodium nitroprusside at 10-minute intervals. RESULTS: There was a linear correlation between RCBF and MPI (r= 0.878, P < 0.0001). MPI in both CK and NK significantly increased after the infusion of captopril, while no significant change was observed in both CK and NK after the infusion of sodium nitroprusside, despite similar reduction of mean arterial blood pressure. CONCLUSION: Our data suggest that the acute inhibition of angiotensin-converting enzyme increased RCBF in both CK and NK of chronic 2K-1C dogs. The quantitative analysis of PD flow signals in
The kidney is noninvasive and a useful method to evaluate regional changes of renal tissue blood flow in various renal diseases.


**Hypertensive encephalopathy in cats with reduced renal function.**

**Brown CA, Munday JS, Mathur S, Brown SA.**

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The clinical, hemodynamic, and pathologic features of hypertensive encephalopathy in two cats with reduced renal mass are described. The cats developed a progressive syndrome of lethargy, ataxia, blindness, stupor, and seizures following an abrupt increase in blood pressure associated with a surgical reduction in renal mass. The cats had severe gross brain edema, evidenced by cerebellar changes of caudal coning and cranial displacement over the corpora quadrigemina and cerebral changes of widening and flattening of the gyri. Histologically, interstitial edema was most pronounced in the cerebral white matter. Hypertensive vascular lesions were present as hyaline arteriolosclerosis in one cat and hyperplastic arteriolosclerosis in the other. Rare foci of parenchymal microhemorrhages and necrosis were also observed. Systemic hypertension (especially severe or rapidly developing) accompanied by neurologic signs and the pathologic findings of diffuse brain edema with cerebral arteriolosclerosis are consistent with an etiologic diagnosis of hypertensive encephalopathy.


**Primary hyperaldosteronism in the cat: a series of 13 cases.**

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Thirteen cases of feline primary hyperaldosteronism were diagnosed based on clinical signs, serum biochemistry, plasma aldosterone concentration, adrenal imaging and histopathology of adrenal tissue. Two cases presented with blindness caused by systemic hypertension, whilst the remaining 11 cases showed weakness resulting from hypokalaemic polymyopathy. Elevated concentrations of plasma aldosterone and adrenocortical neoplasia were documented in all cases. Seven cases had adrenal adenomas (unilateral in five and bilateral in two) and six had unilateral adrenal carcinomas. Three cases
underwent medical treatment only with amlodipine, spironolactone and potassium gluconate; two cases survived for 304 and 984 days until they were euthanased because of chronic renal failure, whilst the third case was euthanased at 50 days following failure of the owner to medicate the cat. Ten cases underwent surgical adrenalectomy following a successful stabilisation period on medical management. Five cases remain alive at the time of writing with follow-up periods of between 240 and 1803 days. Three cases were euthanased during or immediately following surgery because of surgical-induced haemorrhage. One cat was euthanased 14 days after surgery because of generalised sepsis, whilst the remaining cat was euthanased 1045 days after surgery because of anorexia and the development of a cranial abdominal mass. It is recommended that primary hyperaldosteronism should be considered as a differential diagnosis in middle-aged and older cats with hypokalaemic polymyopathy and/or systemic hypertension and should no longer be considered a rare condition.

Publication Types:
• Case Reports


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Hypertension is a common sequela to renal disease in cats and dogs, affecting as many as 61% cats and 93% of dogs, respectively. Undiagnosed and untreated, elevations in blood pressure can have deleterious effects on the brain and heart as well as promote further renal injury. In this article, we discuss the identification of patients at risk for hypertension as well as methods for measuring blood pressure and the treatment of hypertensive patients.

Publication Types:
• Review

Tijdschr Diergeneesk. 2005 Apr 1;130(7):198-201.

[Non-invasive blood pressure measurement in dogs and cats]

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Bloodpressure measurements are of interest for todays veterinary practice. It can be used for screening of incoming patients, the emergency case, the intensive care patient and sedated animal. Furthermore, like in human medicine, blood pressure can be influenced by several diseases. The most reliable method of arterial blood pressure measurement is the direct or invasive method. Only the non-invasive methods doppler and oscillometric methods are used in veterinary medicine. The article describes the method of measurement, and provides a review of the literature. The oscillometric method especially in dogs. Both methods measure a lower bloodpressure if compared with an invasive method. The difference in bloodpressure is for the oscillometric method in cats greater then in dogs and appears to increase at higher blood pressures. Keeping these facts in focus, and if one is able to work in a quiet environment, repeat the measurements and maintain a critical attitude, blood pressure measurements can be performed in veterinary practice.

Publication Types:
- Review


Ventricular structure and function in aged dogs with renal hypertension: a model of experimental diastolic heart failure.

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BACKGROUND: Heart failure (HF) with normal ejection fraction (diastolic HF [DHF]) usually occurs in elderly patients with hypertension. The presence and significance of altered systolic and diastolic ventricular function in DHF is increasingly controversial. Our objective was to develop a clinically relevant large-animal model to better understand the pathophysiology of DHF. METHODS AND RESULTS: Ventricular structure and function were characterized in young control (YC group; n=6), old control (OC group; n=7), and old dogs made hypertensive by renal wrapping (experimental DHF [ExDHF] group; n=8). The ExDHF group was associated with normal left ventricular (LV) volume, increased LV mass, and myocardial fibrosis. LV relaxation was impaired in ExDHF (tau=53+/−6 ms) compared with OC (tau=35+/−3 ms; P<0.05) and YC (tau=33+/−6 ms; P<0.05) dogs. The percent diastole at which relaxation is complete was increased in ExDHF (116+/−30%) compared with OC (69+/−8%; P<0.05) and YC (35+/−5%; P<0.05) dogs. The coefficient of LV diastolic stiffness was similar in OC, YC,
and ExDHF dogs. Diastolic pressures increased dramatically in response to increases in blood pressure. End-systolic LV stiffness was enhanced in ExDHF dogs and after load enhancement of myocardial performance was maintained. Arterial stiffness was increased in ExDHF dogs. CONCLUSIONS: Aged dogs with chronic hypertension exhibit LV hypertrophy and fibrosis with impaired LV relaxation but no increase in the coefficient of LV diastolic stiffness. LV systolic and arterial stiffness are increased, which may exacerbate load-dependent impairment of relaxation and contribute to increased filling pressures with hypertensive episodes. This model mimics many of the structural and functional characteristics described in the limited studies of human DHF and provides insight into the pathogenesis of DHF.


Canine glomerulonephritis: new thoughts on proteinuria and treatment.

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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
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.

Publication Types:
- Review

Spectrum of m-mode echocardiographic abnormalities in 75 cats with systemic hypertension.

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A retrospective study was performed in 75 hypertensive cats to determine the spectrum and frequency of M-mode echocardiographic abnormalities. Results indicated that 21.3% of the cats had M-mode measurements within normal
reference ranges. For cats with echocardiographic abnormalities, changes were variable. Thirty-nine percent of hypertensive cats had hypertrophy of the interventricular septum in diastole, and 41.3% had hypertrophy of the left ventricular (LV) posterior wall in diastole. One cat in five had a dilated left atrium, while fractional shortening and LV internal dimension in diastole were normal in 82.7% and 86.7% of the cats, respectively. The marked variability of echocardiographic findings in hypertensive cats made echocardiography an unreliable screening test for hypertension.


Evaluation of a technique of inducing hypertensive renal insufficiency in cats.

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OBJECTIVE: To compare 2 techniques of inducing combined renal insufficiency and systemic hypertension in cats. ANIMALS: 22 cats 6 to 12 months of age. PROCEDURES: Cats were randomly assigned to 1 of 3 groups. Control (C) group cats had 2 intact kidneys, remnant kidney (RK) group cats underwent unilateral partial renal infarction and contralateral nephrectomy, and remnant-wrap (W) group cats underwent unilateral partial renal infarction and partial ablation and wrapping of the contralateral kidney. Systemic arterial blood pressure (BP) was measured continuously by use of implanted radiotelemetric devices. Renal function was assessed via determination of glomerular filtration rate, measurement of serum creatinine and BUN concentrations, and determination of urine protein-to-creatinine ratio (UP/C). Serum aldosterone concentration and plasma renin activity were measured on day 75. RESULTS: Systolic BP was significantly higher in groups RK and W than in group C, and systolic BP was significantly higher in group W than in group RK. Serum aldosterone concentration and plasma renin activity were significantly higher in group W, compared with groups C and RK. Glomerular filtration rate was significantly lower in groups RK and W, compared with group C. Histologic indices of renal injury and UP/C were significantly higher in group W, compared with groups C and RK. CONCLUSIONS AND CLINICAL RELEVANCE: Hypertensive renal insufficiency in group W was characterized by marked sustained systemic hypertension, decreased renal function, proteinuria, activation of the renin-angiotensin-aldosterone axis, and renal structural injury. Results support the hypothesis that marked systemic hypertension, activation of the renin-angiotensin-aldosterone axis, and proteinuria may damage the kidney of cats with preexisting renal insufficiency.
Association of systemic hypertension with renal injury in dogs with induced renal failure.

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Systemic hypertension is hypothesized to cause renal injury to dogs. This study was performed on dogs with surgically induced renal failure to determine whether hypertension was associated with altered renal function or morphology. Mean arterial pressure (MAP), heart rate (HR), systolic arterial pressure (SAP), and diastolic arterial pressure (DAP) were measured before and after surgery. Glomerular filtration rate (GFR) and urine protein:creatinine ratios (UPC) were measured at 1, 12, 24, 36, and 56-69 weeks after surgery, and renal histology was evaluated terminally. The mean of weekly MAP, SAP, and DAP measurements for each dog over the 1st 26 weeks was used to rank dogs on the basis of MAP, SAP, or DAP values. A statistically significant association was found between systemic arterial pressure ranking and ranked measures of adverse renal responses. When dogs were divided into higher pressure and lower pressure groups on the basis of SAP, group 1 (higher pressure, n = 9) compared with group 2 (lower pressure, n = 10) had significantly lower GFR values at 36 and 56-69 weeks; higher UPC values at 12 and 56-69 weeks; and higher kidney lesion scores for mesangial matrix, tubule damage, and fibrosis. When dogs were divided on MAP and DAP values, group 1 compared with group 2 had significantly lower GFR values at 12, 24, 36, and 56-69 weeks; higher UPC values at 12 and 56-69 weeks; and higher kidney lesion scores for mesangial matrix, tubule damage, fibrosis, and cell infiltrate. These results demonstrate an association between increased systemic arterial pressure and renal injury. Results from this study might apply to dogs with some types of naturally occurring renal failure.

Effects of dietary sodium chloride intake on renal function and blood pressure in cats with normal and reduced renal function.

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OBJECTIVE: To determine effects of variations in dietary intake of sodium chloride (NaCl) on systemic arterial blood pressure (ABP) in cats with normal and reduced renal function. ANIMALS: 21 adult cats (7 with intact kidneys [control cats; group C], 7 with unilateral renal infarction with contralateral nephrectomy [remnant-kidney model; group RK], and 7 with unilateral renal infarction and contralateral renal wrapping and concurrent oral administration of amlodipine [remnant-wrap model; group WA]). PROCEDURE: All cats were sequentially fed 3 diets that differed only in NaCl content (50, 100, or 200 mg of Na/kg); each diet was fed for 7 days. The ABP was recorded continuously by radiotelemetry, and renal function (glomerular filtration rate [GFR]) was determined on the sixth day of each feeding period. RESULTS: Dietary supplementation with NaCl did not affect ABP, but it increased GFR in groups C and WA. The renin-angiotensin-aldosterone axis was activated in groups RK and WA at the lowest NaCl intake, but supplementation with NaCl suppressed this activation in group WA. The lowest NaCl intake was associated with hypokalemia and a high fractional excretion of potassium that decreased in response to supplementation with NaCl. Arterial baroreceptor resetting was evident after chronic hypertension but was not modified by dietary supplementation with NaCl. CONCLUSIONS AND CLINICAL RELEVANCE: Low NaCl intake was associated with inappropriate kaliuresis, reduced GFR, and activation of the renin-angiotensin-aldosterone axis without evidence of a beneficial effect on ABP. Therefore, this common dietary maneuver could contribute to hypokalemic nephropathy and progressive renal injury in cats.


Management of hypertension in a geriatric cat.

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Hyperthyroidism and chronic renal disease occur commonly in geriatric cats, often in association with potentially life-threatening primary or secondary hypertension. Early treatment of hypertension minimizes damage to vital organs. This case illustrates the complexity of managing hypertension in a geriatric cat with both hyperthyroidism and renal disease.


Blood pressure assessment in healthy cats and cats with hypertensive retinopathy.

Sansom J, Rogers K, Wood JL.
OBJECTIVE: To determine whether there was an association between hypertensive retinopathy and high systolic, diastolic, and mean arterial blood pressures in cats. ANIMALS: 181 cats. PROCEDURE: Systolic, diastolic, and mean arterial blood pressures were measured by use of a noninvasive oscillometric technique. The range of blood pressure measurements in healthy cats from various age groups was determined. Associations among systolic, diastolic, and mean arterial blood pressure; hypertensive retinopathy; hyperthyroidism; left ventricular cardiac hypertrophy; chronic renal failure; and serum biochemical abnormalities were determined. RESULTS: All blood pressure measurements increased with age in healthy cats. The frequency of hypertensive retinopathy also increased with age and with blood pressure, and hypertensive retinopathy was particularly found in cats with systolic blood pressures > 168 mm Hg. There was an increased risk for hypertensive retinopathy in cats that were female, > 10 years old, and neutered. The risk of chronic renal failure also increased as blood pressure, particularly systolic blood pressure, increased. CONCLUSIONS AND CLINICAL RELEVANCE: Hypertensive retinopathy was common in cats > or = 10 years of age and was associated with systolic blood pressures > 168 mm Hg when measured by the noninvasive oscillometric technique.


Hypertensive retinopathy and choroidopathy in a cat.

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Bilateral hypertensive retinopathy and choroidopathy with bullous retinal detachment was diagnosed in a 17-year-old, female spayed Domestic Short-haired cat. The underlying cause of the systemic hypertension could not be determined. The blood pressure was lowered successfully with the oral application of the L-type calcium channel blocker amlodipine besylate. The cat subsequently regained vision. The improvement in retinal function was documented using electroretinography.

Publication Types:
• Case Reports
Influence of experimental chronic hypertension on the cerebral and renal arteries of wild cats.

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The influence of chronic hypertension (HT) on the cerebral and renal arteries was examined pathologically and morphometrically in wild cats without a specific genetic background. Chronic HT for 8-15 months was induced by uninephrectomy and salt-loading, and the blood pressure was monitored for a maximum of 5 months. The grade of systolic blood pressure elevation in each cat during the monitoring period was 21-51 mmHg. Histologically, the cerebral arachnoid and medullary arteries of all hypertensive cats showed a well-preserved medial layer, and neither loss of medial smooth muscle cells, adventitial fibrosis or fibrinoid exudation was detected. This experimental model of chronic HT in wild cats for 8-15 months induced segmental intimal elastofibrosis of the arachnoid and renal arteries, but spared the cerebral medullary artery. The parenchymal changes in the brain were negligible. Morphometrically, the arachnoid artery in control cats had a significantly thinner media than the renal artery, and the medial hypertrophy of the arachnoid artery resulting from HT occurred significantly less frequently than that of the renal artery. These findings suggest that the arachnoid and medullary arteries are relatively well protected from HT, and that this may be characteristic of cerebral arteries in general and ascribed to autoregulation.

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


Hypertensive retinopathy in a cat.

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A 12-year-old cat presented for sudden blindness was diagnosed with hypertensive retinopathy on the basis of ophthalmologic and ultrasonic examination. Renal failure due to a large intranephric cyst obstructing the right ureter and renal artery was the suggested cause of the systemic hypertension. The cat died 8 hours after unilateral nephrectomy.

Publication Types:
- Case Reports


Spontaneous feline hypertension: clinical and echocardiographic abnormalities, and survival rate.
Chetboul V, Lefebvre HP, Pinhas C, Clerc B, Boussouf M, Pouchelon JL.

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Systemic hypertension was diagnosed in 58 of 188 untreated cats referred for evaluation of suspected hypertension-associated ocular, neurologic, cardiorespiratory, and urinary disease, or diseases frequently associated with hypertension (hyperthyroidism and chronic renal failure). Hypertensive cats were significantly older than normotensive subjects (13.0 +/- 3.5 years versus 9.6 +/- 5.0 years; P < .01), and had a greater prevalence of retinal lesions (48 versus 3%; P < .001), gallop rhythm (16 versus 0%; P < .001), and polyuria-polydipsia (53 versus 29%; P < .01). Blood pressure was significantly higher (P < .001) in cats with retinopathies (262 +/- 34 mm Hg) than in other hypertensive animals (221 +/- 34 mm Hg). Hypertensive cats had a thicker interventricular septum (5.8 +/- 1.7 versus 3.7 +/- 0.64 mm; P < .001) and left ventricular free wall (6.2 +/- 1.6 versus 4.1 +/- 0.51 mm; P < .001) and a reduced diastolic left ventricular internal diameter (13.5 +/- 3.2 versus 15.8 +/- 0.72 mm; P < .001) than control cats. Left ventricular geometry was abnormal in 33 of 39 hypertensive subjects. No significant difference was found in age or blood pressure at the initial visit between cats that died or survived over a 9-month period after initial diagnosis of hypertension. Mean survival times were not significantly different between hypertensive cats with normal and abnormal left ventricular patterns. Further prospective studies are needed to clearly identify the factors involved in survival time in hypertensive cats.


Comparative diagnostic test characteristics of oscillometric and Doppler ultrasonographic methods in the detection of systolic hypertension in dogs.

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Comparison of test characteristics allows a clinician to choose the optimal diagnostic test method for an individual patient. This study assessed the comparative test characteristics of noninvasive (NI) blood pressure measurement methods (oscillometric and Doppler) and used this information to develop optimal cutoff values for diagnosis of systolic hypertension in dogs by these NI methods. Simultaneous NI (oscillometric or Doppler methods) and invasive (arterial puncture [AP]) systolic blood pressure (SBP) measurements
were obtained prospectively from normal dogs and dogs suspected of having systemic hypertension based on clinical signs. Oscillometric SBP readings were obtained from the distal hind limb (Osc-L, n = 54) or the proximal tail (T, n = 27). Doppler BP measurements were obtained using a forelimb cuff (n = 57). AP-SBP was categorized as hypertensive if > or = 160 mmHg, and sensitivity (Se), specificity (Sp), and likelihood ratios (LR) were calculated for diagnostic cutoff values ranging from 130 to 220 mmHg. Receiver operator characteristic (ROC) curves were analyzed to determine optimal cutoff values for diagnosis of AP-SBP > or = 160 mmHg. Optimal NI SBP cutoff values considered to reflect AP values > or = 160 mmHg were: Osc-L = 160 mmHg (Se: 65%, Sp: 85%, LR = 4.33: 1), Osc-T = 150 mmHg (Se: 84%, Sp: 75%, LR = 3.36: 1), and Doppler = 160 mmHg (Se: 71%).

Publication Types:
• Clinical Trial


Increased mean arterial pressure and aldosterone-to-renin ratio in Persian cats with polycystic kidney disease.


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Polycystic kidney disease (PKD) in Persian cats has been increasingly reported and compared to human autosomal dominant polycystic kidney disease (ADPKD) in the last decade. In cats, however, few studies have dealt with the occurrence and hormonal determinants of hypertension, one of the most common extrarenal manifestations of ADPKD in humans. The purpose of this study was to compare Persian cats >4 years old with PKD to unaffected control cats with regard to blood pressure (BP), plasma renin activity (PRA), serum aldosterone concentration, plasma atrial natriuretic peptide (ANP) concentration, and aldosterone-to-renin ratio (ARR). Three gender- and age-matched groups were studied, each consisting of 7 cats: (1) a control group without cysts, (2) a group with mild PKD, and (3) a group with severe PKD (multiple cysts and renal enlargement). Mild renal insufficiency was found in only 1 of 14 cats with PKD. Cats with PKD had a higher mean arterial pressure (P = .04) and more often had a high ARR (P = .047) than did control cats. Tendencies toward higher diastolic and systolic arterial pressures (DAPs and SAPs, respectively) and lower PRAs were observed in cats with PKD compared to controls (.05 < P < or = .1). No significant differences were found between the groups in serum aldosterone and plasma ANP concentrations. None of the cats had echocardiographic evidence of cardiac hypertrophy. In conclusion, cats with PKD had a minor increase in mean arterial pressure compared to
control cats, and half of the cats had a high ARR.

**J Am Vet Med Assoc. 2003 Feb 1;222(3):322-9.**

**Association between initial systolic blood pressure and risk of developing a uremic crisis or of dying in dogs with chronic renal failure.**

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**OBJECTIVE:** To determine whether high systolic blood pressure (SBP) at the time of initial diagnosis of chronic renal failure in dogs was associated with increased risk of uremic crisis, risk of dying, or rate of decline in renal function. **DESIGN:** Prospective cohort study. **ANIMALS:** 45 dogs with spontaneous chronic renal failure. **PROCEDURE:** Dogs were assigned to 1 of 3 groups on the basis of initial SBP (high, intermediate, low); Kaplan-Meier and Cox proportional hazards methods were used to estimate the association between SBP and development of a uremic crisis and death. The reciprocal of serum creatinine concentration was used as an estimate of renal function. **RESULTS:** Dogs in the high SBP group were more likely to develop a uremic crisis and to die than were dogs in the other groups, and the risks of developing a uremic crisis and of dying increased significantly as SBP increased. A greater decrease in renal function was observed in dogs in the high SBP group. Retinopathy and hypertensive encephalopathy were detected in 3 of 14 dogs with SBP > or = 180 mm Hg. Systolic blood pressure remained high in 10 of 11 dogs treated with antihypertensive drugs. **CONCLUSIONS AND CLINICAL RELEVANCE:** Results suggested that initial high SBP in dogs with chronic renal failure was associated with increased risk of developing a uremic crisis and of dying. Further studies are required to determine whether there is a cause-and-effect relationship between high SBP and progressive renal injury and to identify the risks and benefits of antihypertensive drug treatment.

**Tijdschr Diergeneeskd. 2003 Jan 1;128(1):2-10.**

[Arterial hypertension in the cat. A pathobiologic and clinical review with emphasis on the ophthalmologic aspects]

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Arterial hypertension in cats appears to be an often underdiagnosed problem. Sudden disturbances of vision caused by intraocular haemorrhage and/or detached retina are often related to hypertension. The ability to measure blood pressure routinely in cats, by using an indirect method, has increased knowledge of feline hypertension in recent years. In cats mainly secondary hypertension is described, caused by as a consequence of renal disease, hyperthyroidism, chronic anaemia, primary aldosteronism, and a high-salt diet. This article describes the (patho) physiology of blood pressure control, the different methods of blood pressure measurements and the causes, clinical manifestations, and possibilities of antihypertensive therapy. Given our current knowledge, blood pressure should be measured regularly in older cats (> 10 years), especially in those with renal insufficiency, hyperthyroidism, or visual disturbances of unknown origin. Blood pressure measurements using the Doppler method is a relatively cheaply, quick and simple, method with enough reliability. Hence this method should be incorporated in veterinary practice.

Publication Types:
- Review


**Effect of renal insufficiency on the pharmacokinetics and pharmacodynamics of benazepril in cats.**

**King JN, Strehlau G, Wernsing J, Brown SA.**

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The effect of renal insufficiency was studied on the pharmacokinetics (PK) and pharmacodynamics (PD) of the angiotensin-converting enzyme (ACE) inhibitor benazepril in cats. The active metabolite of benazepril, benazeprilat, is eliminated principally (approximately 85%) via biliary excretion in cats. A total of 20 control animals and 32 cats with moderate renal insufficiency induced by partial nephrectomy were used. Assessments were made at steady state after treatment with placebo or benazepril (0.25-2 mg/kg) once daily for a minimum of 10 days. The PK endpoint was the AUC (0-->24 h) of total plasma benazeprilat. The PD endpoints were systolic, diastolic and mean blood pressures (respectively SBP, DBP and MBP) measured by telemetry, and plasma ACE activity, assessed by an ex vivo assay. Renal function was assessed by glomerular filtration rate (GFR), measured by inulin clearance, and plasma creatinine concentrations (1/PCr). As compared with control animals, the renal insufficient cats had a 78% reduction in GFR (0.57 +/- 0.41 mL/min kg), increased plasma creatinine (2.7 +/- 1.0 mg/dL), urea (44.0 +/- 11.9 mg/dL), and plasma ACE activity (5.0 +/- 4.0 U/mL).
mg/dL) and ACE activity, and moderately increased blood pressure (SBP 171.8 +/- 5.1 mmHg) (all parameters P < 0.05). Renal insufficient cats receiving benazepril had significantly (P < 0.05) lower SBP, DBP, MBP and ACE, and higher GFR values as compared with placebo-treated animals. There were no significant differences in SBP, DBP, MBP, benazeprilat or ACE values according to the degree of renal insufficiency in cats receiving benazepril. It is concluded that no dose adjustment of benazepril is necessary in cats with moderate renal insufficiency.

**Evaluation of an oscillometric blood pressure monitor for use in anesthetized cats.**

**Pedersen KM, Butler MA, Ersboll AK, Pedersen HD.**

OBJECTIVE: To determine accuracy of an oscillometric blood pressure monitor used over a wide range of pressures in anesthetized cats. DESIGN: Prospective study. ANIMALS: 6 healthy cats. PROCEDURE: 4 female cats and 2 male cats that weighed 2.7 to 4.5 kg (5.9 to 9.9 lb) and were 2 to 8 years old were anesthetized. Blood pressure was measured directly with an arterial catheter placed in the right femoral artery and indirectly from the left antebrachium by use of an oscillometric monitor. A series of diastolic arterial pressure (DAP), mean arterial pressure (MAP), and systolic arterial pressure (SAP) measurements were obtained during hypotension, normotension, and hypertension. Values obtained indirectly and directly were compared. RESULTS: The oscillometric monitor was accurate for DAP and MAP throughout the entire pressure range and met the standards of the Association for the Advancement of Medical Instrumentation (mean +/- SD difference from values obtained directly, < or = 5 +/- 8 mm Hg). The SAP was increasingly underestimated with increasing overall pressure; mean differences from direct measurements were -5.2, -12.1, and -17.7 mm Hg during hypo-, normo-, and hypertension, respectively. Standard deviations for SAP were all < or = 8 mm Hg. The monitor gave readings during all attempts. The direct blood pressure recording system appeared to perform well with neither under- nor overdamping. CONCLUSIONS AND CLINICAL RELEVANCE: Except for a minor underestimation of SAP during normo- and hypertension, the oscillometric monitor yielded reliable and easily obtainable blood pressure measurements in anesthetized cats.
Echocardiographic and radiographic changes associated with systemic hypertension in cats.

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The purpose of this study was to assess the effects of systemic hypertension (SHT) on echocardiographic and radiographic cardiovascular variables in affected cats compared with healthy geriatric cats. Secondary objectives were to determine whether there were any relationships between these findings and age or systolic blood pressure (SBP). Fifteen healthy cats (>8 years of age with normal SBP) and 15 hypertensive cats (SBP > 180 mm Hg) were studied. Each cat was evaluated for standard echocardiographic parameters and 4 different aortic root dimensions. Seventeen variables were measured from right lateral and dorsoventral radiographic views. Left ventricle wall thickness was greater in the SHT group (5.1 +/- 0.9 mm) than in the healthy cats (4.2 +/- 0.5 mm). Left ventricular hypertrophy in the SHT cats often was not severe, and mean measures were considered normal. Some cats had asymmetrical septal hypertrophy (ASH) in the basilar portion of the septum as determined from the 2-dimensional view of the left ventricular outflow tract. ASH was greater in cats with SHT. Comparisons of the proximal ascending aorta indicated the presence of dilatation in the SHT cats, and comparison of the ascending aorta to the aortic annulus was helpful in differentiating between the 2 groups. The distal aortic root measurements and ratios evaluated by echocardiography were significantly different between the 2 groups of cats (P = .0001) and were significantly correlated with SBP (P = .0001) but not age (P > .3).

Prevalence of systolic hypertension in cats with chronic renal failure at initial evaluation.

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OBJECTIVE: To determine prevalence of systolic hypertension and associated risk factors in cats with chronic renal failure evaluated in first-opinion practice.
DESIGN: Prospective study. ANIMALS: 103 cats with chronic renal failure. PROCEDURE: Systolic arterial blood pressure (SABP) was measured with a noninvasive Doppler technique, and cats that had SABP > 175 mm Hg on 2 occasions or that had SABP > 175 mm Hg and compatible ocular lesions were classified as hypertensive. Information from the history (previous treatment for hyperthyroidism, age), physical examination (sex, body weight), routine plasma biochemical analyses (creatinine, cholesterol, potassium, sodium, chloride, and calcium concentrations), and thyroid status were evaluated as potential risk factors for systolic hypertension. Variables associated with systolic hypertension were evaluated by use of logistic regression. RESULTS: 20 (19.4%; 95% confidence interval, 13 to 28%) cats had systolic hypertension. Plasma potassium concentration was significantly and inversely associated with systolic hypertension. CONCLUSIONS AND CLINICAL RELEVANCE: Prevalence of systolic hypertension, although clinically important, was lower than that reported previously. The cause of the inverse association between systolic hypertension and plasma potassium concentration is not yet known.


Effects of the calcium channel antagonist amlodipine in cats with surgically induced hypertensive renal insufficiency.


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OBJECTIVE: To determine whether amlodipine besylate decreases systemic arterial blood pressure (BP) and reduces the prevalence of complications in cats with induced hypertensive renal insufficiency. ANIMALS: 20 cats with partial nephrectomy. PROCEDURE: Following reduction in renal mass, 10 cats were administered 0.25 mg of amlodipine/kg, PO, q 24 h (group A). Ten cats served as a control group (group C). Systolic BP (SBP), diastolic BP (DBP), and mean BP (MBP), physical activity, and pulse rate were measured continuously for 36 days by use of radiotelemetric devices. RESULTS: Compared with values for clinically normal cats, SBP, DBP, and MBP were significantly increased in cats of group C. Cats in group A had significant reductions in SBP, DBP, and MBP, compared with values for cats in group C. Albuminuria but not urine protein-to-creatinine ratio was significantly correlated (R² = 0.317) with SBP in hypertensive cats. Prevalence of ocular lesions attributable to systemic hypertension in group C (7 cats) was greater than that observed in group A (2). Two cats in group C were euthanatized on day 16 because of nuerologic complications attributed to systemic hypertension. One normotensive cat in group A was euthanatized because of purulent enteritis of unknown cause on
day 27. CONCLUSIONS AND CLINICAL RELEVANCE: Amlodipine had an antihypertensive effect in cats with coexistent systemic hypertension and renal insufficiency. Its use may improve the prognosis for cats with systemic hypertension by decreasing the risk of ocular injury or neurologic complications induced by high BP.


**Systemic hypertensive disease and the feline fundus.**

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The fundoscopic appearance and some of the histopathological findings of arterial hypertension in the cat are reviewed in relation to the anatomical and physiological features that place retinal function at particular risk when the eye is subjected to sustained increased arterial blood pressure. The fundus changes fall into three categories: hypertensive retinopathy, hypertensive choroidopathy and hypertensive optic neuropathy, and information from cases with confirmed arterial hypertensive disease is used to provide a basis for discussion and future investigation.

Publication Types:
- Review


**Feline hypertension: clinical findings and response to antihypertensive treatment in 30 cases.**

**Elliott J, Barber PJ, Syme HM, Rawlings JM, Markwell PJ.**

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Systolic hypertension was diagnosed in 30 cats. At diagnosis, 16 of those were found to be in chronic renal failure only, while five were azotaemic and either receiving treatment for hyperthyroidism (four cases) or were untreated hyperthyroid cases (one case). Two cases were untreated hyperthyroid cases with no evidence of azotaemia and the remaining seven cases had no definitive diagnosis of the underlying cause of their hypertension. The successful treatment used for the majority of cases was amlodipine, which lowered
systolic blood pressure from 202.5+/-16.8 to 153.2+/-21.6 mmHg (mean+/-SD; n=29) within the first 50 days. Each case was followed for at least three months, or to the end of its natural life, and each cat was re-examined every six to eight weeks. Systolic blood pressure was kept below a target value of 165 mmHg in 58 per cent of cases treated for three months or longer. At the time of writing, 19 of the cases had died or been euthanased with a median treatment time of 203 days, one case was lost to follow-up and 10 cases were still alive, nine of which had been treated for six months or more. Amlodipine can be used for long-term control of feline systemic hypertension.


Effects of the angiotensin converting enzyme inhibitor benazepril in cats with induced renal insufficiency.


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OBJECTIVE: To determine effects of the angiotensin converting enzyme inhibitor benazepril in cats with induced renal insufficiency. ANIMALS: 32 cats. PROCEDURE: Renal mass was surgically reduced, and cats were assigned to 1 of 4 eight-cat groups. Group 1 received placebo, whereas groups 2, 3, and 4 received benazepril hydrochloride orally once daily for approximately 6.5 months at the following doses: group 2, 0.25 to 0.50 mg/kg of body weight; group 3, 0.50 to 1.00 mg/kg; and group 4, 1.00 to 2.00 mg/kg. Arterial blood pressures, glomerular filtration rate (GFR), and renal plasma flow were determined before treatment and during the treatment period. Other determinants of renal hemodynamics were measured by use of micropuncture techniques. Renal biopsy specimens were examined microscopically. RESULTS: Compared with cats that received placebo, mean systolic arterial blood pressure was significantly less and GFR significantly greater in cats that received benazepril. Glomerular capillary pressure and the ratio of efferent to afferent arteriolar vascular resistance were also significantly less in treated cats. However, histologic differences in renal specimens were not detected. CONCLUSIONS AND CLINICAL RELEVANCE: Treatment with benazepril sustained single nephron GFR in remnant nephrons of cats with induced renal insufficiency. Administration of benazepril was also associated with a small but significant reduction in degree of systemic hypertension and an increase in whole kidney GFR. Benazepril may be an effective treatment to slow the rate of progression of renal failure in cats with renal disease.
Effect of amlodipine on echocardiographic variables in cats with systemic hypertension.

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Left ventricular hypertrophy signals a poor prognosis in hypertensive humans. Cardiac disease is common in cats with systemic hypertension. The aims of this study were to characterize the echocardiographic findings of cats with systemic hypertension and to determine if reducing the degree of hypertension is associated with resolution of cardiac hypertrophy. Echocardiographic examinations were performed on 19 cats with naturally occurring systemic hypertension. Fourteen of these cats were subsequently studied after a minimum of 3 months of treatment with the antihypertensive agent amlodipine. Hypertensive cats had a significantly thicker interventricular septum in both systole and diastole, thicker left ventricular free wall in both systole and diastole, and larger left atrium compared to the published normal values and 74% (14/19) of the cats met criteria for left ventricular hypertrophy (diastolic septal or free-wall thickness > 0.60 cm). Systolic blood pressure was lower after treatment (217 +/- 25 mm Hg, range: 180-275 mm Hg; and 142 +/- 27 mm Hg, range: 90-200 mm Hg). No difference was found in any of the echocardiographic measurements between the untreated and treated cats, although more cats had ventricular hypertrophy before treatment (11/14) than after initiating amlodipine (6/14; P = .006). Ventricular hypertrophy is common in hypertensive cats and may resolve after the initiation of amlodipine.

Arterial blood pressure measurement in a population of healthy geriatric dogs.

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The purpose of this study was to evaluate healthy geriatric dogs for the presence of systemic hypertension. Thirty-three geriatric dogs (i.e., dogs exceeding the geriatric age range for their weight group) and 22 control dogs (i.e., dogs less than six years of age) were evaluated by measuring blood
pressure with an oscillometric monitor. Five consecutive blood pressure measurements were taken in each dog, averaged, and compared. Diastolic and mean blood pressure measurements were significantly lower in the geriatric group as compared to the control group. Systolic blood pressure measurements were not significantly different between the two groups. Systemic hypertension does not appear to be a common clinical problem in the healthy geriatric dog.


Effects of enalapril versus placebo as a treatment for canine idiopathic glomerulonephritis.

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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.

Publication Types:
- Clinical Trial
- Multicenter Study

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OBJECTIVE: To characterize clinical and clinicopathologic findings, response to treatment, and causes of systemic hypertension in cats with hypertensive retinopathy. DESIGN: Retrospective study. ANIMALS: 69 cats with hypertensive retinopathy. PROCEDURE: Medical records from cats with systemic hypertension and hypertensive retinopathy were reviewed. RESULTS: Most cats (68.1%) were referred because of vision loss; retinal detachment, hemorrhage, edema, and degeneration were common findings. Cardiac abnormalities were detected in 37 cats, and neurologic signs were detected in 20 cats. Hypertension was diagnosed concurrently with chronic renal failure (n = 22), hyperthyroidism (5), diabetes mellitus (2), and hyperaldosteronism (1). A clearly identifiable cause for hypertension was not detected in 38 cats; 26 of these cats had mild azotemia, and 12 did not have renal abnormalities. Amlodipine decreased blood pressure in 31 of 32 cats and improved ocular signs in 18 of 26 cats. CONCLUSIONS AND CLINICAL RELEVANCE: Retinal lesions, caused predominantly by choroidal injury, are common in cats with hypertension. Primary hypertension in cats may be more common than currently recognized. Hypertension should be considered in older cats with acute onset of blindness; retinal edema, hemorrhage, or detachment; cardiac disease; or neurologic abnormalities. Cats with hypertension-induced ocular disease should be evaluated for renal failure, hyperthyroidism, diabetes mellitus, and cardiac abnormalities. Blood pressure measurements and funduscopic evaluations should be performed routinely in cats at risk for hypertension (preexisting renal disease, hyperthyroidism, and age > 10 years). Amlodipine is an effective antihypertensive agent in cats.

Effects of dietary polyunsaturated fatty acid supplementation in early renal insufficiency in dogs.

Dietary supplementation with polyunsaturated fatty acids (PUFAs) alters the course of experimental kidney disease in dogs. In particular, supplementation with omega-6 PUFAs hastens the decline of kidney function, and omega-3 PUFAs are renoprotective. We investigated the early stages of renal insufficiency to determine whether PUFA supplementation altered the magnitude of hypercholesterolemia or glomerular hemodynamics. Two months after 11/12 nephrectomy, dogs were randomly divided into three groups of 6 animals each. Each group of dogs was then 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 were rich in omega-3 PUFAs (menhaden fish oil, group FO), omega-6 PUFAs (safflower oil, group SO), or saturated fatty acids (beef tallow, group C). Early in renal insufficiency, before significant kidney damage, group FO had a lower (P<.05) serum cholesterol concentration and tended to have a lower urinary prostaglandin E2 (PGE2) and thromboxane A2 (TxA2) excretion than group C. In contrast, group SO had a higher mean glomerular capillary pressure (P<.05) and more glomerular enlargement (P<.05) and tended to have higher eicosanoid excretion rates than group C. These differences in lipid metabolism, glomerular hypertension and hypertrophy, and urinary eicosanoid metabolism could explain, in part, the beneficial effects of omega-3 PUFAs and the detrimental effects of omega-6 PUFAs when administered on a long-term basis in this model of renal insufficiency.


New insights on effect of kidney insufficiency on disposition of angiotensin-converting enzyme inhibitors: case of enalapril and benazepril in dogs.

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The influence of a renal injury on the disposition of benazeprilat, the active moiety of benazepril, and of enalaprilat, the active moiety of enalapril, two angiotensin-converting enzyme (ACE) inhibitors (ACEI), having different routes of elimination in dog was investigated during a mild renal insufficiency obtained by a nephrectomy-electrocoagulation method reducing glomerular filtration rate by approximately 50%. Plasma concentrations of the active moieties were analyzed with a physiologically based model taking into account
the binding to ACE (high affinity, low capacity). An influence of renal insufficiency on enalapril disposition was shown with an increase in its plasma concentration, which was correlated to the reduction of the glomerular filtration rate. No such effect was evidenced for benazepril. With the physiologically based model analysis, it was shown that renal impairment led to an increase of the apparent benazeprilat clearance (260%), whereas that of enalaprilat was reduced to 40 to 55%. Renal insufficiency had no significant effect either on the apparent volume of distribution of each drug or on the binding parameters [i.e., maximal binding capacity (B(max)) and affinity (K(d))]. Enalaprilat and benazeprilat inhibitory action on ACE also was evaluated ex vivo. Similar patterns of inhibition were observed for both drugs. Renal injury had no significant influence on the overall effect of benazeprilat, whereas the inhibition effect of enalaprilat was significantly increased. It was concluded that renal insufficiency may have effects on the ACEI disposition but that the measurable active moiety plasma concentration is not the most appropriate endpoint to describe and interpret the consequence of a renal injury on ACEI.


Effect of enalapril on blood pressure, renal function, and the renin-angiotensin-aldosterone system in cats with autosomal dominant polycystic kidney disease.

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OBJECTIVE: To evaluate blood pressure, renal function, and the renin-angiotensin-aldosterone system (RAAS) in cats with autosomal dominant polycystic kidney disease (ADPKD) and to assess the effect of enalapril on these variables. ANIMALS: 6 cats with ADPKD and 6 age-matched healthy cats. PROCEDURE: To measure blood pressure and heart rate, a radiotelemetry catheter was placed in the left femoral artery of each cat. Baseline data collection included 24-hour blood pressure, heart rate, and motor activity. Blood was then collected for analysis of RAAS status and renal function. Enalapril (0.5 mg/kg of body weight, p.o., q 24 h) was administered for 1 week, and data collection was repeated. RESULTS: Differences in baseline blood pressure, heart rate, motor activity, RAAS status, and renal function were not detected between cats with ADPKD and control cats. Hypertension was not documented in cats with ADPKD. Blood pressure was significantly reduced for 15 to 17 hours after treatment with enalapril in both groups. Administration of enalapril also resulted in significant increases in plasma renin activity and significant decreases in angiotensin converting enzyme activity and atrial natriuretic peptide concentration but only minimal changes in
glomerular filtration rate and effective renal plasma flow in both groups of cats. CONCLUSIONS AND CLINICAL RELEVANCE: Although hypertension is common in humans with ADPKD, cats with ADPKD were normotensive. Treatment with enalapril (0.5 mg/kg, p.o., q 24 h) significantly reduced blood pressure in normotensive healthy cats and cats with ADPKD, and resulted in predictable changes in RAAS enzyme activities and hormone concentrations. Enalapril had minimal effects on renal function.

Publication Types:
- Clinical Trial


Progression of chronic renal disease in the dog.

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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


Venous thromboembolism and renal cell carcinoma.

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There is a vast amount of literature documenting the relationship between cancer and venous thromboembolism. Nevertheless, many aspects of this association remain obscure and the best approach to be taken towards a patient with apparently idiopathic venous thromboembolism has yet to be defined. We present a case of a patient with venous thromboembolism in whom abdominal ultrasonography, prescribed as a cautionary measure to rule out the presence of a tumour, revealed liver metastases, while the subsequent CAT scan showed hepatic angiomatosis and two small bilateral renal carcinomas. Although there are as yet no indications in the literature on screening patients with idiopathic venous thromboembolism for occult tumours, our case shows how the clinical decision to perform abdominal ultrasonography saved the patient's life.

Publication Types:
- Case Reports


Evaluation of the white-coat effect in cats.

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The diagnosis and management of systemic hypertension in cats requires a reliable method for measurement of systemic arterial blood pressure (BP) in
clinical patients. Unfortunately, the setting of a clinical practice and the act of measuring BP might raise BP and heart rate (HR), an effect referred to as the white-coat effect in human patients. The purpose of the present study was to determine if a white-coat effect was experienced by cats. Radiotelemetric implants were used to measure BP and HR in 13 conscious cats in a research colony while undisturbed in their cages and while subjected to simulated visits to a veterinarian’s office. The white-coat effect was taken to be the difference between the overall 24-hour average value for parameters of BP and HR and the corresponding value during the simulated office visit. A white-coat effect was observed in cats. In healthy cats, the systolic BP measured during the examination period of the simulated office visit exceeded the 24-hour average systolic BP by 17.6+/−1.5 mm Hg. However, marked heterogeneity occurred in the pattern and magnitude of the increase in systolic BP above the 24-hour baseline and the increase varied between 75.3 and -27.2 mm Hg for the healthy cats. Variation in response to the simulated office visit was observed among cats and among visits by the same cat. During an office visit, the magnitude of the white-coat effect tended to decrease, but not disappear, over time. The magnitude of the white-coat effect varied when cats were subjected to 5 repeat office visits, but did not diminish in the group as a whole. The mean increase in systolic BP during the examination (22.3+/−0.9 mm Hg) was greater (P < .05) in cats with renal insufficiency. Although the heterogeneity of response expected from companion animals might be greater than that observed in these colony cats, these results indicate that veterinarians should carefully consider the white-coat effect in evaluation of BP in cats. A quiet, undisturbed environment and adequate time for acclimation should be included in the standard protocol for measurements of BP. Because of day-to-day variation in the white-coat effect in individual cats, multiple serial measurements following a standard protocol should provide the best estimate of BP in cats.


Effects of renal impairment on the disposition of orally administered enalapril, benazepril, and their active metabolites.

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The pharmacokinetics of benazepril, enalapril, and their active metabolites (benazeprilat and enalaprilat) were compared after a single administration of each product by the oral route at the recommended dosage (0.5 mg/kg for both drugs) in the dog before and after moderate experimental renal impairment. Ten dogs were randomly assigned to 2 groups of 5 animals in a 2-period crossover design for angiotensin-converting enzyme inhibitor administration. Renal failure was surgically induced by right nephrectomy and
electrocoagulation of the remaining kidney. Renal mass reduction induced a significant decrease (P < .001) in glomerular filtration rate (GFR) (1.7 +/- 0.3 versus 3.3 +/- 0.7 mL/kg/minute). No significant differences before and after surgery were observed for enalapril and benazepril kinetics. The area under the curve (AUC) for enalaprilat increased after surgery from 23.6 +/- 14.7 to 42.4 +/- 20.9 micrograms.minute/mL (P < .01). Mean peak plasma concentration (Cmax) was increased in the impaired dogs (59.1 +/- 23.3 versus 43.9 +/- 32.9 ng/mL), but this variation was not significant (P > .05). Renal failure had no significant effect on AUC for benazeprilat (13.8 +/- 9.8 versus 14.9 +/- 5.0 micrograms.minute/mL) (P > .05), but Cmax decreased significantly (from 55.0 +/- 26.4 to 31.9 +/- 17.7 ng/mL) (P < .05). Multiple regression analysis showed that both GFR and AUC for enalapril were highly significant variables that explained the variation in AUC for enalaprilat (R2 = .86, P < .001) but not for benazeprilat (R2 = .12, P > .05). The results of this study indicate that exposure to enalaprilat, but not to benazeprilat, is increased in dogs with subclinical renal impairment.


Diagnosis and treatment of systemic hypertension.

Brown SA, Henik RA.

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Systemic hypertension is often observed in dogs and cats with chronic renal failure and other metabolic and endocrinological abnormalities. High systemic arterial blood pressure has been associated with chronic renal failure, ocular injury, neurologic complications, and cardiovascular changes. Recent advances in our knowledge of the prevalence and consequences of systemic hypertension dictate that proper diagnosis and treatment of this problem should become a component of routine therapy for many of our patients.

Publication Types:
- Review


Epidemiological study of blood pressure in domestic cats.

Bodey AR, Sansom J.

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Blood pressure was measured indirectly in 203 cats using an oscillometric technique in conjunction with a tail cuff. Systolic blood pressure was found to be log normally distributed across the population, while diastolic pressure was log log normally distributed. Blood pressure was found to rise with age (systolic, diastolic, mean arterial and pulse pressure were significantly higher in animals aged 11 years or over than in animals aged under 11 years) but this rise did not parallel an increase in plasma urea or creatinine. Cats with clinical renal disease did however have higher blood pressures than normal cats, as did cats with ocular change consistent with hypertensive retinopathy.


Is there a role for dietary polyunsaturated fatty acid supplementation in canine renal disease?

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Dogs with spontaneous renal diseases frequently develop progressive uremia. After partial nephrectomy, a similar pattern of progressively declining renal function develops. This pattern may be attributed in part to the development of glomerular hypertension in remnant canine nephrons. Changes in the composition of dietary polyunsaturated fatty acids (PUFA) modify glomerular hemodynamics in normal rats and affect the chronic course of renal disease in partially nephrectomized rats. Thus, dietary PUFA supplementation might alter progressive canine nephropathies. However, the response of dogs with renal insufficiency to dietary manipulations frequently differs substantially from that of laboratory rodents, and the effects of dietary PUFA composition have been poorly characterized in dogs with chronic renal disease. Here we address the hypothesis that dietary PUFA supplementation may delay the progression of chronic renal insufficiency in dogs. In particular, dogs ingesting diets supplemented with (n-6) PUFA exhibited severe glomerular hypertension associated with rapidly progressive renal failure. In contrast, dietary supplementation with (n-3) PUFA prevented deterioration of the glomerular filtration rate and preserved renal structure. The results of these model studies demonstrate that dietary PUFA supplementation may alter renal hemodynamics and the long-term course of renal injury in dogs. Clinical trials to address the potential benefits of dietary (n-3) PUFA supplementation in a variety of spontaneous renal diseases seem warranted.

Publication Types:
- **Review**
Obesity in dogs: effects on renal function, blood pressure, and renal disease.

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Publication Types:
- Review

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,
Non-invasive blood pressure measurements in cats: clinical significance of hypertension associated with chronic renal failure.

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The systolic, mean and diastolic pressures as well as the heart rate were measured using the oscillometric method, on a total of 104 cats (60 cats in the normal group, and 44 in the renal disease group) which were brought into Azabu University Animal Hospital. The blood pressure in the normal group was systolic: 115.4 +/- 10.1 mmHg, mean: 96.2 +/- 12.2 mmHg, and diastolic: 73.7 +/- 10.7 mmHg. Although no difference in heart rate, the renal disease group showed significantly (p < 0.05) higher values for systolic, mean, and diastolic pressure when compared with the normal group. Moreover, when plasma renin activity, angiotensin I and II, and aldosterone concentrations were measured in other cats (11 normal and seven with chronic renal failure), all cats with chronic renal failure showed significantly (p < 0.05) higher values than the normal group. It is, therefore, indicated that hypertension due to stimulating renin-angiotensin-aldosterone system may have manifested in cats with renal dysfunction.

Amlodipine: a randomized, blinded clinical trial in 9 cats with systemic hypertension.

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The efficacy of amlodipine (AML) was tested in hypertensive cats in a placebo-controlled, randomized, blinded clinical trial. Five cats were randomized to receive 0.625 mg AML once daily and 4 cats to receive placebo (PLA) once daily. The average systolic blood pressure (SBP) recorded by the Doppler method on day 0 was 212 +/- 21 mm Hg in the AML group and 216 +/- 32 mm Hg in the PLA group. On day 7, the cats receiving AML had a significantly
lower average daily SBP (160 +/- 30 mm Hg) but SBP in the PLA group was unchanged (207 +/- 31 mm Hg). On day 7, all cats receiving PLA and one cat receiving AML were crossed over to the other group because of inadequate response. Blood pressure did not decrease adequately in 3 cats by day 14 (7 days of PLA and 7 days AML) and the treatment code was broken. Each of these cats was subsequently administered 1.25 mg AML daily. Cats requiring 1.25 mg AML once daily (6.1 kg +/- 0.7 kg) weighed significantly more than cats that responded to 0.625 mg AML once daily (4.1 +/- 0.7 kg). The average daily SBP recorded in the 6 cats that completed the study was significantly lower after 16 weeks of treatment (152 +/- 14 mm Hg) compared to day 0 (221 +/- 24 mm Hg). Three cats were euthanized before completion of the study. All 3 cats were responders to AML on day 7. SBPs measured 24 hours after AML administration were similar to the average daily SBP, suggesting that AML effectively controlled SBP for a 24-hour period. AML was shown to be an effective once-daily antihypertensive agent when administered to cats at a dosage of 0.18 +/- 0.03 mg/kg sid.

Publication Types:
- Clinical Trial
- Randomized Controlled Trial


[Indirect blood pressure measurement in cats with diabetes mellitus, chronic nephropathy and hypertrophic cardiomyopathy]

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In the present study blood pressure was measured in cats comparing two indirect methods (oscillometric versus Doppler-sonographic) over a wide pressure range. It was shown, that at the lower pressures Doppler and oscillometric measurements were basically equivalent. However for higher pressures oscillometric measurements were consistently lower than Doppler measurements. This difference became greater as blood pressure increased. The determination of blood pressure by the Doppler-sonographic method was always possible, whereas the measurement by the oscillometric method was often not possible, especially at higher blood pressure levels. In a second step, the frequency of hypertension was determined in cats with diabetes mellitus, chronic renal failure and hypertrophic cardiomyopathy. Eight cats with diabetes mellitus had oszillometric blood pressure values of 101-155 mmHg systolic, 42-105 mmHg diastolic and 65-125 mmHg mean arterial pressure determined at the front leg and 110-167 mmHg systolic, 44-98 mmHg diastolic, and 61-125 mean arterial pressure determined at the tail. The Doppler-sonographic values were 120-180 mmHg. Only the oscillometric measurement (at the tail)
of the systolic pressure was significantly higher than that of normal cats. In 11 cats with chronic renal failure the following values were determined by the oszillometric method: at the front leg 137-182 mmHg systolic, 74-138 mmHg diastolic, 100-162 mmHg mean arterial pressure and at the tail 134-189 mmHg systolic, 53-109 mmHg diastolic, 80-135 mmHg mean arterial pressure. With the Doppler-sonographic technique the blood pressure was between 120 and 280 mmHg. All blood pressure measurements were significantly higher than those of healthy cats, except the oscillometric measurements of diastolic blood pressure. In 12 cats with hypertrophic cardiomyopathy systolic pressure was 108-179 mmHg, diastolic pressure was 64-135 mmHg, and mean arterial pressure was 89-154 mmHg at the front leg using the oscillometric method. At the tail results were as follows: 121-201 mmHg systolic, 61-141 mmHg diastolic, and 85-160 mmHg mean arterial pressure. By the Doppler-sonographic technique determined blood pressure was 110-260 mmHg. All oscillometric measurements except the diastolic pressure determined at the front leg were significantly higher than in normal cats. Four cats with chronic renal failure and five cats with hypertrophic cardiomyopathy showed retinal hemorrhages and/or detachments. Eight of this nine cats had blood pressure measurements above the normal range. We conclude that hypertension can be detected in cats with several diseases. In most cases reliable measurements can only be obtained by Doppler-sonographic methods.


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

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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.


Pathophysiology and management of progressive renal disease.

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Recently, the hypothesis that all renal diseases are inherently progressive and self-perpetuating has focused attention on adaptive changes in renal structure and function that occur whenever renal function is reduced. These glomerular adaptations to renal disease include increases in filtration rate, capillary pressure and size, and are referred to as glomerular hyperfiltration, glomerular hypertension and glomerular hypertrophy, respectively. Extrarenal changes, such as dietary phosphate excess, systemic hypertension, hyperlipidaemia, acidosis and hyperparathyroidism occur in animals with renal disease and may be contributors to progression of renal disease. Emphasis in the management of companion animals with renal disease has shifted to identifying, understanding and controlling those processes that play a role in the progression from early to end-stage renal failure. Advances made by veterinary nephrologists in the past 15 years permit resolution of old controversies, formulation of new hypotheses and discussion of unresolved issues about the nature of progressive renal disease in dogs and cats.

Publication Types:
• Review


Ocular signs in four dogs with hypertension.

Sansom J, Bodey A.

Animal Health Trust, Newmarket, Suffolk.

Four dogs suddenly developed visual problems associated with retinal detachment and haemorrhage. They all had a high arterial blood pressure
measured with a Doppler ultrasonic blood pressure monitor. Two of the dogs showed evidence of cardiac hypertrophi

y and one had hypercholesterolaemia; in three of them there was no conclusive evidence of underlying systemic
disease. The condition was treated and assessed over a period of 12 months. In the absence of any findings suggesting the presence of underlying systemic
disease, it is possible that the ocular changes were the result of primary hypertension, although not every possible cause of secondary hypertension could be excluded.

Publication Types:
• Case Reports


Treatment of systemic hypertension in cats with amlodipine besylate.

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Amlodipine besylate, a calcium channel blocker, was used to treat (mean +/- standard deviation [SD], 127 +/- 68 days) 12 cats with systemic hypertension. Amlodipine was administered orally at a dosage of 0.625 mg per cat (range, 0.08 to 0.23 mg/kg body weight; mean dose +/- SD, 0.17 +/- 0.04 mg/kg body weight) once daily as a single agent. Average indirect systolic blood pressure measurements in the 12 cases decreased significantly from 198 to 155 mmHg during amlodipine treatment. Significant changes in body weight and serum creatinine and potassium concentrations were not detected. Amlodipine appears to be a safe and effective oral treatment for systemic hypertension in cats when used chronically once daily as a single agent.


Plasma renin activity and angiotensin I and aldosterone concentrations in cats with hypertension associated with chronic renal disease.

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OBJECTIVE: To determine plasma renin activity (PRA), angiotensin I (Ang I), and aldosterone (ALDO) values in clinically normal cats and hypertensive cats with renal disease, and the relation of renin-angiotensin-aldosterone activation
in response to treatment with beta-blockers or angiotensin-converting enzyme inhibitors. ANIMALS: 5 normotensive healthy control cats and 12 Untreated hypertensive cats with chronic renal disease. PROCEDURE: Untreated hypertensive cats received either propanolol (n = 6) or enalapril (n = 6) as initial antihypertensive treatment. PRA and baseline plasma Ang I and ALDO concentrations were measured prior to treatment. The difference in Ang I values at 2 hours (Ang I generated) and at time 0 (baseline Ang I) was divided by 2 to give the PRA value. Values for PRA, Ang I, and ALDO were obtained from 5 clinically normal, normotensive cats, and compared with those of hypertensive cats. RESULTS: Mean +/- SD PRA and baseline Ang I concentration were not significantly different between normotensive and hypertensive cats. Mean ALDO concentration was significantly (P = 0.0235) higher in hypertensive cats with renal disease (186.18 +/- 145.15 pg/ml), compared with that in normotensive controls (51.1 +/- 16.76 pg/ml). Eight hypertensive cats with ALDO concentration > 2 SD above the mean concentration in control cats had low (n = 3), normal (n = 4), or high (n = 1) PRA, suggesting variable activation of the renin-angiotensin-aldosterone axis in the hypertensive state. Overall, enalapril was effective long-term monotherapy in only 1 of 6 cats, and propranolol was ineffective as long-term monotherapy. CLINICAL RELEVANCE: Evaluation of the renin-angiotensin-aldosterone system in cats with hypertension associated with renal disease may lead to greater understanding of the pathophysiologic mechanisms of this disorder. In addition, identification of biochemical markers in hypertensive cats may permit selection of appropriate antihypertensive drugs. Propranolol and enalapril were ineffective antihypertensive agents in most cats of this study.

Publication Types:
- Clinical Trial
- Randomized Controlled Trial


Comparison of blood pressure measurements obtained in dogs by use of indirect oscillometry in a veterinary clinic versus at home.

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OBJECTIVE: To compare blood pressure and heart rate measurements performed in a veterinary clinic to similar measurements performed in a dog's home. DESIGN: Prospective study. ANIMALS: 14 client-owned, clinically normal dogs. PROCEDURE: Sequential blood pressure and heart rate measurements were recorded from the metatarsus and metacarpus of conscious dogs by indirect oscillometry. Measurements were performed in the dogs' homes and were repeated in a veterinary clinic. Blood pressures and
heart rate were derived from 7 serial estimates over 8 to 10 minutes. Statistical differences between the home and clinic and between recording sites were calculated. RESULTS: Systolic, diastolic, and mean blood pressure and heart rate measurements obtained from the metatarsus and metacarpus in the dogs' homes were significantly lower than measurements from the metatarsus in the clinic, but were similar to measurements from the metacarpus in the clinic. Significant differences were not found between blood pressure measurements from the metatarsus and metacarpus in the dogs' homes, but systolic and mean blood pressure and heart rate measurements from the metacarpus in the clinic were significantly lower than measurements from the metatarsus. Whereas all dogs had normal blood pressure in their homes, 5 of 14 dogs had transient hypertension (systolic pressure > 165 mm of Hg or diastolic pressure > 95 mm of Hg) in the clinic. CLINICAL IMPLICATIONS: Blood pressure and heart rate measurements obtained in the clinic initially overestimate comparable measurements in a dog's home. The differences are best explained by transient autonomic responses to the stress of the clinic. Blood pressure must be measured by use of standardized techniques on dogs acclimated to the clinic environment.


Erratum in:

Effects of parathyroidectomy on induced renal failure in dogs.

Finco DR, Brown SA, Crowell WA, Hoenig ME, Ferguson DC, Brown CA, Cooper TA.

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OBJECTIVE: To determine the effects of parathyroid hormone (PTH) depletion on dogs with induced chronic renal failure. ANIMALS: 2 groups of 26 mixed-breed dogs of both sexes (13 were parathyroidectomized [PTX] and 13 had sham surgery). PROCEDURE: After surgical reduction of renal mass and PTX, dogs were selected for a 24-month period of study and monitored for clinical, hematologic, blood biochemical, and organ function status. On development of uremia or after 24 months, dogs were euthanatized, and tissues were examined. RESULTS: Higher survival rate and smaller decrement in renal function (glomerular filtration rate) were observed in PTX dogs, compared with those that had sham surgery, but values did not reach statistical significance. The PTX dogs remained hypocalcemic during the study and had lower serum Ca2+ X P product values. Regardless of parathyroid state, survivors and fatalities could be separated on the basis of serum Ca2+ X P product values. Parathyroidectomy did not prevent renal deposition of calcium, and renal
lesions were poorly correlated with renal cortical calcium concentration. Abnormalities reported in dogs with renal failure, which were attributed to PTH (glucose intolerance, pulmonary hypertension), were not observed in PTX dogs or those that had sham surgery. CONCLUSIONS AND CLINICAL RELEVANCE: PTX had beneficial effects, but these were mediated via changes in mineral homeostasis rather than via direct effects of PTH. Results attributable to PTX were similar to those previously obtained by dietary restriction of phosphate intake.


Absence of hypertension in dogs with renal insufficiency.

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Dogs have provided classic models of induced hypertension. This paper shows that despite being susceptible to hypertension, they are naturally resistant to its development even when renal function is severely compromised. The proportion of hypertensive dogs was almost as low among those with reduced glomerular filtration rate (GFR) (9%) as those with normal GFR (6%). Dogs with GFR less than 33% of the normal lower limit (with an average GFR equivalent to 10 mL min⁻¹ in a 70-kg patient) had arterial pressures not significantly above normal. Only dogs with a GFR 33-75% of the lower limit of normal had significantly elevated systolic pressure, though none was actually hypertensive. Since there was no correlation between arterial pressure and GFR below 33% of lower limit, the dogs in the 33-75% range may be showing an effect of increased pressure, rather than a cause. In humans with GFR less than 33% of normal, the majority are hypertensive. Since various aspects of canine cardiovascular and renal function are comparable with humans, the question is why dogs, despite being capable of developing hypertension, are resistant to it, even when they have chronic renal insufficiency.


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

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USA.

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 hyper-adrenocorticism 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.


Hypertension and renal disease.

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Systemic hypertension is commonly associated with chronic renal failure in dogs and cats. Consequences of systemic hypertension are manifested by pathologic changes involving the eyes, heart, central nervous system, and/or kidneys. These changes may be prevented or reversed by diagnosing and treating systemic hypertension. Therefore, blood pressure determination and ophthalmic examination should be performed routinely in animals with chronic renal failure. Therapy for systemic hypertension associated with chronic renal failure should be initiated cautiously with the goal being to lower arterial pressure below values considered to be hypertensive. Therapy may involve nonpharmacologic strategies and/or hypertensive drugs. This article discusses
pathophysiologic mechanisms, consequences, diagnosis, and treatment of systemic hypertension associated with chronic renal failure in dogs and cats.

Publication Types:
• Review


Mineralocorticoids, salt and high blood pressure.

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Essential hypertensive patients often respond to treatments mitigating mineralocorticoid action, even though circulating levels of these steroids are within normal ranges. In addition to the kidney, mineralocorticoid or Type I receptors are found in the brain and vascular smooth muscle where they mediate effects associated with several forms of experimental hypertension. Studies in which discrete anatomic or functional areas of the brain have been ablated demonstrate that the periventricular areas of the hypothalamus and the central sympathetic and baroreceptor systems are crucial for the development of hypertension in the renoprival, DOCA salt, and Dahl salt-sensitive rat. Intracerebroventricular (i.c.v.) infusion of aldosterone in both rats and dogs at doses that do not raise serum levels above normal produce hypertension. The hypertension produced by systemic mineralocorticoid excess, adrenal regeneration, and i.c.v. or oral administration of glycyrrhetinic acid or carbenoxolone in genetically normotensive rats and by dietary salt in the Dahl salt-sensitive rat is inhibited by the i.c.v. infusion of a mineralocorticoid receptor antagonist or a Na+ channel-selective amiloride analog. Recent data demonstrate the extraadrenal synthesis of steroids in aortic endothelial cells, smooth muscle cells and the brain. The role of the extraadrenal synthesis of steroids raises new avenues for research into the causes of hypertension.

Publication Types:
• Review


Epidemiological study of blood pressure in domestic dogs.

Bodey AR, Michell AR.
Previous experience has shown that a non-invasive (indirect) technique using an oscillometric monitor in conjunction with a tail cuff makes routine clinical blood pressure measurement practicable in dogs. The relationship between indirect and direct readings has been evaluated in both anaesthetised and conscious dogs (Bodey and others 1994, 1996). In this study, more than 2000 pressure measurements were taken from 1903 dogs. It was found that systolic is the most variable pressure parameter and that it depends on age, breed, sex, temperament, disease state, exercise regime and, to a minor extent, diet. Diet was not a significant determinant of diastolic and mean arterial pressure. Age and breed were the major predictors for all parameters. Heart rate was primarily affected by the temperament of the animal, though other factors also play a part in prediction. The distribution of systolic, diastolic, mean arterial pressure and heart rate across the dog population approximates to a log normal distribution. On the basis of these results it is possible to describe normal ranges for canine blood pressure; definition of hypertension, though, demands attention to age and breed normal values. The existence of statistically defined hypertension in an individual or breed does not imply adverse effects justifying therapy. Among the secondary causes of hypertension, such as diabetes, obesity and hyperadrenocorticism, hepatic disease was a new addition also undocumented in humans. The hypothesis that dogs, though classic model animals for hypertension, are resistant to its development found support from the modest increase in mean pressure values observed among dogs with renal disease, notably those with substantial reduction of glomerular filtration rate. The existence of breeds such as deerhounds with average pressures in the borderline range for hypertension in humans (and many individuals, therefore, well above) suggests that dogs may also be resistant to some of the adverse effects of high blood pressure.


Single-nephron adaptations to partial renal ablation in cats.

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To evaluate remnant nephron hyperfiltration, cats underwent sham surgery (group 1, n = 6) or three-fourths nephrectomy (group 2, n = 6). Four to six weeks later, micropuncture studies demonstrated increases (P < 0.01) of single-nephron glomerular filtration rate (SNGFR) in group 2 (28.1 +/- 2.8 vs. 56.0 +/- 5.9 nl/min). In group 2 the mean estimated glomerular capillary pressure of 74.0 +/- 1.7 mmHg exceeded (P < 0.01) the value for group 1 (62.6 +/- 1.4 mmHg). The mean effective filtration pressure (EFPm) for group
2 (28.7 +/- 3.1 mmHg) was greater (P < 0.05) than that in group 1 (20.8 +/- 1.9 mmHg). Similarly, the mean ultrafiltration coefficient (kf) in group 2 of 2.03 +/- 0.24 nl.min^{-1}.mmHg^{-1} exceeded (P < 0.05) the corresponding value for group 1 of 1.35 +/- 0.06 nl.min^{-1}.mmHg^{-1}. Morphological studies demonstrated glomerular enlargement and mesangial matrix expansion in group 2 (P < 0.05). Proteinuria, as assessed by the urine protein-to-creatinine ratio, was increased (P < 0.05) after partial renal ablation. These results demonstrate that increases in SNGFR in feline remnant nephrons occur in association with glomerular hypertension, glomerular hypertrophy, expansion of mesangial matrix, and proteinuria, and furthermore, that the observed increases in SNGFR are attributable to an augmentation of EFPm and Kf.


Hypertension induced by chronic renal adrenergic stimulation is angiotensin dependent.

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We designed these studies to assess the role of the renin-angiotensin system in mediating the hypertensive and renal functional effects of chronic renal adrenergic stimulation. Norepinephrine was infused at 0.1 microgram/kg per minute for 7 days directly into the renal artery of uninephrectomized dogs under control conditions (n = 5) or after plasma angiotensin II (Ang II) concentration was fixed at control levels (n = 5) by chronic intravenous infusion of captopril (14 micrograms/kg per minute) and Ang II (0.58 +/- 0.04 ng/kg per minute). During the first 60 minutes of norepinephrine infusion in control dogs, mean arterial pressure increased 9 +/- 4 mm Hg in association with a twofold to threefold rise in plasma renin activity. Additionally, glomerular filtration rate, renal plasma flow, sodium excretion, and fractional sodium excretion decreased to 70 +/- 5%, 64 +/- 5%, 31 +/- 4%, and 38 +/- 6% of control, respectively, while filtration fraction increased 15 +/- 2%. In contrast to the pronounced short-term effects of norepinephrine on renal function, during chronic norepinephrine infusion, all indexes of renal function returned to control levels. However, elevations in both plasma renin activity and mean arterial pressure were sustained and on day 7 were 2.3 +/- 0.6 ng angiotensin I/mL per hour (control, 0.5 +/- 0.1) and 110 +/- 7 mm Hg (control, 90 +/- 3). In dogs with fixed plasma levels of Ang II, acute and chronic changes in renal function induced by norepinephrine were similar to those in control dogs except that acute reductions in glomerular filtration rate tended to be more severe, and changes in filtration fraction and fractional sodium excretion were either attenuated or abolished. Moreover, in the absence of a rise in plasma Ang II concentration, mean arterial pressure did
not change either acutely or chronically during norepinephrine infusion. These findings suggest a critical role for Ang II in mediating the hypertension associated with elevated levels of renal adrenergic stimulation that have little or no long-term effect on renal blood flow.


The link between hypertension and nephrosclerosis.

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Nephrosclerosis is literally defined as hardening of the kidneys (Greek derivation: nephros, kidney; sklerosis, hardening). It is the result of scarring or replacement of the normal renal parenchyma by dense collagenous tissue. In practice, nephrosclerosis refers to diseases with predominant pathologic changes occurring in the preglomerular microvasculature and secondarily involving the glomeruli and interstitium. The relationship between mild to moderate hypertension and either nephrosclerosis or end-stage renal disease (ESRD) remains circumstantial, although these syndromes have long been associated in the medical literature. Nephrologists credit hypertension as the etiology of nephrosclerosis in 25% of patients initiating Medicare-supported renal replacement therapy, even though other processes may cause similar renal pathologic findings. Strikingly, serum creatinine values infrequently increase in patients with long-standing mild to moderate hypertension. Patients classified as having hypertensive ESRD typically present with advanced disease, making the processes that initiated the renal disease difficult to detect. Nephrologists are twice as likely to label an African-American patient as having hypertensive nephrosclerosis, compared with a white patient, when presented with identical clinical histories. This review proposes that many patients classified as having hypertensive nephrosclerosis actually have intrinsic renal parenchymal diseases, renal artery stenosis, unrecognized episodes of accelerated hypertension, or a primary renal microvascular disease. The familial clustering of ESRD attributed to hypertension in African-Americans and the identification of genes associated with renal injury in animals support the concept that inherited factors may predispose to renal failure. African-American families often have members with ESRD from disparate etiologies, including hypertensive ESRD. This suggests that common mechanisms, be they inherited or environmental, underlie the development of progressive renal failure in diverse forms of nephropathy. Identification of the mechanisms producing susceptibility to progressive renal disease would support the concept that mild to moderate elevations in blood pressure per se are uncommon causes of nephrosclerosis.

Salt, hypertension and renal disease: comparative medicine, models and real diseases.

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Dogs are well established as experimental animals for the study of both renal disease and hypertension, but most work is based on surgical or pharmacological models and relatively little on spontaneous diseases. This review argues for the latter as an underexploited aspect of comparative medicine. The most important feature of canine hypertension may not be the ease with which models can be produced but the fact that dogs are actually rather resistant to hypertension, and perhaps to its effects, even when they have chronic renal failure. The importance of natural models of chronic renal failure is strengthened by the evidence that self-sustaining progression is a consequence of extreme nephron loss, that is, a late event, rather than the dominant feature of the course of the disease. The role of salt in hypertension is discussed and emphasis given to the importance of understanding the physiological basis of nutritional requirement and recognizing that it is unlikely to exceed 0.6 mmol/kg/day for most healthy adult mammals except during pregnancy or lactation. Such a perspective is essential to the evaluation of experiments, whether in animals or humans, in order to avoid arbitrary definitions of 'high' or 'low' sodium intake, and the serious misinterpretations of data which result. An age-related rise in arterial pressure may well be a warning of excess salt intake, rather than a normal occurrence. Problems of defining hypertension in the face of variability of arterial pressure are also discussed.


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

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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.