

HOW I TREAT...

Hypertension



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Introduction

Hypertension is the most important cardiovascular disease of the aged cat and the most important vascular disease in cats, making up approximately 1% of NCSU admissions from 1990-1995 (*Figure 1*). Its

recognition and appropriate treatment is therefore emerging as a critical component of small animal geriatric medicine. There are a number of target organs for systemic hypertension (*Figure 2*); our experience has shown that hypertensive cats have associated disease, in approximate order of clinical presentation, of the eye, kidney, heart, and central nervous system (CNS) (1). Any discussion of management of hypertension must be preceded by a discussion of the causes of hypertension, the specific target organs affected, and the mechanism by which target organs are damaged.

Etiology

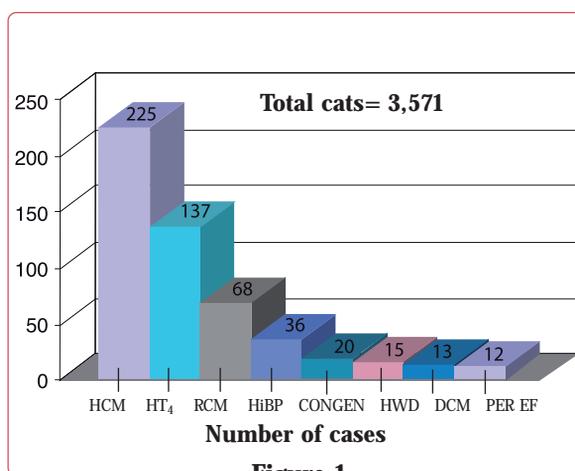
Hypertension in animals has largely been considered to be secondary to other diseases (e.g. renal disease and endocrinopathies), as opposed to idiopathic (primary or essential), as is the case in most human hypertensives. This has recently been questioned. One study of hypertensive cats referred for ocular disease revealed that at least 17%, and possibly as many as 50%, of cats had no identifiable cause for their systemic hypertension (1). Another study showed that approximately 20% of hypertensive cats diagnosed in "primary-care" practice were idiopathic (2). In a retrospective review of hypertensive cats, using more rigorous inclusion criteria (Atkins, Grauer, unpublished), > 10% of affected cats were determined to be idiopathic. It is important to note that the average age for hypertensive cats is 14.8 years (1).

Described and potential etiologies of secondary hypertension include chronic and acute renal disease, hyperthyroidism, hypothyroidism, hyperadrenocorticism, hyperaldosteronism, pheochromocytoma, diabetes mellitus, and possibly obesity. Clearly, chronic kidney disease (CKD) has the greatest association with hypertension and may often be causal. A recent report suggested ~ 29% of elderly cats with CKD were hypertensive (3) with a further four studies giving a range of 19-65% (4).

KEY POINTS

- ➔ Fundic examination and blood pressure measurement should be performed in all cats > 10 years of age.
- ➔ Some cats do not have an identifiable cause for their hypertension. These should be considered as idiopathic and managed aggressively to prevent damage to target organs.
- ➔ Early intervention, especially to spare the eye and central nervous system, is imperative, with amlodipine as the drug of choice.
- ➔ In most feline hypertensive patients, the renin - angiotensin - aldosterone system is abnormally activated and should be suppressed with an ACE-inhibitor or aldosterone receptor blocker.
- ➔ Tachycardia not only contributes to hypertension but is also harmful to the cardiovascular system; persistent tachycardia should be managed with atenolol.

HOW I TREAT...



The relative prevalence of cardiac disease and hyperthyroidism seen at NCSU over a 5-year period. HCM= hypertrophic cardiomyopathy. HT₄= hyperthyroidism. RCM= restrictive cardiomyopathy. HiBP= systemic hypertension. CONGEN= congenital heart disease. HWD= heartworm disease. DCM= dilated cardiomyopathy. PER EF= pericardial effusion.

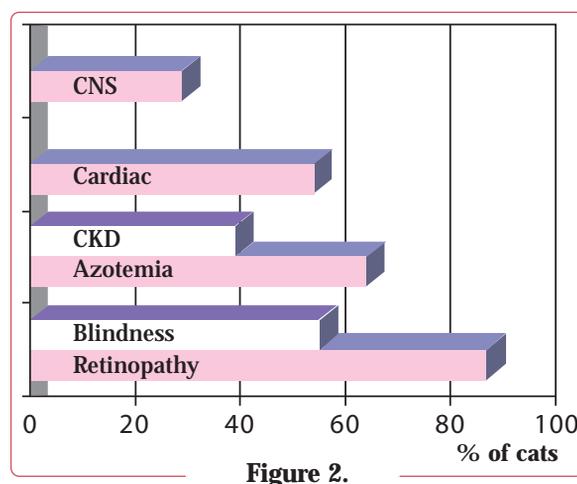
⊕ Pathogenesis

The pathogenesis of hypertension is complex, not well understood, and beyond the scope of this paper. However, several studies have indicated that the renin-angiotensin-aldosterone system (RAAS) is probably abnormally activated in many (if not most) cats with systemic hypertension, particularly with concurrent renal disease, and certainly after therapy with drugs such as loop diuretics and vasodilators (4-6). My therapeutic approach is based on target organ damage (present vs. absent, and, if present, which organ system(s) is in peril), and a brief review of the target organs of hypertension, and how they are injured, is appropriate.

Tissues such as the eye, brain and kidney are able to protect their microcirculation from pressure fluctuation by “autoregulation”. In the normal individual the glomerular pressure is maintained between 60-160 mmHg. However, in hypertension, this protective measure is lost and elevated systemic pressures are translated directly to the capillary beds, producing barotrauma.

Ocular damage

The eye is the organ at greatest risk because of its vulnerability to the insult. Hypertension disrupts the “blood-ocular barriers” and produces “protective” vasoconstriction; this is followed by secondary vascular hypertrophy/hyperplasia and vascular dysfunction with leakage of blood components into



Clinical diseases associated with hypertension in a study of 69 cats.

ocular tissues and fluids. Clinical findings include arteriolar tortuosity, retinal edema, hemorrhage, detachment, and hyphema (**Figure 3**). Blindness often results from the complications of intraocular hemorrhage (tractional retinal detachment, cataract, extensive vitreal hemorrhage, and secondary glaucoma) or, more commonly, from progressive neurosensory retinal degeneration. Blindness is usually, but not inevitably, permanent. If vision returns, it may be temporary; this is because retinal degeneration from progressive ischemic injury or excitotoxicity can develop, sometimes months afterwards. Early detection of hypertensive retinopathy is imperative, arguing strongly for yearly ophthalmic examination in aged cats.

Renal damage

Failure of renal autoregulation results in elevated intraglomerular capillary pressure and ongoing renal destruction. This may occur with acute or chronic kidney disease and, adding to the confusion in understanding the pathogenesis of hypertensive renal disease, renal disease begets hypertension and hypertension begets renal disease. Furthermore, activation of the RAAS contributes to renal damage. Not surprisingly, ACE-Inhibitors have been shown to spare the kidney by reducing intraglomerular pressures, inhibiting mesangial cell growth and fibrosis, and possibly by reducing proteinuria. The renal arteries and arterioles are themselves damaged and contribute to the pathogenesis (see vascular damage, below).

The kidney, like the eye, is an important target organ for hypertension, even if hypertension is secondary

HYPERTENSION

to renal disease. As renal disease is a major problem in the aging cat population, correction of hypertension is one way which the duration and quality of life can be improved. Yearly or more frequent fundic examination, urinalysis, microalbuminuria screening, and measurement of serum urea and creatinine, coupled with measurement of systemic blood pressure (BP), are essential in these cats.

CNS damage

With hypertension, the CNS also loses its ability to autoregulate. Cerebral blood pressure is normally maintained at 60-150 mmHg, but higher pressures affect the vasculature resulting in damage, leakiness, and cerebral edema, possibly with brainstem herniation (*Figure 4a*). Hypertension-induced over-perfusion also contributes to the edema. Vascular barotrauma may induce ischemia and brainstem or spinal cord hemorrhage (*Figure 4b*). Clinical signs may include cranial nerve lesions, seizures, somnolence, paralysis/paresis and behavioral abnormalities.

Vascular damage

Hypertension produces endothelial dysfunction with impaired vasodilation, thus worsening hypertension. Over time this results in vessel arteriosclerosis and hyperplasia of the myointimal layer, altering the vessels' ability to protect other target organs through autoregulation. Control of BP alone does not reverse these changes, but lowering BP, while blunting the RAAS, normalizes both vascular function and anatomy (7).

Cardiac damage

Hypertension and the concomitant vascular changes produce increased cardiac afterload. This is compounded by sympathetic nervous system (SNS) activation. Cardiac hypertrophy and fibrosis is produced by the combination of hypertension (increased afterload) and RAAS and SNS activation. A review of 99 hypertensive cats (Atkins, unpublished data) revealed that the vast majority had suffered cardiac changes (*Figure 5*), including auscultatory abnormalities (murmur and/or gallop), cardiomegaly, left ventricular hypertrophy and/or electrocardiographic evidence of hypertensive heart disease. Despite this, only 3% of these cats developed heart failure.

❖ Diagnosis of hypertension

Although a detailed discussion of the diagnosis of hypertension is beyond the scope of this work, a brief



Figure 3.

Ocular changes in a hypertensive cat. Note the tortuous retinal arteries, hyper-reflective retinal degeneration, and punctate retinal hemorrhage.

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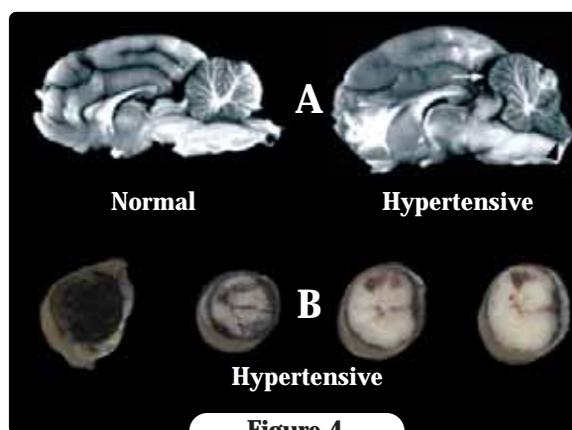


Figure 4.

A: Comparison of normal (left) and acutely hypertensive cat brain cut in sagittal section. There is cerebral edema and the swollen cerebellum (white arrow) has prolapsed through the foramen magnum producing a "coning" effect (black arrow).

B: Hypertensive spinal cord hemorrhage. Note there is both subdural and intrathecal hemorrhage.

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overview is pertinent. The veterinary profession has relied upon the Doppler method for determining BP in cats. Whilst thought to be more reliable than the oscillometric method for smaller patients, it has the distinct disadvantage of not providing diastolic or mean blood pressures in most instances. For this reason, we continue to explore the use of oscillometric equipment and newer units show promise for use in small dogs and cats. At NCSU, the tail is the appendage of choice for BP measurement, followed by the palmar surface of the front foot and finally the dorsal surface of the rear foot. Cuff width is important and should

HOW I TREAT...

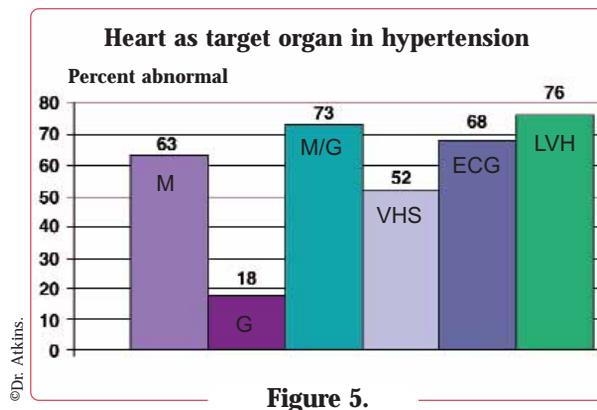


Figure 5.

Cardiac changes in 99 hypertensive cats. Note that there is a high prevalence of cardiac abnormalities. M= murmur. G= cardiac gallop. M/G= murmur and gallop. VHS= vertebral heart score. ECG= electrocardiographic abnormality. LVH= left ventricular hypertrophy, determined by echocardiography.

approximate to 30-40% of the circumference of the appendage used. Too small a cuff tends to over-estimate and too large a cuff to under-estimate true systemic BP. The cuff position should approximate the level of the heart. Current recommendations are that measurement should be done in a quiet area prior to examining the patient, typically in the presence of the owner and after 5-10 minutes of acclimatization. The ACVIM Panel on Hypertension suggests discarding the first measurement, then obtaining a minimum of 3, preferably 5-7, consecutive measurements with less than 20% variability in systolic BP. The conditions (including animal's disposition, cuff size, site and all measurements) should be recorded. Many clinicians require that hypertension be documented on more than one occasion before accepting the diagnosis. Note that in animals < 10 years of age the risk of "false positive" diagnosis is increased, especially in cats because of the high prevalence of "white coat" (stress-induced) hypertension in "normotensive" animals. The possibility of misdiagnosis is reduced if concurrent predispositions (e.g. renal disease) or findings (e.g. retinopathy or murmur) are detected.

What drugs are available?

Therapies for feline hypertension have varied and have rarely been systematically evaluated. Drugs that have been employed and/or reported upon include:

- Diuretics (furosemide and spironolactone).
- Angiotensin-converting enzyme inhibitors (ACE-I) (captopril, enalapril, lisinopril).

- Beta-blockers (propranolol and atenolol).
- Calcium channel blockers (diltiazem and amlodipine).

Various studies have reviewed different regimes; the literature and clinical experience leads one to conclude that amlodipine is the single best agent for managing feline systemic hypertension (1,8-11). This said, specific roles for other drugs can be identified; betablockers slow the heart rate and block the cardiovascular effects of T3 in hyperthyroidism; ACE-I combat drug-induced or spontaneous activation of the RAAS, preserve renal function (12,13), and lower BP (14,15); spironolactone counters the effects of aldosterone (16); and furosemide (possibly with nitroglycerin) aids heart failure secondary to hypertension.

Treating hypertension

It is important to consider the following factors; establishing if the RAAS is activated (initially or iatrogenically); assessing the role of the SNS; evaluating renal function and the effects of hypertension on renal function; noting salt intake; checking for heart failure (uncommon); investigating for reversible causes of hypertension (e.g. hyperthyroidism, diabetes mellitus, adrenal tumors); and establishing the target organ(s) affected or suspected to be at risk. I essentially divide cats as follows: reversible or irreversible cause; with or without presumed RAAS activation (RAAS activated in renal failure, heart failure, or with vasodilator or loop diuretic administration); presence or absence of tachycardia (> 200 bpm); and by target organ damage.

In all cases, I use a moderately salt-restricted diet (typically a renal diet) and avoid salt-laden fluids, such as lactated Ringers solution. This lessens total body sodium without worsening renal function or severely activating the RAAS, which can happen with heavily salt-restricted diets. I appreciate that salt restriction has minimal, if any, effect on blood pressure in the cat, but salt has been shown to play a permissive role in hypertensive cardiac disease.

Hyperthyroidism, the only common treatable cause of feline hypertension, is treated by standard methods. However because of the effects of T3 on beta receptors, I employ a beta-blocker such as atenolol (6.25-12.5 mg PO daily) to reverse the cardiovascular effects until more definitive therapy is efficacious, and if

HYPERTENSION

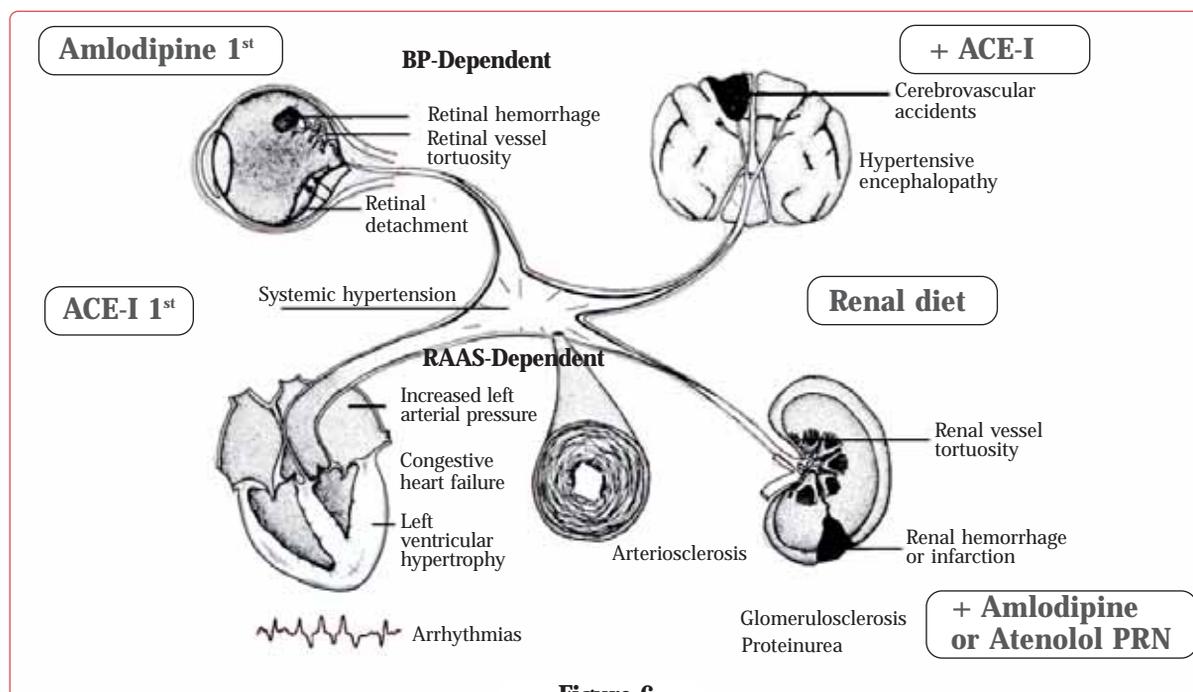


Figure 6.

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The approach to the management of systemic hypertension using target organ risk. The organs more susceptible to barotrauma and without obvious RAAS involvement are the eye and brain. The risk to these organs is generally more acute, and immediate reduction in blood pressure is desirable using amlodipine; an ACE-Inhibitor can be added either immediately or later. For organs such as the heart, arteries and kidneys, the acute risk is less and the RAAS is important in the damage to these target organs. For these reasons, an ACE-Inhibitor is instituted first, even though blood pressure decline may well be inadequate. Amlodipine (to ensure a decrease in blood pressure) or atenolol (to lower the heart rate) can be added as necessary. Lastly, a modest reduction in salt intake is instituted. PRN= pre-required need (19).

hypertension control is unsuccessful I add enalapril at 0.5 mg/kg/day PO.

In the euthyroid, non-tachycardic cat with hypertension, I simplify the approach by administering amlodipine and enalapril daily, 1 tablet in the morning and 1 in the afternoon if the owner's schedule allows. If hypertension is not controlled, first the amlodipine dosage is increased and/or other drugs such as beta-blockers are employed. When compliance is an issue and only 1 pill can be administered daily, amlodipine is the choice.

• Target organ damage

Using target organ damage as a criterion, my therapeutic approach is to employ amlodipine as a sole initial therapy if the barotrauma itself is probably the greatest detrimental effect (CNS and ocular lesions) and acute blood pressure reduction is necessary. An ACE-I is added later. If the kidneys, blood vessels, or heart are felt to be at greater risk, then I block the RAAS, typically with an ACE-I such as enalapril, with betablockers or amlodipine being added if further depression of blood pressure is necessary (Figure 6).

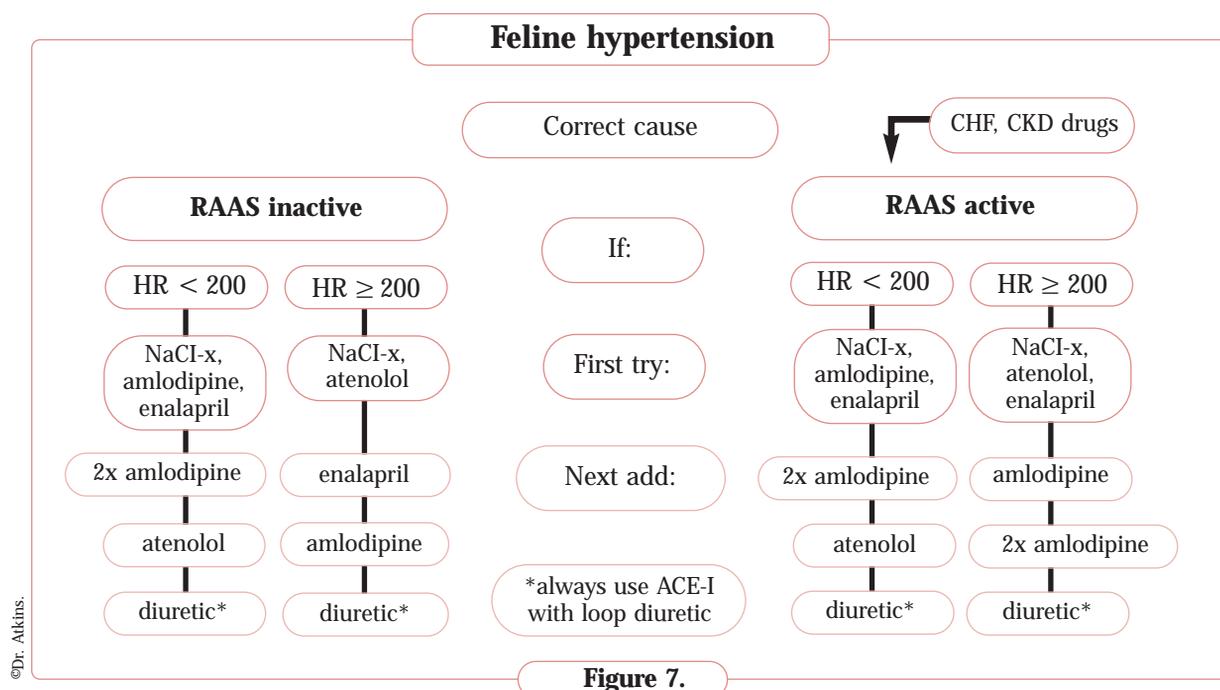
• RAAS activation

The RAAS is probably activated in most or all feline hypertensives. For this reason, though not the most effective class of drugs at lowering blood pressure, ACE-I are employed in most cases of hypertension. This is particularly apropos when one considers that amlodipine activates both the RAAS (6) and SNS (17). Betablockers are employed if persistent tachycardia is noted or, as mentioned above, with concurrent hyperthyroidism.

• RAAS not activated

If the RAAS is not thought to be activated (this may be an erroneous assumption) and tachycardia is not problematic, my approach is as follows: amlodipine (0.625-1.25 mg PO daily, or even higher if unresponsive) plus a moderately salt-restricted renal diet and enalapril (Figure 7). The ACE-I counteracts activation of the RAAS by amlodipine (6). If unsuccessful, I first double the dosage of amlodipine, then sequentially add atenolol and finally (rarely) add diuretics (furosemide 6.25-12.5 mg daily or spironolactone 1-2 mg/kg daily PO), if needed. It should be pointed out that in cats unresponsive to amlodipine plus a second drug,

HOW I TREAT...



An algorithmic approach to the management of feline hypertension using RAAS activation and heart rate to determine the course of action, but also considers target organ involvement. If the practitioner is unsure about RAAS activation, the safest approach is to assume that it is activated. NaCl-x= moderate salt restriction; HR= heart rate; CHF= congestive heart failure; CKD= chronic kidney disease.

owner compliance and BP measurement technique should be scrutinized.

If tachycardia is present (without RAAS activation), I begin with moderate salt restriction and atenolol. However even though heart rate typically falls, blood pressure control is often inadequate, in which case I sequentially add amlodipine plus enalapril, then, if needed, double the amlodipine dosage, and finally (rarely) add a diuretic. However if the tachycardia is not initially controlled, the atenolol dose is first increased. If this does not bring the exam room heart rate to < 160 or the at-home heart rate to < 140, I would substitute diltiazem (30 mg PO bid) for amlodipine to better control heart rate and then follow the same sequence mentioned above.

• RAAS abnormally activated

When conditions (heart failure, renal failure, or drug therapy) indicate the RAAS is inappropriately activated, I begin therapy with amlodipine, a moderately salt-restricted diet and enalapril (**Figure 7**). If a normotensive state does not result, I add, sequentially, increased amlodipine dosage, atenolol, and finally diuretics (furosemide or spironolactone).

Alternatively, if tachycardia is a concern, moderate salt restriction, atenolol, and enalapril would be used initially. If unsuccessful control of hypertension results, amlodipine would be added, and followed sequentially, as needed, by a doubling of the amlodipine dosage, and finally diuretic therapy if needed. If, after initial therapy, heart rate control is inadequate, the atenolol dose is first increased. If this does not adequately control heart rate, I would substitute long-acting diltiazem (30 mg PO bid) for amlodipine to better control heart rate and then follow the stepwise sequence mentioned above for blood pressure control, if needed. Heart failure secondary to hypertension is rare and will not be discussed except to note that diuretics will often be necessary in such patients to control signs and that enalapril is indicated.

Lastly, if renal failure or significant renal disease is present, the etiology should be sought (at least by urinalysis and culture) in the hopes of finding a reversible cause. Otherwise, treatment of renal disease is standard and beyond the scope of this article. It is wise to consider the routes of excretion of the drugs being used in deciding dosage and dosing interval in the face of renal insufficiency. Note that hypoten-

HYPERTENSION

sion may rarely occur due to over-exuberant anti-hypertensive therapy. This should be avoided as it may further compromise renal function.

🔍 Prognosis and conclusion

The prognosis for feline hypertension is guarded but not grave. Vision lost rarely returns. However, with diagnosis and treatment, survival averages have ranged from 18-21 months from the date of diagnosis (1,3). Data comparing survival times for

cats with hypertrophic cardiomyopathy (average age 6.5 years) (18) with those with treated hypertension (average age 14.8 years) (1) shows that survival times are not markedly different despite the differently aged cats. This argues strongly for vigilance, allowing early diagnosis and intervention in the hypertensive geriatric cat. This is best accomplished with twice yearly physical examination, fundic examination and blood pressure monitoring in cats over 10 years of age. 📌

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