

ISFM Consensus Guidelines on the Diagnosis and Management of Hypertension in Cats



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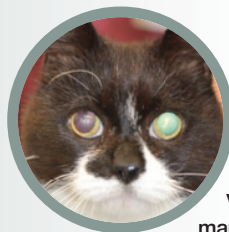
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Practical relevance: Feline hypertension is a common disease in older cats that is frequently diagnosed in association with other diseases such as chronic kidney disease and hyperthyroidism (so-called secondary hypertension), although some cases of apparent primary hypertension are also reported. The clinical consequences of hypertension can be severe, related to 'target organ damage' (eye, heart and vasculature, brain and kidneys), and early diagnosis followed by appropriate therapeutic management should help reduce the morbidity associated with this condition.

Clinical challenges: Despite being a common disease, routine blood pressure (BP) monitoring is generally performed infrequently, probably leading to underdiagnosis of feline hypertension in clinical practice. There is a need to: (i) ensure BP is measured as accurately as possible with a reproducible technique; (ii) identify and monitor patients at risk of developing hypertension; (iii) establish appropriate criteria for therapeutic intervention; and (iv) establish appropriate therapeutic targets. Based on current data, amlodipine besylate is the treatment of choice to manage feline hypertension and is effective in the majority of cats, but the dose needed to successfully manage hypertension varies between individuals. Some cats require long-term adjuvant therapy and, occasionally, additional therapy is necessary for emergency management of hypertensive crises.

Evidence base: These Guidelines from the International Society of Feline Medicine (ISFM) are based on a comprehensive review of the currently available literature, and are aimed at providing practical recommendations to address the challenges of feline hypertension for veterinarians. There are many areas where more data is required which, in the future, will serve to confirm or modify some of the recommendations in these Guidelines.

Introduction

Systemic arterial hypertension (referred to simply as hypertension in these Guidelines) is a well recognised condition in cats, but probably remains significantly underdiagnosed. The clinical consequences of hypertension can be severe, due to target organ damage (TOD) affecting the eyes, heart, brain and kidneys,¹ and some damage may be irreversible. Unless marked TOD is detected, the presence of hypertension is unlikely to be immediately apparent. Therefore, more widespread routine monitoring of feline blood pressure (BP) would likely enable an earlier diagnosis of hypertension and facilitate the prompt provision of effective therapy to prevent TOD and hopefully reduce the morbidity associated with hypertension.

Indirect measurement of BP in cats can be readily performed, although care is needed

with both the choice and use of the equipment to ensure meaningful and accurate results are obtained. Systolic blood pressure (SBP) has been shown to increase with age in cats,² as does the risk of hypertension.³ The majority of cats diagnosed with hypertension have other systemic disease(s) which may cause or contribute to the hypertension,^{3,4} although in up to 20% of cases no underlying cause is found.^{5–7} Cats with an underlying disease are often referred to as having 'secondary hypertension', although the relationship between the hypertension and the underlying disease may not always be understood. When secondary hypertension is found, there is a need to manage both the hypertension and the underlying disease concurrently.

These Guidelines have been created to offer practitioners up-to-date information on the causes, clinical signs, diagnosis and management of feline hypertension, as well as practical advice on measurement of BP and interpretation of results. Where clinical studies and scientific data are not available, the Guidelines represent consensus opinion of the Panel.




Regulation of blood pressure

Blood pressure (BP) is the product of cardiac output (CO), which in turn is the product of heart rate and stroke volume ($HR \times SV$), and systemic vascular resistance (SVR). Thus: $BP = HR \times SV \times SVR$.

In health, despite potential changes to blood volume, CO and SVR, complex neural and hormonal homeostatic mechanisms involving the brain, heart, vasculature and kidneys combine with local tissue factors to maintain BP within a relatively narrow range (Figure 1).

The predominant factor controlling SVR is arteriolar size, which is affected by many systemically circulating, local tissue and endothelial-derived factors (Figure 1).⁶ Blood volume is regulated by the kidneys, mainly through pressure natriuresis and the renin–angiotensin–aldosterone system (RAAS). Pressure natriuresis couples water and sodium excretion in response to changes in blood volume and CO (through alterations in renal perfusion), while the RAAS directly affects SVR via the potent vasoconstrictor angiotensin II, and affects blood volume through renal reabsorption of sodium and water via aldosterone.

Some organs, including the kidney, have the capacity to regulate their own BP ('autoregulation') to some extent. As a result, renal blood flow and glomerular filtration rate are maintained over a range of SBP (~80–160 mmHg). Outside of these limits, and also when significant kidney disease is present, direct transfer of elevated pressures to the glomerular capillaries results in glomerular hypertension and the potential for glomerulosclerosis.

Pathogenesis

The pathogenesis of feline hypertension remains poorly understood and will vary with differing aetiologies. Altered renal function, RAAS activation and pressure natriuresis likely play a role, but local factors (including local [tissue-specific] RAAS activation) are increasingly recognised as possible contributors.⁸ The good response seen in many hypertensive cats to the use of the vasodilator amlodipine^{5,6,9–15} suggests that increased vascular tone may be a common component of feline hypertension.

Blood pressure is labile and varies considerably within and between cats, depending in part on their level of arousal, activity or stress.



Classification of feline hypertension

Hypertension is classified as:¹

- ✦ Idiopathic (or primary) where there is no apparent underlying disease; or
- ✦ Secondary (thought to be due to underlying diseases or the use of therapeutic agents).

'White coat hypertension' is the increase in BP that occurs as a consequence of excitement- or anxiety-related sympathetic activation. This is important in veterinary medicine as the neurohormonal changes associated with the stress and/or excitement surrounding a veterinary visit can create a temporary physiological increase in BP.^{16,17}

Idiopathic hypertension

It is reported that 13–20% of hypertensive cats have idiopathic hypertension.^{5–7} Further work is required to determine the degree to which non-azotaemic chronic kidney disease (CKD) might be a factor in some of these patients, and whether there are environmental factors or genetic predispositions, as have been identified in humans with 'essential hypertension'.¹⁸

Secondary hypertension

Secondary hypertension may be seen with many diseases including CKD, hyperthyroidism, primary hyperaldosteronism (PHA), hyperadrenocorticism (HAC) and pheochromocytoma. Secondary hypertension is the most common form of hypertension seen in cats.

Chronic kidney disease

CKD is the most common condition associated with feline hypertension. Azotaemia has been found in up to 74% of hypertensive cats, and conversely between 19% and 65% of cats with CKD have been found to be hypertensive.^{19–22} However, the prevalence and severity of hypertension does not appear to be related to the severity of the CKD.^{2,19,23}

In humans, factors such as sodium and water retention, activation of the RAAS and the sympathetic nervous system, structural changes to arterioles, endothelial dysfunction,

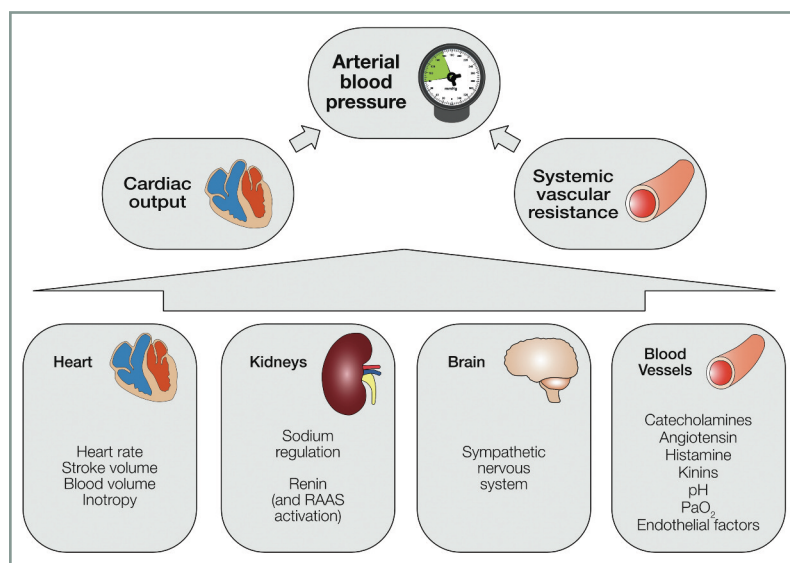


Figure 1 Overview of some of the important mechanisms involved in the regulation of blood pressure. RAAS = renin–angiotensin–aldosterone system

oxidative stress and genetics all play a role in the pathogenesis of CKD-associated hypertension.⁸

Less is known about the pathogenesis of hypertension in feline CKD, but the limited change in renin, aldosterone or BP in response to the use of angiotensin-converting enzyme (ACE) inhibitors,^{24,25} suggests systemic RAAS activation is unlikely to be the major factor involved. Elevated aldosterone independent of RAAS activation is recognised in some hypertensive humans, and may also play a role in cats with hypertension.^{13,26} Some mechanisms worthy of investigation in cats with CKD-associated hypertension include local (tissue-specific) RAAS activation (independent of systemic RAAS), and impaired sodium handling by the tubules or collecting ducts,^{18,27–29} although there is limited evidence to suggest salt-sensitive hypertension exists in cats.^{30–32} The profound response of cats with CKD-associated hypertension to amlodipine⁵ suggests that increased vascular tone may be particularly important, although this has not been specifically investigated.

Hyperthyroidism

Hypertension has been documented in 10–23% of cats with hyperthyroidism at the time of diagnosis,^{21,33–35} although some of these cats may also have had CKD. Additionally, nearly 25% of hyperthyroid cats normotensive at the time of diagnosis may develop hypertension after successful control of their hyperthyroidism.^{34–36}

The pathophysiology of hyperthyroid-associated hypertension remains poorly understood. Studies in other species suggest that hyperthyroidism may increase cardiac sensitivity to circulating catecholamines, and thyroid hormones may also have direct effects on cardiac myocytes.³⁷ Hyperthyroidism may also decrease SVR (through direct and indirect effects on blood vessels), with subsequent stimulation of the RAAS.³⁸ However, in studies of hyperthyroid cats, there is no evidence that RAAS activation causes hypertension, although RAAS dysfunction may be present in some cats that develop hypertension after treatment for their hyperthyroidism.³⁶

Primary hyperaldosteronism

PHA is an excess of aldosterone independent of its regulator, angiotensin II. Hypertension is reported in around 40–60% of cats with PHA.^{39,40} It could initially be the consequence of sodium retention and volume expansion leading to increased CO, but sustained hypertension should result in pressure natriuresis, returning plasma volume to normal. This, together with the fact that not all cats with PHA develop hypertension, suggests

that other mechanisms are involved;⁴¹ potentially these include effects on blood vessels, vascular tone, vascular remodelling and responses to sympathetic stimulation.^{42–44}

Other diseases

Diabetes mellitus (DM) is a well recognised risk factor for hypertension in humans, but there is little current evidence to show the same is true in cats, although further work is needed. Severe hypertension in cats with DM appears uncommon,^{7,45} and the prevalence of hypertension in cats with DM is typically low, but often confounded by the presence of concomitant conditions such as CKD.^{7,46} However, BP in cats with DM has been found to be higher than in healthy, age-matched controls,⁴⁷ and hypertensive ocular disease has occasionally been reported in diabetic cats with no other underlying cause identified,⁷ suggesting a link could exist.

Phaeochromocytomas are rare tumours in cats^{48–52} associated with excessive circulating catecholamines, and can result in sustained or paroxysmal bouts of hypertension. There is also a report of severe hypertension in a cat associated with HAC,⁵³ although the prevalence of hypertension in cats with this disease is unknown.

Consequences and clinical signs of hypertension

Hypertension is most likely to cause disease in tissues with a rich arteriolar supply^{1,54} and in the cardiovascular system as a result of increased SVR.^{1,54} The eyes, brain, kidneys and myocardium are thus particularly vulnerable to hypertensive injury (TOD).^{1,20,54} Clinical manifestations of TOD can be striking and may be the reason for presentation to the veterinarian.^{7,20,55} However, TOD is not always present and in some cats clinical signs of their underlying disease may predominate^{5,19,56} or there may be no overt clinical signs.

Target organ damage: eyes

Hypertensive ocular changes have been reported in approximately 50% of hypertensive cats,^{6,21,22,57} and studies suggest that retinal changes can develop at an SBP of approximately 160 mmHg and above.^{58,59} However, the high prevalence of reported ocular lesions may reflect the relatively late diagnosis of hypertension in many studies.

The retina and choroid have separate blood supplies and both can suffer hypertensive damage,⁶⁰ with an array of fundic lesions visible on ophthalmoscopy.^{7,61}

✦ Hypertensive retinopathy can manifest as haemorrhages of varying size and number^{21,55} (Figure 2).



Ocular lesions not associated with an impaired menace response or pupillary light deficits are more amenable to anti-hypertensive treatment, hence early diagnosis is key.

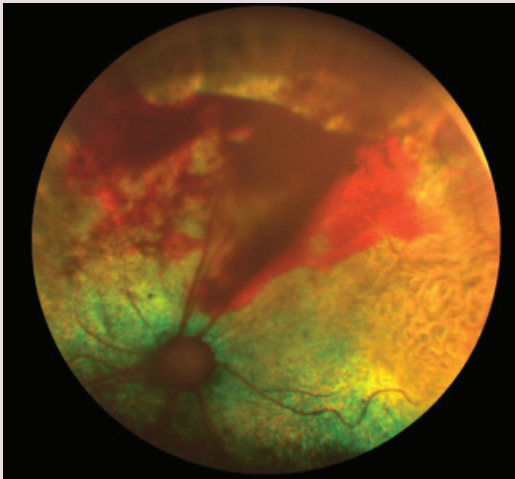


Figure 2 SBP 182 mmHg. Left eye. Dorsal to the optic nerve head is substantial fresh vitreal haemorrhage. There are also some areas of retinal thinning and laterally there is retinal degeneration

Ocular changes have been reported in approximately 50% of hypertensive cats.

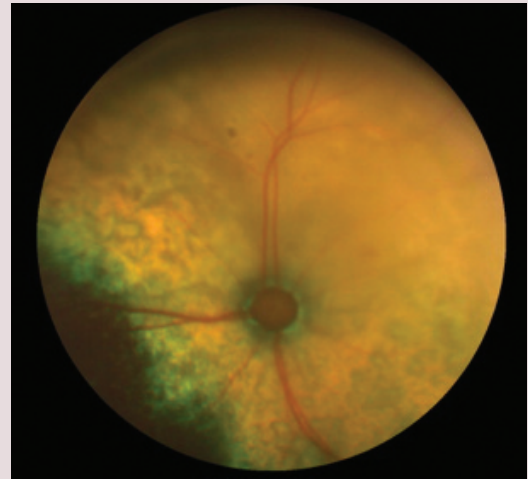


Figure 3 SBP 172 mmHg. Left eye. Note the generalised tapetal retinal oedema and retinal vessel attenuation. Throughout the tapetal fundus there are areas of hyperreflectivity due to retinal thinning and hyporeflexivity because of localised retinal oedema

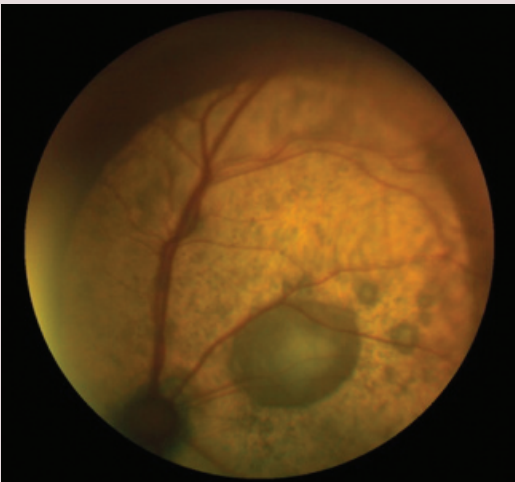


Figure 4 SBP 170 mmHg. Left eye. There is a large bullous retinal detachment, with several smaller foci of detachment lateral to this. Throughout the fundus are multifocal areas of pigmentary disturbance



Figure 5 SBP 195 mmHg. The right eye of this cat has vitreal haemorrhages present; the fundus was not visible

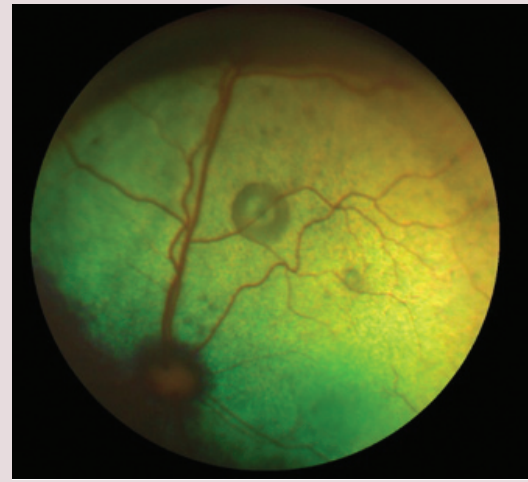


Figure 6 SBP 167 mmHg. Left eye. Note the large bullous retinal lesion associated with a blood vessel; smaller bullous lesions are also present. This eye had an intact menace response and pupillary light reflex, and was completely visual

- ❖ Hypertensive choroidopathy can cause changes in the appearance of the retinal vessels.⁷ Retinal oedema and breakdown of the blood–ocular barrier in the retinal pigment epithelium can create the impression that the vessels, particularly the arterioles, are narrowed⁶¹ (Figure 3).
- ❖ Hypertensive choroidopathy can also cause retinal detachment, which can appear bullous, flat, or may involve the whole retina⁶¹ (Figure 4), with the overlying retinal arterioles often appearing more tortuous than normal.⁶¹ Photoreceptors often sustain irreversible damage from retinal detachment.⁶²
- ❖ Hypertensive optic neuropathy is diagnosed rarely in cats, possibly because the nerve head appears recessed, making pathology more difficult to appreciate.⁶¹

Other ocular signs associated with hypertension include hyphaema and vitreal haemorrhage (Figure 5),⁷ and hyphaema can in turn lead to secondary glaucoma.⁵⁵

Many cats with severe hypertensive ocular damage present with blindness and bilateral mydriasis resulting from complete retinal detachments and/or intraocular haemorrhage; the changes are often irreversible.^{7,20,21} Lesions that are not associated with an impaired menace response or pupillary light deficits (Figure 6) are much more amenable to anti-hypertensive treatment,⁷ highlighting the importance of early diagnosis and management. Detection of early hypertensive ocular lesions requires an ocular examination to be performed on all cats at risk of developing lesions.

Target organ damage: brain

Hypertensive encephalopathy occurs when BP is high enough and sustained long enough to overcome the autoregulatory ability of the cerebral vasculature.⁶³ Cerebral oedema and arteriosclerosis have been described in cats with hypertensive encephalopathy.^{64,65} Studies have reported neurological signs in 15–46% of hypertensive cats,^{7,20,57,66,67} including disorientation, seizures, ataxia, depression and vestibular signs. Confirmation that clinical signs are due to hypertension is rarely achieved without advanced imaging, but a presumptive diagnosis can be made if signs improve following normalisation of BP.⁶⁵ Anecdotally, owners often report improvement in some behavioural signs (eg, depression, lethargy) after antihypertensive therapy.

Target organ damage: heart and vasculature

The elevated SVR associated with hypertension can increase left ventricular wall stress and result in concentric left ventricular hypertrophy (LVH). This may commonly produce auscultatory abnormalities such as gallop sounds, and perhaps less commonly murmurs and arrhythmias, in hypertensive cats.^{7,20,57} Echocardiography frequently reveals LVH,^{57,68} although the degree of hypertrophy does not correlate with the magnitude of hypertension.⁶⁹ Occasionally severe complications such as heart failure^{7,20} or aortic dissection^{70,71} have been reported in affected cats.

Target organ damage: kidneys

A controlled study of over 200 cats demonstrated increased glomerulosclerosis and arteriosclerosis in cats with higher BP,⁷² supporting the concept of kidney TOD in feline hypertension. However, such lesions are not solely caused by hypertension; and, as many cats with hypertension have concomitant CKD, the importance of hypertension in causing nephrosclerosis and in causing or contributing to the progression of CKD remains uncertain.⁷³

There is an association between SBP and the magnitude of proteinuria in cats with CKD,⁷⁴ and treatment with amlodipine reduces the proteinuria.⁶ This may be important, as proteinuria has been linked to reduced survival in cats with either CKD^{74,75} or hypertension,⁶ although managing hypertension has not yet been demonstrated to provide a survival benefit. In contrast, hypertension is recognised as both an important causal factor in human CKD, and a factor contributing to disease progression in human and canine CKD.^{8,76}

Panel recommendations

Monitoring blood pressure in cats

| Category | Frequency of SBP monitoring |
|--|--|
| Healthy adult cats (3–6 years of age) | Consider every 12 months* |
| Healthy senior cats (7–10 years of age) | At least every 12 months |
| Healthy geriatric cats (≥11 years of age) | At least every 6–12 months |
| Cats with recognised risk factors including: | Measure immediately and reassess at least every 3–6 months |
| ❖ Underlying diseases: CKD, hyperthyroidism (including treated cats), PHA, HAC, phaeochromocytoma, etc | |
| ❖ Drug therapy (eg, erythropoietin) ^{77,78} | |
| ❖ Evidence of TOD | |

*The main purpose of monitoring in this age group is to obtain baseline measurements for the individual cat. As few cats in this age category have hypertension, great care is needed in the interpretation of elevated BP measurements, especially in the absence of TOD or a clear underlying disease. SBP = systolic blood pressure; CKD = chronic kidney disease; PHA = primary hyperaldosteronism; HAC = hyperadrenocorticism; TOD = target organ damage

More widespread routine monitoring of blood pressure would likely reduce the morbidity associated with hypertension in cats.



Patient groups benefiting from blood pressure measurement

Hypertension is much more common in older cats (>10 years old), with current studies suggesting a median age at diagnosis of 13–15 years,^{6,7,57} although it has been reported in cats as young as 5–7 years.^{7,12,20,22,53,59,65} As early diagnosis (and management) of hypertension is considered valuable to help prevent TOD, this data helps to provide a rationale for which cats should undergo routine BP assessment (Table 1).

Additionally, as secondary hypertension is common in cats, individuals with recognised risk factors such as CKD, hyperthyroidism or PHA should undergo more frequent BP measurement. Further, the presence of any unexplained disease compatible with hypertensive TOD (eyes, brain, kidneys and heart) warrants careful BP assessment.

Recommended equipment and procedures for measuring blood pressure

Direct assessment of BP (via arterial cannulation) accurately measures SBP, diastolic blood pressure (DBP) and mean arterial pressure (MAP). Radiotelemetric implants allow direct BP measurements to be monitored over time in conscious animals, without direct intervention. However, this technique is not practical for clinical use in client-owned cats.^{54,79}

Equipment for routine clinical use

In clinical settings and with conscious cats, BP is usually measured using indirect techniques such as Doppler sphygmomanometry (Figure 7a) or oscillometry. The Doppler technique has been extensively used in feline medicine, with investigators demonstrating good correlation and accuracy compared with direct BP assessment.⁸⁰ It has been shown that traditional oscillometry is less accurate than Doppler in conscious cats, often underestimating BP at higher values, and there are many cats for which it is difficult or impossible to achieve BP measurements with this equipment.^{80–85}

Recently, high-definition oscillometry (HDO) equipment (Figure 7b) has been developed to overcome the problems of traditional oscillometry. Although there are fewer reports of its use in cats, it has been compared with direct BP assessment in conscious cats over a range of different BPs and has shown to provide accurate results.⁸⁶ It also appears that there are fewer cats for which it is difficult to obtain a reading compared with traditional oscillometry.^{86,87}

It should be noted that neither the Doppler nor HDO technique has been fully validated according to the ACVIM 2007 criteria.^{1,88} Although HDO equipment will generate figures for SBP, DBP and MAP, it has been shown that in conscious cats it is only the SBP value that has acceptable accuracy.⁸⁶ Further, although DBP can be measured with Doppler equipment, this measurement also lacks acceptable accuracy and repeatability.^{80,89} However, systolic hypertension is generally thought to be the most clinically important form of hypertension; although isolated diastolic hypertension may occur in cats,¹ the limitations of current measurement methodologies make this challenging to diagnose and any clinical significance uncertain.

As in other species, BP in cats is labile and varies considerably within and between individuals, depending in part on their level of arousal, activity or stress.^{16,79,90} Clinical assessment of SBP is also affected by many external variables including the operator, conditions, environment, equipment, position of the cat, size of the cuff, and site of measurement.^{16,17,80,81,87,89,91–94}



Figure 7 Examples of (a) Doppler sphygmomanometry and (b) high-definition oscillometry (HDO) equipment

Defining normal blood pressure

Some studies have evaluated direct SBP, DBP and MAP in healthy cats using radiotelemetry (Table 2), the results of which were not dissimilar to those of other mammalian species, including humans.^{16,79,90,95} These studies also highlight the lability of feline BP in individual cats, with one demonstrating up to 80 mmHg change in SBP in response to a simulated clinic visit,¹⁶ showing the potential magnitude of ‘white coat hypertension’ in healthy cats.

(‘Defining normal blood pressure’ continues on page 296)

Table 2 Direct blood pressure measurements (mmHg) in studies of healthy conscious cats

| Study (number of cats) | SBP mean ± SD | MAP mean ± SD | DBP mean ± SD |
|--|------------------|------------------|------------------|
| Brown et al (n = 6) ⁹⁵ | 125 ± 11 | 105 ± 10 | 89 ± 9 |
| Belew et al (n = 6) ¹⁶ | 126 ± 9 | 106 ± 10 | 91 ± 11 |
| Slingerland et al (n = 21) ⁷⁹ | 132 ± 9 | 115 ± 8 | 96 ± 8 |
| Mishina et al (n = 16) ⁹⁰ | 117 ± 12 | 94 ± 11 | 78 ± 10 |

SBP = systolic blood pressure; MAP = mean arterial pressure; DBP = diastolic blood pressure

Panel recommendations

Use of equipment and procedures

- ❖ For assessment of BP and hypertension in conscious cats, either Doppler sphygmomanometry or HDO equipment should be used.
- ❖ Only SBP measurements should be used for clinical assessment. (DBP and MAP readings are less accurate and should generally be ignored.)
- ❖ Use of standardised protocols (see pages 294–295 for Panel recommendations) is imperative to improve the accuracy and reproducibility of measurements.



Panel recommendations

Standardised protocols to assess SBP in cats

Environment

- ❖ The cat should be in a calm quiet room, away from other animals.
- ❖ In a calm and quiet environment, SBP can sometimes be measured in hospitalised cats while they are in their cage.
- ❖ Have the cat resting on its own bedding (with its own scent) and/or consider using a synthetic facial pheromone (Feliway; Ceva) in the environment or on the bedding, which may help to reduce stress.⁹⁶

Acclimatisation

- ❖ Allow the cat at least 5–10 mins in the room to acclimatise.¹⁷
- ❖ The cat should be free to explore the room and interact with people.
- ❖ A cat carrier with a removable top will allow the cat to stay in the bottom of the carrier if it prefers.

Personnel

- ❖ Use the minimum number of people necessary (usually two).
- ❖ Having the owner present may be valuable if they are able to reassure the cat in a quiet, gentle way.
- ❖ Having a trained, experienced individual measure SBP improves reproducibility of results.⁸⁹
- ❖ A nurse or technician who is empathetic with cats may often be the best person to measure SBP.

Restraint and positioning of the cat

- ❖ Use of minimal and gentle restraint is vital.
- ❖ Cats should be in a settled, relaxed, comfortable position.
- ❖ If the cat becomes agitated, stop and let it settle rather than use firmer restraint.
- ❖ Try to keep the cat in the same position throughout the procedure.
- ❖ Avoid measuring BP while the cat is moving.

Choice and position of cuff

- ❖ The site for BP measurement will depend partly on what is tolerated best by the cat, but the forelimb may be better for Doppler measurements⁹¹ while the tail is better for HDO⁸⁷ (Figure 8).
- ❖ The cuff width for cats should be 30–40% of the circumference of the limb/tail where it is used.⁹³
- ❖ Cuffs are usually secured with a Velcro fastener; fit them snugly but avoid restricting blood flow. A small piece of adhesive tape may also be used if necessary, but this should never be wrapped around the limb/tail.
- ❖ Where possible, the site of BP measurement should be roughly on the same horizontal plane as the heart.
- ❖ Handle and manipulate limbs gently – older cats especially may suffer from osteoarthritis.

Using Doppler equipment

- ❖ Detection of blood flow requires good contact between the Doppler probe and the skin. This is best achieved with alcohol to dampen the hair and skin, and the use of plenty of ultrasound gel.
- ❖ Clipping the hair at the site is not usually necessary. It may be considered if detection of blood flow is difficult, but use quiet clippers and allow the cat time to settle before measuring BP.
- ❖ Ensure the inflatable portion of the cuff is positioned over the artery to be occluded.
- ❖ Using headphones to avoid sound from the Doppler unit disturbing the cat is highly recommended; if not available, ensure the volume is turned down when the procedure starts, and use the lowest volume needed to hear pulsatile blood flow.
- ❖ Position the Doppler probe with gentle pressure to avoid restricting blood flow, and adjust the position slowly until pulsatile blood flow is heard.
- ❖ Inflating and deflating the cuff a few times before making recordings helps the cat to get used to the sensation.
- ❖ Slowly inflate the cuff to 20–40 mmHg above the point where blood flow is no longer heard.
- ❖ Allow air to slowly bleed from the cuff. SBP is the point at which pulsatile blood flow is first detected.



Figure 8 Positioning of the cuff for blood pressure measurement. Forelimb (a) and tail (b) for Doppler measurement; tail (c) for measurement by high-definition oscillometry

Continued from page 294

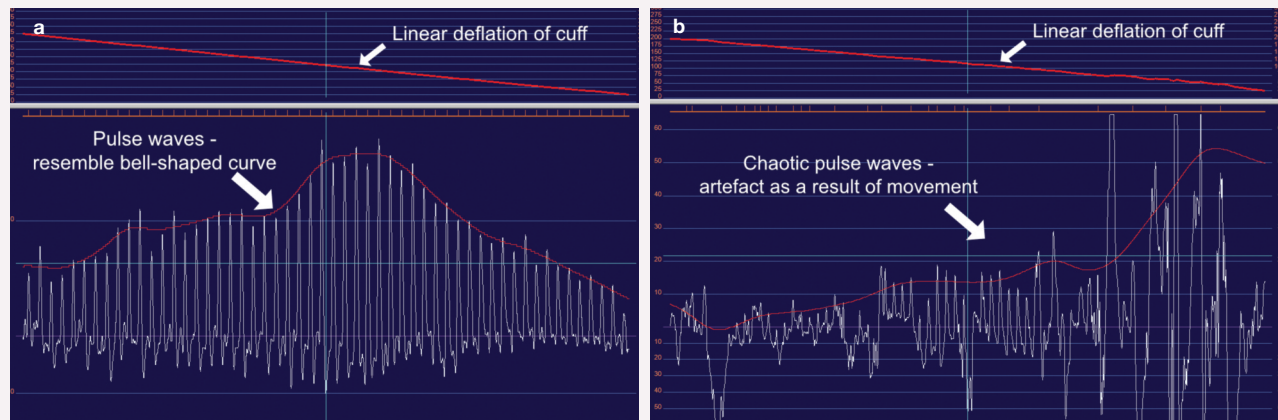


Figure 9 HDO traces recorded on a computer. (a) Good trace, providing a reliable reading. (b) Poor trace showing interference (as a result of patient movement)

Using HDO equipment

- ❖ Patient movement can readily cause false SBP readings. Using the tail and ensuring the cat is as still as possible helps to reduce this error.^{86,87}
- ❖ The area where the inflation tube enters the cuff should be placed closest to the artery, as this maximises the sensitivity of the HDO equipment.
- ❖ When the machine is activated, the cuff will automatically inflate and deflate at a constant rate, and BP values will be generated. Only the SBP should be used.
- ❖ The HDO device should always be linked to a desktop computer or tablet – this allows confirmation that the deflation of the cuff is steady and that the pulse waves are smooth, with an outline approximating a bell-shaped curve (Figure 9a). If these criteria are not met, the reading should be discarded as unreliable (eg, due to movement artefact; Figure 9b).

Taking and interpreting measurements

- ❖ The first SBP measurement is usually discarded. Subsequently, ideally five to seven consecutive and consistent (<20% variability) measurements should be made and SBP calculated as the mean of these.
- ❖ All readings should be recorded, whether or not used to calculate SBP.
- ❖ If there is a consistent downward (or upward) trend in readings, or $\geq 20\%$ variation, further measurements should be made until consistent readings are achieved, using only the consistent readings to calculate the average SBP.
- ❖ If there is doubt over SBP validity, the procedure should be repeated – either immediately, after further acclimatisation, or later. Consider also changing the position of the cuff, and reassess the environment for causes of stress.

Consistency

- ❖ Careful records should be kept (Figure 10).
- ❖ For meaningful SBP comparisons in a cat, the assessment should be replicated using the same equipment, personnel and procedures as far as possible each time.

Blood pressure evaluation form

| | | | |
|-------|-------------|--------|------------|
| Date: | Cat's name: | Owner: | Clinician: |
| Age: | Sex: | Breed: | Time: |

Position of the cat:

Sitting

Standing

Sternal

Lateral

Other (specify):

Site of the cuff:

Right forelimb

 Left forelimb

Right hindlimb

 Tail

 Left hindlimb

| | |
|-------------------------|------------------------|
| Equipment used: | Size of cuff: |
| Location (room): | Others present: |
| Performed by: | |

Subjective assessment of stress:

Relaxed
 Slightly tense
 Nervous
 Very nervous
 Agitated

Record of all SBPs measured (mmHg):

| | | | | |
|----|----|----|----|-----|
| 1. | 2. | 3. | 4. | 5. |
| 6. | 7. | 8. | 9. | 10. |

Mean Systolic Blood Pressure (mmHg):
Mean of stable values above (ignore outliers)

Figure 10 Example of a blood pressure assessment form. This document is available to download from jfms.com as a supplementary material file

The ISFM has produced a set of videos on measuring blood pressure in cats – see page 300 for more information.

Table 3 Indirect SBP (mmHg) measurements in studies of healthy conscious cats

| Equipment used (number of cats) | SBP (mean ± SD) |
|--|-----------------|
| Traditional oscillometry* | |
| Bodey and Sansom (n = 104) ⁵⁶ | 139 (± 27) |
| Mishina et al (n = 60) ⁹⁴ | 115 (± 10) |
| Curtet et al (n = 72) ⁹² | 123 |
| Morar et al (n = 54) ⁹⁷ | 124 |
| Haberman et al (n = 13) ⁸⁰ | 133 (± 28) |
| Doppler sphygmomanometry | |
| Kobayashi et al (n = 33) ¹⁹ | 118 (± 11) |
| Sparkes et al (n = 50) ¹⁷ | 162 (± 19) |
| Lin et al (n = 53) ⁹⁸ | 134 (± 16) |
| Bijsmans et al (n = 124) ² | 131 |
| Conti et al (n = 30) ⁹¹ | 135 (± 21) |
| Haberman et al (n = 13) ⁸⁰ | 146 (± 50) |

*Note that traditional oscillometry is not suitable for assessing clinical hypertension as it tends to underestimate BP at higher values, and produces less reliable readings – see text
BP = blood pressure; SBP = systolic blood pressure

Establishing reference intervals for estimated SBP in healthy cats using Doppler or oscillometric equipment is fundamental to the clinical diagnosis of hypertension, and also for determining therapeutic targets in affected cats. Results of studies in healthy cats are shown in Table 3, but it should be noted that there is a wide discrepancy between different studies; this reflects, at least in part, the different populations examined, and differences in types of equipment and the way equipment was used. Thus, having a standardised technique is of paramount importance.

Table 4 International Renal Interest Society staging for SBP¹⁰³

| SBP (mmHg) | Category | Risk of TOD |
|------------|-------------------------|-------------|
| <150 | Normotensive | Minimal |
| 150–159 | Borderline hypertensive | Low |
| 160–179 | Hypertensive | Moderate |
| ≥180 | Severely hypertensive | High |

SBP = systolic blood pressure; TOD = target organ damage

A recent large longitudinal study showed a small, but significant, increase in blood pressure as cats age: ~1–2 mmHg a year for cats >9 years old.



Unlike in humans, to date in feline medicine no gender effects on BP have been identified;^{56,94} in addition, there are no documented breed effects on feline BP.^{56,94} Similar to humans, however, a recent large longitudinal study of cats established a small but significant increase in BP as cats age,² equating to ~1–2 mmHg per annum for cats >9 years old. Humans with a higher baseline BP may be at increased risk of future development of hypertension (termed pre-hypertension),^{99–101} and there is evidence that the same may be true of cats.²

The majority of cats reported in the literature to have TOD associated with hypertension have had indirect SBP measurements in excess of 160 mmHg,^{5,7,14,20,22,53,55–57,59,64,65,71,102} although there are occasional exceptions to this.⁵⁸ The International Renal Interest Society (IRIS) has proposed four categories of BP in cats – based on potential risk of TOD – to help with the diagnosis of hypertension (Table 4).¹⁰³ However, along with the lability of BP already noted, it is likely the TOD in hypertension will not only be related to the severity of the hypertension, but also to the duration and relative change in BP that occurs, thus strict categorisation is problematic.

Panel recommendations

Criteria justifying antihypertensive therapy

While individual circumstances should always be carefully assessed, based on current knowledge the Panel suggests that antihypertensive therapy is generally justified if SBP is measured carefully (see pages 294–295) and when:

- ✦ Indirect SBP is ≥150 mmHg on a single occasion, and there is clear evidence of ocular or neurological TOD. Note: if clinical signs do not respond appropriately to adequate antihypertensive therapy, the diagnosis should be reassessed and other potential causes of the signs investigated.
- ✦ Indirect SBP is ≥160 mmHg on at least two separate occasions, and there is evidence of TOD including ocular, neurological, cardiac or kidney damage.
- ✦ Indirect SBP is ≥170 mmHg on at least two separate occasions, and the clinician does not consider ‘white coat hypertension’ is likely to be the cause.
- ✦ Indirect SBP is <150 mmHg, but there is clear evidence of active ocular TOD. Note: cats should be monitored carefully. If there is any doubt about the diagnosis of hypertension, the need for long-term therapy should be reassessed by trial withdrawal of therapy once stable, and monitoring of BP and clinical signs.

Cats with SBP <150 mmHg and evidence of potential TOD should have their clinical signs and BP monitored carefully, and other possible causes of the signs investigated.

Panel recommendations

Investigation of hypertensive cats

Along with measuring SBP, hypertensive cats should be carefully evaluated for both TOD and the presence of underlying disease. Assessments should include:

- ❖ **Complete physical examination** (including thorough cardiac, neurological and ocular assessment, including indirect ophthalmoscopy) and **thorough clinical history**. Indirect ophthalmoscopy is a very valuable technique and readers are referred elsewhere for full details¹⁰⁴
- ❖ **Laboratory evaluation** to identify any underlying disease(s):
 - Serum creatinine and/or SDMA*
 - Urinalysis, including specific gravity and quantitative proteinuria assessment
- Serum thyroxine
- Serum sodium, potassium and chloride
- ❖ **Additional investigations** that may be of value include:
 - Diagnostic imaging (cardiac and abdominal imaging)
 - Serum aldosterone (ideally with measurement of renin or renin activity)
 - Further endocrine testing where appropriate (eg, dynamic adrenal function testing, glucose monitoring)

*SDMA (symmetric dimethylarginine) is a renal biomarker

Routine treatment of hypertension

Whenever hypertension is diagnosed, it is important to search for, and treat, underlying diseases as most cases of feline hypertension are secondary. Treatment of underlying diseases is outside the scope of these Guidelines, but does not obviate the need for appropriate antihypertensive therapy.

The goal of therapy for hypertension is to decrease the risk of TOD, and help maintain or improve the health of the cat. This is generally achieved with an initial target SBP of <160 mmHg.¹ Given that the IRIS group¹⁰³ suggests the risk of TOD is minimal if SBP is <150 mmHg, and that some cats with TOD have pressures below 160 mmHg, a target of <150 mmHg may be an appropriate long-term goal.

Amlodipine besylate

Based on current data,^{5,6,9,11,12,14,66} the dihydropyridine calcium channel blocker amlodipine besylate is the drug of choice for the management of hypertension in cats, and there is

now a product licensed for feline use in some countries.

Amlodipine is a potent peripheral arterial dilator that acts directly on vascular smooth muscle, causing a reduction in SVR and BP with minimal cardiac effects.¹⁵ The reduction in SBP following treatment of hypertensive cats is generally around 30–70 mmHg,^{5,6,11,12,14,66} with 60–100% of cats responding to amlodipine as a monotherapy, albeit with dose adjustment being needed in some.^{5,6,9,12,14} Amlodipine has also been shown

Dosing of amlodipine

Amlodipine has typically been used orally, at a starting dose of 0.625 mg/cat (0.125 mg/kg) q24h, with doubling of the dose if the response is inadequate within 1–3 weeks.^{5,6,9,11,12,14,66} The reduction in SBP appears to be dose-related;^{9,105} thus cats with a higher SBP (eg, ≥ 200 mmHg) may benefit from a starting dose of 1.25 mg/cat (0.25 mg/kg) q24h.^{9,105} Infrequently, higher doses of amlodipine (up to 2.5 mg/cat or 0.5 mg/kg q24h) may be needed,¹² but compliance should be checked as few cats appear to require these doses.^{5,6,9,11,12,14,66} Transdermal amlodipine has also been used in cats,⁶⁷ but may be less effective than oral therapy and further studies are required to determine optimum dosage and formulation.

Figure 11 (a) 18-year-old, female, domestic shorthair cat with an SBP of 180 mmHg. Left eye. There is a large bullous retinal detachment medial to the optic nerve head. Also focal areas of retinal oedema lateral to the optic nerve head, with an area centrally that has coalesced to form a region of serous retinal detachment. (b) Same eye, 10 weeks after commencing amlodipine besylate treatment (current dose 1.25 mg q24h). The bullous lesion has resolved and the area of serous retinal detachment appears now as a hyporeflective, thickened area of the retina

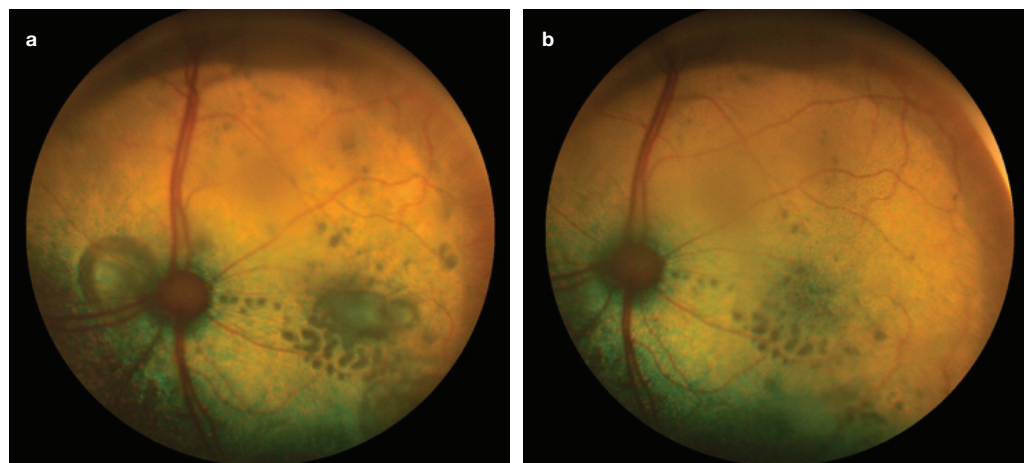


Table 5 Drugs used for management of feline hypertension

| Drug | Suggested dose | Comments |
|-------------|--|--|
| Amlodipine | 0.625–1.25 mg/cat (0.125–0.25 mg/kg) q24h PO | Calcium channel blocker and drug of first choice. Dose may be doubled if response is inadequate up to a maximum of 2.5 mg/cat (0.5 mg/kg) q24h ^{1,12} |
| Benazepril | 0.5–1.0 mg/kg q24h PO | ACE inhibitor ^{24,25,108,110} |
| Enalapril | 0.5 mg/kg q12–24h PO | ACE inhibitor ^{24,25} |
| Ramipril | 0.125–0.25 mg/kg q24h PO | ACE inhibitor ¹⁰⁶ |
| Telmisartan | 1 mg/kg q24h PO (experimentally, a dose of 3 mg/kg produced a greater effect on blood pressure) ¹⁰⁷ | ARB, licensed at 1 mg/kg q24h in some regions for management of CKD-associated proteinuria. Not assessed clinically for managing feline hypertension, but one study showed greater response than benazepril to angiotensin I-induced pressor response when given at 1–3 mg/kg ¹⁰⁷ |
| Atenolol | 1–2 mg/kg q12h PO | β -blocker ¹⁰⁹ |

PO = orally; ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker

to reduce the magnitude of proteinuria in hypertensive cats with CKD.^{6,74} Adverse events associated with amlodipine therapy appear to be uncommon.^{12,15} Although hypotension is a rare complication,^{5,15} monitoring of SBP is always recommended.¹⁵

Other treatments

ACE inhibitors,^{24,25,106–108} angiotensin receptor blockers (ARBs)¹⁰⁷ and beta-blockers⁴ have all been used to treat feline hypertension. They appear to have poorer efficacy in reducing SBP than amlodipine (typically only achieving a reduction in SBP of 10–20 mmHg),^{24,25,106–109} and fewer cats respond adequately to their use as monotherapy. These drugs are, therefore, best considered as second (or occasionally third) agents to add in to therapy if treatment with amlodipine is not sufficient to control the SBP (Table 5),¹¹⁰ or if their use is indicated by any concurrent or underlying disease.

The choice of adjunctive therapy to help manage hypertension may in part be dictated by any concurrent or underlying disease. For example, ACE inhibitors or ARBs may be indicated in CKD patients to help manage proteinuria; atenolol may be indicated in some hyperthyroid cats to manage tachycardia; prazosin (an alpha-adrenergic blocker) may be indicated in phaeochromocytoma; and spironolactone in hyperaldosteronism. These drugs are usually combined with amlodipine and titrated to effect.

Panel recommendations

Routine therapy and monitoring

- ❖ **Routine treatment** of cats with hypertension should commence with amlodipine at 0.625 mg/cat (0.125 mg/kg) q24h PO.
- ❖ **For cats with SBP ≥ 200 mmHg**, consideration should be given to commencing therapy at 1.25 mg/cat (0.25 mg/kg) q24h PO.
- ❖ **Cats with evidence of TOD at the time of diagnosis and/or cats with SBP ≥ 200 mmHg** should have their SBP and clinical signs monitored closely during the first 24–72 h. For some cats (eg, those with overt hypertensive encephalopathy or severe cardiac complications) hospitalisation may be required to allow close monitoring and control of the SBP. In other cases, initial daily re-evaluation may be sufficient. See also 'Emergency treatment of hypertension' on page 299.
- ❖ **Cats without evidence of TOD** should initially have their SBP reassessed at least every 7–10 days (depending on severity, concomitant disease, etc), together with evaluation of clinical signs (including thorough ocular examination). Re-evaluation of laboratory parameters may also be prudent, depending on the presence and severity of concomitant disease.
- ❖ **If response to therapy is inadequate**, the amlodipine dose can be doubled up to a maximum of 2.5 mg/cat (or 0.5 mg/kg) q24h. Dose increases are generally made at intervals of 7 days or more, but may be shorter (eg, after 24 h) if the SBP is high (≥ 200 mmHg) or there is ongoing TOD (see 'Emergency treatment of hypertension', page 299).
- ❖ **If response to amlodipine is inadequate, or if there is concomitant disease** (eg, persistent proteinuria), suggesting another antihypertensive agent would be useful, a second drug can be added together with the amlodipine.
- ❖ **The aim of therapy** in the short term (ideally within 1–2 weeks) should be to reduce SBP to < 160 mmHg. In the longer term (weeks), aiming for an SBP of < 150 mmHg may be prudent to minimise any risk of TOD. A safe lower limit for indirectly measured SBP in cats on antihypertensive therapy has not been well established, but the Panel recommends SBP should be kept above 110 mmHg.
- ❖ **Once SBP is controlled**, SBP should be reassessed at least every 3 months. Along with SBP measurement, clinical signs of TOD should be monitored (ocular examination, neurological examination, cardiac auscultation \pm echocardiography); and laboratory tests re-evaluated (eg, serum creatinine and/or SDMA concentrations, urinalysis with urine protein:creatinine ratio, assessment of other parameters as indicated). Fundic examination with indirect ophthalmoscopy¹⁰⁴ provides the easiest way to monitor the progress of ocular TOD with antihypertensive treatment (Figure 11). Once SBP is controlled there should be no further progression of lesions, but existing fundic lesions may take weeks to months to show improvement (depending on the presenting severity of the lesions and the control of SBP). Mild fundic lesions (eg, retinal oedema and small bullous lesions) respond better to antihypertensive treatment than advanced lesions (eg, retinal detachment, severe retinal haemorrhage).^{7,58}

Panel recommendations

Emergency treatment

Hypertensive emergencies are those cats with hypertension and evidence (or at high risk) of acute, severe and progressive TOD.

- ❖ Affected cats should be hospitalised and have their SBP monitored frequently and carefully (eg, every 4 h until the target SBP is achieved and then two to four times daily until stable).
- ❖ Whenever possible, oral amlodipine should be administered immediately at a starting dose of 0.625–1.25 mg/cat (0.125–0.25 mg/kg), depending on the severity of both the clinical signs and SBP.
- ❖ The dose of amlodipine could be repeated after 4–8 h if necessary, in increments up to a maximum of 2.5 mg/cat in the first 24 h.
- ❖ If oral amlodipine cannot be used, or if additional therapy is required, short-acting parenteral antihypertensive drugs can be administered (Table 6).
- ❖ Once the cat is stable, standard treatment should be instituted (see page 298 for Panel recommendations on routine therapy and monitoring).

Table 6 Parenteral drugs for emergency management of hypertension

| Drug | Suggested dose | Comments |
|---------------|---|---|
| Hydralazine | 0.2–0.5 mg/cat SC; repeat after 15 mins if necessary | Direct arterial vasodilator. Add a β -blocker if reflex tachycardia occurs ^{1,102,112} |
| Acepromazine | 50–100 μ g/cat IV or SC | Phenothiazine and α -blocker, non-specific vasodilator ^{102,117} |
| Nitroprusside | 1 μ g/kg/min CRI; titrate up to 3 μ g/kg/min if needed | Nitric oxide donor, non-specific vasodilator ¹¹² |
| Labetolol | 0.25 mg/kg IV over 2 mins, repeat up to a total of 3.75 mg/kg, then 25 mg/kg/min as CRI | α - and β -blocker ¹ |
| Esmolol | 50–100 μ g/kg/min CRI | β -blocker ^{1,112} |

SC = subcutaneously; IV = intravenously; CRI = constant rate infusion

Emergency treatment of hypertension

Hypertension is generally a chronic condition, although some cats may present with an acute onset of severe clinical signs associated with TOD (usually ocular, neurological or cardiovascular). Acute elevations of BP may also be seen in some diseases such as acute kidney injury. Although hypertensive emergencies are not as clearly established as in humans,¹¹¹ the severity of TOD may prompt more aggressive antihypertensive therapy,^{1,112} despite a lack of definitive evidence that this approach is any more beneficial, and a potentially greater risk of adverse events.¹¹³

Emergency treatment is aimed at halting ongoing TOD and preventing further damage. In human medicine, the initial goal of emergency therapy is to smoothly reduce SBP by up to 25% in the first 1–2 h, and then towards a level of 160 mmHg within a total of 6 h.⁹⁹ Uncontrolled, abrupt reduction in SBP or development of hypotension can precipitate myocardial, cerebral or renal ischaemia and should be avoided.^{114,115}

Cats requiring emergency therapy should be hospitalised to allow close monitoring of BP and treatment adjustments. Where feasible, direct arterial pressure monitoring is preferred, to provide the most accurate measurement of BP. Generally, antihypertensive agents (especially parenteral agents) should be titrated upward to effect.^{116,117} Amlodipine monotherapy may still be effective

Uncontrolled, abrupt reductions in SBP or development of hypotension can potentially precipitate myocardial, cerebral or renal ischaemia.

in emergency situations and should be used whenever oral administration is possible, safe and likely to be adequate. Detailed pharmacokinetic data for amlodipine use in cats are lacking. In humans, peak serum concentrations occur after 6–8 h.¹¹⁸ Data provided for licensing in cats suggest peak serum concentrations are reached at 3–6 h in this species, with a half-life of 53 h.¹¹⁹ Amlodipine has also been reported to have a BP lowering effect within 4 h and to last up to 30 h in clinical cases.¹⁰ Parenteral treatments may need to be considered if the oral route cannot be used, if the response to oral therapy is inadequate, or if an underlying disease dictates their use.

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Conflict of interest

The Panel members have no conflicts of interest to declare.



The ISFM welcomes endorsement of these Guidelines by the American Association of Feline Practitioners (AAFP).

A series of four short videos has been produced by the ISFM in various languages. Available on the YouTube channel of ISFM's parent charity International Cat Care at www.youtube.com/user/iCatCare, they may be accessed individually by searching for 'blood pressure', or as a group via the 'ISFM hypertension resources' playlist. The videos are also available at jfms.com as supplementary material.

Doppler blood pressure measurement in the cat: use of the leg



Doppler blood pressure measurement in the cat: use of the tail



Blood pressure measurement in the cat: use of HDO (high definition oscillometry) equipment



Blood pressure measurement in the cat: getting the environment right



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