# Systemic Hypertension: A Step-Wise Treatment Approach

Randolph L. Winter, DVM, DACVIM
Assistant Professor, Cardiology
PhD candidate, Biomedical Sciences
Auburn University

## Outline

- Introduction
  - Common etiologies
  - Organs affected
- Real vs. artifact
- Chronic therapy
  - Consensus guidelines
  - My approach
- Hypertensive crisis

## INTRODUCTION

## Common Etiologies

- Kidney disease – chronic or acute
  - high prevalence in dogs and cats (>50%)
  - Impaired $Na^+$ excretion
    - Increased circulating blood volume
  - RAAS activation
    - vasoconstriction
    - endothelial cell dysfunction
    - sympathetic stimulation


## Common Etiologies

- Canine Hyperadrenocorticism
  - ~59-86% of all cases of HAC in dogs
  - ↑mineralcorticoid activity
  - glucococorticoid excess = ↑blood volume
  - RAAS activation
- Canine Diabetes mellitus
  - ~35% of dogs with DM
  - Increased vascular smooth m. tone


## Common Etiologies

- Feline Hyperthyroidism
  - ~5-23% of unregulated cats
  - Excess thyroxine causes RAAS activation
  - Thyroid hormone sensitizes to catecholamines
    - increased heart rate
    - increased cardiac inotropy

} Increased CO

## Common Un-etiologies

- Obesity
  - not significant in dogs
  - no effect in cats
- Hypothyroidism
- Feline Diabetes Mellitus
- Pheochromocytoma
  - causes ↑BP in dogs and cats
  - very rare disease

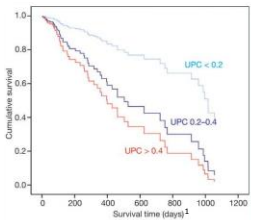

## Target Organs

- Renal
- Ocular
- Cardiovascular
- Central Nervous System

AUBURN UNIVERSITY
COLLEGE OF VETERINARY MEDICINE

## Renal damage

- Glomerular damage
  - proteinuria
  - independent predictor
- Local RAAS activation
- Azotemia – cause/effect



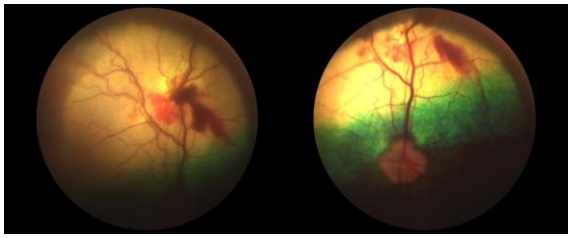

AUBURN UNIVERSITY
COLLEGE OF VETERINARY MEDICINE

1. Syme HM. J Feline Med Surg 2009

## Ocular Damage

- Hypertensive Choroidopathy/Retinopathy
  - as auto-regulation limit exceeded
  - breakdown of blood-retinal barrier
- Tortuosity of retinal vessels
- Retinal detachment
- Hemorrhage/multifocal edema

## Ocular Damage



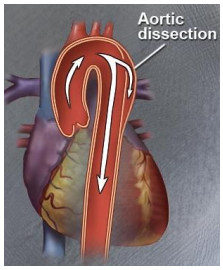
Photos courtesy of Dr. Anthony Moore

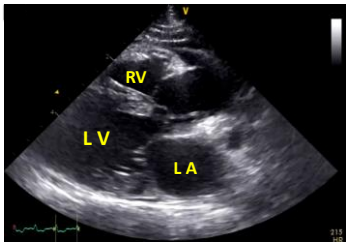
## Cardiovascular damage

- Vascular damage
  - Endothelial dysfunction
  - Intimal thickening
  - Reduced vasodilatory ability
- Cardiac damage
  - Left ventricular concentric hypertrophy
  - Worsening of mitral (or aortic) regurgitation
    - hastens progression toward CHF

## Vascular damage

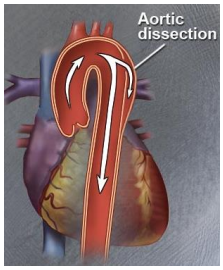
- Aortic dissection

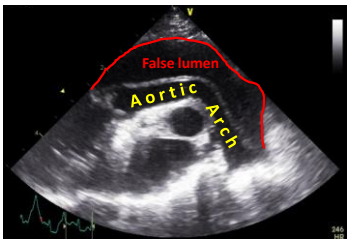


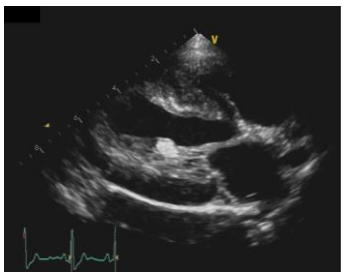

## Vascular damage

- Aortic dissection



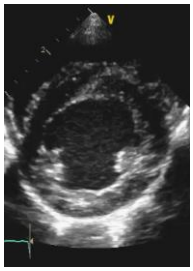




## Cardiac damage



## Cardiac damage

- More subtle



| Weight (kg) | 3 | 5 | 7 | 10 | 15 | 20 | 25 | 30 | 35 | 40 | 50 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| LVIDd (cm) | 2.46 ±0.62 | 2.74 ±0.52 | 3.00 ±0.45 | 3.27 ±0.35 | 3.71 ±0.24 | 4.14 ±0.22 | 4.48 ±0.29 | 4.83 ±0.39 | 5.17 ±0.50 | 5.48 ±0.61 | 6.07 ±0.82 |
| LVIDs (cm) | 1.36 ±0.55 | 1.60 ±0.47 | 1.79 ±0.40 | 2.06 ±0.31 | 2.43 ±0.21 | 2.80 ±0.20 | 3.16 ±0.29 | 3.39 ±0.34 | 3.68 ±0.45 | 3.96 ±0.54 | 4.46 ±0.74 |
| LVPWd (cm) | 0.50 ±0.22 | 0.54 ±0.17 | 0.57 ±0.15 | 0.62 ±0.12 | 0.68 ±0.08 | 0.74 ±0.07 | 0.76 ±0.10 | 0.84 ±0.13 | 0.89 ±0.17 | 0.93 ±0.20 | 1.02 ±0.26 |
| LVPWs (cm) | 0.72 ±0.17 | 0.79 ±0.16 | 0.84 ±0.14 | 0.92 ±0.13 | 1.02 ±0.11 | 1.13 ±0.11 | 1.21 ±0.12 | 1.30 ±0.13 | 1.38 ±0.15 | 1.45 ±0.17 | 1.60 ±0.22 |
| IVSd (cm) | 0.58 ±0.21 | 0.62 ±0.17 | 0.65 ±0.15 | 0.70 ±0.12 | 0.76 ±0.08 | 0.82 ±0.07 | 0.87 ±0.09 | 0.92 ±0.13 | 0.97 ±0.17 | 1.02 ±0.20 | 1.10 ±0.27 |
| IVSs (cm) | 0.90 ±0.26 | 1.02 ±0.22 | 1.04 ±0.20 | 1.09 ±0.17 | 1.15 ±0.12 | 1.23 ±0.11 | 1.30 ±0.15 | 1.39 ±0.23 | 1.46 ±0.26 | 1.54 ±0.35 | na |
| LA (cm) | 1.27 ±0.53 | 1.40 ±0.45 | 1.50 ±0.38 | 1.63 ±0.30 | 1.83 ±0.20 | 2.02 ±0.16 | 2.18 ±0.24 | 2.33 ±0.33 | 2.48 ±0.43 | 2.62 ±0.52 | 2.89 ±0.71 |
| Ao (cm) | 1.30 ±0.36 | 1.53 ±0.30 | 1.64 ±0.25 | 1.81 ±0.20 | 2.04 ±0.14 | 2.25 ±0.13 | 2.46 ±0.16 | 2.64 ±0.22 | 2.83 ±0.29 | 3.00 ±0.35 | 3.31 ±0.48 |

Key: values shown as mean ± standard deviation

References: Bonagura et al. Echocardiography: principles of interpretation. Vet Clin North Am 15:1177, 1985

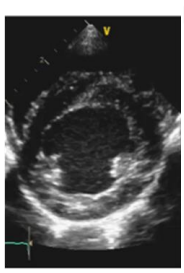
AUBURN UNIVERSITY
COLLEGE OF VETERINARY MEDICINE

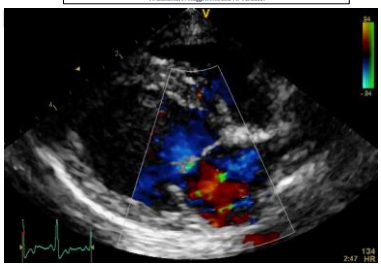
## Cardiac damage

- More subtle

**Survival Characteristics and Prognostic Variables of Dogs with Mitral Regurgitation Attributable to Myxomatous Valve Disease**

M. Borgarelli, P. Savarino, S. Crosara, R. A. Santilli, D. Chiavegato, M. Poggi, C. Bellino, G. La Rosa, R. Zanatta, J. Haggstrom, and A. Tarducci

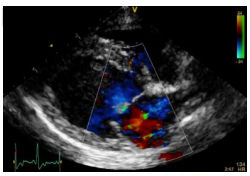




## Cardiac damage

**Survival Characteristics and Prognostic Variables of Dogs with Mitral Regurgitation Attributable to Myxomatous Valve Disease**

M. Borgarelli, P. Savarino, S. Crosara, R. A. Santilli, D. Chiavegato, M. Poggi, C. Bellino, G. La Rosa, R. Zanatta, J. Haggstrom, and A. Tarducci

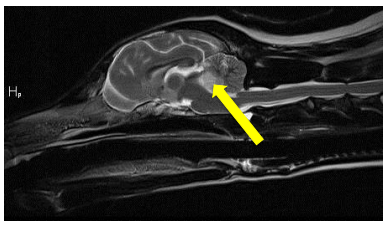


AUBURN UNIVERSITY
COLLEGE OF VETERINARY MEDICINE

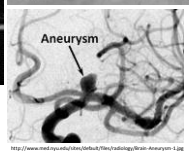
## CNS damage

- Small vessel disease
  - thrombosis
  - hemorrhage
  - infarction
- Disruption of blood-brain barrier
- Hypertensive encephalopathy

## CNS damage



https://img.webmd.com/dtmcms/live/webmd/consumer_assets/site_images/media/medical/hw/h0091190.jpg


http://www.med.nyu.edu/sites/default/files/radiology/Brain-Aneurysm-1.jpg

13 yo MC JRT
Right sided torticollis and head tilt
Vertical nystagmus
BP 230 mmHg

**REAL VS. ARTIFACT**

## Real vs. artifact

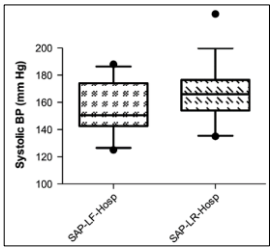
- How do I trust the reading?
  - Is white-coat effect real?
    - Dogs
    - Cats

## White-coat effect

- Artifactual increase in measured BP
  - mostly SBP, but DBP as well
- Hard to predict stress level
  - particularly for cats
- DOES happen in SOME animals

## White-coat in dogs

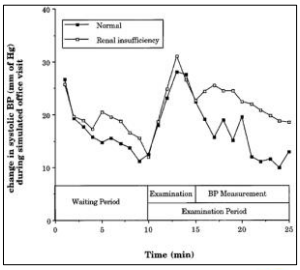
- Greyhounds with BP measured at home and in the hospital
  - higher in hosp




CL Marino et al. JVIM 2011

## White-coat in cats

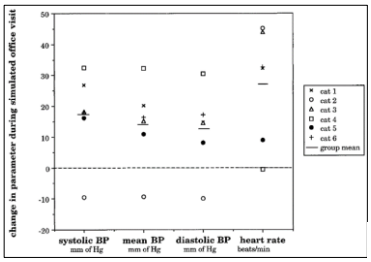
- BP measured in cats
  - normal and renal insuff.
  - 24-hr BP vs. mock exam/visit




AM Belew et al. JVIM 1999

## White-coat in cats

- Exam/Visit values varied
  - some higher, some lower




AM Belew et al. JVIM 1999

## How to address white-coat

- Prevent
  - quiet exam rooms
  - cat only exam rooms
  - Feliway®
  - Tech/nurse take BP first
    - in room with owner

## How to address white-coat

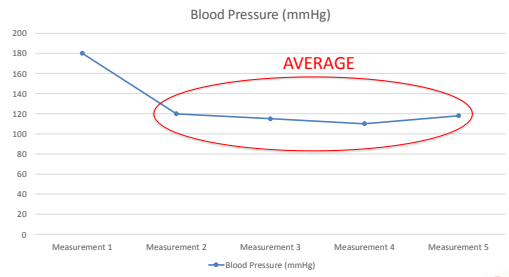
- Repeat
  - Repeat BP later
  - Repeat BP after butorphanol 0.1-0.2 mg/kg
    - Kappa receptor agonist / weak mu receptor antagonist
    - No real cardiovascular effects
      - removes anxiety / stress component

## How to measure

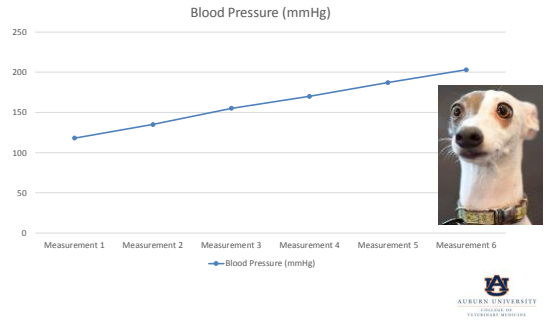
- Measure 5 – 7 times
  - discard the first
  - then average (hopefully consistent values)
- Note site, cuff size, body position

Oral communication. M Acierno (chair of SAIM Hypertension Consensus Group). ACVIM Forum 2017

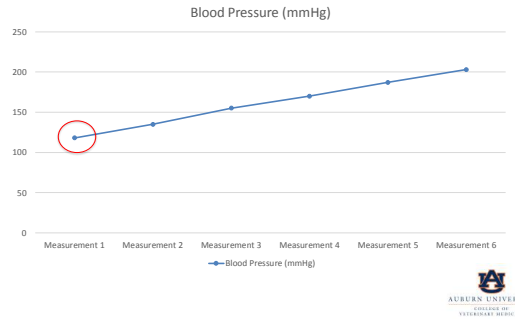
## How to measure



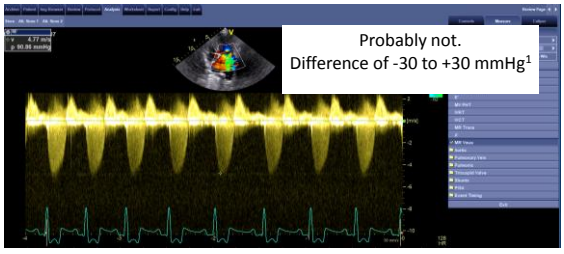
## How to measure




## How to measure




## Can we verify?




1. SP Tou et al. JVIM 2006

## CHRONIC THERAPY

## Do we treat?

| Risk Category | Systolic BP (mmHg) | Diastolic BP (mmHg) | Risk of EOD |
|---|---|---|---|
| I | < 150 | < 95 | Minimal |
| II | 150 – 159 | 95 – 99 | Mild |
| III | 160 – 179 | 100 – 119 | Moderate |
| IV | ≥ 180 | ≥ 120 | Severe |

[1]

- 2 repeat measurements to confirm[2]
  - 4-8 wks apart if Category III
  - 1-2 wks apart if Category IV
  - NO REPEAT NEEDED IF **EOD**

1. S Brown et al. ACVIM Consensus Statement. JVIM 2007
2. Oral communication. M Acierno (chair of SAIM Hypertension Consensus Group). ACVIM Forum 2017

## Do we treat?

| Risk Category | Systolic BP (mmHg) | Diastolic BP (mmHg) | Risk of EOD |
|---|---|---|---|
| I | < 150 | < 95 | Minimal |
| II | 150 – 159 | 95 – 99 | Mild |
| III | 160 – 179 | 100 – 119 | Moderate |
| IV | ≥ 180 | ≥ 120 | Severe |

[1]

- Routine screening not advised[2]
  - risk of false positive
- Hypertensive retinopathy risk at 168 mmHg
- Cats with 140 – 160 mmHg may be pre-hypertensive
  - likely to develop > 180 mmHg as they age

1. S Brown et al. ACVIM Consensus Statement. JVIM 2007
2. Oral communication. M Acierno (chair of SAIM Hypertension Consensus Group). ACVIM Forum 2017

## What can we use?

- ACEi
  - enalapril
  - benazepril
- $Ca^{++}$ channel blocker
  - amlodipine
- Aldosterone antag.
  - spironolactone
- Direct vasodilator
  - hydralazine

- ARB
  - losartan
- $\alpha_1$ blocker
  - acepromazine
  - prazosin
- β blocker
  - atenolol
  - carvedilol (some α)
- Diuretic
  - furosemide
  - hydralazine

AUBURN UNIVERSITY COLLEGE OF VETERINARY MEDICINE

## What is recommended in dogs?

- If BP < 200 mmHg
  - ACEi alone[1]
    - Enalapril and Benazepril: 0.5 mg/kg q12h
- If BP > 200 mmHg
  - ACEi and amlodipine
    - amlodipine dose: 0.1 – 0.25 mg/kg q12-24h
- Recheck BP in 1-2 weeks

AUBURN UNIVERSITY COLLEGE OF VETERINARY MEDICINE

1. Oral communication. M Acierno (chair of SAIM Hypertension Consensus Group). ACVIM Forum 2017

## What do I use in dogs?

- ACEi expected to decrease BP 10 – 20 mmHg
- Enalapril vs. Benazepril
  - metabolism/clearance favors benazepril (~70/30)
- RAAS major player – primary or secondary

Benazepril 0.5 mg/kg q24h
+
Amlodipine 0.1 mg/kg q24h

AUBURN UNIVERSITY COLLEGE OF VETERINARY MEDICINE

## What do I use in dogs?

- Goal is Category I (SBP < 150 mmHg)
- At recheck, assess if too low or too high
- If too low
  - D/C amlodipine
  - recheck in 1-2 wks
- If too high
  - ↑ amlodipine: 0.1 mg/kg q12h
  - recheck in 1-2 wks
- If perfect
  - recheck in 1-3 months
  - BP and chem/UA

AUBURN UNIVERSITY COLLEGE OF VETERINARY MEDICINE

## What do I use in dogs?

- Benazepril 0.5 mg/kg q12h + Amlodipine 0.1 mg/kg q24h
- Benazepril 0.5 mg/kg q12h + Amlodipine 0.1 mg/kg q12h
- Benazepril 0.5 mg/kg q12h + Amlodipine 0.2 mg/kg q12h
- Benazepril 0.5 mg/kg q12h + Amlodipine 0.25 mg/kg q12h
- Benazepril 0.5 mg/kg q12h + Amlodipine 0.25 mg/kg q12h + Spironolactone 2 mg/kg q24h
- Ace, hydralazine, βblock, low diuretic dose, ARB, α1 block

AUBURN UNIVERSITY COLLEGE OF VETERINARY MEDICINE

## What is recommended in cats?

- If BP < 200 mmHg
  - amlodipine 0.625 mg/CAT q24h
- If BP > 200 mmHg
  - amlodipine 1.25 mg/CAT q24h
  - ACEi or spironolactone

AUBURN UNIVERSITY COLLEGE OF VETERINARY MEDICINE

Oral communication. M Acierno (chair of SAIM Hypertension Consensus Group). ACVIM Forum 2017

## What do I use in cats?

- Enalapril vs Benazepril
  - ~50% don't respond to enalapril
  - proteinuria poor prognostic (regardless)
    - benazepril 70/30 metabolism/clearance
  - benazepril can be q24h

Amlodipine 0.625 mg/CAT q24h

## What do I use in cats?

- Goal is Category I (SBP < 150 mmHg)
- At recheck, assess if too low or too high
- If too low
  - literally never happened
- If too high
  - amlodipine 0.625 mg/CAT q24h
  - benazepril 0.5 mg/kg q24h
  - recheck in 1-2 wks
- If perfect
  - recheck in 1-3 months
  - BP and chem/UA

## What do I use in cats?

- Amlodipine 0.625 mg/CAT q24h
- Amlodipine 0.625 mg/CAT q24h + Benazepril 0.5 mg/kg q24h
- Amlodipine 1.25 mg/CAT q24h + Benazepril 0.5 mg/kg q24h
- Amlodipine 1.25 mg/CAT q12h + Benazepril 0.5 mg/kg q24h
- Amlodipine 1.25 mg/CAT q12h + Benazepril 0.5 mg/kg q24h + Spironolactone 2mg/kg q24h
- Amlodipine 1.25 mg/CAT q12h + Benazepril 0.5 mg/kg q12h + Spironolactone 2mg/kg q24h
- Amlodipine 1.25 mg/CAT q12h + Benazepril 0.5 mg/kg q12h + Spironolactone 2mg/kg q12h

**HYPERTENSIVE CRISIS**


## What is a hypertensive crisis?

- Severe systemic hypertension
  - concurrent, progressive EOD
- Typically SBP > 180 mmHg
  - often much higher
- No repeat measurement recommended


## What is a hypertensive crisis?

- Local and systemic increases:
  - catecholamines
  - angiotensin II
  - aldosterone
  - endothelin I
- Severe endothelial dysfunction
  - lack of vasodilators
- Vascular inflammatory/oxidative injury
  - increased vascular permeability

## What is a hypertensive crisis?

- Sudden onset blindness
  - retinal detachment
- Intraocular hemorrhage
- Neurologic acute decline
  - progressive ↑ frequency seizure activity
- Acute worsening of renal function
- Active, worsening pulmonary edema

## Hypertensive crisis - therapy

- Goals:
  - Decrease mean BP ~25% within 1 hr
    - no more (organ ischemia)
  - Decrease SBP/DBP to < 160/110 mmHg in 2-6hrs
    - Category II = mild risk of EOD

## Hypertensive crisis - therapy

- Want immediate decrease in BP
- Direct arterial measurement ideal
- Fenoldopam[1] 0.1 – 0.8 mcg/kg/min CRI
  - dopamine-1 agonist
- Hydralazine 0.2 mg/kg IV, repeated q2h
  - direct (unknown) arterial vasodilator
- Acepromazine 0.01 – 0.02 mg/kg IV, repeated q1-4h
  - α1 antagonist
- Oral amlodipine 0.2 mg/kg q12h
  - $Ca^{++}$ channel blocker

1. Oral communication. M Acierno (chair of SAIM Hypertension Consensus Group). ACVIM Forum 2017

Questions?