# Anesthesia for patients with cardiac disease

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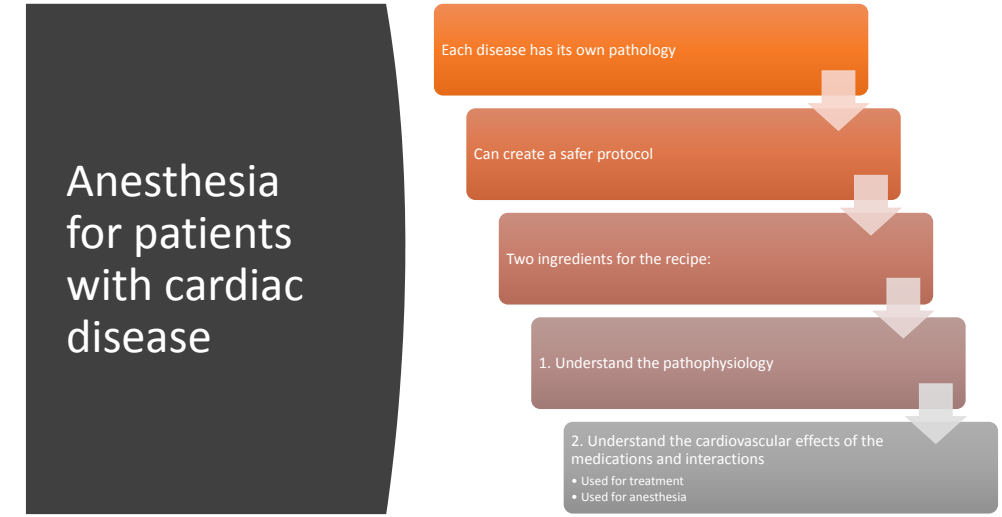
## Anesthesia for patients with cardiac disease




## Anesthesia for patients with cardiac disease

Two ingredients for the recipe: understand the pathology

Is the heart to thick and over-muscled

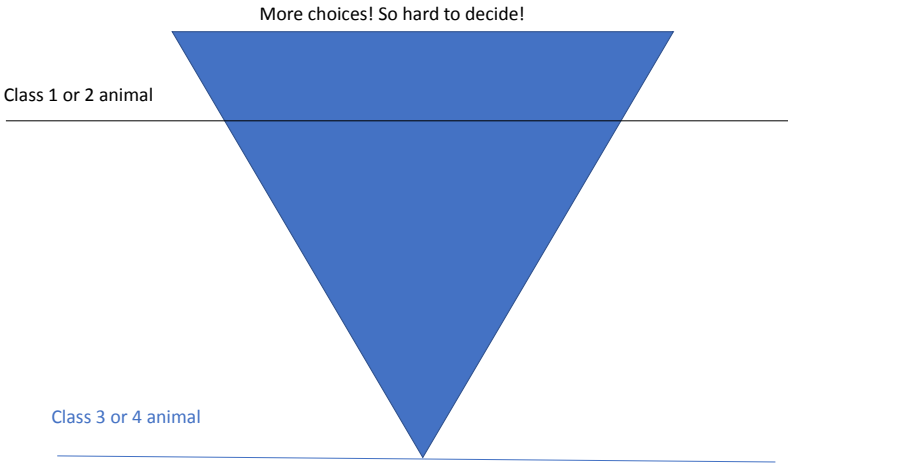
Is the heart to thin and dilated, flabby weak

Is the valve problem affecting the blood flow to the lungs or to the body

## Why one needs to care

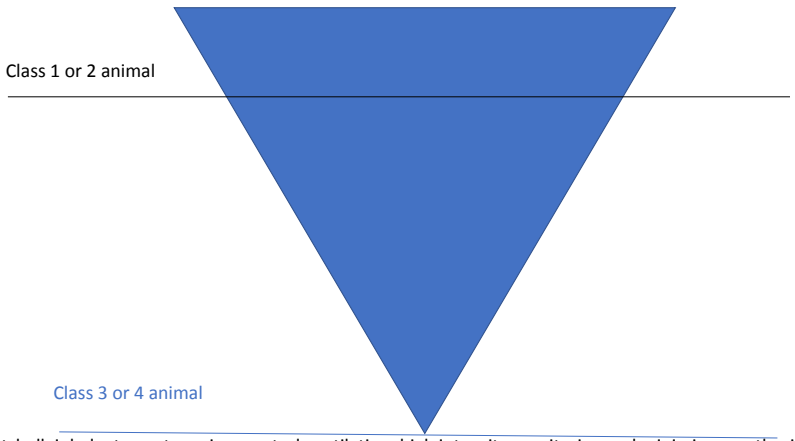
Cardiac disease can take normally benign protocols and create morbidity/mortality incidents
Acute pulmonary edema after diazepam-ketamine in a dog
J. Boutureira Et al. VAA 2007

*My theory of basic protocol creation*




Fewer choices- almost makes it *faster to choose a protocol* once knowledgeable

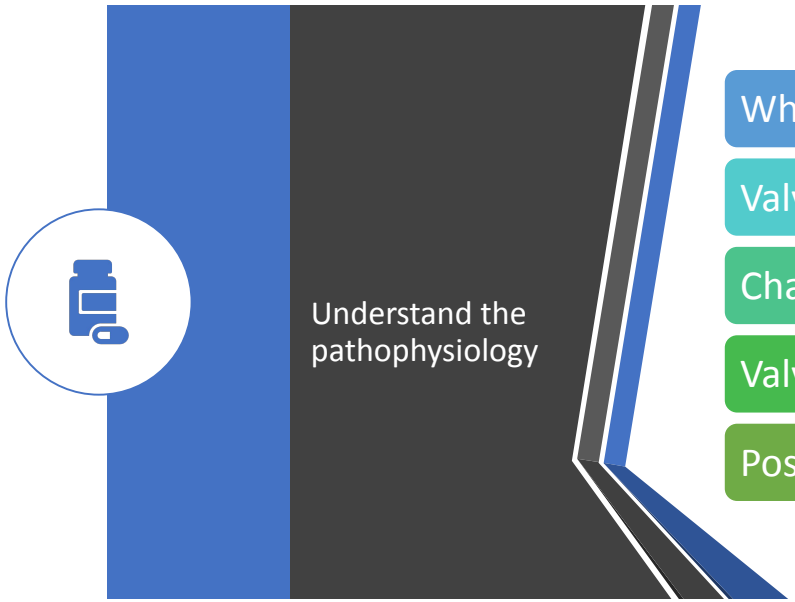
*My theory of basic protocol creation*




Nutshell: inhalant agent sparing, control ventilation, high intensity monitoring and minimize anesthesia
Effects on patient with cardiac disease

# Pharmacology

- Understand the drugs used for the disease
- Example:
- Calcium channel blocker and dobutamine
- Antihypertensive and isoflurane
- Antiarrhythmic (*antidysrhythmic) and anticholinergic



## Imaging

Gold standard is complicated

Suggest echocardiogram

- Offer access
- But it doesn't often happen same day

Chest rads, auscultation, asking about activity level still count even if echo'd

## List of current medications

Get list of current cardiac meds

Many who are on cardiac meds are ok to anesthetize

Some who are untreated are not ok

Meds usually but not always indicate a disease that has progressed

## Understanding when to refer

Charge for a dedicate veterinary nurse before during and after

Refer cases to an anesthesiologist for a few reasons/invite us to attend when

- Owner concern
- Time required to monitor/sufficient staff issue
- Unfamiliarity with meds and
- Lack of anesthesia equipment for monitoring

## A few suggestions: induction

- Etomidate
- Alfaxalone
- Propofol
- Prime doses of Propofol or alfaxalone reduce total amount needed for induction

Give small amount first, wait, then IV to effect.

## What is priming?

Priming alfaxalone and alfaxalone–midazolam co-induction techniques in dogs
Lagos-Carvajal, P. Queiroz-Williams, J. Nevarez, C. Ricco, A. da Cunha, J. Cremer, C. Liu
*Veterinary Anaesthesia and Analgesia* Volume 44, Issue 5, Pages 1016-1026 (September 2017)

- A potential way to reduce induction dose in alfaxalone and propofol
- Both agents have dose dependent cardiovascular depression

## A few suggestions: induction

- Benzodiazepine
  - Midazolam- use it
  - 0.1- 0.2 mg/kg
- Some studies say it supports HR and BP, some say it has no difference
- No cited neg effect
- Reduces amount of alfaxalone or propofol
- More effect as co induction than as premedication (excitement?)

## A few suggestions: induction

- Benzodiazepine
  - Midazolam- use it
  - 0.1- 0.2 mg/kg

*Induction dose and recovery quality of propofol and alfaxalone with or without midazolam coinduction followed by total intravenous anesthesia in dogs*

*PenTing Liao, Melissa Sinclair, Alexander Valverde, Cornelia Mosley, Heather Chalmers, Shawn Mackenzie, Brad Hanna*

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## Inhalant agent sparing techniques

- Choose an inhalant-sparing regimen with minimal cardiovascular effects
- Inhalant anesthetics: can be compared to exercise
- Is your patient able to exercise?
  - Example, vasodilation, heart rate increase
- *Isoflurane minimum alveolar concentration sparing effects of fentanyl in the dog* – A.J Williamson et al. VAA 2017.

A few suggestions:

Fentanyl & midazolam* cri (49:1 ml, 1 ml/kg/hr)

Lidocaine CRI
3 mg/kg/hr plus bolus, dogs only

Alfaxalone CRI
Many options PIVA

Propofol CRI
Many options PIVA

## Inhalant agent sparing regimen and controlled ventilation

Good in theory, takes practice, monitoring and experience to avoid prolonged recovery

Example: short or ultrashort opioid constant rate infusion (CRI)
- Fentanyl, remifentanil

Benzodiazepine CRI

Alfaxalone CRI

Lidocaine CRI

Can bolus intermittently or use fluid bag method of CRI

## Monitoring

- Gold standard: arterial blood pressure
  - Offers beat to beat information
- Second choice: monitor using two methods
- Oscillometric and Doppler
  - oscillometric is better, say some studies
  - Doppler is more “real-time”

## Monitoring

*Continuously and thoroughly (use the clinician’s brain to integrate the monitors; alter expectations)*

- Perfusion by SPO2
- ECG but keep in mind, rhythm not diagnostic and affected by body position (it’s not always right lateral)

## Pulse oximetry: the under appreciated indicator of perfusion

- Oxygenation info without drawing blood, beat to beat
- New technology is better
- Needs a pulse to read
- Information about perfusion and oxygenation
- Information with a set of caveats
  - Too slow HR may not read
  - Patient being moved (scrub, surgery) may not read
  - Best on tongue, not always possible

## Pulse oximetry: under appreciated indicator of perfusion

- Solution
  - Too slow HR may not read
    - Add anticholinergic if patient can tolerate
  - Patient being moved (scrub, surgery) may not read
    - Ask for a “pause” and get an intermittent good pulse ox
    - Better than an inaccurate continuous
  - Best on tongue, not always possible
    - Again, intermittent sampling

# Pharmacology

## Common drugs used for cardiac disease and their effects on anesthesia

**Diuretics**

Lower BP/hypovolemia?

Need to monitor bladder

## Common drugs used for cardiac disease and their effects on anesthesia

Vasodilators

Lower blood pressure

So do both isoflurane/sevoflurane

Less so with desflurane*

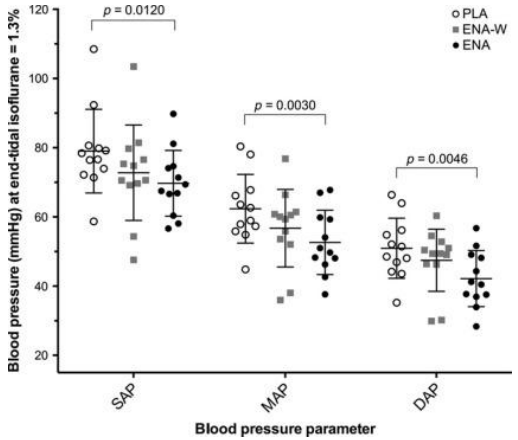
## Common drugs used for cardiac disease and their effects on anesthesia

- Ace inhibitors

*Effects of orally administered enalapril on blood pressure and hemodynamic response to vasopressors during isoflurane anesthesia in healthy dogs*

*Amanda E. Coleman, Molly K. Shepard, Chad W. Schmiedt, Erik H. Hofmeister, Scott A. BrownVeterinary Anaesthesia and Analgesia*

Volume 43, Issue 5, Pages 482-494 (September 2016)

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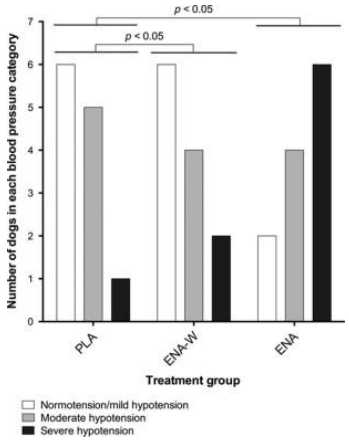


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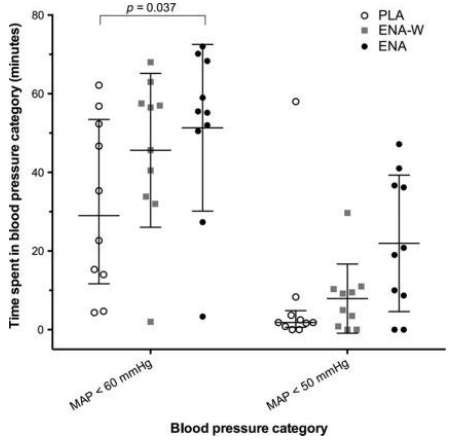


## Thought exercise

Can have great blood pressure and poor tissue perfusion i.e. dexmedetomidine

Can have lower BP and better perfusion

If a cardiologist has given a combo of meds and is echo'ing the dog and everything looks, good, keep on that combo of meds despite the risk the numbers on a machine might be less than that of a healthy normal patient

To a degree, lower afterload = lower bp = better CO; until preload catches up- more later

## Thought experiment

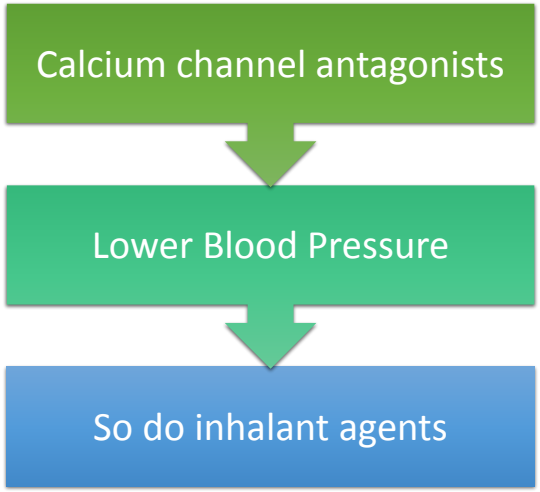
Preload is the pressure filling of the right atrium

Afterload is the pressure in the system in the aorta

Contractility is also the fractional shortening/ejection fraction you see in echo reports but is the strength of the muscle

Here's how isoworks: initially in the healthy heart it lowers afterload by vasodilation, has mild effects on contractility but eventually the preload isn't filling adequately. Hence, we give patients IV fluids!

## Common drugs used for cardiac disease and their effects on anesthesia




Common drugs used for cardiac disease and their effects on anesthesia

Beta adrenergic antagonists; B1 heart B2 lung

Lower blood pressure

Arrhythmias

Make bronchodilators less or ineffective; Increased selectivity for Beta 1 drugs are safer for bronchoconstriction treatment; drugs are rarely pure

## Common drugs used for cardiac disease and their effects on anesthesia

- Inotropes
- Contractility enhancers: increases the contractile power of the heart muscle, enabling a disease-weakened heart to keep up with the body's demand for heart action
- Digitalis- old
- Pimobendan- very popular dogs and cats PD3 inhibition

## Common drugs used for cardiac disease and their effects on anesthesia

- Antiarrhythmics
- Decrease the frequency
- Fast sodium channel blocker (lidocaine, mexiletine)
- Beta blocker (propranolol atenolol) NEG INOTROPE, lowers BP
- Calcium channel blocker (diltiazem or verapamil) NEG INOTROPE
  - Also won't work well with dobutamine
- Digitalis glycosides (digoxin)

## Common drugs used for cardiac disease and their effects on anesthesia

- Anticoagulants
- Feline Cardiogenic Arterial Thromboembolism
- Effect is that of increased risk for hemorrhage

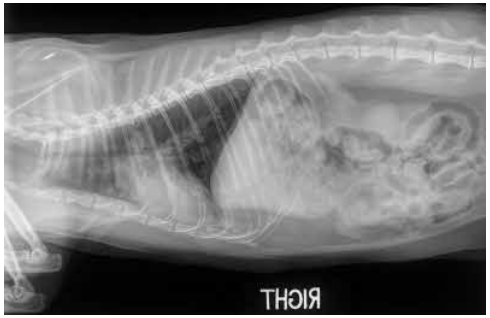
## Things to look for on radiology of thorax for CHF

In Cats, radiographic infiltrates of cardiogenic pulmonary edema typically are described as patchy and are not consistently localized

In contrast to the perihilar description often given to such infiltrates in dogs.

Cats have atrial enlargement as a consequence of high cardiac filling pressures.

## Cat with HCM and pulmonary edema





## Small animal cardiac health council vs. ASA classifications

**Class I** - Patients with confirmed cardiac disease but no signs of heart failure. These patients would be considered **ASA category II** if clinically normal without cardiac medications and **ASA category III** if cardiac medications are required to achieve clinical normalcy. These patients should tolerate a properly managed anesthetic/sedative event without difficulty.

**Class II** - Patients with mild to moderate signs of heart failure at rest or with mild exertion. These patients would be considered **ASA category IV.** These patients should have additional diagnostics and therapeutic adjustments to stabilize prior to anesthesia or sedation.

**Class III** - Patients in fulminate heart failure requiring aggressive measures to stabilize prior to any procedures. These patients would be considered **ASA category IV to V.**

## Other signs of CHF

- Dyspnea
- Cats have a gallop sound

## Dogs: most common disease of the valves

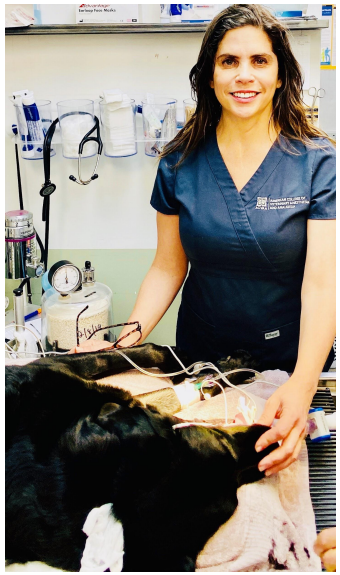
Asymptomatic mature dogs with systolic heart murmurs characteristic of mitral regurgitation should undergo diagnostics to determine the presence or absence of heart enlargement and to document that the dog is normotensive.

Treatment is not recommended in dogs with stage B1 degenerative valve disease (asymptomatic with normal heart size)

Treatment with pimobendan has been shown to extend symptom-free and overall survival of dogs with stage B2 degenerative valve disease (asymptomatic with heart enlargement).

# If symptomatic and on meds

- Plan ahead
- Dobutamine is your friend for pressors in “floppy” heart disease like valvular, not in thickened
- Except for calcium blockers
- Avoid increases in afterload



## Dogs

- Arrhythmias (now dysrhythmias)
- Boxers
- Others
- How to approach: avoid arrhythmogenic drug
- Example: Boxer
- Example: Belgian Malinois

## Cats

- HCM
- Asymptomatic
- Symptomatic

Hypertrophic cardiomyopathy (HCM) is the most common form of feline cardiovascular disease

May affect up to approximately 15% of the domestic cat population, primarily as a subclinical disease.

Severe HCM, leading to heart failure or arterial thromboembolism (ATE), only occurs in a small proportion of these cats.

HCM is the non-physiologic hypertrophy of the left ventricle and resultant diastolic dysfunction. HCM is genetic with multiple mutations identified in purebred cats. Autosomal dominant variable penetrance Maine Coon, Ragdoll

HCM may or may not produce a heart murmur or gallop sound.

Systolic anterior motion of the mitral valve (SAM) is the most common cause of dynamic left ventricular outflow tract obstruction (DLVOTO); the most common cause of a heart murmur with feline HCM.

HCM without obstruction and HCM with obstruction (HOCM)

Diastolic dysfunction leads to abnormally increased atrial pressure leading to signs of heart failure, and sluggish atrial blood flow leading to ATE, is the primary abnormality that causes clinical signs and death in affected cats.

## Cats

- Valvular insufficiencies
- Asymptomatic

*Arrhythmias and transient changes in cardiac function after topical administration of one drop of phenylephrine 10% in an adult cat undergoing conjunctival graft*

*Paolo Franci, Elizabeth A Leece, J Fraser McConnell*

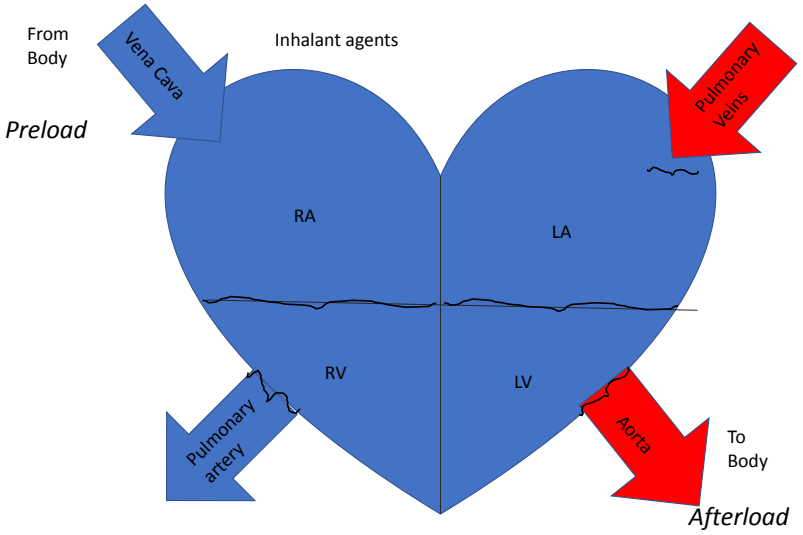
*Veterinary Anaesthesia and Analgesia*
Volume 38, Issue 3, Pages 208-212 (May 2011)
DOI: 10.1111/j.1467-2995.2011.00607.x

# How I visualize cardiac pathophysiology for anesthesia

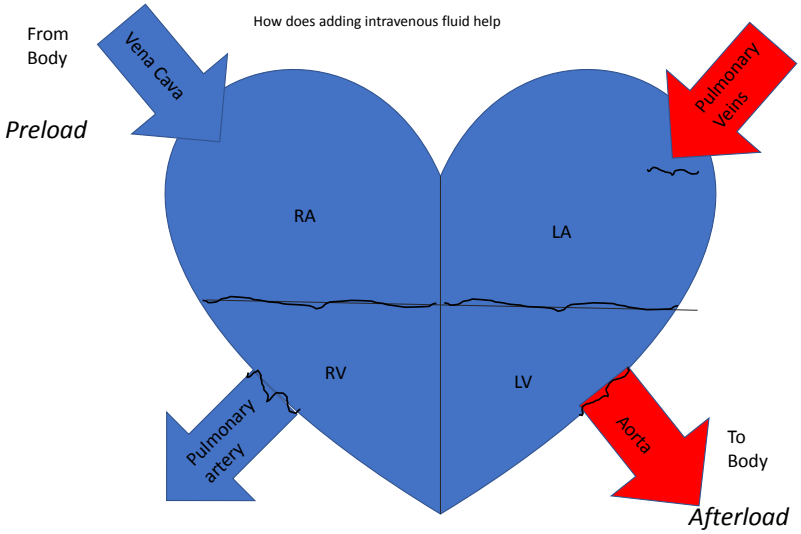
## Detailed Schematic cardiac diagram

Not drawn to scale

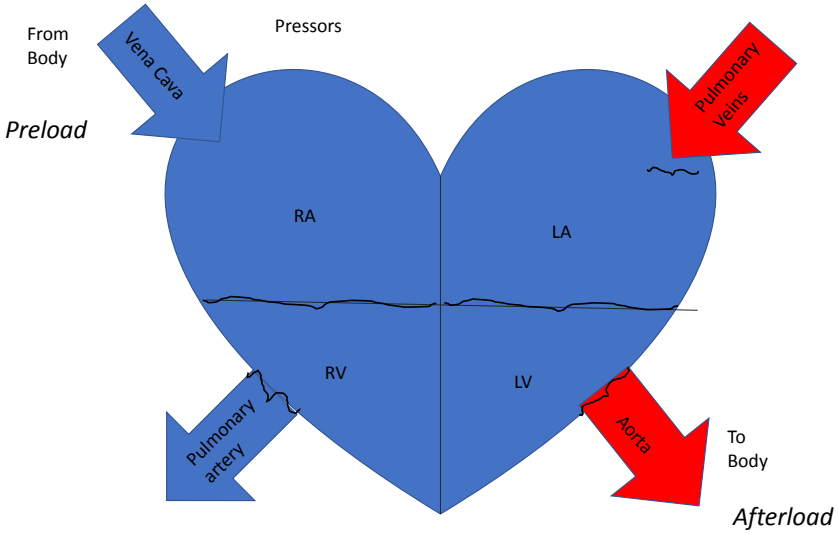
Abstract representation



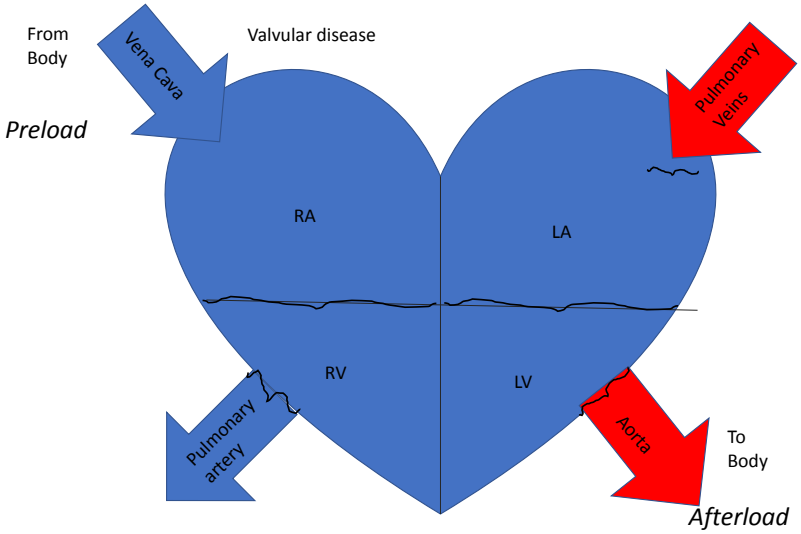
How does adding intravenous fluid help



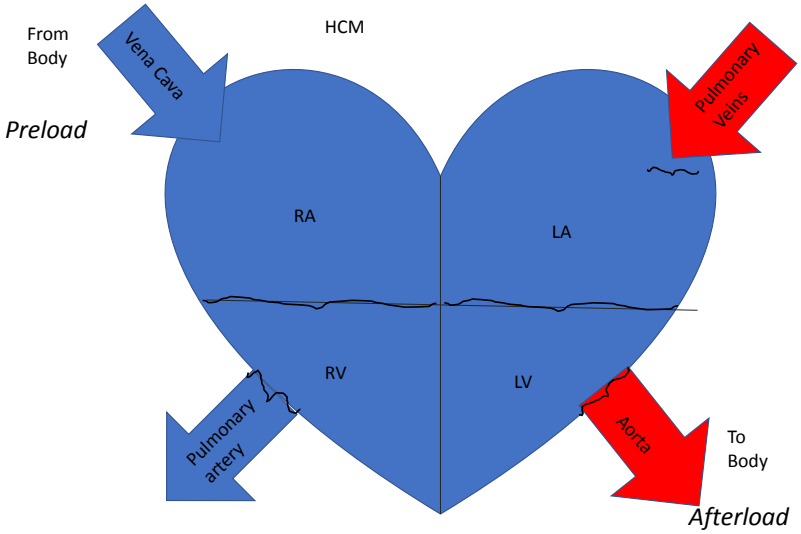

Pressors

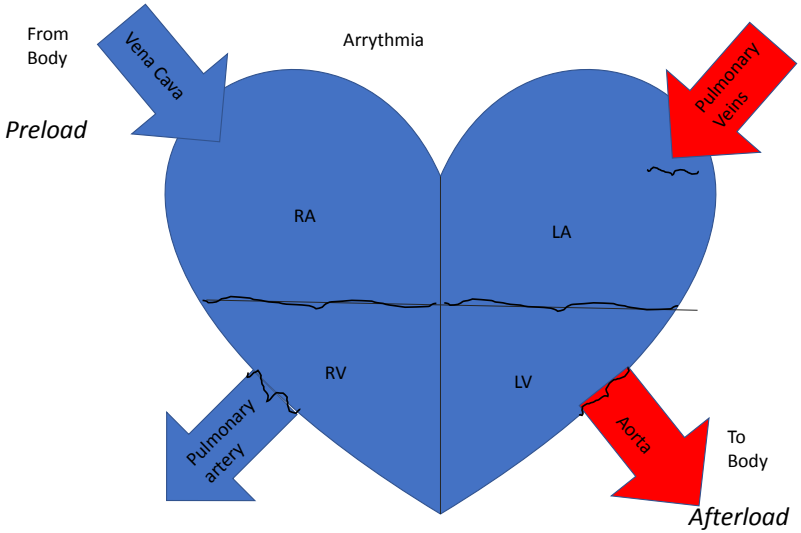


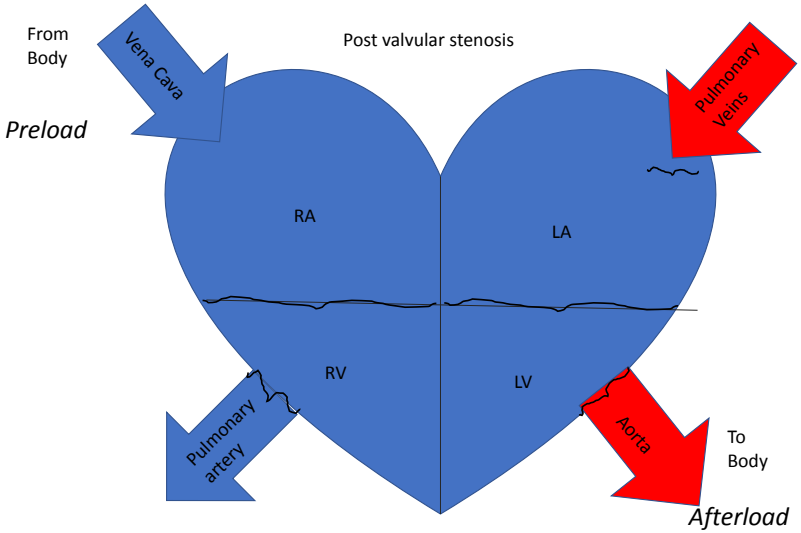

Valvular disease

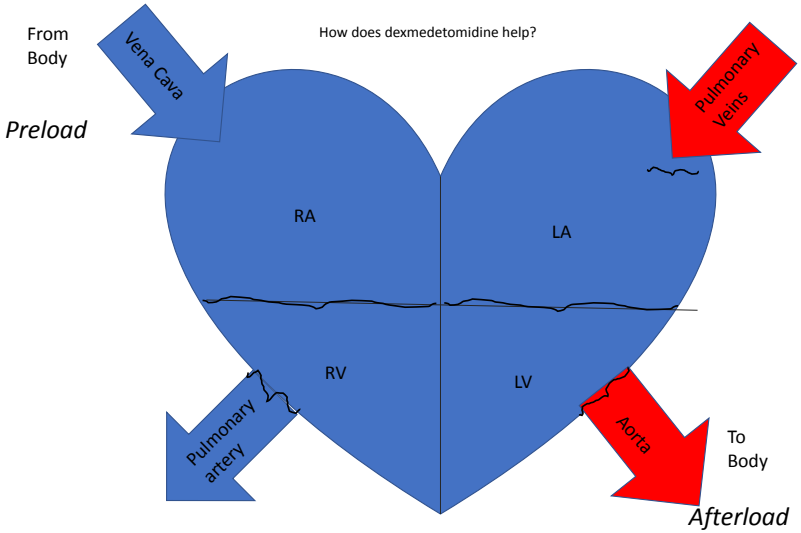



HCM




From Body
Arrythmia
Vena Cava
Pulmonary Veins
Preload
RA
LA
RV
LV
Pulmonary artery
Aorta
To Body
Afterload


From Body
Post valvular stenosis
Vena Cava
Pulmonary Veins
Preload
RA
LA
RV
LV
Pulmonary artery
Aorta
To Body
Afterload


From Body
How does dexmedetomidine help?
Vena Cava
Pulmonary Veins
Preload
RA
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Pulmonary artery
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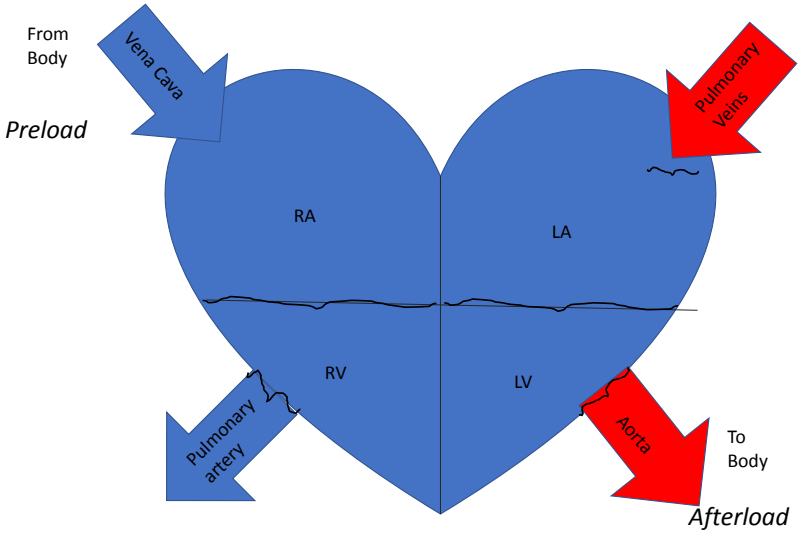
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Afterload

# Normal ECG dog

RHYTHM DIAGNOSIS: SINUS RHYTHM

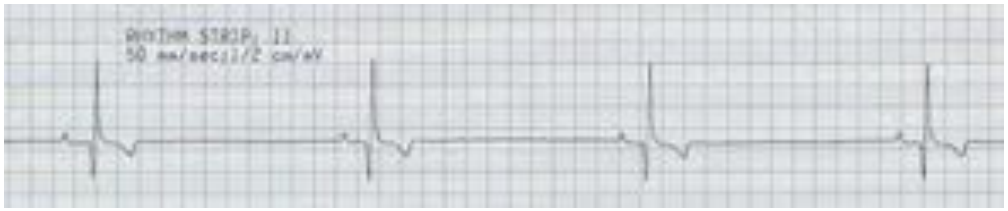
▸ What are the criteria for a normal sinus rhythm?

▸ P wave preceding every QRS complex

▸ Constant PR interval

▸ P wave positive in lead II

# ECG abnormality: what's your impression?




SINUS BRADYCARDIA

▸Often a physiologic response to systemic disturbance

▸ Increased vagal tone due to primary respiratory, GI, CNS disease DRUGS

▸ Hypothermia, hypothyroidism, hypoglycemia

▸ Electrolyte abnormalities

Normal for a very fit dog

# ECG abnormality

SINUS ARREST/SINUS BLOCK

▸ Defined as an intermittent absence of P waves, two P-R intervals or longer

▸ Pauses may be terminated by an escape beat NOT a VPC

▸ QRS without a P that often has a wide and bizarre shape that follows a pause - NOT a VPC

▸ May be an early sign of SA node disease (sick sinus syndrome)or drugs or physiologic disturbance

What does an escape beat mean??????

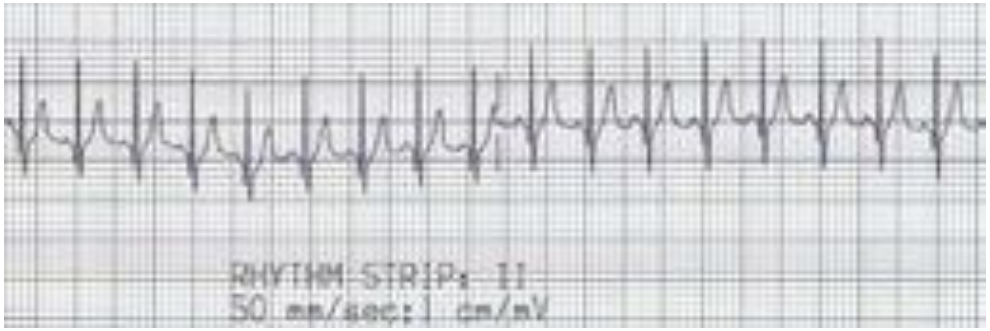
TACHYARRHYTHMIAS

▸ Defined as a heart rhythm with a  rate above the normal range for that species

▸ Originates from either the SA node,supraventricular region (atria, AV node/junction) or the ventricle

▸ Determining origin => understand the cause of the arrhythmia & need for intervention

# ECG ABNORMALITY




# ECG ABNORMALITY SINUS TACHYCARDIA

▸ A secondary response to some systemic disturbance

▸ Hypotension, pain, sepsis, fever, hyperthyroidism, cardiac tamponade, drug effects

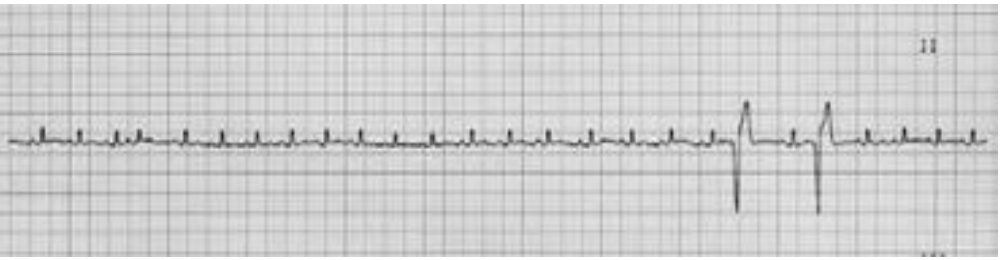
▸ Not associated with primary cardiac disease

▸ However can be seen in patients with CHF

▸ Treatment is aimed at correcting the underlying cause

Dog: 180 is tachycardia, treat-WHY?

# ECG Abnormality




# ECG Abnormality VENTRICULAR ARRHYTHMIAS VPC

▸ Common, pain, injury to myocardium; ectopic impulses which originate from the ventricular myocardium

▸ SA node continues to fire independent of these

ventricular ectopic impulses = AV dissociation

▸ Complexes are wide, bizarre and different than the sinus complexes due to conduction delay

Can have fusion beats

# ECG Abnormality

VENTRICULAR TACHYCARDIA

▸ 4 or more VPCs in a row

▸ Can be short in duration (paroxysmal) or sustained

▸ Can occur suddenly and abruptly terminate

▸ AV dissociation is a feature

▸ Can precede ventricular fibrillation = terminal rhythm

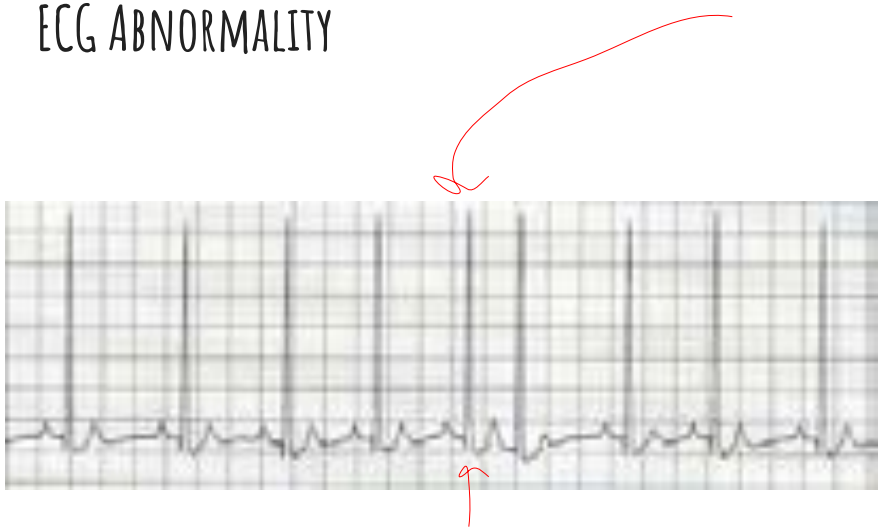
# ECG abnormality HR is 150

Accelerated idioventricular rhythm

- Characterized by a regular run of VPCs with a rate similar to that of the normal sinus rate
- Common in anesthetized patients, hospitalized patients, post GDV, post splenectomy, etc.

“Slow VTach”

# ECG Abnormality

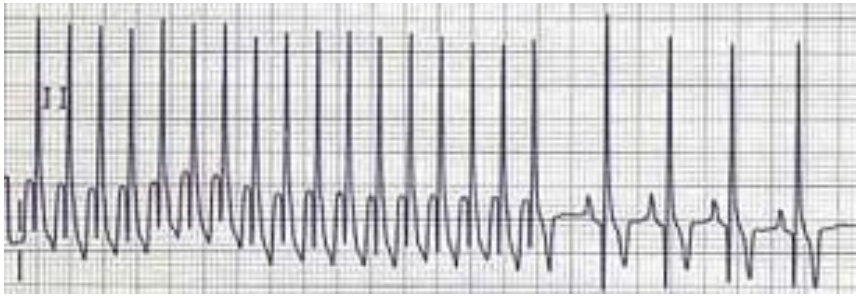


# ECG Abnormality SUPRAVENTRICULAR PREMATURE CONTRACTIONS (SVPC)

- From ectopic atrial focus
- Conducts via the same ventricular conduction pathway as sinus beats therefore ***similar*** looking QRS
- Premature P wave may or may not be obvious
- **Interrupts the normal P-P and R-R intervals**
- Typically occurs secondary to atrial stretch/disease but can be cardiac neoplasia and non-cardiac causes

NO fusion beats

# ECG Abnormality



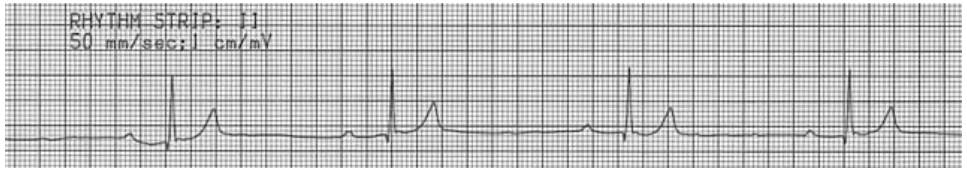

# ECG Abnormality SUPRAVENTRICULAR TACHYCARDIA

- 4 or more SVPCs in a row with a rate that generally is >150 bpm
- Abrupt onset and offset is common
- How differs from a sinus tachycardia?

  Often regular

  QRS morphology similar to sinus beats
- Premature P waves may be buried

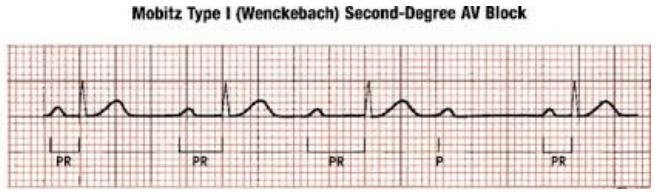
# ECG Abnormality




# ECG Abnormality 1ST DEGREE AV BLOCK

- Defined as a prolonged PR interval (> 0.13 seconds in the dog, > 0.09 seconds in the cat)
- PR interval represents conduction time from SA node through AV node, Bundle of His, bundle branches and Purkinje fibers
- Typically associated with **increased vagal tone**
- No treatment indicated

# ECG Abnormality





# ECG Abnormality ▸ 2nd degree AV block - Mobitz type I

▸ Presence of P waves not followed by QRS complexes

▸ QRS morphology normal

▸ PR interval progressively lengthens prior to block and then shortensimmediately after block

▸ Generally associated with high vagal tone; common in patients during GA/sedation

▸ Resolves with atropine administration

# ECG Abnormality


# ECG Abnormality 2nd degree AV block type II

▸ P waves not followed by QRS complexes

▸ Can have multiple P waves not followed by QRS (= high grade AV block)

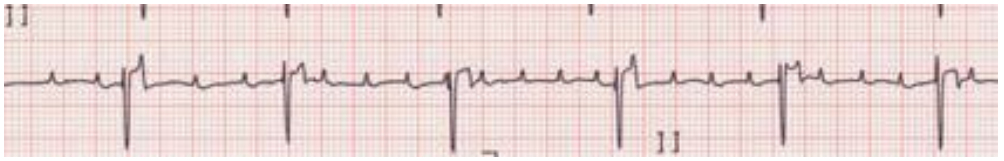
▸ PR interval is constant

▸ QRS complexes may be normal or wide

▸ Not common but can happen under GA

▸ try atropine,several doses, wake up patient?

# ECG Abnormality



# ECG Abnormality 3rd degree AV block

▸ Complete AV dissociation/ rate less than 60 dogs 100 cats

▸ P waves unassociated with QRS with faster atrial rate (P-P)

▸ Slow ventricular escape rhythm

▸ Patients are symptomatic - syncope, weakness, lethargy

▸ Cats is often incidental as escape rate does not cause observable signs
Wake up?

# ECG Abnormality

# ECG Abnormality BUNDLE BRANCH BLOCK

▸ Defined as delayed conduction through the bundle branches

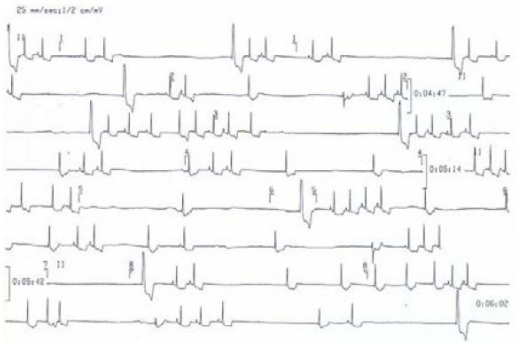
▸ Right bundle branch block is common and considered nonpathologic

▸ Can be noted with increased vagal tone, anesthesia,

or may be incidental finding

▸ Left bundle branch block is uncommon; a precursor to higher grades of heart block (3rd degree AV block)?

# ECG Abnormality



## SICK SINUS SYNDROME

- A 'catch-all' term used to describe ECGs with the following features:
  - Sinus bradycardia
  - Periods of sinus arrest
  - AV block
  - Bursts of SVT
- Most common in older small breed dogs - Westies, Schnauzers, Cocker Spaniels

## Balance anesthesia

- Appropriate stabilization of the critically ill animal before sedation or anesthesia is imperative to minimize anesthetic complications.
- Problems should be anticipated and an appropriate and efficient therapeutic plan should be formulated before anesthetic induction.
- **Consider the use of a balanced anesthesia technique to minimize potential deleterious effects of single-use drug therapy. Using a combination of different classes of analgesics may be more effective in the treatment of established pain than the use of a single agent.**
- **Example: ketamine, lidocaine for pain**

## Inotropic support-When do I use it?

These agents are given as an IV CRI because of their short half-life, at a dose of 2 to 10 mg/kg/min

- Must be close to normal blood volume for inotropes to work
- Dopamine tends to vasoconstrict
- Dobutamine tends to vasodilate
- Patients on inotropes and vasopressors should be monitored carefully for tachycardia; decrease the rate of the infusion
- or change to another inotrope.
- Other agents that may be used include ephedrine (0.05–0.5 mg/kg IV as a single bolus), norepinephrine (0.1–1 mg/kg/min IV as a CRI), and vasopressin (0.01–0.04 U/kg/h IV as a CRI).

## Inotropic support-When do I use it?

If the initial inotrope is not successful in correcting the hypotension, a

- Second agent is added while continuing administration of the first agent
- Norepinephrine is most often used in combination with dopamine or dobutamine, and
- Vasopressin can also be used in combination with inotropes ($)

## TIVA or PIVA: intravenous anesthesia

- Inhalant agents by their nature cause trend towards lower BP
- "If the patient has persistent hypotension after appropriate fluid therapy and inotropic support, discontinuation of the inhalant anesthetic should be considered, and injectable anesthetic drug therapy should be instituted" Quandt 2013.

## TIVA or PIVA: intravenous anesthesia

- Total or partial intravenous anesthesia- must be ready to control ventilation and slower recovery
- Adequate liver fcn OR use plasma metabolized meds: remifentanil, propofol
- Alfaxalone cri or boluses
- Propofol cri or boluses
- CRI of fentanyl (where available) in combination with midazolam or ketamine and/or lidocaine.
- Ketamine works best in more stable patients, vet opinion
- Ketamine safe for trauma, human med opinion "a little ketamine for you"

## Anticholinergics for bradycardia

- Atropine, 0.04 mg/kg IM, 0.02 mg/kg IV
- Glycopyrrolate, 0.01 mg/kg IM, IV
- May make respiratory secretions more viscous
- Increase heart rate and can increase myocardial work and oxygen consumption
- Glycopyrrolate does not cross the blood brain barrier or the placenta

## Opioids, mu-agonists

- MAY DELAY RECOVERY & EXTUBATION
- **Fentanyl,** 0.005 to 0.04 mg/kg IM, IV, SC
- CRI loading dose for dog, 5 to 10 mg/kg, then 0.05 mg/kg/min
- CRI loading dose for cat, 5 mg/kg, then 0.05 mg/kg/min.
- MIDAZOLAM 0.1 MG/KG/HR AFTER 0.1 BOLUS HELPS; IS REVERSIBLE; can lower total opioid dose needed
- Bradycardia hypoventilation
- **Remifentanil**, 3 mg/kg IV, then CRI, 0.1 to 0.3 mg/kg/min
- Antagonist Naloxone, 0.002 to 0.02 mg/kg IM, IV

## Opioids, mu-agonists

- Morphine, 0.2 to 2.0 mg/kg IM, subcutaneous (SC) CRI, 0.1 to 0.3 mg/kg loading dose, then 0.1 to 0.3 mg/kg/h
- Oxymorphone, 0.05 to 0.20 mg/kg IM, IV, SC
- Hydromorphone, 0.1 to 0.2 mg/kg IV, IM, SC CRI, 0.025 to 0.050 mg/kg IV loading dose, then 0.01 to 0.04 mg/kg/h

## Benzodiazepines

- Benzodiazepines are  cardiac- neutral muscle relaxants, anti-anxiety, co-induction
- Diazepam, 0.2 to 0.5 mg/kg IVpropylene glycol
- Midazolam, 0.1 to 0.4 mg/kg IM, SQ, IV; CRI, 0.1 to 0.5 mg/kg/h
- Can decrease other drug doses
- Mild sedation and muscle relaxation
- Diazepam has Antagonist: Flumazenil, 0.08 to 0.2 mg/kg IV

## INDUCTION

- Techniques such as clipping the surgical site with the animal awake
- Critically ill patients are often depressed and lethargic, and require minimal drug therapy
- for induction.
- often be reduced to as much as half of the dose used in more stable patients.
- Induction- PRIMING IS IN VOGUE NOW
- Drugs should be slowly titrated IV to effect, and the minimal amount of drug necessary
- to intubate the patient should be used.
- balanced anesthetic technique (eg, the use of multiple drug classes) will help minimize the side effects
- “The use of local anesthesia and epidural analgesia should be used, if appropriate, to decrease the amount of general anesthesia that is required” Quandt 2013

# Alfaxalone

Alfaxalone, 2 to 5 mg/kg intravenously. Small volume IM cats, small dogs

May need sedation to improve recovery

CAN REDOSE 1/3 TO ½ INITIAL VOLUME

# Etomidate

Giving a benzodiazepine first

Etomidate should not be used as the sole induction agent, because it may lead to retching and myoclonus

The use of etomidate for induction of critically ill patients that are cardiovascularly unstable because of its minimal cardiovascular effect.

The use of etomidate in the critically ill human patient- controversial

Adrenal dysfunction: The duration of the adrenal dysfunction can last from 24 to 48 hours in the critically ill patient. The use of hydrocortisone totreat the etomidate-induced adrenal insufficiency had no effect on outcome.

# Propofol

Use with a benzodiazepine to decrease the negative cardio and pulmonary effects

Propofol decrease intracranial and intraocular pressure and would be indicated for induction of the patient with a traumatic brain injury

The new formulation of propofol, PropoFol 28, is not labeled for use in cats but has been safely used in healthy cats with no indications of toxicity . The new formulation contains the preservative benzyl alcohol,

# Lidocaine

Loading dose, 1 to 2 mg/kg IV, then CRI, 1–3 mg/kg/h

CRI not recommended for use in cat

Analgesia body-wide, antiarrhythmic, slows heart rate, anti-inflammatory, free radical scavenger

Example: Spinal cord injuries

# Thank you !

Anesthesia for patients
with cardiac disease

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