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Cardiology Crash Course Online 'Mini Series'

Session 1:
Feline Cardiology
What You Need to Know

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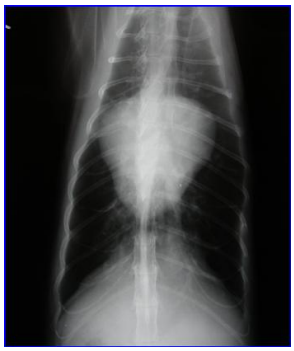

Cats and Clots: Feline Arterial Thromboembolic Disease

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Introduction

- Feline arterial thromboembolism (FATE) is one of the most serious complications associated with cardiomyopathy in the cat.
- Thrombosis represents clot formation within a cardiac chamber or vascular lumen.
- Thromboembolization occurs when a clot or part of a clot embolises from the site where it has formed and lodges within a vessel.
- In cats, the most frequent site of thrombus formation is the left atrium and atrial appendage.
- Right-sided heart and deep vein thrombosis are rare in cats (compared with humans).
- Emboli most commonly lodge in the distal aorta (and are termed "saddle thrombi"), but can also occlude a brachial, renal, coronary, cerebral or mesenteric artery.
- FATE can occur with any type of cardiomyopathy.
    - FATE is seen in HCM cats most frequently as this is the most common type of feline cardiomyopathy.
- In cats > 90 % FATE episodes are due to underlying cardiac disease.
- Arterial thromboembolism is also sometimes seen in cats with no underlying heart disease, in which the hypercoagulable state is due to systemic disease, E.g.
    - Protein losing disease (e.g. kidney disease)
    - Infection (e.g. endocarditis)
    - Neoplasia
    - Steroid administration.

Pathophysiology

- Thrombosis requires one or more of three essential conditions (Virchow's triad) to be present:
    1. Local vessel or tissue injury
        - Endothelial damage induces platelet adhesion and aggregation, and activates clotting cascade.
    2. Circulatory stasis
        - Enlarged left atrium/left atrial appendage due to diastolic/systolic impairment and poor atrial emptying (evident as "smoke" on echo).
        - Decreased clearance of activated clotting factors.
    3. Altered blood coagulability

        - Feline platelets are very reactive (platelet reactivity increased further in cardiomyopathic cats).
- Collateral circulation plays critical role in progression and resolution of clinical thromboembolic disease, and is modulated by vasoactive substances released by the clot (e.g. serotonin, prostaglandins, thromboxane A_2).
- Sudden complete arterial occlusion, coupled with decreased collateral circulation, causes substantial tissue injury and ischaemic neuromyopathy.

Clinical manifestations

- Clinical consequences of FATE are dependant on:
    - Site of arterial obstruction
        - 90% distal aorta
        - 5% brachial artery
        - 5% other sites (brain, kidney etc.)
    - Functional patency of collateral circulation.
    - Duration and completeness of obstruction.
    - Development of serious complications (e.g. self-mutilation, limb necrosis, hyperkalaemia etc).

History

- Often per acute onset of symptoms.
- Can be mistaken for trauma/neurologic disease.
- Often no history of heart disease.

Physical examination

- Dependant on specific tissues/organs that are embolised.
    - Hind limb paresis/paralysis (unilateral or bilateral) from distal aortic thromboembolism ("saddle thrombus").
    - Forelimb paresis/paralysis from brachial artery thromboembolism (R forelimb affected >L forelimb).
- Thromboemboli affecting extremities result in clinical signs that relate to the four "P"s:
    1. Paralysis/Paresis
    2. Pain
    3. Pulselesness
    4. Polar (cold distal limbs and pads).
- Painful/firm muscles
    - With saddle thrombus, cranial tibial and gastrocnemius muscles become firm from ischaemic myopathy by 10-12 hours post embolization; become softer 24 – 72 hours later.
- Vocalization due to pain.

- Dehydration and hypothermia (hypothermia is a poor prognostic indicator).
- Dyspnoea, tachypnoea, anorexia and syncope may also be present due to congestive heart failure (CHF).
- Sudden death is a possible initial clinical finding.

Cardiac evaluation

- Thoracic auscultation:
    - Tachycardia
    - Cardiac arrhythmias
    - Heart murmur
    - Gallop (S_4) sounds
    - Pulmonary crackles
    - Muffled heart and lung sounds.
- Thoracic radiography:
    - Cardiomegaly usually evident.
    - Evidence of CHF (pulmonary oedema, pleural effusion) may be present.
- Electrocardiography (ECG):
    - Abnormalities present in most cases, which include enlargement pattern, conduction system disturbance, supraventricular tachycardia, ventricular tachycardia, isolated premature atrial and ventricular complexes, and atrial standstill with sinoventricular rhythm (secondary to hyperkalaemia as a result of reperfusion injury).
- Clinical Pathology:
    - Abnormalities present in most cases, which include azotaemia, increased lactate dehydrogenase and creatine phosphokinase (consistent with widespread muscle cell injury), hyperglycaemia, hyperkalaemia, hypokalaemia.
- Echocardiography:
    - Provides rapid, non-invasive assessment of cardiac structure and function and detects intra-cardiac thrombi when present.
    - Left atrial enlargement usually present.
    - May see spontaneous echo contrast (“smoke”), associated with blood stasis and considered to be a marker for increased thromboembolic risk.
- Blood pressure measurement:
    - Rule out systemic hypertension as a cause for underlying heart disease (increased cardiac afterload causing secondary left ventricular hypertrophy).
    - Ophthalmoscopy can also be performed to check for hypertensive retinal disease (retinal vessel tortuosity and retinal haemorrhage).

Other diagnostic tests

- Blood flow in affected limb can be assessed by:
    - Cutting nail to quick to check for bleeding.
    - Doppler to detect blood flow in artery.
- Ultrasound to image thromboembolus in abdominal aorta.

Differential diagnoses

- For acute posterior paresis:
    - Trauma
    - Intervertebral disc extrusion
    - Spinal lymphosarcoma or other neoplasia
    - Fibrocartilagenous embolus.

- For acute forelimb monoparesis:
    - Trauma
    - Foreign body
    - Brachial plexus avulsion.
- Arterial thromboembolism is relatively easy to confirm from physical examination and cardiac evaluation.

Therapy

- Manage congestive heart failure or serious cardiac arrhythmias when present.
- Anticoagulant therapy
    - These drugs have no effect on established thrombi, but help to prevent further thrombus formation from the activated blood-clotting pathways.
    - E.g. Unfractionated heparin, low molecular weight heparin (LMWH).
    - Little published data on efficacy of anticoagulant therapy in cats.
    - Must monitor clotting profiles closely.
    - Bleeding is a major complication (less so with LMWH) and can be fatal.
        - Unfractionated Heparin:
            - Binds to plasma ATIII to neutralise thrombin and activated factors XII, XI, X and IX, preventing activation of coagulation cascade.
            - Doses vary widely:
                - Initial dose of 100-200 IU/kg IV
                - Then 50-100 IU/kg SQ q 6-8 hrs
            - Adjust dose to prolong APTT to 1.5 to 2.0 x pre-treatment values.
        - LMWH:
            - Derived from de-polymerization of unfractionated heparin.
            - Maintain ability to inhibit activation of factor X.

- Minimally affect thrombin, thus aPTT activity is not affected.
- Cats have rapid absorption and elimination kinetics with LMWH and need frequent dosing.
- Current dosage recommendations may not be adequate for all cats (need further studies):
    - Enoxaparin 1-2 mg/kg SQ only q12-24 hr
    - Dalteparin 100-200 IU/kg SQ only q12-24 hr
- Many cats will require at least q8 hr treatment (expensive).
- Monitoring via anti-FXa is recommended when initiating therapy (expensive).
- But not sure of 'target' anti-FXa levels in healthy cats or cats prone to ATE.

- Anti-Platelet therapy
    - Little published data on efficacy of anti-platelet therapy in cats at preventing thrombosis / re-thrombosis.
    - E.g. Aspirin, Clopidogrel
    - GI side-effects are recognized side-effect .
        - Aspirin:
            - COX-1 inhibitor - causes Thromboxane A2 (TxA2) inhibition.
            - TxA2 needed for platelet recruitment and activation.
            - By modifying platelet aggregation, may prevent further thrombus formation.
            - Effectiveness is debatable - retrospective studies show cats have high re-embolisation rates on aspirin.
            - Recommended dose for cats: 18.75 mg per cat PO q 48-72 hr.
        - Clopidogrel:
            - ADP receptor antagonist.
            - Prevents primary and secondary platelet aggregation.
            - Reduces release of serotonin (important for promoting collateral circulation).
            - Effectiveness? – *"FAT CAT" study – Feline Aortic Thromboembolism Clopidogrel vs. Aspirin Trial (ongoing at Purdue Uni, USA).*
            - Recommended dose for cats is 18.75 mg per cat PO q 24 hr.
        - N.B. The concurrent usage of aspirin and clopidogrel is recommended in human patients to prevent platelet aggregation through two separate pathways.
        - No studies have been done on the efficacy of this combination in cats.
- Supportive measures
    - Analgesia is very important, as these cats are often extremely painful!!
        - Opioids rather than NSAIDs as renal status often unknown.

- Most cats are hypothermic, dehydrated, anorexic and hypokalaemic, so it is important to maintain body temperature, hydration, nutritional support and electrolyte balance.
    - CARE with IV fluid therapy if cat is in congestive heart failure, as very prone to fluid overload and worsening of CHF.
- Bandage limbs to prevent self-mutilation of devitalized extremities.
    - Monitor limb viability closely.
    - Limb amputation or skin grafts may be necessary once stabilized.
- Monitor blood parameters closely (renal function, electrolyte status, coagulation profiles).
    - If cat has embolised renal artery this will become evident with sequential blood parameter monitoring.
- N.B. Vasodilator therapy (E.g. ACP, hydralazine) has been suggested to encourage opening of collateral circulation – no proof of efficacy and may exacerbate systemic hypotension, so use with caution!

Reperfusion injury

- Hydrogen and potassium ions are released from damaged cells once reperfusion occurs to damaged muscle tissue.
- Can lead to severe metabolic acidosis and hyperkalemia.
- Life threatening complication!

FATE prognosis

- Short-term prognosis will depend on nature of underlying cardiomyopathy and response of congestive heart failure to therapy.
- Can take up to 2 weeks for motor function to begin to return in limbs after saddle thrombus, and up to 6 weeks for motor function to be normal.
    - May require limb amputation or skin grafts.
    - May be high-risk general anaesthetic candidates.
- Most cats experience further arterial thomboembolic episodes within days to months after initial episode, although some studies report survival for several years.

Feline Systemic Hypertension: Diagnosis and Management

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Background

- Average values for systolic/mean/diastolic systemic arterial blood pressure in calm, unsedated cats is 125/100/80 mmHg, respectively.
- Systemic hypertension is defined as a persistent, abnormal elevation of blood pressure.
- This can refer to an elevation in systolic pressure, diastolic pressure, or both.
- In cats, age has an effect on blood pressure, i.e. healthy cats greater than 11 years of age have been shown to have significantly higher blood pressure compared with healthy cats less than 11 years of age.

Indications for measuring blood pressure

- It is critical to measure blood pressure in animals with clinical signs that might be referable to systemic hypertension.
- Animals at risk should also be assessed to enable early identification of hypertension and appropriate intervention.
- Most cats with severe systemic hypertension are older (> 12 years).
- Systemic hypertension in cats is almost always secondary to another systemic disease process.
- Chronic renal failure and hyperthyroidism are most commonly implicated.
    - N.B. Heart disease does not cause systemic hypertension (in fact, cats with advanced heart disease are more likely to be hypotensive).
- This is in contrast with humans, in which most systemic hypertension is primary (essential).

Typical clinical signs of systemic hypertension

- Presenting signs associated with severe systemic hypertension include:
    - blindness and hyphaema
    - ataxia, seizure and sudden collapse (signs associated with cerebrovascular accident)
    - epistaxis
    - occasionally laboured breathing (signs related to congestive heart failure).
- Cats with acute severe hypertension may have a syndrome of progressive stupor, head pressing, seizures and death.
- If a diagnosis is established early, these clinical signs will usually resolve rapidly (within 24 hours) with effective anti-hypertensive treatment.

Organs at risk from systemic hypertension

- Systemic hypertension can damage a variety of tissues.
- The **eyes** are the organ most commonly reported to be affected by systemic hypertension in cats.
    - The findings associated with hypertensive ocular injury include haemorrhage of the retina, vitreous or anterior chamber, retinal detachment and atrophy, retinal oedema, retinal vessel tortuosity and glaucoma.
- The **kidney** is susceptible to hypertensive damage.
    - In a healthy kidney, the pre-glomerular arterioles constrict when blood pressure is elevated, to protect the renal glomerulus.
    - In cats with renal insufficiency, these preglomerular arterioles are dilated and poorly responsive to changes in blood pressure.
    - This allows increased blood pressure to be transmitted directly to the glomerula capillary bed.
    - This glomerular hypertension may cause glomerular damage and a progressive fall in renal function unless the hypertension is effectively treated.
- The **heart** is susceptible to hypertensive damage.
    - As a result of it working against increased afterload, left ventricular hypertrophy may develop.
    - This may regress with effective anti-hypertensive treatment.
- The **brain** is also susceptible to hypertensive damage.
    - Signs associated with cerebrovascular haemorrhage (head tilt, depression, seizures) are seen clinically in cats with uncontrolled hypertension and are associated with a poor prognosis.

Blood pressure measurement techniques

- Blood pressure may be measured by either direct or indirect methods.
- Attention to the technique of blood pressure measurement is more important than which equipment is used.
- The procedure should be standardized within the clinic and carried out in the same way for each patient, by trained operators.

- **Direct** blood pressure measurement is the “gold standard”.
- This involves placement of a 22-25-gauge needle or indwelling catheter into a peripheral artery (typically femoral or dorsal pedal artery).
- The needle or catheter is then attached to a calibrated pressure transducer, zeroed at the level of the sternum in the laterally recumbent patient, and the pressure is then displayed on a screen or recording chart.
- Advantages of this method are that it yields systolic, diastolic and mean pressures and it provides a “true” measurement.

- Disadvantages of this method are that it is technically difficult in unsedated animals, obese or small patients (and is therefore rarely performed in feline patients).
- It requires more physical restraint and induces more pain than non-invasive methods, thereby giving rise to sympathetic stimulation and raised blood pressure.
- Systemic hypertension is considered to be present when blood pressure measurements exceed 160/100 mmHg using direct arterial puncture in unacclimated animals.
- This method is best suited for anaesthetic or acute critical care blood pressure monitoring.

- **Indirect** blood pressure measurement is more applicable in a clinical setting as it is technically easier and requires less patient restraint.
- Indirect blood pressure assessment can be made with Doppler or Oscillometric technique.
- In cats the **Doppler method** is preferred as it is the more accurate of the two indirect methods.
- All indirect techniques involve wrapping an inflatable cuff around an extremity to constrict a peripheral artery.
- Choice of cuff size is very important.
- In cats, cuff width should measure 30-40% of the circumference of the limb (at cuff site).
- An oversized cuff may give falsely low readings and an undersized cuff may give falsely high readings.
- If the ideal cuff size is midway between two available sizes, the larger cuff should be used, as it will theoretically produce the least error.
- If a limb is used, the limb should be kept at the level of the heart.
- Inflate the cuff slowly if the patient is awake to ensure they are not startled.
- The cuff size and the position of the cuff (limb or tail) should always be recorded in the animal's medical record for future reference, so that future results are comparable.

- The Doppler method utilizes a piezoelectric crystal to detect blood flow as a change in the frequency of reflected sound waves (Doppler shift) due to the motion of red blood cells in the underlying artery.
- For the Doppler technique, the cuff is usually placed over the median artery and the transducer is placed between the carpal and metacarpal pad.
- The transducer detects blood flow in the constricted artery once systolic blood pressure overcomes the pressure of the inflated cuff.
- The diastolic blood pressure may be estimated when the pitch of the Doppler flowmeter's sound changes.
- The Doppler signal is enhanced if the hair is clipped and acoustic gel is placed at the site of transducer placement.
- Use headphones to ensure that the sound does not stress the patient, and to enable the sound of the machine to be heard more effectively, thus increasing accuracy.
- Just the right amount of pressure on the transducer is essential: too much and the flow will be reduced, too little and it will slip out of position.

- The technique is technically easy, does not cause the patient discomfort, and requires minimal restraint.
- This is the least expensive equipment.
- The major limitation of the Doppler method is imprecise discrimination of sounds designating the diastolic, and therefore the mean blood pressure.
- Therefore the Doppler method may be unreliable for the routine diagnosis of diastolic hypertension.
    - N.B. In cats and dogs, little is known about the clinical significance of diastolic hypertension, so clinical importance is focused primarily on systolic hypertension.
- Despite the relative ease of use, obtaining reliable values from an indirect device is not easy.
- Multiple blood pressure measurements should be obtained from each patient, rather than a single recording that is prone to inaccuracies.
- An average of all values should then be taken as an estimate of blood pressure.
- If in doubt, the session can be repeated on another day and with cuff placement at another site.

Anxiety-induced artifact: The "White Coat Effect"

- The visit to the veterinary clinic, hospitalisation and other unusual environmental conditions in the veterinary hospital may induce anxiety in an animal.
- "White Coat Effect" refers to the false elevation in blood pressure that may be obtained secondary to catecholamine release associated with anxiety.
- The magnitude of this effect varies widely among animals and among visits in the same animal.
- Blood pressure should be measured in a calm, motionless cat, before physical examination is performed, in a quiet room, away from other animals, humans and background noise to minimize the risk of anxiety-induced hypertension.
- The owner should be present if possible to calm the cat.
- The cat should be allowed a minimum of 10 minutes to acclimatize to its surroundings.
- Sedatives will affect blood pressure, so animals should not be sedated for blood pressure measurement.
- Multiple readings should be taken on an individual animal, preferably over several days, rather than relying on a single measurement for the basis of treatment.

Which animals to treat

- Systemic arterial blood pressure is a product of cardiac output and total peripheral resistance.
- Therefore antihypertensive therapy is generally aimed at reducing cardiac output, total peripheral resistance, or both.
- When treating a hypertensive animal, it is not usually possible to restore blood pressure to normal values with antihypertensive medications.
- The goal should be to restore blood pressure to within 30-50 mmHg of the normal range.
- Antihypertensive medications have a variety of side effects, so it is important that the clinician is confident of the diagnosis before embarking on therapy.

- The effectiveness of therapy should be judged on the basis of repeated blood pressure measurements.
- Due to the difficulties and uncertainty associated with blood pressure monitoring in cats, only those animals with marked elevations of indirectly measured blood pressure and /or clinical signs directly attributable to hypertensive injury, should be considered candidates for treatment.
- Although opinion between authors varies, as a general guideline, treatment is indicated in any animal with sustained systolic blood pressure greater than 200 mmHg or diastolic blood pressure greater than 120 mmHg, regardless of other clinical findings, due to the risk of ocular injuries with severe hypertension.
- Any cat with sustained elevations in systolic blood pressure greater than 170 mmHg or diastolic blood pressure greater than 100 mmHg, with clinical signs of retinal lesions, chronic renal disease or left ventricular hypertrophy, that could be caused or exacerbated by systemic hypertension, should also be treated.
- However, opinion still varies as to whether antihypertensive therapy is indicated in animals with moderate elevations of blood pressure (170-200/100-120 mmHg), but without clinical signs.
- Animals with mildly elevated blood pressure 120-170/80-100 mmHg should not be treated as these may be false elevations (e.g. white coat syndrome).
- Animals with normal blood pressure or in which blood pressure has not been measured, should not be treated.
- Hypertension associated with chronic renal disease necessitates life long treatment with antihypertensive agents.
- Hypertension associated with hyperthyroidism can usually be expected to resolve within 1-3 months following effective treatment of the underlying condition, unless chronic renal failure is also present.
- Periodic dosage adjustments based on blood pressure measurements are indicated.

Treatment options

- Non Pharmacologic therapy
    - Treatment of underlying medical conditions
        - E.g. hyperthyroidism
    - Avoidance of drugs that can cause/exacerbate hypertension
        - Glucocorticoids
        - Phenylpropanalomine
        - Nephrotoxic agents (e.g. cyclosporine, aminoglycosides)
    - Dietary modification
        - N.B. Role of sodium restriction in feline hypertension is undetermined
    - Weight control
        - Controlling obesity may help
- Pharmacologic therapy
    - Calcium channel blockers

        - E.g. Amlodipine (second-generation calcium channel blocker has more effect on peripheral vasculature and less on cardiac contractility and heart rate).
        - Potential side effects include anorexia, lethargy, hypotension, vomiting.
        - Amlodipine appears to be safe and effective as monotherapy for systemic hypertension in cats
        - Amlodipine dose: 0.625-1.25 mg per cat PO q 24h.
    - Angiotensin-converting enzyme (ACE) inhibitors
        - E.g. Enalapril, benazepril, ramipril
        - Inhibit Angiotensin II production (potent vasoconstrictor), decrease aldosterone secretion (thus reducing renal sodium retention), increase vasodilatory prostaglandin synthesis, inhibit vascular hypertrophy.
        - Potential side effects include renal insufficiency, vomiting, diarrhoea, systemic hypotension.
        - May be particularly useful if proteinuria or heart failure present.
        - Limited data, but can be effective as monotherapy in cats with mild-moderate systemic hypertension associated with chronic renal failure; may be more efficacious if combined with a second anti-hypertensive drug, such as amlodipine.

Feline Cardiomyopathies: Diagnosis and Treatment

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Introduction

- Cardiomyopathies represent the most important type of feline cardiovascular disease seen in clinical practice.
    - Congenital heart disease is relatively rare in cats.
- Cardiomyopathies can be described as:
    - Primary
    - Secondary
        - E.g. secondary to systemic, metabolic or nutritional disorder.

- N.B. There is a generally accepted classification scheme for feline cardiomyopathies.
    - However, it is important to note that many cases may have overlapping features, so categories do not have sharply defined boundaries:
        - Hypertrophic cardiomyopathy (HCM).
            - Sub-classified into non-obstructive form (HCM) and obstructive form (HOCM).
        - Dilated cardiomyopathy (DCM).
        - Restrictive cardiomyopathy (RCM).
        - Unclassified cardiomyopathy (UCM).
        - Arrhythmogenic right ventricular cardiomyopathy (ARVC).

Hypertrophic Cardiomyopathy

- Most commonly encountered type of feline cardiomyopathy and therefore much more is known about HCM than other types of feline cardiomyopathy.
- Characterised by hypertrophied, non-dilated left ventricle, in the absence of other cardiac disease (e.g. aortic stenosis) or systemic disease (e.g. hyperthyroidism, systemic hypertension) capable of causing left ventricular hypertrophy.
- Left ventricular hypertrophy is defined as end-diastolic measurements of interventricular septum and / or left ventricular free wall > 6 mm in diameter.

- Some cats with HCM have a dynamic left ventricular outflow tract obstruction that causes a sub-aortic pressure gradient (obstructive form of HCM).
    - This is also termed hypertrophic obstructive cardiomyopathy (HOCM).

    - HOCM is typically caused by systolic anterior motion of mitral valve (SAM).
    - SAM results in a left sided systolic heart murmur caused by a combination of mitral regurgitation and dynamic sub-aortic stenosis.
- Cats with non-obstructive form of HCM may not have a heart murmur, as there is no turbulent flow within the cardiac chambers or great vessels.
- So it is important to remember that the absence of a heart murmur does NOT exclude the possibility of myocardial disease such as HCM!
- Non-obstructive form of HCM is more common than obstructive form of HCM.
- All age ranges are affected with HCM, but mean age is reported to be 4.8 – 7 years.
- Male predominance.
- Domestic shorthairs are most frequently affected.
- Inherited in some breeds:
    - Maine Coons, Ragdolls (each has a different mutation in the same gene MYBPC3)
    - Genetic test available, BUT:
        - Not all Maine Coons with HCM have this mutation so probably other genetic mutations involved.
        - Not all Maine Coons with this mutation appear to develop HCM.
- HCM is uncommon in Siamese, Burmese and Abyssinians.

Pathophysiology of HCM:

- Heart failure with HCM is due primarily to diastolic dysfunction.
- Left ventricular filling depends on:
    - Ventricular relaxation, which is an active, energy dependent process, i.e. the thicker the ventricular wall, the longer it will take to relax.
    - Chamber compliance, which is a passive process and is affected by amount of fibrosis within myocardium etc.
- Left ventricular filling pressure increases in cats with HCM, due to delayed ventricular relaxation and myocardial stiffness, which causes left atrial pressure to increase.
- As a result, pulmonary venous pressures increase and eventually pulmonary congestion develops.
- In <u>cats</u>, congestive heart failure may manifest as:
    - Pulmonary oedema (with left-sided CHF only).
        - Same as in dogs.
    - Pleural effusion (with both left and right-sided CHF).
        - Unlike dogs which only develop pleural effusion with right-sided CHF.
    - Pericardial effusion can also develop in some cats with advanced left-sided CHF as well as right-sided CHF.
        - Rarely see pericardial effusion in dogs with CHF.
    - <u>It is the vascular anatomy that makes cats different to dogs!</u>

        - In cats, visceral pleural veins drain into the pulmonary venous circulation, rather than into the systemic venous circulation (the parietal pleural veins drain into the systemic circulation).
        - The pericardium is lined with visceral pleura, so it is possible that the pericardial venous drainage also empties into the pulmonary venous circulation.
        - Therefore increases in pulmonary venous pressure are transmitted to the visceral pleural veins and probably, the pericardial veins.
        - CHF in cats can produce a serous, serosanguinous, pseudochylous or chylous effusion.
            - Not unusual for a serous effusion to progress to a pseudochylous or a chylous effusion (mechanism unknown).
- Other HCM sequelae include:
    - Myocardial ischaemia
    - Coronary arteriosclerosis
    - Ventricular and supraventricular arrhythmias
    - Left atrial thrombus formation.

Dilated Cardiomyopathy

- Rare since routine dietary supplementation with Taurine (essential amino acid in cats).
- Diagnosis is based on echocardiography.
    - Dilated, hypokinetic LV with relatively thin walls.

Restrictive Cardiomyopathy

- Normal to mildly hypertrophied LV walls.
- Mild ventricular dilation.
- Marked atrial dilation (often biatrial).
- Mitral +/- tricuspid insufficiency.
- Low-normal fractional shortening.
- Often have extensive endocardial, sub-endocardial or myocardial fibrosis causing severe diastolic dysfunction.

Unclassified Cardiomyopathy

- Some feline myocardial diseases have features that do not fit into a discrete category of HCM, RCM or DCM etc.
- OR may display characteristics of more than one type of cardiomyopathy.

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

- Fibro-fatty infiltration of the right ventricular myocardium.
- Right ventricular chamber enlargement (+/- tricuspid regurgitation).
- Rule out congenital tricuspid valve dysplasia.
- Ventricular arrhythmias are common.
- Signs of right-sided congestive heart failure predominate.

Typical Cardiac History

- Asymptomatic cat with heart murmur, arrhythmia or gallop rhythm detected at routine evaluation.
    - Owner may report cat to be asymptomatic ("normal") at home.

  OR
- Tachypnoea, dyspnoea noticed by owner.
    - N.B. Coughing is rarely observed in cats with pulmonary oedema, unlike dogs (coughing is predominantly a feature of primary lower airway disease in cats e.g. feline asthma).
- Clinical signs associated with arterial thromboembolic episode.
- Syncope
    - Usually exertional syncope associated with left ventricular outflow tract obstruction (i.e. HOCM).
    - But tachy/bradyarrhythmias are also a possible cause of syncope in cats.
- Anorexia, vomiting (may precede overt signs of heart failure by a few days).

Physical Examination and Diagnostic Tests:

- **Thoracic auscultation**
    - Tachycardia
    - Cardiac arrhythmias
    - Heart murmur
    - Gallop (S_4) sounds
    - Pulmonary crackles
    - Muffled heart and lung sounds.
    - Careful cardiac auscultation while palpating femoral pulses.
        - Murmurs in cats are often sternal or parasternal.
        - Murmur intensity may be variable.
        - Gallop rhythms and arrhythmias in cats may be intermittent.
    - Pay close attention to the pulmonary auscultation, breathing pattern and rate.

- The majority of murmurs in cats arise from the left ventricular outflow tract (LVOT) and right ventricular outflow tract (RVOT).
    - In the dog LVOT and RVOT are up on the side of the chest, at the "heart base".
    - In the cat, they are down on the sternum.
- Higher incidence of physiologic or iatrogenic murmurs in cats vs. dogs
    - i.e. Heart murmurs in the absence of structural heart disease.
    - Cats have very compliant thoracic cages.
    - It is possible to induce a soft murmur in a cat by pressing too hard with a stethoscope while auscultating, effectively "squashing" the heart, most likely the compliant right ventricle, producing dynamic right ventricular obstruction.
    - Important to auscultate cats in a standing or sitting position and to only gently apply the stethoscope to the chest

- **Thoracic radiography**
    - Cardiomegaly usually evident (unless cat only has mild or early cardiomyopathy without significant left atrial enlargement – more likely in asymptomatic patient).
    - Evidence of congestive heart failure (pulmonary oedema +/- pleural effusion).

- **Electrocardiography (ECG)**
    - ECG abnormalities are highly variable.
        - If present, these can include enlargement pattern, conduction system disturbance (left anterior fascicular block), supraventricular tachycardia, ventricular tachycardia, isolated premature atrial and ventricular complexes.

- **Echocardiography**
    - Provides rapid, non-invasive assessment of cardiac structure and function.
    - Required for definitive diagnosis of type of cardiomyopathy:
        - Allows assessment of severity of left ventricular hypertrophy in HCM.
        - Allows detection of left ventricular outflow tract obstruction in HOCM.
        - Allows diagnosis of other causes of turbulent blood flow giving rise to cardiac murmur (e.g. mitral regurgitation).
        - Allows evaluation of myocardial function (diastolic and systolic).
        - Allows detection of intra-cardiac thrombi.
        - Allows detection of other concurrent cardiac conditions (e.g. aortic stenosis, which could be a possible cause of left ventricular hypertrophy).

- **Blood tests**
    - Haematology.
        - Typically normal.
    - Biochemistry
        - May see pre-renal azotaemia in CHF.
        - Otherwise non-specific, but important as baseline for medication monitoring.
        - Renal parameters and electrolytes should be monitored with ACE inhibitors, diuretics and antiarrhythmic therapy.
    - Thyroid (T4)
        - Rule out hyperthyroidism as potential cause of left ventricular hypertrophy in older cats (check for goiter).
    - NT-proBNP
        - BNP is neurohormone secreted by the ventricle in response to increased wall stress (pressure +/- volume).
        - It counteracts the effects of RAAS stimulation, resulting in natriuresis and vasodilation.
        - Commercially available assay utilises ELISA technology (feline specific).
        - Assay detects inactive NT-proBNP, as more stable than active compound.
        - Potential roles of NT pro-BNP
            - Distinguishing cardiac from non-cardiac dyspnea:
                - NT-pro BNP is increased in cats with clinically relevant structural heart disease.
                - Highest increase is seen in symptomatic cats with CHF.
                - Therefore may be useful additional diagnostic test for distinguishing cardiac from non-cardiac dyspnoea in the cat, particularly when symptoms are ambiguous.
                - Do not use as sole test for CHF!
                - NOT a substitute for good physical exam, history, Xrays.
                - Recent study *(Singletary et al JVIM 2012)* showed that NT-pro BNP, when used together with standard diagnostic tests, significantly improved diagnostic accuracy and confidence in a general practice setting.
            - As a screening test for occult cardiomyopathy:
                - Conflicting data on utility of NT-pro BNP to detect cats with asymptomatic (occult) cardiomyopathy.
                - Study by *Fox et al JVIM 2011* showed that NT-pro BNP could reliably discriminate normal cats from cats with occult cardiomyopathy in a selected study population of > 200 cats.
                - Was most reliable for identifying moderate to severe occult cardiomyopathy.

        - Further studies needed to assess NT-pro BNP test performance in unselected general feline population (i.e. true screening test).
    - Limitations:
        - Not 100% reliable!
        - If NT-proBNP is normal in a cat suspected of having heart disease (e.g. cat with heart murmur), an echo is still needed to rule out cardiomyopathy.
        - Renal dysfunction, systemic and pulmonary hypertension can affect the levels of circulating NT-proBNP in cats and produce false positive results.
        - Indiscriminate testing of patients with little likelihood of CHF will lead to high incidence of false positive results and frustration for clinician and owner.
        - No "cage-side" SNAP test available.
        - 24 hour minimum turn-around time for results.
        - Limits utility in emergency situations.

Therapy:

- The clinical course and outcome of cats with cardiomyopathy is hard to predict, which complicates therapy decisions.
- Diuretics are certainly NOT indicated in asymptomatic cats that have never had congestive heart failure and may in fact be detrimental in these patients by stimulating the renin-angiotensin-aldosterone system (RAAS) prematurely.
- However, it is unclear whether beta-blockers, calcium channel blockers and ACE-inhibitors delay disease progression, protect against sudden cardiac death, or improve prognosis in asymptomatic cats with cardiomyopathy.

- **Treatment considerations for asymptomatic but potentially high-risk patients**

    - Several important features may increase the risks of morbidity and mortality in asymptomatic cats, and therefore may warrant prophylactic treatment.

    i. Cats with occult HCM and marked left ventricular hypertrophy.
        - "Marked hypertrophy" refers to interventricular septum and/or free wall thicknesses in diastole > 8 mm.
        - The following drugs may be beneficial:
            - Beta-blockers
                - To slow heart rate, decrease dynamic left ventricular outflow tract gradients and decrease myocardial oxygen demand.
            - Calcium channel blockers

        - To improve ventricular diastolic relaxation and filling.
    - ACE Inhibitors
        - To blunt neuroendocrine (RAAS) activation and prevent cardiovascular remodelling.

ii. Spontaneous echo contrast (“Smoke”)
    - Indicative of left atrial blood stasis and considered to be associated with increased thromboembolic risk.
    - Anti-coagulant or anti-platelet therapy could be considered (please refer to notes on feline arterial thromboembolic disease for further detail).

iii. Tachyarrhythmias
    - Rapid heart rates will decrease diastolic filling time, which can:
        - Increase dynamic left ventricular outflow tract gradients in cats with HOCM.
        - Decrease cardiac output.
        - Increase myocardial oxygen demand.
        - Decrease coronary artery perfusion.
    - Beta-blockers are useful for controlling supraventricular AND ventricular tachyarrhythmias in cats.

iv. Syncope
    - Recurrent syncope is a risk factor for sudden death in humans with HCM.
    - In cats with HCM, this is usually exertional syncope associated with left ventricular outflow tract obstruction (i.e. HOCM).
    - Beta-blocker therapy may help to decrease or abolish dynamic left ventricular outflow tract obstruction, and therefore control syncope.
    - NB. Arrhythmias (tachycardias & bradycardias) can also cause syncope.

v. “High risk” family history
    - Maine Coon, Ragdoll, Sphynx, British Shorthair, Persian, Norwegian Forest Cat are all predisposed breeds for HCM.
    - N.B. Maine Coons, Ragdolls, Sphynx often develop HCM at a young age.
    - Recommend serial echocardiographic monitoring of any at-risk cat.
    - In the case of familial HCM early intervention with Ca-channel blocker or Beta-blocker may be helpful?? (mixed opinions).

- **Treatment of symptomatic cats**
  - **Initial emergency treatment (first 24-48 hrs):**
    - Therapy should be aimed at:
      - Eliminating life-threatening pulmonary oedema and pleural effusions.
      - Controlling haemodynamically significant tachyarrhythmias – to improve ventricular filling and relaxation, and to decrease dynamic left ventricular outflow tract obstruction.
      - Managing arterial thromboembolism and its consequences (please refer to accompanying notes on feline arterial thromboembolic disease (FATE) for more detail).
      - N.B. Avoid stressing dyspnoeic cats – these are VERY unstable patients!
      - Hospitalisation for cage rest and close monitoring.
      - Oxygen therapy.
      - Thoracocentesis as required
        - Significant volume pleural effusions must be drained initially – will not resolve with furosemide therapy.
      - Blood pressure if possible.
      - Furosemide IV or IM (1-2 mg/kg boluses).
        - Usually need to give IV every 2-6 hours as peak IV effect at 30 mins.
        - Cats are more sensitive to furosemide side effects (e.g. dehydration, hypokalaemia, azotaemia) than dogs - monitor closely!
      - Pimobendan for systolic support?
        - Off licence use.
        - Suggested dose: 1.25 mg per cat PO q 12 hr.
      - ACE I
        - Continue if already on ACE I.
        - If not, stabilise any hypotension before starting ACE I in acute phase.
      - Nitroglycerine ointment (2%)?
        - Venodilation to decrease venous congestion.
        - WEAR GLOVES!
        - Pea sized bleb applied to hairless area inside pinna q 6-8 hr.
      - Address heart rate and rhythm if necessary to stabilise patient
        - Calcium channel blockers
        - Beta-blockers
          - CARE in cats with low FS% as may decrease systolic function further and worsen CHF.
        - Digoxin not used for acute situation.

        - Consider any concurrent systemic disease when deciding on best treatment options.
            - Systemic hypertension, Hyper T4, CRF.

- **Chronic maintenance therapy**
    - Therapy should be aimed at:
        - Maintaining cardiac compensation.
        - Preventing arterial thromboembolism.
        - Preventing further myocardial remodelling.
        - Improving quality of life.
        - Prolonging survival.
        - Identifying and treating underlying systemic conditions and risk factors.
            - E.g. systemic hypertension, hyperthroidism, taurine-deficient diets etc.
    - Diuretics
        - Goal of diuretic therapy is to control signs of congestive heart failure.
        - As soon as breathing normalises (< 30 breaths / min), furosemide is changed from IV IM to PO administration and the dose is gradually decreased to lowest possible effective dose.
        - **Furosemide**
            - Typically start off by giving 5 mg per cat PO q 12-24 hrs.
            - May need higher maintenance dose in some cats
            - It may be possible to gradually decrease this dose further, as long as owners are instructed to monitor respiratory rate and effort closely at home.

        - As heart failure progresses, cats will require increasing doses of furosemide and may benefit from the addition of a second diuretic, such as a potassium sparing diuretic (e.g. spironolactone).
        - **Spironolactone**
            - Weak diuretic. NOT first line diuretic (not a substitute for furosemide).
            - Aldosterone antagonist, independent of diuretic action.
                - May be more important role?
            - 2 mg/kg PO q 24 hr effectively inhibits aldosterone and has diuretic effect in dogs.
            - Appropriate dose in cats not known, so start lower and increase to effect:
            - Suggested starting dose: 3.125 - 6.25 mg per cat PO q 24 hr.
            - Increased absorption if given with food.
            - Usually well tolerated (but can cause facial pruritus, lethargy, vomiting, diarrhoea, hyperkalaemia).

- N.B. BUN, creatinine and electrolytes should be monitored in all cats on chronic diuretic therapy.

- Additional pharmacologic options can be considered for the following theoretical reasons:
  - Beta-blockers
    - To decrease dynamic left ventricular outflow tract gradients.
    - To control tachyarrhythmias.
    - To decrease dynamic LVOT gradients (HOCM).
    - To control tachyarrhythmias.
    - SVTs and VTs in cats.
    - Start dosing low and increase to effect.
    - **Atenolol**: 6.25 mg per cat PO q 12-24 hr.
    - Also available as liquid - Tenormin syrup (Atenolol 5mg/ml).
    - Enables a lower dose to be given (e.g. small or geriatric cat).
    - May improve compliance (easier than giving pill?).
    - Absorption of liquid seems to be better than tablet form so start cautiously.
    - Can cause lethargy and bradycardia.

  - Calcium channel blockers
    - To improve ventricular diastolic relaxation and filling.
    - Improve diastolic relaxation and LV filling.
    - Decrease dynamic LVOT gradients in cats with HOCM (less effective than beta-blockers?).
    - Control tachyarrhythmias (SVTs only).
    - Start low and increase dose to effect.
    - Can cause lethargy, vomiting, bradycardia.
    - **Diltiazem** (Hypercard 10mg)
    - May need to give PO q 8 hr, which often makes compliance a problem.

  - ACE inhibitors
    - To blunt neuroendocrine (RAAS) activation and prevent cardiovascular remodelling.
    - N.B. theoretical concern that decreasing blood pressure with ACE inhibitors could be deleterious in cats with severe dynamic left ventricular outflow tract obstruction or syncope.

  - Inodilators
    - Positive inotrope.

- Vasodilation.
- Anti-cytokine effects (clinical relevance?).
- Anti-platelets effects (clinical relevance?).
- **Pimobendan** licensed for CHF in dogs.
- Benefit in cats with systolic dysfunction?
- Not licenced for cats.
- Suggested dose (from personal experience): 0.625 – 1.25 mg per cat PO q 12 hr (depending on size of cat and degree of systolic dysfunction).

- However, there is a paucity of data to indicate which is the optimal therapy for chronic management of HCM.
- Is combined therapy better than monotherapy with furosemide?
- How easy is the cat to medicate?
    - Detrimental effect of stressing cat.
- How dedicated is owner?
    - Long term cost / inconvenience etc.

HCM prognosis

- Minimal survival data for other types of cardiomyopathy, as most studies have focused on HCM.
- Asymptomatic HCM / HOCM cats:
    - Variable prognosis reported.
    - Most progress very slowly over 3-5 years.
    - Predisposed breeds that develop HCM at young age can have more rapid progression (e.g. Maine Coon, Ragdoll, Sphynx) with earlier onset of clinical signs.
- Cats with HCM and CHF:
    - Variable prognosis reported.
    - Study in 1992 showed a 3 month survival rate.
    - Study in 2002 showed a 1.5 year survival rate.
        - Is this because we are becoming better at diagnosing and treating CHF?
- Cats with HCM and systemic thromboembolism:
    - Also variable prognosis reported!
    - But in general considered poor.
    - 2 months to 11 months depending on study.