Although there are highly sophisticated and advanced diagnostic modalities in cardiology, the basic technique of a good cardiovascular examination is still an essential fundamental element of the cardiovascular workup. An overview of the common diagnostic modalities in cardiology and their uses and pitfalls will also be presented at the end of the lecture.

The initial assessment of the patient begins with the signalment and history. In pediatric or juvenile patients, signalment helps increase suspicion for certain congenital defects. Rottweiler, Golden Retriever, Great Dane, Boxer, and German Shepherd dogs are particularly predisposed to develop subaortic stenosis. In contrast, terriers and small breed dogs are more likely to develop pulmonic stenosis. Tricuspid valve dysplasia +/- mitral valve dysplasia are the most common defects of Labrador Retrievers, which cannot be excluded based on the absence of a murmur on physical examination. Small breed dogs such as the poodle, Yorkshire terrier, Shetland sheep dog, and many others typically develop patent ductus arteriosus. Developmental heart diseases are more common in middle age to older animals, and include myxomatous mitral valve disease in small dogs (especially the Cavalier King Charles Spaniel), dilated cardiomyopathy in large breed dogs, and hypertrophic cardiomyopathy in cats. Highly predisposed breeds for development of DCM include Boxer dogs, Doberman Pinschers, and giant breed dogs.

Objectives for cardiac auscultation include assessment for a murmur, extra heart sound (gallop or systolic click), or arrhythmia. The murmur is localized to left or right side, basilar versus apical point of maximal intensity, with the timing defined as systolic (90% of murmurs), diastolic, continuous, or to-and-fro (i.e. subaortic stenosis with aortic insufficiency). Certain murmur characteristics are pathognomonic for specific diseases, such as a continuous left basilar murmur heard in patients with a patent ductus arteriosus. Murmurs in cats may be present due to underlying heart disease, systemic diseases causing volume overload to the heart or high output state (significant anemia, fluid overload, hyperthyroidism, fever), or may be innocent. Most innocent murmurs are relatively soft (I-III/VI), whereas loud murmurs are most common in hypertrophic obstructive cardiomyopathy or congenital heart defects. The typical murmur of mitral regurgitation is a left apical holosystolic or pansystolic murmur. Pansystolic murmurs obscure the second heart sound, and are usually present in the face of severe mitral regurgitation. In small breed dogs diagnosed with mitral valve degeneration, the murmur intensity roughly parallels the degree of mitral regurgitation: soft murmurs (I-II) are associated with mild mitral regurgitation and loud murmurs (≥ IV) are associated with severe mitral regurgitation. The typical auscultation abnormalities in dilated cardiomyopathy include a soft left apical holosystolic murmur from secondary mitral regurgitation and a S3 gallop. A gallop heart sound is an extra heart sound, either S3 or S4, and occurs in diseases causing a stiff left ventricle (in cats mostly) or significant volume overload to the heart (cats: anemia, hyperthyroidism, fluid overload; dogs: severe AV insufficiency, dilated cardiomyopathy). A mid-systolic click is a classic feature of mitral valve prolapse and myxomatous valve degeneration, and is often heard when the mitral regurgitation is mild. Arrhythmias may consist of premature beats, runs of
tachycardia, irregularly irregularly rhythm, or bradycardia. Auscultation alone cannot
 diagnose the type of premature beat (ventricular versus atrial premature complex), and an
electrocardiogram must be done to diagnose the specific rhythm abnormality. An
irregularly irregular rhythm may be caused by atrial fibrillation or frequent atrial or
ventricular premature complexes, and must be distinguished by an ECG.

Assessment of femoral arterial pulse intensity and whether pulses are synchronous
with the heart beat are also essential objectives in the cardiac examination. Femoral
pulses reflect the pulse pressure which is the difference between the systolic and the
diastolic arterial blood pressure. Decreased femoral arterial pulse strength may be
present in dogs with significant left ventricular outflow tract obstruction such as subaortic
stenosis, or in dogs with very low cardiac output (most commonly due to dilated
cardiomyopathy or cardiac tamponade). Bounding femoral arterial pulses are present in
diseases with increased pulse pressure such as patent ductus arteriosus or aortic
insufficiency, which cause a diastolic runoff of blood from the aorta to the pulmonary
artery or left ventricle respectively. Jugular venous distension or pulsation may reflect
elevated right heart diastolic pressure in dogs with right heart failure. Concurrent
abnormalities typically include hepatomegaly and abdominal effusion.

Evaluation of respiratory abnormalities is initially done by observation of the
animal’s breathing pattern in the examination room prior to handling the animal.
Abnormal respiratory patterns include tachypnea, dyspnea, orthopnea, or cough. Cough
is not specific for heart failure, and is often present in dogs with respiratory disease
including collapsing trachea or chronic bronchitis. Dogs with heart failure may cough
due to pulmonary edema or compression of the left mainstem bronchial compression by
an enlarged left atrium. A cardiac cough is typically soft, compared to the loud honking
cough caused by collapsing trachea, or the loud, productive hacking cough typical of
chronic bronchitis. Animals with heart failure may have increased adventitious lung
sounds, although harsh crackles are more common in animals with primary respiratory
disease. Muffled lung sounds are common in animals with pleural effusion, and are
typically coupled with a restrictive breathing pattern (fast, shallow breaths). Absence of
adventitious lung sounds does not eliminate congestive heart failure, as many animals
with mild cardiogenic pulmonary edema do not have increased lung sounds.

Diagnostic Modalities and Techniques

Electrocardiogram

The primary indication for obtaining an electrocardiogram (ECG) is to evaluate
an arrhythmia. Patients with a history of syncope, episodic weakness, or collapse should
be evaluated with an ECG. An ECG is an insensitive test for assessment of specific
cardiac chamber enlargement, and interpretation of structural heart disease is best done
using radiography and echocardiography. In order to simplify and standardize the
process of ECG analysis, the interpreter should evaluate ECG’s in a specified order,
which aids in interpretation of difficult arrhythmias. The first step is to calculate the
heart rate, either an average or an instantaneous rate. Average heart rate is the number of
beats in 6 seconds x 10, or the number of beats in 3 seconds x 20. The instantaneous rate
obtained by measuring the R-R interval (in seconds) of the particular beat (preceeding
beat is the first R to the beat of interest R), and dividing it into 60 s. The second step of
ECG analysis is to assess whether the rhythm is regular or irregular, and if there is a
pattern of the irregularity. Next, and most importantly, the rhythm is classified as either supraventricular or ventricular in origin. Supraventricular rhythms typically have narrow, upright QRS complexes in lead I, II, AVF, III, unless there is a bundle branch block. Ventricular arrhythmias have wide, tall or deep (negative) S waves, and have wide and bizarre T waves, and are not associated with a P wave. Assessment of the relationship of P waves to the QRS complexes is critical for determining many supraventricular and ventricular arrhythmias. At 50 mm/s and typically standard amplitude of 10 mm/mv, complex morphology (height and width of complexes, PR interval) should be measured. Lastly, the mean electrical axis is calculated, which can indicate whether there is a marked left or right axis deviation (normal MEA is 40-100 in dogs, 0-160 in cats). Right axis deviation is seen with right ventricular hypertrophy (normal QRS duration) or right bundle branch block (prolonged QRS duration).

Pitfalls of the electrocardiogram are that it may miss intermittent arrhythmias that may be clinically significant, and the lack of ability to diagnose cardiac structure and function. For more comprehensive evaluation of intermittent arrhythmias, a holter monitor or an event monitor may be necessary, especially when evaluating animals with intermittent signs of syncope or weakness, or in animals predisposed to cardiomyopathies causing ventricular arrhythmias such as Boxer dogs or Doberman Pinschers.

**Blood pressure measurement**

Systemic hypertension is an often overlooked, nebulous disease causing multiple target organ diseases. Blood pressure is part of the minimum data base in patients with evidence of target organ damage such as ocular abnormalities (retinal detachment, hyphema, etc), stroke-like event or brain abnormalities consistent with hypertensive encephalopathy, cardiac abnormalities such as left ventricular concentric hypertrophy, or progressive renal disease or proteinuria. Predisposed patients with the following diseases should also have blood pressure measured as part of standard recheck examinations: chronic kidney disease (prevalence 60-93%, dog; 46-65%, cat), protein losing nephropathy (prevalence 90%), acute kidney disease (prevalence 87%), hyperadrenocorticism (Native, prevalence 73%; iatrogenic, prevalence 80%), diabetes mellitus (prevalence 34-46%, dog), adrenal mass (pheochromocytoma, prevalence 43-86%, dog; up to 100% cat; aldosterone secreting adrenal cortical tumor, 50-100% prevalence, cat; unknown dog), and hyperthyroidism (prevalence 23-87%, cat; pre-treatment or post-treatment). Animals with cardiac disease, especially those with cardiomegaly with or without heart failure, should also have blood pressure measured as a part of the minimum data base, since increased afterload can greatly worsen the magnitude of the cardiac disease.

Measurement of blood pressure should be done with as minimal stress and restraint as possible, prior to other stressful procedures. Animals should be allowed to acclimate to the room for 5-10 minutes prior to BP measurement, and the owner is preferably present to calm the animal. The Doppler ultrasonography method of blood pressure measurement is the preferred in cats and small dogs, since oscillometric methods may underestimate blood pressure in very small animals. In cats, an extremity or the tail can be used, whereas in dogs the metacarpal or metatarsal artery is used. The cuff size should be 30-40% of the limb or tail circumference. The first measurement should be discarded, and five consecutive measurements (with < 20% variability) are averaged.
Systemic hypertension is diagnosed based on the systolic blood pressure. Systolic blood pressure is normally less than 160 mmHg, with a grey zone of 160-180 mmHg, and elevated blood pressure >180 mmHg.1

The main pitfall of blood pressure measurement is the difficult in distinguishing a normal physiologic elevation in blood pressure due to sympathetic drive in a frightened animal from true pathologic systemic hypertension. Measurement of the blood pressure in the examination room with owner present and prior to other stressful procedures such as measurement of body temperature or other diagnostic tests are ways to lessen stress and reduce likelihood of white coat hypertension. In patients with elevated blood pressure (>160 mmHg), repeated measurements should be done over the next 30 minutes to a couple hours, and may be repeated on different days if it is still elevated. At-home blood pressure measurement may be useful to minimize the effect of stress on blood pressure, and can be done in nervous patients that have elevated blood pressure (160-210 mmHg).

**Thoracic radiographs**

Thoracic radiographs are an essential tool for assessment of overall heart size, assessment of the great vessels (aorta, pulmonary artery and main branches, caudal vena cava), pulmonary parenchyma, pulmonary vasculature, and airways. Thoracic radiographs are an essential tool to diagnose congestive heart failure. Presence of left atrial dilation and cardiomegaly, as well as perihilar to caudodorsal interstitial to alveolar pulmonary infiltrates, with or without pulmonary vascular distension is pathognomonic for left heart failure in dogs. Thoracic radiographic abnormalities of left heart failure in cats is much more variable, but classic abnormalities include cardiomegaly and left atrial dilation, pulmonary venous distension, diffuse interstitial to alveolar pulmonary infiltrates and/or pleural effusion.

Vertebral heart score may be useful to quantify heart size. The length of the long axis of the heart is measured from the level of the carina to the left ventricular apex. A perpendicular line is drawn at the widest part of the short axis of the heart. The long axis and short axis lengths are then converted to the length of vertebrae, starting at the cranial aspect of T4, and then added together for total vertebral heart scale. Normal VHS in cats is 6.9-8.1, and normal VHS in dogs is 9.7 +/- 0.5 (99% confidence interval 8.5-11).2,3 VHS of 10.7 vertebrae or larger accurately (78% accuracy) discriminates dogs with cardiomegaly and heart disease from normal dogs.4 Assessment of left atrial dilation in dogs indicates significant left heart disease and increased left ventricular diastolic filling pressure, and is always present in animals with left heart failure.

Great vessels: Dilation of the ascending aorta may be seen in animals with subaortic stenosis, patent ductus arteriosus (i.e. the ductal bump), or as a normal variant in aged cats. Using the dorsoventral or ventrodorsal view, the aorta is located at the 12-1 o’clock position. The main pulmonary artery lies just to the left of the aorta on the “clock face”, and may be dilated in animals with pulmonic stenosis, pulmonary hypertension, or heartworm disease. Measurement of an increased caudal vena caval to aortic diameter of >1.5 is highly suggestive of right heart failure in dogs, and is always accompanied with
evidence of right heart enlargement (reverse D appearance of the heart on dorsoventral view, increased sternal contact on lateral view).

Pulmonary vasculature: Pulmonary venous distension (i.e. venous congestion) is a common abnormality in animals with left sided heart failure. However, absence of pulmonary venous congestion does not eliminate heart failure from the differential list. Pulmonary overcirculation pattern is identified when the pulmonary arteries and pulmonary veins are both dilated, and occurs in left to right shunting congenital heart defects such as patent ductus arteriosus. Pulmonary undercirculation (small pulmonary arteries and veins) occurs in animals with hypovolemia or right to left shunting congenital heart disease.

Pleural effusion is a common manifestation of left or right heart failure in cats, or right heart failure in dogs. Most cats and dogs with right heart failure also have concurrent ascites. Repeat thoracic radiographs should be done after thoracocentesis to allow better visualization of the heart and pulmonary vasculature.

Abnormal pulmonary patterns include pulmonary infiltrates (interstitial or alveolar), bronchial pattern, or nodular pattern. It is essential to assess whether infiltrates are cardiogenic (left heart failure) or non-cardiogenic (infectious, parasitic, inflammatory, neoplastic, or non-cardiogenic (neurogenic) pulmonary edema. In dogs, the pattern of the infiltrate is helpful, as congestive heart failure causes perihilar to caudodorsal pulmonary edema. Left atrial dilation and cardiomegaly should be present in left heart failure. In cats, there is no typical distribution pattern of cardiogenic pulmonary edema, and cardiac size may be obscured. These patients often benefit from an echocardiogram to assess for significant cardiomegaly and atrial dilation. A nodular pulmonary pattern may be seen in neoplastic or fungal pulmonary disease.

Pitfalls of thoracic radiographs include the inability to detect specific chamber enlargement and assess myocardial function or blood flow abnormalities, which require an echocardiogram. Therefore, radiographs are unable to specifically diagnose the etiology of heart disease but are helpful to establish whether there is cardiomegaly or evidence of heart failure. Radiographs may demonstrate non-specific pulmonary patterns such as interstitial pulmonary infiltrates caused by disparate etiologies ranging from heart failure to primary pulmonary disease, or pleural effusion caused by many different etiologies, and additional diagnostic tests are needed to discriminate between heart failure and other etiologies of respiratory disease.

**Biomarkers: Natriuretic peptides**

Brain natriuretic peptide is a neurohormone synthesized by the ventricular myocardium in response to increased wall stress as well as other stimuli such as neurohormones, or hypoxia, in a wide range of cardiac diseases. The large pro-hormone is cleaved into the biologically active BNP and the inactive fragment NT-proBNP. NT-proBNP has a longer circulating half-life and at the time of this writing has been evaluated more extensively than BNP in veterinary medicine. BNP and NT-proBNP have been shown to be increased in dogs with cardiac disease and further elevated in
dogs with heart failure, with some overlap between patient populations and normal dogs. The main indication for its use is to evaluate whether heart failure is the likely cause of respiratory clinical signs in animals with cough or dyspnea. Other indications are to screen predisposed breeds for occult dilated cardiomyopathy, since these animals may not have overt cardiovascular abnormalities on physical examination. Given the challenges of diagnosing heart failure in cats, NT-proBNP may help differentiate heart failure from primary respiratory disease in dyspneic cats. Likewise, given the high prevalence of cardiomyopathy in cats, NT-proBNP has also been used to screen for occult disease with variable results. Biomarkers are not a substitute for radiographs or echocardiography, but provide complimentary information, and may provide further rationale for pursuing additional diagnostic workup with an echocardiogram or radiographs, and help guide medical therapy. There may be false negative results, especially in animals with mild cardiac disease. Likewise, false positives may occur in animals with no overt cardiac disease. Additional pitfalls include the specific technique required for appropriate sample handling to avoid erroneous values, and requirement of special blood tubes with protease inhibitors. Point of care testing is on the horizon but is not commercially available at this time, so a delay of 1-3 days may occur before results are available currently. Further areas of interest are to evaluate the use of BNP or NT-proBNP as prognostic markers for early cardiac death or progression to development of congestive heart failure in specific populations, and the utility of natriuretic peptides to help refine heart failure therapy during recheck examinations.

**Echocardiography**

The echocardiogram is an essential tool for the cardiologist to evaluate the cardiac structure and function. An echocardiogram is useful to identify the source of a murmur, assess heart size and function in animals with a gallop heart sound, and screen for occult cardiomyopathy in dogs and cats. It is an essential test in patients with episodic weakness, collapse, or syncope to evaluate whether there is pericardial effusion, pulmonary hypertension, or severe myocardial failure. An echocardiogram may distinguish various causes of valvular regurgitation (myxomatous valve degeneration, infective endocarditis, or functional mitral regurgitation due to marked ventricular dilation in DCM) in patients with a new murmur, which helps direct appropriate medical therapy. However, an echocardiogram is not useful to evaluate for arrhythmias or pulmonary abnormalities, whereas an electrocardiogram and radiographs are the most appropriate tests, respectively.

A basic “triage” echocardiogram can be done to help triage the case to either primary cardiac versus non-cardiac disease. A triage echocardiogram is used to evaluate for significant left atrial dilation, moderate to severe myocardial failure, and presence and severity of pericardial and/or pleural effusion. In dyspnic animals, the left atrial size should be assessed either subjectively or quantified by measurement of the ratio of the left atrial diameter to the aortic diameter in the right parasternal short-axis basilar view. Normal LA:Ao is <1.5, and significant left atrial dilation is >1.8. Dogs with severe mitral regurgitation and cardiogenic pulmonary edema typically have severe left atrial dilation (LA:Ao ≥ 2) except in the rare instance of acute major chordae tendinae rupture. Likewise, congestive heart failure is a higher differential than primary respiratory disease
in cats with pulmonary infiltrates or pleural effusion and echocardiographic evidence of moderate or severe left atrial dilation.

A higher level, comprehensive echocardiogram is done in stable patients for quantification of systolic and diastolic myocardial function, careful evaluation of cardiac anatomy and diagnosis of the specific cardiac disease present, careful evaluation for cardiac masses in patients with pericardial effusion, and evaluation for presence of pulmonary hypertension +/− cor pulmonale. The comprehensive echocardiogram requires specialized training and a specialized echocardiogram machine, and is best served by a cardiologist or person with advanced echocardiographic training. It is the only non-invasive test that can diagnose pulmonary hypertension, which makes diagnostic cardiac catheterization for this disease nearly obsolete in current days.

The largest pitfall of echocardiography is the inability to visualize pulmonary edema, so it is used in conjunction with radiographs to confirm a diagnosis of congestive heart failure. Many abnormalities such as marked left atrial dilation, pulmonary venous distension, and increased left ventricular filling measurements suggestive of elevated left atrial pressure are commonly seen in patients with heart failure, but radiographs are essential to confirm presence and severity of heart failure. Another pitfall of echocardiography is the variability of cardiac measurements depending on level of operator skill and training. It takes years of training and experience to be proficient in advanced echocardiography. Unlike thoracic CT or MRI, there are limited acoustic windows for imaging with echocardiography, and inability to visualize the great vessels distal to their insertion to the heart. A financial limitation of echocardiography is the expense of the ultrasound machine and the cost of the test to the client.

References


The primary indication for obtaining an electrocardiogram (ECG) is to evaluate an arrhythmia. Patients with a history of syncope, episodic weakness, or collapse should be evaluated with an ECG. An ECG is an insensitive test for assessment of specific cardiac chamber enlargement, and interpretation of structural heart disease is best done using radiography and echocardiography. In order to simplify and standardize the process of ECG analysis, the interpreter should evaluate ECG's in a specified order, which aids in interpretation of difficult arrhythmias. The first step is to calculate the heart rate, either an average or an instantaneous rate. Average heart rate is the number of beats in 6 seconds x 10, or the number of beats in 3 seconds x 20. The instantaneous rate obtained by measuring the R-R interval (in seconds) of the particular beat (preceeding beat is the first R to the beat of interest R), and dividing it into 60 s. The second step of ECG analysis is to assess whether the rhythm is regular or irregular, and if there is a pattern of the irregularity. Next, and most importantly, the rhythm is classified as either supraventricular or ventricular in origin. Supraventricular rhythms typically have narrow, upright QRS complexes in lead I, II, AVF, III, unless there is a bundle branch block. Ventricular arrhythmias have wide, tall or deep (negative) S waves, and have wide and bizarre T waves, and are not associated with a P wave. Assessment of the relationship of P waves to the QRS complexes is critical for determining many supraventricular and ventricular arrhythmias. At 50 mm/s and typically standard amplitude of 10 mm/mv, complex morphology (height and width of complexes, PR interval) should be measured. Lastly, the mean electrical axis is calculated, which can indicate whether there is a marked left or right axis deviation (normal MEA is 40-100 in dogs, 0-160 in cats). Right axis deviation is seen with right ventricular hypertrophy (normal QRS duration) or right bundle branch block (prolonged QRS duration).

Bradyarrhythmias are classified if the heart rate is < 80 bpm in small dogs, <70 bpm in medium-large dogs, and < 60 bpm in giant breed dogs, and < 120 bpm in cats. **Sinus bradycardia** is seen in animals with high vagal tone, sedation, hypothermia, sinus nodal disease, or increased intracranial disease (i.e. Cushings reflex). **Sinus arrhythmia** is a common normal variant, and often occurs in a pattern associated with respirations, where the heart rate increases during inspiration and decreases on exhalation. Often there is a wandering pacemaker, with changes in the P wave amplitude following the pattern of irregular rhythm (often there are taller P waves during inspiration when the heart rate increases) and is due to a shift in the location of sinus nodal depolarization associated with high vagal tone. Sinus arrhythmia is often caused by high vagal tone, but some animals with early sick sinus syndrome may have what appears to be a pronounced sinus arrhythmia, which must be differentiated using an
atropine challenge test. **Sick sinus syndrome** (SSS) is the most common arrhythmia in Schnauzers and Cocker Spaniels, and may also occur in other dogs. SSS is composed of several arrhythmias, with sinus arrest (pause > 2 x RR interval) the signature of the disease. Other abnormalities include: sinus bradycardia, sinus arrhythmia, first and second degree atrioventricular block (2DAVB). Supraventricular tachycardia (SVT) may preceed sinus arrest (i.e. tachy-brady syndrome). Syncope usually occurs when there is a pause of sinus arrest of ≥ 6 seconds. An atropine challenge test is necessary to help differentiate sinus bradycardia or sinus arrhythmia due to high vagal tone from SSS. High dose atropine (0.04 mg/kg SC) is given and the ECG repeated 30 minutes later. Dogs with high vagal tone have regular sinus tachycardia, with HR ≥ 140, and no pauses of sinus arrest or AV block. Dogs with SSS often have pauses of sinus arrest or suboptimal increase in rate (<130 bpm). If there is a significant atropine response and the resting rate is slow (<65), terbutaline, a nonselective beta agonist, can be given. If there is no clinical improvement, other anticolinergic agents such as propantheline could be given. Asymptomatic dogs with SSS have a significant risk of sudden death during general anesthesia, and require either a temporary pacemaker or isoproterenol constant rate infusion (CRI). A permanent pacemaker is the treatment of choice for symptomatic dogs with SSS. **Atrial standstill** is a rare bradyarrhythmia, caused by severe hyperkalemia (reversible atrial standstill) or a serious atrial myopathy (permanent atrial standstill). ECG consists of lack of P waves and a nodal or less commonly purkinje escape. Electrolytes should be measured if this arrhythmia is seen, and atropine should be given. The prognosis for patients with atrial standstill and myopathy is very poor, and they are not ideal pacemaker candidates because they often quickly progress to develop severe right heart failure.

Atrioventricular blocks are another group of bradyarrhythmias. **First degree AV block** is defined by a prolonged PR interval, and all P waves are conducted and associated with QRS complexes. It does not cause a clinical problem, and is often caused by high vagal tone or cardiac antiarrhythmic medications. **Second degree atrioventricular block** (2DAVB) is divided into Mobitz type I (i.e. Wenkebach) where there are progressively prolonging PR intervals preceeding the dropped P wave, Mobitz type II where the PR interval does not prolong prior to the dropped P wave, and high grade 2DAVB where there are never 2 consecutively conducted P waves (can describe the ratio of P's to QRS, such as 2:1, 3:1). High vagal tone may cause Mobitz type I 2DAVB. AV nodal disease can cause Mobitz type I, II, and always causes high grade 2DAVB. An atropine challenge test should be done for any animal with 2DAVB to assess the role of high vagal tone in the arrhythmia. **Third degree AV block** (3DAVB) is evidenced by lack of any association of P waves with QRS complexes, and is caused by severe AV nodal disease. Nodal escape beats have a supraventricular morphology and typically a rate of 40-60 bpm in dogs, and 80-100 in cats. Purkinje escape beats are wide and bizarre, ventricular beats occurring at a slower rate of 20-40 bpm in dogs, and 60-80 bpm in cats. Patients
with high grade 2DAVB and 3DAVB often present for lethargy, collapse, or syncope. Lidocaine or other ventricular antiarrhythmic therapy (beta blockers, mexilitene, sotalol) is contraindicated for treatment of 3DAVB, even if there are ventricular premature beats, as it will likely eliminate the life-saving purkinje escape beats. Dogs with high grade 2DAVB have equal risk to dogs with 3DAVB for sudden death, and have a 30% risk of dying suddenly within 6 months of diagnosis regardless of whether clinical signs are present. Dogs with high grade 2DAVB and 3DAVB should be treated with a permanent pacemaker. (1) 3DAVB is much better tolerated in cats than in dogs, because their escape rates are often quite fast (often 80-140 bpm). In a recent study, median survival of cats with 3DAVB was 386 days, and most died of non-cardiac causes. Only 1 cat received a permanent pacemaker, and no cats died suddenly. (2)

Supraventricular tachyarrhythmias are a broad category of arrhythmias arising from the AV node or atria. Sinus tachycardia consists of heart rate >160 bpm, with narrow upright QRS complexes and associated P waves. The tachycardia gradually increases and decreases without an abrupt onset or break. It is often an important physiologic compensation for hypovolemia, anemia, fever, hypoxia, sepsis, hyperthyroidism, and many other systemic abnormalities, and does not require antiarrhythmic treatment. On the contrary, supraventricular tachycardia (SVT) is caused by an ectopic atrial focus or a re-entrant pathway involving the AV node or an accessory pathway. SVT may be initiated by a P wave that appears different from the sinus nodal P wave, and may be negative or buried in the preceding T wave. PR interval may be different than the sinus derived PR interval. Often SVT has a rapid rate of 200-300 bpm, and typically has an abrupt onset and termination. SVT in cats is often 300-400 bpm. SVT often causes syncope, and requires emergency treatment with intravenous antiarrhythmics including IV diltiazem (0.125-0.25 mg/kg slow IV over 1-2 minutes, repeating dose if ineffective), esmolol (0.25-0.5 mg/kg IV over 1-2 minutes), or adenosine. Cardioversion may be another option for refractory SVT. Ideally, an echocardiogram is done to assess myocardial function, since beta blockers should not be given if there is severe myocardial failure. Choices, in order of preference, for chronic therapy include diltiazem (1-4 mg/kg PO TID, often high doses are needed), atenolol (1-2 mg/kg PO BID) and sotalol (1-3 mg/kg PO BID). Chronic tachycardia >180 bpm for longer than a couple of weeks may lead to pacing induced myocardial failure, which is indistinguishable from idiopathic dilated cardiomyopathy (DCM) on echocardiography. Tachycardiomyopathy, however, is rapidly reversible once rate control has been established. Atrial flutter is an irregularly irregular supraventricular arrhythmia with narrow upright QRS complexes and saw-toothed flutter (F) waves with rate of 250-350 bpm. The ventricular rate is variable and depends on amount of vagal tone at the AV node, but is often very fast if heart failure is present. Atrial fibrillation appears similar to atrial flutter, except there are less distinct fibrillatory waves or undulating baseline. Both atrial flutter and atrial fibrillation are often associated with severe underlying cardiac disease, and heart failure is
often present. Antiarrhythmic therapy is aimed at decreasing the AV nodal conduction by prolonging AV nodal conduction time and refractory period, which decreases the number of wavelets that depolarize the ventricles. Chronic oral therapy is used to maintain the heart rate ≤140 bpm, and choices include: diltiazem (0.5-3 mg/kg PO TID, starting at low dose), atenolol (0.5-2 mg/kg PO BID), or sotalol (1-3 mg/kg PO BID). Digoxin increases vagal tone and may aid in slowing the ventricular response rate, but is not usually adequate to maintain adequate rate control in severely tachycardic cases. Some cardiologist prefer electrical cardioversion to regain sinus rhythm, but there may be high recurrence rates in patients with significant cardiac disease and cardiomegaly. Giant breed dogs may develop “lone” atrial fibrillation in the absence of structural heart disease, and may not require antiarrhythmic therapy if heart rates are in the normal range. “Lone” atrial fibrillation often foreshadows development of DCM in Irish Wolf hounds, so serial echocardiograms are needed over time.

Ventricular arrhythmias may occur due to abnormal automaticity of non-excitatory ventricular myocardial cells, enhanced automaticity of purkinger cells, or most commonly re-entrant circuits involving diseased ventricular myocardium. Ventricular premature complexes (VPC’s) are premature beats, with wide and bizarre QRS and T waves and no P wave. VPC morphologies include tall and wide QRS complexes (left bundle branch block morphology) that likely arise from the right ventricle or basilar interventricular septum, or deep (negative) S waves that likely arise from the left ventricle. R on T phenomenon, couplets, and triplets are a higher grade of malignancy. Although VPC’s may not be hemodynamically deleterious, they may identify patients with significant structural or functional heart disease that require an echocardiogram. Ventricular arrhythmias are also common with other systemic diseases, after trauma, in post-surgical splenectomy or gastric dilation volulus patients, and often improve with treatment of the underlying problem and tincture of time. Greater than 3 VPC’s in a row (instantaneous ventricular rate > 160 bpm) is considered non-sustained ventricular tachycardia, and signifies a highly malignant arrhythmia grade and risk of sudden death. Sustained ventricular tachycardia lasts longer than 30 seconds, and often requires emergency treatment. Accelerated idioventricular rhythm consists of a ventricular derived rhythm with a rate of 80-160 bpm, and is most often seen in systemically ill dogs or post-operative splenectomy or GDV patients, and does not typically require therapy. Holter monitors are necessary to help quantify the severity of ventricular arrhythmias, and are especially useful in Doberman Pinschers and Boxer dogs. Normal dogs have < 50 VPC’s in 24 hours and there is a grey zone of 100-500 VPC’s/24 hours (for Boxer dogs).(3) > 50 VPC’s in 24 hrs, 1 couplet or triplet in overtly normal Doberman Pinschers with normal echocardiographic studies was highly predictive of development of DCM.(4) Couplet, triplets, and non-sustained ventricular tachycardia are abnormal and require antiarrhythmic treatment. Sustained ventricular tachycardia requires acute antiarrhythmic therapy and hospitalization. Lidocaine is the drug of choice (2-4 mg/kg IV, repeated to 6 mg/kg total cumulative dose followed by CRI 30-90 mcg/kg/min). Intravenous procainamide, esmolol, or
amiodarone are other choices for refractory ventricular arrhythmias. Chronic antiarrhythmic treatment choices include sotalol (1-3 mg/kg PO BID), atenolol (1-2 mg/kg PO BID), mexilitene (5-7 mg/kg PO TID), and amiodarone (10-15 mg/kg PO BID x 7 days then 5-7 mg/kg PO q24 hr). If there is severe decompensated DCM, atenolol and possibly sotalol should be avoided as they will further decrease contractility. Sotalol or the combination of atenolol and mexilitene effectively decreases the severity of arrhythmia and reduces syncopal episodes in Boxer dogs with arrhythmogenic right ventricular cardiomyopathy. Follow-up ECG and ideally holter monitoring is important after starting antiarrhythmic medication. Often combination antiarrhythmic therapy is needed, such as sotalol and mexilitene, or amiodarone and low dose atenolol or mexilitene. Amiodarone is typically reserved for refractory ventricular arrhythmias or for treatment of severe ventricular arrhythmias in dogs with severe DCM.

Terminal arrhythmias include **asystole**, where there is lack of any electrical cardiac activity, and **ventricular fibrillation**. Both should be treated aggressively with immediate cardiac defibrillation (5-10 joules/kg extrathoracic), as well as emergency drugs including atropine and epinephrine. Asystole has very little chance of cardioversion, given the lack of electrical activity.

**Reference List**


New Perspectives on Diagnosis and Treatment of Canine Congestive Heart Failure
Kristin MacDonald, DVM, PhD, Diplomate ACVIM (Cardiology)
VCA- Animal Care Center of Sonoma

Congestive heart failure (CHF) is a common sequela to severe cardiac disease. Myxomatous mitral valve disease and dilated cardiomyopathy (DCM) are the most common heart diseases in dogs to result in CHF. CHF develops when the left ventricular diastolic filling pressures are substantially increased, leading to elevated left atrial and pulmonary capillary wedge pressure. Pulmonary venous distension may be seen on thoracic radiographs prior to overt pulmonary edema. When the left atrial pressure increases above 20 mmHg, pulmonary edema forms. Initially, there is interstitial pulmonary edema, and alveolar edema occurs with progressive increase in pulmonary capillary wedge pressure.

Right sided CHF occurs when right ventricular diastolic pressure, right atrial pressure, and central venous pressures increase over 15 mmHg. Right sided CHF is evidenced by jugular venous distension, hepatomegaly and ascites, and possibly pleural effusion and peripheral edema.

When stroke volume is decreased, there is decreased renal blood flow and decreased sodium delivery to the macula densa of the kidney, which activates the renin-angiotensin-aldosterone system (RAAS) to increase intravascular volume by increasing sodium and water retention. The net effect of RAAS activation is maintenance of systemic organ perfusion by increased systemic vascular resistance, increased blood volume through sodium and water retention, increased sympathetic tone by increasing norepinephrine, vasopressin and endothelin-1, and counter-regulate nitric oxide, natriuretic peptides, and prostaglandins to further increase systemic vascular resistance. Except for the generation of renin by the kidney, all components of RAAS are present at the myocardial level (as well as in many other organs), and are capable of generating high levels of angiotensin II (ATII) and aldosterone locally, which induce myocardial hypertrophy and fibrosis. Aside from cardiac ACE, other pathways including chymase, ACE-2, cathepsins, and tonin convert ATI to ATII. In fact, in dogs, cats, and humans, chymase is responsible for 90% of myocardial ATII formation.

Diagnosis of CHF

Clinical signs of coughing, tachypnea, dyspnea, orthopnea may be seen in animals with heart failure. Other nonspecific history may include exercise intolerance, lethargy, anorexia, or weight loss. Syncope may be seen in dogs with heart failure. The main diagnostic tool for diagnosis of CHF is thoracic radiographs. Vertebral heart score may be useful to quantify heart size. The length of the long axis of the heart is measured from the level of the carina to the left ventricular apex. A perpendicular line is drawn at the widest part of the short axis of the heart. The long axis and short axis lengths are then converted to the length of vertebrae, starting at the cranial aspect of T4, and then added together for total vertebral heart scale. Normal VHS in cats is 6.9- 8.1, and normal VHS
in dogs is 9.7 +/- 0.5. VHS of 10.7 vertebrae or larger accurately (78% accuracy) discriminates dogs with cardiomegaly and heart disease from normal dogs. In dogs, identification of perihilar to caudodorsal interstitial to alveolar pulmonary infiltrates, along with cardiomegaly and in particular left atrial dilation are the main criteria for diagnosis of CHF, and pulmonary venous distension is also often seen. An echocardiogram is necessary to identify the etiology of the heart disease, and is also helpful to confirm whether there is significant enough heart disease present to cause dyspnea in patients with pulmonary infiltrates.

The ACVIM consensus statement of diagnosis and treatment of mitral valve disease utilized an ABCD staging system to help define appropriate workup and treatment depending on the severity of the disease, which can be helpful to adopt into general clinical practice. Dogs with no cardiovascular abnormalities that are genetically predisposed to develop cardiac disease may be considered Stage A (i.e. Cavalier King Charles Spaniels). Asymptomatic dogs with a cardiovascular abnormality (i.e. murmur) are a Stage B, which is subdivided into B- no cardiac enlargement, and B2- cardiac enlargement but no congestive heart failure. A Stage C dog has either current congestive heart failure or history of heart failure and receives heart failure medications. Dogs with refractory heart failure that have symptoms despite maximal furosemide dose of 4 mg/kg PO TID, an ACE inhibitor, and pimobendan are Stage D.

Measurement of circulating biomarkers such as brain natriuretic peptide (BNP) is useful to help distinguish whether dyspnea is due to CHF or primary respiratory disease in dogs and cats. NT-proBNP, the precursor of the biologically active BNP, has a longer circulating half-life and data suggests that it is a promising cardiac biomarker of disease and failure. A commercially available test (Cardiocare®, IDEXX laboratory) has been evaluated for differentiation of CHF from primary respiratory disease in dyspneic dogs, and a cutoff of >1725 pmol/L is highly sensitive (88%) and specific (77%) for diagnosis of CHF. Likewise, a cutoff of >445 pmol/L is moderate to highly sensitive (83%) and specific (90%) for distinguishing dogs with asymptomatic heart disease from normal control dogs. A strict protocol exists for collection and processing of NT-proBNP samples.

**Treatment of Congestive Heart failure**

Recently, the ACVIM Cardiology consensus committee on treatment of myxomatous mitral valve degeneration outlined the standard of care for treatment of heart failure to include triple therapy of furosemide, an ACE inhibitor, and pimobendan. We have summarized the most pertinent findings from clinical trials in dogs with heart disease below, to justify why the consensus statement has been made.

ACE inhibitors have been the standard choice for RAAS antagonism, and are indicated for treatment of CHF in people, dogs, and cats. Dogs and people benefit from improved quality of life as well as survival. The IMPROVE trial showed that enalapril resulted in very modest acute reductions of pulmonary capillary wedge pressure and arterial blood pressure in dogs, but greater long term clinical improvement was seen only
in the DCM group and not the mitral regurgitation group. Other clinical trials found improved symptoms and survival in both DCM and mitral regurgitation groups. There is a lack of evidence showing beneficial effects of early ACE inhibitor treatment in asymptomatic dogs with mitral regurgitation in the absence of CHF. Two large-scale, blinded, randomized, placebo controlled clinical studies (SVEP and VETPROOF) of dogs with mitral regurgitation without CHF failed to show an improvement in survival or increased time until development of CHF when treated early with enalapril. ACE and aldosterone escape is a problem in some people and animals (dogs and cats) treated with ACE inhibitors, and is characterized by progressive increases in ATII and aldosterone over time despite low ACE activity. Aldosterone antagonists or angiotensin receptor blockers may be added in conjunction with ACE inhibition for more complete RAAS inhibition.

The standard therapy for CHF of all causes includes furosemide (1-4 mg/kg PO BID-TID for stable patients), an angiotensin converting enzyme (ACE) inhibitor, and pimobendan. The dose and route of administration of furosemide varies depending on the severity of the CHF and the stability of the patient. Dogs with mild heart failure may be managed with lower furosemide doses (1-2 mg/kg PO q24 hr – BID), while dogs with severe or refractory heart failure require the highest oral dose of 4 mg/kg PO TID. Furosemide is within the most powerful class of diuretics, the loop diuretics, which inhibit the Na\(^+\)/K\(^+\)/2Cl\(^-\) cotransporter in the thick ascending loop of henle, leading to urinary loss of water, sodium, chloride, potassium, calcium, and magnesium. It is highly protein bound (86-91%), which traps the diuretic in the vascular space to deliver it to the proximal renal tubule, where 55% is excreted in the urine, and 45% is eliminated by the liver. Therefore, there must be adequate blood flow to deliver the furosemide to the kidney (a problem with low output heart failure), and adequate renal function to excrete the drug. Renal insufficiency prolongs the plasma half life of furosemide since the excretion is slower. Non-steroidal anti-inflammatory drugs also reduce the diuretic response to furosemide by increasing the solute reabsorption at the thick ascending LOH. Oral bioavailability is only ~50% with marked individual variability. When administered intravenously, the diuretic effect is seen 5 minutes post-IV injection, with a peak diuretic effect 30 minutes post IV injection, and duration of diuresis 2-3 hrs. Venodilation is seen 5-15 minutes after IV injection. When given orally, the diuretic effect is seen by 1 hr, with a peak effect at 1-2 hrs, and duration of diuresis 6 hrs.

Pimobendan (0.25 mg/kg PO BID) is an exciting drug used for treatment of dogs with CHF secondary to DCM or mitral regurgitation. Pimobendan is a phosphodiesterase III (PDE III) inhibitor and a calcium sensitizer, which exerts powerful positive inotropic and vasodilatory effects. Inhibition of PDE III results in decreased degradation of cAMP, resulting in increased phosphorylation of protein kinases and positive inotropic and lusitropic (relaxation) effects. Pimobendan also sensitizes the myofilaments (troponin C) to calcium to enable increased contraction. PDE III inhibition in the vasculature leads to vasodilation of the systemic arterioles and pulmonary vasculature. The combination of a positive inotrope and vasodilation leads to increased cardiac efficiency without increasing the myocardial oxygen consumption. In normal dogs, pimobendan produces moderate reductions in systemic and pulmonary vascular resistance, a decrease in left ventricular
filling pressure, a moderate increase in heart rate, and a moderate increase in cardiac output. It also increases myocardial blood flow and improves diastolic function. Pimobendan reduced the mitral regurgitant fraction in dogs with experimentally created mitral regurgitation.

In an open label study, pimobendan reduced heart failure score in dogs with CHF compared to digoxin. Pimobendan improved survival in 15 Dobermans with DCM (mean survival 128 days versus 63 days for placebo group) and had greater time before treatment failure.9 Similarly, another small scale blinded, placebo controlled study in 16 Dobermans with CHF showed a marked improvement in survival in dogs treated with pimobendan as well as background therapy of benazepril, spironolactone, and furosemide compared to placebo and background therapy (median survival time 130 days vs. 14 days respectively).10 Pimobendan has also been studied in dogs with heart failure due to myxomatous valve degeneration. VETSCOPE was a placebo controlled, blinded, prospective, randomized trial that compared the effects of pimobendan versus benazepril in 76 dogs with mitral regurgitation and moderate CHF.11 Dogs treated with pimobendan had greater improvement in heart failure score, vertebral heart score, and increased overall efficacy compared to the benazepril group. There was a dramatic improvement in survival in the pimobendan group (430 days versus 228 days in the benazepril group). Similarly, The Quality of Life and Extension of Survival Study (QUEST) was a multicenter, blinded, positive controlled study that evaluated the effect of pimobendan (n= 124 dogs) compared to benazepril (n= 128 dogs) in dogs with mild to moderate congestive heart failure secondary to myxomatous mitral valve degeneration.12 Like the VETSCOPE study, the QUEST study found a significant improvement in survival time (91% extension of survival) in dogs given pimobendan (MST 267 days) compared to dogs given benazepril (MST 140 days), and there was a 25% reduction in risk of dying or being removed from the study due to treatment failure, and greater than 20% reduction in risk over a prolonged period of time (120- 329 days). There was no difference in number of dogs reaching the end-point, but they lived longer and reached the clinical end-points later than dogs treated with benazepril.12

In patients with myocardial failure (i.e. DCM), positive inotropic therapy with digoxin is indicated. Large dogs with severe mitral regurgitation also often develop myocardial failure, although not to the degree of dogs with DCM, and they may benefit from digoxin. Small dogs with chronic refractory severe mitral regurgitation may possibly have symptomatic improvements when given digoxin. Digoxin increased vagal tone, improves baroreceptor function, and increased diaphragm muscle tone, which may help patients with progressive heart failure. An important use of digoxin is to help slow the ventricular response rate of atrial fibrillation by increasing vagal tone and prolonging atrioventricular nodal conduction.

In refractory cases of severe CHF that have maximized the oral lasix dose, addition of a second diuretic such as a thiazide may be necessary to control fluid accumulation. Spironolactone is a much weaker diuretic than both thiazides and loop diuretics, and may not add enough additional diuresis for adequate fluid control, but may have attractive ancillary properties as a neurohormonal antagonist. Since up to 40-50%
of dogs and cats have elevated aldosterone concentrations despite receiving ACE inhibitors (i.e. ACE escape), there is rationale to add an aldosterone receptor blocker to the medical regimen in animals with progressive heart failure. In dogs with refractory CHF due to mitral regurgitation, another option is afterload reduction with an arteriolar vasodilator. Amlodipine and hydralazine are effective in reducing systemic arterial pressure (10-40 mmHg) and reducing the mitral regurgitant fraction by approximately 15%. Low salt diets are indicated in refractory CHF patients receiving the previously mentioned pharmacologic treatments. Low salt diets (0.15-0.2 g sodium/1000 kcal) will help limit sodium and water retention. Dogs with mitral regurgitation and CHF fed low salt diets along with standard background therapy had smaller left atrial and left ventricular diastolic and systolic dimensions than when they were fed a moderate sodium diet.

Aldosterone receptor antagonists (i.e. spironolactone and eplerenone) have gained great attention in the veterinary community following the announcement of improved survival in people treated with spironolactone in the RALES clinical trial. Caution should be exerted before extrapolating positive effects seen in people who mostly had ischemic heart disease to dogs with other cardiac diseases. The mortality benefit was due to a decrease in sudden death, and was mostly seen in people with higher baseline circulating collagen markers of myocardial fibrosis. Recently, the only large scale, blinded, placebo controlled, multicenter clinical trial has been completed evaluating the effect of spironolactone in dogs with moderate or severe mitral regurgitation. Although the dogs (n= 212) were classified as having mild (Class II) or moderate (Class III) heart failure, the inclusion criteria were not specific for heart failure, and only 40% of dogs required furosemide at baseline. Although the study demonstrated that dogs treated with spironolactone (+ ACE inhibitor, +/- furosemide, +/- digoxin) had a 55% reduction in risk of cardiac related death, euthanasia due to worsening mitral regurgitation, or severe worsening in mitral regurgitation, there was a very low event rate (with many dogs having less severe mitral regurgitation), making it questionable whether many of the dogs actually had congestive heart failure at entry. It is difficult to assess when in the clinical course of mitral regurgitation that a possible beneficial effect of spironolactone could be seen based on this study. There are no other clinical trials in dogs with spontaneously developing CHF, and more studies are needed to evaluate whether these seemingly strong benefits are reproducible, and at what stage of disease the benefit may occur.

Reference List


Current Strategies on Diagnosis and Treatment of Feline Cardiomyopathy
Kristin MacDonald, DVM, PhD, Diplomate ACVIM (Cardiology)  
VCA - Animal Care Center of Sonoma County

Diagnosis
Feline heart disease is common and can be challenging to diagnose. Cats are often asymptomatic until they develop severe disease. While clinical signs and radiographs may suggest presence of heart disease in cats, echocardiography is required for diagnosis of the specific etiology and severity of heart disease. Feline cardiomyopathies are the most common heart diseases in cats, and are divided into 4 etiologies: hypertrophic cardiomyopathy, dilated cardiomyopathy, unclassified or restrictive cardiomyopathy, and arrhythmogenic right ventricular cardiomyopathy. It is important to define the specific type of heart disease since it helps determine the treatment and prognosis.

Thoracic radiographs are useful to assess whether there are pulmonary infiltrates or pleural effusion, and may identify significant cardiomegaly. Calculation of the vertebral heart scale may be useful to quantify cardiac size and confirm cardiomegaly. The long- and short-axis measurements of the heart, expressed in vertebral lengths starting at the fourth thoracic vertebrae, are added to yield vertebral heart size (VHS). Normal VHS is 7.4 +/- 0.3 in cats.1 Left sided congestive heart failure (CHF) may be evidenced by presence of patchy interstitial to alveolar pulmonary infiltrates with no typical pattern of distribution, unlike the dog that has a classic pattern of perihilar to caudal distribution. Pulmonary venous distension and left atrial dilatation are commonly seen with CHF. Pleural effusion may be caused by left or right heart failure. Dorsal deviation of the trachea has not been shown to be specific for cardiomegaly in cats with pleural effusion.2 Thoracic radiographs are insensitive for diagnosis of mild cardiac disease, and are not helpful to detect concentric hypertrophy of the ventricle, as overall heart size is not increased. Thoracic radiographs are essential to monitor for presence and severity of heart failure as well as adequacy of heart failure treatment. The electrocardiogram is useful to evaluate for arrhythmias in cats presenting for complaint of syncope or episodic weakness, or in cats with an arrhythmia detected on auscultation. Electrocardiography is insensitive for diagnosis of ventricular hypertrophy in cats with HCM.

Measurement of circulating biomarkers, such as brain natriuretic peptide (BNP), may identify cats with cardiac disease or CHF. BNP is synthesized normally in the atria, but there is increased synthesis in the ventricle with cardiac disease. N-terminal proBNP is a fragment formed by the cleavage of proBNP, and has a longer circulating half-life than BNP. In a study of 66 dyspnic cats with primary respiratory disease and 101 cats with dyspnea secondary to heart failure, NT-proBNP was significantly increased in cats with heart failure (P<0.001, median for CHF= 846 pmol/L; 1st respiratory = 53 pmol/L).3 NT-proBNP >180 was highly sensitive (94%) and specific (86%) for detection of CHF in dyspnic cats. NT-proBNP was also measured in 14 normal control cats and 23 asymptomatic cardiomyopathic cats, and was significantly higher in asymptomatic cardiomyopathic cats (P<0.001, median for control= 24 pmol/L, median for
asymptomatic cardiomyopathy = 283 pmol/L.\textsuperscript{4} NT-pro-BNP > 70 pmol/L was highly sensitive (87.5%) and specific (100%) for detection of asymptomatic cats with cardiomyopathy.

**Echocardiography** is the essential diagnostic tool to diagnose the specific etiology of heart disease as well as characterize the severity of the disease. Criteria for diagnosis of the specific cardiomyopathies by echocardiography are discussed below. Assessment of left atrial size is an essential tool for risk stratification for congestive heart failure or arterial thromboembolism. Cats with left atrial dilation have increased diastolic filling pressure and are at risk for development of heart failure or may have concurrent heart failure at the time of examination. Cats with echocardiographic evidence of left atrial dilatation need to be further evaluated with thoracic radiographs to assess for presence of congestive heart failure. Echocardiography is also essential for assessment of spontaneous echocardiographic contrast, which is present when red blood cells aggregate, and often precedes development of an intracardiac thrombus. Cats with spontaneous echocardiographic contrast or an intracardiac thrombus (often within the left atrium or auricle) need to be placed on an anticoagulant, and the owner appropriately counseled regarding the high likelihood of an impending arterial thromboembolism.

**Electrocardiogram**

An electrocardiogram (ECG) is the test of choice for evaluation of arrhythmias. An ECG should be done on any cat with history of episodic weakness or syncope, or if an arrhythmia was ausculted on examination. Common arrhythmias include ventricular premature complexes, atrial premature complexes, supraventricular tachycardia, ventricular tachycardia, or atrial fibrillation. Certain arrhythmias including ventricular tachycardia, supraventricular tachycardia, or atrial fibrillation with a rapid ventricular response rate warrant immediate antiarrhythmic therapy.

**Other diagnostic tests:**

Systolic blood pressure and serum thyroxine concentration must be measured in cats with concentric hypertrophy to rule out secondary causes of concentric left ventricular hypertrophy. Genetic screening tests have been developed for detection of two mutations of myosin binding protein C occurring in Maine Coon cats and Ragdoll cats, and may be useful for breeding programs.\textsuperscript{5,6} Plasma and whole blood taurine concentration should be measured in any animal with myocardial failure. Normal plasma and whole blood taurine concentrations are > 60 nmol/ml and > 250 nmol/ml respectively. Taurine deficiency induced DCM must not be missed as it is a curable form of DCM compared to the grave prognosis of idiopathic DCM.

**Specific Cardiomyopathies**

**Hypertrophic cardiomyopathy**

HCM is diagnosed by echocardiographic measurement of the end-diastolic left ventricular wall or interventricular septal thickness of ≥ 6 mm. Hypertrophy may be symmetrical or asymmetrical. Papillary hypertrophy may be an early abnormality even when the wall thickness is normal. Systolic anterior motion (SAM) of the mitral valve should be assessed in the right parasternal long-axis left ventricular outflow tract view.
using 2 dimensional echocardiography and color flow Doppler. Color flow Doppler depicts mitral regurgitation and turbulent blood flow in the left ventricular outflow tract and aorta arising from the obstruction of the left ventricular outflow tract by the anterior mitral leaflet. Pulsed wave and continuous wave Doppler are performed in the left apical 5-chamber view to measure the aortic blood flow velocity and determine the severity of the SAM. Left atrial size is measured by 2-dimensional echocardiography in the right parasternal short-axis view at the base of the heart. Left atrial to aortic diameter ratio ≥ 1.5 identifies left atrial dilation. Evaluation of spontaneous contrast of red cell aggregation or thrombus formation in the left atrium is also important. Diastolic dysfunction may be assessed using pulsed wave Doppler of the mitral inflow and pulmonary venous flow. Delayed relaxation or restrictive patterns may be identified which denote worsening stages of diastolic dysfunction respectively. However, there is an intermediate flow pattern termed “pseudonormalization” which may mask diagnosis of diastolic dysfunction. Tissue Doppler imaging (TDI) echocardiography is useful to detect diastolic impairment, which is evidenced by reduced early diastolic myocardial velocities of the left ventricular free wall in short-axis or reduced lateral mitral annular velocity or septal velocity in the left 4-chamber apical view.

Treatment of asymptomatic cats is debatable. The same scenario exists in human medicine, and treatment of asymptomatic people is on an “empiric basis without controlled data to either support or contradict is potential efficacy”. Treatment goals include reduction in LV hypertrophy, reduction in systolic anterior motion (SAM) of the mitral valve if it is more than mild, and improvement in diastolic function. Asymptomatic cats with severe HCM are often treated. Beta blockers and calcium channel blockers have anecdotally been shown to reduce hypertrophy is some cats. There is a lack of studies evaluating beta blockers and calcium channel blockers in cats with HCM. A small, unblinded, uncontrolled study evaluated the effect of diltiazem on left ventricular (LV) hypertrophy and diastolic function in 12 cats, and found that diltiazem reduced LV hypertrophy and improved LV relaxation time over the 6 months of therapy.6 A recent abstract presented at the 2007 ACVIM forum by Schober et al. evaluated the effects of atenolol versus diltiazem in asymptomatic cats with HCM. Results were relatively underwhelming. Atenolol had modest effects with improvement in one variable of diastolic function and slightly reduced septal wall thickness, and there were no significant effects of diltiazem on diastolic function, left atrial size, or LV hypertrophy. Atenolol also reduced the severity of SAM of the mitral valve, and diltiazem did not.

Angiotensin converting enzyme (ACE) inhibition has been shown to reduce LV hypertrophy in 2 small, uncontrolled or retrospective studies, where LV hypertrophy was assessed by either M-mode or 2-dimensional echo.8,9 However, 2-dimensional echocardiographic assessment of LV hypertrophy is fraught with high inter-and intraobserver variability of 18-20% respectively. The author completed a double blinded, placebo controlled, randomized, prospective study evaluating the effect of ramipril on LV mass, diastolic function, neurohormones, and blood pressure in 26 Maine coon and Maine coon-cross cats with mild to severe familial HCM without CHF.10 LV mass was quantified by cardiac magnetic resonance imaging, diastolic function was assessed by
pulsed wave tissue Doppler imaging (TDI), and plasma concentration of aldosterone and brain natriuretic peptide were measured. There was no difference in LV mass, diastolic function, delayed contrast enhancement assessment of myocardial fibrosis, blood pressure, or neurohormones between the placebo and ramipril treatment groups.

A small, double blinded, placebo controlled prospective study evaluating the effect of spironolactone on diastolic function assessed by TDI and on LV mass quantified by echocardiography was done on 26 Maine Coon cats with familial HCM without CHF. All cats had diastolic dysfunction at baseline. Cats were given 2 mg/kg PO BID of placebo or spironolactone for 4-months, and echocardiography was performed every 2 months. There was no difference in diastolic function or systolic function assessed by TDI, LV mass, or left atrial size. Serum aldosterone concentration was markedly elevated in cats treated with aldosterone. Approximately one-third of cats given spironolactone developed severe facial ulcerative dermatitis, which may have been caused by a drug reaction.

The largest multicenter clinical study to date has evaluated the effect of atenolol, diltiazem, and enalapril on survival in symptomatic cats with CHF or arterial thromboembolism secondary to cardiomyopathy (mostly due to HCM). Cats received a background therapy of furosemide if CHF was present. None of the drugs improved survival, and there was a trend in reduced survival in the atenolol group.

**Dilated Cardiomyopathy**

Dilated cardiomyopathy (DCM) consists of primary systolic myocardial failure. In response to reduced contractility, there is reduced cardiac output, which triggers volume expansion through the renin-angiotensin-aldosterone system, which leads to compensatory development of left ventricular eccentric hypertrophy. Less blood is ejected during systole and remains in diastole, which further increases left ventricular diastolic filling pressure. Pulmonary edema and pleural effusion may occur secondary to left sided CHF, and ascites and pleural effusion may occur secondary to right sided CHF. Other cardiac diseases that can lead to myocardial failure and may mimic DCM include severe volume overload of the left ventricle such as severe mitral regurgitation or left to right shunts. The myocardial failure and shortening fraction are not as severely reduced as in primary DCM. Taurine deficiency induced DCM was discovered in 1987, and was secondary to inadequate dietary intake of this essential amino acid in cats. Only 30% of taurine deficient cats develop echocardiographic evidence of myocardial failure. There is a prolonged occult phase when the cat is asymptomatic. Since modern feline diets are supplemented with taurine, these cases are rarely seen and the majority of cases are idiopathic. Cats fed exclusively one canned diet or vegetarian diets occasionally develop taurine deficiency induced DCM. Echocardiographic diagnosis of DCM is relatively straight-forward. Increased end systolic diameter (> 10 mm), reduced shortening fraction (<28 %, <20% in severe DCM), increased E point to septal separation (> 4 mm), and compensatory increased end diastolic diameter (> 18 mm) are abnormalities seen on echocardiography of the left ventricle. Left atrial enlargement is present in moderate to severe cases. Right ventricular and right atrial dilation may also be seen. TDI reveals
reduced systolic myocardial velocity. Color flow Doppler often shows centrally arising mild mitral regurgitation secondary to annular dilation and lack of valve coaptation.

Positive inotropic treatment with digoxin (1/4 of 0.125 mg PO q 24 -48 hours) and likely pimobendan (0.25-0.3 mg/kg PO BID, not labeled for use in cats) is recommended for severe DCM (when fractional shortening is 20% or lower). Treatment of moderate DCM without CHF is debatable. Although taurine deficiency induced DCM is much less common now than idiopathic DCM, supplementation with taurine (250 mg PO BID) should be started while whole blood and plasma taurine concentrations are pending. Taurine supplementation in deficient cats leads to clinical improvement in several weeks, and measurable improvement in systolic function in 2-4 months (sometimes earlier). Myocardial function normalizes in these patients. Furosemide and an ACE inhibitor should be started if there is evidence of CHF. Thoracocentesis should be performed to remove pleural effusion. Antiarrhythmic drugs are not usually necessary, but can be used if there are severe tachyarrhythmias such as ventricular tachycardia, atrial fibrillation, or supraventricular tachycardia, with avoidance of strong negative inotropes such as beta blockers or high doses of calcium channel blockers. Severe ventricular arrhythmias may be treated with mexilitene 5-8 mg/kg PO TID +/- sotalol (2 mg/kg PO BID). Supraventricular arrhythmias may be treated with diltiazem or sotalol and digoxin.

Feline Unclassified Cardiomyopathy
This nebulous category consists of cats with left atrial enlargement +/- right atrial enlargement in the absence of significant concentric hypertrophy and normal to only mildly reduced systolic function. Significant valvular insufficiency must be ruled out, which may be difficult given the high heart rates of cats. Atrial dilation in cats with unclassified cardiomyopathy may be secondary to diastolic dysfunction or due to a form of atrial myopathy. Diastolic function assessed by TDI echocardiography in unclassified cardiomyopathy may be normal.

Restrictive cardiomyopathy is a subset of unclassified cardiomyopathy that is characterized by severe diastolic impairment and increased stiffness secondary to infiltration of the endocardium, subendocardium, or myocardium with fibrosis. There is normal to only mildly increased wall thickness, normal to mildly decreased systolic function, and atrial dilation. Echocardiography may reveal severe fibrotic bands bridging the left ventricle or extensive left ventricular endomyocardial fibrosis. Early diastolic myocardial velocity is reduced in cats with restrictive cardiomyopathy. Delayed relaxation, pseudonormal, or restrictive patterns may be seen using PW Doppler of mitral inflow. Left atrial thrombus or spontaneous contrast may be seen in cats with severe RCM, and 45% of cats suffer from arterial thromboembolism.

Treatment of Unclassified or Restrictive Cardiomyopathy
Restrictive cardiomyopathy is characterized by severe endomyocardial fibrosis and bridging fibrotic bands, which greatly reduces the compliance of the left ventricle and leads to diastolic heart failure. Beta blockers or calcium channel blockers are not useful to treat endomyocardial fibrosis, but may be used to treat significant
tachyarrhythmias. Anticoagulant therapy (as discussed above) is often necessary in cats with moderate or severe atrial dilation as there is a high incidence of arterial thromboembolism of 45% in cats with restrictive cardiomyopathy. Heart failure treatment is outlined above.

**Arrhythmogenic right ventricular cardiomyopathy (ARVC)**

ARVC is a rare form of cardiomyopathy in cats, and is more common in Boxer dogs and people. It consists of fatty or fibrofatty infiltration of the right atrium and right ventricle, with subsequent severe dilation of those chambers. The etiology of ARVC in cats is unknown. In a case series of 12 cats, middle aged, male domestic shorthair cats were most commonly affected with ARVC. Fatty replacement of the cardiomyocytes results in systolic myocardial failure +/- diastolic dysfunction. Echocardiography reveals right atrial and right ventricular dilation. The right ventricular wall is commonly thin and there may be right ventricular aneurysms. Centrally arising tricuspid regurgitation occurs secondary to tricuspid annular dilation and lack of valve coaptation. Right sided CHF including pleural effusion and ascites was seen in 67% of cats with ARVC. Ventricular tachyarrhythmias are common (75%), as well as supraventricular tachyarrhythmias (42%). Changes mostly involve the right heart, but changes may also occur to a lesser extent in the left ventricle and left atrium. The main differential diagnosis of ARVC is tricuspid valve dysplasia, a congenital heart defect. Prognosis of cats with ARVC is grave, with a median survival of 1 month (range 2 days to 4 months).

Arrhythmogenic right ventricular cardiomyopathy is typically treated similarly to idiopathic DCM, with use of positive inotropes, furosemide, and an ACE inhibitor. Since ventricular tachyarrhythmias are common (75%), as well as supraventricular tachyarrhythmias (42%), antiarrhythmic therapy may be needed as described above. Indications for anticoagulant therapy are outlined above.

**Treatment of Congestive Heart failure**

Treatment of CHF is similar regardless of the specific cardiac disease present, and includes furosemide and an angiotensin converting enzyme (ACE) inhibitor. Furosemide may be given parenterally (1-3 mg/kg every 1-4 hours) in cats with fulminant CHF, and the furosemide dose should be rapidly tapered once the respiratory rate and effort begin to improve. Although efficacy is unknown, the venodilator nitroglycerin may be applied transdermally every 6 hours for 2 days (until tolerance develops) for hospitalized patients. Oxygen therapy is necessary in severe cases, and the fractional inspired oxygen percentage should be decreased to 50% or less if possible within 12 hours to avoid further barotrauma. An ACE inhibitor can be slightly postponed in cats receiving aggressive diuresis, until the cat is eating, drinking, and not severely dehydrated since it may potentiate azotemia in dehydrated cats. Chronic oral dosing of furosemide may be started at 1 mg/kg PO q24 hr- BID and increased over time as the severity of CHF worsens to a maximal ceiling dose of 4 mg/kg PO TID. Pimobendan (0.25 mg/kg PO BID) is used in cats with myocardial failure and heart failure, and also may be useful in cats with unclassified or restrictive cardiomyopathy, a diagnosis made by echocardiography. In cats receiving maximal furosemide doses that have refractory CHF, an additional diuretic
may be added such as hydrochlorothiazide (1-2 mg/kg PO q24 hr – BID). Some degree of azotemia is expected in cats receiving aggressive diuretic therapy.

**Anticoagulant therapy**

Anticoagulant therapy is necessary in cats that have suffered from arterial thromboembolism or who have echocardiographic evidence of a thrombus or spontaneous contrast within the left atrium, and may be considered in cats with moderate or severe left atrial dilation. Aspirin (5 mg – 81 mg PO q 3 days) has relatively underwhelming and variable success in prevention of thromboembolism. In cats suffering from arterial thromboembolism, survival with or without thrombolytic therapy is only 30-40%. Recurrence rate with aspirin (standard or low dose) is variable and ranges from 28-90%.

Clopidogrel is a novel anti-platelet agent that irreversibly inhibits ADP receptors on platelet membranes. Clopidogrel has been shown to inhibit platelet aggregation, increase oral mucosal bleeding time, and reduce plasma serotonin concentration in normal cats at doses as low as 18.75 mg PO q 24 hours. Low molecular weight heparins (LMWH) such as dalteparin and enoxaparin are attractive alternatives to unfractionated heparin given their increased bioavailability and prolonged half lives. Compared to unfractionated heparin, LMWHs work more specifically upstream in the coagulation cascade against Factor X with much lower activity against thrombin (Factor II). Since there is less anti-II activity, LMWHs do not alter PT and APTT times, and therapeutic efficacy must be assessed by measurement of anti-Xa activity. There are only a few pilot studies evaluating pharmacokinetics of dalteparin and enoxaparin in healthy cats. 1.5 mg/kg of enoxaparin SQ appears to adequately suppress factor Xa activity, but the optimal dosing interval is less clearly defined. Dosing frequencies of BID to TID are likely necessary for sustained anti-Xa activity. In cats suffering from arterial thromboembolism, thrombolytic therapy with streptokinase, tissue plasminogen activator, or urokinase are generally not recommended as they are associated with approximately 50% mortality, the same mortality as conservative supportive therapy.

**Reference List**