Congenital heart diseases are an important cause of morbidity and mortality in pediatric veterinary patients. The incidence of such defects is listed below.

**CONGENITAL HEART DISEASES:**

North American Study (canine) 0.46%-0.85%
- PDA 31.7% (female predominance 2:1)
- SAS 22.1%
- PS 18.3%
- VSD 6.6%
- PRAA 4.5%
- ToF 2.7%
- TVDys 2.4% (male predominance)
- ASD 0.7%

North American Study (feline) 0.2-1.0%
- AV septal defects 23% (male predominance)
  VSD, ASD, AV canal
- M&TVDys 17%
- PDA 11%
- AS 6% (male predominance)
- ToF 6%
- PS 3%

**Patent Ductus Arteriosus:**

Is the most common congenital defect in dogs. It is a L- R shunting defect resulting from failure of closure of the left sixth aortic arch. If left untreated it results in left sided congestive heart failure. Clinically animals present with a Continuous (Machinery) Murmur at the left heart base with Hyperkinetic Femoral Pulses. A systolic murmur of mitral regurgitation may also be ausculted secondary to annular dilation from volume overload of the left ventricle.

**Signalment:** toy breeds (Corgi, Poodle, Maltese), German Shepard, Rottweiller are common large breeds affected. There tends to be a female: male (2:1) ratio.

**Thoracic radiographs:** Left ventricular enlargement, +/- L atrial enlargement, pulmonary overcirculation, “Ductus bump” (dilatation of the descending aortic), +/- pulmonary edema
**Treatment** – Multiple options to close the ductus now exist. Surgical closure has been the gold standard however interventional closure has overtaken surgery as the most common method in cardiology centers. Three devices have been studied and proven successful in our patients, Gianturco coil, Amplatz Plug, and the Canine ductal occluder.

**Subaortic Stenosis:**

Subaortic stenosis (SAS) is the second most common congenital defect in canine patients. It results in significant pathology and may cause sudden death. A fibrous, muscular or fibromuscular narrowing is formed just below the aortic valve in the LVOT that may involve the base of the aortic valve and the anterior leaflet of the mitral valve and anterior leaflet of the mitral valve since the annulus of these two structures is formed contiguously. The lesion may not be present at birth, can worsen over the first few months of life. MV dysplasia commonly associated.

Pathophysiology: stenotic ring induces increase in LV afterload

- pressure overload $\rightarrow$ concentric hypertrophy associated coronary arterial changes reduce coronary flow
- increased wall tension especially in subendocardial regions ($\uparrow$ MVO2) $\rightarrow$ ischemia/arrhythmias.

**Signalment:** It is most commonly seen in large breed dogs such as Newfoundland, Golden Retriever, Rottweiller, Boxer, German Shepard; exact genetics unknown, suspect autosomal dominant with modifying genes or polygenic.

**Clinical signs**

Exercise intolerance, syncope, sudden death, L-CHF (unusual) may all be present however a number of patients will present perfectly normal. **Physical exam** Cardiac auscultation often reveals an Ejection-type systolic murmur around left heart base (3rd- 4th ICS) of variable intensity radiates cranial and to the right, up the carotids and calvarium in some circumstances. The quality of the femoral pulses gives a strong physical exam clue as the severity of the stenosis. Reduced and late rising Pulses parvus et tardus suggest more severe disease.

**Treatment** – B-blockers, balloon dilation not as productive as the narrow often returns in about 6 months. If necessary however given the relative non-invasiveness of ballooning it can be performed at multiple times.

**Pulmonic Stenosis:**

Pulmonic stenosis results from malformation (dysplasia) or fusion of the pulmonic valve. Our patients tend to have a combination of both types. This results in obstruction to blood flow from the right ventricle. **Signalment** Breed predisposition Bulldog, Boxer, Labrador, Beagle (polygenetic), Mastiff, terriers, many others.

Pathophysiology: stenosis induces increase in RV afterload; pressure overload $\rightarrow$ concentric hypertrophy; associated coronary arterial changes reduce coronary flow; increased wall tension especially in subendocardial regions ($\uparrow$ MVO2) $\rightarrow$ ischemia/arrhythmias reduced coronary flow increased heart rate ($\downarrow$ diastolic filling time, $\uparrow$MVO2) critical stenosis can lead to $\downarrow$ CO and syncope

Physical exam Cardiac auscultation Ejection-type systolic murmur around left heart base (3rd ICS) of variable intensity radiates dorsally. Femoral pulses may be reduced if critical PS but usually NORMAL Jugular pulses may display a Prominent a-wave (RVH) distension if R-CHF

**ECG RVE, +/- RAE** TREATMENT: $\beta$-blockers (atenolol) to $\downarrow$HR, $\downarrow$MVO2, $\downarrow$ ischemia and risk of arrhythmias. **Balloon valvuloplasty** is used best with thin fused valve excellent results
with little morbidity/mortality even in apparently dysplastic valves. However the

**Ventricular Septal Defect:**

Ventricular septal defects are common defects especially seen in cats and not uncommon in dogs that often results in left to right shunting of blood. Generally they are placed in two broad categories:

- **“Restrictive” VSD** small hole with large pressure gradient from LV→RV high on IVS L→R shunt directly into the RVOT/PA Volume overload of the L heart
- **“Non-restrictive” VSD** large defect with equilibration of LV and RV pressures if RV afterload is normal, L→R shunt with L-CHF or biventricular failure. Increased RV afterload (PS, pulmonary hypertension) may result in either bidirectional or R→L shunting. **Signalment** Dogs (breed predisposition) Bulldog, Springer Spaniel, Keeshonds (autosomal recessive) Cats. **Clinical signs** Often asymptomatic exercise intolerance, coughing, poor growth, syncope, exercise intolerance, cyanosis (R→L VSD) **Physical exam** Pansystolic murmur over the right cranial sternal border, +/- ejection-type systolic murmur left heart base (3rd ICS) of variable intensity (relative PS), Split S2 Diastolic decrescendo over left heart base (AI, PI), S3 gallop, **Clinical management** Most are asymptomatic; congestive heart failure usually develops early in life unlikely to develop after 6 months of age. Medical management could include Diuretics, positive inotropes, ACE inhibition, +/- afterload reducers. Surgical therapy is either definitive closure (cardiopulmonary bypass); or **PA banding** Create supravalvular PS to reduce the amount of L→R shunting. There are interventional devices that are available to close ventricular septal defects however, due to perimembranous location of most VSD’s in veterinary patients, placement of available devices may result in disruption of atrioventricular (AV) valve function.

**Tetralogy of Fallot**

Is a defect that results from 4 changes in the heat. Ventricular septal defect, Overriding aorta, pulmonic stenosis, and right ventricular hypertrophy. Cranial deviation of the infundibular septum is responsible for all 4 defects of Tetralogy. Direction of VSD flow is primarily dependent upon the severity of RV obstruction; RV pressures must be suprasystemic to get R→L shunting; Mild to complete atresia of the PA “pink” tetralogy.

Desaturation of arterial blood causes ↑erythropoietin which leads to polycythemia. **cyanosis** of entire body R→L shunting worsens with exercise ↓systemic arterial resistance ↑in RV obstruction (dynamic) return of more desaturated mixed venous blood to R heart **Systemic bronchial collaterals form tortuous network that supplies blood flow from aorta to lungs Can participate in gas exchange** **Physical exam:** ejection-type systolic murmur left heart base (3rd ICS) of variable intensity (RV obstruction). On rare occasions one may hear no murmur. The mucous membranes may be cyanotic, especially with exertion or normal. **Thoracic radiographs** Normal to small “club-shaped” cardiac silhouette MPA is not dilated (compared to PS with intact IVS) Pulmonary Undercirculation. **Clinical management** Medical: β-blockers (reduce exercise-induced R→L shunting), periodic phlebotomy, crystalloid fluid replacement moderate to severe exercise restriction, hydroxyurea; **Surgical:** Create L→R shunt, **Blalock-Taussig shunt** (left subclavian→PA), **Potts shunt** (ascending aorta→PA **Waterston-Cooley shunt** (descending aorta→PA).

Other common defects include:

**Vascular Ring Anomalies**
- Most common are associated with regurgitation in puppies
- Abnormal embryological development

**Persistent Right Aortic Arch**
- Persistence of the R 4\(^{th}\) aortic arch instead of L 4\(^{th}\) aortic arch
- Left 6\(^{th}\) aortic arch (ductus) remains which forms a constrictive band around the esophagus at the heart base
- Ductus can be patent or a ligamentum

**Atrial Septal Defects**
Defect in formation of IAS 2 septa Septum secundum is to the right of septum primum Clinical findings are usually limited depending on the size of the defect. A soft murmur of relative pulmonic stenosis may also be ausculted at the left heart base with larger defects that are cause hemodynamic changes. **Signalment** Boxers, standard poodles; cats. **Treatment**: Larger defects may be amendable to closure via catheter based delivery of an Amplatz Ductal Occluder.

**Reference:**
Available upon request.
Managing Feline Arterial Thromboembolism

Henry W. Green, III, DVM, DACVIM – Cardiology
Department of Veterinary Clinical Sciences
Purdue University College of Veterinary Medicine, West Lafayette, IN 47907

Thrombotic and thromboembolic complications have long been recognized as some of the most difficult to manage complications of feline myocardial disease. This syndrome is often referred to as feline aortic thromboembolism (FATE). Thrombosis represents clot formation within a cardiac chamber or vascular lumen. Thrombus formation has been historically linked to the presence of one of three predisposing factors known as Virchow’s triad: 1) local vessel or tissue injury, 2) circulatory stasis, and 3) altered blood coagulability. These thrombi typically form in the left atrium, left ventricle or both. Embolization occurs when a clot fragment or other foreign material lodges within a distal vessel. Although the distal aorta is the most common site of embolization, various other organs (i.e. the kidney, intestine) may become affected during embolic showers.

The prevalence of thromboembolism has been widely reported. In studies of FATE in necropsied cats, thromboembolism was seen in up to 48% of cats with hypertrophic cardiomyopathy (HCM), 29% with restrictive cardiomyopathy (RCM) and 25% with dilated cardiomyopathy (DCM). The prevalence in clinical settings obviously; is much less, being reported from a range of 12% in HCM cats to 18% in taurine deficient DCM cats. In recent clinical study FATE was seen in 0.57% of all feline clinical cases seen at a single referral institute. Incidentally, FATE is rarely seen in cats with hyperthyroidism; it has only been reported in 2% and 3% of cats in retrospective studies of cats with thyrotoxicosis.

CLINICAL PRESENTATION AND EVALUATION:

The clinical presentation of cats suffering FATE may vary substantially depending on the location of the thrombus, the extent and duration of arterial occlusion, the degree of functional collateral circulation, whether the cat is suffering from concurrent congestive heart failure (CHF), and the development of other severe complications such as renal failure. Classically cats will present with paralysis, paresis, and painful; firm cold limbs and pale footpads, along with pale or cyanotic nail beds and potentially very weak to non-palpable femoral pluses. Clinical signs are attributable to substantial tissue injury (ischemic neuropathy) due to the sudden arterial occlusion with almost instantaneous and complete interruption of blood flow, coupled with decreased collateral circulation secondary to vasoconstrictive substances being released from the thrombus.

If FATE is suspected based on clinical presentation, a minimum data base should include a complete blood count, coagulation and biochemical profiles; urinalysis, blood pressure, thoracic radiographs, electrocardiogram, and echocardiogram. Common clinical pathology abnormalities include elevated blood urea nitrogen (BUN) and creatinine, elevated serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) as well as increases in creatine phosphokinase (CPK). Hyperglycemia, and stress leukogram characterized by a mature neutrophilia and lymphopenia may also be present.

Thoracic radiographs are indicated to assess for cardiomegaly and CHF. Echocardiography gives a non-invasive assessment of cardiac structure and function. It also allows for investigation of the cardiac chambers for thrombi and spontaneous contrast (smoke) which is believed to result from blood stasis and subsequent rouleaux formation of red blood cells. Smoke may be present in the LA or LV and is a harbinger for thromboembolic potential.

MANAGEMENT OF FATE:

Treatment of acute FATE should address general patient support; management of concomitant CHF and/or arrhythmias, and thrombus therapy to limit thrombus growth and formation. Chronic therapy is aimed at prevention of repeated thromboembolic events.
Analgesic therapy is essential for cats with FATE to alleviate pain, discomfort and stress associated with the ischemic myopathy during the first 24 to 48 hours following a thromboembolic event. Butorphanol, morphine, oxymorphone and fentanyl have all been used for this purpose. Maintenance of hydration, electrolyte balance and nutrition is also important during the first days of therapy. Thus it may be necessary to place nasoesophageal feeding tube, particularly when CHF has been resolved but there is persistent anorexia present.

Thrombolytic therapy with Tissue plasminogen activator (t-PA) can be attempted within the first few hours of a thromboembolic event in attempt to lyse the clot and rapidly restore perfusion to affected limbs. Therapy with this agent has not gained as great of popularity in veterinary medicine as has been seen in human medicine. The expense associated with its use, the need for emergency availability and difficulty found in using these drugs as well as managing related complications in cats have all led to their minimal utilization veterinary medicine. We currently only use these drugs on rare occasions. Streptokinase and urokinase are no longer available in the US.

Anticoagulant therapy has been a mainstay of therapy for thromboembolic disease. Anticoagulants work by retarding the synthesis or accelerating the inactivation of clotting factors but they have no effect on established thrombi. Their use is therefore based on the premise of prevention of thrombus formation or preventing thrombus extension resulting in subsequent further reduction in arterial blood flow. Coumarin (warfarin) impairs hepatic vitamin K metabolism, thereby interfering with production of the procoagulant factors II, VII, IX and X. Given the lack of evidence of preventing thromboembolism as well as the difficulty associated with monitoring these patients, and the potential for complications; warfarin therapy has not really gained favor in the treatment of this disease. Heparin has also been used as acute and chronic anticoagulant therapy in cats. Heparin also binds and inhibits von Willibrand factor thus exhibiting some direct antiplatelet effects. Classically unfractionated heparins (UFH) have been used for this purpose. Low molecular weight heparins (LMWH) are fractionated particles of heparin that are now available and have greater bioavailability, a longer plasma half life than UFH and can reportedly be given as a fixed subcutaneous dose once daily however most pharmacokinetic studies of this drug suggest the need for more frequent 2 to 3 times a day dosing. The problem with these studies however is the endpoint that was being studied prolongation of anti factor Xa has not been proven to necessarily correlate to preventing thrombus formation. Thus studies need to be performed that directly assess dosing affects on clot formation or prevention thereof.

Antiplatelet aggregating drugs are used to prevent the activation of platelets in response to exposure of blood to subendothelial connective tissue. Aspirin has traditionally been used in this manner as it induces a functional defect in platelets by irreversibly inactivating cyclo-oxygenase. Although aspirin should theoretically be beneficial, there is no evidence that aspirin is effective at preventing first time or recurrent thromboembolism. Also there is recent research that questions the ability of aspirin to decrease platelet stimulation and aggregation or to suppress overall thromboxane A2 production. Current research with aspirin is focusing on the use of low dose aspirin (5 mg/cat q 72hrs) base of the theory of sparing endothelial prostaglandin I2 synthesis. Newer antiplatelet drugs include the thienopyridine derivatives ticlopidine and clopidogrel. They function by irreversibly binding ADP to its receptor on platelets, thereby preventing the transformation of the IIb/IIIa glycoprotein receptor to its active form. Clopidogrel however effectively inhibited platelet aggregation with no apparent gastrointestinal side effects when dosed at 18.75 - 75 mg/cat/day PO. Current trials with clopidogrel are ongoing at Purdue University to assess drug efficacy versus aspirin in the FATCAT study.

So what do we do with our patients?

Acute Stage:
Supportive care is the mainstay of our treatment: Pain management and control signs of congestive heat failure – if present.

Owners are offered the option of thrombolytic therapy
A loading dose of Clopidogrel 75mg is given if the blood work is relatively normal along with a loading dose of unfractionated or low molecular weight heparin.

Chronic Stage:
Depending on the cat’s status (to be discussed further) chronically we recommend Clopidogrel-Plavix® 18.75 mg PO q 24 hrs. We also commonly will use chronic therapy with LMWH. We commonly utilize these drugs in combination as they could offer synergistic effects of preventing clot formation. In such cases we often use Dalteparin 100UI/kg q 24 - 12 hrs or Enoxaparin 1-1.5 mg/kg q 24 - 12 hrs SQ.

Preventative:
Cats that appear to be at risk for FATE (i.e. Thrombus, or spontaneous contrast of those with large diameter LA are seen on echocardiogram) we suggest starting therapy with Clopidogrel - Plavix® 18.75 mg PO q 24 hrs. Therapy with aspirin is also discussed as an alternative if affordability or tolerance is an issue.

Low molecular weight heparins are also often discussed/offered as an alternative or additive to therapy for a number of potentially at risk cats.

OUTCOMES:
Honestly outcomes are still somewhat unpredictable in these patients. Poor prognostic indicators appear to include hypothermia on presentation in the acute stage, thrombus present in the LA, and signs of renal dysfunction along with congestive heart failure. Historically most studies assessing survival of acute episodes report a 33%-39% rate of survival to discharge. These numbers may be skewed significantly since this represents data mostly from referral institutions where cases may be significantly more severely affected. More recent data suggest improved survival rates with up to 73% of cats being discharged after acute events. The Feline Arterial Thromboembolism: Clopidogrel vs Aspirin Trial (FAT CAT) was the first study designed to be the first prospective study to evaluate antithrombotic therapy for the secondary prevention of CE in cats to better assess drug therapy outcomes. Results of the FATCAT trial showed that cats receiving clopidogrel tolerated it well and survived longer, with a longer time to repeat thrombosis than did cats receiving aspirin. This is the first demonstration of a clinical benefit to the use of clopidogrel to treat cats that have experienced thromboembolism secondary to heart disease. While there are study limitations, it provides objective data supporting the use of clopidogrel in the treatment of thromboembolism in cats with heart disease and sets the stage for future studies addressing treatment of this very important disease of cats.

References:
Available upon request.
INTRODUCTION:

Syncope is the sudden temporary loss of consciousness that is associated with loss of postural tone as a result of an abrupt decrease in cerebral perfusion or decreased delivery of essential nutrients (i.e. glucose) to the brain. The true incidence of syncope is unknown however it has been reported to occur in a referral database in 0.15% of dogs and 0.03% of cats. This number may be due to the fact that one it is a referral database and two that often to both the trained and untrained eye it may be difficult to distinguish syncope from seizure activity.

During a syncopal event, animals will usually collapse into lateral recumbency and may have concurrent stiffening of the limbs, opisthotonous, urination and vocalization. However it is uncommon to see persistent facial fits, persistent tonic/clonic motion, defecation, postictal dementia and neurologic deficits with cardiovascular mediated syncope. What may often confuse one who witnesses a syncopal event is that on occasion some animals may have “convulsive syncopal episodes” (CSE) that results from severe hypotension or asystole. Typically CSE are preceded by loss of muscle tone whereas seizure activity is usually preceded by atypical limb or facial movement or even staring spells prior to the loss of body tone.

ETIOLOGY AND PATHOPHYSIOLOGY:

The mechanisms underlying syncope are usually rather acute in nature. These mechanisms usually involve reduced cardiac output resulting from arrhythmias or decreased cardiac filling, obstruction of blood flow from the heart, hypoxia or hypoglycemia (with normal cerebral flow) or severe decreased vascular resistance related to neurocardiogenic reflexes. There are numerous diseases that can result in any one or a combination of these mechanisms. A partial list is presented in Table 1.

The vast majority of syncopal events in veterinary medicine are due to a transient reduction in brain blood flow. A sudden decrease in cardiac output (CO) or vascular resistance reduces mean arterial pressure may both result in reduction of cerebral blood flow. The most common causes we see in our patients are cardiogenic in nature. Two-thirds of dogs and cats with syncope also have a cardiac disease. Most of these are related to rhythm disturbances which are secondary to inherent cardiac disease. Underlying cardiac functional or structural abnormalities exacerbate the negative effect of arrhythmias on cardiac output. Poor myocardial contractility, impaired filling as with pericardial disease or outflow obstructions can all result in an inability of the heart to maintain sufficient cardiac output to meet increased demand during excitable states; even under normal cardiac rhythms.

Non-cardiogenic diseases such as those that result in increased intracranial pressure can result in syncope also by reducing cerebral perfusion pressure by compressing intracranial vessels. While the majority of animals with severe hypoglycemia will present with weakness or seizures, a fair number may present with syncope or CVE while maintaining normal cardiac output. Hypoxia as a result of right to left shunts, severe acute anemia or pulmonary disease can result in insufficient cerebral oxygen delivery and syncope.

Another common occurrence that we see is cough (tussives) syncope. Some like to use the term ‘cough drop’ to describe syncope induced in this manner. This form of situational syncope occurs most often in brachoecephalic dogs however is also common in dogs with airway disease,
tracheal collapse or those with sever left atrial (LA) enlargement causing compression of the left mainstem bronchus. Coughing results in increased intrathoracic pressure which decreases venous return (preload) and cardiac output. It also decreases intracranial pressures both of which may cause a decrease in cerebral perfusion if severe enough coughing occurs. Coughing may also induce reflexive bradycardia by stimulation of the vagal nerve.

Neurocardiogenic (vasovagal) reflex resulting in syncope is less common in animals than in people however there are reports of syncope that occurs secondary to sudden bradycardia following bouts of tachycardia in especially in small breed dogs with advanced valvular disease. In cases of neurocardiogenic syncpe acute sympathetic activity (induced by excitement) provokes a strong reflex vagal response that results in bradycardia. Ventricular mechanoreceptors play a huge role in this reflex in that their activation due to forceful contraction results in a surge in afferent neural traffic stimulating paradoxical brainstem response to vagal activation.

**APPROACH TO THE PATIENT WITH SYNCOPE:**

Clues as to the underlying cause of the episodes can be elicited through a thorough history and physical examination of the animal. Getting a detailed (almost dramatic) description of the events as they occurred as well as the preceding events, prodromal signs, and the animal's mentation and behavior prior to and after the event can help in differentiating cardiovascular syncope from seizure activity and other causes of collapse. In a nice human prospective study the etiology of the syncopal event was able to be correctly elicited in 32% of patients based on obtaining a thorough history and physical examination. Performing diagnostic testing in a stepwise manner is critical in diagnosing the syncopal patient.

Some questions you should consider asking when obtaining a history include:
- What was the animal doing immediately prior to the event?
- How long did the event last?
- Did the animal lose consciousness during the event?
- Did the animal have muscle (motor activity) movement during the event?
- If not; did the muscles appear stiff or relaxed?
- Did the animal urinate or defecate?
- Was the animal normal after the event or disoriented and confused and if so for how long after.
- Current medications.
- Any possible exposure to toxins?
- Have there been any changes in behavior recently?
- Was there any vomiting or coughing prior to the event?

While this is not an all inclusive list of questions and the answers may take you down different lines of questioning, answers to most of these questions may help you decide to follow the path of seizure or syncope for your next steps in diagnostic testing.

Routine database of CBC, biochemical profile, urinalysis, heartworm test, and arterial blood pressure measurement should be performed. In some cases testing for adrenal and thyroid abnormalities should also be performed. In the syncopal patient however these test are most usually normal however it is important to perform them to rule out some non cardiogenic causes of collapse.

A resting electrocardiogram (ECG) should be obtained and the rhythm should be evaluated for at least 1 minute if not longer and while the animal is calm and it is excited. In dogs with bradycardia ECG should be evaluated a second time following the administration of atropine 0.04 mg/kg IV or SC. Dogs with underlying sinus node disease will show an inadequate response (heart rate increase to <140 bpm). Dogs with vagal tone as the underlying mechanism for bradycardia
typically have heart rates that increase above 160 bpm. Normal heart rates on transient baseline ECG’s however does not completely rule out arrhythmias as the underlying cause of the syncopal episode.

Thoracic radiographs should be performed to evaluate lungs, pleural space, mediastinum and pulmonary vasculature as well as normal cardiac size and shape. Echocardiogram should be performed even if no murmurs are ausculted on physical examination to assess global cardiac function and to rule out the present of pericardial disease and obstructive cardiac masses.

In the face of finding all of the aforementioned test to be relatively normal (blood work, ECG, radiographs, and echocardiography) the clinician should consider ambulatory ECG monitoring with either Holter or event monitoring. Ambulatory monitoring can help identify or exclude cardiac arrhythmias as a cause for syncope in some animals.

**Holter monitoring** is twenty-four to forty-eight hours of continuous ECG monitoring. They are most likely to be diagnostic of syncopal events in animals with multiple and frequent syncopal episodes. To make a definitive diagnosis a syncopal episode must occur while the monitoring is occurring. However, just because frequent events are occurring doesn’t increase the likelihood of an event occurring during testing. Holter monitoring does allow one to identify any arrhythmia and quantitate the severity of arrhythmias that might increase the suspicion that the syncopal events are induced by arrhythmias. Because arrhythmias often occur without clinical signs this ability to evaluate the entire recording period is a very useful aspect of Holter monitoring. Holter monitors are also very useful for assessment of anti-arrhythmic therapy efficacy.

**Event monitors** are typically worn for 1-2 weeks periods in our patients that allow longer periods of assessment than with Holter monitoring. The event recording system does need to be activated when an event is observed. The monitor then saves to memory a portion of the recording prior to and after activation. The save recording is then transmitted via telephone to be printed. Event recorders have a higher diagnostic yield than Holter monitors however there biggest disadvantage is that they do not save recordings of potentially significant arrhythmias unless activated and they can not quantify the frequency of arrhythmias.

**TREATMENT:**

Therapy of animals with syncope episodes is intended to manage the underlying disease and avoidance of precipitating activities such as excitement as much as one can. In as such treatment of specific causes is sometimes obvious for example correcting anemia or treating respiratory or metabolic disorders.

In the case of heart failure patients: addressing proper management of the patient in heart failure: Institute appropriate therapy with diuretics, angiotensin converting enzyme inhibitors (ACE-I), and inotropic support if needed. In the case of patients who are already being treated with triple therapy, optimizing drug therapy dosages or stacking additional medications such as additional diuretics or vasodilators may help to place the patient in a more positive hemodynamic state and thus resolving syncopal signs.

If tachyarrhythmias are the apparent cause, treating with the appropriate anti-arrhythmic (or combination of anti-arrhythmic) will reduce or eliminate the number and severity of the arrhythmias such that the signs are eliminated. In the case of those arrhythmias that can not be eliminated such as atrial fibrillation associated with advanced heart disease, than using drug combinations that slows the number of impulses that cross the AV node to the ventricles will appropriately slow the heart rate enough to allow for appropriate ventricular filling and contraction that syncopal signs are eliminated or reduced significantly.
In the case of bradyarrhythmias, than pacemaker therapy may be warranted; especially those cases that don’t respond to atropine trials. Other strategies that have been effective, at least anecdotally include using Theophylline or Aminophylline to attempt to increase heart rate. We have found that often this therapy may be effective early but becomes ineffective as time passes on. We have also successfully employed pacemaker therapy in animals where syncope was apparently induced by coughing and the cause of the cough could not be resolved (i.e. severe LA enlargement).

In the rare cases of neurocardiogenic syncope pacemaker therapy is not likely to alter the hypotension that results. In suspected cases therapy with beta-blockers can be used to blunt the initiating sympathetically-induced tachycardia and the hyperkinetic ventricular contractions that stimulate the mechanoreceptors. The concern with utilizing beta-blocker therapy along is exacerbation of the resultant bradycardia thus these patients should be monitored very closely and combination of drug and pacemaker therapy may be the most appropriate for these animals.

SUMMARY:

Syncope can be a very difficult diagnosis and hard to distinguish from seizures or other causes of collapse. An adequate physical examination and understanding of the etiology and pathophysiology along with a stepwise approach to animals presenting with this clinical complaint can expedite uncovering the underlying cause and allow for early intervention for these animals.

Table 1.

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th>Hypotensive/Reflexive</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A) Arrhythmias</strong></td>
<td><strong>A) Neurologic</strong></td>
</tr>
<tr>
<td>1. Tachyarrhythmias</td>
<td>1. Brain Tumor</td>
</tr>
<tr>
<td>2. Bradyarrhythmias</td>
<td>2. Thromboembolism</td>
</tr>
<tr>
<td>a) Ventricular Tachycardia</td>
<td>3. Seizures</td>
</tr>
<tr>
<td>b) Supraventricular tachycardia</td>
<td></td>
</tr>
<tr>
<td>c) Atrial fibrillation</td>
<td></td>
</tr>
<tr>
<td>2. Bradyarrhythmias</td>
<td></td>
</tr>
<tr>
<td>a) Sinus node disease</td>
<td></td>
</tr>
<tr>
<td>b) Atioventricular block (high grade)</td>
<td></td>
</tr>
<tr>
<td><strong>B) Impaired Forward cardiac output</strong></td>
<td><strong>B) Metabolic/ Hematologic</strong></td>
</tr>
<tr>
<td>1. Myocardial Failure</td>
<td>1. Acute Hemorrhage</td>
</tr>
<tr>
<td>a) Dilated cardiomyopathy</td>
<td>2. Anemia</td>
</tr>
<tr>
<td>2. Severe Valvular Regurgitation</td>
<td>a) Hemolysis</td>
</tr>
<tr>
<td><strong>C) Impaired Filling</strong></td>
<td>3. Hypoxemia</td>
</tr>
<tr>
<td>1. Hypertrophic cardiomyopathy</td>
<td>a) Primary respiratory disease</td>
</tr>
<tr>
<td>2. Pericardial effusion</td>
<td>b) Pleural space</td>
</tr>
<tr>
<td>3. Intracardiac tumor</td>
<td>4. Hypoglycemia</td>
</tr>
<tr>
<td><strong>D) Outflow obstruction</strong></td>
<td><strong>C) Neurocardiogenic</strong></td>
</tr>
<tr>
<td>1. Subaortic stenosis</td>
<td><strong>D) Tussive (cough)</strong></td>
</tr>
<tr>
<td>2. intracardiac tumor</td>
<td><strong>E) Micturition, defecation</strong></td>
</tr>
<tr>
<td>3. Pulmonic stenosis</td>
<td></td>
</tr>
<tr>
<td>4. Pulmonary hypertension</td>
<td></td>
</tr>
<tr>
<td><strong>E) Cyanotic Heart Disease</strong></td>
<td></td>
</tr>
<tr>
<td>1. Tetralogy of Fallot</td>
<td></td>
</tr>
<tr>
<td>2. Other right to left shunting defects</td>
<td></td>
</tr>
</tbody>
</table>

References:
Diagnosis and Treatment of Congestive Heart Failure

Henry W. Green, III, DVM, DACVIM – Cardiology
Department of Veterinary Clinical Sciences
Purdue University College of Veterinary Medicine, West Lafayette, IN 47909

Introduction:

There are many different diseases that can cause signs of congestive heart failure (CHF) thus there are numerous approaches one can take for therapy depending on the patient’s particular circumstance(s). There is a heavy reliance on medical management to control clinical signs of heart failure. The ultimate goal of which is to improve the patient’s quality and potentially length of life generally accomplished by reducing retention of salt and water, improving cardiac function and reducing cardiac workload. Owners must be made aware of this goal as there are very few of curable diseases that cause congestive heart failure.

In recent years, there has been a greater understanding and appreciation for the role of neuroendocrine system changes in heart failure. With this understanding came a new focus on therapy, not concentrating specifically on symptomatic relief but attempting to halt progression of disease. Improvement in clinical signs is simply a consequence of modification of these changes. This approach appears to be of primary importance and therapeutic considerations include how disease states affect activation of these systems. Current therapeutic options are facilitated not only by knowledge of pharmacology, hemodynamic effects of drugs, the nature and prevalence of drug side effects, drug efficacy, and the effects of drugs on quality of life but also how given drugs will alter neuroendocrine function.

These systems include but are not limited to the Renin Angiotensin Aldosterone System (RAAS), Sympathetic Nervous System (SNS), the Natriuretic peptides and Arginine Vasopressin (ADH). The RAAS system involves the generation of angiotensin II (ANG II) and aldosterone (ALD) in response to reduced renal perfusion, reduced sodium load to the distal convoluted tubule and increased sympathetic tone. ANG II and ALD both cause increased sodium and water retention along with inducing significant myocardial and vascular smooth muscle remodeling and fibrosis. These latter effects represent irreversible changes and progression of disease. ANG II is also a potent direct vasoconstrictor which increases afterload. ALD has more of a permissive effect on maintaining vascular smooth muscle tone rather than inducing vasconstriction. The prognosis for heart failure is inversely proportional to the degree of sympathetic nervous system activity. Increased sympathetic tone causes vasoconstriction, renin release, arginine vasopressin release (a potent vasoconstrictor and water retainer) and has been shown to induce myocardial and vascular smooth muscle remodeling and fibrosis. It has been proven that there is baroreceptor dysfunction in heart failure patients and it is felt that this plays the central role in increased sympathetic tone in these patients. Natriuretic peptides (ANP and BNP) are produced by the atria and ventricles in response to increased stretch induced by volume overload and increased pressure. They antagonize the vasoconstriction and sodium/water retention from other neuroendocrine actions and acts as the body’s internal regulator. Unfortunately, it is not very effective as they are broken down rather quickly and their effects are essentially neutralized.

In veterinary medicine alas there is very little data available to assist us in determining the optimal therapy for our patients with congestive heart failure (CHF). To date, only data generated using the ACE inhibitors enalapril and benazepril and the positive inotrope pimobendan have been shown to improve the length and quality of life in the dog. Given the paucity of clinical data in veterinary patients, we have become reliant on data generated in human patients with similar disorders with a view to considering these data for our patients. Thus long term multi-center trials need to be completed to optimize CHF therapy for veterinary patients.

MEDICAL MANAGEMENT
Diuretics are the most commonly drugs for patients with CHF. These drugs reduce the preload on the heart and thus reduce backward pressure on the venous system. Asymptomatic heart disease is usually not associated with measurable activation of certain neuroendocrine systems; however, these neuroendocrine responses are stimulated following diuretic therapy secondary to the decreased preload induced reduction of cardiac output. Because activation is presumably counterproductive, most cardiologists do not recommend single agent use of furosemide for chronic treatment of heart failure. This does not mean that appropriate diuretics should not be used when congestion develops. The combined use of ACE inhibitors and diuretics can compromise one of the kidneys’ normal compensatory mechanisms (vasoconstriction of the efferent arteriole) and can lead to azotemia when excessive diuretic dose is initiated. While it is this author’s experience that this is not a common occurrence I strongly recommend assessing renal function if possible prior to onset of this therapy and adjusting therapy accordingly. We currently use the lowest possible dose of furosemide in animals with CHF. This often means a degree of experimentation must be performed to best evaluate an individual animal’s needs. In most instances of mild CHF, canine patients are released from our hospital on 1 mg/kg q 12 PO q 12 hrs, and in most cats we initially try to use 6.25 mg/cat/day for chronic therapy. When a dose of 2.2 mg/kg twice to three times a day is exceeded during chronic therapy, a thiazide diuretic (hydrochlorothiazide) is “stacked” on to therapy as an opposed to further increase in furosemide dosing. At this level of dosing some degree of diuretic resistance has been reached the addition of a synergistic diuretic is often of great benefit to your patient. While others suggest utilizing spironolactone in this capacity we typically will not due to the minimal diuresis affects of this drug. Spironolactone has however gained a more constant place in therapy due to the additional benefit of aldosterone-antagonism, and has been shown to have survival benefits in human CHF studies. Thus we often will have spironolactone on board concurrently at the onset of therapy for the CHF patient. The dosing spironolactone to this end point in dogs is highly empirical as no study has been repeated to mimic that seen in humans although in numerous animal models this antifibrotic effect has been duly noted.

Angiotensin-Converting Enzyme Inhibitors (ACE-I) are commonly used in the management of heart failure. Their benefits include reductions in plasma concentrations of angiotensin II and aldosterone; therefore, fluid retention and vasoconstriction are inhibited. ACE inhibition also is known to reduce the progressive cardiac enlargement and remodeling that attends most forms of heart failure. Enalapril (0.5 mg/kg SID to BID) is the ACE inhibitor most frequently used for dogs in the United States. We standardly employ twice a day dosing for dogs and feel this is most appropriate to achieve benefits for CHF and has been safe in the absence of significant pre-existing renal disease or excessive concurrent diuretic use. Although enalapril is licensed for use only in dogs, its successful use has been described in cats with hypertrophic cardiomyopathy (HCM). Other ACE-I commonly used in the U.S. is Benazepril (Dogs) 0.25 – 0.5 mg/kg PO q 24 – 12 hours and (Cats) 1.25 mg PO q 24 hours.

Other direct acting arteriolar vasodilators such as Amlodipine or Hydralazine may be very useful as disease progresses. While these drugs lack the favorable neuroendocrine effects that are associated with ACE-I, we often consider use of one of these (preferably Amlodipine) patients with CHF resulting from mitral valve disease or those with significant mitral regurgitation secondary to annular dilation especially when standard therapy (discussed below) appear inadequate.

With myocardial failure (dilated cardiomyopathy, end-stage mitral regurgitation), positive inotropes play an integral role. Positive inotropes may also have a beneficial effect in early mitral regurgitation by reducing the severity of regurgitation through reduction in isovolumetric contraction time and geometrical changes on the mitral annulus. Pimobendan is a new cardiac medication which acts as a calcium-sensitizing agent to increase inotropy. Because the drug increases the sensitivity of the contractile elements to the existing calcium, there seem to be fewer deleterious effects than drugs that act by increasing calcium flux into the myocardium. Inhibition of phosphodiesterase also may account for some of the beneficial effects of pimobendan. There has been no documentation of increased mortality in dogs treated with pimobendan and improvements in clinical signs may result in longer survival for dogs as quality of life impacts an owner’s decision to euthanize the dog. This will be determined as more study results are released on this drug. The dose of pimobendan for dogs is 0.25 mg/kg q 12 hrs. The dose for cats (those with systolic dysfunction) has been proposed to be 1.25 mg/cat q 12 hours but there is very limited experience with this drug in cats.
The use of digoxin in heart failure has been debated for hundreds of years. It is certainly recognized as a drug with beneficial effects but with a significant risk for toxicity. There is no argument against its use with atrial fibrillation but some controversy still exists about its use with normal sinus rhythm especially in human medicine. The arguments for using digoxin include its positive inotropic effect, as well as restoration of blunted baroreceptor responses and reduction of excessive sympathetic tone which is important in the neuroendocrine based treatment of CHF. In a large trial in people with heart failure, digitalis did not impact mortality, but did reduce the need for hospitalization. Those who are not enthusiastic users of digoxin point out that the drug has significant potential for toxicity, that it can be difficult to dose in veterinary patients, and that it has not been documented to improve survival. This author has not experience such frequent difficulties with toxicities or dosing. We historically employed digoxin as the third wing of triple therapy for CHF however since the FDA approval of pimobendan we employ ACE inhibitors, pimobendan, and diuretics for the early stages of CHF, and add digoxin when significant supraventricular arrhythmias (i.e. atrial fibrillation), recurrent syncope, or advancing CHF requires additional therapies.

Beta Blockers (propranolol and atenolol) have been used for many years in cats with HCM. While there benefit in this disease is under fire at the moment, more recently, beta blockade has gained favor in dogs as a therapeutic modality for treatment of heart failure. Many human studies on the use of beta blockers (i.e., metoprolol, carvedilol) have documented the benefits of chronic treatment with beta-blockers. These effects are often not seen for several months after initiation of beta blockade. Such benefits include up regulation of previously down regulated beta-receptors, improved cardiac performance (improved stroke volume), and improved survival. Because beta-blockers have negative inotropes and chronotropes effects, it is this author’s opinion that they may be best employed in animals that are minimally symptomatic with early/mild heart failure where long term favorable affects (if present) on mortality and hemodynamics may take place with minimal risk of resultant decompensation of the patient.

Finally one should not leave out the impact of nutrition for treatment of heart disease. Very interesting data have been revealed to show the effects not only of adding low salt diets to therapeutic regimes but also fish oils that contain n-3 fatty acids help to reduce to production of cytokines and other inflammatory mediators in both people and dogs.

Specific treatment decisions are made possible by an accurate diagnosis of the primary cause of the clinical signs (systolic or diastolic pump failure). Other considerations include, the timing of clinical signs (acute vs chronic HF), the severity of disease (mild, moderate, or severe HF), and the predominant manifestation of clinical signs (i.e. left vs. right heart failure and congestive vs. low-output failure). One method to attempt to help with classification of heart failure patients is given below.

**International Small Animal Cardiac Health Council (ISACHC) Heart Failure Classification**

**Class I: Asymptomatic**

Heart disease is detectable (a murmur or arrhythmia detected on auscultation) but the patient is showing no clinical signs of heart failure. Treatment is not indicated at this stage.

**Class II: Mild to moderate heart failure**

Clinical signs of heart failure are present at rest or with mild exercise. Clinical signs include exercise intolerance, cough, tachypnea, mild respiratory distress, and mild to moderate ascites. Home treatment is often indicated at this stage.

**Class III: Advanced heart failure**
Clinical signs of advanced congestive heart failure are immediately obvious. Clinical signs include profound exercise intolerance, respiratory distress, and marked ascites. In the most severe cases, the patient suffers from cardiogenic shock. Death or severe debilitation is likely without therapy.

a) Home care is possible
b) Hospitalization is mandatory

**Drug therapy for HCM or RCM patient:**

**Acuteley Decompensated- Class III(b):**
- Oxygen Therapy
- IV or IM Lasix (hourly dose or CRI)
- +/- Thoracocentesis
- +/- Venous Dilators
  - Nitroglycerine 2% Ointment

**Chronic Non-HF Therapy-Class I:**
- +/- Ca**++** Channel Blockers
  - Diltiazem extended release tablets for cats
  - OR-
- β-Blockers (For HOCM cats or those with significant arrhythmias)
  - Atenolol
- +/- Anti-platelet/coagulation therapy

**Chronic Compensated Therapy- Class II:**
- Ca**++** Channel Blockers or Atenolol
- Lasix (optimize dose)
- ACE Inhibitor
  - Benazepril (cats)

**Moderate to Severe Refractory HF- Class III(a):**
- Diltiazem or Atenolol (for cats with HOCM)
- Lasix (optimize dose)
- ACE Inhibitor (Remember this is not an emergency drug)
  - Benazepril (cats)
- +/- Thiazide Diuretic
- +/- Nitroglycerine Ointment
  - Once daily

**Other therapies**

Thrombolytic agents
- FATE in cats
  - +/- Tissue plasminogen activator (tPA)
- Antiplatelet agents
  - Aspirin
  - Clopidogrel (Plavix®)
- Anticoagulants
  - Heparin
  - Low molecular weight heparin
    ▪ Fragmin®

**Therapy for DCM patient:**

**Early Disease - Class I:** Know there is early activation of the RAAS and Sympathetic nervous system prior to the onset of heart failure. Thus therapy is aimed improving function and slowing progression of myocardial remodeling.

- ACE Inhibitors
- Spironolactone
- +/- positive inotropic therapy (Early use of Pimobendan is being investigated)
- Early therapy with β-blockers is currently being evaluated in clinical research
- Omega 3 Fatty Acids also may beneficial

**Acutely Decompensated-Class III:**

- Oxygen
- Lasix - IV
- Sodium Nitroprusside - IV
- Dobutamine infusion or Pimobendan if Infusion is not available

**Chronic Therapy-Mild CHF- Class II and III(at home):**

- Positive Inotrope : Pimobendan and or Digoxin (some cardiologists use both)
- ACE Inhibitors
- Spironolactone
- Lasix- low dose
- Patient Follow-up
  - Renal and electrolyte recheck in 3-5 days
  - Serum digoxin levels in 7-10 days or anytime signs of toxicity develops
  - Bloodwork is followed up every 6 months or with changes in dosing regime

**Chronic Therapy- Moderate to Severe CHF- Class III:**

- Same as above, may add periodicdobutamine infusions
- Maximize positive inotropic therapy
- Increase Lasix dose or decrease interval
- +/- Thiazide diuretic
- +/- Vasodilators

**Therapy for Chronic Valve Heart Disease (CVHD) Patient**

ACVIM Cardiologist developed a specific classification scheme for patients with chronic valve disease:

- A - Identifies high risk patients but no current structural disease
There are no current recognized benefit to currently available therapies.

- **B - Asymptomatic patients w structural heart disease**
  - **B1 - no radiographic or echocardiographic changes**
    - No treatment
  - **B2 - evidence of structural change**
    - Recent studies have proven that ACE inhibitors have no benefit at slowing progression of MVD. Thus therapy recommendations are limited. For animals with significant cardiomegaly we might recommend afterload reduction;
      - Amlodipine is what we often use for this purpose

- **C - Past or current clinical signs of heart failure associated with structural heart disease**
  - Acute or chronic
    - **Chronic Therapy-Mild CHF - Class (II):**
      - Positive Inotropes (usually Pimobendan however with atrial fibrillation we will use digoxin)
      - ACE Inhibitors
      - Spironolactone
      - Lasix- low dose
      - Patient Follow-up
        - Renal and electrolyte recheck in 3-5 days
        - If necessary serum digoxin levels in 7-10 days or anytime signs of toxicity develops
        - Bloodwork is followed up every 6 months or with changes in dosing regime

- **D - End-stage refractory to “standard therapy”**
  - Acute or chronic
    - **Acutely Decompensated- (Class IIIb):**
      - Oxygen
      - Lasix
      - +/-Sodium nitroprusside
      - +/- Dobutamine infusion
    - **Chronic Therapy- Moderate to Severe CHF- (Class IIIa):**
      - Same as above, may add periodic dobutamine infusions
      - Maximize positive inotropic use
      - Increase Lasix dose or decrease interval
      - +/- Vasodilators
      - +/- Thiazide diuretics

**CONCLUSION**

It is currently believe the maladaptive neuroendocrine responses play a very important role in the pathogenesis of heart failure. While traditional treatments such as diuretics remain important, most aspects of current management are directed toward blunting of the body’s neuroendocrine responses even through dietary modification.

References: Available upon request