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MANAGEMENT OF ACQUIRED HEART DISEASE IN THE DOG

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INTRODUCTION
Acquired heart diseases of dogs include chronic degenerative valvular diseases (endocardiosis), pericardial diseases, cardiac neoplasia, dilated cardiomyopathy (DCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), pulmonary hypertension (PH), infective endocarditis, and heart rhythm disturbances, some of which represent primary electrical disorders and others that develop secondary to cardiac remodelling. These conditions can lead to clinical signs of limited exercise capacity, heart failure, weakness/collapse, or sudden cardiac death. Effective management of cardiac diseases in dogs requires an appreciation of these different disorders, understanding of diagnostic criteria for these diseases, and delivery of appropriate patient monitoring and interventional strategies.

Congestive heart failure (CHF) is a clinical syndrome characterized by a cardiac lesion that limits cardiac output, causing arterial under-filling and evoking maladaptive compensations to restore blood pressure (BP). Most compensatory responses triggered in heart failure, including activation of the sympathetic nervous system, renin-angiotensin-aldosterone system, and pro-inflammatory cytokines, ultimately injure heart muscle and blood vessels. Furthermore, CHF is characterized by renal sodium retention that promotes elevated venous pressures behind the failing side(s) of the heart. Effective management controls these compensations with multifaceted medical therapy.

CAUSES OF HEART DISEASE – OVERVIEW
The most common heart diseases leading to CHF in dogs are valvular endocardiosis, dilated cardiomyopathy, pulmonary hypertension, and pericardial effusion. Various congenital malformations (including patent ductus arteriosus, pulmonic stenosis, subaortic stenosis, atrioventricular valve dysplasia) are important causes of heart disease and heart failure young animals.

Valvular endocardiosis (1,2) is characterized by progressive mitral/tricuspid valvular degeneration and apical systolic murmurs typical of mitral regurgitation (MR) and tricuspid regurgitation (TR). Atrial arrhythmias, left mainstem bronchus compression, PH, and rarely atrial tearing may complicate the clinical picture. Systemic hypertension from renal or Cushing’s disease increases the regurgitant fraction and represents a comorbid condition. In contrast to endocardiosis, infective endocarditis is a multisystemic inflammatory disorder originating from a cardiac infection and is a relatively rare cause of CHF in dogs. The conditions should not be confused.

Dilated cardiomyopathy (DCM) is a primary myocardial disorder caused by an inexplicable loss of myocardial contractility. This idiopathic/genetic disease is often associated with cardiac arrhythmias, such as atrial fibrillation (AF) and ventricular tachycardia (VT). Occult or preclinical DCM refers to the echocardiographic finding of reduced left ventricular (LV) ejection fraction in the absence of CHF. Left- and right-sided CHF as well as sudden cardiac death are common outcomes of DCM. In some breeds such as Doberman pinschers, development of ventricular or atrial arrhythmias may predate the development of DCM. Right ventricular arrhythmogenic cardiomyopathy (ARVC), is especially common in boxers and English bulldogs.

Pulmonary hypertension (PH) stems most often from three disorders: chronic left sided heart failure; dirofilariasis; and severe interstitial lung disease. This disorder also can be idiopathic (primary) in dogs. PH is very common in dogs with chronic mitral regurgitation (MR) and typically leads to a progressively louder murmur of tricuspid regurgitation, signs of low cardiac output, right sided failure (including ascites and exertional syncope). With the exception of heartworm disease, PH due to primary lung disease infrequently leads to heart failure.

Pericardial effusion is a frequent cause of heart failure in dogs but often is misdiagnosed. Acute effusions can provoke collapse related to hypotension. Right-sided CHF, including pleural effusions, can develop in chronic cardiac tamponade. In younger dogs (and some older ones)
idiopathic pericardial hemorrhage is the underlying cause and carries a very good prognosis with proper management. In dogs >7 years of age there is often a cardiac-related neoplasia involved with the effusion (hemangiosarcoma, chemodectoma, mesothelioma, ectopic thyroid neoplasia). Treatment of pericardial disorders does not involve drugs, but instead, pericardiocentesis often followed by form of surgical or endoscopic procedure.

Cardiac arrhythmias often complicate the atrial and ventricular remodeling observed in structural heart diseases. Heart rhythm disturbances can precede the development of heart failure in some disorders, especially in forms of cardiomyopathy. Tachyarrhythmias, if relentless (as with atrial flutter, atrial fibrillation, reentrant supraventricular tachycardia, or sustained ventricular tachycardia) induce a potentially-reversible decrease in ventricular function called tachycardia-induced cardiomyopathy. This impairment of cardiac output is additive to any preexisting structural heart disease. Bradyarrhythmias such as sinus arrest and atrioventricular blocks are more often related to primary disease (degeneration) of the conduction system in dogs and can lead to collapse, syncope, or CHF. Management approaches for arrhythmias may involve directed follow-ups (with no therapy), antiarrhythmic drugs, cardiac pacing, or catheter based interventions.

DIAGNOSIS OF HEART DISEASE & HEART FAILURE
The diagnosis of heart disease and the recognition of CHF require a careful history and clinical examination. There is clearly epidemiologic risk for cardiac disease related to species, age, breed, and sometimes sex. These predispositions are learned with experience or can be identified by consulting reference textbooks. The historical findings of cardiac disease are not specific. Exercise intolerance often can be identified and respiratory signs are common in patients with heart failure.

Physical diagnosis may identify objective signs of CV disease. Auscultation may indicate a heart murmur, arrhythmia, or gallop sound. The lungs may be abnormal to auscultation if there is pulmonary edema or cor pulmonale. Blood pressure in heart failure may be normal (from cardiac, autonomic, endocrine, and renal compensations); low in profound CHF (cardiogenic shock); or surprisingly high, indicating the co-morbid condition of systemic hypertension.

Diagnostic imaging is an important aspect of cardiac diagnosis. Echocardiography is the noninvasive gold standard for diagnosis of heart disease and is helpful in confirming the cause in cases of suspected CHF. While not necessary in all cases, Echo studies are pivotal for confirmation of DCM, pericardial diseases, endocarditis, and pulmonary hypertension (as well as for the diagnosis of congenital heart defects). Thoracic radiography is useful for evaluating heart size and following the progression of cardiomegaly. Radiographs are also essential in the differential diagnosis of respiratory signs. Many dogs with compensated heart disease are asymptomatic because of a primary respiratory, pleural, or thoracic disorder, not CHF. When CHF is suspected, chest radiographs obtained before and after diuretic treatment can support the clinical diagnosis because radiographic findings of acute or severe CHF are significantly "improved" following successful therapy.

The electrocardiogram (EKG, ECG) in advanced heart disease may delineate cardiac-enlargement patterns (wide or tall P-waves or QRS complexes), conduction disturbances, or arrhythmias. Unfortunately the 6- or 9-lead ECG is too often within normal limits or equivocal and therefore cannot be relied on for establishing a diagnosis of heart disease. Simply stated, the EKG has low diagnostic sensitivity for heart disease in many dogs. Of course the EKG is the test of choice for delineating heart rhythm disturbances.

Confirmation of the diagnosis of left-sided CHF requires integration of history, physical examination, and radiography; echocardiography can also be instructive when performed by an experienced examiner. Most CHF patients have some cardiac abnormality on auscultation, but it may be subtle, such as soft heart sounds (pericardial disease, DCM) or a gallop sound. Resting tachycardia is common but not always evident. Key radiographic findings of left sided heart failure include left atrial and ventricular enlargement; pulmonary venous congestion or distension (this is variable); and pulmonary infiltrates compatible with cardiogenic edema. These are typically bilateral, caudo-dorsal interstitial and alveolar infiltrates when heart failure is severe. There may be a slight, right-sided preponderance to the infiltrates. Radiographic signs of cardiogenic pulmonary edema should improve within 24 to 48 hours of diuretic therapy, and will often be accompanied by reduction in overall heart size, indicating reduced venous pressures and cardiac filling. Pleural effusions also may be evident in biventricular CHF and especially with pericardial disease or end-stage CHF complicated by atrial fibrillation.
The diagnosis of right-sided CHF is usually suspected from physical examination (resting tachycardia, jugular venous distention, abnormal jugular pulses, abdominal distension from hepatomegaly and ascites, and abnormal cardiac auscultation). Confirmation requires identification of cardiomegaly or pericardial effusion by radiography and often with echocardiography (to establish the exact type of heart disease).

Clinical laboratory tests may be contributory in canine patients with heart disease. Elevated blood troponin (cTnI) indicates heart muscle injury and is likely to be high in cases of myocarditis or acute ischemic injury. High circulating NT pro-BNP (brain natriuretic peptide) suggests structural heart disease and heart failure. There are emerging data regarding the use of this biomarker for both diagnosis and prognosis in canine heart disease, but the test should not be assessed in isolation (as it may be high in some dogs with primary respiratory disease and with other noncardiac conditions). Serum biochemistries, especially renal function tests and electrolytes, should be evaluated in CHF patients. These can be abnormal owing to pre-existing disease or drug therapy. Anemia and hyperthyroidism (from excess or inappropriate supplementation) increase demands for cardiac output and should also be ruled out in cardiac patients. Thyroid function tests (including free T4 and TSH) are indicated in dogs with inappropriate sinus bradycardia or when serum cholesterol is significantly elevated. A heartworm antigen test should obtained from dogs living in (or coming from) geographic regions endemic for dirofilariasis.

DRUGS USED IN THERAPY OF HEART FAILURE

A large number of drugs can alter heart and vascular functions (3). Some treatments for CHF affect ventricular pumping (inotropes), while others reduce venous pressures and ventricular preload (diuretics and venodilators), improving or preventing CHF. Most drugs with arterial vasodilator effects will decrease ventricular afterload, decrease mitral regurgitant volume, and increase cardiac output. Some drugs, demonstrate very rapid hemodynamic effects (IV diuretics, inotropes); while others modulate chronically-activated neurohormonal or inflammatory mediators of CHF (offering “cardiac protection”). The clinician should be mindful of the clinical pharmacology of these agents and appreciate that many drugs used in veterinary practice are prescribed in an extra-label manner.

Furosemide (2–4 mg/kg IV, IM, SQ, PO) is a potent loop diuretic used firstly for mobilization of edema and chronically to prevent fluid retention (on a b.i.d. – t.i.d. basis). A relatively high initial furosemide dose (2–4 mg/kg, IV) is administered in cases of severe CHF as renal blood flow may be reduced. Once diuresis begins, the dose can be reduced to 2 mg/kg q6–12h, IV, IM, or SQ depending on severity and response. In life-threatening pulmonary edema, a constant rate infusion of furosemide should be considered (after one or two IV boluses, a constant rate infusion 2 mg/kg/hour can be administered over the next 6 hours until diuresis begins). Oral maintenance dosages of furosemide typically range from 2 to 4 mg/kg two to three times daily but can be increased to 6 mg/kg in refractory cases of heart failure; alternatively, intermittent subcutaneous dosing (2 mg/kg) can be helpful (see below).

Spironolactone (2 mg/kg PO daily in one or two divided doses) is a weak, cardioprotective, potassium-sparring diuretic. It also may normalize baroreceptor function. There is some evidence—though not definitive—for a survival benefit in canine heart failure. Spironolactone is prescribed as chronic co-therapy with furosemide for management of CHF. Some also use this drug empirically in preclinical DCM for potential cardioprotection.

Adverse effects of diuretics include polydipsia, polyuria, a reduction in blood pressure, azotemia, electrolyte depletion, and elevated blood potassium (with spironolactone). Clients should be instructed not to administer the drug at bedtime and should not restrict water except in rare circumstances. Mild azotemia is not a reason to discontinue diuretic therapy, but moderate to severe azotemia should prompt a dosage reduction. Potassium supplements are rarely needed in dogs receiving combined therapy of furosemide, spironolactone, and enalapril as the latter two drugs “spare” potassium, reducing urinary losses.

Diet – There is evidence supporting the use of sodium restricted diets for reduction of plasma volume and heart size. Conceivably this diet would also reduce daily diuretic dosages. Restriction of salt must be balanced with issues of palatability and protein/caloric intake, which can be insufficient in dogs with CHF and cardiac cachexia. Rigid sodium restriction is generally considered to be ~12 mg sodium/kg bodyweight/day, but this is rarely achieved. Freeman has
recommended moderate restriction of 50 to 80 mg sodium/100 kcal of dietary energy as a starting point for dogs. Both prescription diets (Cardiac Support diet, h/d – Heart Diet, and CV Diet) and over the counter senior diets restrict sodium to varying degrees. Perhaps as important is avoidance of high-sodium treats (processed meats, hot dogs, sausages, some cheeses, etc.) that clients may use to entice pill-taking. Lower sodium treats can be identified including carrots, apple slices, and a number of dog biscuits (read the labels).

There is also some evidence for using fish oils (omega-3 fatty acids like EPA at 40 mg/kg/day and DHA at 25 mg/kg/day) in preventing cardiac cachexia.

L-arginine supplementation (250 to 500 mg PO three times daily) is added when severe PH is documented and especially when sildenafil has been prescribed to treat this problem (this amino acid is the precursor of nitric oxide, the endothelial vasodilator maintained in an active state by phosphodiesterase-V inhibitors).

Other supplements have minimal evidence for their use, except in very specific situations. These nutriceuticals also can be very costly! Among this group are the supplements L-carnitine (50 to 100 mg/kg every 8 hours) and taurine (500 to 1000 mg daily). Taurine can be measured in some commercial laboratories but it is not feasible to measure other amino acids or proteins. L-carnitine is considered for some boxers with DCM. Taurine is considered for treating dogs eating exclusive lamb-rice, restricted-protein, or “off-brand” diets; it is also considered in spaniel breeds, golden retrievers, and Newfoundland dogs with DCM. While there is hypothetical value to coenzyme Q10 supplementation, there is no evidence this costly compound should be used; the author never prescribes it.

Angiotensin Converting-Enzyme Inhibitors / Vasodilators – The ACE-inhibitors and vasodilators are mainstays of CHF therapy. Venodilation pools blood in systemic veins and reduces venous pressures, while arterial dilation reduces BP and LV afterload. Mitral regurgitation is usually reduced by lowering diastolic blood pressure, a potential benefit of ACE-inhibitors and especially more potent arterial vasodilators such as amlodipine or hydralazine. The ACE-inhibitors, including benazepril, enalapril, and ramipril, inhibit the renin-angiotensin-aldosterone system by blocking the converting enzyme (a kininase) leading to decreased plasma angiotensin-II and delayed degradation of vasodilating kinins. Reducing serum aldosterone concentration limits sodium retention and potassium loss in the urine. Additionally, ACE-inhibitors protect cardiac muscle, renal and vascular tissues from RAAS induced injury while also down-regulating the sympathetic nervous system.

The usual dosage of enalapril and benazepril in North America is 0.25 mg/kg twice daily; the dose is often increased to 0.5 mg/kg twice daily at the time of first reevaluation if BP and renal function are acceptable.

Direct acting vasodilator drugs used for acute, life-threatening pulmonary edema include 2% nitroglycerine ointment (15 mg/inch; dosed between ¼ to one inch topically q12h for 24 to 48h), and sodium nitroprusside (infused at 0.5 to 5.0 micrograms/kg/minute to titrate the systolic BP to approximately 85–90 mm Hg). The phosphodiesterase-5 inhibitor sildenafil (usual dose: 1–3 mg/kg PO q12h) is reserved for treatment of severe, symptomatic pulmonary hypertension. The dihydropyridine calcium channel blocker amlodipine is used mostly for intercurrent systemic hypertension or as an afterload reducer in end-stage left-sided CHF (to further reduce afterload). The initial dose of amlodipine for CHF patients is 0.05–0.1 mg/kg PO q12h; however, much higher doses (up to 0.4 mg/kg PO q12h) may be needed to treat dogs with refractory systemic hypertension. The drug has a long elimination half-life, so it may take a number of days before dosage changes are manifest.

The main adverse effects of vasodilator drugs are systemic hypotension (causing weakness or lethargy) and impairment of renal function. Some drugs, including amlodipine and the less-often used hydralazine (1–3 mg/kg PO q12h), also may cause reflex neurohormonal activation and sinus tachycardia. Hyperkalemia is a risk with the ACE-inhibitors, especially when combined with spironolactone (mild hyperkalemia is ignored).

Inotropic Drugs – The positive inotropic drugs include catecholamines (dobutamine, dopamine), the glycoside digoxin, and the inodilator pimobendan (Vetmedin®).

Dobutamine (2.5–20 micrograms/kg/minute constant rate infusion) is reserved for dogs with cardiogenic shock (defined clinically as: CHF accompanied by systolic BP <80 mm Hg + hypothermia + impaired peripheral perfusion + elevated blood lactate); dobutamine is infused for 24 to 48 hours. Tachycardia and ectopic complexes are signs of overdose.
**Digoxin** (0.005–0.0075 mg/kg PO q12h in dogs with normal renal function) is a modest positive inotropic drug that also slows heart rate by sensitizing baroreceptor function and altering autonomic neural tone to the CV system. The main indications for digoxin are refractory CHF or CHF with AF where its vagal-stimulating effect helps to slow AV nodal conduction and heart rate. Adverse effects of digoxin – anorexia, vomiting, diarrhea, depression, and cardiac arrhythmias (sinus node and AV nodal depression; PVCs) – are best avoided by monitoring therapy with a serum digoxin level.

**Pimobendan** (0.2–0.3 mg/kg PO q12h) is a potent, orally administered inotropic drug with vasodilator properties. It is classified as a calcium sensitizer with phosphodiesterase-3 inhibitory properties. Pimobendan is combined with furosemide, an ACE-inhibitor, and spironolactone for management of chronic CHF due to chronic valvular disease or DCM.

**Beta-adrenergic Blockers** – Beta-blockers, particularly carvedilol, metoprolol (long acting), bisoprolol (in clinical trial), and atenolol are increasingly prescribed to protect the heart muscle. The hope is that with chronic use, myocardium will be protected, heart rate controlled, and LV ejection fraction will improve (as observed in human patients). In canine model studies, beta-blockers are cardioprotective, but this effect has not been proven in preliminary clinical studies of dogs with DCM or chronic mitral regurgitation. Dogs with advanced heart disease but not yet in CHF (e.g. occult or preclinical DCM) tolerate beta-blockade reasonably well. While beta-blockers should never be used in uncontrolled CHF, gradual dose up-titration is possible in some dogs following stabilization. Concurrent use of pimobendan seems to offset some of the negative inotropic effects of beta-blockers in dogs with heart failure. Major adverse effects are weakness, hypotension, bradycardia, and worsening of edema or effusions. Beta-blockers are not yet considered a standard of care for CHF in dogs and their use in other forms of heart disease is empirical.

**Antiarrhythmic Drugs** – As a general rule, antiarrhythmic drug therapy should be limited to patients with “clinically-significant” heart rhythm disturbances and avoided whenever possible in patients with CHF (since most are negative inotropes). However, there are some dogs with serious rhythm disturbances requiring therapy. In atrial fibrillation (AF) heart rate can be especially rapid due to sympathetic activation, further deteriorating ventricular function and leading to ineffective cardiac cycles. Rate control is usually gained by the combination of digoxin plus the calcium channel blocker diltiazem (starting dose of 0.5 mg/kg PO q8h uptitrated every 8 hours to as high as 2 mg/kg PO q8h for standard diltiazem; an alternative is long-acting diltiazem at a dosage range of 0.5 to 3 mg/kg q12h). Once CHF is stabilized, the addition of a beta-blocker (if tolerated) will further slow the ventricular rate response to AF, potentially allowing for a dose-reduction of diltiazem. Carvedilol, metoprolol, or atenolol can be used for this purpose. Target in-hospital heart rate response for dogs with AF is about 120–160/minute, and an ambulatory ECG (Holter) monitoring can be done to objectively assess rate control.

Management of ventricular arrhythmias is a separate topic, and control of these in the setting of CHF is very difficult because most drugs depress ventricular function and represent yet another “pill” for clients to administer. IV lidocaine (2–4 mg/kg IV boluses to 8 mg/kg; 50 microgram/kg/minute constant rate infusion) can be used in the hospital in dogs with rapid or dangerous-morphology ventricular. Oral mexiletine (5–8 mg/kg PO q8h) may be effective if adverse effects (anorexia, vomiting, and tremors) are not severe and i.t.d. dosing is acceptable to the client. Sotalol (1–2 mg/kg PO q12h) depresses myocardial contractility and is best avoided in CHF, but sotalol is sometimes the only reasonable choice because of an otherwise good tolerance profile (start at the low dose). Flecainide has not been studied sufficiently in dogs, but can be administered at an initial dosage of 1-2 mg/kg PO, q8-12h. Amiodarone is sometimes used for rhythm control of AF after cardioversion and for suppression of malignant ventricular arrhythmias (dose: 8 to 10 mg/kg PO once daily for one to two weeks; thereafter 4–6 mg/kg PO once daily). However, owing to liver toxicity, liver enzymes/function tests (as well as a complete blood count) must be followed. Dogs who become ill from amiodarone may take days to recover owing to the very long elimination half-life.

**STAGES OF HEART DISEASE**
The ACC/AHA classification of human heart disease (Stages A-B-C-D) can be readily applied to dogs. Treatment approaches can be based on these modified ACC/AHA stages, especially when considering chronic home management of heart disease.

Stage A includes dogs at high risk for development of heart disease/failure, but currently without signs of structural disease. Examples include the Doberman pinscher (risk for DCM) and the Cavalier King Charles spaniel (risk for chronic MR). No therapy is indicated, but monitoring by auscultation or other methods (e.g. echocardiography or perhaps biomarkers like NT proBNP) may be appropriate in some cases.

Stage B includes dogs with a structural heart abnormality (e.g. murmur of MR or echo findings compatible with “occult” DCM) but never showing signs of heart failure. Subclass B1 includes dogs with a normal-sized heart and subclass B2 includes dogs with remodeling (cardiomegaly). There is some tendency to consider treatment in dogs in subclass B2 (see below).

Stage C includes those dogs with current or previously-treated heart failure. Once in stage C, the patient can never return to stage B. Dogs in this stage are prescribed life-long cardiac therapy.

Stage D includes dogs with clinical signs of CHF that are refractory to “standard therapy” (defined by a consensus panel as “standard dosages of furosemide, spironolactone, ACE-inhibitor, and pimobendan”). These dogs require more aggressive treatment and may benefit from referral to a cardiologist.

Dogs with acute CHF requiring hospital stabilization are somewhat difficult to classify in this system. Some dogs may have never received therapy before and with hospital stabilization will reside in stage C. Other dogs with long-standing CHF will clearly fall into Stage D.

MANAGEMENT OF PRECLINICAL (ASYMPTOMATIC) HEART DISEASE (STAGES B1 and B2)

Early introduction of CV drug therapy in “preclinical” or “asymptomatic” dogs with heart disease is controversial. There is a greater tendency to treat dogs with echo-evidence of dilated cardiomyopathy or dogs with chronic valvular heart disease with severe remodeling. In these cases cardioprotective drugs may be useful. In the future additional guidance might be provided by serial measurements of BNP, but this cannot be advanced as a blanket recommendation now.

There is some evidence that early “cardioprotective” therapy is of value to dogs with well defined, preclinical (“occult”) DCM. In these dogs, an ACE-inhibitor such as enalapril or benazepril is initiated at a minimal dose of 0.25 mg/kg b.i.d. and then increased to 0.5 mg/kg b.i.d. after two weeks. Consideration also should be given to the use of a beta-blocker considering these are likely to be well tolerated at this time. The use of inotropic drugs (i.e., digoxin or pimobendan) is not recommended in this setting unless radiographs indicate that pulmonary edema is imminent, there is demonstrable exercise intolerance, or LV systolic dysfunction is severely reduced (e.g. LV shortening fraction less than ~15%). There is an ongoing clinical trial assessing treatment with pimobendan in preclinical DCM. Large breed dogs with chronic mitral regurgitation and demonstrable cardiomegaly or LV dysfunction are treated as if they have occult DCM.

Studies of chronic degenerative valvular heart disease in dogs have failed to show clear benefit of ACE-inhibition for this group and certainly no therapy can be justified for dogs in subclass B1. In dogs in subclass B2 (i.e. significant remodeling) an ACE-inhibitor can be considered for empirical use to delay development of CHF based on the “trend” for benefit in the VETPROOF trial (this is the author’s personal approach). Others are uncompelled by the evidence for early ACE-inhibition and offer no therapy until there are signs. Certainly in this group there may be other indications for considering an ACE-inhibitor prior to CHF, including dogs with cough from left bronchial compression or dogs with other medical disorders (systemic hypertension, chronic kidney disease). In our practice we also initiate enalapril (or benazepril) therapy if six-monthly interval evaluations indicate a marked increase in cardiac size (based on vertebral heart score or echocardiography) or if radiographs suggest impending CHF. Another clinical trial (EPIC) has begun studying pimobendan in dogs in Stage B2 with advanced valvular heart disease, but results will take years to assess.

MANAGEMENT OF INITIAL CLINICAL SIGNS IN ADVANCED MITRAL VALVE DISEASE

The onset of clinical signs in dogs with advanced valvular endocardiosis is often very gradual and usually heralded by intermittent coughing related to compression of the left mainstem bronchus (between the descending aorta and dorsal left atrium). This is common even in the
setting of radiographically-normal lung fields. This feature of chronic MR in dogs is not synonymous with left-sided CHF, but can be difficult to distinguish from signs of pulmonary edema. The author’s approach to management of these dogs is initial treatment with enalapril or benazepril (0.25 mg/kg q12h for two weeks then 0.5 mg/kg q12h thereafter) along with low-dose furosemide (1-2 mg/kg PO once daily). In most cases the cough improves if it’s due to bronchial compression (or early CHF). If the cough returns weeks to months later or if respiratory rate increases at home (>40/min), radiographs are repeated and often full CHF therapy is initiated (see below).

It should be emphasized that failure of the cough to respond to a very low dose of a diuretic and full dose of an ACE-inhibitor should prompt reconsideration of the diagnosis; in particular, the clinician should rule out chronic bronchitis, other airway diseases (laryngeal disease, tracheal collapse), and pulmonary parenchymal disorders (pneumonia, neoplasia, heartworm disease, etc.). These patients are ideally evaluated by radiography (consider obtaining a second opinion on the chest films) and by appropriate respiratory diagnostics (such as bronchoscopy with airway cytology/culture). When diagnostic testing is limited, a trial course of doxycycline or prednisone may be instructive (and relieve signs related to infection or bronchitis). Cough suppressants can be prescribed as a last resort for symptom relief.

HOSPITAL MANAGEMENT OF CONGESTIVE HEART FAILURE

A number of standard treatment approaches that have proven useful for management of established CHF in dogs (please see above sections for drug dosages).

Hospital Therapy of Acute Pulmonary Edema from Left-Sided CHF – The combination of furosemide, oxygen, nitroglycerine (or sodium nitroprusside) & sedation with butorphanol (0.25 mg/kg IM, repeated in 30 to 60 minutes if needed) closely followed by oral administration of pimobendan (0.25 to 0.3 mg/kg q12h) represents the initial treatment plan applicable to most cases of CHF regardless of cause. With this protocol, diuresis is initiated; oxygen saturation is increased; ventricular loading is reduced; the tendency towards pulmonary edema is decreased; anxiety is relieved; and myocardial contractility is supported; If patients are heavily sedated, the torso is positioned in sternal recumbency, the chin supported with a towel or soft pad, and nasal oxygen prongs are inserted for better oxygenation. After an initial IV or IM bolus of 2 to 4 mg/kg, the dosage, route, and frequency of furosemide can be adjusted to the clinical response (respiratory rate, anxiety, auscultation). In life-threatening pulmonary edema due to mitral disease, a constant rate infusion of furosemide along with aggressive afterload reduction with sodium nitroprusside should also be considered. Administration of pimobendan also is helpful, since it functions as a preload and afterload reducer as well as a potent inotrope. Less-potent and less controllable alternatives to sodium nitroprusside include oral hydralazine or an ACE-inhibitor.

Cardiogenic Shock – The findings of cardiogenic pulmonary edema or pleural effusion with severe hypotension (BP <80 mm Hg) along with other indicators of low cardiac output (pallor, hypothermia, depression, elevated blood lactate) are highly suggestive of cardiogenic shock. Dogs with dilated cardiomyopathy (often Doberman pinschers) represent the typical case of cardiogenic shock. Other potential causes of cardiogenic shock include myocardial infarction and massive pulmonary embolus as might occur following treatment for adult heartworms or after a spontaneous pulmonary embolism. Initial treatment is the same as discussed above with Furosemide-Oxygen-Nitrate-Pimobendan. As these patients are hypotensive and often very depressed, sedation is not often needed and diuretics alone may further depress BP, so more aggressive therapy is needed. The clinician should determine if centesis is necessary, as dogs with cardiogenic shock may have both pulmonary edema and large cavity effusions. Volume infusion (i.e. fluid therapy) is not appropriate to raise BP in this setting, as it will only worsen edema. In most cases, there is a need to stimulate myocardial contractility to improve pump function and facilitate diuresis. Dobutamine (or dopamine) is administered as a constant rate intravenous infusion, starting at 2.5 micrograms/kg per minute and increasing the infusion by 1-2 micrograms/kg/minute every 15 to 30 minutes until systolic BP is 90 mm Hg. This end-point is generally reached at an infusion of 5–10 micrograms/kg/minute, though higher infusion rates may be needed. Once the BP is stable (systolic BP in the 90 to 100 mm Hg range), other vasoactive drugs, such as nitroprusside or an ACE-inhibitor, can be added to unload the left ventricle further. Again, the approach to cardiogenic shock treatment, aside from the addition of a catecholamine, is similar to that discussed in the previous section. After 24 to 48 hours of
dobutamine therapy, the dobutamine rate is reduced by 50% every 2-4 hours, and once the dose has been lowered to ~1.25 micrograms/kg for 2-4 hours, the infusion is discontinued.

**Arrhythmias in Acute CHF** – Atrial fibrillation can precipitate CHF in previously stable canine patients. This problem is usually managed with heart rate control as opposed to cardioversion (back to normal rhythm). Rate control involves initiation of oral digoxin followed within 24 hours by up-titration of oral diltiazem (see above section on Cardiac Drugs). Effective treatment of CHF is also useful as it allows for some withdrawal of sympathetic tone and reduction of ventricular rate response. Electrical cardioversion from AF to sinus rhythm has been used by some in managing this arrhythmia, but our experience is that dogs in CHF usually revert back to AF in short time, so we mainly recommend rate control in our practice.

Isolated premature ventricular complexes (PVCs) are not treated in CHF cases. However, sustained runs of rapid ventricular tachycardia require treatment to maintain BP and are managed with boluses of lidocaine followed by a constant rate infusion of lidocaine if required.

**CHRONIC HOME MANAGEMENT OF CHF** (Stages C & D)

The transition from hospital to home therapy of CHF usually begins within 48 hours of admission. During that interval, the initial diagnostic workup should have been completed. The typical transition to ‘Home Therapy’ includes the following steps:

1. parenteral furosemide is replaced with oral furosemide; 2) oxygen is discontinued; 3) nitrates (if used) are replaced by an ACE-inhibitor; 4) pimobendan is continued (digoxin is used only for rate control in AF); 5) spironolactone is initiated mainly for cardioprotection at the time of release or at the time of first follow-up; and 6) the client is counseled regarding a sodium-restricted diet and pros/cons of nutriceuticals. These specific uses of these drugs (as well as dosages) have been summarized above in the section on ‘DRUGS USED IN THERAPY OF HEART FAILURE’.

The long term (home) therapy of CHF in the dog includes oral furosemide, spironolactone, pimobendan, and an ACE-inhibitor along with dietary sodium restriction. Additional therapy may be added for special reasons. In the dog with echocardiographic evidence of LV systolic dysfunction, beta-blockade is considered at the first or second follow up examination (assuming the dog is “dry” and very stable). As previously stated, it can be very difficult to initiate therapy with beta-blockers due to their negative effect on contractility. In cases of severe PH with symptoms such as exertional collapse or ascites, sildenafil is considered as a relatively selective pulmonary vascular vasodilator to unload the right ventricle. When AF complicates CHF, both digoxin and diltiazem are added to the treatment plan to gain better heart rate control as discussed previously. Premature ventricular complexes (PVCs, VPCs) and nonsustained runs of VT are not treated, unless the QRS morphology or timing appear “dangerous” (such as R on T; very rapid; multiform VT; or torsade de pointes): In reality, most clients are very willing to assume a risk of sudden death for their dog (and most hope that will occur instead of intractable CHF or euthanasia). However, sustained ventricular arrhythmias – especially when causing signs – are managed with mexiletine, amiodarone, flecainide, or sotalol. Each of these drugs has a poor adverse effect profile in dogs with CHF, and is used as a last resort.

Strategies for managing refractory edema or ascites (Stage D) include first reviewing client compliance and optimizing the dosages of currently-prescribed drugs. Pimobendan (Vetmedin®) dosage is generally increased to 0.25 mg/kg PO q8h (extra-label). Client administration of subcutaneous furosemide is suggested (begin by substituting one oral dose of furosemide for a subcutaneous injection, three times weekly then go to every other day if necessary). Alternatively, a low dose of hydrochlorothiazide can be started (1-2 mg/kg daily or every other day) with monitoring of serum biochemistries within a week (or earlier). Abdominal paracentesis should be considered to reduce tense ascites. Sildenafil (Viagra®) plus L-arginine supplementation are offered when severe PH is documented by echocardiography.

**Follow up evaluations** for dogs with chronic CHF are scheduled initially at 7-14 days after release, then one month later, then every 3 to 4 months if possible. Drug dosing and adverse effects of treatments are discussed with the client at all stages of therapy. Emphasis for effective treatment is on quality of life (eating well, sleeping comfortably, capacity for walking/mobility, family interaction, resting respiratory rate, and clinical signs of disease or drug toxicity). Additional examinations of importance include: physical examination findings of controlled CHF; bodyweight/cachexia; BP; renal function; heart rhythm; and thoracic radiography if respiratory symptoms are still present.
PROGNOSIS

Prognosis is a key client question and it is very difficult to predict the outcome for a single canine patient. The general prognosis for canine heart disease and CHF in particular depends on the cause, severity, and care received. Many dogs survive > 1 year following the first signs of CHF provided they receive optimal veterinary and home care. It may take weeks to obtain complete stabilization of the seriously-ill dog with CHF. Understand that not every dog will be well overnight, and regrettably, some clients run out of patience or financial resources and request euthanasia. As patients become well-managed, other problems may become evident.

Some dogs with chronic left-sided CHF appear to develop pulmonary fibrosis at an accelerated rate – this should be recognized, not misdiagnosed as uncontrolled CHF (usual findings are tachypnea + crackles + “clear lung fields” radiographically). Dogs with chronic airway disease (tracheal or primary bronchus collapse, chronic bronchitis) may become symptomatic due to these diseases requiring other treatments for control (doxycycline, prednisone, cough suppressants). Development of chronic renal failure with moderate azotemia is a poor prognosis, especially if diuretic dosages cannot be reduced due to fluid accumulation.

References


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