

DEGENERATIVE VALVE DISEASE

Degenerative valve disease (DVD) is *the most common heart disease of dogs and the most common cause of congestive heart failure*. The prevalence of this disease approaches 100%, especially in senior small breed dogs. It is a chronic, slowly progressive process, potentially affecting dogs for > 5 years before resulting in heart failure and death. The mitral valve is most commonly and most severely affected, although concurrent tricuspid valve involvement occurs in 30% of cases. Isolated DVD of the tricuspid valve is relatively uncommon, and DVD of the aortic and/or pulmonic valves is rare. Synonyms for DVD include myxomatous valve disease, endocardiosis, chronic valvular insufficiency, myxomatous valvular degeneration, and mitral valve disease. The condition rarely occurs in cats. The condition is common in large animals and will also be covered in Large Animal Medicine 3.

Etiology

The cause(s) of DVD is (are) unknown. An inheritable basis has been reported in Dachshunds and Cavalier King Charles Spaniel breeds, suggesting a polygenic mode of inheritance. However, the genetic mechanisms remain to be identified. Likely, multiple genes are at play.

Pathology and Pathophysiology

DVD often progresses over many years, and morbidity is directly related to the degree of valvular insufficiency and subsequent volume overload to the heart. The degree of valvular insufficiency is affected by numerous factors including the degree of structural change to the valve leaflets, integrity of the chordae tendineae, myocardial contractility and chamber dilation. Mitral and tricuspid valve competence relies upon the structural and functional performance of six basic components that comprise the valve apparatus: the atrial wall, valve annulus (where the leaflets attach to), valve leaflets, chordae tendineae, ventricular papillary muscles, and associated ventricular wall. The valve apparatus operates through complex interplay, with each element acting both independently and synergistically to maintain valve integrity. During systole, the atrio-ventricular opening is covered by the valve leaflets. Each leaflet appears as thin, translucent structure without nodules or thickening at the valve margins. Each leaflet is adjoined to the papillary muscles through the chordae tendineae. Tensile forces on the chordae generated through ventricular and papillary muscle contraction act to pull the valve leaflets into apposition and effectively seal the atrioventricular opening.

DVD affects all components of the valve apparatus in varying degrees. Marked structural, thickening changes in the valve leaflets are common. The severity of lesions vary and progress from small nodules on the free margins of the valves to large, coalescing plaques that result in severe thickening and distortion of the valve leaflets. As the leaflet edges thickened, they often roll inward, creating a rounded contour and reduce leaflet apposition during systole. Consequently, affected valves become incompetent with the amount of insufficiency influenced

by the degree of structural changes to the leaflets. The chordae tendineae are also usually affected in DVD, becoming thickened, elongated, weakened and often rupture. Elongation and/or rupture of the chordae prevents adequate closure of the valve leaflets across the atrio-ventricular opening as the leaflet tips now prolapse or even flip out (flail) into the atrium during systole. Severe valvular insufficiency develops secondary to a fail leaflet with acute decompensation and development of congestive heart failure. This can occur with even relatively minor structural changes to the leaflets.

Secondary changes related to valvular insufficiency contribute to progressive valvular insufficiency. *Mitral regurgitation begets mitral regurgitation*. Chamber and annular dilation reduce leaflet co-aptation as the valve leaflets are literally pulled apart from one another as the heart dilates. Decreased myocardial contractility may develop (common in large breeds) further reducing leaflet apposition due to diminished tensile forces on the chordae and progressive chamber dilation (see DCM notes). Arrhythmias which commonly develop in this disease even contribute by weakening and distorting the synchrony of contraction, which again directly reduces the degree of leaflet co-aptation. All of these changes lead to progressive valvular regurgitation and subsequent greater volume overload states, triggering additional chamber dilation and eventual heart failure.

The basic pathophysiology of DVD involves volume overload of respective atria and ventricle and the veins on the affected side of the heart i.e., increased preload. As valve regurgitation worsens, an ever-increasing volume of blood moves back and forth between ventricle and atrium causing cardiac output to diminish, thereby increasingly stimulating a variety of compensatory mechanisms. These compensatory mechanisms augment blood volume to ensure that circulatory needs of the body are met. This is achieved primarily by an increase in preload or blood volume as the Frank-Starling relationship shifts downwards and to the right. Such compensation is clearly advantageous, but an increased preload also has important consequences: first, increased preload coupled with the growing regurgitant fraction results in eccentric hypertrophy of the affected ventricle and atrium. Second, preload may eventually increase to the point where capillary homeostasis can no longer be maintained, and the patient develops edema or *congestive heart failure* (CHF, i.e., congestion and edema secondary to an underlying cardiac disorder):

- With mitral regurgitation, increased left-sided preload may lead to *pulmonary* venous congestion and *pulmonary* edema (*left-sided CHF*).
- With tricuspid regurgitation, increased right-sided preload may lead to *visceral* venous congestion and edema, usually manifested as hepatomegaly and ascites (*right-sided CHF*).
- Both *left- and right-sided failure* lead to various combinations of the above abnormalities, as well as pleural effusion.

In most cases with DVD that develop CHF, congestive signs occur *without* any decrease in forward cardiac output, i.e., blood pressure is normal and tissues are well-perfused with a normal capillary refill time. As valve disease progresses, the compensatory mechanisms further expand blood volume and increase peripheral vascular resistance (afterload). Thus preload and

afterload continue to increase, exacerbating congestion and edema, and further increasing regurgitation. In *late* stages of the disease, the various compensatory mechanisms may be insufficient to maintain forward cardiac output, leading to hypotension, weakness, pale mucous membranes with a prolonged refill time, and weak pulses as a result of hypoperfusion. This is defined as forward heart failure.

Compensatory changes in atrial and ventricular size and blood volume allow patients to remain asymptomatic for potentially years, and some patients never show clinical signs of CHF, despite severely affected valves. Most patients maintain adequate tissue perfusion and cardiac output at the time of development of congestive heart failure due to compensation from increased preload and afterload. Decreased tissue perfusion and cardiac output develop during the end stages of this disease as inadequate tissue perfusion is not sustainable with life (forward failure).

Complicating Factors

Progression of this disease process is usually slow but certain events can induce acute clinical signs in cases that were previously asymptomatic or well-controlled on medications:

- development of tachyarrhythmias such as frequent APCs, atrial tachycardia, atrial fibrillation, and even ventricular tachycardia
- left atrial perforation with hemorrhage into the pericardial sac, which can cause acute deterioration due to cardiac tamponade
- major chordae tendineae rupture which can acutely worsen or precipitate CHF

Histopathology

The histopathological changes observed with DVD is described as myxomatous degeneration, which basically results in loss of collagen and other connective tissue within the valve leaflet and excessive accumulation of proteoglycans. This process results in loss of the normal support structure of the valve as well as the endothelial covering. A more detail description is provided below starting with normal mitral valve histology.

Mitral Valve Histology

Valve leaflets are laminated, structures composed of four distinct layers. From the atrial to ventricular aspect

- atrialis comprises a thin layer of endothelial cells supported by scattered collagen fibers, elastic fibers, fibroblasts, and smooth muscle cells
- spongiosa, a layer rich in proteoglycans, glycosaminoglycans and ground substance
- fibrosa, a dense layer of compact collagen bundles with scattered fibroblasts, attaches to the chordae tendineae *Predominate source of structural support for the leaflet.*
- ventricularis, thin layer of endothelium on the ventricular surface of the leaflet similar to the atrialis.

Lesions include progressive expansion of the spongiosa layer and disruption of the fibrosa layer. Such changes can be detected most readily along the region of leaflet apposition (leaflet tips). The spongiosa valve layer becomes thickened with increased extracellular matrix containing glycosaminoglycans (GAG) and proteoglycans, and proliferation of edematous ground substance. The normal arrangement of layered collagen in the fibrosa layer becomes disrupted and attenuated. In advanced stages, it is difficult to recognize distinct spongiosa and fibrosa layers. In moderate and severe DVD, changes in the extracellular matrix and connective tissue components become substantial with significant reduction in connective tissue density of the valve leaflets. Endothelial injury is also extensive with areas of loss, exposing the subendothelial basement membrane and valvular interstitial cells.

Epidemiology

DVD is common in middle-aged and older dogs. Smaller breed dogs are affected much more often than large. Males are more commonly affected than females (~ 1.5:1). Predisposed breeds include Cavalier King Charles Spaniel, Dachshunds, Miniature and Toy Poodles, Whippets and most Terrier breeds. However, this disease may develop within any breed including the giant breeds and even cats. Disease incidence is estimated within the general population to involve 1:7 dogs. The incidence is greater than 90% for predisposed breeds, especially senior animals.

Clinical signs

A systolic murmur with its point of maximal intensity over the left apex is the most distinctive clinical finding in a dog with DVD. The murmur usually radiates dorsally and cranially on the left side, and a similar but softer murmur is frequently heard on the right side. The intensity of the murmur correlates poorly with the hemodynamic significance of valve insufficiency. A grade 2/6 murmur maybe associated with severe mitral regurgitation, whereas a grade 6/6 murmur may result from trivial mitral regurgitation. A second auscultatory abnormality associated with DVD is a systolic click, which is a high frequency “click” sound heard in midsystole. A systolic click sound is caused by mitral valve prolapse associated with elongation and/or tearing of the chordae with DVD. Typically, the systolic click is transient and quickly replaced with the murmur of mitral regurgitation.

In many cases, the murmur is an incidental finding in an otherwise completely asymptomatic dog. Clinical signs in dogs with symptomatic disease usually result from the onset of left-sided CHF, i.e., pulmonary congestion and edema. Coughing, restlessness, tachypnea, dyspnea, reduced exercise tolerance, weight loss and inappetence are common complaints. In the initial stages, coughing is nocturnal and/or occurs with rest.

Syncope may also be reported, frequently in association with bouts of coughing (cough syncope or "cough-drop"). Several mechanisms for cough syncope have been proposed, including the following:

- Acutely increased intrathoracic- and intraabdominal pressure associated with coughing leads

to venous compression, decreased venous return, and decreased cardiac output as a consequence.

- Acutely increased intrathoracic- and intraabdominal venous pressure associated with coughing is transmitted to the spinal- and intracranial veins. This, in turn, results in an acute increase in intracranial pressure and decreased cerebral perfusion.

Syncope may also occur as a result of severe arrhythmias, or hypoxia due to pulmonary edema. Syncope is common with the initial development of congestive heart failure. Generally, the syncope will resolve once the heart failure is managed.

Physical examination findings in milder cases of CHF may be limited to the presence of a murmur and a slightly increased respiratory rate with increased broncho-vesicular sounds noted on pulmonary auscultation. In more severe cases, dyspnea is evident, and crackles and wheezes may be heard on auscultation. Dogs with concurrent tricuspid insufficiency may have signs of right-sided CHF such as hepatomegaly, a high protein- or modified transudate ascites, and pleural effusion. Dogs in active heart failure are generally tachycardia due to a state of elevated sympathetic tone secondary to the heart disease.

Bear in mind that coughing, respiratory distress and pulmonary crackles are common signs of several pulmonary diseases, especially chronic bronchitis. Crackles ascribable to CHF usually only occur when pulmonary edema is severe and respiratory distress is clearly apparent. Nevertheless, in a dog with mitral DVD, it is often difficult to differentiate early congestive failure caused by mitral insufficiency from symptomatic pulmonary disease, with mitral valve disease as an incidental finding (not in heart failure). Thoracic radiography and a therapeutic trial with a diuretic are helpful in these situations (see below). Also, patients with CHF often have sinus tachycardia, whereas dogs with chronic pulmonary disease frequently have a normal-to-slow heart rate and a marked respiratory sinus arrhythmia (presumably because of a reflex increase in vagal tone).

A common cause of coughing in patients with DVD is collapse of the left mainstem bronchus associated with left atrial enlargement. The cause of this collapse is controversial, but it is likely a combination of factors including impingement from the dilated left atrium and concurrent weakening of the cartilaginous rings as with tracheal collapse. Resulting inflammation and mucus production from the airway collapse is a common cause of coughing in patients with mitral valve disease.

Radiography

In the early stages of DVD, thoracic radiographs may be unremarkable. However, as the disease progresses thoracic radiographs reveal a progressive increase in the size of the cardiac silhouette relative to the thorax, with left atrial and ventricular enlargement predominating. Early in the disease only mild left atrial enlargement is seen, but severe dilatation of the left atrium (sometimes with elevation of the left mainstem bronchus to cause a so-called "cowboy sign")

can develop over time. Left-sided congestive failure is diagnosed when radiographic signs of pulmonary edema develop. Radiographically, cardiogenic pulmonary edema appears as a progressive *interstitial and even alveolar pulmonary infiltrate*. In dogs, infiltrates consistent with cardiogenic pulmonary edema have a fairly characteristic distribution, i.e., *marked in the dorsocaudal lung fields*. The infiltrate may be symmetric or predominately involving one side of the lung (usually the right). If right-sided CHF is present, pleural effusion, a distended caudal vena cava, hepatomegaly and/or ascites may be seen. Generally, the lobar pulmonary veins are distended secondary to venous congestion. However, the lack of venous distension does not rule out CHF as the lobar veins will shrink secondary to diuretic administration and dehydration.

Electrocardiography

The ECG is often normal especially in the early stages of this disease, although the ECG may also show changes consistent with left or biatrial enlargement (p wave changes) and left ventricular enlargement (tall R waves). In advanced stages, arrhythmias become common. These are mainly supraventricular (APCs, atrial tachycardia, atrial fibrillation) but ventricular ectopy may occur. These arrhythmias may be associated with acute exacerbations of CHF, as well as weakness and syncope.

Echocardiography

Two-dimensional echocardiography usually indicates chamber enlargement on either side of the affected valve(s). Prolapse, flail, and irregular, knobby thickening of the affected valve leaflets may be seen. In most dogs, M-mode echocardiography reveals exuberant interventricular septal- and left ventricular posterior wall motion (this is termed a hyperdynamic appearance). This is because increased preload increases the left ventricular diameter in diastole, while the left ventricular diameter in systole remains unchanged. Doppler echocardiography (color-flow and/or spectral) interrogation of the valves reveals high velocity, retrograde flow from the ventricles into the atria during systole. The presence of the disease and hemodynamic significance is readily diagnosed on echo.

Treatment

Definitive therapy of DVD involves surgical replacement or repair of the diseased heart valve(s). Valve repair and replacement is predominately performed as an open heart procedure requiring the need for cardiac by-pass. Open heart surgery is quickly becoming more common place in veterinary medicine with a growing number of centers offering such procedures. However, costs and equipment needs drastically limit the number of patients referred for surgery. A number of interventional (per-catheter) treatment modalities are under investigation as upcoming therapeutic options independent of cardiac by-pass.

Consequently, the main goal of therapy is to provide symptomatic relief by controlling congestion and edema and delay disease progression. Many dogs with advanced mitral insufficiency can be maintained for months to years with appropriate therapy, although frequent reevaluations and medication adjustments become necessary as the disease progresses. Treatment is guided by determining the dog's "Functional Class" of CHF. We utilize the American College of Veterinary Internal Medicine (ACVIM) classification scheme as outlined below for our treatment recommendations. The ACVIM classification scheme is based on a letter grade evaluating the hemodynamic significance of the mitral regurgitation. The classification is helpful in making consistent treatment recommendations and for assessing prognosis in patients with mitral valve disease. This classification system can also be adapted to other forms of heart disease. Patients may move up stages as their heart disease progresses but not downward unless their disease is cured with surgical intervention.

Stage A: Stage A consists of patients that do not have heart disease but that are considered to be predisposed or at a high risk for developing the disease. Such breeds include: Cavalier King Charles Spaniel, Dachshunds, Miniature and Toy Poodles, Whippets and Terrier breeds.

Stage B: Stage B consists of patients that have developed mitral and/or tricuspid regurgitation. These patients will have a corresponding murmur of valvular regurgitation, which is confirmed on echocardiography. However, stage B patients are asymptomatic in that they have not developed congestive heart failure, exercise intolerance or syncope (Stage C). Stage B is subdivided into B1 and B2 categories based on the presence of chamber enlargement, which indicates that the valvular regurgitation is hemodynamically significant or not. Stage B1 consists of normal chamber dimensions. Stage B2 is associated with chamber dilation (atrium and/or ventricle).

Stage C: Stage C consists of patients that are or have shown clinical signs secondary to their heart disease. Stage predominately consists of animals that are in congestive heart failure with pulmonary edema, pleural effusion and/or ascites. Other common signs for stage C include exercise intolerance and syncope.

Stage D: Stage D patients are in refractory heart failure, which is defined as the recurrence of edema while receiving proper heart failure therapy: furosemide, ACE-inhibitors and pimobendan. Stage D patients may also have evidence of decreased cardiac output and tissue perfusion (forward failure).

Therapy for Degenerative Valve Disease

Stage A: Stage A patients do not currently have heart disease, they are just predisposed. Therefore, no therapy is recommended for stage A. Client education on valvular disease is essential as well as at a minimum yearly auscultation for the detection of the murmurs of mitral and tricuspid regurgitation. Ideally, biannual cardiac auscultation should be performed in those dogs that are over the age of 4 years for early detection of this disease. Clinical signs of heart disease should also be reviewed with

the client as well as the importance of maintaining ideal body weight and regular exercise. Life style changes may be necessary for the prevention of heart disease. Have you exercised recently??????

Potential breeding animals should no longer be bred if a murmur or echocardiographic evidence of degenerative valve disease is noted prior to 8 years of age.

Stage B: Mitral and tricuspid regurgitation has now developed, announced by the presence of a heart murmur. When the murmur is first noted, imaging is necessary to determine if the individual is a stage B1 versus B2. Ideally, an echocardiogram is performed for determination of B1 versus B2 status, but thoracic radiographs would suffice. Blood pressure measurement is also recommended to identify hypertension if present and provide a baseline for recheck comparison when starting medical therapy.

Stage B1: Stage B1 patients have normal cardiac chamber dimensions and function. The valvular regurgitation is not considered hemodynamically significant. For stage B1, currently we do not recommend any medical therapy as no medication has shown to be beneficial at this stage. Client education is essential on the topics of congestive heart failure, ideal body weight, exercise recommendations and the need for routine follow up with blood pressure monitoring and cardiac imaging (echo versus radiographs). Many patients will remain in stage B1 for the rest of their lives as DVD is a very slowly progressive disease. Blood pressure monitoring is important in these patients as systemic hypertension would greatly enhance the rate of disease progression. The increased afterload on the left ventricle with systemic hypertension would result in an increased volume of mitral regurgitation and greater damage to the valve leaflets due to a higher velocity jet of mitral regurgitation. Recheck imaging is recommended every 6 – 12 months for small breed dogs and every 6 months for larger breeds due to a faster rate of disease progression.

Stage B2: Stage B2 patients have evidence of chamber dilation secondary to a volume overload state from hemodynamically significant valvular regurgitation. These are the patients that will likely continue to progress and develop congestive heart failure and/or arrhythmias. Recently, it has been demonstrated that the inodilator pimobendan (Vetmedin) delays disease progression and the onset of congestive heart failure in B2 patients. Therefore, we recommend pimobendan in all B2 patients. Pre-emptive therapy with an ACE-inhibitor is highly controversial in dogs with asymptomatic DVD (stage B2). The rationale behind therapy is that the RAAS cascade is up-regulated in this disease resulting in the renal retention of sodium and water with subsequent increases in preload ultimately leading to congestive heart failure. Angiotensin-2 and aldosterone also appear to play a substantial role in triggering eccentric hypertrophy and myocardial fibrosis, which can lead to decreased contractility, arrhythmias and death. ACE-inhibitors also reduce blood pressure or afterload, which would reduce the severity of mitral regurgitation. Despite these theoretic benefits, many studies have failed to demonstrate a difference between an ACE-inhibitor and placebo in delaying the onset of heart failure in dogs with DVD. Generally, ACE-inhibitors are only recommended for B2 patients with moderate to marked chamber dilation and imminent CHF or in B2 patients with evidence of decreased contractility. ACE-inhibitors are

utilized as first line of therapy in hypertension and are likely beneficial in dogs with concurrent DVD. The potassium sparing diuretic spironolactone may also be recommended for B2 patients. Spironolactone blocks aldosterone receptors on the myocardium. Aldosterone appears to play a substantial role in disease progression and myocardial fibrosis and has shown benefit in decreasing disease progression in those patients with decreased contractility. A sodium restricted diet should be implemented in B2 patients for prevention of excessive blood volume expansion and hypertension, which both could trigger congestive heart failure. Ideally, the diet should contain ≤ 80 mg Na per 100 Kcal. Excessive sodium restriction (≤ 40 mg/100 Kcal) is not warranted due to poor palatability and up regulation of the RAAS cascade. Supplementation with fish oil also appears beneficial for B2 patients for prevention of cardiac cachexia and their anti-arrhythmic efficacy. Owners should be instructed to monitor respiratory rate daily for early detection of congestive heart failure. Any B2 patient that develops respiratory signs, exercise intolerance or syncope should seek prompt veterinary attention! The importance of maintaining a healthy weight and moderate exercise should be stressed to the owner. B2 patients should be restricted from strenuous exercise (hunting, retrieving, agility, jogging on leash, excessive swimming) due to increased demands on the diseased heart with potential collapse and development of heart failures and/or arrhythmias. Working dogs should be retired. B2 patients should be re-evaluated every 3 to 6 months.

Stage C Mild-to-Moderate CHF

Many cases will present when dogs have obvious clinical signs ascribable to CHF, and thoracic radiographs show pulmonary changes consistent with cardiogenic edema. These cases are treated with diuretics (almost always furosemide), usually in combination with an ACE-inhibitor, pimobendan and spironolactone. Diuretic therapy and inhibition of the renin-angiotensin-aldosterone system reduce the signs of CHF by reducing intravascular volume and therefore preload, decreasing the edema. In addition, pimobendan and ACE inhibition causes arteriolar vasodilatation, which reduces systemic vascular resistance. This allows greater forward flow from the left ventricle and a reduction in the regurgitant volume. ACE-inhibitors and spironolactone inhibit aldosterone induced sodium retention and secondary volume expansion. Spironolactone also inhibits the direct myocardial toxic effects of aldosterone.

I recommend re-evaluation every 3 months for mild-to-moderate CHF cases (or sooner if the owner observes clinical signs suggestive persistent/recurrent CHF), both to assess for any progression and to make appropriate adjustments to therapy. The recheck examinations usually involve a review of the history to assess how the dog is doing at home, a thorough physical examination, thoracic radiographs to check that the CHF is controlled, a blood chemistry panel to check for any adverse effects (e.g., progressive azotemia and significant electrolyte abnormalities) ascribable to the medications and/or disease progression and blood pressure measurement as many stage C and D patients become hypotensive as a consequence of their medications and underlying heart disease. ACE-inhibitors should be reduced or discontinued in hypotensive animals as they are potent vasodilators and in azotemic patients.

Stage C patients will benefit from the dietary and exercise restrictions described under B2 patients. Mild to moderate exercise is important for stage C patients, and so a severe exercise restriction should never be recommended unless for orthopedic or neurologic reasons. We strongly recommend leash walks at a modest pace for our heart failure patients.

In some cases it may be difficult to differentiate between mild CHF, and primary pulmonary disease. The owner reports signs consistent with left-sided CHF such as coughing at night and with exercise, a mitral murmur is ausculted, but the thoracic radiographs show little and possibly equivocal signs to suggest cardiogenic pulmonary edema (left sided cardiomegaly and an interstitial infiltrate within the caudal-dorsal lung fields). As mentioned above, the physical examination (and electrocardiographic) findings may be helpful in cases such as these. Patients with CHF often have sinus tachycardia, whereas dogs with chronic pulmonary disease frequently have a normal-to-slow heart rate and marked respiratory sinus arrhythmia (presumably because of a reflex increase in vagal tone). A therapeutic trial with a diuretic (e.g., furosemide at ~ 2 mg/kg PO q8-12h for a few days) is also frequently very useful to clarify whether the reported signs are due to primary pulmonary disease or early CHF. A diagnosis of mild CHF can be made if:

- the cough improves *markedly* with this therapeutic trial, and
- the clinical improvement is associated with radiographic improvement, i.e., with clearing of any pulmonary infiltrate on thoracic radiographs.

Such cases are then treated as above, i.e., with a combination of furosemide and adjunctive therapy (an ACE inhibitor and pimobendan), with re-evaluations recommended every 3 to 6 months as described above. However, if significant clinical and radiographic improvement does not occur with the furosemide therapeutic trial, it is then likely that the clinical signs are related to primary respiratory system disease, and the murmur is an incidental finding. The furosemide should be discontinued, but standard B2 therapy is still warranted as outlined above.

Some dogs will continue to cough despite seemingly appropriate therapy for CHF. The most important first step in these cases is to take thoracic radiographs to assess whether the pulmonary edema has resolved. If radiographic signs of cardiogenic edema persist, then the diuretic dose should be increased (usually by 1 mg/kg increment). If the edema has resolved, concurrent primary respiratory system disease (e.g., chronic bronchitis, tracheal collapse, etc.) is probably present. Many small breed dogs suffer from primary airway disease, and increasing the diuretic dose in such cases will not improve the coughing. In fact, increasing the diuretic dose may be contraindicated because dehydration will increase the viscosity of tracheobronchial secretions. Many of these cases require additional therapy specifically for concurrent airway disease, especially bronchodilators such as theophylline or terbutaline. In addition to prescribing bronchodilator therapy, we also recommend a thorough tracheobronchial and pulmonary evaluation, as discussed during the Respiratory Disorders lectures.

Advanced CHF Stage D

Stage D patients are considered to be in refractory heart failure as defined by the presence of edema while receiving standard stage C therapy. Generally, stage D develops after 3 to 12 months following stage C. Always look for an underlying cause for decompensation such as arrhythmias, hypertension, high salt diet, etc and treat accordingly. Stage D patients are treated with higher doses of furosemide (4 mg/kg BID – TID) and the addition of other diuretics that target downstream regions of the nephron such as hydrochlorothiazide. Occasionally, furosemide will be replaced with the loop diuretic torsemide (Demadex), which acts on the same NaK₂Cl symporter within the ascending loop of Henle as furosemide. Torsemide is approximately 10 times more potent than furosemide and appears to be less affected by diuretic resistance. Recently, off label high dose pimobendan (0.9-1.2 mg/kg/day) has shown to increase survival times and quality of life in stage D patients. Stage D patients may benefit from the addition of vasodilators such as amlodipine if their blood pressure remains normal despite their heart disease and other cardiac medications. See the congestive heart failure notes for additional information on Stage D.

Prognosis

The prognosis for cases of DVD is unpredictable for the early stages (B1) as many cases will never progress into the advanced stages. Those that do progress may take a number of years to do so. Generally, B2 patients will develop CHF within 1-4 years of diagnosis. The median time to development of CHF in B2 cases treated with pimobendan was 3.5 years (EPIC trial). Senior patients may succumb to other diseases before the onset of CHF. The median survival time for stage C dogs has been reported from 9 to 15 months based on numerous studies. Approximately 25% of these dogs will survive greater than 1.5 years with survival times of > 2 years being somewhat common. Survival time for stage D patients is typically 3 to 6 months.

Cases of DVD are extremely rewarding to treat but the disease is progressive. Clients must be well informed about the clinical signs of CHF, as well as warned about the side-effects of the drugs, and that medication dose adjustments are required from time to time. Effective client education and communication is the key to the successful management of these cases. End of life discussion is necessary for CHF patients as most patients are ultimately euthanized due to quality of life concerns.