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CARDIOLOGY

Congestive Heart Failure in Canines

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Heart failure is a syndrome of clinical signs that, although well recognized by clinicians, is difficult to define precisely. It involves the heart's inability to maintain output sufficient to meet the body's needs, or to do so at normal filling pressures. Elevated filling pressures can lead to congestion as increased venous pressures cause fluid to leak from the vessels, resulting in congestive heart failure (CHF), which moves the patient into stage C (**BOX 1**).

With right-sided heart failure, increased right atrial and vena caval pressures cause hepatomegaly to develop, and the fluid then weeps into the abdomen as ascites; drainage is only required if the effusion compromises respiratory function. The elevated filling pressures can also be documented as jugular venous distention.

For left-sided heart failure, the increased left atrial and pulmonary venous pressures cause fluid to seep into the interstitial spaces and then flood the alveoli with pulmonary edema. Dogs occasionally present with pleural effusion when in CHF, and respiratory effort can increase significantly if this effusion is not drained.

When heart failure develops, a number of mechanisms are activated to maintain cardiac output and blood pressure. Unfortunately, this neurohormonal activation is deleterious in the long run and increases the damage to the heart and circulation. The best-known mechanism is the renin-angiotensin-aldosterone system. Chronic elevations in angiotensin II and aldosterone are known to have harmful effects.

BOX 1. Classification scheme of canine heart disease

STAGE	
A	A dog at risk of heart disease
B1	Signs of heart disease (eg, a murmur but no structural changes; eg, left atrial enlargement). The dog is asymptomatic.
B2	Signs of heart disease (eg, a murmur with structural changes; eg, left atrial enlargement). The dog is asymptomatic.
C	Congestive heart failure is present or has been present and the dog is receiving treatment.
D	Congestive heart failure is present and refractory to standard therapies. The patient requires hospitalization.

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Aldosterone can increase myocardial fibrosis and cell death. It also potentiates the sympathetic nervous system, increasing the heart rate, and decreases potassium, predisposing the heart to arrhythmias.

Treatment of CHF in dogs can be divided into two phases: acute and chronic.

- The acute phase is aimed at treating the congestion and supporting cardiac output. This is potentially more critical for left-sided heart failure, as pulmonary edema will result in dyspnea, and urgent treatment is needed to avert death.
- The chronic phase of treatment involves the long-term management of stable, compensated CHF. The goals are to prevent recurrence of decompensation, control clinical signs, and slow progression of the disease.

TABLE 1 provides an overview of treatment options for CHF.

ACUTE TREATMENT OF CONGESTIVE HEART FAILURE

It is important to appreciate that patients in acute CHF may have little reserve cardiorespiratory function. Treatment should be prompt, and further investigations may need to be minimized, pending improvement in the clinical condition.

Diagnosis of Congestive Heart Failure

While a cage-side echocardiogram (eg, assessment of left atrial size) can provide support for a diagnosis of CHF if needed, the stress of a full echocardiogram could further decompensate the patient without providing additional information.

Thoracic radiographs often confirm the diagnosis of left-sided CHF but should be postponed if the patient is unstable (**FIGURE 1**). Radiographic cardiomegaly can be documented, and the presence of an interstitial/alveolar pattern centered on the perihilar region, consistent with pulmonary edema, confirms the diagnosis of CHF. While dilated pulmonary veins can be suggestive of left heart failure, in acute cases, it is not uncommon for these to be normal in size.

The clinical signs and history can also help in increasing the clinical suspicion of CHF. Sympathetic stimulation associated with heart failure should cause tachycardia, while cough and crackles are nonspecific signs.

For example, an 8-year-old Cavalier King Charles spaniel presenting with tachycardia, pulmonary crackles on auscultation, and a several-year history of a left apical systolic murmur with progressively increasing intensity could be considered likely to have developed CHF secondary to degenerative mitral valve disease (DMVD). However, an 8-year-old Cavalier King Charles spaniel with a recently documented quiet murmur that presents with crackles on auscultation, a heart rate of 90 beats/min, and a cough is unlikely to be in CHF.

First-Line Therapy

Any dyspneic patient should initially be provided oxygen supplementation to increase tissue oxygenation. This can be achieved several ways. The most effective

TABLE 1 Summary of Treatment Options for Congestive Heart Failure

ACUTE TREATMENT		
FIRST LINE	**SECOND LINE**	**LONG TERM**
▪ Oxygen supplementation ▪ Furosemide ▪ Pimobendan	▪ Arterio dilators (eg, hydralazine) ▪ Dobutamine or dopamine	▪ Furosemide ▪ Potassium supplementation (if needed)
CHRONIC TREATMENT		
STANDARD	**ADDITIONAL**	
▪ Furosemide ▪ Pimobendan ▪ ACE inhibitor (eg, enalapril, benazepril) ▪ Spironolactone	▪ Antiarrhythmic drugs (eg, mexiletine, sotalol, digoxin, diltiazem) ▪ Dietary modification ▪ Omega-3 fatty acid supplementation ▪ Carnitine and taurine supplementation	

is an oxygen cage with the ability to vary the oxygen content and control temperature. Oxygen cages have the additional benefit of reducing activity, hence reducing oxygen use by the muscles. However, some larger dogs can become hyperthermic in small oxygen cages. If an oxygen cage is not an option, flow-by oxygen, masks, and nasal prongs may be used.

In dogs with a diagnosis of acute congestive heart failure, oxygen should be used in conjunction with a potent loop diuretic, such as furosemide. Ideally, an intravenous catheter is placed and furosemide is given IV. If the patient is too unstable, furosemide can be administered IM and the patient returned to the oxygen cage, pending improvement.

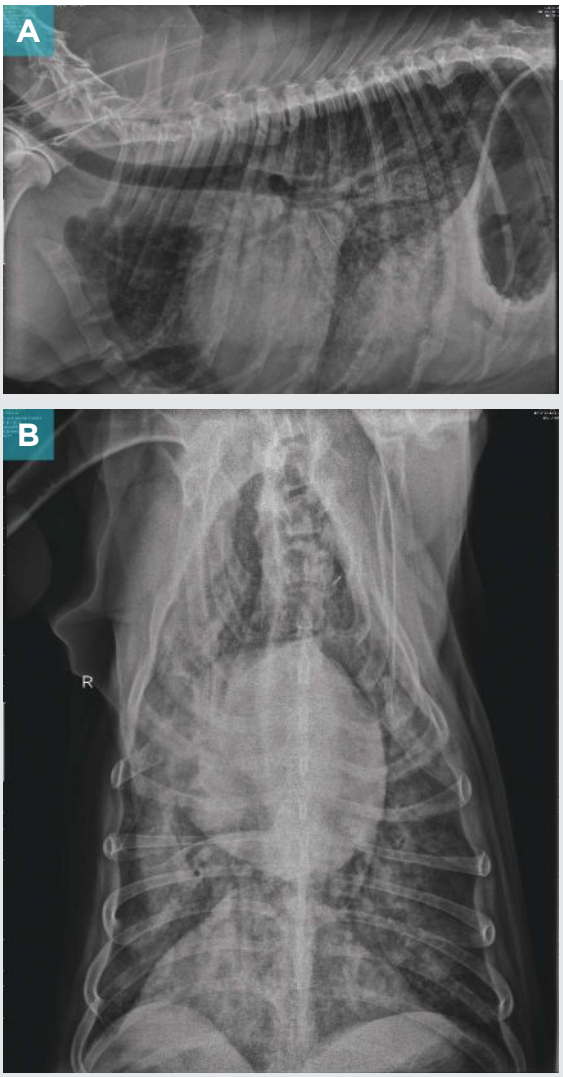


FIGURE 1. (**A**) Lateral and (**B**) dorsoventral thoracic radiographs of an 8-year-old Doberman pinscher with DCM in CHF. Note the cardiomegaly with a straightened caudal border, prominent left atrium, and tracheal elevation. There is a diffuse alveolar/interstitial pattern in the lung fields with air bronchograms and dilated pulmonary veins.

Exact doses depend on the severity of the presenting signs; furosemide 2 to 4 mg/kg IV or IM is used initially. Response to treatment should be closely monitored over the next 1 to 2 hours.[1] Ideally, after 1 hour, the respiratory rate and effort should start to decline; however, some severely affected dogs require several doses before improvement is noted. However, if the patient has not responded after oxygen and furosemide have been administered, referral consultation with a specialist should be considered.

Close monitoring of respiratory rate is a noninvasive way to tailor diuretic therapy. The production of large amount of dilute urine is an encouraging sign that furosemide is having an effect. If there is no improvement, the dose can be repeated as a bolus, or the patient can be placed on a constant-rate infusion (CRI). CRI doses of furosemide 0.6 to 1 mg/kg/hr IV have been suggested; this high dose should be carefully monitored and decreased by 50% as the patient improves, or major electrolyte disturbances will be seen.[1]

Pimobendan should also be administered as soon as CHF is diagnosed. This inodilator causes vasodilation via phosphodiesterase 3 inhibition and augments contractility of the heart, supporting the failing heart by promoting calcium binding to troponin C within the cardiomyocyte. Left atrial pressure declines with pimobendan in experimental models and likely in the clinical setting.[2]

If the patient appears stressed as a result of dyspnea, opioids can be beneficial to reduce anxiety and provide mild sedation. This must be balanced against the potential to depress the respiratory centers. Butorphanol at 0.1 to 0.2 mg/kg IV or IM is often used.

Second-Line Options

Following these treatments, the next parameter to evaluate is blood pressure. Due to the sympathetic drive, these patients may be normo- or hypertensive, and this afterload is an extra burden on the failing myocardium. If the patient is hypertensive, arterio dilators can be used to decrease the afterload for dogs with severe mitral regurgitation to achieve a systolic blood pressure of about 100 mm Hg.

Historically, sodium nitroprusside was the treatment of choice. This drug was given as a CRI, and the dose was increased to reduce the blood pressure to the required level. It required close monitoring of the blood pressure and could only be used for 24 to 48 hours at the risk of developing cyanide toxicity. Unfortunately, it has now become prohibitively expensive.

Topical nitroglycerine ointment has been used, but studies and clinical experience have questioned its effectiveness. Amlodipine can be given orally but is slower in onset of action. Injectable nitrate compounds have been used anecdotally.

Hydralazine is a potent arterio dilator and has been used at 0.5 to 3 mg/kg IV bolus q12h or as a CRI at 1.5 to 5 mcg/kg/min IV. Reflex tachycardia and hypotension are the most serious side effects seen.

For patients that are hypotensive (eg, dogs with dilated cardiomyopathy (DCM) and some dogs with DMVD), pressor agents may be required to increase blood pressure.[3] Dopamine or, more commonly, dobutamine (which is less arrhythmogenic) have been used as CRIs, and, in my clinical experience, the beneficial effects seem to last for 4 to 6 weeks.

Hospital Monitoring

Clinical improvement can be seen with normalization of breathing rate and effort. It can be confirmed with thoracic radiographs, remembering that radiographic improvement often lags clinical improvement by 1 to 2 days (**FIGURE 2**). In a small subset of patients that are equivocal for the diagnosis of CHF, repeating thoracic radiographs after 1 week on furosemide at 2 mg/kg q12h can be very helpful in confirming the diagnosis; this is usually accompanied by clinical improvement.

It is also important to check electrolytes and renal parameters, as high-dose diuretics — especially in patients that are not eating — can rapidly result in electrolyte disturbances and renal insufficiency. Hyponatremia, hypokalemia, hypochloremia, and metabolic alkalosis can occur. When electrolytes and renal parameters are checked before the start of treatment, blood urea nitrogen and creatinine are often mildly elevated due to prerenal causes, as the heart does not supply sufficient pressure to make the kidneys work effectively. This finding should not discourage appropriate treatment of heart failure with diuretics, as the values will improve as the heart failure resolves.

In some patients with severe CHF, the dose of diuretics necessary to resolve pulmonary edema can cause dehydration and azotemia with depression and poor appetite/anorexia. In these patients, the diuretic dose should be reduced as soon as the heart failure is controlled; allow for rehydration and resolution of azotemia while monitoring closely for recurrence of heart failure. It is difficult to imagine a situation where IV fluids are indicated at the same time as treating CHF with diuretics.

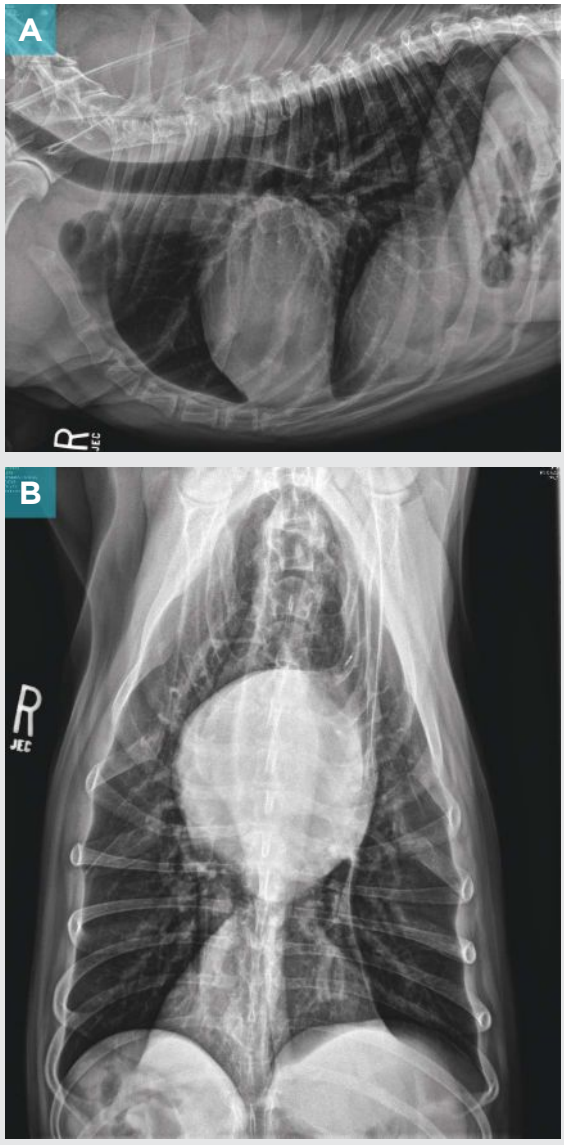


FIGURE 2. (**A**) Lateral and (**B**) dorsoventral thoracic radiographs from the same dog as Figure 1. Note the resolution of the pulmonary edema after treatment for acute congestive heart failure with furosemide and pimobendan. The cardiac silhouette is still enlarged but is smaller (the vertebral heart score decreased from 11.6 to 11).

Follow-Up Care

Over the next 24 to 48 hours as the patient improves, intravenous diuretics are typically transitioned to oral diuretics, often furosemide 2 mg/kg PO q8h initially, with a plan to titrate the dose to q12h after 3 to 4 days. Treatment regimens will vary based on patient response, renal function, and clinician preference and experience.

The first recheck appointment is usually at 7 days, although many owners appreciate a phone consultation to check progress after 2 to 3 days at home. At that appointment, thoracic radiographs and blood samples should be taken to confirm resolution of CHF and to check electrolyte and renal status. If the dog is eating normally, electrolytes are usually in the normal range. If hypokalemia is present, potassium supplementation can be added to the treatment regimen. Follow-up visits are usually planned at 1 month and then every 3 months.

Owners are strongly advised to record their dog's resting respiratory rate. There are several apps available for smartphones that can help do this. Involving clients in their dog's care and treatment increases client compliance and allows them to recognize when CHF is returning, which will prompt a return to the clinic. Client compliance is extremely important, as the owners will need to medicate their pet daily for the rest of its life and be vigilant for the return of decompensation.

CHRONIC TREATMENT OF CONGESTIVE HEART FAILURE

Chronic treatment of patients with CHF shifts from trying to control pulmonary edema to trying to negate deleterious effects of neurohormonal stimulation. The aim of chronic CHF treatment is to increase longevity of the patient, as well as improve quality of life. As a result, treatment for chronic CHF generally involves the use of 4 medications: furosemide, pimobendan, an angiotensin-converting enzyme (ACE) inhibitor, and spironolactone. These drugs are usually continued indefinitely. Other drugs may also be required.

Standard Regimen

Furosemide: The dose can gradually be decreased toward 1 mg/kg q12h, but with each dose reduction the owner should monitor for any change in the dog's respiratory rate and effort. Thoracic radiographs can be helpful to monitor response to therapy, although they often mirror what is anticipated from the respiratory status.

Chronically, renal failure may start to develop, especially with escalating doses of furosemide. Ultimately, many patients cannot be kept out of heart failure without using doses of diuretics that induce renal failure.

Pimobendan:[4,5] The dose is 0.2 to 0.3 mg/kg PO q12h on an empty stomach, as a recent meal significantly decreases absorption. In cases of refractory heart failure, some cardiologists increase the dose of pimobendan to 0.2 to 0.3 mg/kg PO q8h, although there are no supporting studies.

There has been debate regarding whether pimobendan would increase ventricular arrhythmias, increasing the rate of cardiac death, as other phosphodiesterase 3 inhibitors do in humans. However, this has not been supported in clinical trials.[5,6] Indeed, pimobendan has been shown to increase life expectancy when compared to standard therapy.

ACE inhibitors have been shown to help in the control of CHF and increase longevity for dogs with DMVD and DCM. Commonly used ACE inhibitors include enalapril and benazepril, while ramipril and quinapril are also available in Europe for dogs.[7-9] All of the modern ACE inhibitors have a similar duration of action and should be used once to twice daily.

Often, an ACE inhibitor dose is started once daily and is increased to twice daily as the disease progresses. Enalapril is excreted via the kidneys, whereas benazepril is excreted 50% by the kidneys and 50% by the liver; therefore, benazepril may be preferable in patients with some renal compromise.

Typically, an ACE inhibitor is dispensed as the patient is discharged from the hospital with instructions not to start the drug until the patient is eating well. There is always a concern that an ACE inhibitor could exacerbate pre-existing renal failure and starting an ACE inhibitor should prompt evaluation of renal parameters after one week.

While blocking the conversion of angiotensin I to angiotensin II, some vasodilation should be seen and systolic blood pressure would be expected to decrease. However, the change is usually about 5 to 10 mm Hg, and it is uncommon for hypotension to be clinically apparent. Indeed, in dogs these drugs are generally well tolerated, improving survival and quality of life.[7,8]

Elevated aldosterone levels are very harmful to the myocardium. Angiotensin II is one of the potent

stimuli for aldosterone release; therefore, ACE inhibition should reduce aldosterone levels. While this may true in the short term for some dogs, many dogs experience aldosterone escape and levels rapidly rise again.[10] These patients will probably benefit from additional aldosterone blockade from spironolactone.

In humans, ACE inhibitors may cause cough, and these patients are generally switched to an angiotensin receptor blocker, such as losartan. These drugs have been used in dogs, but as canine patients are coughing anyway, it is difficult to justify the increased costs or identify increased coughing.

Spironolactone, an aldosterone antagonist, is an extremely mild diuretic—it is difficult to document an increase in thirst in a dog given this drug. As a single agent, spironolactone is rarely sufficiently potent to control CHF, and clinical improvements are unlikely to be seen. However, there is good evidence that dogs with DMVD live longer if they receive spironolactone.[11]

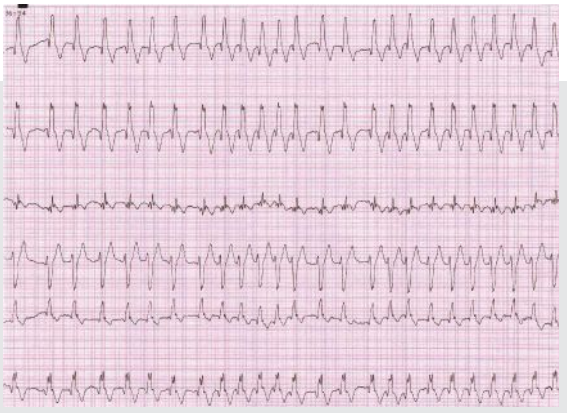


FIGURE 3. Electrocardiogram from a dog in atrial fibrillation. There is a lack of P waves on any limb lead and a supraventricular tachycardia with an irregularly irregular rhythm. 50 mm/sec and 1 cm/mV.

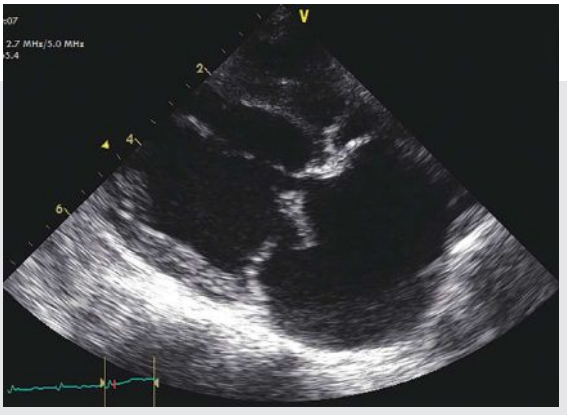


FIGURE 4. Echocardiogram from right parasternal long axis showing the left side of the heart and the mitral valve from a dog with degenerative mitral valve disease. A flail anterior mitral valve leaflet can be seen prolapsing back into the left atrium during systole.

If not started right away, spironolactone can be introduced at the first or second recheck visit to allow the owner to come to terms with the number and frequency of the dog's medications before adding another tablet. The dose of spironolactone is 1 to 2 mg/kg PO q24h with food, as it is fat soluble, and absorption is increased with a meal.

The main side effect of spironolactone in humans, gynecomastia, has not been reported in dogs. However, dogs should be monitored for the development of hyperkalemia.

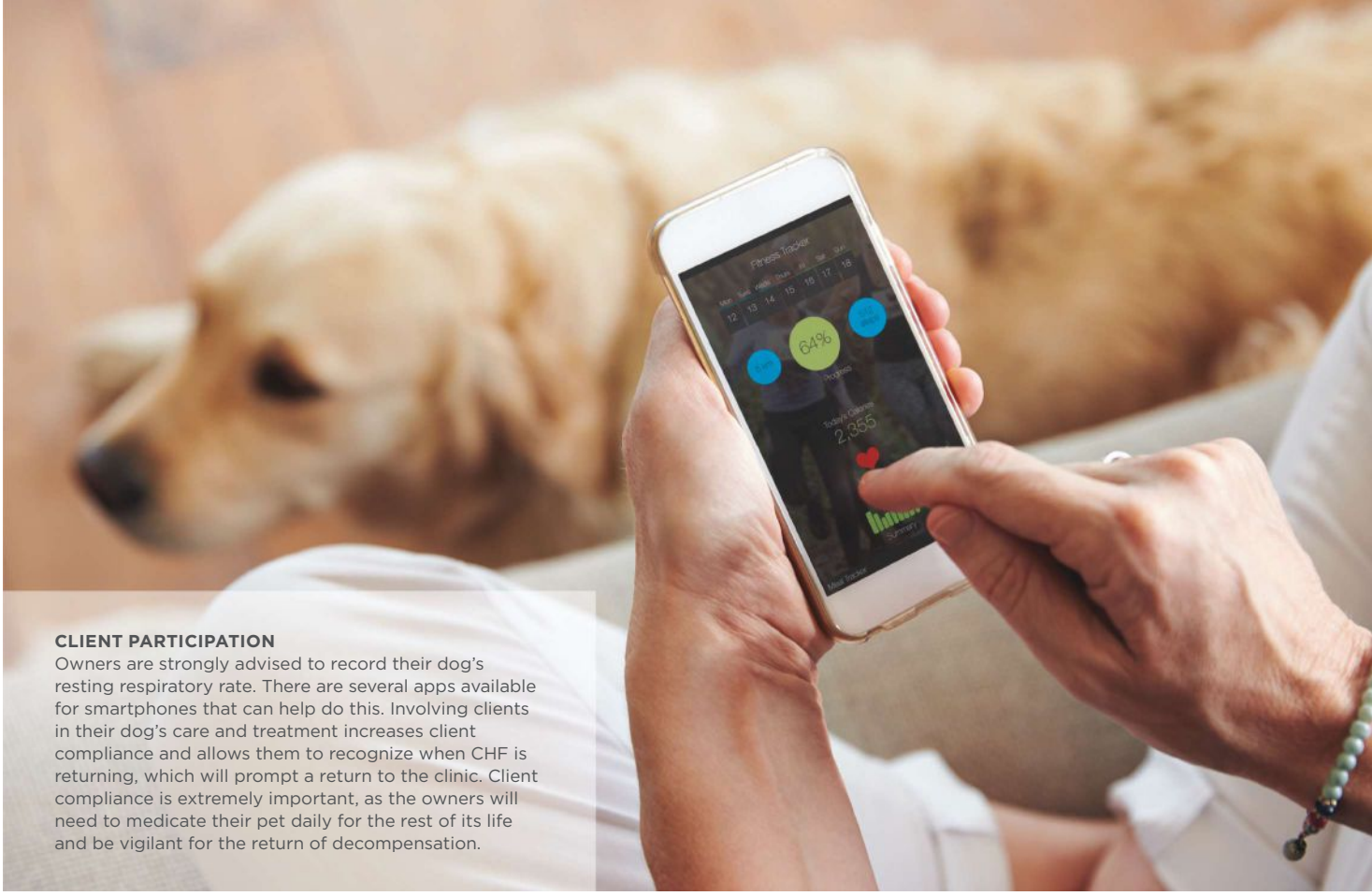
Additional Options

If an arrhythmia is present, **antiarrhythmic drugs** may be indicated.

Ventricular arrhythmias severe enough to require treatment are more common in DCM than mitral regurgitation; class 1 and 3 agents are used, with drugs such as mexiletine and sotalol being the most effective.[12] Side effects of mexiletine are usually gastrointestinal. Sotalol can exacerbate bradyarrhythmias and should be used with caution in patients with CHF.

Atrial premature complexes, caused by stretching of the atrial myocardium, may not require specific treatment if they are infrequent. However, sustained atrial tachycardia and atrial fibrillation (**FIGURE 3**) which is characterized by an irregularly irregular rhythm usually require rate control, as the sustained fast rate can result in a chronic tachy cardiomyopathy. A combination of digoxin and diltiazem gives better rate control in atrial fibrillation than either drug alone, but it has yet to be demonstrated that this combination results in an increased life expectancy.[13]

Beta-blockers may seem a logical approach to rate control as they are used extensively in human patients with CHF and improved longevity is well documented. Unfortunately, the negative inotropic effects can be significant, particularly in canine patients with poor systolic function (eg, DCM). Furthermore, in the acute setting, the patient may require the extra inotropic and chronotropic support that beta stimulation provides to maintain output. For that reason, beta-blockers should never be administered to patients with acute CHF.



CLIENT PARTICIPATION
Owners are strongly advised to record their dog's resting respiratory rate. There are several apps available for smartphones that can help do this. Involving clients in their dog's care and treatment increases client compliance and allows them to recognize when CHF is returning, which will prompt a return to the clinic. Client compliance is extremely important, as the owners will need to medicate their pet daily for the rest of its life and be vigilant for the return of decompensation.

The role of dietary modification in the treatment of CHF is uncertain. Ideally, moderate sodium restriction in a calorie-dense diet seems a sensible approach, but it is important that the dog continues to eat well, as unintended weight loss (cardiac cachexia) is a feature of advancing heart failure and a poor prognostic sign. Very low sodium diets can stimulate the renin-angiotensin-aldosterone system and be counterproductive.

Supplementation with omega-3 fatty acids has been shown to be beneficial in human patients with CHF, and the same is likely to be true in dogs, especially if cardiac cachexia is present. Doses of eicosapentaenoic acid (EPA) 40 mg/kg PO q24h and docosahexaenoic acid (DHA) 25 mg/kg PO q24h have been suggested.[14]

Carnitine and taurine supplementation has been suggested and may be appropriate in cases with poor systolic function. However, apart from anecdotal reports, there is little evidence to support their use.

Management of Recurrent Acute Signs

If decompensated heart failure (ie, pulmonary edema) returns, the patient should be admitted and diuretics given intravenously to regain control. A higher dose of furosemide may be needed and is often achieved by increasing the frequency of administration to 3 times daily or more. If the dose of furosemide starts to exceed 3 to 4 mg/kg q8h, furosemide resistance may be present. At that point, options include adding another diuretic, such as a hydrochlorothiazide, to achieve sequential nephron blockade.

Alternatively, the more potent loop diuretic torsemide can be prescribed. The starting dose is generally obtained by taking the total daily furosemide dose and dividing it by 10; that total daily dose of torsemide is divided to be given PO twice daily. For example, if a dog is receiving a total daily dose of 100 mg furosemide, the dose of torsemide would be 5 mg PO q12h.[15]

After switching diuretics, renal parameters and electrolytes should be checked in 5 to 7 days.

COMPLICATIONS

The most common cause of a recurrence of acute decompensated heart failure is a ruptured chorda tendinea. An echocardiogram can confirm the presence of the new flail mitral leaflet (**FIGURE 4**). Emergency treatment of the acute heart failure is

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required, pending left atrial adjustment, usually dilation, to the increased regurgitation.

Eventually, in some dogs, systolic failure develops from the chronic volume overload. In the early and middle stages of DMVD, the fractional shortening is elevated. A finding of low or low-normal fractional shortening in a dog with advanced DMVD is a poor prognostic sign, as it suggests the patient is in the terminal stages of the disease.

An uncommon cause of decompensation in a stable CHF patient with DMVD is the development of a hemopericardium secondary to left atrial rupture. These patients are difficult to manage, as draining the pericardium tends to encourage further hemorrhage. As this is an acute bleed, an echocardiogram may show clots developing in the pericardium. Given time, the defect can scar over and the patient recover, but recurrence is common.

PROGNOSIS

The development of heart failure represents a specific measurable point in the development of heart disease. For DMVD, the average survival of dogs with CHF is 9 months.[5] However, within survival times in this group vary widely, with some patients living over 3 years.[5] Survival in dogs with DCM is similar.[16]

Parameters that can help stratify risk by suggesting poorer prognosis include large left atrial and left ventricular size and high mitral E wave velocity.

When owners are questioned, it is evident that most would trade some longevity for improved quality of life. With a logical approach, heart failure can be controlled for many months with a good quality of life in most dogs. TVP

Simon Swift

After qualifying from Cambridge University, Dr. Swift spent 2 years in mixed practice before moving to a specialist small animal practice in the Northwest of England. He developed an interest in cardiology taking the RCVS cardiology certificate in 1990. He became a partner in a large emergency and referral hospital building up the cardiology referral service until he left in 2005 to follow an alternative residency program at Liverpool University. Since becoming a European Diplomate in cardiology, he worked in a private referral hospital before moving to Florida to join the College of Veterinary Medicine as Clinical Associate Professor. He is service chief for cardiology and has recently been appointed medical director. He has been involved in breeding programs and the treatment of degenerative valvular disease especially in the cavalier King Charles spaniel having been adviser to the UK CKCS club for 20 years and more recently has helped develop advanced interventional techniques at the University of Florida.

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Congestive Heart Failure in Canines

LEARNING OBJECTIVES

After reading this article, readers should be able to recognize congestive heart failure (CHF) and have a logical approach to its treatment, categorize treatment priorities, administer them appropriately in the acute setting, and explain their use in the chronic situation.

OVERVIEW

This article provides an overview of the recognition of CHF and the treatment of both acute and chronic CHF, using logical choices based on evidence-based medicine.

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1. **A 12-year-old, female, spayed Shih Tzu presents with a short history of exercise intolerance and increased respiratory rate and effort. She is a longstanding patient who has had a left apical murmur for 3 years, which has increased in volume. The optimal initial treatment plan for this dog is:**
   a. Administer high-dose furosemide IV, then obtain a detailed echocardiogram.
   b. Sedate to obtain diagnostic thoracic radiographs before starting medical treatment.
   c. Place in an oxygen cage and administer furosemide SC.
   d. Place in an oxygen cage with inotropic support, such as dobutamine.
   e. Place in an oxygen cage with high-dose furosemide IM, and delay further investigations pending clinical improvement.

2. **A 6-year-old Cavalier King Charles spaniel is examined for routine vaccinations, and a grade 4 left apical systolic murmur is detected. Thoracic radiographs show an elevated trachea and left atrial enlargement but no evidence of pulmonary edema. Echocardiography confirms degenerative mitral valve disease (DMVD) with thickened leaflets and left sided volume overload. Using the heart failure classification scheme, this dog would be classified as stage:**
   a. A
   b. B1
   c. B2
   d. C
   e. D

3. **Regarding the action of pimobendan in dogs, which of the following statements is true?**
   a. Pimobendan should be given with food to increase its absorption.
   b. Pimobendan increases the sensitivity of troponin I to calcium, which causes an increase in contractility.
   c. Pimobendan increases the risk of sudden death by causing an increase in ventricular arrhythmias.
   d. Pimobendan causes vasoconstriction helping to maintain blood pressure in dogs with congestive heart failure.
   e. Pimobendan increases life expectancy in dogs with congestive heart failure.

4. **Thoracic radiographs are obtained from a dog with acute congestive heart failure. What are the common findings:**
   a. A hypervascular lung pattern
   b. An alveolar/interstitial pattern in the dorso caudal lung fields
   c. A generalized bronchial pattern
   d. An alveolar/interstitial pattern in the cranio ventral lung fields
   e. Patchy alveolar pattern

5. **Which of the following statements regarding the diuretic, furosemide, is correct:**
   a. It is called a loop diuretic as it works on the loop of Henle in the kidney.
   b. The dose can be tapered down and eventually stopped in cases of congestive heart failure.
   c. It can be replaced by the potassium sparing diuretic, spironolactone, in cases of congestive heart failure.
   d. It causes minimal electrolyte imbalances so it is not necessary to check these levels occasionally.
   e. It causes minimal effects on renal function with escalating doses.

NOTE Questions online may differ from those here; answers are available once CE test is taken at **vetfolio.com/journal-ce**. Tests are valid for 2 years from date of approval.

6. **An 11-year-old small-breed dog presents with an increased respiratory rate and effort. The dog has had a left apical systolic murmur for years that has increased in intensity to a grade 4. The heart rate is 120 beats/min with normal femoral pulses. The best method to evaluate the cause of this dog's clinical signs is:**
   a. Echocardiography
   b. Electrocardiography
   c. Thoracic radiography
   d. Blood testing troponin and a proBNP assay
   e. Blood pressure measurement

7. **A 10-year-old Shih Tzu presents with a 2-week history of coughing. Clinical examination reveals the presence of a grade 4 left apical systolic murmur and pulmonary crackles. The heart rate is 130 beats/min with normal pulses, and the respiratory rate is 28 breaths/min. Based on these findings, a likely diagnosis is**
   a. CHF requiring furosemide IV and pimobendan PO.
   b. Respiratory disease that warrants further investigation.
   c. Respiratory tract infection requiring antibiotics.
   d. Heartworm disease.
   e. Impossible to narrow down without further investigation.

8. **A 10-year-old German shepherd with stable compensated congestive heart represents with dyspnea. Examination reveals a heart rate of 220 bpm with an irregularly irregular rhythm. This is most likely caused by:**
   a. Supraventricular premature complexes
   b. Supraventricular tachycardia
   c. Ventricular tachycardia
   d. Atrial fibrillation
   e. Ventricular premature complexes

9. **Which statement about spironolactone is correct?**
   a. It is a powerful potassium-sparing diuretic.
   b. It can be used to replace the loop diuretic furosemide in the control of CHF.
   c. There is evidence it may delay the onset of heart failure, so it can be used in asymptomatic patients.
   d. It is not helpful as an aldosterone antagonist, as ACE inhibitors prevent the angiotensin II mediated release of aldosterone.
   e. There is evidence it may prolong life in patients with CHF secondary to DMVD.

10. **When dogs become resistant to the loop diuretic furosemide, which of the following measures is not appropriate:**
   a. Increase the frequency of administration to 3 or 4 times daily.
   b. Add a thiazide diuretic such as hydrochlorothiazide.
   c. Switch to the more potent loop diuretic, torsemide.
   d. Limit the water intake of the patient.
   e. Ensure that all the other cardiac medications are optimally dosed.

090340591/0
NADA 141-273, Approved by FDA

Vetmedin®(pimobendan) Chewable Tablets

Cardiac drug for oral use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Description: Vetmedin (pimobendan) is supplied as oblong half-scored chewable tablets containing 1.25, 2.5, 5 or 10 mg pimobendan per tablet. Pimobendan, a benzimidazole-pyridazinone derivative, is a non-sympathomimetic, non-glycoside inotropic drug with vasodilatative properties. Pimobendan exerts a stimulatory myocardial effect by a dual mechanism of action consisting of an increase in calcium sensitivity of cardiac myofilaments and inhibition of phosphodiesterase (Type III). Pimobendan exhibits vasodilating activity by inhibiting phosphodiesterase III activity. The chemical name of pimobendan is 4,5-dihydro-6-[2-(4-methoxyphenyl)-1H-benzimidazole-5-yl]-5-methyl-3(2H)-pyridazinone.

Indications: Vetmedin (pimobendan) is indicated for the management of the signs of mild, moderate, or severe (modified NYHA Class II[a], III[b], or IV[c]) congestive heart failure in dogs due to atrioventricular valvular insufficiency (AVVI) or dilated cardiomyopathy (DCM). Vetmedin is indicated for use with concurrent therapy for congestive heart failure (e.g., furosemide, etc.) as appropriate on a case-by-case basis.

[a] A dog with modified New York Heart Association (NYHA) Class II heart failure has fatigue, shortness of breath, coughing, etc. apparent when ordinary exercise is exceeded.

[b] A dog with modified NYHA Class III heart failure is comfortable at rest, but exercise capacity is minimal.

[c] A dog with modified NYHA Class IV heart failure has no capacity for exercise and disabling clinical signs are present even at rest.

Contraindications: Vetmedin should not be given in cases of hypertrophic cardiomyopathy, aortic stenosis, or any other clinical condition where an augmentation of cardiac output is inappropriate for functional or anatomical reasons.

Warnings: Only for use in dogs with clinical evidence of heart failure. At 3 and 5 times the recommended dosage, administered over a 6-month period of time, pimobendan caused an exaggerated hemodynamic response in the normal dog heart, which was associated with cardiac pathology.

Human Warnings: Not for use in humans. Keep this and all medications out of reach of children. Consult a physician in case of accidental ingestion by humans.

Precautions: The safety of Vetmedin has not been established in dogs with asymptomatic heart disease or in heart failure caused by etiologies other than AVVI or DCM. The safe use of Vetmedin has not been evaluated in dogs younger than 6 months of age, dogs with congenital heart defects, dogs with diabetes mellitus or other serious metabolic diseases, dogs used for breeding, or pregnant or lactating bitches.

Adverse Reactions: Clinical findings/adverse reactions were recorded in a 56-day field study of dogs with congestive heart failure (CHF) due to AVVI (256 dogs) or DCM (99 dogs). Dogs were treated with either Vetmedin (175 dogs) or the active control enalapril maleate (180 dogs). Dogs in both treatment groups received additional background cardiac therapy.

The Vetmedin group had the following prevalence (percent of dogs with at least one occurrence) of common adverse reactions/new clinical findings (not present in a dog prior to beginning study treatments): poor appetite (38%), lethargy (33%), diarrhea (30%), dyspnea (29%), azotemia (14%), weakness and ataxia (13%), pleural effusion (10%), syncope (9%), cough (7%), sudden death (6%), ascites (6%), and heart murmur (3%). Prevalence was similar in the active control group. The prevalence of renal failure was higher in the active control group (4%) compared to the Vetmedin group (1%).

Adverse reactions/new clinical findings were seen in both treatment groups and were potentially related to CHF, the therapy of CHF, or both. The following adverse reactions/new clinical findings are listed according to body system and are not in order of prevalence: CHF death, sudden death, chordae tendineae rupture, left atrial tear, arrhythmias overall, tachycardia, syncope, weak pulses, irregular pulses, increased pulmonary edema, dyspnea, increased respiratory rate, coughing, gagging, pleural effusion, ascites, hepatic congestion, decreased appetite, vomiting, diarrhea, melena, weight loss, lethargy, depression, weakness, collapse, shaking, trembling, ataxia, seizures, restlessness, agitation, pruritus, increased water consumption, increased urination, urinary accidents, azotemia, dehydration, abnormal serum electrolyte, protein, and glucose values, mild increases in serum hepatic enzyme levels, and mildly decreased platelet counts.

Following the 56-day masked field study, 137 dogs in the Vetmedin group were allowed to continue on Vetmedin in an open-label extended-use study without restrictions on concurrent therapy. The adverse reactions/new clinical findings in the extended-use study were consistent with those reported in the 56-day study, with the following exception: One dog in the extended-use study developed acute cholestatic liver failure after 140 days on Vetmedin and furosemide.

In foreign post-approval drug experience reporting, the following additional suspected adverse reactions were reported in dogs treated with a capsule formulation of pimobendan: hemorrhage, petechia, anemia, hyperactivity, excited behavior, erythema, rash, drooling, constipation, and diabetes mellitus.

Effectiveness: In a double-masked, multi-site, 56-day field study, 355 dogs with modified NYHA Class II, III, or IV CHF due to AVVI or DCM were randomly assigned to either the active control (enalapril maleate) or the Vetmedin (pimobendan) treatment group. Of the 355 dogs, 52% were male and 48% were female; 72% were diagnosed with AVVI and 28% were diagnosed with DCM; 34% had Class II, 47% had Class III, and 19% had Class IV CHF. Dogs ranged in age and weight from 1 to 17 years and 3.3 to 191 lb, respectively. The most common breeds were mixed breed, Doberman Pinscher, Cocker Spaniel, Miniature/Toy Poodle, Maltese, Chihuahua, Miniature Schnauzer, Dachshund, and Cavalier King Charles Spaniel. The 180 dogs (130 AVVI, 50 DCM) in the active control group received enalapril maleate (0.5 mg/kg once or twice daily), and all but 2 received furosemide. Per protocol, all dogs with DCM in the active control group received digoxin. The 175 dogs (126 AVVI, 49 DCM) in the Vetmedin group received pimobendan (0.5 mg/kg/day divided into 2 portions that were not necessarily equal, and the portions were administered approximately 12 hours apart), and all but 4 received furosemide. Digoxin was optional for treating supraventricular tachyarrhythmia in either treatment group, as was the addition of a β-adrenergic blocker if digoxin was ineffective in controlling heart rate. After initial treatment at the clinic on Day 1, dog owners were to administer the assigned product and concurrent medications for up to 56±4 days.

The determination of effectiveness (treatment success) for each case was based on improvement in at least 2 of the 3 following primary variables: modified NYHA classification, pulmonary edema score by a masked veterinary radiologist, and the investigator's overall clinical effectiveness score (based on physical examination, radiography, electrocardiography, and clinical pathology). Attitude, pleural effusion, coughing, activity level, furosemide dosage change, cardiac size, body weight, survival, and owner observations were secondary evaluations contributing information supportive to product effectiveness and safety. Based on protocol compliance and individual case integrity, 265 cases (134 Vetmedin, 131 active control) were evaluated for treatment success on Day 29. At the end of the 56-day study, dogs in the Vetmedin group were enrolled in an unmasked field study to monitor safety under extended use, without restrictions on concurrent medications.

Vetmedin was used safely in dogs concurrently receiving furosemide, digoxin, enalapril, atenolol, spironolactone, nitroglycerin, hydralazine, diltiazem, antiparasitic products (including heartworm prevention), antibiotics (metronidazole, cephalexin, amoxicillin-clavulanate, fluoroquinolones), topical ophthalmic and otic products, famotidine, theophylline, levothyroxine sodium, diphenhydramine, hydrocodone, metoclopramide, and butorphanol, and in dogs on sodium-restricted diets.

Manufactured for:
Boehringer Ingelheim Vetmedica, Inc.
St. Joseph, MO 64506 U.S.A.

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