

## **Congestive Heart Failure**

Congestive Heart Failure (CHF) is the clinical syndrome where abnormal cardiac function due to heart disease results in the up-regulation of sympathetic (adrenergic) activity with the retention of sodium and water and subsequent organ congestion and edema. Congestion and edema develop as a consequence of elevated atrial and venous pressures as blood accumulates behind the diseased ventricle. Heart failure is classified based on the affected ventricle and subsequently where the fluid accumulates.

1. Left-sided CHF = pulmonary edema secondary to elevated left atrial and pulmonary venous pressures. The pulmonary edema results in severe respiratory compromise including respiratory distress, coughing and potentially death secondary to fluid flooding the alveoli. Cats may develop pleural effusion secondary to left sided congestive heart failure instead of pulmonary edema. This occurs due to a difference in their venous anatomy with the pleural veins draining into the left atrium versus the right atrium as seen in most species.

2. Right-sided CHF = modified- transudate ascites (high protein fluid with low cell count) secondary to elevated right atrial and caudal vena caval pressures. The ascites results in severe abdominal distension secondary to fluid accumulation. Severe ascites will result in abdominal pain and respiratory distress secondary to the diaphragm being pushed up against the lungs.

3. Bilateral CHF = both right- and left-sided CHF = manifested as a pleural effusion secondary to elevated left and right atrial pressures. The pleural effusion is usually a modified transudate, but other types of pleural effusions are possible, e.g., chylous effusions are quite common in cats with various forms of cardiomyopathy. Bilateral CHF can also manifest as concurrent ascites and pulmonary edema.

Heart failure is also classified as either backward, forward or both. Backward failure refers to organ congestion and edema secondary to increased atrial pressure as blood “backs up” behind the failing ventricle. Forward failure refers to decreased tissue perfusion and blood pressure secondary to decreased cardiac output as there is not enough “forward” blood flow to maintain tissue perfusion. Generally, animals in heart failure present with backward (congestion) signs first followed by forward signs in chronic stages. Survival times in animals with forward failure is extremely short as diminished tissue perfusion results in multiple organ dysfunction.

## **Causes of Congestive Heart Failure**

1. Volume overload due to valvular regurgitation and shunting of blood. Examples include mitral regurgitation, aortic insufficiency, patent ductus arteriosus and septal defects (atrial or ventricular). *Predominate cause in most dogs with heart failure.*

2. Systolic dysfunction due to decreased ventricular contractility. Examples include dilated cardiomyopathy, cardiomyopathy secondary to chronic volume overload and secondary

myocardial diseases (myocarditis, taurine deficiency, toxins and neoplasia). Common in dogs, usually with concurrent volume overload.

3. Diastolic dysfunction due to decreased myocardial relaxation or reduced ventricular compliance. Examples include hypertrophic cardiomyopathy, concentric hypertrophy secondary to aortic or pulmonic stenosis, and restrictive cardiomyopathy. *Predominates in most cats with heart failure.*

4. Pericardial disorders resulting in cardiac tamponade (collapse of the right heart). When pericardial pressures are elevated secondary to fluid accumulation or constriction, blood is unable to return to the right atrium due to compression. This increases vena caval pressures and results in signs of right sided CHF. Examples include pericardial effusion and constrictive pericarditis.

5. Arrhythmias can result in CHF by causing an abnormal heart rate and decreasing cardiac output. Examples include tachyarrhythmias (atrial fibrillation, ventricular tachycardia) and bradyarrhythmias such as third-degree atrioventricular block and atrial standstill. Persistent tachycardia may also result in progressive systolic dysfunction attributed to myocardial exhaustion.

## **How do we Treat CHF?**

One must accurately diagnose and specifically treat the cardiac disorder(s) whenever possible. For example:

- CHF due to a persistent bradycardia should be treated by pacemaker implantation.
- CHF due to pericardial effusion should be treated by pericardiocentesis
- CHF due to the presence of a shunt should be treated by occlusion of the shunt.

However, the great majority of cases are caused by cardiac disorders that are not readily amendable to correction. This includes the cardiomyopathies, valvular disease and some intracardiac shunts. Thus, the management of these conditions is focused on the resolution of the edema of congestive heart failure. In addition, there may be a known medication that acts to improve the primary cardiac problem as with positive inotropic drugs with systolic dysfunction.

The basic therapeutic approach to the treatment of CHF involves the combined use of diuretics, suppression of the renin angiotensin aldosterone system (RAAS), sodium restriction and ancillary therapy. Intermittent thoraco- and abdominocentesis in cases with pleural effusions and/or ascites due to CHF may also play a part of therapy. We will also discuss additional therapeutic modalities for the management of congestive heart failure including pimobendan, digoxin and others.

## **Diuretics**

- *Diuretic therapy is the mainstay of CHF treatment.* Appropriate diuretic therapy is responsible for most of the improvement that we obtain when we treat a case of CHF! All other treatments should be considered as merely adjunctive.
- *Diuretics reduce blood volume and thereby lower atrial and venous pressures, which alleviates edema and its associated clinical signs.*
- Diuretics should be prescribed at the lowest effective dose for managing the edema and clinical signs of congestive heart failure.

Whenever possible, before initiating diuretic therapy, obtain blood for at least a serum chemistry (including renal variables - BUN and creatinine) with electrolytes, and collect urine for a full urinalysis, or at least measure urine specific gravity. This will enable you to make sense of future clinical pathology results. For example, once a case is receiving furosemide, urine specific gravity will frequently be isosthenuric (or even hyposthenuric). If the dog becomes azotemic (a common side effect of both diuretic and ACE-inhibitor therapy), it will be difficult, if not impossible to distinguish between renal- and prerenal azotemia without the benefit of a pre-diuretic urine specific gravity measurement. Such a distinction has clear therapeutic and prognostic implications.

## **Furosemide**

*Furosemide (Lasix/Salix) is the most important drug used for management of CHF* as it is one of the most potent diuretics and most familiar in veterinary medicine. Furosemide is a loop diuretic, which inhibit sodium and chloride transport in the ascending Loop of Henle of the nephron. This inhibition results in an obligatory loss of sodium and water into the urine, reducing blood volume.

### Dosages

Chronic Management of CHF:

Dogs: 1 - 4 mg/kg orally every 8 to 12 hours. Typically start at 2 mg/kg every 12 hours and adjust dose based on clinical signs, presence of edema and blood chemistry profiles. Again, you want to administer the lowest effective dose in managing edema without serious complications (see below).

Cats: 0.5 – 4 mg/kg orally once to twice daily. Cats are more sensitive to the effects of furosemide and require smaller dosages. Again adjust dose based on clinical signs, presence of edema and blood chemistry profiles, and administer the lowest effective dose.

Acute Pulmonary Edema:

The management of acute pulmonary edema is dependent on the patient's level of distress as assessed by respiratory rate and effort. Severe, crisis situations will require larger and frequent furosemide dosing than in patients with mild to moderate distress. Adjunctive therapy includes strict cage rest, oxygen therapy, and minimal restraint. Furosemide may be administered in

dosages as high as 4 - 8 mg/kg IV every 1 – 3 hours and quickly tapering the dose based on respiratory rate and effort. Alternatively, after an initial IV bolus, furosemide may be administered as a constant rate IV infusion at 0.25 - 1 mg/kg/hr adjusted per level of respiratory distress.

#### Side Effects:

The side effects associated with furosemide (seen mainly but by no means exclusively at higher dosages) include:

- Polyuria and polydipsia - these are the side effects that are most frequently reported by owners and that are most concerning to them
- Volume depletion (frequently leading to prerenal azotemia and/or exacerbating preexisting renal azotemia)
- Hyponatremia
- Hypochloridemia
- Metabolic alkalosis (Increased Bicarbonate)
- Hypokalemia
- Hypocalcemia
- Hypomagnesemia

With the exception of polyuria and polydipsia, these side effects are infrequent in patients that are receiving low-to-modest furosemide dosages, and eating and drinking well. Side effects are common with higher dosages, especially in anorectic animals receiving additional diuretics. *Hypokalemia and its associated clinical sign of muscle weakness is common in cats and usually requires potassium supplementation.* Encourage oral food and water intake and consider a naso-esophageal tube or appetite stimulants if necessary.

#### **Torsemide**

Torsemide is another loop diuretic that functions similar to furosemide by blocking the sodium chloride resorption across the ascending loop of Henle. Torsemide is approximately 10 to 20 times as potent as furosemide. Torsemide is largely used in patients with Stage D (refractory) heart failure or in earlier stage C cases that are demonstrating a lack of responsiveness to furosemide due to diuretic resistance. Some cardiologists advocate for the use of torsemide for all stage C patients, but caution needs to be taken over the drug's potency as it is relatively easy to trigger acute renal failure due to the drug's potent diuretic effects. Torsemide may be administered on an once to twice daily basis. Never give torsemide concurrently with furosemide. Torsemide is not used for acute management of pulmonary edema. As with all diuretics, close monitoring of kidney values is a must as azotemia is a common side effect.

Dosages (dog and cat): 0.1-0.3 mg/kg PO q 24 to q 12 hour. Some clinicians dose at 1/20 – 1/10 the furosemide dose.

## Hydrochlorothiazide

Hydrochlorothiazide is a thiazide diuretic, which are a class of diuretics that inhibit sodium and chloride absorption from the distal tubule of the nephron. This class is not as potent as furosemide in stimulating diuresis. This class is predominately used in combination with furosemide in treatment of advanced, refractory CHF (Stage D). *Thiazide diuretics should never be used in place of furosemide in CHF.*

### Dosages:

Dogs: 0.5 - 1 mg/kg 1 – 2 times daily. Start low and adjust based on presence of edema and blood chemistry profile.

Cats: 0.5 – 1 mg total every 1 – 2 days. Start low and adjust based on presence of edema and blood chemistry profile.

Side effects are similar to furosemide therapy. It is very common to see side effects as usually prescribed in combination with furosemide.

## Potassium Sparing Diuretics

The potassium sparing diuretics are weak diuretics that should never be used as single agent therapy in CHF. Spironolactone is most commonly used from this drug class. Its mechanism of action is to inhibit aldosterone receptors within the collecting ducts, preventing aldosterone from stimulating sodium reabsorption and potassium secretion. In addition to its weak diuretic effects, *spironolactone has beneficial effects in prevention of myocardial fibrosis and heart disease progression.* This effect is covered in greater detail under ancillary therapy. Due to their potassium sparing effects, spironolactone should be used cautiously with concurrent ACE-inhibitors and/or potassium supplementation to avoid life threatening hyperkalemia.

### Dosages:

Dogs: 1-2 mg/kg PO BID.

Cats: 1-2 mg/kg PO BID. Rare reports of facial excoriations have been noted within cats. These lesions resolve with discontinuation of this drug.

## ACE-Inhibitors

ACE-inhibitor therapy should be considered routine adjunctive therapy in the chronic treatment of CHF. In addition to allowing us to prescribe a lower furosemide dose, ACE-inhibitor therapy increases both quantity and quality of life when used as adjunctive therapy in the treatment of CHF. ACE-inhibitors are also vasodilatory, thereby reducing blood pressure (left ventricular afterload). The reduction in afterload improves forward stroke volume and cardiac output and directly reduces the volume of mitral regurgitation. All of these effects are beneficial in managing left sided congestive heart failure. ACE-

inhibitors are also commonly used for management of systemic hypertension with concurrent heart disease.

#### Dosages:

##### Dogs:

Enalapril 0.5 mg/kg once to twice daily. Generally start at the once daily dose for one week and then increase to twice daily administration if eating well.

Benazepril 0.25 – 0.5 mg/kg once to twice daily. Typically administered twice daily if kidney function permits.

Cats: Benazepril: 0.25 – 0.5 mg/kg once daily. *Benazepril appears to be better tolerated in cats versus enalapril.*

Enalapril: 0.25 – 0.5 mg/kg once daily. Commonly associated with GI side effects.

#### Side Effects:

As in the case of furosemide, ACE-inhibitor therapy should not be started prior to performing a serum chemistry profile and urinalysis. Side effects are typically mild and include gastro-intestinal signs, hypotension and azotemia. Anorexia, vomiting and diarrhea are commonly seen with initiation of therapy. Cats seem most prone to the GI effects. Azotemia is usually mild but may on occasion be severe. The azotemia will usually resolve following discontinuation or dose reduction.

### **Positive Inotropic Drugs**

This is a class of drugs that acts to increase the strength of the myocardial contractions. Such an increase is known as a positive inotropic response. There are three such drugs that are widely used in veterinary medicine. These drugs have the most benefit with dilated cardiomyopathy and other causes of decreased ventricular contractility. They also appear to benefit patients with chronic CHF secondary to volume overload as seen with mitral regurgitation and congenital left to right shunts. These drugs are contraindicated in patients with stenosis. A positive inotropic drug will increase the severity of the stenosis and potentially trigger congestive heart failure and sudden death.

### **Digoxin and the Cardiac Glycosides:**

The cardiac glycosides indirectly increase intracellular calcium through inhibition of the Na/K ATPase pump. The increase in calcium triggers a more forceful contraction from the myocardium (positive inotropic response). The cardiac glycosides also slow conduction across the AV node through vagal influences, slowing the heart rate in face of supraventricular tachycardias. Digoxin is indicated in virtually every patient with CHF

secondary to systolic dysfunction (dilated cardiomyopathy). Digoxin is also indicated in patients with structural heart disease and concurrent supraventricular tachycardias (atrial fibrillation and concurrent mitral regurgitation).

### Dosage:

*Digoxin has a very narrow therapeutic window, thereby toxicity commonly occurs with administration. The dosage is determined by several factors:*

- Drug form: Elixir is associated with a higher rate of intestinal absorption compared to the tablet form. The total dose should be reduced by 15% when using the elixir.
- Lean body mass: Obesity and ascites fluid should be accounted for in dosing. Often subtract 15 – 25% of body weight pending the animal's body condition score.
- Renal Function: Digoxin is predominately eliminated via renal filtration. The presence of renal disease necessitates a 25-50% dose reduction.
- Electrolyte status: Hypokalemia results in digoxin toxicity as potassium and digoxin compete for the same cellular receptors. Correct for hypokalemia before administering digoxin.

Dogs: 0.24mg/M<sup>2</sup> body surface area (BSA). BSA is calculated following correction for above parameters.

Cats: 0.007-0.015 mg/kg once daily to every other day.

Measure serum digoxin levels within 7 – 10 days of initiation and periodically every 6 months afterwards. Therapeutic serum concentration is 0.6 to 2 ng/ml. Serum levels should be measured 6 – 8 hours post administration.

### Toxicity

Clinical signs of toxicity usually start off as gastro-intestinal and consist of anorexia, nausea and vomiting. Affected patients are usually lethargic as well. A variety of arrhythmias may develop, some of which can be life threatening. The more common arrhythmias include ventricular bigeminy, atrial tachycardia, second degree AV block and ventricular tachycardia. Treatment of toxicity involves discontinuation of digoxin for 24 to 36 hours and restarting at a lower dose. Arrhythmias may require the use of an antiarrhythmic.

### **Pimobendan**

Pimobendan (*Vetmedin*®) is an inodilator, a drug with both positive inotropic and vasodilatory properties. Pimobendan acts as a calcium sensitizer and as a phosphodiesterase III inhibitor. A calcium sensitizer acts to increase the responsiveness of the myofilaments to calcium, triggering greater number of cross bridges (actin - myosin binding) and hence a stronger contraction. Pimobendan also inhibits phosphodiesterase III. Phosphodiesterase is the enzyme that metabolizes cyclic adenosine monophosphate (cAMP), which is an intracellular secondary messenger of sympathetic nervous stimulation. Inhibition of phosphodiesterase results in accumulation of cAMP and enhanced sympathetic stimulation on the heart. This increases myocardial contractility and relaxation as well as vasodilation of arteries and veins. Pimobendan

has been shown to increase survival times and the quality of life of patients with heart failure secondary to valvular disease and dilated cardiomyopathy. Pimobendan is considered to be exceptionally safe with rare GI side effects reported.

#### Dosages:

Dogs and cats: 0.2 – 0.3 mg/kg twice daily.

#### **Dobutamine**

Dobutamine is a sympathomimetic that stimulates Beta-1 adrenergic receptors on the myocardial cells, increasing cAMP and calcium influx. Dobutamine has a short half-life, and therefore must be administered as a constant rate infusion. Dobutamine is indicated for use in patients with severe CHF secondary to systolic dysfunction (dilated cardiomyopathy). Highly recommended for patients that need hospitalization within an oxygen cage. Monitor closely for arrhythmias and tachycardia. Dobutamine is contraindicated with pre-existing tachyarrhythmias.

Dose: 5 to 20 micrograms/kg/min IV. Dose according to heart rate. Recommend to start low and continue to increase while monitoring heart rate. Caution with use in cats as it has been reported to trigger seizures. We have never observed this effect, however.

#### **Ancillary Therapies:**

##### **Abdomino- and/or Thoracocentesis:**

Patients presenting with significant fluid accumulation within the pleural or abdominal cavities benefit from manual removal of this fluid. This is especially true with pleural effusion resulting in respiratory compromise as manual removal of this fluid will quickly correct the respiratory distress. Removal of the fluid with diuretic therapy will take too long and likely result in the demise of the patient. As much fluid as possible should be removed from either cavity if resulting in clinical signs (abdominal discomfort, respiratory signs). Caution must be taken not to remove the pleural fluid too quickly in patients with large volumes as cardiovascular collapse may result (rare occurrence). Following manual removal, the patient should be started on diuretic therapy in attempt to prevent recurrence. Often patients will require additional taps for resolution of associated clinical signs. Again, it is recommended to remove as much fluid as possible and then adjust the diuretic dose. This fluid tends to be high in protein, which is then lost with its removal. *Therefore, it is ideal to tap less than once per month if possible to prevent significant protein loss and subsequent hypoproteinemia. Adjust diuretic dose based on rate of fluid accumulation, clinical signs and kidney values.*

#### **Sodium Restricted Diets**

Sodium restricted diets are generally recommended for patients with advanced heart disease and congestive heart failure. Such recommendations are largely based on human recommendations and theory versus actual data. However, we have seen many cases respond well to modest sodium restriction. Currently, the Cardiology Service recommends feeding a diet that is modestly restricted in sodium ( $\leq 80$  mg sodium per 100 kcal). Many non-prescription diets will meet this sodium restriction. Numerous prescription diets will also meet this recommendation including diets specifically formulated for heart disease and kidney disease. Most of these diets are not recommended however due to the marked protein restriction which is detrimental to the patient with heart disease due to cachexia. Adequate protein intake is critical in preventing

cardiac cachexia and heart disease progression.

## **Supplements**

Supplements for heart disease are endless! We generally recommend avoiding supplements other than omega-3 fatty acid and co-enzyme Q 10. The recommendation for omega-3 fatty acids has the most science behind it with omega-3s having antiarrhythmic effects and preventing cardiac cachexia. Heart disease is now considered an inflammatory disease with the up regulation of pro-inflammatory cytokines. Such cytokines appear responsible for triggering cardiac cachexia and can be suppressed with omega-3 fatty acid supplementation. We recommend a target dose of 40 mg/kg EPA and 25 mg/kg DHA per day. Some diets (cardiac and joint diets) have an appropriate level of EPA and DHA within them.

There is emerging evidence that co-enzyme Q 10 supplementation improves survival times in humans with heart failure. Q 10 is an integral component to mitochondrial oxidation and appears to become deficient in humans with heart failure. There is also evidence that levels are deficient in dogs with heart failure. We do not know if there is any benefit in supplementing Q 10 to veterinary patients with heart failure, but such supplementation has been shown to be safe.

## **Spironolactone**

Spironolactone was covered previously as a potassium sparing diuretic that works by inhibiting aldosterone receptors. Aldosterone plays a significant role in the pathophysiology of heart failure including sodium retention and promoting myocardial necrosis and subsequent fibrosis. Blocking the effects of aldosterone decreases mortality in humans with advanced heart disease. It is suspected that the addition of spironolactone to conventional cardiac therapy (furosemide and ACE-inhibitor) in dogs with CHF decreases the risk of cardiac related death, euthanasia or severe progression of clinical signs. There is growing evidence of Aldosterone Break Through with ACE-inhibitors being unable to chronically suppress aldosterone upregulation with heart disease.

## **Beta-Blockers**

Beta-blockers have been advocated in patients with diastolic dysfunction, including hypertrophic and restrictive cardiomyopathy. These drugs act to slow the heart rate by blocking sympathetic adrenergic responses. The rationale behind their use in diastolic dysfunction is that slowing the heart rate could improve diastolic function by increasing the amount of time available for ventricular filling. Their use in diastolic dysfunction is controversial with veterinary cardiologists on both sides of the argument. In theory, beta-blockade would have beneficial effects. However, there is limited evidence that beta-blockade may hasten the recurrence of CHF in cats with hypertrophic and restrictive cardiomyopathy. It is suggested that cats may do better with furosemide and an ACE-inhibitor alone.

## **Vasodilators**

### Venous Vasodilators

Nitrates are venous vasodilators used in patients presenting in acute, severe left sided CHF. Venous vasodilators reduce pulmonary edema by decreasing venous blood return to the heart. Dilation of the systemic veins will result in retention of large proportion of blood volume (70-80%) within the systemic veins, thereby decreasing return to the heart. This decreased return will lower left atrial and pulmonary venous pressures and subsequently reduce pulmonary edema. Venous vasodilators should never be used as sole therapy for left sided CHF and have no merit with treatment of right sided CHF. The vasculature may become refractory to continuous

use of nitrates. Tolerance may be avoided by intermittent use of these agents (skipping dosing intervals).

### **Nitroglycerine**

Cutaneous Paste. (2% nitroglycerine paste)

Dogs: 0.5 – 1.5 cm strip applied cutaneously every 8 to 12 hours

Cats: 0.5 cm strip every 8 – 12 hours

Recommend to remove strip after the 8-12 hour interval and wait an additional 8 – 12 hour interval before re-applying to prevent tolerance.

Cutaneous Patch (nitroglycerine patch)

Dogs and Cats: 0.1 – 0.2 mg/hour

Avoid continuous administration due to tolerance

### **Isosorbide dinitrate**

Oral tablets.

Dogs: 0.2 to 2 mg/kg every 8 hours, alternating with dosage free interval

### Arterial Vasodilators

Arterial vasodilators are used to reduce systemic arterial resistance and blood pressure. They constitute an important therapy for systemic hypertension. In addition, they may be useful in managing left sided CHF secondary to mitral and aortic valvular insufficiency (regurgitation). By decreasing the systemic arterial pressure that the left ventricle must contract against (afterload), they decrease regurgitant volume (amount of blood that leaks across the mitral valve) and increase forward blood flow (stroke volume). Caution must be taken with their use in patients with heart disease as severe hypotension may result. They should only be used if blood pressure can be monitored. It is not recommended to use more than one arterial vasodilator concurrently.

### **Amlodipine**

Amlodipine is a calcium channel blocker that predominately affects the vascular smooth muscle triggering vasodilation and a drop in blood pressure.

Dose: Oral tablets

Dogs and Cats: 0.05 – 0.1 mg/kg once to twice daily. The dose is gradually increased while monitoring blood pressure, clinical signs and pulmonary edema. Recommend to start once daily and increase to twice daily if necessary.

### **Hydralazine**

Hydralazine is a direct acting arterial vasodilator. It appears reasonable for short term use in patients with decompensated left sided CHF. However, it is not recommended for long term use due to poor patient tolerance. *When administered orally, effects begin within one hour, peaks within 3 hours and total duration is approximately 12 hours.* Adverse effects include hypotension, gastrointestinal signs and reflex tachycardia.

Dose: oral tablets

Dogs: 0.5 to 1.0 mg/kg twice daily. Dose is gradually increased to a maximum of 3.0 mg/kg twice daily while monitoring blood pressure.

### **Sodium Nitroprusside**

Sodium nitroprusside is a direct mixed vasodilator (arterial and venous). *It is extremely potent*

*vasodilator primarily used for in hospital treatment of severe left sided CHF. Continuous blood pressure monitoring should be utilized during its administration.*

Dose:

Dogs: CRI of 1.0 microgram/kg/minute. Rate of administration titrated to effect and blood pressure.