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**American College of Veterinary Pharmacists** 

# MANAGEMENT OF CARDIOVASCULAR DISEASE IN THE HOUSEHOLD DOG

PETTALK

#### What is Cardiovascular Disease?

Cardiovascular disease (CVD), also known as heart disease, is not just a condition that affects humans, but our four legged pets as well! As awareness of heart disease increases in human medicine, there is now a trend of increasing awareness within veterinary medicine also. The availability of information on this topic can be overwhelming so an overview of heart disease and the medications used to manage it will be assessed in this article, hopefully giving better insight to owners about what heart disease means for their dog. The heart is essential for operation of the circulatory system. Cardiac performance is essentially determined by how much, how hard, and how often the heart pumps blood (stroke volume, cardiac output, preload, afterload, heart rate, contractility, and synchrony). Alteration of any of these operations can lead to cardiac dysfunction. Cardiac failure (aka heart failure) is defined as the physiologic state in which the heart cannot receive or eject blood properly resulting in erratic blood volume balance and in turn creating clinical signs and symptoms of heart failure.



#### How prevalent is this condition?

The prevalence of heart disease, or heart failure, is somewhat breed specific. The more veterinarians are learning about heart disease, the more documentation is being recorded about the prevalence of certain breeds that correlate with specific forms of heart disease. Heart disease has many causes! One example of heart failure is Dilated Cardiomyopathy (DCM) which primarily affects large breed dogs such as Dobermans. Irish Wolfhounds, Great Danes, and Newfoundlands, but also male Dalmatians and American and English Cocker Spaniels. Of these dogs, 50% will develop the arrhythmia Atrial Fibrillation (AFib) which is essentially an abnormal or irregular fast heartbeat, known as an arrhythmia, which occurs in the atria, the upper chambers of the heart. Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC), also known as Boxer Cardiomyopathy, appears to be exclusively represented by the Boxer breed. This is caused by a genetic defect of the parts of heart muscle that primarily involve the right ventricle which is a bottom chamber of the heart. On the other hand. Myxomatous Mitral Valve Disease (MMVD), which makes up 75% of canine congestive heart failure, is prevalent in smaller breeds such as Cavalier King Charles Spaniels, Papillons, Chihuahuas, Dachshunds, and Toy Poodles. This disease normally affects older dogs with the exception of Cavaliers and Dachshunds who may experience onset of this dis-

ease as early as 2 to 4 years of age. This disease manifests as a series of progressions but essentially the progressive myxomatous (connective tissue) degeneration of the atrioventricular valves which separate the atria from the ventricles. The mitral valve, also known as the bicuspid valve, specifically separates the left atrium from left ventricle. As with humans, there are also many congenital heart diseases, but these are often surgically corrected, such as Patent Ductus Arteriosus (PDA) or Tetralogy of Fallot, and are therefore not included in this newsletter as the focus is primarily on medication management.

#### What causes heart disease?

As with most diseases in the veterinary world, the exact cause or causes of heart failure are varied depending on the breed of dog, age, gender, and any other diseases they may have,

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#### Continued from Page 1

such as kidney or lung disease. To briefly summarize, one reason heart failure can occur is from an inability of the heart to fill with blood because one of the heart's valves isn't working properly. A second cause of heart failure may be a result of the heart muscle being unable to push enough blood out of the heart due to a clot or other obstruction. A third source for heart failure is from the heart receiving too much blood and the cardiovascular tissue isn't strong enough to pump the blood back out due to a reduced heart muscle and this can be from a disease such as Dilated Cardiomyopathy where the heart physically becomes enlarged and weakened and cannot pump blood. The cause of this disease is likely genetic but could also be from injury to the heart muscle (myocardium) itself due to infection or an origin of unknown cause. The fourth reason for heart failure is from abnormal rhythms or heart beats such as atrial fibrillation or heart block. Atrial fibrillation may be due to high blood pressure, genetics, or other forms of heart disease that cause this rapid, irregular heartbeat. Heart block is a problem with the electrical system of the cardiovascular tissue and has many causes including heart infection, inflammation, or electrolyte imbalances, for example potassium. Since there are so many nuances involved with CVD, and this newsletter isn't meant to be a textbook on cardiology, these functional classifications will be further examined from a treatment perspective and any questions about the disease states themselves can certainly be answered by your trusted veterinarian.

# How will I know if my pet is has heart disease?

Symptoms of heart disease depend largely on which type of heart disease your dog has. Commonly dogs will present with exercise intolerance, difficulty breathing, coughing, a general lack of energy, blue or purple tinged coloration of the gums, and they may

also experience consistent or intermittent episodes of fainting. Also, instead of laying down flat on their sides as usual, they may prefer to sit sternal with their bellies on the ground and their heads elevated. MMVD (as mentioned above) will often present in a young male Cavalier with coughing, labored breathing, and exercise intolerance. A depressed, coughing, exercise intolerant Doberman with a rapid, irregular heart beat is likely to have DCM. Sick sinus syndrome (a group of abnormal heart rhythms) often presents in a middle age female Miniature Schnauzer that has intermittent fainting yet a Boxer who also faints is likely to have ARVC. These problems, if not addressed right away by a veterinarian, can become life threatening just as they would in a human. Cardiovascular disease can lead to fluid in the lungs, kidney failure, decreased blood flow to critical organs and if not medically managed, will eventually lead to death.

## What are signs of heart disease?

- 1. New onset weakness and fatigue
- 2. Decreased interest in food
- 3. Exercise intolerance
- 4. Coughing or wheezing
- 5. Increased panting
- 6. Blue-purple membranes
- 8. Episodes of unexplained fainting
- 9. Shortness of breath when lying down

\*If you notice any of these changes in your pet, please contact your veterinarian as soon as possible\*



# What will my vet do for my dog's heart disease?

When you bring your animal in for an appointment, your vet will likely take a complete history of your pet which includes what symptoms have been going on, when they occur, and for how long they have been happening. You want to be as detailed with you veterinarian as possible so they can give you the best diagnosis and treatment. The primary means of diagnosing a dog with heart disease is through a complete history and thorough physical exam, followed by xrays, electrocardiogram (test that records the electrical activity of the heart), and/or an echocardiogram (ultrasound image of the heart). Blood from your dog may also be drawn in order to identify and rule out other disease processes such as diabetes, kidney disease, or an underlying infection. Chest x-rays, an electrocardiograph (ECG), and/or an echocardiograph (Echo) allow your veterinarian to have a better understanding to what is going on within your pet without having to be invasive.

#### Diagnostic Test Summary

In order to increase quality of life and extend your pet's overall survival, medical treatment must be instituted as soon as possible. Diagnostic testing should be performed to better understand which form of heart disease your pet is experiencing in order to treat and alleviate symptoms and decrease chances of morbidity and mortality.

- 1. Thorough history and physical exam with auscultation of heart and lungs
- 2. Complete Blood Count
- 3. Chemistry Panel
- 4. Radiographs
- 5. ECG
- 6. Echo or TTE

## How is heart disease treated?

There are several drug classes available for veterinarians to treat heart failure in your pet and each class is specific to where in the heart the problem is occurring. Because of the intricacies of heart disease, the choice of therapy, or therapies, must be individualized to each dog specifically. Within each drug class are often spe-

Continued from Page 2	mias, would not be sent home with your pet and therefore will not be dis-	in humans for heart failure, its absorp- tion in dogs is very unpredictable and
cific medications that may be chosen	cussed in this article. Phenytoin has	therefore its use is not recommended.
over another due to safety, side ef-	poor efficacy and with side effects of	These medications can cause ex-
fects, and cost.	sedation, gingival hyperplasia, skin	tremely low heart rates and even heart
	reactions and CNS toxicity, its use is	block which is why you will often
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#### ACE Inhibitors

Angiotensin-converting enzyme inhibitor (ACEi) is a group of medications that are typically used to treat hypertension and congestive heart failure as they cause vasodilation or widening and relaxation of blood vessels. Commonly used ACEi's in dogs are benazepril, enalapril, and lisinopril though captopril may also be used but it is older and its use has decreased. Ramipril is a newer ACEi and has not been studied as much in animals but it appears to have similar effects. These medications are often used in combination with other cardio -medications. Benazepril, enalapril, lisinopril, and ramipril are generally well tolerated though they can cause kidney dysfunction in at-risk patients, especially those on high doses of diuretics. All ACEi's are contraindicated for pregnant dogs.

## Antiarrhythmic Agents

There are actually 4 groups of drugs within this class. The first medications discussed are disopyramide and quinidine which are class 1a antiarrhythmics that are primarily used to control ventricular arrhythmias. The ventricles are the two large lower "pumping chambers" of the heart. Side effects have not been specifically reported in dogs though adverse reactions in humans include constipation and dry mucous membranes. At higher doses disopyramide can induce arrhythmias in human patients. Ouinidine has the same mechanism of action but it can also be used to convert atrial fibrillation to sinus rhythm (NSR). Side effects include nausea, vomiting, diarrhea, hypotension, tachycardia, and AV block. Class Ib antiarrhythmics are lidocaine, phenytoin, mexelitine, and tocainde, and they treat ventricular arrhythmias. Lidocaine, though the most likely to be used for acute ventricular arrhyth-

not preferred. Mexiletine's use in veterinary medicine is also not very common and its side effects include excitation, tremors, and vomiting. Tocainide also has limited use in animals but clinical studies do demonstrate efficacy. Its side effects include anorexia, vomiting, and ataxia. Class II antiarrhythmics are the Beta Blockers but due to their limited use for heart failure specifically, they are discussed later on with the exception of sotalol. Sotalol is unique in that it is a Class II antiarrhythmic beta blocker but also a Class III antiarrhythmic as well. This medication is indicated for the management of refractory ventricular arrhythmias and refractory atrial fibrillation. Side effects include shortness of breath. difficulty breathing, nausea, vomiting, and pro-arrhythmic activity. Amiodarone is a Class III antiarrhythmic and it is used to treat refractory ventricular arrhythmias and is reserved for life-threatening arrhythmias refractory to treatments. Side effects include decreased appetite, decreased heart rate, congestive heart failure, low blood pressure, heart block, liver dysfunction, and a decrease in red blood cells. Dobermans appear especially affected by amiodarone experiencing high levels of anorexia, fatigue, liver toxicity, and vomiting. Class IV antiarrhythmics are the nondihydropyridine calcium channel blockers and due to their unique pharmacologic mechanism, will be discussed in another section.

## Beta Blockers

This group of medications work to slow the heart rate and are used to treat supraventricular (above the ventricle) fast arrhythmias and certain ventricular contractions. Choices for use in dogs include atenolol, propranolol, and metoprolol. While carvedilol, has been very successful tion in dogs is very unpredictable and therefore its use is not recommended. These medications can cause extremely low heart rates and even heart block which is why you will often hear from your veterinary pharmacist "start low and titrate slow" and when discontinuing therapy, your veterinarian will institute a gradual tapering down regimen. These medications can also cause fatigue and mask clinical signs associated with low blood sugar so be aware of this if your dog has diabetes. Propranolol may create difficulty of breathing in certain patients like those who have asthma.

# Calcium Channel Blockers (dihydropyridine)

Dihydropyridine calcium channel blockers, amlodipine and nifedipine, are a group of medications that act to dilate vessels of the heart. They are often used in combination with a beta blocker. Side effects include low blood pressure and a decrease in heart rate though a few cases of overgrowth of the gums (gingival hyperplasia) have been observed in dogs.

## Calcium Channel Blockers (nondihydropyridine)

These calcium channel blockers, diltiazem and verapamil, are nondihydropyridines and are used for many reasons such as control of various arrhythmias, cardiomyopathies, and other forms of tachycardia (rapid heartbeat). Side effects generally include slow heart rate, fatigue, GI distress, low blood pressure, rashes, or elevations in liver function tests.

## Cardiac Inotropic Agents

The first medications in this drug class are digitoxin and digoxin, though only digoxin is available in the USA. Digoxin, which originates from the Foxglove plant, is used in dogs for the treatment of heart failure. It can also be used to decrease supraventricular (above the ventricle) arrhythmias. It is often used in combination with an ACEi and a diuretic such as furosemide. It can also cause

#### Continued from Page 3

such side effects as vomiting, anorexia, and diarrhea. Dobermans appear to be most sensitive to these adverse effects. The second group in this class consists of one medication, pimobendan, that is used for the management of congestive heart failure and either valvular insufficiency or cardiomyopathy (heart muscle disease). Side effects include anorexia, fatigue, diarrhea, difficulty breathing, renal dysfunction, weakness, and fainting.

#### Diuretics

Furosemide is a loop diuretic that is the most effective of the diuretics and creates very dilute urine. One of its uses in dogs is to treat edema caused by heart disease. Adverse effects are related to its diuretic effects such as loss of fluid creating dehydration and electrolyte losses. Another group of diuretics are chlorothiazide and hydrochlorothiazide, thiazide diuretics which are really just mentioned for sake of completeness as thiazide diuretics are not used very often in veterinary medicine. These medications have far less of a diuretic effect than furosemide. Side effects are limited to electrolyte imbalance and allergic reactions. The third group of diuretics are the potassium-sparing diuretics, specifically spironolactone and triamterene, which are used to treat congestion caused by heart failure and are often used with an ACEi. When treating congestive heart disease in animals, spironolactone is more frequently used. Side effects of both include electrolyte abnormalities (especially increased potassium), dehydration, anorexia, vomiting, fatigue, and abnormal muscle movements.

## Vasodilators

Hydralazine is a vasodilator and is used primarily for treatment of congestive heart failure and valvular heart disease. Side effects include low blood pressure and dangerously reduced cardiac output. Nitroglycerin is another vasodilator, used to alleviate the symptoms of heart failure. The primary side effects are hypotension, rash at site of application, and tolerance that can develop with repeated use. It's very important that owners apply this medication to their pet while wearing gloves! Irbesartan and losartan are another group of vasodilators though due to cost and questionable efficacy, they are rarely used but if so, side effects are minimal and limited to low blood pressure.



# What is the prognosis for heart disease?

Once present, heart disease is a lifelong condition. If your dog has an arrhythmia, or abnormal heart beat, the prognosis is not as optimistic long term. When an arrhythmia is detected on routine examine, your veterinarian may place a Holter monitor on your pet to wear for a full day so that they can interpret the results and evaluate the frequency and complexity of the arrhythmia over the course of 24 hours. Pimobendan has demonstrated a 4 month survival versus no drug treatment in Dobermans with DCM while Fish Oil in Boxers has demonstrated some improvement in ventricular premature contractions (VPC's) and a decrease in fainting episodes but not a decrease in mortality. For heart failure in the absence of arrhythmias, the outlook is slightly more encouraging. Management focuses on enhancing quality of life by improving clinical signs and increasing survival. Prognosis depends on how your pet presents and what stage of heart failure they are in as assessed by your veterinarian using the New York Heart Association and International Small Animal Cardiac Health Council guidelines. If they have heart disease without overt symptoms and are treated right away, then likely

they have many years left with their families. However, those dogs that have severe and life threatening heart disease, often requiring oxygen therapy, may only have a few months of survival left. If their quality of life cannot be managed effectively, then euthanasia may be the most humane option and will need to be discussed with your veterinarian.

# How can my veterinary pharmacist help?

Treating pets with heart failure offers a unique opportunity for veterinary pharmacists to help you and your pet. Many of the aforementioned products must be compounded because they are not palatable or in a dose properly concentrated for your dog. While pimobendan is approved for veterinary use and comes in chewable tablets, others such as atenolol and furosemide do not. Often a dog with heart failure will be on many medications and pharmacists have the ability to address drug compatibility issues. Veterinary pharmacists can even combine medications into one acceptable dosage form improving compliance making life much easier for you and your pet. In addition to making compounded medications, veterinary pharmacists can also provide proper counseling on how to administer these medications and what side effects to look for. Your veterinary pharmacist will be supportive and work with you and your dog to the best of their abilities as you manage heart disease together!



## Further Reading Upon Request

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