Alternative Approach to managing Heart Disease and supporting Cardiovascular Health in Dogs

A Comprehensive Nutritional Program that works with the body to promote better structure and function of the heart and vascular system

Cause and Prevalence of Acquired Heart Disease in Dogs

Cardiovascular disease and congestive heart failure are common in dogs especially as they age. Heart failure is a clinical syndrome characterized by inadequate cardiac output and insufficient delivery of nutrients to the tissues of the body.

According to the American Veterinary Medical Association, one in ten dogs has developed heart disease. Some breeds have a genetic predisposition toward the development of heart disease, while others develop conditions as a result of aging, dietary factors, including nutritional deficiencies, infections, obesity, or cachexia (chronic weight loss). A 1991 informal survey by the Morris Animal Foundation showed that the third leading cause of non-accidental death in dogs was due to heart problems. The two most prevalent canine heart diseases are dilated cadiomyopathy and mitral valve disease. Chronic mitral valve disease (endocardosis) is the most common acquired heart abnormality in dogs affecting more than 35% of dogs 10 years or older.

Cardiovascular disease can involve one or more heart structures. Early symptoms are often so subtle that they can be undetected on routine exam, so by the time symptoms are noticed, there can be significant damage. Early signs of cardiac failure can include lethargy, decreased activity or exercise tolerance, dyspnea, orthopnea, wheezing, and cough, particularly after rest. Abrupt weakness, syncope, and even sudden death due to heart rhythm disturbances can also occur. In later stages, ascites can create greater respiratory effort and cause abdominal distention requiring medical intervention.

As the condition progresses, the body tries to compensate with adrenergic stimulation of the heart, but this increases arterial pressure, against which the heart must contract more forcefully. An increased renin production in the kidney further increases arterial pressure and causes structural changes in the heart. Ultimately, these effects put additional stress on the heart, increase cardiac cell death, and cause disease progression.

Choice of Drugs or Nutritional Intervention

Many of the drugs currently used in the treatment of heart disease in dogs have significant side effects. The use of diuretics to reduce edema may decrease the contractile performance of the heart and contribute to arrhythmias, as a result of hypovolemia, electrolyte and acid-base imbalances. Venodilators work by shifting the volume of blood from the heart into peripheral circulation, which reduces pulmonary edema, but may result in severe hypotension, in animals with an already reduced stroke volume. Positive inotropes are used to increase the heart's contractile ability, but are thought to exacerbate hypertrophic cardiomyopathy and to cause arrhythmias. They often drive the heart beyond its capacity to perform. Pharmaceuticals do have a place, but there are often natural substances which are kinder to the cardiovascular system.

There are a number of heart pathologies for which nutritional supplementation is considered effective, including diseases of the heart valves (mitral regurgitation and valvular disease), ventricles (primary diastolic dysfunction), heart muscle tissue (cardiac hypertrophy, dilated and restrictive cardiomyopathy, congestive heart failure), ischemic and reperfusion damage, infarction, cardiac arrhythmias. Many of the treatments used for heart failure target these processes to slow the rate of progression. For example deficiencies of taurine and L-carnitine can lead to idiopathic dilated cardiomyopathy, characterized by left ventricular dilation and systolic

dysfunction. Similar findings can be found with a deficiency of CoQ10 and the development of congestive heart failure.

There are three major goals of Nutritional Supplementation therapy:

- **Correct any dietary deficiencies that lead to cardiac disease**
- **Provide active cardio-protective supplements that improve cardiovascular function**
- **Support metabolic pathways and structural integrity of the cardiovascular system**

The following supplements are under clinical investigation regarding their mechanisms of action, and their beneficial role in the support of cardiovascular structure and function in dogs. Many of these nutrients have been found to work in a synergistic manner to help restore cardiovascular health.

L-carnitine

Carnitine is an amino acid-like cofactor that seems to have a positive inotropic effect on the heart muscles. Deficiency results in development of cardiomyopathy as it is essential to normal cellular energy metabolism, in the transport of long-chain fatty acids to beta-oxidation sites in the mitochondrial matrix. L-carnitine can improve heart rate, lipid patterns, and exercise tolerance, and protect against cardiac necrosis, all of which are important to returning an animal to normal cardiac function. Of all antioxidant and cardio-protective compounds studied, L-carnitine in combination with taurine, has shown the greatest direct effect on improving life expectancy and mortality rates in some animals with congestive heart disease. L-carnitine demonstrated a return of myocardial function and decreased clinical signs of dilated cardiomyopathy,

The clinical evidence looks promising. Carnitine seems to improve symptoms, ejection fraction, and exercise tolerance. Carnitine seems to increase ejection fraction by up to 14% and exercise tolerance by as much as 21% in human patients, and appears to decrease cardiac remodeling. While myocardial function did not completely return to normal in all animals treated with carnitine therapy, it provided the dogs a normal quality of life for months to years. It is valuable to understand L-carnitine in relation to taurine deficiency and supplementation, as the two nutrients have interrelated roles in management of heart disease in dogs.

Taurine

Taurine, an amino acid found in relatively high concentration in heart tissue, is thought to be a cardioprotectant, Taurine may help reduce salt and fluid load. It improves contractile function , as it exhibits positive inotropic effects on myocytes, thereby lessening congestive symptoms. In addition, it may inhibit the actions of angiotensin II, thereby mimicking the actions of ACE inhibitors. Taurine has also been shown to decrease the level of lipid peroxides (and hence, oxidative damage) in hypoxic tissues, and is anti-arrhythmic. In patients with acute myocardial infarction or unstable angina, the combination of taurine and CoQ10 supplementation resulted in a significant decrease in the mean infarct size, and the EKGs were significantly improved. Further, total complications were shown to be significantly lower in the intervention group than the control group. Taurine supplementation reduced mortality rates, improved clinical condition, and enhanced myocardial contractility in dogs with congestive heart failure as compared to controls. Other researchers have found taurine to slow the rapid progression of heart failure and prolong life expectancy in animals.

Arginine

L-arginine is an amino acid produced by the body. The most common explanation for its cardiovascular benefits has to do with L-arginine's effect on nitric oxide. L-arginine is a substrate for the enzyme nitric oxide synthase (NOS), which converts L-arginine to nitric oxide. This leads to vasodilation, which can moderate hypertension, improved coronary endothelial function, and increased coronary blood flow. In addition to increasing nitric oxide, there is some evidence that L-arginine decreases the activity of the angiotensin-converting enzyme (ACE). Theoretically, this could have benefits in interrupting the progressive nature of congestive heart failure. Patients seem to have improved kidney function and increased fluid elimination. Many demonstrate improved functional status, exercise tolerance, and quality of life.

Dimethlglycine

N,N-dimethylglycine (DMG) is an important amino acid that has been shown to support the cardiovascular system as well as a broad range of immune functions. DMG improves circulation, hypertension, detoxification, and physical performance in stressed animals. It has been found to increase cellular energy and, improve oxygen utilization which are important for cases of heart failure characterized by insufficient cardiac output. DMG enhances both humoral and cell mediated immune function. It can act as a "metabolic enhancer" by supporting transmethylation pathways via SAMe, as an indirect methyl donor. DMG has been studied extensively and has shown a positive effect on stamina and endurance due to its ability to reduce lactic acid build-up. DMG has been found to be especially helpful in boosting vitality and mobility in older dogs.

Coenzyme Q 10

Coenzyme Q10 is a fat-soluble quinone, found in the inner mitochondrial membrane, where it acts as a membrane stabilizer and a free radical scavenger by suppressing the formation of reactive oxygen species during lipid peroxidation that occurs in the pathogenesis of degenerative heart disease. It protects heart tissue from functional and structural changes resulting from ischemia and reperfusion. CoQ10 is essential to a number of cellular processes, including synthesis of adenosine triphosphate (ATP). It acts as an electron carrier in respiration and oxidative phosphorylation. CoQ10 appears to be the first therapy that significantly improves the strength of myocardial contraction and maintains this improvement over months to years. No conventional cardiac drugs can biochemically substitute for CoQ10 because of their different organic structure. CoQ10 was found to enhance cardiac output by exerting a positive inotropic effect upon the myocardium as well as mild vasodilation. They also noted that in some studies CoQ10 was also shown to exhibit an antiarrhythmic effect.
Supplementing the diet of dogs which had experimentally-induced congestive heart failure with CoQ 10 was found to decrease hypertrophy and reduce myocardial injury. Maintaining adequate myocyte nutrition and enhancing myocardial function by dietary addition of CoQ 10 in cases of canine heart disease can be important in decelerating disease progression and improving overall heart health. Clinical improvement appears to be directly related to the use of higher doses of CoQ 10.

Berberine

Berberine (BBR) is a flavonoid contained along with isoquinolone alkaloids, including berberine, hydrastine, and sanguinarine, which are found in herbs such as barberry, Oregon grape root, goldenseal, and bloodroot. Among the actions of these alkaloids: antimicrobial, antioxidant anti-inflammatory, inotropic, and antineoplastic. Berberine can be extracted from the root of the coptis chinensis plant. It has traditionally been used as a natural remedy against candida and other yeast infections, and both viral and bacterial infections Two of its main uses are to treat skin inflammation, and to reverse inflammation. Berberine may also have an effect on immune cells in the body, as it has been shown to prevent and suppress some proinflammatory cytokines. A

recent study from Nanjing Medical University has indicated that Berberine - a natural extract found in Berberis (Goldenseal) (and in Coptis chinensis) has the potential to help overcome the problems in ensuring bone marrow stem cells stay alive after they have been transplanted. It has been reported that berberine is valuable for long-term treatment of ventricular premature beats (VPBs) and leads to a decrease in mortality for patients with congestive heart failure (CHF). berberine improved quality of life and decreased VPCs and mortality in patients with CHF. Berberine has been found to reduce platelet aggregation, possibly by inhibiting the arachidonic pathway. In addition, a 2004 study showed berberines to be effective in lowering serum cholesterol and triglycerides, by a mechanism different than statins.

Hawthorne (Crataegus spp.)

Hawthorne (Crataegus oxycantha) has been used traditionally as a cardiac therapy since the first century A.D. and is currently used as a cardio-tonic for a variety of functional heart disorders. Recent research shows Crataegus extracts exert a wide range of positive actions on heart function, due primarily to its flavonoid content, particularly the oligomeric proanthocyanidins (OPCs), which are highly concentrated in the leaves, berries, and flowers, and act as antioxidants. These flavonoids have very strong vitamin P (also known as citrin bioflavonoid) activity, and work synergistically with vitamin C to promote capillary stability by improving collagen integrity. Other constituents of Crataegus include quercetin, quercetrin, triterpene saponins, vitamin C, and several cardioactive amines. Hawthorne has been shown to reduce oxidative stress in reperfused myocardium and appears to inhibit apoptosis, resulting in a cardio-protective effect. It has been shown to increase coronary blood flow, and enhance oxygen flow and utilization by the heart, has positive inotropic effect on the contraction amplitude of myocytes, is cardiotropic and vasodilatory. Crataegus exerts mild blood pressure-lowering activity, which appears to be a result of a number of diverse pharmacological effects. It dilates coronary vessels, (18) inhibits ACE, (19) acts as an inotropic agent, (10) and possesses mild diuretic activity. Crataegus also prevents elevation of plasma lipids, including total cholesterol, triglycerides, and LDL- and VLDL-fractions and prevents the accumulation of cholesterol in the liver by enhancing cholesterol degradation to bile acids, promoting bile flow, and suppressing cholesterol biosynthesis. A study in mice investigated the mechanism behind hawthorn flavonoids' effect on blood lipid levels and found they significantly up-regulate adipogenesis gene expression and modulate both lipogenesis and lypolisis, resulting in decreased blood lipid concentrations.

Crataegus provides effective and low-risk phytotherapy for patients with coronary heart disease, atherosderosis, hypertension, or hypercholesterolemia. Human patients with congestive heart failure have reported improvement in subjective symptoms, such as reduced performance, shortness of breath, and ankle edema. An added benefit is a trend toward reduced anxiety episodes, which is often observed in cardiac patients.

Magnesium

Magnesium is thought to have a direct cardio-protective effect in dogs with acute myocardial infarction due to its antiarrhythmic and antithrombotic actions. It is also believed there is a correlation between magnesium deficiency in dogs and the development of mitral valve prolapse, although this hypothesis is still under investigation. Intravenous magnesium sulfate can be a safe and effective antiarrhythmic intervention which should be considered more often in medical practice before resorting to pharmacological antiarrhythmic medications, as it causes a significant decrease in the number of ventricular ectopic beats, couplets, and episodes of nonsustained ventricular tachycardia. Iseri et al also noted that magnesium deficiency can induce coronary spasm and create an ischemic environment for ionic balance. They cited four double-blind randomized studies that have shown infusion of magnesium during the first 24 hours after acute myocardial infarction reduced the development of VT and ventrical fibrillation (VF). A 1997 double-blind study with 232 patients experiencing frequent ventricular arrhythmias, showed that

patients treated either with a relatively small dose of magnesium and potassium (only 50% above recommended minimum daily dietary intake) combination of oral magnesium and potassium, or with a placebo, produced a moderate but significant antiarrhythmic effect when compared to placebo. Bean et al in 1994 speculated that hypomagnesemia, like hypokalemia, may potentiate arrhythmias caused by catecholamine excess. They reported that acute administration of magnesium in normal dogs increased the arrhythmogenic threshold for epinephrine, further supporting the use of magnesium as an antiarrhythmic agent.

In CHF, chances are that there are concurrent low blood levels of magnesium because the disease depletes this mineral, as do diuretic medications. Patients with low magnesium had more severe symptoms, greater risk of kidney failure, and a one-year survival rate of just 45 percent. But for those with high levels, symptoms were milder and survival was 71 percent.

Potassium

There is abundant research demonstrating that several nutritional supplements help to significantly control ventricular arrhythmias. Magnesium therapy, coupled with potassium, usually brings about the most immediate improvement. The membrane and action potential of cardiac cells, including formation of tachyarrhythmias, is affected by the fluxes of sodium, potassium, calcium and magnesium ions. Iseri et al reported that a decrease in magnesium ions can induce triggered ectopic impulses, and a decrease in potassium ions can delay conduction of these impulses to set up reentrant tachycardia. In another review article, Iseri et al noted that in some cases when magnesium was used to successfully abort the recurrence of VT and VF, serum potassium levels decreased. When potassium was added to the regimen, control of arrhythmias was made more effective. In a separate report, Iseri noted several cases where serum potassium and/or sodium levels fell precipitously during magnesium treatment. Potassium and magnesium supplementation should be considered even if serum levels are normal since serum magnesium and potassium levels do not necessarily reflect the levels of these elements within the myocardium.

The use of diuretics as the first-line treatment of hypertension and CHF is in question since diuretics are the most common cause of magnesium and potassium depletion. Furosemide use has been implicated in the development of hypokalemia due to increased urinary loss of potassium. Hypokalemia can contribute to arrhythmias directly and by potentiating the arrhythmogenic effects of digitalis toxicosis. Hypokalemia occurs infrequently in animals with cardiac disease but the increased use of angiotensin converting enzyme (ACE) inhibitors, which decrease potassium excretion, makes hyperkalemia a possibility. Many commercial diets designed for animals with cardiac disease have increased concentrations of potassium so monitoring serum potassium concentrations for both increases and reductions is important.

Folic Acid

Folic acid has remarkable antioxidant potential which can promote activity of nitric oxide synthase in oxidatively stressed endothelial cells. Folate likely has comparable activity in cardiomyocytes which can reduce the extent of cardiac tissue death. Folate treatment can help to preserve bioenergetic status and efficient cardiac function during the ischemic phase of a cardiac event, perhaps by preserving cardiac mitochondria and thus, may have outstanding potential as a myocardial antioxidant in the face of cardiac remodeling. Folic acid and vitamin B12 supplementation improve vascular endothelial function in patients with coronary heart disease, possibly as a result of reduced blood levels of homocysteine.

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