

DCM Study Review

by Chelsea Kent April 11, 2021

Summary:

“Board Invited Review: Review of canine dilated cardiomyopathy in the wake of diet-associated concerns,”

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“Confounding variables and lack of controlling for independent variables can introduce bias and suggest a correlation when none exists.”

Incidence of heart disease:

“Despite no definitive correlation for grain-free diets or their ingredients to DCM, some veterinary cardiologists and researchers are recommending pet owners switch their dogs to grain-based diets, without exotic protein sources and avoiding boutique brands. Yet, others state there is insufficient evidence-based research on whether diet is the cause for the subjective claims.”

Requirements for an effective review of data:

Sampling bias* – “Regardless of what diet the dog is eating, asking the veterinary community and the public for DCM cases in dogs only eating grain-free or exotic protein diets will result in sampling bias.”

Diagnostics** - “Echocardiography is necessary to definitively differentiate DCM from other cardiovascular diseases. It is important to note that a normal ECG does not rule out the presence of DCM, as most arrhythmias are intermittent and have high day-to-day variability.”

“In 2018 a longitudinal study was noted for having one of the largest sample size populations that assessed taurine concentration in Golden Retrievers. ... (implemented treatments included) a diet change, administration of supplemental taurine, with or without L-carnitine, inotropic agents, diuretics, ACE inhibitors, and calcium channel blockers. **Despite inconsistencies**, the study concluded that taurine supplementation could slow down the progression of DCM in dogs fed commercial diets. **Since not all dogs received the same treatment, determining which variables had any**

75% of cardiovascular disease in dogs is chronic degenerative valve disease

The 2nd most common cardiovascular disease in dogs is DCM

0.5%-1.3% of all dogs suffer from a form of cardiovascular disease

“A review of the current literature reveals gaps within DCM studies in dogs, including:

- *Sampling bias,**
- *Inconsistencies in sampling parameters, - Confounding variables,*
- *Lack of complete data for case studies in DCM, and*
- *Known genetic predisposition in certain dog breeds.”*

Additional, generally unmet, scientific requirements include:

- *Knowledge of the incidence*
- *Clinical manifestations, complete medical records (identify confounding variables)*
- *Diagnostics***

- *Potential treatment required and*

standardization of treatments (diet,

supplements, pharmaceuticals) provided

- *Knowledge of duration of previous diet - Use of a single laboratory for analyzing blood parameters to prevent the use of*

different reference ranges

- *Analysis of one variable at a time*

correlations to these improvements can be challenging if not impossible.

Scientifically proven contributing factors to the development of DCM and Heart Disease:

“Prevention of non-inherited cases of DCM is difficult in most cases,

as arrhythmias, infectious disease, and hypothyroidism are not preventable.”

Hypothyroidism and Endocrine Disease – “Thyroid hormones regulate key proteins involved in positive cardiac ionotropy and chronotropy. Clinically hypothyroid dogs may have decreased systolic function, low QRS voltages, weak apex beat, and sinus bradycardia due to poor hormone regulation. Thus, hypothyroidism can lead secondarily to DCM.” Large amounts of “spinach, cassava (tapioca), peanuts, soybeans, strawberries, sweet potatoes, peaches, pears, broccoli, brussels sprouts, cabbage, canola, cauliflower, mustard greens, radishes and rapeseed have properties that suppress the function of the thyroid gland, increasing the risk of hypothyroidism.”

Myocarditis (Infectious/inflammatory insults) – “Myocarditis in humans and dogs is commonly viral in origin. Myocarditis is reported in cases infected with Parvovirus, *Borrelia burgdorferi* (Lyme disease), *Bartonella*, *Trypanosoma cruzi*, *Neospora caninum*. In many cases of suspected myocarditis, the source of infection is not identified.”

Genetics - Dystrophin (DMD) in German Shorthair Pointer’s, Striatin (STRN) in Boxers, Pyruvate Dehydrogenase Kinase 4 (PDK4) and a locus on chromosome 5 in Dobermans

Elevation of Cardiac Troponin-I (cTnI) as seen in Doberman Pinscher research.

Chronic Tachycardia/ High Arrhythmic Load –“results in increased oxygen demand, decreased myocardial blood supply, loss and eccentric hypertrophy of myocytes, abnormal calcium handling and reduced ATP production.”

Results of laboratory analysis done by Know Your Pet Food, an initiative of Paws for Change, found the following Amino Acid results in five (5) randomly selected consumer accessible dry kibble dog foods:

Natural Balance (grain-free) – Lowest in Cysteine/Taurine, #2 in Methionine

Purina Pro Plan (grains) – Highest in Cysteine and Methionine

Royal Canin (grains) – 2nd lowest in Cysteine, Moderate in Methionine

Taste of the Wild (grain-free) – Mod. Cysteine, 2nd lowest in Methionine **V-Dog** (Vegan, grains) – 2nd highest in Cysteine, Lowest in Methionine

Methionine & Cysteine Deficiency – “these Sulphur containing amino acids are used to synthesize taurine. Deficiencies of these amino acids may occur from poor bioavailability of ingredients, degradation during high-heat processing (as is done with most kibble and canned pet foods), or failure to add sufficient supplementation to a diet. One study demonstrated that dogs eating diets containing such as animal “meals” (rendered meats), turkey, whole grain rice, rice bran or barley had low plasma methionine and cysteine concentrations.”

Choline deficiency – “As a methyl donor, choline is important for the regeneration of methionine from homocysteine. When choline stores are deficient, the capacity to methylate homocysteine to methionine is diminished resulting in increased plasma homocysteine concentration. Elevated homocysteine concentrations are associated with increased risk of cardiovascular diseases in humans.”

Taurine deficiency – “While Taurine is not currently considered an essential amino acid in dogs, it is considered an essential amino in cats. This is due to cats having a lower activity of cysteine sulfinic acid decarboxylase affecting the biosynthesis of taurine. Studies evaluating if taurine should be considered an essential amino acid in dogs have not been conclusive. Studies have found that breeds that are predisposed to DCM often have normal taurine concentrations, indicating that taurine was not contributing to the development of DCM. Currently, studies suggest that there may be breed-specific taurine concentration reference ranges and that one range cannot be applied across all breeds. Certain breeds are more associated with

taurine-deficient DCM than others.”

Carnitine deficiency – “Carnitine is ... synthesized endogenously in the liver. Carnitine assists in the transport of long chain fatty acids from the cytosol to the mitochondrial matrix; once inside, it undergoes beta-oxidation to generate energy. Roughly, 60% of the total energy production for the heart is through beta-oxidation. Carnitine also plays an important role in the buffering of toxic levels of acyl CoA in the mitochondria to allow beta-oxidation to continue. Therefore, deficiency in carnitine could cause cardiac dysfunction leading to cardiac diseases, including DCM.

Results of laboratory analysis done by Know Your Pet Food, an initiative of Paws for Change, found the following mineral/heavy metal results in five (5) randomly selected consumer accessible dry kibble pet foods:

(Products tested were as follows – Purina Pro Plan Chicken/Rice (contains grains), Royal Canin GI Low-Fat (RC) (contains grains), Taste of the Wild Pacific Stream (TOTW) (grain-free), Natural Balance Sweet Potato/Fish (NB) (grain-free), V-Dog Vegan (contains grains))

Selenium – All of the products tested contains Sodium Selenite. None of the dry kibble products tested contained detectible levels of Selenium.

Copper deficiency – “Copper is necessary in the production of hemoglobin, myelin, and melanin, as well as maintaining the strength of blood vessels, epithelial tissue and connective tissue. Thus, deficiency in copper can have detrimental implications for cardiac function. The effects of copper deficiency range from anemia, CHF, myocardial necrosis, calcification, and cardiac hypertrophy. Research into relative copper deficiencies which **could be caused by excessive dietary zinc or iron** and the correlation with potential copper deficiency and cardiac health in dogs.”

Scientific literature notes that iron intake in excess of 60mg/kg can result in severe toxicity and lead to severe morbidity and mortality in humans (AAFCO indicates that no studies have been done in dogs).

Therefore, **toxic levels of iron were found in as little as 1.8oz of Natural Balance (1/2 cup) to 9.4oz of Purina (2 ¾ cups).**

Iron Toxicity – Ho-Wang Yuen; Wenxia Becker, 2020

<https://www.ncbi.nlm.nih.gov/books/NBK459224/>

Vitamin E and Selenium deficiency – “Vitamin E works with the selenium-containing enzyme, Glutathione Peroxidase, to scavenge free radicals & prevent oxidative damage to polyunsaturated fatty acids. Dogs with DCM have significantly lower vitamin E concentrations and reduced glutathione peroxidase, which is involved in cysteine synthesis when compared to healthy dogs. Selenium is more available in its organic forms, seleno-cysteine & seleno-methionine, rather than the inorganic form, selenite. Selenium deficiency increases the occurrence of myocarditis and cardiomyopathy in mice exposed to both virulent and avirulent Coxsackie virus due to reduced glutathione peroxidase. Thus, glutathione peroxidase may protect against virally induced cardiac inflammation because reactive oxygen species may enhance viral replication.”

Copper –

AAFCO requires a minimum of 7.3mg/kg of Copper Purina Pro Plan – 18mg/kg

Royal Canin – 16.5mg/kg

Taste of the Wild – 14mg/kg

Natural Balance – 31.5mg/kg

V-Dog – 24.5mg/kg

No tested products were deficient in Copper. However...

Zinc/Iron –

AAFCO requires a minimum of 80mg/kg of Zinc

AAFCO requires a minimum of 40mg/kg of Iron

Purina Pro Plan –

Zinc = 257mg/kg (3.2x min), Iron = 224mg/kg (5.6x min) Royal Canin –

Zinc = 242mg/kg (3x min), Iron = 281mg/kg (7x min) Taste of the Wild –

Zinc = 190mg/kg (2.4x min), Iron = 365mg/kg (9x min) Natural Balance –

Zinc = 170mg/kg (2x min), Iron = 1,200mg/kg (30x min)

Potassium deficiency – “decreased potassium intake can induce a taurine depletion that can contribute to cardiovascular diseases in cats. *50% of cats*

provided diets sufficient in supplemental taurine, but deficient in potassium, still developed DCM and thromboembolisms while those fed sufficient potassium did not.”

V-Dog –

Zinc = 170mg/kg (2x min), Iron = 301mg/kg (7.5x min)

Lead/Arsenic/Cadmium/Mercury –

Lead – Purina/TOTW – 84.9ppb, Royal Canin – 284ppb, Natural Balance – 303ppb, VDog – 140ppb Arsenic – Purina/Royal Canin/ Natural Balance – 176ppb, TOTW – 147ppb, VDog –

Heavy Metals – “Since Taurine detoxifies heavy metals, there is an increase in the demand, which may result in a taurine deficiency. More specifically, taurine depletion can occur during arsenic-induced cardiomyocyte viability, reactive oxygen species products, intracellular calcium, and apoptotic cell death. Taurine has also been observed to reduce cadmium-induced damages in murine hearts and hypothalamus. A similar effect is exhibited in rats with taurine and its hepatoprotective effects against mercury toxicosis.”

160ppb

Cadmium – Purina – 58ppb, Royal Canin – 84.7ppb, TOTW/Natural Balance – 52.9ppb, VDog – 66.2ppb Mercury – Purina and VDog – Not Detected, RC/TOTW/ NB – Detected under 10.7ppb

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Purina Pro Plan – (grain containing diet)

Carbohydrate – 45%

Fiber/Ash – 5.94% (stated maximum = 3%) Protein (includes vegetable/filler protein) – 32.22% (max 0.7oz “meat” per cup)

Fat – 11.01% (stated minimum = 14%)

Phytic Acid (antinutrient) – 5566mg/100g (5.6%)

Royal Canin GI Low Fat – (grain containing diet) Carbohydrate – 59%

Fiber/Ash – 6.39% (stated maximum = 3.6%) Protein (includes vegetable/filler protein) – 21.59% (max 0.4oz “meat” per cup)

Fat – 4.21% (stated minimum = 4.5%)

Phytic Acid – 3837mg/100g (3.8%)

Taste of the Wild Pacific Stream – (grain free diet) Carbohydrate – 47%

Fiber/Ash – 7.02%

Protein (includes vegetable/filler protein) – 27.08% (max 0.6oz “meat” per cup)

Fat – 12.01% (stated minimum = 15%)

Phytic Acid – 5014mg/100g (5%)

Natural Balance Sweet Potato& Fish – (grain free diet) Carbohydrate – 54%

Fiber/Ash – 9.73% (stated maximum = 4.5%) Protein (to include all vegetable/filler protein) – 20.7% (stated minimum = 21%)

(max 0.4oz “meat” per cup)

Fat – 7.48% (stated minimum = 10%)

Phytic Acid – 6289mg/100g (6.3%)

VDog Vegan – (grain containing diet)

Carbohydrate – 53%

Fiber/Ash – 7.8% (stated maximum = 5%)

Protein (to include all vegetable/filler protein) – 25.35%

(while this product should contain 0% meat, beef protein was detected in one lab analysis, likely due to cross-contamination)

Fat – 6.25% (stated minimum = 9%)

Phytic Acid – 5898mg/100g (5.9%)

Excessive Levels of Insoluble Fibers – “The GI tract has been identified as the primary location where sulfur-containing amino acids are metabolized... it has been demonstrated that certain dietary fiber, such as non-starch polysaccharides, are relatively nonfermentable and have anti-nutritive effects. This can lead to a decrease in sulfur-containing amino acids and result in nutrient deficiencies, such as taurine or carnitine.”

“(One) study hypothesized that diets, which were formulated to meet AAFCO requirements, may not actually be meeting the dogs’ nutritional needs due to fiber’s negative effect on nutrient absorption. Fiber can also influence fermentation by products from microbes in the hindgut and hinder reabsorption of taurine, even if taurine is biosynthesized in sufficient amounts. For example, fiber in the form of unrefined cereals, legumes, nuts, oilseeds, fruits and vegetables can reduce the absorption of fats and fat-soluble vitamins”

Tofu-based Diets – “While (tofu is) lower in protein, AAFCO requirements for protein were met. Tofu is made from soybean curd, which is low in sulfur-containing amino acids, devoid of taurine and may have contributed to the cause.”

Low-Protein Diets Designed for the Management of Urate Stones – “this may be due to low protein diets being low in essential and nonessential amino acids or vital precursors for carnitine and taurine synthesis.”

Cassava (tapioca) and cyanide – “Cassava is known to accumulate cyanogenic glycosides, cyanide. When cyanide is consumed, it is converted into thiocyanate, which requires sulfane sulfur from sulfur-containing amino acids during detoxification. There is an increased demand for sulfur containing amino acids during detoxification. This can limit the availability of sulfur-containing amino acids used to biosynthesize taurine and carnitine.”

Popular brands that use Tapioca (Cassava) – Nature’s Variety Instinct, Merrick, Eden, Petcurean Go!, Nutri Source, Earthborn Holistic & Zoic

<https://petfoodreviewer.com/tapioca-in-dog-food/>

Phytic Acid can bind to necessary minerals and block enzymes, leading to digestive trouble or mineral deficiencies. Mineral deficiencies can result in pain syndromes similar to fibromyalgia. Despite some potential antioxidant properties, it is recommended that intake is limited to 100-400mg per day.

Of the 5 kibble products tested by Know Your Pet Food, Phytic Acid levels averaged 5,321mg per cup of food.

<https://www.integrativepainscienceinstitute.com/> - Phytic Acid – Top Reasons to Avoid this Anti-Nutrient

Where FDA publications have failed the public and vets:

“The use of the acronym “BEG” (Boutique, Exotic, Grain-Free) and its association with DCM are without merit because there is no definitive evidence in the literature...it is impossible to draw any definitive conclusions... linking specific diets or specific ingredients to DCM.”

“Descriptors of pet foods implicated to have a subjective association with DCM are diets with specific characteristics, such as, but not limited to, containing legumes, grain-free novel protein sources and ingredients, and smaller manufactured brands. However, an exhaustive review of the literature provides evidence of conflicting information. For example, boutique diets, defined as produced by a small manufacturer, have been implicated in association with DCM. However, when the FDA report is broken down into which pet food manufacturers made the called-out diets, 49% of the brands listed were made by one of the six largest pet food manufactures in North America. Given that almost half of the brands listed on the FDA report on June 27, 2019, are not manufactured by boutique pet food companies it is unlikely that an association can be made to DCM.”

Breeds prone to DCM regardless of diet:

DCM in dogs is more prevalent in males than in females

DCM is also a disease of middle aged to older dogs

Doberman Pinschers Irish Wolfhounds

Great Danes

“The FDA ... lists the top seven proteins of the implicated diets: chicken, lamb, salmon, whitefish, turkey, beef and pork. These comprised 75% of the diets named in the FDA report which are not exotic pet food proteins... suggesting exotic protein sources may not lead to the development of DCM.”

“(One) study concluded that *whole blood taurine concentrations were lower in dogs fed whole grain diets, such as rice bran and barley*, while another study observed that beet pulp, rather than rice, had a greater impact on lowering the concentrations of plasma and whole blood taurine. This suggests that these

Boxers

American Cocker Spaniels

Bulldogs

Golden Retrievers

ingredients are likely not a cause of the taurine-deficiency in dogs. However, the FDA has currently raised concern for diets that contain legumes as one of the top seven ingredients. According to the FDA’s 2018 report, lentils, peas, and other legumes (pulse ingredients) have been speculated to be responsible for diet-associated DCM. However, *this hypothesis may be unsupported by evidence-based research*. In a study conducted at the University of Illinois, in a controlled environment, dogs were fed 45% legumes or fed a diet primarily comprised of poultry byproduct. Interestingly, over the 90-d study, there was no significant difference when comparing plasma amino acids between groups. Additionally, comparing the plasma and whole blood taurine concentrations between groups was not significantly different. Therefore, since there was no change in taurine concentrations with dogs being fed a diet containing 45% legumes, legumes are more than likely not a cause of taurine deficient DCM.”

Saint Bernards

Airedale Terriers

Newfoundlands

Scottish Deerhounds English Cocker Spaniels

German Shorthair Pointers

A 2020 publication on DCM “was not well-controlled from a nutritional standpoint. The study evaluated two groups: traditional diets and non-traditional diets; however, the non-traditional diet group was comprised balanced AND those used only for supplemental feeding, which are

not formulated to meet AAFCO requirements. Furthermore, the majority of the dogs eating the non traditional diets did not have low taurine or abnormal cardiac parameters. Moreover, not all dogs with decreased systolic function had low taurine concentrations, and the relationship between whole blood taurine, plasma taurine, and cardiac muscle taurine concentration remains unknown.”

“In recent FDA reports, of the 340 dogs’ medical records reviewed, 202 (only 36%) had a definitive diagnosis of DCM, confirmed by an echocardiogram. The FDA Vet-LIRN states that 176 (only 31%) of the dogs diagnosed with cardiovascular disease had taurine measurements and echocardiograms. However, the report does not provide details on whether it has been suggested that whole blood taurine may be more indicative of the actual taurine status of the dog than plasma taurine.” Further, “the FDA reports do not have complete medical records and diet histories for all dogs... of the 515 dogs,

14 dogs(only 2.7%) have provided initial samples for the 1 to 2-mo follow-up. 44% of DCM diagnosed dogs had concurrent conditions which can lead to the development of cardiovascular diseases. 15% of the dogs had valvular degeneration, 12% had atrial fibrillation, 9% had hypothyroidism and 8% had Lyme disease. 61% of dogs with chronic valvular disease or DCM have another concurrent condition... therefore, dogs with these conditions... should not be included. *The information cannot be properly analyzed if a case report does not contain all required information, therefore, it should not be included in studies.*”

“In the FDA report, 13 (4%) of the dogs were reported “unknown breed”, 62 (20%) mixed breeds, and the remaining were named by breed. Of the 305 dogs that had breeds listed 223 (73%) were identified as a breed predisposed to DCM...(leaving only 3% of dogs that could effectively be analyzed for “new” or “abnormal” DCM cases) overrepresentation and breed reporting bias possibly inflated the number of reported cases. An increase in

A study done on 64 dogs with DCM showed that only 24 (37.5%) had blood samples submitted, only 14 (22%) of those had low taurine and 6 were DCM prone breeds. 100% of the taurine deficient dogs were consuming lamb & rice diets, 8 (67%) of which were consuming the exact same product. Yet, all boutique brand products are villainized as potential causes of DCM.

reports due to awareness or concern regarding diet history and veterinarians knowledge of predisposed breeds resulted in reporting bias and overrepresentation. To further understand incidence rate and if there is a

possible increase in DCM, multi-clinic, retrospective studies are warranted to identify a percentage of the population seeking referral to diagnose DCM, the incidence in specific breeds, and diet history, comparison to market share.”

Limiting factors in research:

“Difficulty of antemortem testing of the myocardium and out of pocket cost to screen for nutritional deficiencies and infectious agents.”

“Most definitive diagnoses in dogs are obtained through postmortem histopathology. Due to limitations in definitive testing modalities in dogs, myocarditis is suspected to be underrepresented as a cause of DCM.”

To read the full report, see:

Required tests to effectively diagnose cardiac disease:

- 25-h Holter monitoring
- Comprehensive thyroid panel (T3, T4, TSH, TPO) - cTnI concentration
- Infectious disease testing
- L-Carnitine (free, total and carnitine ester concentrations) - Plasma and Whole Blood Taurine
- hs-CRP
- Homocysteine
- Mineral/Heavy Metal Analysis (HTMA Test ParsleyPet.com)

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