Development and Management of Canine Adverse Food Reactions and its Connections to the Grain-Free Dog Food Movement

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Abstract

Canine Adverse Food Reactions include immunologically-mediated food allergies as well as non-immunological food intolerances. Although popular belief holds grains are responsible for AFR, the majority are aggravated by the common protein sources found in commercial dog foods. Elimination diets, a time-intensive method in which suspected allergens are removed from the dog's diet, are the most effective form of diagnosis, though alternative techniques including patch testing and serum antibody tests have been explored. Presently, avoidance of allergens is the recommended management approach. The erroneous association of grains with AFR has led to the rise of grain-free dog food. However, these nontraditional diets have been connected with a surge in diagnoses of dilated cardiomyopathy, hinting at a detrimental nutritional deficit.

Keywords: adverse food reactions, grain-free, veterinary medicine, food allergies, dogs

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Introduction

A few decades ago, tossing the dog a chicken bone or filling his bowl with table scraps was no cause for concern. Any itching or diarrhea that followed was likely attributed to fleas or a raided garbage can and quickly forgotten. However, it is now a different era of veterinary medicine, one in which owners are far more conscientious as to what they feed their pets, and veterinary researchers diligently work to understand canine nutrition and the many associated medical conditions. In fact, one of the most common issues faced in private veterinary practice is directly related to food—Adverse Food Reactions (AFR), often referred to as food allergies or food intolerances. It is believed up to 25% of dogs with existing skin conditions may suffer from AFR (Pali-Schöll et al., 2017; Olivry & Mueller, 2017), which most commonly manifests in the gastrointestinal and integumentary systems and serves as a leading cause of canine Atopic Dermatitis.

The customary approach to treating Adverse Food Reactions is diagnosis through an elimination diet, followed by strict avoidance of known allergens. However, this process is time-intensive and heavily dependent on owner compliance (Martín et al., 2004). Further complicating proper responses to the condition is the rise of grain-free diets, colloquially believed to mimic the ancestral diet of wild canines and reduce the occurrence of allergies. Unfortunately, the most frequent aggravators of AFR are not grains, but the protein sources—such as chicken, beef, and lamb—that serve as the backbone of the majority of commercial pet foods. Furthermore, the elimination of grains from dog food has created unexpected nutrient deficits, leading to a rise in deadly conditions such as dilated cardiomyopathy. Misconceptions concerning the use of grains

in dog food, in addition to the widespread use of allergenic ingredients, have rendered it difficult for veterinary professionals to determine a cost-effective and efficient method for diagnosing and managing AFR while maintaining the nutritional integrity of commercially processed dog food. Though the pathology of AFR is poorly understood, researchers are continuing to explore the various traditional and experimental approaches to detecting and treating the condition in an effort to educate owners and aid dogs affected by the condition.

Effect of Domestication on Dog Digestion

Dogs were the first animal man ever domesticated, remaining humanity's sole animal companion for several thousand years. Along with cats, they are the only animals not domesticated as livestock (Driscoll et al., 2009). It is widely believed that, when human tribes still lived as hunter-gatherers, wolves began to dwell near human encampments in search of food. Over time, the humans may have welcomed the wolves' presence as sentries and eventually hunting companions, leading to a naturally-selected breeding pool of wolves who were friendly toward humans. Artificial selection, however, would ultimately be the most important factor in the domestication of wolves, with humans raising wolf pups and controlling which animals bred, selecting for docility and other traits similar to those of modern dogs (Driscoll et al. 2009). Over the millennia, dogs have coevolved alongside their human caregivers, gradually separating themselves from their lupine ancestors. For example, dogs have retained noticeable paedomorphic (juvenile) features, which humans find appealing, thus enabling them to be more readily accepted in human homes (Nagasawa et al., 2015). Along with modified behavioral traits, modern dogs possess a number of physiological differences from wolves, including an enhanced ability to digest starches. Starch breakdown begins with cleavage by

alpha-amylase, which is present in human saliva. Canines, however, produce this enzyme only in the pancreas. A study published in *Nature* found that dogs produce an average 7.4 times more amylase than wolves, giving them a significant advantage in digesting starchy foods (Axelsson et al., 2013). Despite this, meat remains an essential part of the canine diet, and when offered a choice between animal- and plant-based proteins, both wolves and dogs consistently chose meat. Nevertheless, dogs are less discerning about their food sources and are content to scavenge, whereas wolves tend to hunt fresh meat (Rao et al., 2018). It is theorized that physiological adaptations favoring starch digestion, such as increased amylase production, enabled dogs to feed—and thrive—on human refuse, resulting in their reliance on humans for food (Axelsson et al., 2013).

Most commercial dog foods contain both animal and plant-based ingredients. A recent study published in the *Journal of Animal Science* compared the digestibility of various ingredients in two similar diets, one animal protein-based and the other vegetable (plant) protein-based. Although both diets met the nutritional standards of the Association of American Feed Control Officials (AAFCO), the researchers predicted the animal-based diet would be the more digestible, citing a similar study performed in pigs, another omnivorous domestic species. Interestingly, however, the study concluded animal- and plant-based diets are equally effective in providing adult dogs with essential minerals, which suggests dogs are as capable of digesting plant-based diets as animal-based (Cargo-Froom et al., 2019). Through domestication, dogs have adapted to thrive on omnivorous diets and are therefore not innately intolerant of either animal or plant-based foods. Nevertheless, food allergies in domestic dogs have become an issue

of increasing importance in the world of veterinary medicine, as has the perceived safety of plant-sourced ingredients.

Definition of Canine Adverse Food Reactions

Food allergies are extensively researched in the field of human medicine. Although a majority of studies are performed on laboratory animals such as mice, food allergies in companion animals remain poorly characterized. In dogs, immunologically-based food allergies and non-immunological food intolerances are often exceedingly difficult to distinguish from each other. As a result, they are collectively referred to as Canine Adverse Food Reactions, a condition typically characterized by the occurrence of dermatological or gastrointestinal symptoms. Nonseasonal pruritis (itching) is among the most common symptoms, with pruritis of the ears, paws, and ventral region being particularly characteristic of AFR (Hillier & Griffin, 2001). Other skin symptoms known to manifest in dogs with AFR include erythema (reddening) and self-inflicted wounds from scratching, which can result in infection. Typical gastrointestinal symptoms include diarrhea, increased defecation, vomiting, and flatulence. In up to 44% of dogs with AFR, dermatological and gastrointestinal symptoms appear concurrently (Mueller & Unterer, 2018). However, due to the broad variety of conditions with digestive and skin-related symptoms seen in dogs—both of which are among the most prevalent issues presenting in veterinary practices—the diagnosis of

Figure 1. Pattern of pruritis and erythema in dogs with immunological AFR. Irritation of these particular regions allows veterinarians to identify food-based allergens as the offending agent (Hensel et al., 2015).

AFR in animals experiencing gastrointestinal and/or dermatological symptoms can prove challenging.

Association with Atopic Dermatitis

Adverse food reactions are closely associated with the condition Atopic Dermatitis (AD), characterized by chronic erythema and pruritis. AD is the result of a genetic immune response to environmental or food-based allergens (Olivry et al., 2010), both of which result in identical symptoms, although the former is typically more common (Mueller & Unterer, 2018). Though considered separate conditions, AFR and AD often occur concurrently, and can therefore prove difficult to distinguish (Pucheu-Haston, 2016). This is particularly true in the absence of gastrointestinal symptoms, which are not associated with AD as with AFR. It is also believed dogs with AD are more susceptible to developing AFR, which can serve as a trigger for AD episodes (Olivry et al., 2007). However, as previously mentioned, environmental allergens are also known to aggravate AD (Hillier & Griffin, 2001), requiring an elimination diet—the "gold standard" test for AFR—to determine if the flareup is of environmental or food-based origin (Hardy et al., 2014). Many aspects of the connection between Adverse Food Reactions and Atopic Dermatitis remain misunderstood, with the conditions both intricately interwoven yet capable of presenting independently from one another.

Pathogenesis of the Allergy

Immune-mediated food allergies are found in approximately 8.96% of United States citizens. The epidemiology of the condition in dogs is less easily determined, due to the discrepancy between owner reports and official diagnoses. Nevertheless, AFR typically manifests in dogs younger than one year or older than six years. Certain breeds, including

German shepherds, West Highland white terriers, pugs, and boxers are more likely to develop AFR (Mueller & Unterer, 2018). Currently considered incurable, the pathogenesis of food allergies in humans is extensively studied, though far less is understood about its development in companion animals, including dogs. In humans, food allergies are directly linked to immunoglobulin E (IgE). The best understood mechanism of reaction occurs when the immune system encounters an allergen, launching B-cells which then class-switch to IgE antibodies. The antibodies induce the allergic response to the offending food item by binding effector cells, which release inflammatory agents upon exposure to the specific allergen. This results in the symptoms of an allergic reaction when the cells encounter the allergen in the future. Though the IgE pathway is the most common, a variety of other pathways is known to exist in humans, such as those involving other immunoglobulins or T cells. In some instances, a similar IgE response can be observed in dogs exposed to a known allergen (Pali-Schöll et al., 2017).

It was previously assumed dogs and other companion animals experience a similar mechanism (Mueller & Unterer, 2018). However, it has been demonstrated the presence or absence of IgE (or IgG) antibodies does not reliably predict the occurrence of an allergic reaction. An article in *BMC Veterinary Research* reported that two separate studies found food-specific IgE tests yield low repeatability, even when using the same blood sample (Mueller & Olivry, 2017). This suggests AFR is not always the result of an immune response. Similarly, a study of immunotherapy in treating AFR found, although IgE antibodies were high when a dog was exposed to an allergen, the antibodies were also present when the animal did not experience a reaction (Maina & Cox, 2016). Though IgE-mediated mechanisms may play some role in canine Adverse Food Reactions, it can be reasonably concluded they are not the chief source of

its development nor a reliable indicator of its occurrence. Therefore, the accurate pathogenesis of AFR remains to be discovered.

Diagnosis through Elimination Diets

As with human food allergies, formal diagnosis of canine Adverse Food Reactions is a lengthy and rather difficult process. The traditional method of diagnosis, still considered the most effective, is an elimination diet, in which the suspected allergen is removed from the animal's diet for a significant period of time. If the symptoms resolve, the allergen may be reintroduced in order to determine if the symptoms will return, strengthening the diagnosis (Martín et al., 2004). Elimination trials can last from 3-12 weeks, with 80% of dogs experiencing symptom absolution after 5 weeks. Continuing the diet for 8 weeks increases the percentage to 90%. The majority of veterinarians still employ elimination diets due to their reliability in determining the offending allergen (Olivry et al., 2015).

However, elimination diets present certain drawbacks. The method is extremely reliant on the compliance of the owner, as they will be solely responsible for monitoring the dog's food intake. In its ideal form, an elimination diet consists of a single protein source and single carbohydrate source homecooked by the owner. It is essential both food items have never been previously fed to the dog (Bethlehem et al., 2012). Although homecooked diets allow for complete knowledge of what the dog is ingesting, many owners are understandably avoidant of such a time-consuming approach. Furthermore, homecooked diets (particularly those consisting of only two ingredients) are often severely lacking in essential nutrients such as vitamins, minerals, and fatty acids and require extensive supplementation, adding to their inconvenience (Maina et al., 2018). As a result, many owners and veterinarians prefer commercial elimination

diets—specially formulated foods developed without traditionally allergenic ingredients. Other commercial foods use a hydrolyzed form of the allergenic protein, which is broken down into small molecules typically undetectable by the immune system. Despite their convenience, commercial diets may contain "hidden allergens" further down the ingredients list, such as animal fat of unknown origin. Elimination diets produced in the same factory as non-hypoallergenic diets may become cross-contaminated, provoking a reaction in especially sensitive dogs. Dogs may also react to allergenic proteins that have been incompletely hydrolyzed—a risk of improperly manufactured commercial hydrolyzed diets (Maina et al., 2018).

Alternative Methods of Diagnosis

Despite the reliability of elimination diets, veterinary researchers continue to search for more convenient yet equally effective methods of diagnosing canine AFR. Serological tests which test for IgE/IgG antibodies to specific food allergens are widely used to diagnose food allergies in humans and have become increasingly popular in veterinary practice. However, some researchers have raised concerns about the tests' accuracy, as some dogs testing positive for an allergy to a certain food still experience symptoms even when the food is removed from their diet (Hardy et al, 2014). A study by the Royal Veterinary College compared the results of IgE and IgG food allergen tests between two different laboratories. Unfortunately, the results showed significant variation, despite testing the exact same dogs. For example, the dogs tested positive for IgE immunological responses to common animal-based allergens (beef, lamb, and cow's milk) up to 26 times more frequently at the first laboratory than the second. Likewise, the second laboratory reported IgE responses to plant-based allergens (corn, wheat, soy, and rice) up to 6

times more frequently than the first laboratory (Hardy et al., 2014). Such discrepancies could potentially result in false diagnoses of AFR, placing undue stress on the owner and dog, or prevent a proper diagnosis from being made, resulting in continued suffering for the patient. Furthermore, as previously noted, not all cases of AFR are immunologically mediated, in which cases antibody tests would be entirely ineffective (Bethlehem et al., 2012).

Another alternative diagnosis approach is patch testing, in which the suspected allergen is applied to an exposed portion of skin to determine if a cutaneous reaction occurs. Although not a common method in human medicine, patch testing is attractive in veterinary medicine as it is a much more time-efficient process than elimination diets. A study published in *Veterinary Immunology and Immunopathology* explored the accuracy of patch tests when used alongside elimination diets and serum tests. The researchers concluded that although patch tests in dogs are highly *sensitive* (a term indicating minimal production of false negatives), they lack high *specificity* (indicating minimal production of false positives). Therefore, patch testing can be a useful tool in selecting appropriate ingredients for an elimination diet. For example, a dog which experiences no reaction to a chicken patch test will likely not need chicken removed from its diet; however, a dog which does experience a reaction to a chicken patch test cannot be safely diagnosed with a chicken allergy without elimination and later reintroduction of chicken to its diet (Bethlehem et al., 2012). A similar study concluded that patch testing is more accurate in

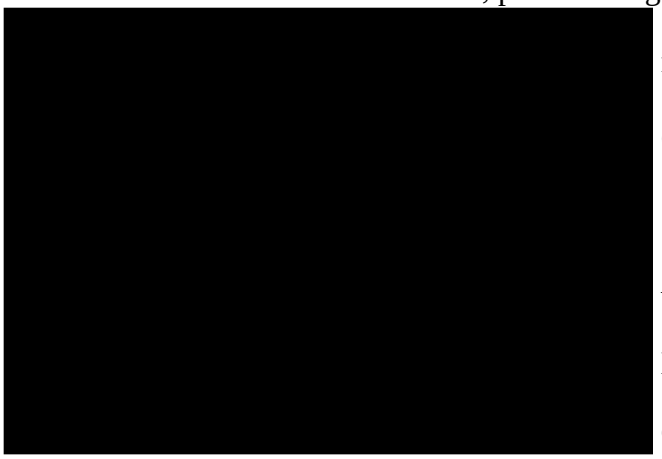

Figure 2. Application of a patch test to a dog in a study similar to that described in the text. (Sancak et al., 2009).

identifying allergenic proteins than allergenic carbohydrates and is not particularly effective in determining the allergenicity of commercial dog foods (Johansen et al., 2017). Although serum and patch testing offer promise as more convenient methods of diagnosing AFR, elimination diets currently remain the only trustworthy means of achieving an accurate diagnosis (Mueller & Olivry, 2017).

Managing AFR

Not only is an altered diet the most effective means of diagnosing Adverse Food Reactions, it also remains the best approach to managing the condition. In severe cases, anti-inflammatory drugs may be prescribed in order to combat extreme pruritus or irritated lesions, although this treatment will be ineffective long term if the dog's allergens are not removed from its diet (Olivry et al., 2010). Once the diet change is made, 90% of dogs achieve remission (Olivry et al., 2015). Although this management approach is simple in theory, preventing a dog's exposure to offending allergens can prove difficult for owners, who ultimately bear the majority of the responsibility for the diet's success (Martín et al., 2004). As with an elimination diet, only homecooked meals completely ensure that the dog does not come into contact with allergens, but these diets are time-intensive for owners and often not nutritionally complete. Commercial "limited ingredient" diets present challenges as well, as dogs may still react to unlisted or mislabeled ingredients or to the dyes and additives commonly found in processed foods (Olivry & Mueller, 2018; Maina et al., 2018).

The majority of commercial hypoallergenic diets use "novel" protein sources not commonly found in most dog foods. These proteins can include duck, salmon, and venison as well as exotic ingredients such as rabbit, bison, kangaroo, and wild boar. While in the past these

ingredients were reserved for prescription diets specifically designed for use in elimination diets or managing food allergies, recently they have become more commonplace, particularly in "boutique" brands of pet food (Freeman, 2018a). As a result, it is now considerably more difficult for owners and veterinarians to find commercial diets containing ingredients the dog has not yet been exposed to (Bizikova & Olivry, 2016). Hydrolyzed diets offer a solution to this issue. Although not without setbacks (as previously mentioned), properly manufactured hydrolyzed diets allow dogs suffering from AFR to consume diets containing allergens without experiencing a reaction. However, not all hydrolyzed diets yield the same results. A study by North Carolina State University College of Veterinary Medicine compared two different hydrolyzed diets—one containing hydrolyzed chicken liver and the other hydrolyzed chicken feathers—fed to client-owned dogs with known chicken allergies. While 40% of the dogs eating the liver-based diet developed pruritis, none of those eating the feather-based diet did (Bizikova & Olivry, 2016). Despite its difficulties, diet change remains the most highly recommended method of managing AFR.

Due to the difficulty of completely avoiding exposure to a dog's allergens, researchers continue to investigate alternative means of managing the condition. Among the most promising possibilities is immunotherapy, in which an individual is exposed to small amounts of an allergen, gradually increasing over time, in order to build a tolerance. Immunotherapy has been met with great success in human medicine, prompting

Figure 3. A dog participating in the study described below is administered a dose of allergenic concentrate as FA-SLIT (Maina & Cox, 2016).

veterinary researchers to explore its efficacy in combatting Adverse Food Reactions in pet dogs. Although the first recorded use of immunotherapy in a dog took place in 1941, only recently have researchers begun to explore its potential against canine AFR (DeBoer, 2017). Additionally, the few studies which have been performed have dealt with canine Atopic Dermatitis rather than AFR. A 2016 study performed in northern Italy was among the first to test the efficacy of food allergen-specific sublingual immunotherapy (FA-SLIT) in dogs diagnosed with AFR. Over 6 months, 13 client-owned dogs were administered small doses of allergen extract beneath their tongues. The dose concentration was increased every 2 weeks. Although 2 dogs were removed from the study by their owners due to symptom flares, those that completed it experienced noticeably less severe symptoms when exposed to their offending allergens. Unfortunately, total remission was not achieved, necessitating further studies with altered techniques and larger study pools before immunotherapy can be considered a viable treatment option (Maina & Cox, 2016). Nevertheless, this study displays the promise of immunotherapy as a simpler approach to managing—and potentially curing—AFR.

Are Grains the Source of Adverse Food Reactions?

Modern media has popularized the concept of a lasting evolutionary connection between wolves and dogs, leading many dog owners to attempt feeding their pets diets mimicking those of their wild ancestors. Phrases such as “grain-free,” “low carbohydrate,” and “ancestral diet” now frequently appear in advertising for commercial dog food brands. In fact, approximately 40% of current American dog food brands can be classified as grain-free (Pezzali et al., 2020). Though the association between wolves and dogs is reasonable due to their biological history, as previously noted, dogs have adapted to thrive on an omnivorous diet unique from that of wolves.

Unfortunately, many pet owners erroneously believe dogs are intolerant of non-meat ingredients and attribute Adverse Food Reactions to grain products such as corn and wheat (Coates, 2015). In truth, grain allergies are fairly rare in dogs. For example, corn—an extremely common carbohydrate source in commercial dog food—is considered relatively nonallergenic, particularly in the form of cornstarch. A 2018 study found cornstarch failed to elicit a significant allergic response even from dogs with known corn allergies, prompting the authors to propose cornstarch be considered a hypoallergenic ingredient relative to corn flour (Olivry & Bexley, 2018). According to a recent survey of 297 dogs diagnosed with cutaneous Adverse Food Reactions, the grains corn and rice were among the least common allergens, with 4% and 2% of the dogs reacting to these ingredients respectively. The most allergenic grain—wheat—induced an allergic response in 13% of the dogs. Fortunately, dogs allergic to wheat do not typically react to other grains, allowing them to continue eating grain-inclusive diets (Freeman & Heinze, 2012). Similarly, gluten intolerance, despite its pervasiveness in human medicine, is an extremely rare condition in dogs (Freeman et al., 2016). Resultingly, promotion of a dog food brand as “gluten-free” has little to do with the diet’s health.

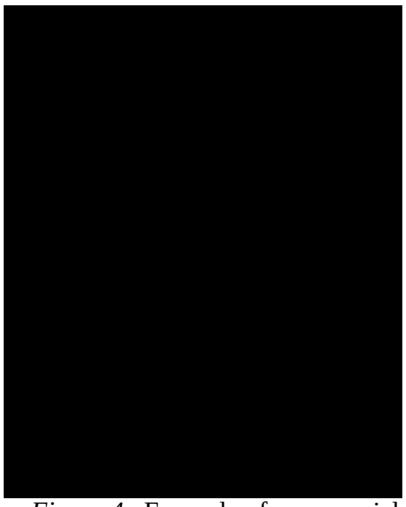

Figure 4. Example of commercial dog food advertising promoting the evolutionary link between dogs and wolves. (https://www.albertsons.com/shop/product-details.960497029.html)

In comparison, animal products such as beef (34%), dairy (17%), and chicken (15%) were noticeably more likely to result in an adverse reaction (Mueller et al., 2016). Furthermore, unlike with grain products, many cross reactions occur between animal-based allergens. Many of

these cross-reactions are a result of the close relationship between allergens—for example, dogs allergic to beef often react to cow's milk as well. Similar cross-reactions are seen between chicken and eggs or beef (or cow's milk) and lamb, as cattle and sheep are both members of the taxonomic family *Bovidae* (Bexley et al., 2017). However, though less common, cross reactions among unrelated allergens are not unheard of. A 2019 study published in *Veterinary Dermatology* found 49% of dogs challenged with chicken, white fish, and salmon experienced an IgE reaction against all three allergens, despite the seemingly significant divide between poultry and fish (Bexley et al., 2019) As both chicken and fish are widely used in commercial dog food, identifying a food containing neither poultry nor fish-sourced ingredients can prove difficult.

Alternative Starch Sources

Proponents of grain-free diets often consider grains to be mere filler products of no nutritional value to dogs. Additionally, some pet owners mistakenly believe dogs, as a result of their carnivorous ancestry, do not require the carbohydrates grain products provide. While true the majority of mammals, including dogs and humans, can survive without dietary carbohydrates due to gluconeogenesis, consuming carbohydrates remains extremely beneficial (Laflamme et al., 2014). According to Drs. Freeman and Heinze (2012) of Tufts University's Cummings School of Veterinary Medicine, dogs do, in fact, nutritionally benefit from the common grain ingredients found in commercial pet food. In addition to carbohydrates, grains provide dogs with highly digestible protein (including essential amino acids), fats, vitamins, and fiber (Laflamme et al., 2014). The label "filler" is therefore erroneous; since a food product's digestibility is heavily correlated with its nutritional value, the dog's enhanced ability to process starchy foods allows for the absorption of these nutrients. Although grains play an important role in the diet of modern

domestic dogs, the wariness many pet owners hold toward grain products prompts many pet food companies to seek grain-free starch sources. Increasingly popular grain substitutes in contemporary dog food include legumes and potatoes, the latter of which is considered more similar to the non-meat foods consumed by wild canines than traditional grains products. Interestingly, diets utilizing these ingredients are perceived as low-carbohydrate, despite containing approximately the same amount of carbohydrates as grain-inclusive diets (Laflamme et al., 2014). Furthermore, when grain allergies do occur in dogs, it appears due to the grain's protein content rather than the carbohydrates (Laflamme et al., 2014).

Potato starch is reportedly more digestible and palatable than corn, partly as a result of its lower density. Subsequently, potato is now considered an especially appropriate starch source for puppies (Domingues et al., 2018). Certain studies have determined diets utilizing potato allow for greater nutrient digestion than those containing grains. For example, a study performed on Labrador retrievers in a guide-dog training program found that dogs eating a potato-based, grain-free diet enjoyed increased protein and fat uptake and less loss of body mass than those eating conventional grains. The authors suggested that this sort of high-protein, high-fat diet may be particularly beneficial to working dogs, who face higher energy demands than pets (Chiofalo et al., 2019). However, not all researchers are in agreement. A study from Kansas State University, published in the same year, reported that laboratory beagles fed grain-free diets experienced lower nutrient utilization than those fed grain-inclusive diets. The Kansas State researchers theorized that the excessively high levels of fiber found in the grain-free carbohydrate sources may hinder the gastrointestinal tract from fully absorbing the available nutrients (Lopez et al., 2019).

The Danger of Grain-Free Diets

Unfortunately, a deeper issue than decreased digestibility exists in regard to grain-free carbohydrates. Taurine is an amino acid synthesized in the livers and central nervous systems of dogs and cats from the essential amino acids methionine and cysteine, which are obtained through the diet.. Though taurine has long been recognized as an essential nutrient in cats—with deficiencies known to result in dilated cardiomyopathy (DCM)—it was not until the mid-1990s that taurine deficiencies were also linked to the development of the condition in dogs (Kaplan et al., 2018). DCM, frequently seen in large, deep-chested breeds such as Doberman pinschers and Great Danes (Freeman, 2018a), is characterized by an abnormal enlargement of the heart's left ventricle, which eventually leads to a failure to properly pump blood. Unaddressed, DCM can result in death from congestive heart failure. Though a variety of factors can contribute to the formation of DCM, taurine has long been acknowledged as a dietary factor essential to preventing the condition's development (Pezzali et al., 2020). For many years, DCM was mainly observed in dogs fed improperly supplemented homemade or raw diets (Kaplan et al., 2018), and the number of occurrences appeared to be decreasing in the early 2000s. However, at that same time,

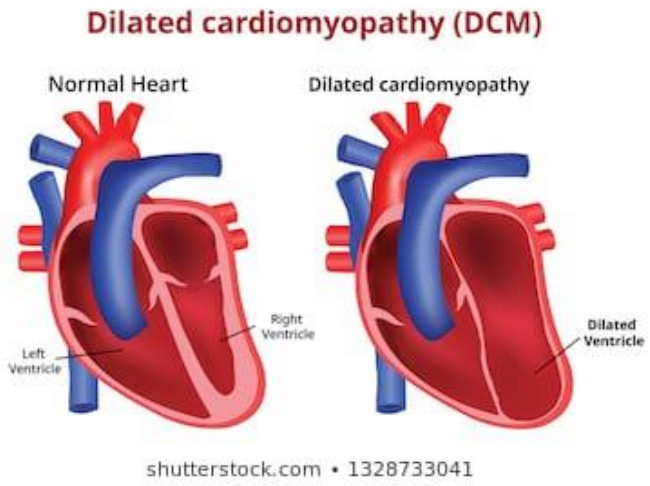

Figure 5. Normal heart vs heart with DCM, frequently associated with grain-free diets. Dilation of the left ventricle eventually results in congestive heart failure due to a decreased ability to pump blood. Taurine deficiency is closely associated with the condition's development. (https://www.shutterstock.com/image-vector/dilated-cardiomyopathy-heart-disease-vector-image-1328733041)

clinicians began observing a rise in the number of DCM cases in breeds not typically associated with the condition, such as golden retrievers, paralleling the emergence of the grain-free movement.

In 2018, the FDA issued a warning that shocked pet owners throughout the United States—grain-free diets, specifically those substituting legumes and potatoes for traditional grain ingredients, had been linked to the development of DCM in otherwise healthy pet dogs (Freeman et al., 2018). The same year, a concerning study by the University of California, Davis found that all 24 client-owned, DCM-diagnosed golden retrievers studied were fed grain-free/legume-rich commercial diets. Additionally, a significant percentage of the 52 healthy golden retrievers also surveyed—all of which were fed grain-free/legume-rich diets—were taurine-deficient. Encouragingly, however, 23 of the 24 dogs improved after receiving taurine supplements and switching to a grain-inclusive diet (Kaplan et al., 2018). A similar case was reported by the teaching hospital at the Cummings School of Veterinary Medicine in the same year. A 4-year-old mixed breed dog was presented with symptoms mimicking that of dilated cardiomyopathy. At the suggestion of the veterinary cardiologist, the dog was switched from a kangaroo and chickpea-based diet to one including grains. After the diet change and additional medications, the dog's symptoms resolved within five months (Freeman, 2018a). What aspect of grain-free diets leads to the development of taurine deficiency is not yet understood. Some theories include a dietary absence of the taurine precursor amino acids cysteine and methionine; loss of taurine through the urinary system; decreased bioavailability of taurine or its precursors; and abnormal taurine metabolism due to interactions between the food and intestinal microbiota (Freeman et al., 2018).

Safety of Grain-Free Starch Sources and Novel Proteins

Due to the public's concern for the safety of grain-free starch sources, particularly legumes, research groups have begun to launch studies into the issue. A study published in 2020 found laboratory beagles fed either grain-free or grain-inclusive diets—both of which were supplemented with taurine—did not develop a deficiency, suggesting legume ingredients are not responsible for suppressing the absorption of the nutrient (Pezzali et al., 2020). Presently, the consensus of veterinary professionals appears to be in favor of grain-inclusive diets, which not only lack the risks now associated with grain-free diets but are inherently more nutritious than many common substitutions. According to the USDA Nutrient Database, oats actually contain more protein, less sugar, and fewer carbohydrates than the grain substitutes potato and tapioca, despite the widespread opinion that grain-free diets provide more protein. Additionally, grain-inclusive diets are typically lower in caloric content, reducing the risk of obesity presented by high-protein, high-fat grain-free diets (Freeman & Heinze, 2012). While these diets may prove beneficial to workings dogs (Chiofalo et al., 2019), the average house pet does not engage in the amount of physical activity required to justify eating such energy-dense foods. The excessive fat and calorie levels found in grain-free diets frequently result in obesity and related health problems, as well as gastrointestinal upsets (Freeman et al., 2016). Finally, grain substitutes such as legumes are low in the sulfur precursor nutrients required for the canine body to manufacture taurine. Though all plant products naturally contain virtually no taurine, the plant ingredients traditionally found in dog foods serve as adequate sources of the precursors (Kaplan et al., 2018).

Non-grain starch sources, however, may not be the only culprit. The increasingly widespread use of novel protein sources in commercial dog food has created an obstacle for

veterinarians attempting to place dogs on diets containing ingredients they have not previously consumed. However, as questions concerning the safety of grain-free diets grow, researchers are left to consider the possibility that the exotic ingredients commonly found in such foods may be the source of the issue. Owners often turn to dog foods containing exotic ingredients believing them to be more holistic and healthy than those made from farmed meat such as beef or chicken (Freeman, 2018a). Researchers from leading veterinary schools including Tufts University, North Carolina State University, and University of California, Davis now theorize the rise of dilated cardiomyopathy in pet dogs is linked not only to grain-free diets but also to "boutique" brand foods and those containing exotic ingredients, collectively referring to them as "BEG" (boutique, exotic, grain-free) diets. Similar problems accompany homemade, raw, and vegetarian/vegan diets (Freeman, 2018b; Freeman et al., 2018). Although pet food marketing frequently claims alternative protein sources are safe and nutritious, exotic ingredients often have completely different nutrient breakdowns than more common animal products. The nutritional components of uncommon meats such as kangaroo or squid are not as widely understood as beef or chicken, making it difficult for pet food companies to devise formulas that allow for optimal utilization of the available nutrients (Freeman, 2018a). Additionally, certain exotic meats, such as rabbit, are naturally lower in taurine and other vital nutrients (Kaplan et al., 2018). Safe use of alternate proteins requires extensive research of nutrient bioavailability, digestion, and

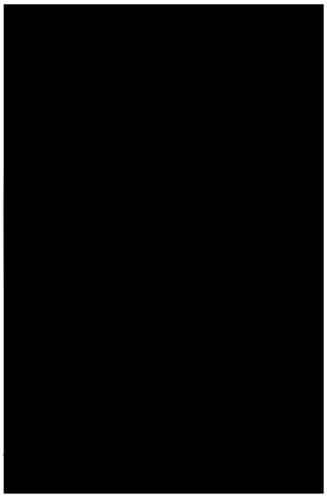

Figure 5. Example of advertisement for commercial dog food containing novel proteins. The slogans promise "holistic," ecofriendly nutrition free from grains. (https://www.earthbornholisticpetfood.com/dog-food-formulas/venture/venture-squid-chickpeas)

absorption the majority of boutique companies lack the resources to provide (Freeman et al., 2018).

Presently, many theories have been proposed as to what characteristic of grain-free diets leads to taurine deficiency and the onset of dilated cardiomyopathy. The absence of traditional grain products, presence of rich starches such as potatoes and legumes, and nutritional deficiencies resulting from the use of exotic proteins have all been discussed as potential factors. Interestingly, however, some dogs on BEG diets have been observed to develop DCM despite normal taurine levels. Nevertheless, these dogs improved on a new diet, just as dogs with a noted taurine deficiency. The researchers hypothesized BEG diets may result in deficiencies of other nutrients associated with cardiac health, including choline, copper, magnesium, thiamine, and selenium or that BEG diets include an as-of-yet unidentified cardiotoxic ingredient (Freeman et al., 2018). However, no theories have yet been proven, and extensive research remains to be performed before a credible answer to the mystery of both taurine and non-taurine associated dietary DCM can be determined.

Treatment of Diet-Associated DCM

As an incredibly new issue in the field of veterinary medicine, few studies have yet been published about treating diet-associated DCM or the long-term effects of the condition. The current recommendations, established by a collaboration of veterinary schools, begin with establishing taurine concentration through either plasma, serum, or whole blood. Veterinarians should make note of taurine concentrations that are “low-normal,” as this could indicate a deficiency is in development. If within the owner’s budget, baseline echocardiograms are also recommended. However, most essential to the diagnosis process is obtaining the dog’s complete

dietary history. This includes not only the specific brand and formula of the dog's commercial food, but also any treats, table scraps, and diet supplementations, as well as how much and how frequently the dog is fed. Other dogs in the household consuming the same diet should also be screened for DCM (Kaplan et al., 2018; Freeman et al., 2018).

Dogs determined to be taurine-deficient should be transitioned to a diet made from traditional protein and carbohydrate sources, such as chicken and rice. The diet ought to be produced by a reputable manufacturer, particularly those that employ veterinary nutritionists in designing their formulas. Taurine supplementation is required if the dog has been determined to be taurine deficient and could also provide benefits even if the dog's levels are normal, although some non-taurine deficient dogs have been observed to enter remission on diet change alone. If possible, a follow-up echocardiogram should be performed within 6 months of the diet change (Freeman et al., 2018). To date, diet change combined with taurine supplementation has been extremely successful in reversing the effects of diet-associated dilated cardiomyopathy. As previously mentioned, the pilot study out of UC Davis saw all but one of the 24 dogs in the study absolved of DCM symptoms. Furthermore, of the 11 dogs in the group in congestive heart failure, nine entered remission. Five of the nine were taken off furosemide, while the remaining four were able to remain symptomless at much lower doses (Kaplan et al., 2018).

Although much research remains to be done, the early results imply diet-associated DCM can be relatively easily reversed. Even more encouraging is the implication that the condition can be avoided entirely through proper nutrition. While many dogs remain perfectly healthy on grain-free, homemade, or other nontraditional diets, the risks associated with them may outweigh any potential benefits. The majority of dogs are completely capable of receiving high-quality

nutrition from traditional grain-inclusive diets. Novel proteins and grain-free starch sources, at the time, seem best reserved for veterinarian-approved diets meant only for dogs diagnosed with Adverse Food Reactions. Avoiding the feeding of nontraditional ingredients to healthy dogs will not only significantly decrease their risk of diet-associated DCM, but also make locating foods the dog has not been priorly exposed to much easier should the animal ever develop AFR.

Conclusion

Thousands of years ago, the wolf ancestors of modern dogs began adapting to life alongside human companions, gaining the ability to thrive on humans' omnivorous diets. The bond between humans and dogs has persisted ever since, and today more than ever dogs are viewed as more than working animals or pets, but as part of the family. Out of love and concern for their four-legged family members, many dog owners have grown wary of traditional dog food ingredients, particularly grains, largely due to wildly successful marketing by grain-free dog food manufacturers which suggest dogs need to eat diets similar to those "naturally" consumed by wolves. As a result, it has become widely accepted that grains in dog food result in food allergies.

However, canine food allergies—more properly referred to as Adverse Food Reactions—are rarely aggravated by grains. Canine AFR, which is closely associated with Atopic Dermatitis, can be immunologically mediated, although the pathogenesis of these and non-immune mediated reactions are currently poorly understood. Various methods of diagnosing AFR have been practiced, including blood serum antibody tests and patch testing. However, these approaches are largely unsuccessful, particularly when compared to elimination diets, a cumbersome but highly effective method that remains the gold standard for diagnosing AFR. Presently, canine AFR can

be successfully managed through strictly feeding a diet free from the dog's known allergens, although researchers continue to explore treatments such as immunotherapy to ease the burden on veterinarians and owners. Unfortunately, misunderstandings about Adverse Food Reactions lead many owners to feed their dogs diets rich in novel proteins and grain-free starch sources. This has not only limited the ingredients veterinarians can turn to in formulating elimination diets but introduced the problem of diet-associated dilated cardiomyopathy. Though research is ongoing, veterinary nutritionists and cardiologists believe the rise in DCM is due to taurine deficiency in grain-free dog foods and other alternative diets. In a nutrition-obsessed society, it is only natural that concern extends to our beloved dogs. Although much remains to be discovered, veterinary medicine continues to strive to provide man's best friend with the diets necessary to live happy, healthy lives.

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