

Diet Trials: The Forgotten Diagnostic Tool in Your Practice

MANAGING DOGS WITH FOOD ALLERGIES

A balanced diet provides nourishment. However, patients with food allergy develop an aberrant immune response to what typically are common dietary components and may exhibit dermatological and gastrointestinal clinical signs.

In this roundtable, experts in veterinary dermatology and gastroenterology discuss the impact of adverse food reactions, particularly food allergy, on canine health; the challenges of conducting elimination diet trials; and the role of therapeutic nutrition in managing dogs with food allergy.

DEFINING THE CONDITION AND ITS IMPACT

Dr. Jason Gagné: Let's start by defining some of the terminology we'll be using. Can you please share definitions for adverse food reaction, allergy and food intolerance?

Dr. Stanley Marks: An adverse food reaction is defined as any abnormal clinical response attributed to the ingestion, contact with or inhalation of a food, its derivatives, or an additive contained in it. Adverse food reactions have been classified according to their underlying mechanisms, including food intolerances, which have no primary immunologic basis; food toxicities; pharmacologic reactions; and food allergies, which have an underlying immunologic basis.

Dr. Craig Griffin: An allergy is a chronic condition involving an immune reaction, called a hypersensitivity, to an ordinarily harmless substance. An allergy can be caused by a food or by an aeroallergen such as a dust mite or weed, tree and grass pollens.

Dr. Alison Manchester: Food intolerance is a type of adverse food reaction and is defined as a non-immune reaction to a wide variety of different dietary components, including carbohydrates, fats or dietary additives. It also includes maldigestion or an idiosyncratic reaction such as a temporary inability to digest a food substance.

Dr. Gagné: What do we know about the prevalence of food allergy in dogs?

Dr. Galia Sheinberg: It depends on who you ask. We see discrepancies between published studies, and dermatologists themselves don't agree how common it is. Speaking for myself, I estimate that approximately 30% of my atopic patients respond to elimination diets.

Dr. Griffin: I agree that much of what is published is too low, and the reason may be that dermatologists are not always



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looking for it, especially partial responders. If you never do a diet trial, you won't find food allergy very much! Meanwhile, a single diet trial isn't always enough to rule it out. The prevalence of food allergy could actually be higher than 30%.

Dr. Sheinberg: Another factor is that sometimes we lose patients to follow up because they improve. We put them on a hydrolyzed elimination diet, they get better—and they never come back. Because we don't get the opportunity to challenge these patients, they're never completely diagnosed.

Dr. Gagné: What are the perspectives of the gastroenterologists in the group?

Dr. Manchester: As with dermatology, I think it's difficult to get a true handle on prevalence. It probably varies geographically. Wheat intolerance in humans is much higher in Italy, whereas shellfish intolerance is very common in Japan. I'm sure there is regional variation in our canine populations as well.

Week in and week out, I see animals being referred to our academic institution for chronic refractory enteropathies refractory to treatment. When I look through a dog's history, I see he has been prescribed medications like metronidazole,



Patients that exhibit subtle signs of allergy, such as paw licking, can be missed if owners don't realize the behavior is a sign of a problem.

tylosin and prednisone and undergone many fecal PCR panels—with no mention of the diet fed. Whatever diet “trial” he may have had was limited to feeding an easily digestible diet for a week. If the patient wasn't better by then, the clinician moved on.

Animals like these have often been going to the veterinarian for months to years. I think we need to do a better job of educating the veterinary profession about the significant potential for diet to help these animals.

CLINICAL PRESENTATION OF CANINE FOOD ALLERGY

Dr. Gagné: Let's move on to clinical presentation and diagnosis. Starting with the dermatologists, what is the typical presentation for dogs with food allergy?

Dr. Sheinberg: Non-seasonal itching and erythema of the skin, mostly along the ventrum, is common in these patients, although it can vary widely. Sometimes we see dogs with otitis or relapsing otitis as the only presentation. Most dogs with food allergy are younger than 1 year of age, although I diagnose senior patients with food allergy, too.

Skin disease that is concurrent with GI manifestations is frequently seen in food allergy patients. When we take a proper history and note that a dog has a host of skin problems and a history of either vomiting, diarrhea, or chronic GI trouble, it is a strong signal that we need to do a food trial.

As the disease advances, we also see chronic skin disease with secondary bacterial or yeast infections.

Dr. Griffin: I see numerous dogs that began getting ear disease when they were 6 months to a year of age; however, the owners learned that if they cleaned the dog's ears as soon as they started getting dirty, it could prevent ear disease. By the time these dogs are 5 years of age, they are exhibiting clear allergy signs. The owner thinks it is just starting, but in reality, the

problem began years earlier. If you don't ask owners about ear cleaning, you miss those cases.

Dr. Sheinberg: Patients also slip through the cracks because owners don't realize that certain behaviors are indicative of allergies. Paw licking is a good example. Owners simply live with their dogs licking their paws and don't realize it's a problem. As clinicians, we have to zero in on those signals and ask the right questions if we want to identify patients when they begin showing signs of problems.

Dr. Gagné: Does the location of skin lesions suggest food allergy vs. environmental allergy?

Dr. Griffin: There is some evidence in the literature that dogs with food allergy have a bit more dorsal lumbar involvement, but it's not true for every breed. If the dog's perianal area looks bad, food allergy typically moves higher on my list of differentials. However, we see perianal signs with both food and non-food allergies, so it's clear that looking at the pattern of lesions is not enough.

Dr. Gagné: Let's discuss GI signs. Do these go beyond vomiting and diarrhea?

Dr. Manchester: I try to keep an open mind and see the whole spectrum of GI signs as possibly being secondary to a food reaction. It can range from a loose stool once every two weeks to vomiting after breakfast three times a week to having difficulty putting on weight to constipation.

Dr. Marks: The GI manifestations of an adverse food reaction are broad, and approximately 70% of affected dogs have large bowel diarrhea or mixed bowel diarrhea signs. Vomiting can also be seen in affected dogs. Secondary manifestations of adverse reaction to food can include increased flatulence and borborygmi. Obtaining a complete GI history that includes determining the frequency of secondary GI signs in addition to concurrent pruritic behaviors is extremely important.

We also need to ensure that our questioning about the stool consistency does not lead to an inaccurate response because most pet owners equate diarrhea with a liquid or watery stool. I prefer to show owners a Nestlé Purina Fecal Scoring Chart and ask them to point to the image that most closely matches their pet's stool over the past week or two to avoid miscommunication.



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Dr. Alison Manchester



When food allergy is suspected, a comprehensive diet history that covers well pet and therapeutic diets, as well as treats, can aid in the selection of an elimination diet.

Dr. Gagné: How commonly do dogs with food allergy have concurrent dermatologic and GI signs?

Dr. Griffin: I used to tell people that 50% of dogs that have skin disease and are diet-responsive will have at least some sort of subtle GI sign. I still think that is true. A complicating factor is that by the time a number of dogs with skin disease make it to a referral center, they have already been on antibiotics and other medications; the GI signs are due to the treatments rather than the disease. To sort through this confusion, I ask the client whether there were GI signs in the history of that dog before a veterinarian may have begun using drugs to treat the skin disease.

Dr. Marks: Approximately 20 to 60% of food allergic dogs have concurrent dermatologic and GI signs, and the reason for the wide range is due to the inconsistent incorporation of secondary GI signs (flatulence, increased borborygmi) that are often ignored in the history. We know that the clinical signs associated with the gastrointestinal tract in food-allergic patients can be used as an indirect method for assessing the downstream effect of how the pruritic behaviors may or may not respond to that dietary intervention. If a patient's diarrhea has resolved within 7-10 days and the animal is still pruritic, I'm more optimistic that the pruritic behavior will be improved or resolved if the diet is continued for another 6-8 weeks.

Dr. Gagné: What do we know about the role of the GI microbiome in these disorders?

Dr. Marks: Without question, the intestinal microbiome plays an important role in early host immunologic development, and the colonization of a diverse microbiota in early childhood is necessary for the induction and maintenance of oral tolerance. In humans, a variety of epidemiological studies have linked environmental factors and intestinal dysbiosis to atopic risk. Examples include children living in rural environments around livestock and children with pets in the household. These

influences in infancy and childhood can have a profound effect on the downstream development of allergic disease involving the skin, respiratory, or gastrointestinal systems. The same is true for administering antibiotics to infants or young children—the intestinal dysbiosis induced by antibiotics shapes the innate and adaptive immune responses, increasing the development of atopy and asthma in adulthood.

Dr. Manchester: It's exciting that we are looking into this. The microbiome is a very important aspect of gut health, although our understanding is in its infancy. When I ask a student these days for differentials for diarrhea, dysbiosis is often one of the top three things they include. The question is what could have driven that dysbiosis in the first place?

THE INS AND OUTS OF CONDUCTING AN ELIMINATION DIET TRIAL

Dr. Gagné: How do you determine when a patient needs an elimination diet trial?

Dr. Griffin: The dog's history is critical for me. If a dog has year-round pruritus, pursuing food allergy is worthwhile. If he also has GI signs, it's foolish not to investigate it promptly. When I see a younger dog with a history of GI disease, I become concerned about food allergy.

Dr. Marks: Most dogs with food-responsive enteropathies are younger dogs with a median age of 3.4 years, with mild to moderate clinical signs and predominantly large bowel diarrhea. If the patient has the above-mentioned features, has a good appetite and has not lost significant body weight, I perform a centrifugation flotation to rule out intestinal parasites and empirically deworm the patient if the fecal is negative. I also start the dog on an elimination diet trial with explicit instructions to feed the diet exclusively with no treats for 10 to 14 days, which reflects the time during which I expect to see a marked improvement or resolution of the animal's diarrhea. The patient should return for a more comprehensive workup if the diarrhea has not resolved within two weeks following the diet trial.

Dr. Gagné: How do you select an elimination diet? Please discuss the advantages and disadvantages of home-cooked, limited-antigen/novel protein and hydrolyzed diets.

Dr. Sheinberg: A commercial hydrolyzed diet—preferably a vegetarian version—is usually my first choice, because it is a practical, complete, and balanced diet for most patients. Home-cooked diets are not my first choice because I find that many owners do not want to cook for their pets. Ensuring the diet is nutritionally balanced can also be challenging, especially with growing dogs. I do use home-cooked diets as a second choice if a pet won't accept a hydrolyzed diet or the patient was unsuccessful on a hydrolyzed diet.

Evaluating Traditional Diet Options for Elimination Trials

	Pros	Cons
Home-cooked Diets	<ul style="list-style-type: none">• Can be tailored for patients with concurrent disorders• Appealing to highly committed owners who want to feel involved	<ul style="list-style-type: none">• Often unbalanced unless formulated by a Board Certified Veterinary Nutritionist®• Owner must be committed to diet preparation and strict adherence (no ingredient substitutions)
Novel Protein Diets	<ul style="list-style-type: none">• Palatability aids diet acceptance• Cost may be lower than other options	<ul style="list-style-type: none">• Can be difficult to find truly novel protein sources for patients with varied diet history• Cross contamination can be a problem, depending on manufacturer
Hydrolyzed Diets	<ul style="list-style-type: none">• Can be fed long-term (complete and balanced)• Effective and well tolerated• Available in vegetarian formulas	<ul style="list-style-type: none">• Expensive• Not palatable for all patients

I tend to stay away from novel protein diets because in Mexico where I practice, novel protein diets are manufactured by over-the-counter food companies and have been proven to be contaminated with other sources. In addition, many clients have already tried several animal proteins or commercially prepared raw diets with multiple animal proteins before they come to me, so we have fewer choices left.

Dr. Griffin: I've been in clinical practice for 44 years and I've tried them all. Long ago, we recommended home-cooked diets because we didn't have the commercial options available today. I even promoted homemade vegetarian diets of pumpkin and pinto beans for a time, but I found they weren't great long-term diets for dogs when clients saw a favorable response and did not follow up to get on a complete and balanced diet.

I'm a big fan of hydrolyzed diets. I haven't yet found a limited-antigen diet that completely eliminated food allergy, but hydrolyzed diets work in about 90% of cases. While cost can be an issue with these diets, I actually use the expense as an incentive for compliance.

Dr. Gagné: Dr. Manchester and Dr. Marks, what are your thoughts on dietary management of dogs with chronic enteropathies?

Dr. Manchester: If there is one category of diet I prescribe most frequently to dogs with chronic enteropathy, it would be a hydrolyzed diet. I think it's important to give the client some direction vs. sending them home with six different diets to try.

Of course, there is no one-size-fits-all approach. A good diet history is so important, because there is a big difference between what I recommend for a dog that has already been on three different over-the-counter diets and four different prescription diets versus a dog that has eaten a single over-the-counter commercial dog food his whole life. It is also important to look at the diet's formulation, especially the fat content, because chronic enteropathy patients often have a limited

tolerance for dietary fat.

Dr. Marks: It's worth emphasizing that dietary fat restriction is especially important for patients with certain food-responsive enteropathies such as intestinal lymphangiectasia. These dogs need diets that contain less than 20% fat on a metabolizable energy basis and are digestible and highly palatable. We tend to be less aggressive with dietary fat restriction when managing dogs that are not hypoproteinemic or hypocholesterolemic and have other food-responsive enteropathies.

I initially try to determine via the patient's diet history whether a limited-ingredient diet might be a feasible option, because these diets tend to be palatable, particularly for small or toy-breed dogs. I typically reserve home-prepared diets for patients with concurrent disorders because there is no single diet that can be used to manage both disorders. Examples include patients with renal disease and a chronic enteropathy, or patients with primary hyperlipidemia and a chronic enteropathy. I strongly advise that these home-prepared diets be formulated by a board-certified veterinary nutritionist.

Dr. Gagné: How long should a practitioner wait to see a decrease in signs with an elimination diet trial?

Dr. Sheinberg: In dermatology, we adhere to an eight-week trial. If I have a severely inflamed dog, I might choose to use prednisone on that patient and try to recheck the dog two or three weeks afterward to see how he is doing and to try to eliminate the prednisone. If I can transition to oclacitinib I will do that to avoid the long-term effects of steroids. I give dogs medication for the first three or four weeks, then take them off of the medication and start measuring the response between four to six weeks. That way, they will be completely off medications once we reach eight weeks.

Dr. Marks: I think veterinary gastroenterologists have one significant advantage in terms of compliance, because GI dietary trials are typically much shorter in duration than those

of our dermatologist colleagues. Clinical signs of diarrhea should resolve within 10 to 14 days following the onset of the dietary trial compared to 8 to 12 weeks for patients with pruritic behaviors.

Dr. Manchester: It's important to stress that success doesn't have to mean 100% improvement. If I have a patient with really severe signs, I'm happy with 50% improvement. It depends on where you are starting. If an animal is having liquid bowel movements four times a day, improving the consistency and decreasing the frequency will improve the pet's quality of life.

Dr. Gagné: **Knowing that it takes at least eight weeks to resolve dermatological signs, how do you get the patient and the owner to stay compliant on the trial?**

Dr. Sheinberg: Choosing the right elimination diet for the patient is critical. You have to consider how the owner feels about the diet you plan to prescribe. If you are going to use a home-prepared diet, are they willing to cook for their dog? If you are going to prescribe a hydrolyzed diet, do they understand the cost? Do they understand what kind of treats are allowed? If a client feels they are being forced to do something they don't want to do, you won't be successful.

I have found it useful to have clients keep what I call an "itch calendar." Starting several weeks before the diet challenge, when we've removed medications, the clients ask themselves each night how itchy their dog was that day on a 0-10 scale. Once they start the diet challenge, they are more aware of their dog's pruritic behaviors and can see changes.

It takes teamwork and good client education to make an elimination diet trial work. If owners lack information or



A 2-week elimination diet trial is typically sufficient to resolve gastrointestinal signs of adverse food reaction; however, dermatologists recommend an 8-week trial to assess dermatological improvement.



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Dr. Craig Griffin

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motivation, they will not do the diet trial correctly or long enough. Follow-up is also important. We usually call clients one week after we prescribe the diet to see how they are doing, if they haven't already contacted us.

Dr. Gagné: **Assume a dog has responded to the elimination diet trial. How important is it to rechallenge the dog?**

Dr. Griffin: If I have a client whose dog is 100% better and she doesn't want to challenge, I probably wouldn't twist her arm. But the vast majority of our cases don't get 100% better. It may be because the dog has a food allergy and an environmental allergy and the clinical signs are only partially due to the food allergy. If we don't challenge and recognize that food allergy is part of the problem, we will have trouble using allergen-specific immunotherapy to get clinical signs under control without using other atopic medications. In other cases, we might unnecessarily raise the dose of the medication because we think the lower dose isn't controlling the environmental allergy, when the problem is that we missed the food allergy.

There are also cases where I do a diet trial and the GI issues clear up, but the owners and I don't perceive any change in the skin. By re-challenging the dog, we may realize that, in fact, the skin had been improving because now there are areas that flare again within four or five days.

Dr. Marks: Speaking as a gastroenterologist, I would say it is not as important to rechallenge the dog compared to my dermatology colleagues. If a patient is doing well on diet X or diet Y, most owners are relieved that their pet's diarrhea has finally resolved and are more reluctant to challenge their pet in the event that the diarrhea could recur. Many owners are willing to pay a bit more for a therapeutic diet if the diet is palatable and resolves the diarrhea.

Dr. Manchester: I agree. If the GI signs are better, owners usually want a lifetime supply of the diet. Rather than rechallenge with the original diet, I advise they begin to slowly add new dietary components to the elimination diet. If they want to give the dog a carrot as a treat or a little piece of banana, we let them try it. Assuming we're successful,

the owner is usually happy to know the dog can have a little more variety.

Dr. Gagné: **What if adverse food reaction is ruled out through the elimination diet trial and the diagnostics indicate atopy is the cause of the dog's clinical signs? How would you approach nutritional management?**

Dr. Griffin: Including omega-3 fatty acids in diets for dogs with environmental allergies has been studied for its use in decreasing pruritus. When I talk to veterinarians about diet for allergic dogs, I tell them that all allergic dogs can potentially benefit from a diet. If they are food allergic, they need a diet that eliminates the protein to which they are allergic. If they are not food allergic, a diet that is higher protein and contains a source of omega-3 fatty acids will benefit them and give the atopy medications a better chance of working.

Dr. Sheinberg: Building on that point, I prefer diet over supplements for dogs with atopy. It can be hard enough for clients to bathe and medicate a dog; feeding a dermatological diet in lieu of giving supplements is easier.

Dr. Gagné: **What are your thoughts on diagnostic strategies such as intradermal, serum IgE, serum IgG, salivary or hair tests?**

Dr. Griffin: There is no alternative test to an elimination diet trial to diagnose food allergy, and some of the alternatives are particularly bad. Even those that statistically correlate to some degree, such as the IgE serum test, don't always correlate with the exact ingredient.

Dr. Sheinberg: It's hard when you have an owner who has had a saliva or hair test that they believe has given them a diagnosis, but those tests are definitely not appropriate for diagnosing food allergy. These owners are disappointed to learn they still have to perform a diet trial.

A NEW TOOL: THE AMINO ACID-BASED ELEMENTAL DIET

Dr. Gagné: **An amino acid-based elemental diet is a new option for veterinarians in the diagnosis and management of food allergy and other types of adverse food reaction. What does a diet like this have to offer?**

Dr. Sheinberg: An amino acid-based elemental diet is something that we as veterinarians have not had available to us. In pediatric medicine, amino acid diets have been used for more than 20 years and are the first choice of many pediatricians for managing allergic gastrointestinal disease in children. I think that being able to have this tool will be very good. Patients that are not doing well with our current diets

and that tend not to respond well to medications are good candidates for using an elemental diet.

Dr. Manchester: I think it will be exciting to have another dietary tool in our armamentarium to combat chronic enteropathy. In human pediatric Crohn's disease, a high percentage of patients go into complete remission on elemental diets. Not only do their clinical signs go away, but when the patients are re-biopsied, the inflammation is gone. Contrast this to the use of steroids, which have a much greater side effect profile and significant ramifications for growing young children.

While chronic canine enteropathy patients are not the same as Crohn's patients, the clinical signs associated with both conditions are probably due more to intolerances and aberrant immune responses than food allergens, but they still respond to these elemental or polymeric diets. We have dogs that come in with an acutely insulted, leaky and damaged gut barrier. A diet like this that is very digestible, well-balanced, and non-immune stimulating will definitely be helpful.

Dr. Marks: I think that the introduction of an amino acid-based elemental diet that is complete and balanced, as well as palatable, is long overdue. A diet like this could be used for a plethora of disorders—not just for patients with adverse food reactions, but in patients with short bowel syndrome, critically ill puppies with parvovirus, and in patients with steroid-responsive enteropathies in which the elemental diet might allow a reduction in the dose of immunotherapy (prednisone, chlorambucil, azathioprine, etc.) administered to the patient. When one considers all of the patients we see in the ICU or the critical care setting with severe intestinal disease, this



An amino acid-based elemental diet for use in elimination diet trials and management of gastrointestinal disease is a recent therapeutic diet innovation.



Dr. Stanley Marks

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elemental formula could prove to be an invaluable therapeutic modality.

Dr. Gagné: What are your thoughts on the inclusion of a prebiotic in the Purina® Pro Plan® Veterinary Diets EL Elemental diet to alter the microbiome?

Dr. Manchester: It needs to be studied, but I think including a prebiotic is a great idea, especially because so many patients being prescribed this diet will have already had their microbiome wiped out by multiple courses of metronidazole and tylosin. I also think we have a slightly better chance of making a positive impact on the microbiome with a prebiotic that promotes the growth of beneficial bacteria versus just peppering the gut with probiotics alone.

Dr. Gagné: Dr. Sheinberg and Dr. Griffin, having been provided the opportunity to try this diet, how and when do you see yourself using it in practice?

Dr. Sheinberg: I have a particular case of a Labrador-mix dog that had been very difficult to control. She was medicated with long-term steroids, but every time we removed the treatment, she would flare up, get secondary infections and do very poorly. We tried all the hydrolyzed diets on the market as well as a pork and sweet potato diet. She has been on the Elemental diet for almost two months, and her skin is doing really well, with no flares.

Dr. Griffin: I have a case on the diet right now that, in order to initially improve clinical signs, had to be on a homemade unbalanced pumpkin and pinto bean diet. On a blinded challenge, she flared to six different ingredients, then she flared with several different hydrolyzed diets and multiple limited ingredient diets. The only commercial food she has tried that keeps her food allergy controlled is the Elemental diet and she loves it. So do her owners, as they were tired of home cooking and adding supplements to try to balance her diet. She also did not particularly like the homemade diet and would try to steal food and had intermittent flare-ups. She is not only thriving on the Elemental diet but has stopped trying to steal food.

WRAP-UP

Dr. Gagné: What do you see as the primary takeaway of this discussion for practitioners? Is there one piece of advice you would give on helping dogs with allergic and food-responsive conditions?

Dr. Griffin: My takeaway is that foods play a very significant role in allergic skin disease. Because it often isn't a pure problem, it takes an astute clinician taking a good history to capture all clinical signs—including GI signs—and conduct a good exam to determine what role the food plays.

Dr. Sheinberg: A correct clinical history is so important. It can also be difficult to diagnose food allergy if the dog has another issue, such as a chronic ear infection, that needs treatment. You may have to take care of that before you can evaluate how the elimination diet is working.

Dr. Manchester: Just because one diet didn't work, it doesn't mean diet should be given up on. The majority of chronic enteropathy dogs will respond to dietary therapy. Finding the right match for an individual patient may take trial and error.

Dr. Marks: The importance of the dietary history cannot be overemphasized when selecting a diet. In addition, veterinarians should remember to inquire about a pet's gastrointestinal signs when the pet is presented for dermatological disease, and vice-versa.

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