

PROCESS OF ELIMINATION

A complete diagnostic elimination-challenge diet trial isolates the cause of adverse food reactions through 4 phases.

NUTRITION NOTES

Performing a Diet Trial to Identify Food Allergies in Dogs and Cats

Sarah Wilson, DVM, Stockton, Calif.

Craig Datz, DVM, MS, DABVP, DACVN, Royal Canin USA, Columbia, Mo.

Adverse food reactions (AFRs) are immunologic (food allergy or hypersensitivity) or nonimmunologic (food intolerance) responses to dietary components. A *food allergy* is an aberrant adverse immune response elicited by exposure to a particular food substance;¹ most often, the culprit allergens are <70 kDa glycoproteins.¹ A *food intolerance* can be a response to carbohydrates, dyes, flavors, and preservatives.

Diagnosis of an AFR goes hand in hand with treatment because confirmation of disease is based on response to therapy. Confirmation of an AFR depends on reduction or resolution of clinical signs while the animal is being fed a strict elimination diet, recurrence of clinical signs when the animal is challenged with the original diet (and anything else given orally), and resolution of signs after the elimination diet has been reinstated.

THE ELIMINATION-CHALLENGE DIET TRIAL

A complete diagnostic elimination-challenge diet trial (ECDT) can be considered a 4-phase process—eliminate, challenge, confirm, and identify—and may last months. The length of each phase is determined by patient response to therapy and client compliance. The trial cannot move to a new phase until the previous

phase has been successfully completed. A drawback is that some clients may not want to proceed to a new phase if their pet's condition has improved.

Phase 1: Eliminate

This initial phase involves strictly feeding only the trial diet for up to 12 weeks while monitoring for reduction of clinical signs; no other treats, supplements, capsules, toothpastes, dental chews, outdoor hunting, or scavenging are allowed. Flavored oral medications should be transitioned to topical (e.g., parasite control). Ideally, the transition to the new diet should be gradual, over 5 to 7 days; however, some pets may tolerate a faster transition. Gastrointestinal signs usually improve within 2 to 3 weeks; cutaneous signs usually improve within 4 to 12 weeks.¹ Critical analysis of multiple studies showed that by 5 weeks (dogs) or 6 weeks (cats), cutaneous signs underwent remission for more than 80% of patients and by 8 weeks for more than 90%. To achieve complete remission, fewer than 5% of patients needed to continue phase 1 for longer than 13 weeks.²

- When phase 1 successfully alleviates clinical signs, some clients choose to not continue on to phase 2.
- Phase 1 completion is determined by satisfactory reduction of clinical signs.



Client communication note: Emphasize that the only things that should enter the pet's mouth are the approved elimination diet and water. Off-leash parks and other free-range options may be problematic, so alternatives should be considered.

Phase 2: Challenge

This phase involves reintroducing the previous diet while monitoring for recrudescence of signs. If the pet has an AFR, signs usually recur within 2 to 3 days but may take up to 2 weeks.

- Ensure control of things that may cloud the clinical picture during future phases, such as secondary infection and appropriate parasite control.
- If the ECDT is stopped during phase 2, an AFR will not be confirmed.
- Phase 2 completion is determined by a flare of clinical signs.

Client communication note: Remind clients to include other things the animal previously consumed, such as treats, supplements, and toothpastes.

Phase 3: Confirm

This phase involves restarting the strict elimination diet; resolution of clinical signs confirms the diagnosis of an AFR. Confirmation may take 2 to 4 weeks while clients monitor for reduction of clinical signs. If the elimination diet is appropriate and balanced for the patient, it may be continued indefinitely.

- Clients may choose to not pursue testing for individual allergens.
- If the ECDT is stopped during phase 3, specific offending food allergens will not be confirmed.
- Phase 3 completion is determined by resolution of clinical signs.

Client communication note: Advise clients that new allergies to this currently tolerated elimination diet may later arise and that not finishing the trial may require another ECDT in the future.

Phase 4: Identify

This final phase of the ECDT is intended to identify the specific ingredients that cause a flare of signs and that should be avoided. The patient continues eating the strict elimination diet while being offered previously fed ingredients (usually proteins, which are the most commonly problematic) as treats or diet toppers. Small amounts (<10% of caloric intake) of 1 ingredient at a time are offered for up to 2 weeks while the pet is monitored for recrudescence of signs. If no signs are noted, the ingredient can be fed; if signs are noted, the ingredient should be avoided. Although lack of response to a specific ingredient translates to tolerance of that ingredient, it does not rule out overall food intolerance. The only way to definitively diagnose a problem food is systematic testing of each ingredient.

- Individual ingredients tested should be based on diet history and offending food or treats from phase 2. For example, if the challenge diet has 3 protein sources—chicken, egg, and soy—consider testing each one of these ingredients separately.
- If a thorough diet history was undetermined (e.g., poor client recollection, new pet with unknown history), a starting point would be foods commonly reported to cause allergies in pets (**TABLE 1**).
- Completing phase 4 helps determine problematic foods to avoid, which significantly improves prognosis. Knowing which ingredients are off-limits may enable clients to feed less expensive over-the-counter (OTC) diets in the future, although the potential for cross-contamination of these diets exists and may pose problems in sensitive individuals. In addition, if an allergy to the diet arises in the future, transitioning to

TABLE 1 Reported Sources of Food Allergies in Dogs and Cats^{3,4}

SPECIES	COMMON FOODS	UNCOMMON FOODS
Dogs	■ Beef ■ Dairy ■ Chicken ■ Wheat ■ Soy	■ Fish ■ Lamb ■ Pork ■ Rabbit
Cats	■ Beef ■ Fish ■ Chicken	■ Barley ■ Egg ■ Lamb ■ Pork ■ Rabbit ■ Wheat

another diet with previously tested and tolerated ingredients may avoid another lengthy ECDT.

- Phase 4 completion depends on the client's willingness to test all potential allergens.

Client communication note: Set realistic expectations together so that trials do not last an undetermined time.

ELIMINATION DIET OPTIONS

Selecting an appropriate diet for a challenge trial depends on patient history. Hundreds of diet options are available at retail stores and online sources; however, an appropriate ECDT for diagnostic purposes should preferably be chosen from 3 broad categories: veterinary therapeutic limited-ingredient diets, veterinary therapeutic hydrolyzed-protein diets, or complete and balanced home-cooked diets. Many limited-ingredient OTC diets are available; however, studies have found some commercial products to be cross-contaminated with undeclared potential allergens.^{5,6} Although these diets may be considered for long-term feeding, for the diagnostic purposes of an ECDT, OTC diets should be avoided because cross-contamination may result in failure to respond to an appropriate diet (**FIGURE 1**).

Veterinary Therapeutic Limited-Ingredient Diets

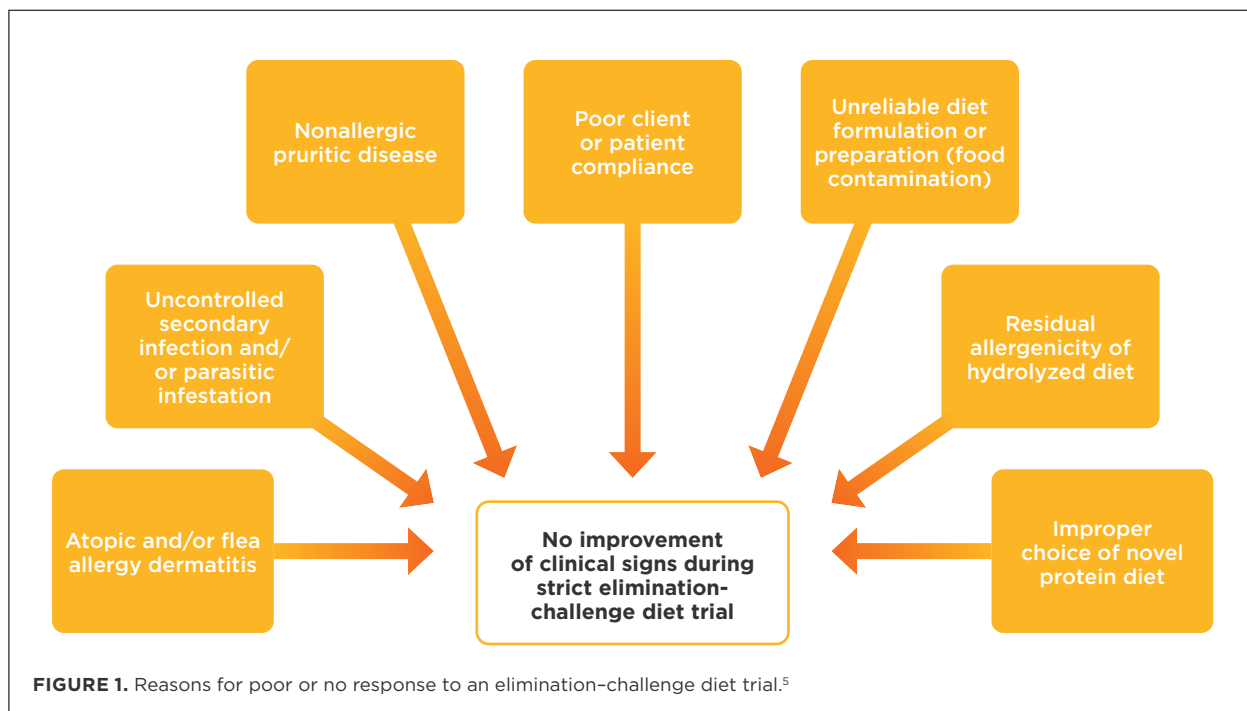
These diets, also called novel protein diets, are formulated for adult maintenance and typically offer uncommon protein sources. The strategy is to feed something to which the pet has not been previously exposed to. Unfortunately, many OTC diets now include previously uncommon ingredients, which makes finding a novel protein difficult. Ingredients such as rabbit, venison, fish, duck, and kangaroo are now present not only in veterinary therapeutic diets but often in OTC diets and treats as well. When choosing a novel protein as part of the diagnostic process, a thorough diet history is necessary to determine which protein source is novel.

Benefits include

- Complete and balanced nutrition
- Palatability
- Appropriateness for long-term feeding
- Moderate cost

Drawbacks include

- Requirement for thorough diet history (Pet may have already been exposed to the ingredient through cross-contamination of an OTC brand.)
- Limited options for growing pets
- Increased nutrients to benefit skin health (fatty acids) in some diets (This may cloud results. Positive





response may not be solely attributed to food allergy if a full ECDT is not performed to confirm an AFR.)

Veterinary Therapeutic Hydrolyzed-Protein Diets

Hydrolyzed-protein diets have been processed to provide small peptides or amino acids rather than intact proteins and large polypeptides. The strategy is to provide the proteins in small peptides, typically <13 kDa, to avoid detection by the immune system and consequent reactions. Currently available hydrolyzed protein sources include chicken, chicken liver, soy, salmon, and feathers.

Benefits include

- Complete and balanced nutrition
- High digestibility
- Diagnostic utility when diet history is limited
- Appropriateness for long-term feeding
- Reasonable palatability
- Adult maintenance formulations (One diet that has undergone feeding trials in puppies is appropriate for growth.)

Drawbacks include

- Higher cost (particularly for large breed dogs)
- Variable palatability
- Retained allergenicity; reactions still possible

Home-Cooked Diets with Novel Ingredients

Home-cooked diets are made with whole food (“human food”) and are usually formulated with a limited number of novel ingredients. Preferably, 1 novel protein and 1 novel carbohydrate source are included to minimize antigen exposure and identify tolerated ingredients. Unless formulated by a veterinary nutritionist, home-cooked diets will likely be incomplete and unbalanced. Studies of dogs and cats have shown that even home-cooked maintenance diets made from recipes found online and in books, written by veterinarians and laypersons, were unbalanced. Approximately 95% of recipes for dogs⁷ and 100% of recipes for cats⁸ evaluated had at least 1, but usually many more, essential nutrients below minimum requirements. Although some ECDTs are performed by using unbalanced home-cooked diets, doing so is not recommended; many nutrients are essential for skin and gastrointestinal health, and clients may choose to continue the tolerated but unbalanced diet for the long term, which may lead to problems such as nutrient deficiencies, toxicities, and other adverse health effects.

Studies of dogs and cats have shown that even home-cooked maintenance diets made from recipes found online and in books, written by veterinarians and laypersons, were unbalanced.

Benefits include

- Complete and balanced nutrition if formulated by a board-certified veterinary nutritionist or someone with a PhD in canine and feline nutrition
- Excellent palatability, often highly digestible
- Ability to be individualized for pet’s needs
- Limited number of potential allergens
- Client participation, which strengthens the human-animal bond

Drawbacks include

- Unbalanced nutrition if not properly formulated
- Can be expensive (particularly for large breed dogs)⁹
- Time-consuming, often inconvenient (preparation, storage of ingredients and prepared diet)
- Probable drift away from home-cooked diet recipe,¹⁰ which could unbalance even a properly formulated diet (switching ingredients, amounts, and/or cooking methods can unbalance a diet)

LONG-TERM MANAGEMENT

After an AFR has been diagnosed as the cause for clinical signs, long-term management involves avoiding problematic foods. No further diagnostics or rechecks are necessary, although future flares may require rechecks and potential transition to another diet or management of other allergic/seasonal disease. Transitioning to an OTC diet may be considered, with the understanding that potential cross-contamination may cause problems for some sensitive individuals. When clients can properly manage the patient’s diet, the prognosis for an AFR is excellent. **TVP**

References

1. Gaschen FP, Merchant SR. Adverse food reactions in dogs and cats. *Vet Clin North Am Small Anim Pract* 2011;1:361-379.

CHEWABLES

CAUTION: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

INDICATIONS: For use in dogs to prevent canine heartworm disease by eliminating the tissue stage of heartworm larvae (*Dirofilaria immitis*) for a month (30 days) after infection and for the treatment and control of ascarids (*Toxocara canis*, *Toxascaris leonina*) and hookworms (*Ancylostoma caninum*, *Uncinaria stenocephala*, *Ancylostoma braziliense*).

DOSAGE: HEARTGARD[®] Plus (ivermectin/pyrantel) should be administered orally at monthly intervals at the recommended minimum dose level of 6 mcg of ivermectin per kilogram (2.72 mcg/lb) and 5 mg of pyrantel (as pamoate salt) per kg (2.27 mg/lb) of body weight. The recommended dosing schedule for prevention of canine heartworm disease and for the treatment and control of ascarids and hookworms is as follows:

Dog Weight	CheWables Per Month	Ivermectin Content	Pyrantel Content	Color Coding On Foil Backing and Carton
Up to 25 lb	1	68 mcg	57 mg	Blue
26 to 50 lb	1	136 mcg	114 mg	Green
51 to 100 lb	1	272 mcg	227 mg	Brown

HEARTGARD Plus is recommended for dogs 6 weeks of age and older. For dogs over 100 lb use the appropriate combination of these chewables.

ADMINISTRATION: Remove only one chewable at a time from the foil-backed blister card. Return the card with the remaining chewables to its box to protect the product from light. Because most dogs find HEARTGARD Plus palatable, the product can be offered to the dog by hand. Alternatively, it may be added intact to a small amount of dog food. The chewable should be administered in a manner that encourages the dog to chew, rather than to swallow without chewing. Chewables may be broken into pieces and fed to dogs that normally swallow treats whole.

Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes after administration to ensure that part of the dose is not lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

HEARTGARD Plus should be given at monthly intervals during the period of the year when mosquitoes (vectors), potentially carrying infective heartworm larvae, are active. The initial dose must be given within a month (30 days) after the dog's first exposure to mosquitoes. The final dose must be given within a month (30 days) after the dog's last exposure to mosquitoes.

When replacing another heartworm preventive product in a heartworm disease preventive program, the first dose of HEARTGARD Plus must be given within a month (30 days) of the last dose of the former medication.

If the interval between doses exceeds a month (30 days), the efficacy of ivermectin can be reduced. Therefore, for optimal performance, the chewable must be given once a month on or about the same day of the month. If treatment is delayed, whether by a few days or many, immediate treatment with HEARTGARD Plus and resumption of the recommended dosing regimen will minimize the opportunity for the development of adult heartworms.

Monthly treatment with HEARTGARD Plus also provides effective treatment and control of ascarids (*T. canis*, *T. leonina*) and hookworms (*A. caninum*, *U. stenocephala*, *A. braziliense*). Clients should be advised of measures to be taken to prevent reinfection with intestinal parasites.

EFFICACY: HEARTGARD Plus Chewables, given orally using the recommended dose and regimen, are effective against the tissue larval stage of *D. immitis* for a month (30 days) after infection and, as a result, prevent the development of the adult stage. HEARTGARD Plus Chewables are also effective against canine ascarids (*T. canis*, *T. leonina*) and hookworms (*A. caninum*, *U. stenocephala*, *A. braziliense*).

ACCEPTABILITY: In acceptability and field trials, HEARTGARD Plus was shown to be an acceptable oral dosage form that was consumed at first offering by the majority of dogs.

PRECAUTIONS: All dogs should be tested for existing heartworm infection before starting treatment with HEARTGARD Plus which is not effective against adult *D. immitis*. Infected dogs must be treated to remove adult heartworms and microfilariae before initiating a program with HEARTGARD Plus.

While some microfilariae may be killed by the ivermectin in HEARTGARD Plus at the recommended dose level, HEARTGARD Plus is not effective for microfilariae clearance. A mild hypersensitivity-type reaction, presumably due to dead or dying microfilariae and particularly involving a transient diarrhea, has been observed in clinical trials with ivermectin alone after treatment of some dogs that have circulating microfilariae.

Keep this and all drugs out of the reach of children.

In case of ingestion by humans, clients should be advised to contact a physician immediately. Physicians may contact a Poison Control Center for advice concerning cases of ingestion by humans.

Store between 68°F - 77°F (20°C - 25°C). Excursions between 59°F - 86°F (15°C - 30°C) are permitted. Protect product from light.

ADVERSE REACTIONS: In clinical field trials with HEARTGARD Plus, vomiting or diarrhea within 24 hours of dosing was rarely observed (1.1% of administered doses). The following adverse reactions have been reported following the use of HEARTGARD: Depression/lethargy, vomiting, anorexia, diarrhea, mydriasis, ataxia, staggering, convulsions and hypersalivation.

To report suspected adverse drug events, for technical assistance, or to obtain a copy of the Safety Data Sheet (SDS), contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS, or online at <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

SAFETY: HEARTGARD Plus has been shown to be bioequivalent to HEARTGARD, with respect to the bioavailability of ivermectin. The dose regimens of HEARTGARD Plus and HEARTGARD are the same with regard to ivermectin (6 mcg/kg). Studies with ivermectin indicate that certain dogs of the Collie breed are more sensitive to the effects of ivermectin administered at elevated dose levels (more than 16 times the target use level) than dogs of other breeds. At elevated doses, sensitive dogs showed adverse reactions which included mydriasis, depression, ataxia, tremors, drooling, paresis, recumbency, excitability, stupor, coma and death. HEARTGARD demonstrated no signs of toxicity at 10 times the recommended dose (60 mcg/kg) in sensitive Collies. Results of these trials and bioequivalency studies, support the safety of HEARTGARD products in dogs, including Collies, when used as recommended.

HEARTGARD Plus has shown a wide margin of safety at the recommended dose level in dogs, including pregnant or breeding bitches, stud dogs and puppies aged 6 or more weeks. In clinical trials, many commonly used flea collars, dips, shampoos, anthelmintics, antibiotics, vaccines and steroid preparations have been administered with HEARTGARD Plus in a heartworm disease prevention program.

In one trial, where some pups had parvovirus, there was a marginal reduction in efficacy against intestinal nematodes, possibly due to a change in intestinal transit time.

HOW SUPPLIED: HEARTGARD Plus is available in three dosage strengths (see DOSAGE section) for dogs of different weights. Each strength comes in convenient cartons of 6 and 12 chewables.

Marketed by
Boehringer Ingelheim Animal Health USA Inc.
Duluth, GA 30096
Made in U.S.A.

©HEARTGARD and the Dog & Hand Logo are registered trademarks of Boehringer Ingelheim Animal Health USA Inc.
©2019 Boehringer Ingelheim Animal Health USA Inc.
All Rights Reserved.

Rev. 08-2018
1050-1999-04.
US-PET-0199-2020.



- Olivry T, Mueller RS, Prélud P. Critically appraised topic on adverse food reactions of companion animals (1): duration of elimination diets. *BMC Vet Res* 2015;11:225.
- Mueller RS, Olivry T, Prélud P. Critically appraised topic on adverse food reactions of companion animals (2): common food allergen sources in dogs and cats. *BMC Vet Res* 2016;12:9.
- Datz C. Food allergy: diagnostic and therapeutic food options. *Today's Veterinary Practice* 2011;6:24-29.
- Ricci R, Granato A, Vascellari M, et al. Identification of undeclared sources of animal origin in canine dry foods used in dietary elimination trials. *J Anim Physiol Anim Nutr* 2013;97:32-38.
- Fossati LA, Larsen JA, Villaverde C, Fascetti AJ. Determination of mammalian DNA in commercial canine diets with uncommon and limited ingredients. *Vet Med Sci* 2019;5(1):30-38.
- Stockman J, Fascetti AJ, Kass PH, Larsen JA. Evaluation of recipes of home-prepared maintenance diets for dogs. *JAVMA* 2013;242(11):1500-1505.
- Wilson SA, Villaverde C, Fascetti AJ, Larsen JA. Evaluation of the nutritional adequacy of recipes for home-prepared maintenance diets for cats. *JAVMA* 2019;254(10):1172-1179.
- Vendramini THA, Pedrinelli V, Macedo HT, et al. Homemade versus extruded and wet commercial diets for dogs: cost comparison. *PLoS One* 2020;15(7):e0236672.
- Johnson LN, Linder DE, Heinze CR, et al. Evaluation of owner experiences and adherence to home-cooked diet recipes for dogs. *J Small Anim Pract* 2016;57(1):23-27.



Sarah Wilson

Dr. Wilson is a 2008 graduate of the veterinary technician program at the University of Guelph, Canada. After 2 years in private practice in Guelph, she went on to study veterinary medicine at St. Matthew's University. In 2013, she completed her clinical year at the Western College of Veterinary Medicine in Saskatchewan, Canada, and in 2014 completed a small animal rotating internship. In 2017, she completed a Small Animal Clinical Nutrition residency at the University of California, Davis Veterinary Medical Teaching Hospital. Dr. Wilson is board eligible and hopes to soon become a diplomate of the American College of Veterinary Nutrition.



Craig Datz

Dr. Datz is a 1987 graduate of the Virginia-Maryland Regional College of Veterinary Medicine. He has spent 14 years in private companion animal practice and 11 years on the faculty at the University of Missouri College of Veterinary Medicine working in the areas of Community Practice and Clinical Nutrition. In 2012, he joined Royal Canin USA, where he is the Director of Scientific Affairs. Dr. Datz is board-certified by the American College of Veterinary Nutrition and is dual board certified in canine/feline and feline practice by the American Board of Veterinary Practitioners.