Diagnosis of Adverse Reactions to Food in Dogs: Efficacy of a Soy-Isolate Hydrolyzate-Based Diet\textsuperscript{1,2}

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EXPANDED ABSTRACT

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Adverse reactions to food include allergy (reaction with an immunological mechanism) and intolerance (nonimmunological reactions, including idiosyncratic, metabolic, and toxic responses) (1). Adverse reaction to food results in dermatological (pruritus, otitis externa, seborrheic dermatitis, recurrent bacterial or fungal dermatitis) and in 10\% of cases in gastrointestinal (diarrhea, abdominal discomfort) signs (2). Food sensitivity is one of the most common causes of nonseasonal allergic skin disease in dogs.

A diagnosis of adverse reaction to food is confirmed by elimination-challenge tests (1,3). The elimination period involves feeding the dog a specialized diet; the diet must include all common foodstuffs and incorporate novel ingredients to which the dog has not had prior exposure. An improvement in clinical signs during this period indicates the likelihood of an adverse food reaction. The elimination period is followed by a challenge with the dog’s usual diet, and if symptoms return, this confirms the diagnosis of adverse food reaction.

Because they are easily customized and assumed to be free of food additives, homemade diets have been recommended by veterinary dermatologists for the diagnosis and management of adverse reaction to food. Although food additives have been linked to adverse reaction in humans, a similar link has yet to be established in dogs and cats (1). A homemade recipe is custom designed so that it provides the dog with novel sources of protein, carbohydrate, and fat. However, owners are often reluctant to feed homemade diets because they are time consuming to prepare, expensive, and might be unpalatable (4). The noncompliance is high (4). In addition, achieving a nutritionally balanced diet using a homemade recipe can be challenging.

Commercially available elimination diets have been marketed for some time (3), utilizing a range of protein sources not normally found in standard dog diets. Such diets are cost effective, convenient, and nutritionally complete, but are not truly hypoallergenic because they contain whole proteins to which the dog may or may not have had prior exposure. This may have contributed to the apparent poor performance reported for some of these diets (5).

A strategy for reducing allergenicity involves hydrolyzing the protein source with enzymes. Food allergens are usually glycoproteins, with the most common ranging in size from 14 to 40 kD (6), although smaller (10 kD) and larger (70 kD) molecules can be immunogenic (1). They are usually stable despite heating, pH, or digestive enzymes (7). By enzymatically breaking the protein down into smaller peptide fragments it becomes intrinsically less allergenic and more digestible. This latter point is probably of great importance, because if a dietary protein is properly digested before contact with the gastrointestinal mucosa, it will not activate the immune system. In a study of veal calves, a soy hydrolyzate diet was utilized more efficiently, and was less immunogenic than a diet containing intact proteins (8). This strategy was also used successfully in babies with allergies to cow’s milk (9).

The purpose of this study was therefore to assess the efficacy of a diet containing soy isolate hydrolyzate for the diagnosis of adverse reaction to food in dogs in a multicentric field study.

MATERIALS AND METHODS

Sixty dogs with suspected skin hypersensitivity were recruited for the study after presentation at one of two dermatology specialist veterinary practices. The dogs represented 26 breeds, 34 males (three castrated) and 26 females (13 spayed), age range from 3 mo to 11 y (mean 4.5 ± 0.4 y). Criteria for inclusion in the study included localized or generalized pruritus, self-trauma, erythema, seborrhea, and recurrent pyoderma and/or malassezia dermatitis as well as otitis. Exclusion criteria included the presence of ectoparasites or underlying disease and the concomitant use of corticotherapy. A dietary history
was taken, and each dog underwent a thorough clinical examination by a board-certified dermatologist, including an assessment of skin lesions. The level of pruritus was subjectively scored, from 0 (no signs) to 5 (very severe). All dogs initially presented with pruritus (mean score $3.4 \pm 0.1$, range 2–5), although other clinical signs varied widely, including conjunctivitis, blepharitis, otitis externa, seborrhea, erythema, recurrent pyoderma, and in eight dogs, diarrhea and flatulence. The duration of these clinical signs varied from 3 wk to 10 y (mean $2.6 \pm 0.4$ y).

After describing the nature of the study and receiving his or her agreement, the owner was provided with a soy hydrolyzate and rice-based elimination diet and was instructed to feed this diet exclusively over the subsequent 2 mo. Care was taken to explain the importance of excluding all other food sources, including treats. Compliance was assessed by owner-interview at the end of the test period.

After the 2-mo test period, the dogs returned to the veterinary practice and were reassessed for the level of pruritus and other clinical signs. If the dog had completely recovered it was returned to its usual diet; a relapse after this challenge confirmed the efficacy of the test diet. If the dog had improved, but not completely recovered while consuming the test diet, it was evaluated for atopy by intradermal skin testing. If the dog showed little or no improvement on the test diet, it was evaluated with another elimination diet and was submitted to intradermal skin tests to confirm a diagnosis of atopy.

### Statistics

Data are presented as mean ± SEM. Treatment effects on pruritus were determined using paired *t* test, with *P* < 0.05 considered significant.

### RESULTS

Fifty-eight dogs completed the study and two others were excluded due to noncompliance. Of these 58 dogs, 36 (62%) markedly improved during the test period and relapsed when challenged with their original diet. Twenty of these 36 dogs (35%, mean age $3.8 \pm 0.6$ y) were diagnosed with an uncomplicated adverse food reaction. Their clinical signs were either completely regressed or very mild during the test period, with a significant reduction of pruritic score (Fig. 1A). Two of these 20 dogs did not respond to the soy isolate hydrolyzate-based diet, but did respond to a soy-based homemade diet and to a rice and rabbit commercially available elimination diet, respectively.

The remaining 16 dogs (28%, mean age $5.7 \pm 0.7$ y) improved during the test period, but their clinical signs remained mild to moderate; although the pruritic score was significantly reduced (Fig. 1B), this was not as dramatic as the adverse food reaction group (Fig. 1A). After more complete work-ups, these dogs were diagnosed with adverse food reaction and concurrent atopy.

Twenty-two dogs (38%, mean age $4.5 \pm 0.6$ y) did not improve when fed the test diet, and there was little or no improvement in clinical signs or pruritic score (Fig. 1C). These dogs were subsequently diagnosed as exclusively atopic, and did not respond to other elimination diets.

### Conclusions

Adverse reaction to food is a nonseasonal, pruritic skin disorder in dogs that is associated with the ingestion of a substance found in the diet. Definitive diagnosis can only be made by the use of an elimination diet. Blood tests (e.g., allergen-specific IgE) or skin tests are not recommended (1,3,5). The gold-standard elimination diet was traditionally a homemade diet. However, this requires complete cooperation by the owner over a period of many weeks, which can reduce compliance and therefore make diagnosis challenging. The reported drop-out rate during a 6–8-wk study using a homemade elimination diet was 36% (4), which would result in 36% of potential canine adverse food reaction cases not being diagnosed using the homemade diet. A commercially available, nutritionally complete, and convenient elimination diet is therefore attractive to owners and veterinarians.

The ingredient source of a commercial elimination diet is critical. Traditionally, lamb and rice were used in diets for "sensitive" dogs, but with their increased use in many standard
diets they can no longer be considered novel. Similarly, there were a surprisingly high number of dogs that had adverse reactions to fish in the elimination diet used by Tapp et al. (4). These authors concluded that the use of fish in standard products could be on the increase thereby reducing its value as a novel protein source.

Diets based on hydrolyzated protein sources represent the next generation of commercially available elimination diets. By hydrolyzing the soy-isolate protein source before its incorporation, intrinsic allergenicity is reduced and digestibility is increased (8).

In our study, 36 of 58 dogs were found to have an adverse food reaction. This high incidence is probably due to the selection of cases. Of these 36 dogs, 34 (94%) responded to the soy hydrolyzate elimination diet. This success rate is considerably higher than the 50% reported in a previous study (4). This study initially identified cases of adverse food reaction using a homemade diet, then transferred the subjects to a "novel" commercially available fish and potato-based elimination diet. Half of the subjects relapsed when placed on the fish and potato diet.

In our adverse food reaction group, two dogs did not respond to the soy isolate elimination diet, but did subsequently respond to homemade or commercial elimination diets. This finding suggests that to exclude a diagnosis of adverse reaction to food the use of several elimination diets is recommended.

Twenty-two dogs presented with skin hypersensitivity did not respond to the soy isolate hydrolyzate diet nor other elimination diets. These dogs were subsequently diagnosed with atopy by intradermal skin tests. Because atopy is not mediated by food these findings are to be expected. Atopy often coexists with adverse reaction to food, as found in 16 of our subjects. The high concentration of essential fatty acids (5.2% as fed), especially from the (n-3) family (0.8% as fed), found in the diet might also explain part of the improvement observed in the dogs of this study (10).

These findings suggest that the use of an elimination diet based on soy hydrolyzate can be a practical and efficient way to diagnose and manage adverse food reactions in dogs. However, as with all elimination diets nonresponse does not necessarily indicate the absence of adverse food reaction and this may require the sequential use of other elimination diets.

LITERATURE CITED