FOOD FIRST Diet trials are the first-line approach to both diagnosis and treatment of chronic enteropathy and could help patients avoid the need for immunosuppressive therapy.

NUTRITION NOTES

Hold That Steroid! Diet Trials for Chronic Enteropathy

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Gastrointestinal (GI) signs such as diarrhea, vomiting, weight loss, and changes in appetite are common presenting complaints in small animal practice.[1] After careful exclusion of extra-GI causes, dogs and cats with GI signs of 3 or more weeks in duration are classified as having a chronic enteropathy.

Chronic enteropathy is a nonspecific term that encompasses food-responsive enteropathy (FRE), antimicrobial-responsive enteropathy (ARE), and immunosuppressant-responsive enteropathy (IRE).[2-5] With no discriminating histopathologic features between these 3 forms of chronic enteropathy, diagnosis of each is dependent on response to various therapeutic interventions (diet, antimicrobials, and immunosuppressive therapies).[4] Diet trials are often the first step in the therapeutic approach, as 50% to 66% of chronic enteropathy patients respond.[5-8]

CLINICAL SIGNS AND LOCALIZATION OF DISEASE

Patients with chronic enteropathy often present with one or more chronic GI signs (**BOX 1**). Many cats present with nonspecific signs that may not be recognized as clinically important to the owner. In one study, 26 of 100 cats were determined to have a chronic enteropathy based on a wellness examination in which the owner reported their cat was doing well.[9]

The first step in approaching the patient with chronic enteropathy is to localize the disease to the small or

BOX 1 Clinical Manifestations of Chronic Enteropathy[a]

Common
- Vomiting (may be intermittent[b])
- Diarrhea (small or large intestinal or mixed)
- Weight loss[b]
- Changes in appetite[b]

Less common
- Constipation
- Hematochezia
- Tenesmus
- Regurgitation (often secondary to esophagitis from vomiting)
- Melena
- Hematemesis

[a]Signs must be observed for ≥3 consecutive weeks and have no extra-gastrointestinal explanation for a diagnosis of chronic enteropathy.
[b]Particularly common in cats.[9]

TABLE 1 Localizing Gastrointestinal Disease

CLINICAL SIGN	SMALL INTESTINE *Function: digestion, absorption*	LARGE INTESTINE *Function: storage*
Stool volume	Normal to increased	Decreased
Blood in stool	Dark, black/tarry if present	Frank blood if present
Mucus in stool	Uncommon	Common
Tenesmus	Absent	Present
Urgency of defecation	Normal	Increased
Frequency of defecation	Normal	Increased
Concurrent vomiting	May be present	Uncommon
Concurrent weight loss	Common	Uncommon
Appetite status	Normal or altered	Typically normal

large intestine (TABLE 1). The diagnostic and therapeutic approach to chronic enteropathy depends on the location of disease and predominating clinical signs. For example, fiber-enriched diets are often employed in the treatment of chronic large intestinal diarrhea, whereas low-fat diets may be helpful for patients presenting with regurgitation.[10,11]

THE ROLE OF NUTRITION IN CHRONIC ENTEROPATHY

Nutrition has a variety of effects on the intestinal system pertaining to epithelial health, microbiota composition, local immune response, general motility, and regulations in gene expression.[2,4] Many patients with chronic enteropathy have evidence of malabsorption such as weight loss and B vitamin deficiency. Hypocobalaminemia, or low vitamin B_{12}, is reported to occur in 30% and 61% of dogs and cats with chronic enteropathy, respectively.[12,13] Associated with clinical signs such as lethargy, dysrexia, and weight loss, hypocobalaminemia should be corrected with supplementation as described elsewhere.[14]

WHY DO A DIET TRIAL?

It has been shown that 50% to 66% of chronic enteropathy patients respond to a change in diet.[5-8] In one study evaluating 136 dogs with chronic diarrhea, 66% demonstrated complete remission and resolution of diarrhea with implementation of an elimination diet (i.e., FRE).[6] Furthermore, dietary management of FRE in dogs has been shown to result in longer remission rates compared with ARE and IRE, for which there are strong data only for short-term remission (<3 months).[3] Given the multimodal aspects of nutrition and clinical response rates, diet trials are the first-line approach to both diagnosis and treatment of chronic enteropathy.

DIET TRIAL CONSIDERATIONS

Unlike the lengthy diet trial required for dermatologic disease (8 to 12 weeks), a clinical response in patients with FRE can be appreciated within 2 weeks.[15] The biggest mistake made is ruling out FRE after only 1 diet trial and, potentially, providing unnecessary immunosuppressive therapy. One study demonstrated that dogs with protein-losing enteropathy (PLE) that previously did not respond to diet trials and immunosuppressive therapies ultimately achieved remission of clinical signs with a diet change.[16] Thus, performing multiple diet trials is recommended prior to definitively ruling out FRE.

Client compliance is crucial to the success of diet trials. It is recommended to slowly transition the diet over 7 to 14 days to reduce any exacerbation of clinical signs a diet change may cause. After this period, it is important for clients to adhere to a strict elimination diet trial for patients receiving hydrolyzed and novel protein sources. These patients cannot receive their usual treats, flavored medications and supplements, or toothpastes. To better encourage compliance, some acceptable treats are listed in BOX 2. Patients on a low-fat or fiber-enriched diet do not require strict elimination of treats, but care should be taken to ensure treats are <5% of the total daily caloric intake.

DIET TRIAL OPTIONS AND SELECTION

A wide variety of commercial options are available for

BOX 2 Acceptable Treats During an Elimination Diet Trial

Fruits
- Bananas
- Apples
- Watermelon
- Strawberries

Vegetables
- Carrots
- Green beans
- Broccoli[a]
- Cauliflower[a]
- Cucumbers

Others
- Marshmallows (aid in administering medications)
- Commercially available veterinary therapeutic hypoallergenic treats

[a]May cause excessive flatulence in some dogs.

diet trials. These include highly digestible, low-residue GI diets, fiber-enriched diets, elimination diets such as hydrolyzed and novel protein, low-fat diets, and limited-ingredient diets. Homemade diets (e.g., ultra–low-fat diets) are also options. Prior to selecting a diet, it is important to consider the patient's specific clinical signs and history (TABLE 2).

Clinical signs should be used in conjunction with diagnostic findings (e.g., B vitamin status, imaging findings) to localize disease to the small intestine, large intestine, or both (BOX 1 AND TABLE 1). Patients with signs of small intestinal disease should initially be trialed on a highly digestible, low-residue diet followed by a hydrolyzed or novel protein diet. Dogs and cats with signs of predominantly large intestinal disease should be trialed on a fiber-enriched diet first. If they fail to respond, they should be escalated to a hydrolyzed or novel protein diet. In patients with concurrent dermatologic signs, the initial diet trial should be a hydrolyzed or novel protein diet. Finally, if a patient has signs of delayed GI motility, concurrent pancreatitis, or evidence of fat malabsorption, the diet should be low in fat.

A comprehensive diet history should be obtained to identify possible previous antigen exposure and to understand the nutrient makeup of the patient's current diet. This history aids in determining potential novel protein sources and desired fiber or fat content of the trial diet based on the patient's baseline. Downloadable forms to facilitate collection of dietary history are available from the World Small Animal Veterinary Association (WSAVA) and the American College of Veterinary Nutrition (BOX 3).

TABLE 2 Recommended Diet Trials[a]

CLINICAL SIGNS AND CONCURRENT DISEASES	DIET TRIAL #1	DIET TRIAL #2	DIET TRIAL #3
▪ **Small intestinal disease**	Highly digestible, low-residue diet	First elimination diet[b]	Second elimination diet[b]
▪ **Large intestinal disease**[17]	Fiber-enriched diet	First elimination diet[b]	Second elimination diet[b]
▪ **Evidence of fat malabsorption (e.g., hypocholesterolemia, steatorrhea)** ▪ **Dilated lacteals**	Low-fat diet (17–26 g/Mcal ME)	Low-fat elimination diet[b] (17–26 g/Mcal ME)	Ultra–low-fat nutritionist-balanced diet (<15 g/Mcal ME)
▪ **Concurrent dermatologic signs (e.g., pruritus, recurrent otitis externa)** ▪ **Erythema**	First elimination diet[b]	Second elimination diet[b]	Third elimination diet[b]
▪ **Concurrent signs of delayed GI motility (e.g., vomiting, ileus, regurgitation)** ▪ **Concurrent pancreatitis**	Chosen diet should be low fat (17–26 g fat/Mcal ME)		

[a]When selecting an initial elimination diet, it is recommended to begin with a hydrolyzed diet due to reported success with these varieties.[2] Subsequent elimination diet trials should contain variable protein sources, fat content, and fiber content. The purpose of trialing 2 elimination diets is to conclude the disease is not diet responsive before initiating immunosuppressive therapy.
[b]Elimination diets include hydrolyzed diets, novel protein diets, and home-prepared elimination diets.
GI=gastrointestinal; ME=metabolizable energy.

Finally, it is important to ensure that the patient's diet follows WSAVA Global Nutrition Committee recommendations to ensure that it is nutritionally balanced and adheres to appropriate quality control.[2]

Highly Digestible, Low Residue

A highly digestible, low-residue diet is often the first-line diet trial for a patient with mild signs of small intestinal disease. These diets contain highly digestible starches and are characterized by a low fiber content (<10 g total daily fiber/Mcal) and low to moderate fat content (30 to 40 g fat/1000 kcal). Some commercial diets also come in a low-fat formulation (18 to 25 g fat/1000 kcal) and a high-energy formulation with a higher fat content (49 to 60 g fat/1000 kcal).

Fiber Enriched

Fiber has various proposed health benefits, including serving as a prebiotic for the microbiome, promoting intestinal wall health, and providing bulk to help improve diarrhea.[18] Solubility of fiber is important to consider when a specific outcome is desired. Soluble fiber sources (e.g., pectin, gums, psyllium husk) have beneficial effects on the immune system and serve as a food source for the gut microbiota; insoluble fiber sources (e.g., cellulose, lignin) provide bulk and aid in intestinal motility.[19]

Fiber may be provided as a supplement (**TABLE 3**) or in a veterinary therapeutic diet that focuses on higher fiber content. Though fiber-enriched diets are not the first-line recommendation in the dietary approach to chronic enteropathy, they are likely to be beneficial in management of chronic large intestinal diarrhea.[10,11]

Hydrolyzed

Hydrolyzed diets are indicated for patients with small intestinal disease that do not respond to a highly digestible, low-residue diet or those with large intestinal disease that do not respond to a fiber-enriched diet.

BOX 3 Diet History Forms

- **American College of Veterinary Nutrition:** acvn.org/wp-content/uploads/2020/04/ACVN-Diet-History-Form-2020-FINAL_fillable.pdf
- **World Small Animal Veterinary Association:** wsava.org/wp-content/uploads/2020/01/Nutritional-Assessment-Checklist.pdf

They are created by enzymatic hydrolysis, which reduces proteins to small polypeptides and amino acids (<3 to 5 kDa). These molecules are too small to cross-link IgE on the surface of mast cells, preventing mast cell degranulation and IgE-mediated (type I) hypersensitivity.[20]

It is important to note that enzymatic hydrolysis may not be complete, and unless it is followed with ultrafiltration, proteins resistant to hydrolysis and the enzymes used for hydrolysis may themselves serve as an antigenic source. As such, 20% to 50% of patients react to hydrolysates of proteins to which they are allergic.[21] Consequently, it is best to select a hydrolyzed diet with a protein that the patient has not received previously, such as a soy-based diet in a dog that has consumed chicken. Hydrolyzed diets have also been proposed to be inherently more digestible due to the protein breakdown and to have beneficial effects on the microbiome.[2,22] When compared to a highly digestible, low-residue diet, feeding a hydrolyzed diet was more likely to lead to 3-year remission in dogs with chronic small intestinal diarrhea.[23]

Novel Protein

For animals that refuse to eat hydrolyzed protein diets, a novel protein diet can be used as an alternative elimination diet. Around 60% of dogs and 50% of cats

TABLE 3 Fiber Supplementation

FIBER TYPE	EXAMPLE SOURCE	PURPOSE	SUGGESTED TARGET DOSING
Soluble	Psyllium husk[a]	Prebiotic, colonocyte health	1–2 teaspoon(s) per 10 kg body weight per meal[10,b]
Insoluble	Canned pumpkin, bran cereals	Provide bulk, accelerate transit time (may increase vomiting)	0.5–1 tablespoon per 10 kg body weight per meal[b]

[a]Psyllium may increase defecation, loosen stools, or increase flatulence, especially if the patient is not gradually transitioned to the suggested target dose.
[b]Always start with smaller amounts and increase slowly to effect.

When selecting a diet, it is important to consider the taxonomic relationship between meat sources, as there can be cross-over between dietary antigens.[2]

with chronic enteropathy have been found to respond to a novel protein diet.[7,8] Novel protein diets contain protein and carbohydrate sources to which the patient has not previously been exposed. Common novel proteins include venison, rabbit, duck, and kangaroo; common novel carbohydrate sources include potato, sweet potato, oats, barley, and green peas. Though it has become increasingly difficult to provide a truly "novel" diet due to the variety of over-the-counter (OTC) pet foods on the market, a benefit may still be seen with these diets as the limited ingredient profile may reduce antigen exposure in the gut.

When selecting a diet, it is important to consider the taxonomic relationship between meat sources, as there can be cross-over between dietary antigens.[2] For example, it may be wise to avoid duck-based diets in patients that have previously consumed a chicken-based diet.[24] Similarly, a dog that has eaten a beef-based diet should avoid goat-based diets.

Although OTC novel protein diets may seem more cost effective than veterinary therapeutic diets, their quality can vary. OTC diets have frequently been found to be contaminated with animal proteins not listed on the label.[17,25] Therefore, it is strongly recommended to provide a veterinary therapeutic novel protein diet to ensure quality control. After documenting success with the initial therapeutic diet, transitioning to an OTC formulation of the same protein source can be considered, but it is not without risk.

Low Fat

A low-fat diet should be considered in dogs with pancreatitis or evidence of delayed gastric motility or fat malabsorption.[26] Fat often increases palatability, which is likely why maintenance diets are higher in fat.

In dogs with fat maldigestion or malabsorption, passage of fat within the intestinal lumen is increased, which can lead to dysbiosis and induce epithelial cell damage and fluid secretion into the colon. Increased dietary fat has also been shown to have proinflammatory effects.[2] Dietary fat content does not affect the outcome in cats with chronic diarrhea and therefore is likely less important in this species.[27]

A low-fat or ultra–low-fat diet is indicated for dogs with intestinal lymphangiectasia (IL) or idiopathic PLE, especially if there is concurrent hypocholesterolemia. Low-fat diets help alleviate clinical signs of IL and PLE by reducing lymphatic flow and pressure secondary to chylomicron production.[2] Idiopathic IL is common in breeds such as the Yorkshire terrier, Norwegian lundehund, soft-coated wheaten terrier, and Maltese. Although definitive diagnosis requires histopathology, the finding of hyperechoic intestinal mucosal striations on abdominal ultrasound increases suspicion of IL. Many dogs with food allergies may have secondary lymphangiectasia and consequently require a diet that both is low in fat and contains a novel or hydrolyzed protein.

A low-fat diet is considered to contain 17 to 26 g fat/Mcal metabolizable energy (ME).[28] This is much lower than most, but not all, hydrolyzed and novel protein diets, which contain 25 to 52 g fat/Mcal ME. An ultra–low-fat diet is considered to contain <15 g fat/Mcal ME;[28,29] to the authors' knowledge, no such diet is currently commercially available.

Limited-Ingredient Homemade

Commercial formulated diets may not meet the needs of every patient with FRE, such as those that require an ultra–low-fat diet. Other patients may have inherent sensitivities to emulsifiers and preservatives found in commercial diets.[2] Finally, comorbidities (e.g., chronic kidney disease) may necessitate multimodal diet therapy in long-term management. For such cases, it is recommended to seek a board-certified veterinary nutritionist to better evaluate the patient's nutritional needs and develop a tailored diet regimen. In addition, a veterinary nutritionist is best able to provide necessary monitoring and supplementation advice to avoid macronutrient, vitamin, and mineral deficiencies that can be seen in home-prepared diets.[30]

CONCLUSION

FRE is very common in dogs and cats. In stable patients, multiple diet trials may need to be performed before concluding chronic enteropathy is not food responsive. Furthermore, management of chronic enteropathy requires a multimodal approach, like figuring out the combination of a lock. Diet may be one dial, but concurrent modulation of the microbiome with probiotics, supplementation of vitamins, and immunosuppression may be necessary to open the lock. It is best to work with the client to determine their goals of management and discuss possible negative consequences of therapy modalities. If a patient is severely affected or fails to respond to deworming, diet trials, and supplementation of B vitamins, advanced diagnostics (e.g., GI endoscopy, exploratory laparotomy for GI biopsy) should be considered before pursuing immunosuppressive therapy. TVP

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