THE BIG PICTURE It is important to assess a diet's complete nutritional profile, rather than relying on the general marketing, when assessing if it is appropriate for patients.

CASE REPORT: NUTRITION

Dietary Elimination Trial in a Dog with Protein-Losing Nephropathy

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Managing patients with multiple medical conditions can prove challenging when those conditions have contradicting nutritional goals or when a diet that meets the needs of both conditions does not exist, as in the case described here. In these instances, a problem list can be created to compare nutritional goals, priorities, and nutrients of concern among all diet options. Sometimes a trial-and-error approach is required and the deciding factor is the patient's response to the diet.

This case report discusses a dog with protein-losing nephropathy and the need for a dietary elimination trial to diagnose potential food allergies. The dog was referred to the Cummings School of Veterinary Medicine nutrition service for nutritional management that would support his concurrent medical conditions. Diet and management options discussed in this report illustrate the approach taken for this specific patient and should not be generalized to all dogs with similar conditions.

HISTORY

The patient was a 1-year-old intact male boxer originally presented to his primary care veterinarian for polyuria, polydipsia, and incontinence, as well as persistent vomiting and diarrhea with weight loss. He had a history of pruritus that was controlled with oclacinitib (Apoquel; Zoetis, zoetisus.com). His previous diet was Purina Savor Lamb and Rice Canine (dry) and Sojos Complete Beef Freeze-Dried Raw Meat Grain-Free (dry).

His primary care veterinarian diagnosed protein-losing nephropathy (PLN) and initiated medical management, including clopidogrel and enalapril. Empirical treatment for his gastrointestinal signs included a short course of tylosin tartrate and probiotics (Visbiome; ExeGi Pharma, visbiome.com). Initially, his stool quality improved greatly; however, he continued to have intermittent episodes of borborygmus, nausea, vomiting, and anorexia. The patient's diet was changed to Hill's Prescription Diet z/d Canine, dry and canned,

and when this diet change did not fully resolve his symptoms, he was referred to our nutrition service to determine the best diet for both his PLN and his ongoing gastrointestinal signs.

REFERRAL ASSESSMENT

Physical Examination Findings

Physical examination by the nutrition service revealed a body weight of 28 kg and a body condition score (BCS) of 2/9 (based on the World Small Animal Veterinary Association [WSAVA] body condition score system of BCS 1 through 9; wsava.org/wp-content/uploads/2020/01/Body-Condition-Score-Dog.pdf). His medical record indicated a previous weight of 31.8 kg, BCS of 5/9, and moderate muscle wasting (based on WSAVA muscle condition score [MCS] system of normal, mild, moderate, or severe muscle wasting; wsava.org/wp-content/uploads/2020/01/Muscle-Condition-Score-Chart-for-Dogs.pdf). The remainder of his physical examination revealed no significant abnormalities.

Diagnostic Tests and Results

Diagnostics included testing for parasites (blood and intestinal), urinalysis, and blood chemistry. Results were negative for parasites and positive for proteinuria, isosthenuria, and microalbuminuria; blood urea nitrogen (BUN) was slightly elevated (**TABLE 1**).

Abdominal ultrasonography showed hyperechoic renal cortices with poor corticomedullary demarcation, which could be consistent with either renal dysplasia or chronic nephritis/glomerulonephritis. Considering the patient's young age, renal dysplasia was of highest concern, but chronic nephritis/glomerulonephritis could not be excluded. Mildly reactive mesenteric lymph nodes were noted but were a nonspecific finding. No gross gastrointestinal tract abnormalities were detected.

Differential Diagnoses

For the patient's history of poor stool quality, the primary causes under consideration were malabsorptive or protein-losing enteropathies or dysbiosis. The gastrointestinal differentials were:

- Inflammatory bowel disease
- Food allergy
- Food intolerance (i.e., fat or fiber intolerance or sensitivity)
- Fiber-responsive diarrhea

TABLE 1 Initial Diagnostic Tests and Results

TEST	RESULT (REFERENT)	INTERPRETATION
RUN BY PRIMARY VETERINARIAN		
Accuplex 4 (Antech, antechdiagnostics.com)	Negative for *Borellia burgorferi*, *Anaplasma*, *Ehrlichia*, *Dirofilaria immitis*	
Fecal flotation	Negative	
RUN BY REFERRAL NUTRITION SERVICE		
URINALYSIS		
Appearance	Yellow, cloudy	
Urine specific gravity	1.006	Isosthenuria
pH	6.5	
Protein	3+	
White blood cells	2–3 cells/high power field	
Albumin	>30 (<2.5) mg/dL	High, microalbuminuria
Urine protein–creatinine ratio	1.7 (<0.5)	High
Culture	No growth	
BLOOD CHEMISTRY*		
Blood urea nitrogen	33 (6–31) mg/dL	Slightly high
Creatinine	1.4 (0.5–1.6) mg/dL	
Total protein	5.8 (5.0–7.4) g/dL	

**All other chemistry values were within reference range.*

- Stress colitis
- Pancreatitis
- Biliary vomiting syndrome

The renal differentials were:
- Congenital renal dysplasia
- Chronic nephritis/glomerulonephritis

TREATMENT PLAN

Medical management was continued by the primary care veterinarian. For nutritional management, we started by developing nutritional goals and creating a list of nutrients of concern for the patient's multiple confirmed and suspected conditions. Considerations that needed to be addressed included conducting a dietary elimination trial to determine a potential food allergy while balancing nutrient modifications recommended for protein-losing nephropathy. The nutrients of concern for his stage of renal disease (avoiding high protein and phosphorus) did not directly contradict the nutrients of concern for his potential food allergy (hydrolyzed protein diet appropriate for dietary elimination trial); however, in this case, there was not a diet available on the market that met both those needs. We thus had to carefully consider the possible consequences of each potential diet and prioritize the nutrients of concern to select the most appropriate diet available. Dietary management was also not straightforward because the exact cause(s) of the patient's gastrointestinal signs were not known and required a dietary trial. These limitations necessitated a trial-and-error approach to diet while monitoring renal values.

Nutritional Goals

- Provide a complete and balanced diet to achieve ideal body weight (target weight 70 lb [32 kg]); this goal was of the highest priority.

TABLE 2 Nutritional Content of Select Therapeutic Diets*

PRODUCT†	KCAL/CAN OR CUP	PROTEIN (G/100 KCAL)	FAT (G/100 KCAL)	PHOSPHORUS (MG/100 KCAL)	CRUDE FIBER (G/100 KCAL)
Hill's Prescription Diet z/d Canine, canned	352	5.2	3.6	140	1.3
Hill's Prescription Diet z/d Canine, dry	354	4.9	3.7	150	1.1
Purina Pro Plan Veterinary Diets HA Hydrolyzed Chicken Flavor Canine Formula, canned	341	7.7	3.6	380	2.5
Purina Pro Plan Veterinary Diets HA Hydrolyzed Chicken Flavor Canine Formula, dry	342	5.3	3.2	220	0.4
Purina Pro Plan Veterinary Diets Hydrolyzed Canine Formula (Vegetarian), dry	314	5.4	2.7	230	0.4
Royal Canin Veterinary Diet Hydrolyzed Protein HP Dry Dog Food	331	5.2	4.8	200	0.4
Royal Canin Veterinary Diet Hydrolyzed Protein Adult Loaf Canned Dog Food	395	5.8	3.6	170	1.4
Royal Canin Veterinary Diet Hydrolyzed Protein Moderate Calorie Dry Dog Food	306	6.2	3.2	160	0.4
Royal Canin Veterinary Diet Hydrolyzed Protein Small Dog Dry Dog Food	373	6.2	4.2	210	0.3
Royal Canin Veterinary Diet Multifunction Renal Support + Hydrolyzed Protein Dry Dog Food	385	3.4	4.7	50	0.5
Royal Canin Veterinary Diet Ultamino Dry Dog Food	316	4.7	4.3	210	0.6

**AAFCO minimum for adult dogs: protein 4.5 g/100 kcal, fat 1.4 g/100 kcal, phosphorus 100 mg/100 kcal.*
†Some diets listed here have undergone reformulation since this case was initially reported, so confirming the most recent formulations from each company's product guides is recommended.

- Avoid diets with high protein and phosphorus because of the proteinuria and elevated kidney values.
- Avoid diets with high fat because of the history of gastrointestinal signs and potential for fat sensitivity.
- Consider performing a dietary elimination trial as an initial strategy, using a novel or hydrolyzed protein diet.
    - If signs improve, consider limited-ingredient diets after rechallenge with protein sources.
    - If signs do not improve, consider trial and error to determine optimal nutrient profile.

Nutrients of Concern

- **Calories:** Provide enough calories for weight gain.
- **Protein:** Meet Association of American Feed Control Officials (AAFCO, aafco.org) minimum of 4.5 g/100 kcal initially, then modify according to response.[1]
- **Phosphorus:** Meet AAFCO minimum of 100 mg/100 kcal but keep under 200 mg/100 kcal.
- **Fat:** Initially feed the diet with the lowest fat among the diets that otherwise meet nutritional goals. Determining the optimal fat content for minimizing clinical signs while encouraging weight gain may require a trial-and-error approach.
- **Fiber:** Initially feed a diet with low crude fiber, then consider increasing fiber for secondary trial-and-error testing.[2]
- **Omega-3 fatty acids:** Consider supplementing with docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) after the patient is stabilized and stool quality is controlled.[3]

Dietary Elimination Trial

To determine which diet would best meet nutritional goals, we analyzed all the hydrolyzed protein diet options. Because the patient's previous dietary history was unknown to the family, selecting a diet with novel protein sources would have been very challenging, so we considered only hydrolyzed protein options (**TABLE 2**).

Although the patient's current diet (Hill's Prescription Diet z/d Canine) met many of his nutritional goals, the client was concerned that the dog's gastrointestinal signs (episodes of borborygmus, nausea, vomiting, and anorexia) had not resolved. A full dietary history revealed that the dog was still receiving flavored preventives and treats (he was regularly given commercial Milk-Bone biscuits). The client was given the option of pursuing a strict dietary trial with the current diet or considering another option, which may not have been ideal for meeting the other nutritional goals (e.g., protein, phosphorus). Given the patient's proteinuria, a decision was made to pursue a short (6 to 8 weeks) trial with the diet with the lowest hydrolyzed protein that still met the AAFCO minimum for protein: Royal Canin Veterinary Diet Ultamino dry (royalcanin.com). Although we considered Royal Canin Veterinary Diet Multifunction Renal Support + Hydrolyzed Protein dry, given the moderate muscle wasting, we decided to not initially restrict protein too severely and to modify as needed based on response to diet. The clients gradually transitioned the diet to Royal Canin Veterinary Diet Ultamino dry over 7 days, with strict instructions to not give any other food items (including treats, table food, toothpaste, flavored medications, flavored supplements, or flavored toys). To encourage weight gain, they fed him ad libitum.

If the dog needed something to chew on or distract him from getting into other pets' food, human food, or the trash, we recommended that a portion of the dry food be made into a slush with water and frozen into a rubber Kong toy as a substitute for treats, chews, and toys. For enrichment, we also recommended food-dispensing toys.

For medication administration, we recommended that the family learn how to administer pills without food, although as an emergency backup option, we suggested that medication could be given in ⅛ teaspoon of honey. We also considered putting the medications into a slush of the diet, but concerns of food aversion (which had happened previously) eliminated that option. The Visbiome was continued; the capsule was opened and the powder was sprinkled directly onto the food, which did not affect the dog's appetite.

OUTCOME

After 2 weeks of eating the Royal Canin Ultamino Canine dry diet, tylosin was discontinued and the dog's stools remained firm. After 8 weeks, body weight increased to 31 kg, BCS increased to 5/9, and MCS improved to mild muscle wasting. By the end of the dietary trial, the nausea, vomiting, and borborygmus episodes had not completely resolved but had become much more infrequent. Therefore, even without a rechallenge trial, we considered this a positive response to the trial and made a presumptive diagnosis of food allergy.

Diagnostics to determine the effects on the patient's kidney disease after an 8-week dietary trial indicated

relatively stable renal values (slightly increased BUN and creatinine), with significantly improved urine protein–creatinine (UPC, 50% reduction). Slight hematuria and granular casts were possibly indicative of a bacterial infection, but urine culture was negative. (**TABLE 3**).

Because food allergy cannot be 100% confirmed without a rechallenge, we discussed with the clients rechallenge with dietary proteins to confirm a food allergy and determine the source of the protein allergy. The clients, however, elected to not make any changes at that time, given the patient's improved gastrointestinal signs and UPC and stable azotemia.

DISCUSSION

Patients with multiple conditions can be challenging to manage nutritionally, particularly if dietary modification is necessary to diagnose one of the conditions, such as in this case with a suspected food allergy. Although we were able to initiate a dietary elimination trial without exacerbating the patient's other medical condition (renal disease), we lacked the information that might have been gleaned from a dietary rechallenge. Without a rechallenge trial, the food allergy was thus a presumptive diagnosis but not absolutely confirmed. The clients' reluctance, however, is not surprising in that, in the author's experience, many clients are hesitant to challenge or make changes after a dietary regimen has resolved clinical signs.

One interesting consideration of this case was the patient's improvement on one hydrolyzed diet and not another. This discrepancy may have resulted from 1 of 3 possible mechanisms: 1) when the first hydrolyzed diet was fed, treats and flavored medications were not discontinued and thus, a strict dietary elimination trial was not conducted with that food; 2) the patient may have responded to the second hydrolyzed diet because the protein was more hydrolyzed and the patient had an extreme sensitivity to allergens; or 3) the patient does not have a food allergy but rather has a nutrient intolerance and responded to a change in the nutrient profile (i.e., response to higher or lower fat or fiber levels that can affect gastrointestinal signs). Without further rechallenge and trial and error, we cannot know which of the 3 mechanisms applies to this patient.

At that time and without a rechallenge or diet change, we recommended frequent monitoring of all renal values (e.g., BUN, creatinine, phosphorus, potassium), particularly while he was receiving enalapril, and urine protein levels. The UPC reduction from 1.7 to 0.8 was promising and met the glomerular disease goal of a 50% reduction, per the American College of Veterinary Internal Medicine consensus statement.[1] Of biggest concern with the current dietary regimen is the phosphorus level, which is higher than ideal for a dog with renal impairment. However, should phosphorus values increase, a phosphate binder could be added if all other values are stable. In addition, if/when kidney disease advances, the next step could be giving a 50:50 mixture of 2 diets (the current Royal Canin Veterinary Diet Ultamino dry and the Royal Canin Veterinary Diet Multifunction Renal Support + Hydrolyzed Protein dry) and gradually transitioning fully to the latter diet as worsening kidney disease may warrant.

TABLE 3 Recheck Diagnostic Tests and Results (8 Weeks After Start of Diet Trial)

TEST	RESULT (REFERENT)	INTERPRETATION
URINALYSIS		
Urine specific gravity	1.011	
pH	5.0	
Protein	3+	
Glucose, ketones, urobilinogen, bilirubuin	Negative	
Blood	25 cells/hpf	Possible bacteriuria, inflammation, cystocentesis
Urine protein–creatinine ratio	0.8 (<0.5)	
Casts	Granular	Possible bacteriuria
Culture	Negative	
BLOOD CHEMISTRY		
Blood urea nitrogen	38.7 (6–31) mg/dL	
Creatinine	1.5 (0.5–1.6) mg/dL	

At our most recent communication, the clients reported that the dog's gastrointestinal signs were stable and that they planned to have laboratory work rechecked every 3 to 6 months as recommended by their primary care veterinarian. We hope that they may also consider a diet rechallenge trial in the future.

TAKE-HOME POINTS

- Creating a fully inclusive list of nutritional goals requires a full nutritional assessment, including physical examination, BCS, MCS, dietary history, and diagnostic workup.
- Because patients, especially those with gastrointestinal disease, can exhibit varied individual responses to diet, trial and error is often necessary.
- Ensuring appropriate diet selection for each patient requires consideration of a diet's nutritional profile (i.e., calories, protein, fat, fiber) and not just the marketing or advertising of a diet.
- For patients with multiple medical conditions, monitoring is especially important for assessing responses and reprioritizing nutritional goals as each condition may progress. TVP

References

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