Nutritional Management of Protein-Losing Nephropathy in Dogs

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Abstract: *Optimal treatment of protein-losing nephropathy (PLN) should address both medical and nutritional issues. In nonazotemic dogs with PLN, the main nutrients of concern are protein, calories, omega-3 fatty acids, and sodium. In azotemic dogs with PLN, requirements for additional nutrients should be addressed. The amount of protein and the specific diet must be individualized for every patient with PLN because commercial dog foods differ greatly in protein and other nutrients. It is critical to avoid excessive dietary protein restriction, which may contribute to loss of lean body mass. A thorough diet history must be obtained to account for the animal's entire daily intake of protein and other nutrients.*

Protein-losing nephropathy (PLN) is frequently diagnosed in dogs. Diagnosis is based on an elevated urine protein:creatinine (UPC) ratio after excluding other causes of proteinuria. A renal biopsy is often helpful to provide a definitive diagnosis and determine the specific histopathologic form. The primary forms of PLN are glomerulonephritis and amyloidosis. Amyloidosis is associated specifically with infiltration of the glomerulus with amyloid protein. Glomerulonephritis can be classified as primary (i.e., idiopathic) or secondary to an underlying disease (e.g., infectious, inflammatory, neoplastic).[1–3] According to the 2009 International Renal Interest Society (IRIS) staging guidelines for chronic kidney disease (CKD), stage 1 CKD includes persistent proteinuria of renal origin[4]; therefore, dogs with PLN should be assessed for CKD.

The clinical signs of PLN vary depending on the degree of proteinuria and stage of CKD. In some asymptomatic animals, proteinuria is detected incidentally. Anorexia, weight loss, vomiting, and polyuria/polydipsia are common with more advanced disease. Clinical signs also may reflect complications from hypertension (e.g., retinal hemorrhage), hypercoagulability (e.g., pulmonary thromboembolism), or hypoalbuminemia (e.g., ascites, pleural effusion).[1–3,5]

Optimal treatment of PLN should address both medical and nutritional issues, which have synergistic effects. The mainstay of medical therapy for proteinuria is angiotensin-converting enzyme inhibitor (ACEI) therapy.[1,2] Proteinuria is expected to decrease within 4 weeks of instituting ACEI therapy; however, maximal response may take longer.[6] Antithrombotic drugs (e.g., aspirin, clopidogrel) are often recommended to address hypercoagulability.[1,2] Additional medical treatment should be tailored on an individual basis. However, to optimally manage the disease, all dogs with PLN should undergo a careful nutritional assessment and an individualized nutritional plan should be developed. Two excellent review articles[1,2] on the medical aspects of PLN were recently published; this article focuses on the nutritional management of canine PLN.

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Nutrients of Concern

A number of nutrients are of concern (i.e., of particular importance for disease management in an individual animal) for dogs with PLN. In dogs with PLN that are nonazotemic (i.e., IRIS stage 1),[4] the main nutrients of concern are protein, calories, sodium, and omega (n)-3 fatty acids.

Protein

For dogs with PLN, protein restriction is recommended even in early stages of the disease. This recommendation differs from that for dogs with tubulointerstitial CKD, in which protein restriction has not been shown to slow disease progression and is not recommended in early stages of disease.[7] Dietary protein restriction has been shown to reduce proteinuria in dogs with spontaneous hereditary glomerulonephropathy. In one study,[8] proteinuria decreased by 57% to 68% after dogs were switched from 8.0 g/100 kcal to 3.3 g/100 kcal protein. Decreasing dietary protein has also been shown to decrease proteinuria in people with CKD.[9,10] The proposed mechanism for the benefits of protein restriction is a decreased glomerular filtration rate and subsequent reduction in structural damage to the remaining glomeruli.[11]

The recommended degree of protein restriction depends on the individual dog's current diet. We emphasize the importance of obtaining a complete and thorough diet history, as is recommended in the recent AAHA[12] and World Small Animal Veterinary Association (WSAVA) Nutritional Guidelines,[13] when making dietary recommendations for animals with PLN. A thorough diet history includes the specific brand, product, and flavor of pet food (or recipe of the homemade diet) plus amount fed and frequency of feeding, along with specific information about treats, table food, dietary supplements, and foods used for medication administration.

Commercial dog foods (both veterinary therapeutic and over-the-counter foods) differ greatly in protein content (**TABLE 1**); therefore, an individual dog's dietary protein intake can vary widely depending on what food it is eating. Dog food is only one component of an animal's overall protein intake; treats, table food, and foods used for medication administration also contribute. **TABLE 2** illustrates the wide range of calories and protein that a dog could be consuming even with only modest treat intake. Depending on a dog's initial diet, the recommended degree of protein restriction required to reduce proteinuria varies. If the dog's diet is very high in protein when PLN is diagnosed, it is usually not necessary to transition to a food designed for advanced kidney disease. If treats are contributing a large proportion of daily protein intake, modifying the dog's treats may sufficiently reduce the protein intake and eliminate the need for a change of food.

It is critical to avoid excessive dietary protein restriction (i.e., more than the amount required to reduce proteinuria), which may contribute to loss of lean body mass and predisposes animals to malnutrition. We recommend initially reducing total dietary protein intake by 25% to 50%, depending on the severity of proteinuria, azotemia, and clinical signs. Dietary protein restriction typically results in a decline in proteinuria within 1 month.[8,9] If the dog's diet already contains a modest amount of protein (e.g., near the Association of American Feed Control Officials' minimum of 5.1 g/100 kcal), it may be preferable to allow the ACEI time to decrease proteinuria before further restricting dietary protein. If the ACEI successfully reduces proteinuria, further diet modification may not be necessary. However, if the UPC does not decrease sufficiently (e.g., to <50% baseline) on an ACEI alone or with modest protein restriction within 1 month, further dietary protein restriction should be instituted.

Table 1. Calorie Density and Protein Content of a Range of Commercial Dry Dog Foods and Resulting Dietary Protein Intake for a 20-kg Dog

Diet	Caloric Density (kcal/cup)	Protein (g/100 kcal)	Total Protein Intake (g/d)[a]
Hill's Prescription Diet r/d Canine Weight Loss-Low Calorie[b]	242	10.6	98.3
Evo Turkey & Chicken Formula[c]	537	10.2	94.6
Purina Active Senior 7+[d]	351	8.4	77.9
Purina Dog Chow[d]	406	6.0	55.6
Iams Veterinary Formula Renal Plus[e]	259	5.5	51.0
Science Diet Mature Adult Active Longevity[b]	363	4.9	45.4
Purina NF Kidney Function Canine Formula[d]	459	3.6	33.4
Hill's Prescription Diet k/d Canine Renal Health[b]	396	3.3	30.6
Royal Canin Veterinary Diet Renal LP Modified[f]	271	3.3	30.6
Hill's Prescription Diet u/d Canine Non-Struvite Urinary Tract Health[b]	396	2.5	23.2
AAFCO minimum (adult dog)	—	5.1	—

AAFCO = Association of American Feed Control Officials

[a]Calculations are based on a 20-kg dog eating 927 kcal/d (calculated as $1.4 \times [70 \times (BW_{kg})^{0.75}]$).

[b]Hill's Pet Nutrition Inc, Topeka, KS.

[c]Natura Pet Products, Fremont, NE.

[d]Nestlé Purina PetCare, St. Louis, MO.

[e]P&G Pet Care, Mason, OH.

[f]Royal Canin USA, St. Charles, MO.

Calories

Calorie recommendations depend on the animal's body weight, body condition score (BCS), and muscle condition score (MCS). The BCS assesses fat stores, and the MCS assesses muscle.[12,13] In dogs with chronic diseases such as PLN, muscle (lean body mass) is preferentially lost. Therefore, it is critical to assess both fat and muscle stores because a dog can be overweight, or even obese, but still have significant muscle loss. It has been demonstrated that dogs that are underweight when diagnosed with CKD have a worse prognosis than moderately sized or overweight dogs.[14] Thus, weight loss in overweight dogs should not be a priority at the time of diagnosis of PLN. For hospitalized animals, feeding the resting energy requirement (RER; $70 \times [BW_{kg}]^{0.75}$) is recommended as an initial goal. Once the animal is at home, its maintenance energy requirement can be calculated. This may range from 1.2 to 1.8 × RER, depending on the animal's activity level and metabolism.[15] However, it is important to remember that while these calculations provide a starting point, the amount fed often needs to be adjusted over time to prevent undesired weight loss or gain and to maintain optimal body condition.

It also is important to be aware that many dogs with PLN, particularly as it becomes more advanced, exhibit hyporexia or anorexia. To prevent the adverse consequences of malnutrition and to optimize patient outcome, methods to enhance food intake often are required. This may entail switching to a different diet (with an appropriate nutrient profile) or using various measures

Table 2. Effect of Treats on Daily Caloric and Protein Intake for a 20-kg Dog[a]

Treats	kcal From Treats	Total kcal/d	Daily kcal From Treats (%)	Protein From Dog Food (g/d)	Protein From Treats (g/d)	Total Protein (g/d)
Diet alone with no treats	0	927	0	47.3	0	47.3
Diet plus:						
Milk-Bone Original Biscuit[b] (medium), 3/day	120	1047	11.5	47.3	6.9	54.2
Chicken breast cooked, 3 oz	140	1067	13.1	47.3	26.4	73.7
Rawhide (small, 40 g), 1/day	168	1095	15.3	47.3	32.6	79.9
Milk-Bone Original Biscuit[b] (medium), 3/day + Chicken breast, cooked, 3 oz + Rawhide (small, 40 g), 1/day	428	1355	31.6	47.3	65.9	113.2

[a]Calculations are based on a 20-kg dog eating 927 kcal of a commercial adult dog food containing 5.1 g/100 kcal protein (calorie intake calculated as $1.4 \times [70 \times (BW_{kg})^{0.75}]$).

[b]Del Monte Foods, Parsippany, NJ.

to increase food intake (**BOX 1**). If a dog with PLN has hyporexia or anorexia, placement of a feeding tube (e.g., esophagostomy tube, gastrostomy tube) may be beneficial to ensure adequate calorie intake and consistent use of a diet with an optimal nutrient profile, as well as to provide a route for medication administration.

n-3 Fatty Acids

n-3 polyunsaturated fatty acids (PUFAs) have a number of potential benefits, including antiinflammatory and antithrombotic properties, that may make them useful in dogs with PLN. In dogs with experimentally induced renal disease, dietary supplementation with n-3 PUFAs was shown to decrease proteinuria.[16,17] However, this effect was not seen in one study of dogs with spontaneously occurring CKD,[18] nor have results been reported for dogs with naturally occurring PLN.

Although an optimal dose of n-3 PUFAs for dogs with PLN has not been determined, we currently recommend a dosage of fish oil to provide 40 mg/kg eicosapentaenoic acid (EPA) and 25 mg/kg docosahexaenoic acid (DHA) for animals with PLN unless there is a contraindication (e.g., platelet abnormalities, taste intolerance). When recommending an n-3 PUFA supplement, it is important to know the exact amount of EPA and DHA in the specific brand because fish oil supplements vary widely. Fish oil supplements should always contain vitamin E as an antioxidant, but other nutrients should be excluded to avoid toxicities. Cod liver oil should be avoided for use at this dose in dogs because of its high vitamin A and D levels. Flaxseed oil should be avoided because dogs cannot efficiently convert plant-based n-3 fatty acids to EPA and DHA. Because dietary supplements do not require proof of safety, efficacy, or quality control to be marketed, careful selection of type, dose, and brand is important to avoid toxicities or lack of efficacy.

Sodium

Sodium restriction is typically recommended for animals with kidney disease to reduce the risk of systemic hypertension and, subsequently, glomerular hypertension.[7] A definitive causative role for dietary sodium in hypertension has not been proven in dogs. Nonetheless, we recommend avoiding high dietary sodium in dogs with CKD and PLN. Most veterinary renal diets are mildly to severely sodium restricted (i.e., 40 to 103 mg/100 kcal). However, as many treats, table foods, and foods used for medication administration are high in sodium, it is important to specifically discuss these with owners.

Other Considerations

A large proportion of animals with glomerular disease develop azotemia (i.e., IRIS stage 2, 3, or 4 CKD). In these dogs, levels of the following nutrients are also of concern.

Phosphorus

Dietary phosphorus restriction has been shown to play a greater role than protein restriction in slowing the progression of renal disease in dogs with induced CKD.[19] Phosphorus reduction may also benefit animals with azotemia by reducing risks of soft tissue mineralization and renal secondary hyperparathyroidism. Diet modification is typically the first step in lowering serum phosphorus. Phosphorus concentrations vary widely among canine diets, but a veterinary therapeutic diet or a properly formulated, phosphorus-restricted, home-prepared diet is needed if significant dietary phosphorus restriction is required. If diet modification alone is ineffective in adequately reducing the serum phosphorus concentration, a phosphate binder (e.g., aluminum hydroxide) can be used to further reduce serum phosphorus.

Box 1. Tips to Enhance Food Intake in Dogs With Protein-Losing Nephropathy That Are Hyporexic or Anorexic

- Use coax feeding (petting dog while eating, hand-feeding, feeding the dog in a quiet place or outside).
- Change the temperature of the food (some dogs prefer warm food, while others prefer food at room temperature, cold, or even frozen).
- Administer appetite stimulants (e.g., mirtazapine). Be careful to monitor food intake because many animals receiving appetite stimulants do not consume adequate amounts to maintain body weight.
- Move feeding location (i.e., try feeding the dog in a different room than where it is usually fed).
- Change the dish from which the dog is fed (feed from a new dog dish or from a dinner plate).
- Add small amounts of palatability enhancers to the food (e.g., pancake syrup, applesauce, honey, fruit [not grapes or raisins], baked goods [without chocolate or xylitol], fruit-flavored yogurt).

Potassium

In dogs with IRIS stage 2, 3, or 4 CKD, serum potassium concentrations may be normal, increased, or decreased. Potassium concentrations may be affected by renal function, dietary intake, acid-base status, medications (e.g., ACEIs may increase serum potassium), and gastrointestinal disturbances. Hypokalemia and hyperkalemia can each have serious consequences; therefore, serum potassium should be kept within the reference range. This can be achieved by selecting a food that has an appropriate potassium level (i.e., increased potassium for a dog with hypokalemia; decreased potassium for a dog with hyperkalemia). However, in some cases, additional supplementation or medications are required to regulate serum potassium concentrations.[7]

pH

Acid-base status is often affected in animals with CKD because the kidneys play a major role in acid-base homeostasis. The metabolic acidosis that typically ensues may further aggravate loss of lean body mass and progression of disease.[7] The goal of dietary modification is to provide a diet that is nonacidifying. This is not as much of an issue in dogs as it is in cats (most over-the-counter feline diets are acidifying). However, certain canine over-the-counter diets may include acidifiers, so diets for dogs with CKD should be specifically assessed for their target urinary pH. This information is best obtained by contacting the manufacturer. Therapeutic diets for renal disease typically aim for a neutral or alkaline urine pH. If diet alone does not achieve adequate alkalinization, sodium bicarbonate or potassium citrate may be administered.[7]

Monitoring

Regular monitoring of the diet history, body weight, BCS, and MCS should be performed to ensure that animals are maintaining weight and lean muscle mass and getting adequate amounts of dietary protein. The complete blood count, serum biochemistry profile, urinalysis, and UPC should also be monitored, as PLN is usually a progressive disease for which ongoing dietary and medical modifications may be necessary. For example, dogs with PLN may require only protein restriction in early stages of disease, but as the disease progresses and azotemia develops, phosphorus restriction may also be required.

Practical Aspects of Nutritional Therapy

Nutritional intervention plays a valuable role in the optimal treatment of PLN. As discussed, there is no single diet or specific level of dietary protein that is best for every patient with PLN. A thorough diet history, including treats, supplements, table foods, and foods used for administering medications, must be obtained to account for the animal's entire daily intake of dietary protein, calories, and other nutrients of concern. Depending on the individual case, a veterinary therapeutic diet or specific over-the-counter diet may be most appropriate. It is critical to evaluate protein and other nutrient levels in each diet because they can vary widely (e.g., senior diets vary greatly in protein and phosphorus concentrations).[20] A reduction in dietary protein is often beneficial, but excessive protein restriction should be avoided, especially because it may contribute to loss of lean body mass. Other nutrients of concern and all components of the diet should also be addressed. Concurrent diseases, medications, and owner and dog preferences should be considered.

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