Letters to the Editor

Chronic enteropathy and diet

We are writing in response to the study by Dandrieux et al[1] regarding the use of a chlorambucil-prednisolone combination versus an azathioprine-prednisolone combination for treatment of dogs with chronic enteropathy and concurrent protein-losing enteropathy. The authors conclude that the chlorambucil-prednisolone protocol was more efficacious than the azathioprine-prednisolone protocol but appear to have discounted the role of hydrolyzed diets in management of chronic enteropathy.

From the description of diets used as adjunctive treatment for dogs in the study, it appears that only 3 dogs in the azathioprine group were fed a hydrolyzed diet and 10 were fed a nonhydrolyzed diet, whereas 11 dogs in the chlorambucil group were fed a hydrolyzed diet and only 3 were fed a nonhydrolyzed diet. The authors state that the percentage of dogs fed a fat-restricted diet (vs a non–fat-restricted diet) did not differ between groups, but they apparently did not compare the distribution of hydrolyzed versus nonhydrolyzed diets between groups.

A recent study[2] compared the use of hydrolyzed versus nonhydrolyzed diets in dogs with chronic enteropathy and found that hydrolyzed diets were more efficacious for long-term management of clinical signs than were nonhydrolyzed diets. Therefore, we propose that some of the dogs in the chlorambucil group in the study by Dandrieux et al[1] may have had adverse reactions to food as opposed to inflammatory bowel disease. We recognize that because the study was retrospective in nature, the authors did not have any control over the dietary treatment. Because most of the dogs in the azathioprine group were treated earlier in the study period, when access to hydrolyzed diets may not have been as easy as during the latter part of the study period, when most of the dogs in the chlorambucil group were treated, the difference in diets between groups is understandable. However, we believe the authors should have taken this fact into greater consideration before drawing their conclusion.

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1. Dandrieux JRS, Noble PM, Scase TJ, et al. Comparison of a chlorambucil-prednisolone combination with an azathioprine-prednisolone combination for treatment of chronic enteropathy with concurrent protein-losing enteropathy in dogs: 27 cases (2007–2010). *J Am Vet Med Assoc* 2013;242:1705–1714.
2. Mandigers PPJ, Biourge V, van den Ingh TSGAM, et al. A randomized, open-labeled, positively-controlled field trial of a hydrolyzed protein diet in dogs with chronic small bowel enteropathy. *J Vet Intern Med* 2010;24:1350–1357.

The authors respond:

On behalf of our coauthors, we thank Drs. Ghormley and Feldman for their comments about our study.[1] They raise an interesting point about the possible confounding effect of hydrolyzed diets on treatment outcome, considering that more dogs in the chlorambucil-prednisolone group received a hydrolyzed diet than those in the azathioprine-prednisolone group.

During our initial statistical analyses, we examined the effect of diet in various ways, and this included assessing the effect of a hydrolyzed diet. With simple statistical analyses, time to death or first treatment failure was significantly ($P = 0.02$) longer in dogs fed a hydrolyzed diet than in dogs fed a nonhydrolyzed diet. However, when both treatment group and hydrolyzed diet (included as a binary [fed or not fed] variable) were included in a Cox regression model, the diet effect was no longer significant ($P = 0.22$), but the group effect remained ($P = 0.02$). This suggested that the difference in response between treatment groups was not due to diet. We considered including assessment of various diet effects in the original manuscript but eventually decided against it because of the range of diets fed, including 3 hydrolyzed diet formulations. However, after review, we included analysis of the effect of feeding a low-fat diet at the request of a reviewer.

Drs. Ghormley and Feldman are correct that previous work[2] has demonstrated the efficacy of a hydrolyzed protein diet for long-term management of chronic small bowel enteropathy in dogs. However, in that study,[2] dogs with hypoalbuminemia (< 20 g/L) were excluded, whereas in our study, all dogs had moderate to marked hypoalbuminemia (< 18 g/L). Furthermore,

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that previous study[2] was primarily designed to assess the effect of diet, with very few dogs being treated with immunosuppressive drugs. This might explain the apparent difference in efficacy between studies and is consistent with another study[3] demonstrating that dogs with food-responsive diarrhea are seldom hypoalbuminemic. It is possible that a similar dietary effect would be observed if dogs treated with azathioprine or chlorambucil were randomly assigned to receive a hydrolyzed diet or another type of diet, but this was not assessed in our study.

Finally, Drs. Ghormley and Feldman are right to highlight the complexity of analyzing retrospective studies given concerns related to confounding factors. As a result, we are sure that they would agree with the closing statement of our report that prospective randomized controlled trials are now needed to confirm or refute the findings.

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1. Dandrieux JRS, Noble PM, Scase TJ, et al. Comparison of a chlorambucil-prednisolone combination with an azathioprine-prednisolone combination for treatment of chronic enteropathy with concurrent protein-losing enteropathy in dogs: 27 cases (2007–2010). *J Am Vet Med Assoc* 2013;242:1705–1714.
2. Mandigers PPJ, Biourge V, van den Ingh TSGAM, et al. A randomized, open-labeled, positively-controlled field trial of a hydrolyzed protein diet in dogs with chronic small bowel enteropathy. *J Vet Intern Med* 2010;24:1350–1357.
3. Luckschander N, Allenspach K, Hall J, et al. Perinuclear antineutrophilic cytoplasmic antibody and response to treatment in diarrheic dogs with food responsive disease or inflammatory bowel disease. *J Vet Intern Med* 2006;20:221–227.

Calcinosis cutis in relatives of Bulldogs

The case described in a recent Pathology in Practice article[1] concerning an English Bulldog with severe calcinosis cutis caught my attention because I had a similar case a few years ago that also ended badly. My patient was a 9-year-old sexually intact male Bullmastiff with dermatologic lesions involving the dorsum similar to those described by the authors of the Pathology in Practice article. Over a period of 18 months, I prescribed a wide variety of antimicrobials and performed extensive diagnostic testing, including testing for hypercortisolism, thyroid and kidney dysfunction, and even heart disease. During this time, the dog was also examined by a veterinary dermatologist, who confirmed the diagnosis of calcinosis cutis following histologic examination of a skin biopsy specimen. I also spoke with a veterinarian with extensive experience with Bullmastiffs who was also puzzled by this case. Nothing ever did resolve the odorous, ulcerative, cutaneous lesions on the dorsum of the neck and cranial thoracic area. Exasperated and heartbroken, the owners finally elected euthanasia.

This article is the first time I have seen any reference to an inherited susceptibility for this incurable, often idiopathic condition. Knowing that Bullmastiffs are derived from English Bulldogs, I suspect that my patient had the same condition as described by Tan et al,[1] and recommend that veterinarians include Bulldog crosses in their list of patients potentially predisposed to calcinosis cutis.

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1. Tan RM, Stern AW, White AG, et al. Pathology in practice. *J Am Vet Med Assoc* 2013;243:347–349.