





## ISSUES IN GASTROINTESTINAL DISORDERS

# The Diabetic Cat with Inflammatory Bowel Disease

*Audrey K. Cook, BVM&S, MRCVS, MSc Vet Ed, DACVIM-SAIM, DECVIM-CA, DABVP (Feline)  
Texas A&M University College of Veterinary Medicine & Biomedical Sciences*

Diabetes mellitus (DM) is a common feline endocrinopathy, with an estimated prevalence of 1 in 100 to 1 in 500 cats.<sup>1</sup> Although the pathogenesis is complex, sustained insulin resistance often plays a role, and feline DM has strong similarities to type 2 DM in people.<sup>2</sup> Although most cats are treated with exogenous insulin, dietary modification and the mitigation of insulin-resistant disorders are key parts of successful patient management.<sup>1</sup>

Comorbid conditions can complicate the management of cats with DM, and those with concurrent gastrointestinal (GI) dysfunction such as inflammatory bowel disease (IBD) present some unique challenges (**BOX 1**). Inflammatory processes associated with GI disease may affect insulin sensitivity, thereby driving hyperglycemia and weight loss in a previously well-regulated diabetic patient. Conversely, inconsistent food intake secondary to GI dysfunction puts diabetic patients at risk of hypoglycemia, as insulin needs may change unpredictably. In addition, intestinal protein loss with increased albumin turnover lowers serum

fructosamine concentrations and may confuse efforts to assess glycemic control.<sup>3</sup>

Unfortunately, little consensus currently exists in the terminology for chronic GI disease in cats. For the purposes of this article, the term *inflammatory bowel disease* describes chronic signs of GI dysfunction (e.g., vomiting, diarrhea,

### **BOX 1** Diabetes Mellitus and Gastrointestinal Disease: Challenges in Management

- Maintenance of adequate food intake
- Maintenance of acceptable body weight
- Balancing dietary needs for both conditions
- Avoidance of hypoglycemia
- Effect of medical therapy on insulin requirements
- Timely adjustment of insulin as needs change

#### **CHALLENGE ACCEPTED**

Managing inflammatory bowel disease in diabetic cats can be challenging, but certain diets and therapy can improve patient wellbeing.



changes in food intake, and weight loss) accompanied by histologically documented GI inflammation.<sup>4</sup> In practice, the term *idiopathic IBD* is used for cats in which a cause of the inflammation cannot be identified; that is, cats without an infectious (including parasitic), neoplastic, or metabolic cause, as well as cats that fail to improve with appropriate dietary modification (i.e., food-responsive enteropathy) or the administration of an antibiotic (i.e., antibiotic-responsive enteropathy).

## RECOGNIZING AND DIAGNOSING INFLAMMATORY BOWEL DISEASE

The clinical manifestations of IBD are variable and can be confused with those of poorly regulated DM (e.g., weight loss, polyphagia) or concurrent pancreatitis (e.g., vomiting, hyporexia). Changes in stool consistency are highly suggestive of chronic enteropathy; however, grossly normal fecal output does not rule out the possibility of substantial GI dysfunction in cats. Specific diagnostics such as ultrasonographic assessment of intestinal wall thickness and appearance, along with measurement of serum folate and cobalamin concentrations, may confirm the presence of GI disease and guide decisions regarding the collection of appropriate biopsy samples via



**FIGURE 1.** Endoscopic image of the proximal duodenum of a 10-year-old female spayed domestic shorthaired cat with chronic vomiting and weight loss. The mucosa is fragile and irregular. Biopsy revealed moderate lymphoplasmacytic enteritis. Clinical signs resolved following the introduction of a novel antigen diet.

### BOX 2 Diagnostic Approach for Cats With Suspected IBD

- Chemistry profile with electrolytes
- Urinalysis
- Fecal flotation
  - +/- Specific pathogen testing (e.g., *Trichostrongylus*, *Histoplasma*)
- Serum total thyroxine (T4)
  - +/- Free T4
  - +/- Feline leukemia virus and feline immunodeficiency virus testing
- Serum folate and cobalamin<sup>a</sup>
  - +/- Feline pancreatic lipase immunoreactivity<sup>b</sup>
  - +/- Trypsin-like immunoreactivity<sup>b</sup>
- Empirical deworming (patients with diarrhea)
  - Fenbendazole 50 mg/kg PO q24h × 3 days
- Abdominal ultrasonography
- Gastrointestinal biopsy collection
- Food trial: novel antigen or hydrolyzed protein<sup>c</sup>
  - +/- Antibiotic trial for patients with diarrhea (tylosin 15 mg/kg PO q12h)<sup>c</sup>
- Immunomodulatory therapy

<sup>a</sup> Guidelines for supplementation available at [vetmed.tamu.edu/gilab/service/assays/b12folate/](http://vetmed.tamu.edu/gilab/service/assays/b12folate/)

<sup>b</sup> Concurrent pancreatic disease does not rule out IBD

<sup>c</sup> May be performed before biopsy collection

laparotomy or endoscopy (**FIGURE 1**). A recommended workup for cats with signs suggestive of chronic enteropathy is provided in **BOX 2**.

Although clinicians may be reluctant to anesthetize a poorly controlled diabetic cat, careful planning and monitoring mitigate much of the risk.<sup>5</sup> In the author's practice, anesthetic procedures for diabetic patients are scheduled early in the day so that the patients can be monitored for several hours afterward. Breakfast is withheld, and 50% of the usual insulin dose is administered subcutaneously. The blood glucose level should be checked before anesthetic induction and every 30 minutes thereafter, until the cat is extubated and able to eat. A small meal should be offered as soon as the cat is able to eat (ideally within 2 hours of extubation). If necessary, a 2.5% dextrose infusion (50 mL of 50% dextrose in 1 L of fluids) can be administered to prevent hypoglycemia. The author often places an esophageal feeding tube at the time of surgical



or endoscopic biopsy collection in cats with a history of hyporexia, as this facilitates the adequate intake of specific diets and the administration of medications.

If a client declines GI biopsy or the cat's clinical condition precludes invasive diagnostics, it is reasonable to make a presumptive diagnosis of IBD and move forward accordingly. However, it is imperative to exclude regionally endemic infectious conditions (e.g., GI histoplasmosis) before beginning immunomodulatory therapy. Clinicians should also consider the possibility of GI small cell lymphoma, which shares many clinical features with IBD but carries a more guarded long-term prognosis.

## DIETARY CONSIDERATIONS

Research in client-owned cats with unexplained chronic GI inflammation suggests that a substantial proportion will have a positive clinical response to a novel protein diet.<sup>6</sup> It is therefore worthwhile to try a limited-antigen or hydrolyzed protein diet before prescribing antibiotics or immunomodulatory agents. Dietary considerations for cats with concurrent DM are more complicated, however, as current recommendations support the use of low-carbohydrate diets (<14% metabolizable energy [ME]) in diabetic cats.<sup>1,5,7</sup> All cats have an inherently limited ability to digest starches,<sup>8</sup> and their endocrine response to carbohydrates is distinctly different to that from dogs and people.<sup>9</sup> Diets rich in digestible carbohydrates are thought to contribute to postprandial hyperglycemia in diabetic cats, and low-carbohydrate diets appear to support pancreatic  $\beta$ -cell health and facilitate diabetic remission.<sup>7</sup>

### BOX 3 Limited-Antigen Diets With Carbohydrate Content <20% of Metabolizable Energy

- Royal Canin Veterinary Diet Selected Protein PR Canned<sup>a</sup>
- Royal Canin Veterinary Diet Selected Protein PD Canned<sup>a</sup>
- Hill's Prescription Diet d/d Venison Formula Canned<sup>b</sup>
- Hill's Prescription Diet d/d Duck Formula Canned<sup>b</sup>

<sup>a</sup> [royalcanin.com/us/cats/products/vet-products](http://royalcanin.com/us/cats/products/vet-products)

<sup>b</sup> [hillspet.com/products/cat-food#pd](http://hillspet.com/products/cat-food#pd)

All cats have an inherently limited ability to digest starches,<sup>8</sup> and their endocrine response to carbohydrates is distinctly different to that from dogs and people.<sup>9</sup>

All the currently available prescription dry and canned foods with limited ingredients or hydrolyzed proteins exceed the carbohydrate recommendation of <14% ME, although a few of the canned limited-antigen products do provide <20% ME as carbohydrate (BOX 3). The cat's current feeding regimen—free choice versus meal fed; dry food versus canned—must also be considered. It can be very difficult to change preferences, and some cats are very reluctant to eat enough wet food if accustomed to dry.<sup>10</sup> It is very important when making a dietary recommendation to carefully calculate both the cat's current caloric intake and its target intake, based on an estimation of its optimal weight and present body condition score. Online calculators (e.g., [petnutritionalliance.org](http://petnutritionalliance.org)) can be helpful in this regard.

The novel diet should be introduced over several days and then fed exclusively for 3 weeks. As food-responsive enteropathies can be triggered by both antigens and microingredients, it may be worthwhile to switch brands rather than return to the original food. If the cat's clinical signs resolve and the cat is maintaining an acceptable weight, the new diet should be continued. If not, a second diet trial can be considered (in case of unknown prior exposure to the first antigen) or a diabetic diet can be reintroduced.

Cats with colonic IBD may benefit from a high-fiber diet, as soluble fibers provide butyrate and are thought to support a healthy microbiome. Standard high-fiber diets often contain substantial amounts of digestible carbohydrates, which may be problematic from a diabetic perspective. However, the dry formulations of both Royal Canin Glycobalance ([royalcanin.com/us/cats/products/vet-products/feline-glycobalancedry-cat-food](http://royalcanin.com/us/cats/products/vet-products/feline-glycobalancedry-cat-food)) and Hills m/d ([hillspet.com/cat-food/pd-md-feline-dry](http://hillspet.com/cat-food/pd-md-feline-dry)) have a fairly robust fiber content



Cyclosporine is a non-myelosuppressive immunomodulator that is used in the management of canine IBD;<sup>13</sup> there is very little information regarding its efficacy for this condition in cats.<sup>11</sup>

(≈30 g total dietary fiber/Mcal) and may be a useful option for these patients.

## IMMUNOMODULATORY THERAPIES

Many cats with IBD ultimately require immunomodulatory therapy, and glucocorticoids are the mainstay of this approach.<sup>11</sup> Unfortunately, steroids are powerful insulin antagonists that predictably blunt the response to exogenous insulin, resulting in hyperglycemia. Insulin doses must be adjusted to counter this effect and mitigate polyuria and weight loss. To prevent swings in blood glucose levels, it is prudent to use short-acting agents such as prednisolone (starting dose, 1 mg/kg PO q12h). When tapering prednisolone in diabetic pets, the author initially decreases the amount per dose rather than extending the frequency, so that the level of insulin resistance is relatively consistent throughout the day.

Information regarding the clinical utility of “locally active” glucocorticoids such as budesonide in cats with IBD is limited. In theory, the high first-pass effect should limit systemic exposure and associated insulin resistance. The author has rarely found budesonide to be a successful first-line substitute for prednisolone in cats with IBD; it may, however, be a suitable choice for long-term maintenance in some individuals (0.5 to 1 mg/cat q24h). This drug is substantially more expensive than prednisolone and must be reformulated for use in cats.

Chlorambucil is an alkylating antineoplastic agent that is routinely used in cats with lymphoplasmacytic IBD as well as those with small cell lymphoma.<sup>11,12</sup> Although it requires careful handling, this agent is usually well

tolerated and does not affect insulin sensitivity. It is therefore a good first-line choice for cats with DM and IBD. Chlorambucil can be myelosuppressive, so periodic complete blood counts are necessary. Varying regimens have been proposed; the author prefers 2 mg/cat every 2 days or 2 mg/cat 3 times a week.

Cyclosporine is a non-myelosuppressive immunomodulator that is used in the management of canine IBD;<sup>13</sup> there is very little information regarding its efficacy for this condition in cats.<sup>11</sup> Although it may have a steroid-sparing effect, cyclosporine has been shown to inhibit insulin release, increase insulin resistance, and trigger overt DM in people. Post-transplantation DM was reported in a cohort of cats receiving cyclosporine, suggesting similar effects on glycemic events in this species.<sup>14</sup> For this reason, it may not convey any advantages over oral glucocorticoids for cats with DM and IBD.

## GLYCEMIC CONTROL

Changes in glycemic events are to be expected when dietary formulations are changed or when insulin-



**FIGURE 2.** A 12-year-old male neutered domestic shorthaired cat with a continuous flash interstitial glucometer attached to the cervical region.

Courtesy of Dr. Heather Kvitko-White



antagonistic medications such as glucocorticoids or cyclosporine are administered. Clinicians should anticipate an increase in insulin requirements and strategize appropriately. In the short term, modest hyperglycemia is acceptable, but sustained hyperglycemia will result in weight loss and may place cats at risk of diabetic ketoacidosis.

Appropriate monitoring is necessary to guide adjustments in insulin. As in-house blood glucose curves can be affected by stress hyperglycemia, at-home monitoring is generally preferable.<sup>1</sup> All owners should be encouraged to keep a log of food intake, attitude, thirst, and urination, as this can facilitate the identification of important changes. In addition, many owners can be taught to check blood glucose concentrations at home, using lancet devices and handheld glucometers. Long-lasting interstitial glucometers, such as the FreeStyle Libre (Abbott Laboratories, [freestylelibre.us](http://freestylelibre.us)), show promise and can provide continuous data for up to 14 days (FIGURE 2). As veterinary experience with this device is presently limited, it is appropriate to periodically compare results from direct blood collection before relying exclusively on the interstitial readings.<sup>15</sup>

## ADJUNCTIVE THERAPIES

Hyporexia and/or vomiting should be addressed promptly, as variable caloric intake is problematic in cats with DM. A transdermal mirtazapine product was recently FDA approved for the management of weight loss in cats and may be used to support consistent food intake (Mirataz; Dechra, [mirataz.com](http://mirataz.com)). The recommended dose is 2 mg/cat once daily; this should be reduced to every 48 to 72 hours in cats with renal insufficiency. Vomiting may be addressed with maropitant (4 mg/cat once daily).

## SUMMARY

Managing IBD in diabetic cats can be challenging, but establishing the diagnosis and starting appropriate therapy are likely to substantially improve patient wellbeing. Practitioners must anticipate changes in insulin requirements and be prepared to adjust as necessary. Drugs such as prednisolone should be tapered promptly, and doses should be kept to the minimum necessary to address clinical signs. Consultation with a board-certified internist and/or nutritionist may be helpful. **TVP**

## References

1. Sparkes AH, Cannon M, Church D, et al. ISFM Consensus guidelines on the practical management of diabetes mellitus in cats. *J Feline Med Surg* 2015;17(3):235-250.
2. Gilor C, Niessen SJM, Furrow E, et al. What's in a name? Classification of diabetes mellitus in veterinary medicine and why it matters. *J Vet Intern Med* 2016;30(4):927-940.
3. Reusch CE, Haberer B. Evaluation of fructosamine in dogs and cats with hypo- or hyperproteinaemia, azotaemia, hyperlipidaemia and hyperbilirubinaemia. *Vet Rec* 2001;148:370-376.
4. Jergens AE. Feline idiopathic inflammatory bowel disease: What we know and what remains to be unraveled. *J Feline Med Surg* 2012;14(7):445-458.
5. Behrend E, Holford A, Lathan P, et al. 2018 AAHA diabetes management guidelines for dogs and cats. *JAAHA* 2018;54:1-21.
6. Guilford WG, Jones BR, Markwell PJ, et al. Food sensitivity in cats with chronic idiopathic gastrointestinal problems. *J Vet Intern Med* 2001;15(1):7-13.
7. Zoran DL, Rand JS. The role of diet in the prevention and management of feline diabetes. *Vet Clin Small Anim Pract* 2013;43:233-243.
8. Verbrugghe A, Hest M. Cats and carbohydrates: the carnivore fantasy? *Vet Sci* 2017;4(4):55.
9. Gilor C, Rudinsky AJ, Hall MJ. New approaches to feline diabetes mellitus: Glucagon-like peptide-1 analogs. *J Feline Med Surg* 2016;18(9):733-743.
10. Stasiak M. The development of food preferences in cats: the new direction. *Nutr Neurosci* 2002;5:221-228.
11. Trepanier L. Idiopathic inflammatory bowel disease in cats: rational treatment selection. *J Feline Med Surg* 2009;11(1):32-38.
12. Stein JG, Pelin M, Steinberg H, et al. Treatment of feline gastrointestinal small-cell lymphoma with chlorambucil and glucocorticoids. *JAAHA* 2010;46(6):413-417.
13. Allenspach K, Rufenacht S, Sauter S, et al. Pharmacokinetics and clinical efficacy of cyclosporine treatment of dogs with steroid-refractory inflammatory bowel disease. *J Vet Intern Med* 2006;20:239-244.
14. Case JB, Kyles AE, Nelson RW, et al. Incidence of and risk factors for diabetes mellitus in cats that have undergone renal transplantation: 187 cases (1986-2005). *JAAHA* 2007;230(6):880-884.
15. Corradini S, Pilosio B, Dondi R, et al. Accuracy of a flash glucose monitoring system in diabetic dogs. *J Vet Intern Med* 2016;30(4):983-988.



### Audrey K. Cook

Dr. Cook is a graduate of the University of Edinburgh. She completed an internship at North Carolina State University and a residency in internal medicine at the University of California, Davis. She is a Diplomate of the American and European Colleges of Veterinary Internal Medicine and has additional board certification in Feline Practice. After a decade in private referral practice, Dr. Cook joined the faculty at Texas A&M College of Veterinary Medicine & Biomedical Sciences, where she is professor and chief of the Internal Medicine Service. Her clinical interests include canine and feline endocrinology and gastroenterology.