Chapter 60

Small Intestinal Bacterial Overgrowth

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*"The microbe is so very small you cannot make him out at all.
But many sanguine people hope to see him through a microscope."
Hilaire Belloc, More Beasts for Worse Children (1897)*

CLINICAL IMPORTANCE

Small intestinal bacterial overgrowth (SIBO), a diarrheic disorder characterized by excessive numbers of small intestinal bacteria, has received much attention (Willard et al, 1994; Simpson, 1994; Johnston, 1999, 1999a; Davenport et al, 1994). Although the incidence of SIBO is unknown, some authors have suggested that it is present in up to 50% of dogs with chronic small bowel diarrhea (Rutgers et al, 1995), whereas others suggest that it occurs rarely in clinical practice (Johnston, 1999a; German et al, 2003). Controversy exists as to whether SIBO is a synonym for or a subset of a group of chronic enteropathies termed antibiotic- or tylosin-responsive diarrhea (Westermarck et al, 2005; Hall and Simpson, 2000).

PATIENT ASSESSMENT

History and Physical Examination

Affected dogs usually present with a history of weight loss and intermittent small bowel diarrhea. Borborygmus and flatulence are also common complaints. Physical examination findings are often unremarkable. Poor body condition (body condition score [1/5 or 2/5]) and unthriftiness may be present if the condition is longstanding.

Laboratory and Other Clinical Information

The gold standard for diagnosing SIBO is quantitative aerobic and anaerobic culture of undiluted duodenal juice. Samples can be collected via endoscopy or direct needle aspiration at surgery (Davenport, 1996; Papasouliotis et al, 1998; Johnston, 1999b). In dogs and cats, the small intestine normally contains a relatively sparse bacterial flora compared with the densely populated oral cavity and large bowel. Historically, the accepted upper limit for small intestinal bacterial flora has been 10^5 colony-forming units (CFU)/ml based on work done before 1984 (Batt and Needham, 1983). Subsequent studies have demonstrated that the small bowel of healthy dogs may contain bacteria in excess of 10^5 CFU/ml (Davenport et al, 1994, 1994a; Ludlow and

Box 60-1. Oligosaccharides.

Oligosaccharides are naturally-occurring carbohydrates found in some fruits, vegetables and grains. Structurally, oligosaccharides are sugar polymers that contain up to six sugars. Oligosaccharides containing fructose are termed fructooligosaccharides (FOS). Those that contain mannose are termed mannanoligosaccharides or MOS and so on. Typically found in low concentrations in foods, these complex carbohydrates can also be manufactured for commercial purposes using microbial or plant-derived enzymatic digestion of sugars.

Oligosaccharides resist digestion by mammalian digestive enzymes. Thus, they are classified as fibers or resistant starches. Because they resist digestion, oligosaccharides enter the large bowel in an intact form where they are readily fermented by certain colonic bacteria such as *Bifidobacterium* and *Bacteroides* spp. Based on in vitro studies, the fermentability of oligosaccharides is intermediate between that of cellulose and lactulose. Other organisms such as lactobacilli, eubacteria and clostridia do not readily use oligosaccharides. This preferential fermentation pattern suggests dietary supplementation with oligosaccharides may help foster beneficial gut bacteria.

The addition of oligosaccharides to pet foods has been studied with variable results. The inclusion of FOS at 0.75% (dry matter) did not influence the duodenal flora of healthy cats quantitatively or qualitatively. However, the fecal flora of cats was affected, resulting in increased numbers of lactobacilli and reduced numbers of *Escherichia coli*. Similar findings have been reported to occur in healthy cats consuming another oligosaccharide (i.e., lactosucrose). The clinical significance of these findings is unknown.

Investigators studied FOS supplementation in a group of healthy German shepherd dogs thought to have small intestinal bacterial overgrowth based on bacterial counts of specimens obtained by needle aspiration of the proximal small bowel at the time of surgery. In these dogs, the inclusion of FOS at 1.0% (as fed) was associated with changes in duodenal bacterial flora. However these changes were of less magnitude than normal dog variability for these parameters. Again, the clinical significance of these findings is unknown.

In some species, MOS derived from yeast cell walls binds to intestinal pathogens such as *Salmonella* spp. MOS inhibits attachment of salmonella to the intestinal mucosa by preferentially binding lectins. This effect has not been demonstrated to occur in companion animals to date.

The Bibliography for **Box 60-1** can be found at www.markmorris.org.

Davenport, 2000; Johnston, 1999a). Normal cats also have small intestinal bacterial counts in excess of 10^5 CFU/ml (Papasouliotis et al, 1998; Johnston et al, 1993). These findings suggest that laboratories should establish their own control or reference ranges for duodenal juice using their own sampling and microbiologic techniques. Furthermore, quantitative microbiology is cumbersome, invasive and not readily available to practitioners. Therefore, a number of other diagnostic modalities have been explored.

Other tests useful in diagnosing SIBO include serum folate and cobalamin concentrations, breath hydrogen measurements (with or without lactulose administration), serum total unconjugated bile acids and intestinal permeability tests. Determination of fasting serum folate and cobalamin concentrations is a rapid, noninvasive and simple method for evaluating dogs with suspected SIBO. Folate and cobalamin analyses have been useful in an experimental model of SIBO (Davenport, 1986) and in naturally occurring cases (Simpson, 1994; Batt and Morgan, 1982; Williams, 1991). However, these assays have low sensitivity and specificity (Rutgers, 1996; Simpson, 1994; German et al, 2003). Diet can influence serum folate and cobalamin concentrations. An analytical survey of commercial foods performed in 1994 revealed a wide range of dietary folate levels (Davenport et al, 1994a). Serum folate and cobalamin concentrations obtained from healthy dogs consuming foods containing high folate and cobalamin levels often exceed the upper limits of the reference ranges established for these vitamins (Davenport et al, 1994a; Williams, 1991). The influence of food on folate and cobalamin concentrations is responsible in part for the poor sensitivity of these assays for the diagnosis of SIBO.

Breath hydrogen testing has been used in human and veterinary medicine to diagnose SIBO. This technique is based on the fact that hydrogen is produced as a by-product of bacterial rather than mammalian metabolism. When given a carbohydrate substrate such as a sugar solution or ^{14}C-d-xylose, bacteria produce hydrogen, which can be measured in expired breath. Intestinal transit time can influence this technique; therefore, it is best considered a tool for assessment of carbohydrate assimilation (Johnston, 1999a). Recently, a ^{13}C-glycocholic acid blood test was validated for use in dogs. This test, which is based on the bacterial deconjugation of glycocholic acid, has the potential to recognize increased numbers of small intestinal bacteria through the early detection of ^{13}C-glycocholic acid (Suchodolski et al, 2005). Clinical data in affected animals, however, are lacking.

Intestinal permeability tests are nonspecific tools useful for evaluating animal patients with suspected small intestinal disease. These tests are most commonly available at referral centers and veterinary teaching hospitals.

Response to therapy with antibiotics should not be overlooked as an effective diagnostic tool. A therapeutic trial may be particularly useful in situations when quantitative cultures are not possible (Westermarck et al, 2005).

Risk Factors

A number of risk factors have been identified for SIBO. German shepherd dogs appear to be predisposed to this

enteropathy (Willard et al, 1994; Batt and Needham, 1983) possibly because of IgA deficiency (Batt et al, 1991; Whitbread et al, 1984; Willard et al, 1994). The recent development of fecal IgA assays has made detection of IgA deficiency more convenient as compared to measurement of IgA levels in intestinal biopsy samples (Tress et al, 2006; Littler et al, 2006).

Exocrine pancreatic insufficiency is also a predisposing factor for SIBO, and this condition can complicate management of exocrine pancreatic insufficiency (Williams et al, 1987).

Investigators have hypothesized that kenneled dogs (especially beagles) may be more likely to have duodenal fluid bacterial counts in excess of 10^5 CFU/ml (Batt et al, 1992).[a] Kennel-housed beagles, German shepherd dogs, Yorkshire terriers and poodles have subsequently been found to have increased counts (Willard et al, 1994; Davenport et al, 1994, 1994a). Quantitative counts in these apparently healthy dogs have ranged up to 10^8 CFU/ml. Potential causes for abnormal bacterial counts in kennel-housed dogs include environment (i.e., cleanliness), coprophagia and breed-specific characteristics (e.g., IgA deficiency). The bacterial flora of healthy colony cats, healthy pet cats and cats with gastrointestinal (GI) disease has been investigated (Johnston, 1996b). Both healthy colony and pet cats had small intestinal bacterial counts exceeding 10^5 CFU/ml duodenal fluid. Clinically abnormal cats had similar bacterial counts but had lower levels of anaerobic and microaerophilic bacteria.

Etiopathogenesis

SIBO can develop any time normal host defenses are impaired. Loss of gastric acid secretion, normal intestinal peristalsis, interdigestive ("housekeeper") motility, ileocolic valve function or local IgA production can result in SIBO. In people, intestinal stasis is the most common cause of SIBO; however, this particular underlying cause is far less common in dogs.

Key Nutritional Factors

Key nutritional factors for patients with SIBO are listed in **Table 60-1** and discussed in more detail below.

Digestibility

Feeding highly digestible (fat and digestible [soluble] carbohydrate ≥90% and protein ≥87%) foods provides several advantages for managing dogs with SIBO. Nutrients from these low-residue foods are more completely absorbed in the proximal gut. Highly digestible foods are also associated with reduced osmotic diarrhea due to fat and carbohydrate malabsorption and reduced production of intestinal gas due to carbohydrate malabsorption. The ideal food for SIBO patients is lactose free to avoid the complication of lactose intolerance due to loss of brush border disaccharidases.

Fat

Energy-dense foods are preferred for managing patients with chronic enteropathies. Calorie-dense products allow the clinician to provide smaller volumes of food at each meal, which minimizes GI stretch and secretions. Unfortunately, energy-dense foods tend to be high in fat. High-fat foods may contribute to osmotic diarrhea and GI protein losses, which complicate SIBO. Therefore, it is often advantageous to initially provide a food with moderate energy density (3.5 to 4 kcal/g [14.6 to 16.7 kJ/g] dry matter [DM]) that contains moderate levels of fat (12 to 15% DM for dogs and 15 to 25% DM for cats). Higher fat and more energy-dense foods can be offered if the patient tolerates these fat levels.

Table 60-1. Key nutritional factors for foods for dogs and cats with small intestinal bacterial overgrowth.*

Factors	Recommended levels
Digestibility	≥87% for protein and ≥90% for fat and digestible carbohydrate
Fat	12 to 15% for dogs 15 to 25% for cats

*Nutrients expressed on a dry matter basis.

Other Nutritional Factor

Prebiotic Fibers

Fructooligosaccharides (FOS) and other prebiotic resistant starches have been proposed for use in managing patients with SIBO. These indigestible sugars are thought to promote beneficial bacteria at the expense of bacterial pathogens (Fishbein et al, 1988; Hidaka et al, 1990; Hussein et al, 2005) (**Box 60-1**). When FOS was fed (1.0% as fed) to a group of German shepherd dogs with asymptomatic SIBO, total bacterial counts were reduced within the duodenum (Willard et al, 1994a). However, this reduction was smaller than the change in bacterial numbers demonstrated within the same dogs at different sampling intervals. Therefore, the clinical utility of FOS and other oligosaccharides in the treatment of SIBO remains unproven in dogs. In cats, feeding the non-digestible trisaccharide lactosucrose increased fecal counts of the favorable bacteria lactobacilli and bifidobacteria and decreased numbers of potential pathogens such as clostridia and Enterobacteriaceae (Terada et al, 1993).

FEEDING PLAN

The feeding plan is often used in conjunction with other medical therapy. Underlying causes of SIBO (e.g., partial intestinal obstruction) should be identified and treated before specific medical and dietary therapy is instituted. Antibiotic therapy is usually required for effective management of SIBO. Antibiotic selection should be based on culture and antimicrobial sensitivity testing of specific pathogens identified in duodenal aspirates. Tetracycline or tylosin should be used if no pathogen is isolated (Westermarck et al, 2005).

Assess and Select the Food

Levels of key nutritional factors should be evaluated in foods currently fed to patients with SIBO and compared with recommended levels (**Table 60-1**). Key nutritional factors include food digestibility and fat content. Information from this aspect

Table 60-2. Key nutritional factors in selected highly digestible commercial veterinary therapeutic foods marketed for dogs with small intestinal bacterial overgrowth compared to recommended levels.*

Dry foods	Fat (%)	Protein digestibility (%)	Fat digestibility (%)	Carbohydrate digestibility (%)	Ingredient comments
Recommended levels	**12-15**	**≥87**	**≥90**	**≥90**	**–**
Hill's Prescription Diet i/d Canine	14.1	92	93	94	–
Iams Veterinary Formula Intestinal Low-Residue	10.7	na	na	na	FOS, MOS prebiotics
Medi-Cal Gastro Formula	13.9	na	na	na	FOS prebiotic, *Bacillus subtilis* dried fermentation extract
Medi-Cal Low Fat LF 20	6.6	na	na	na	MCT
Purina Veterinary Diets EN GastroENteric Formula	12.6	84.5	91.4	94.4	Sodium silico aluminate, FOS, MOS prebiotics
Royal Canin Veterinary Diet Digestive Low Fat LF 20	6.6	na	na	na	FOS, MOS prebiotics
Moist foods	**Fat (%)**	**Protein digestibility (%)**	**Fat digestibility (%)**	**Carbohydrate digestibility (%)**	**Ingredient comments**
Recommended levels	**12-15**	**≥87**	**≥90**	**≥90**	**–**
Hill's Prescription Diet i/d Canine	14.9	88	94	93	–
Iams Veterinary Formula Intestinal Low-Residue	13.2	na	na	na	–
Medi-Cal Gastro Formula	11.7	na	na	na	FOS prebiotic
Medi-Cal Low Fat LF	9.0	na	na	na	–
Purina Veterinary Diets EN GastroENteric Formula	13.8	85.1	95.6	92.2	MCT
Royal Canin Veterinary Diet Digestive Low Fat	6.9	na	na	na	Inulin prebiotic

Key: na = information not available from manufacturer, FOS = fructooligosaccharide, MOS = mannanoligosaccharide, MCT = medium-chain triglyceride.
*Manufacturers' published values. Nutrients expressed as % dry matter.

Table 60-3. Key nutritional factors in selected highly digestible commercial veterinary therapeutic foods marketed for cats with small intestinal bacterial overgrowth compared to recommended levels.*

Dry foods	Fat (%)	Protein digestibility (%)	Fat digestibility (%)	Carbohydrate digestibility (%)	Ingredient comments
Recommended levels	**15-25**	**≥87**	**≥90**	**≥90**	**–**
Hill's Prescription Diet i/d Feline	20.2	88	92	90	–
Iams Veterinary Formula Intestinal Low-Residue	13.7	na	na	na	FOS, MOS prebiotics
Medi-Cal Hypoallergenic/Gastro	11.5	na	na	na	FOS prebiotic, *Bacillus subtilis* dried fermentation extract
Purina Veterinary Diets EN GastroENteric Formula	18.4	94.0	93.1	79.7	–
Royal Canin Veterinary Diet Intestinal HE	23.7	na	na	na	FOS, MOS prebioti sodium silico aluminate
Moist foods	**Fat (%)**	**Protein digestibility (%)**	**Fat digestibility (%)**	**Carbohydrate digestibility (%)**	**Ingredient comments**
Recommended levels	**15-25**	**≥87**	**≥90**	**≥90**	**–**
Hill's Prescription Diet i/d Feline	24.1	91	89	91	–
Iams Veterinary Formula Intestinal Low-Residue	11.7	na	na	na	FOS prebiotic
Medi-Cal Hypoallergenic/Gastro	35.9	na	na	na	FOS prebiotic
Medi-Cal Sensitivity CR	35.1	na	na	na	–

Key: na = information not available from manufacturer, FOS = fructooligosaccharide, MOS = mannanoligosaccharide.
*Manufacturers' published values. Nutrients expressed as % dry matter.

of assessment is essential for making any changes to foods currently provided. Changing to a more appropriate food is indicated if key nutritional factors in the current food do not match recommended levels.

Commercial veterinary therapeutic foods that are highly digestible and designed for patients with GI disease are recommended for patients with SIBO (**Tables 60-2** and **60-3** for dogs and cats, respectively). Many of these foods contain moderate levels of dietary fat. Young growing dogs and cats with SIBO should receive a food that meets the optimal levels of key nutritional factors for growth.

Assess and Determine the Feeding Method

Because the feeding method is often altered in patients with SIBO, a thorough assessment should include verification of the feeding method currently being used. Items to consider include feeding frequency, amount fed, how the food is offered, access to other food and who feeds the animal. All of this information should have been gathered when the history of the animal was obtained. If the animal has a normal body condition score (2.5/5 to 3.5/5), the amount of food previously fed was probably appropriate.

Ideally, patients with SIBO should be fed multiple small meals per day as indicated by animal acceptance and tolerance for the food. Meal size can be increased as tolerated by the patient after clinical signs have been successfully managed for several weeks.

REASSESSMENT

Owners of affected animals should be asked about frequency of diarrhea, borborygmi and flatus. Body weight and condition should be evaluated frequently to assess resolution of malabsorption. In general, SIBO can be managed effectively with a combination of medical (e.g., antibiotic) and nutritional therapies.

ENDNOTE

a. Williams DA, School of Veterinary Medicine, Purdue University, West Lafayette, IN. Personal communication. 1993.

REFERENCES

The references for **Chapter 60** can be found at www.markmorris.org.