Diarrhea is generally regarded as the most consistent clinical sign of intestinal disease in dogs and cats and is one of the most frustrating disorders for many veterinarians to diagnose and manage. Incomplete resolution of the problem can result in frustration and dissatisfaction for the owner and potential suffering for the animal. Antibiotics are commonly administered indiscriminately to diarrheic animals, with resolution of clinical signs often wrongly attributed to eradication of a putative infectious pathogen.

Chronic diarrhea is persistent or relapsing over a period of 3 to 4 weeks or longer. In contrast to acute diarrhea that is often self-limiting and does not typically require a comprehensive workup, chronic cases warrant a step-by-step approach to obtain a diagnosis and formulate an optimal therapeutic plan. The exception to this rule is in dogs with acute hemorrhagic diarrhea syndrome that can be associated with a number of infectious and non-
infectious causes and typically lasts less than 1 week.

The history and physical examination are paramount for determining whether the diarrhea is caused by primary disease of the gastrointestinal (GI) tract or is secondary to extraintestinal diseases such as pancreatic insufficiency or Addison’s disease (Table 1). The need for performing fecal screening for putative enteropathogens, resting cortisol for Addison’s disease, tests for pancreatitis [canine pancreas specific lipase (Spec cPL, IDEXX Laboratories) and ultrasound], or abdominal radiographs for GI foreign bodies should be based upon the patient’s signalment, history (including vaccination history), and physical examination findings. The categorization of diarrhea into small bowel or large bowel in origin is helpful for prioritizing certain differentials (Table 1) and for determining which segment of bowel to biopsy if indicated. Caution is warranted in this over-simplistic anatomic differentiation of the affected segment of bowel because animals manifesting clinical signs of colitis often have concurrent disease in the small bowel and vice versa. In addition, most veterinary gastroenterologists prefer to biopsy the small and large intestine when feasible to maximize diagnostic yield of the procedure. Failure to consider the role of the diet or dietary supplements in precipitating or alleviating the GI disorder can result in delayed diagnosis or improper dietary recommendations. The history should also focus on the duration of the diarrhea, the appearance of the feces (color, volume, mucus, presence of fresh blood), worming and vaccination history, defecation frequency, aggravating or alleviating factors, and defecation urgency.

**DIAGNOSTIC TESTS & PROCEDURES**

**Fecal Examination for Parasites**

The diagnosis of GI parasites in dogs and cats is an integral component of small animal practice. The following guidelines can help veterinarians maximize the diagnostic yield of fecal examinations for parasites.

1. **Fresh fecal specimens** should be refrigerated to facilitate preservation of eggs, oocysts, and cysts if immediate fecal flotation cannot be performed following collection.

2. **Centrifugation fecal flotation** is vastly superior to standing (gravitational) flotation. The type of flotation solution and its specific gravity does affect the diagnostic yield. Aqueous zinc sulfate (ZnSO₄) with a specific gravity of 1.18 to

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**TABLE 1**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Small Intestine</th>
<th>Large Intestine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary GI Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Infiltrative neoplasia: lymphoma, mast cell tumor, carcinoma</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Endoparasites: helminths, Giardia, Cystoisospora, Cryptosporidium</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Food-responsive enteropathy</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Bacterial, viral, and fungal enteropathogens: Campylobacter, Salmonella, Histoplasma spp, Pythium</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Intestinal obstruction secondary to strictures, intussusception</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Ileus</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

**Extragastrointestinal Disorders**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Small Intestine</th>
<th>Large Intestine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addison’s disease</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Exocrine pancreatic insufficiency</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Pancreatic neoplasia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver failure: uncommon cause of diarrhea</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Uremia</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
## Diagnostic Approach to Dogs with Chronic Enteropathies

### History
- Detailed and accurate, including comprehensive dietary history

### Physical examination

#### Minimum database
- CBC
- Serum biochemistry panel
- Urinalysis
- Fecal centrifugation flotation and direct wet-prep

### Additional fecal tests that may be warranted
- **Fecal Giardia ELISA or IFA test for Giardia and Cryptosporidium:** Fecal ELISA for Giardia should be used only as a screening test to diagnose infection before initiating anthelmintic therapy
- **Fecal enteric panel (culture and toxin assays) or fecal PCR panel:** Reserve for animals developing diarrhea after boarding or show attendance, cats and dogs with acute onset of bloody diarrhea in association with evidence of sepsis or diarrhea, outbreaks occurring in more than one pet in a household, and zoonotic concerns (Campylobacter, Salmonella) in diarrheic pets in contact with immunocompromised humans

### Empirical deworming with broad-spectrum anthelmintic

### Tests of assimilation
- **Serum cobalamin and folate:** Assessment of absorption in the ileum and jejunal, respectively
- **Trypsin-like immunoreactivity (cTLI):** Diagnosis of exocrine pancreatic insufficiency

### Imaging
- **Abdominal ultrasonography:** Evaluation of the pancreas; intestinal wall thickening, layering of the wall, echogenicity of layers; mesenteric lymph nodes; liver; spleen; kidneys; presence of peritoneal fluid
- **Abdominal radiography:** Relatively low-yield procedure in animals with chronic diarrhea but is indicated in animals with suspected partial obstructions from foreign body/intrususceptence/mass or gas distention/torsion of the GI tract

### Dietary trial
- **Elimination diet or hydrolyzed diet:** Selected based on the animal’s dietary history; recommend dietary trial to help rule out food-responsive enteropathy before procuring intestinal biopsies in stable animals (no evidence of hypoalbuminemia, hypocobalaminemia, fever, melanosis)
- **High-fiber diet:** Can be tried in animals with colitis if there is no response to an elimination diet trial; response should be recognized within 7 to 10 days of initiating the trial diet

### Antibiotic trial
- **Antibiotic-responsive diarrhea (ARD):** Affects large and giant breed dogs predominantly and is associated with signs of enteritis or colitis
- **Tylosin (5-10 mg/kg q24h PO):** Is the drug of choice for dogs with suspected ARD and is administered prior to procurement of intestinal biopsies in dogs failing to show an adequate response to dietary therapy

### Miscellaneous tests or procedures
- **Spec cPL:** Pancreatitis
- **Thyroxine (T4):** In dogs with polyphagia, weight loss and diarrhea and no evidence of exocrine pancreatic insufficiency or chronic enteropathy
- **Rectal scraping:** Pythiosis, histoplasmosis, protothecosis, and eosinophilic colitis or proctitis

### GI biopsies
- **Endoscopy:** Recommended to procure ileal biopsies particularly when serum cobalamin concentration is abnormally decreased
- **Full-thickness biopsy specimens:** Laparotomy versus laparoscopy

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1.2 has been widely recommended because it will float cysts, oocysts, and most helminth eggs with a minimum of distortion and fecal debris. Other acceptable solutions include Sheather’s sugar and sodium nitrate.

3. **Giardia and Cryptosporidium immunoassays** increase the diagnostic yield of the fecal exam when performed in平行 with centrifugation flotation. Enzyme-linked immunosorbent assays (ELISAs) detect *Giardia* cyst-wall protein 1 (GCWP 1) and are generally easy to perform and interpret. The SNAP *Giardia* Test (IDEXX Laboratories) is a rapid in-house enzyme immunoassay that can be performed on fresh or previously frozen feces or samples stored at 2°C to 7°C for up to 7 days.3 ELISAs should not be used to assess response to therapy in animals that have completed a recent course of anthelmintics because animals can remain positive for *Giardia* spp on the SNAP ELISA for several weeks following successful eradication of the parasite. A second type of immunoassay called direct immunofluorescence (DIF)6 has the added benefit of detecting both *Giardia* and *Cryptosporidium* in feces, but
requires a fluorescent microscope. A positive result is indicated by apple green fluorescence of the cyst (*Giardia*) or oocyst (*Cryptosporidium*) (Figure 1). Morphologic identification is necessary for this technique.

4. **Polymerase chain reaction (PCR)-based tests for *Giardia* and *Cryptosporidium* spp** are commercially available although the author recommends fecal flotation and DIF or ELISA testing for the routine diagnosis of both organisms. An exception is the use of PCR for determining *Giardia* “assemblages” to assess the infectivity potential of the isolate for animals and humans. Dogs have mainly assemblages C and D; cats have assemblages A1 and F; humans have assemblages A2 and B. Assemblages can be determined via PCR\(^5\) to determine the likelihood of zoonotic transmission from animals to humans, although the risk for transmission of *Giardia* spp to humans is generally very low.

### Fecal Examination for Bacteria

1. **PCR and bacterial culture/toxin immunoassays** are low-yield diagnostic procedures in animals with diarrhea if the tests are performed injudiciously.\(^6\) If bacterial enteritis or enterocolitis is suspected, the feces should be cultured or PCR should be performed for specific enteropathogens, such as *Salmonella* spp or *Campylobacter jejuni*. Fecal PCR is superior to culture for the diagnosis of *Campylobacter* spp, and facilitates the rapid diagnosis of multiple species of *Campylobacter*.\(^7\)

2. **Fecal cytology on stained fecal smears** is commonly performed to identify the underlying cause of diarrhea by looking for spiral-shaped bacteria (*Campylobacter*-like organisms), white blood cells, and fecal endospores associated with *Clostridium perfringens*. Unfortunately, the detection of increased fecal endospores is of no clinical diagnostic utility\(^8,9\) (Figure 2) and the overall value of stained fecal smears is extremely limited. Detection of spiral-shaped organisms resembling *Campylobacter* spp is insufficient when used alone to diagnosis *Campylobacter*-associated diarrhea.

Veterinarians should be cognizant of the fact that most bacterial enteropathogens are associated with self-limiting diarrhea. ... Antimicrobials should be administered only to animals manifesting systemic signs of illness.
Measurement of serum cobalamin and folate concentrations provides insight into the functional integrity of the ileum and jejunum, respectively.

**Tests of Intestinal Function**
Measurement of serum cobalamin and folate concentrations provides insight into the functional integrity of the ileum and jejunum, respectively. Low serum cobalamin has been described in dogs in association with a variety of GI diseases, including IBD, intestinal lymphoma, and lymphangiectasia. Mucosal repair is impeded when cobalamin is deficient and its absorption impaired. Dogs that are deficient in cobalamin are typically administered cyanocobalamin subcutaneously (SC) on a weekly basis at 250 to 1500 µg/dose (depending on the animal’s weight) SC for 6 weeks, followed by dosing every 2 to 3 weeks for the indefinite future.

**Abdominal Imaging**
Survey abdominal radiography is a relatively low-yield procedure in most dogs with chronic diarrhea but is indicated in animals suspected of having partial obstructions caused by foreign bodies, intussusceptions, or masses, or in those with gas distention or displacement of the stomach or bowel. Abdominal ultrasonography is complementary to survey abdominal radiography; it is more sensitive for detection of abdominal masses, intestinal mural thickening, intussusceptions, “tiger-stripe” lines in the mucosa (Figure 3), and mesenteric lymphadenopathy.10 In addition, ultrasound-guided percutaneous biopsy or aspiration of masses is an effective diagnostic procedure. Contrast radiography and fluoroscopy are occasionally indicated for identifying partial obstructions and intestinal motility disorders, respectively.

**Endoscopy & Biopsy**
**Pitfalls & Recommendations**
Endoscopy is a valuable procedure for diag-
The diagnosis of intestinal mucosal disorders associated with morphologic changes, but it does not differentiate intestinal motility disorders, secretory diarrheas, or brush-border enzyme defects. In addition, lesions of the intestinal submucosa and muscularis propria layers of bowel can easily be missed, and endoscopy is limited by the working length of the scope, precluding examination of the jejunum. With the support of the World Small Animal Veterinary Association, the Gastrointestinal Standardization Group has proposed a standardized histologic evaluation system that can be applied to all companion animal gastroenterologic disorders to minimize interobserver observation among pathologists.11

COMMON CHRONIC ENTEROPATHIES IN DOGS

Food-Responsive Enteropathy

Food-responsive enteropathy is a common cause of chronic diarrhea in dogs and the disorder is associated with a relatively high response rate (45%–60%) to the feeding of elimination diets containing novel, single sources of protein (intact or hydrolyzed).12-14 Most dogs with a food-responsive enteropathy show a relatively rapid resolution of clinical signs within 3 to 4 days following implementation of dietary therapy. In a retrospective study of dogs with lymphocytic-plasmacytic colitis, clinical signs resolved in all 13 cases with introduction of an elimination diet, and of 11 dogs rechallenged with their original diet, 9 relapsed.12 The theoretical basis for protein hydrolysate diets is that reduction in immunogenic epitopes being presented to the mucosal immune system during dysregulation will increase the potential for resolution. Thus, the argument for the use of a hydrolysate diet is independent of whether a diet-specific immunologic response is suspected. Experience with protein hydrolysate diets is increasing and anecdotally they appear to be effective adjuncts to pharmacologic therapy or even as the sole therapy. Clinical resolution with histologic improvement has been reported in 4 of 6 dogs with refractory IBD when treated with a hydrolyzed soy-protein diet alone.13 In addition, feeding a hydrolyzed diet to 18 dogs with chronic small bowel enteropathy was shown to be superior to feeding a highly digestible control diet for long-term management.14 It is possible, however, that nutritional factors other than protein hydrolysis were responsible for the improvement. These factors could include dietary digestibility, correction of vitamin or mineral deficiencies, reduced fat content, lowered n-6:n-3 fatty acid ratio, and possible immunomodulatory effect of soy isoflavones within the hydrolyzed diets.

Antibiotic-Responsive Diarrhea (ARD) or Tylosin-Responsive Diarrhea

ARD is essentially a canine phenomenon and is seen more commonly in large and giant-breed dogs. German shepherd dogs appear to be particularly predisposed to ARD that is characterized by small bowel or large bowel diarrhea in the absence of an underlying cause.15 These dogs do not appear to have bacterial overgrowth (SIBO), but rather a dysbiosis of their microbiota. ARD is typically managed with tylosin at 5 to 10...
mg/kg every 24 hours for 3 to 4 weeks; however, many dogs may need to be treated for 4 weeks or longer. Many dogs with ARD have failed to respond to metronidazole administration.

**Inflammatory Bowel Disease**

Diagnosis of IBD is based on compatible clinical signs (chronic diarrhea, vomiting, weight loss, with or without borborygmus and flatulence) and exclusion of metabolic, infectious, neoplastic, and obstructive disorders of the gut. Biopsies must show histologic evidence of moderate to marked infiltration of the GI mucosa by inflammatory cells (predominantly lymphocytes and plasma cells) and changes in mucosal architecture for a diagnosis of IBD to be rendered (Figure 4). Management of canine IBD includes elimination or hypoallergenic diets, antimicrobials (tylosin, metronidazole) and/or immunomodulatory drugs (prednisolone, budesonide, chlorambucil), and cyanocobalamin supplementation.

Administration of probiotics to dogs with IBD represents a novel alternative therapeutic modality that warrants further investigation. Probiotics have also been utilized to facilitate eradication of intestinal parasites. A recent study documented the ability of the probiotic organism *Enterococcus faecium* SF68 (FortiFlora, Nestlé Purina) to antagonize *Giardia intestinalis* infection in mice. Oral feeding of *E. faecium* strain SF68 starting 7 days before inoculation with *Giardia* trophozoites significantly increased the production of specific anti-*Giardia* intestinal IgA and blood IgG and increased CD4(+) T cells, with associated diminution in the number of active trophozoites in the small intestine and decreased shedding of fecal *Giardia* antigens (GSA65 protein). Probiotic administration of VSL #3 strain to dogs with IBD has also been associated with clinical improvement and enhancement of regulatory T-cell markers [FoxP3+ cells and transforming growth factor-β (TGF-β)+ cells] compared with a placebo-control group.

**Intestinal Lymphangiectasia**

Protein-losing enteropathy (PLE) is a syndrome caused by a variety of gastrointestinal diseases causing the enteric loss of albumin and globulin. Intestinal inflammation, infiltration, ulceration, blood loss, and primary or secondary lymphangiectasia (Figure 5) are well-documented causes of PLE. If left untreated, the final outcome of PLE is panhypoproteinemia with decreased intravascular oncotic pressure and the development of abdominal and pleural effusion (Figure 6), peripheral edema, and abdominal distension secondary to ascites associated with intestinal lymphangiectasia.
death. An important sequel to PLE includes thromboembolic disease secondary to the loss of antithrombin. The signalment of the animal is important as certain breeds such as the Yorkshire terrier, soft-coated Wheaten terrier, Norwegian lundehund, and Basenji are predisposed to PLE. Additional abnormalities found on the serum biochemistry profile in association with PLE include hypocholesterolemia (secondary to malabsorption) and hypocalcemia. The multifactorial causes include hypoalbuminemia (affects total calcium), decreased absorption of vitamin D, and malabsorption of magnesium. Measurement of total and ionized serum magnesium is recommended in animals with GI disease and hypocalcemia.

Moderate dietary fat restriction is one of the most important aspects in the management of dogs with intestinal lymphangiectasia. Diets that are highly digestible and contain less than 25% fat calories are most commonly recommended. The author recommends the feeding of a premium commercial-based diet if possible; however, there is a small number of dogs with severe lymphangiectasia that will need further fat restriction than that provided in commercial diets, and home-cooked diets are warranted. These home-cooked diets should be made up by a veterinary nutritionist to ensure that the diets are complete and balanced. Dogs with concurrent IBD and lymphangiectasia are more challenging to manage from a dietary perspective because these animals need a novel, select protein source or hydrolyzed diet that is also moderately fat restricted, such as Purina Veterinary Diets HA Hypoallergenic Canine Formula (Nestlé Purina). The current vegetarian formulation of HA contains a soy-protein hydrolysate and contains 24% fat calories, representing a viable dietary option for dogs with lymphangiectasia with or without concurrent IBD.

References