Treatment of Chronic Gastrointestinal Disease in Dogs

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Profile

DEFINITION, CAUSES, & CLINICAL SIGNS

Gastrointestinal disease present for longer than 3 weeks. Typical causes and clinical signs are shown in **Tables 1 and 2**.

Treatment

- The treatment used depends on the diagnosis. For many conditions, a combination of therapies works best.
- Primary treatment options include antiparasitic medication, dietary management, antibacterial agents, and immunosuppressants. Adjunctive therapies include cobalamin supplementation and probiotic therapy.
- Most gastrointestinal diseases are treated on an outpatient rather than an inpatient basis.
- In some cases, the exact diagnosis is not clear from diagnostic investigations, and a staged approach to therapy is recommended (**Figure 1**).
- Alimentary lymphoma in dogs rarely responds to treatment and prognosis is poor.

DIETARY MANAGEMENT

Many chronic gastrointestinal diseases respond favorably to dietary management, and a range of diets are available (e.g., highly digestible, exclusion, and high-fiber).

Highly Digestible Diets

Used as an adjunct to therapy for gastrointestinal disease.

- High digestibility ensures that components can be readily assimilated when digestive functions are suboptimal.
- High digestibility minimizes the substrate available for metabolism by intestinal bacteria and remaining undigested substrate (which commands an osmotic potential and thus may cause diarrhea).
- Protein should be of high biological value, highly digestible, and preferably restricted to one source.
- Fat restriction was traditionally recommended because of concerns over malabsorption; however, fat restriction has recently been challenged because low-fat diets make it difficult to correct weight loss deficits. Thus, the only diseases for which fat restriction is necessary are pancreatitis and lymphangiectasia—diets with a higher fat content can be used in all other circumstances.

Exclusion Diets

Used when an adverse reaction to food is suspected. Can be either home-prepared or commercially available; commercially avail-

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Table 1. Signs Associated with Chronic Gastrointestinal Disease

Diarrhea	Polyphagia	Abdominal discomfort	Edema
Weight loss/failure to thrive	Anorexia	Dehydration	Melena
Vomiting	Borborygmi	Ascites	Hematochezia
	Flatus		Tenesmus

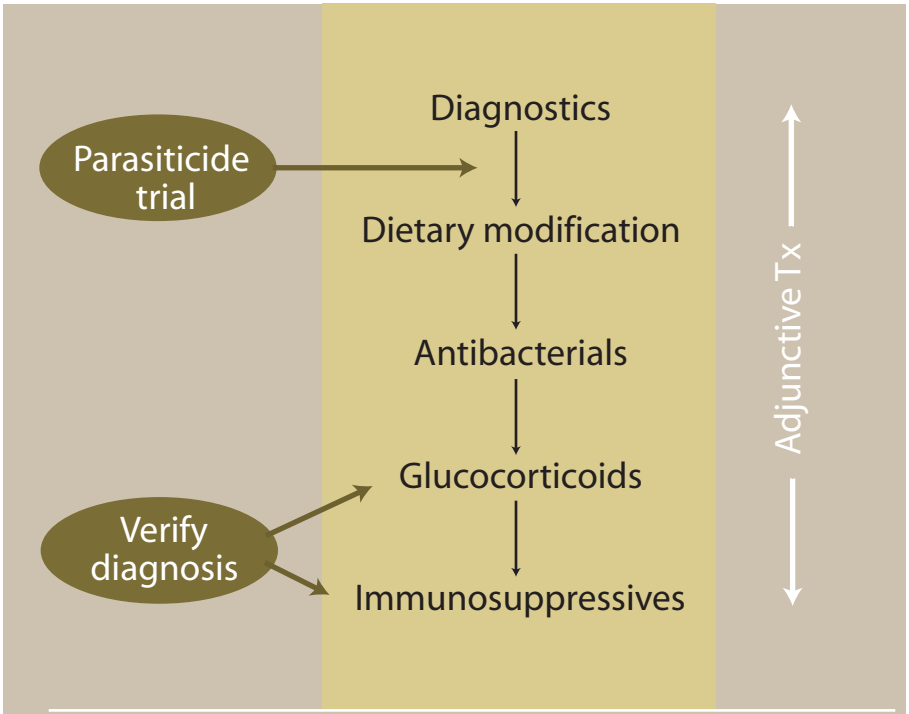
Table 2. Classification of Causes of Chronic Diarrhea

- **Primary small intestinal disease**
  - IBD (e.g., lymphocytic-plasmacytic, eosinophilic)
  - Lymphangiectasia
  - Lymphoma
  - Other neoplastic diseases
  - Primary infections (e.g., giardiasis)
- **Primary large intestinal disease**
  - Fiber-responsive colitis
  - *Clostridium perfringens*–associated colitis
  - IBD (e.g., lymphocytic-plasmacytic; eosinophilic, histiocytic, ulcerative colitis)
  - Infectious disease (e.g., histoplasmosis)
  - Neoplasia
- **Dietary**
  - Food poisoning
  - Overfeeding
  - Sudden change of diet
- **Gastric disease**
  - Achlorhydria (rare)
  - Dumping syndromes (rare)

IBD = inflammatory bowel disease

able diets can be based on a single-source or a hydrolyzed protein.

- If a single-source protein is used, ideally it should be novel to the individual. Options include cottage cheese, egg, rabbit, venison, chicken, fish, kangaroo, and turkey.
- Gluten is perceived to be a common food allergen, and most formulated diets are now gluten-free. However, although undoubtedly responsible for some adverse reactions to food, there is no evidence that gluten is any more antigenic than other commonly fed proteins.
- Some clinicians recommend home-prepared diets and others prefer commercial diets. I prefer the latter because owner compliance is usually better.
- Hydrolyzed protein diets are based on chemically treated, low-molecular-weight protein derivatives of chicken or soy. Such diets are theoretically less antigenic, although no clear evidence supports this theory. However, such diets are highly digestible and are currently the easiest way to feed novel antigens and are now the exclusion diet of choice for most clinicians.
- The optimum duration for an exclusion diet trial is unknown; 3 to 4 weeks has been chosen arbitrarily. However, some cases may take longer to respond (e.g., up to 12 weeks).
- Once remission is achieved, the animal should be challenged with the original diet to demonstrate relapse and confirm the diagnosis. However, many clients are not willing to pursue this approach, particularly if diarrhea is likely to recur during relapse.



KEY	
Parasiticides	Fenbendazole, metronidazole
Dietary modification	Highly digestible, exclusion, high-fiber
Antibacterials	Oxytetracycline, tylosin, metronidazole
Glucocorticoids	Prednisolone (prednisone), budesonide
Immunosuppressives	Azathioprine, cyclosporine, sulfasalazine
Adjunctive therapy	Probiotics, prebiotics, cobalamin, fluid therapy, antiemetics, protectants, adsorbents, motility modifiers

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Recommended staged approach to therapy

High-Fiber Diets

Most commonly used in cases presenting predominantly with large intestinal signs.

Different fiber sources have different physiologic properties.

Low-solubility high-fiber diets, such as those that include cellulose, achieve their effect by increasing bulk in the intestine; they bind nonabsorbed fluid and help to regulate intestinal motility.

Higher-solubility fibers include beet pulp, pectins from carrots or fruits, and gum-like fiber. These fibers can be easily fermented by intestinal bacteria and short-chain fatty acids (e.g., butyric acid) and can be partly utilized by the colonic mucosa. Further, fermentable dietary fiber reduces the concentrations of potentially harmful bacteria and

ARD = acute renal disease; IBD = inflammatory bowel disease

increases the concentrations of potentially beneficial bacteria.

Thus, a mix of insoluble and soluble fiber is usually chosen; a purpose-formulated commercial ration or a fiber supplement added to the existing diet (e.g., Isogel—GlaxoSmithKline) can be used.

Approach to Dietary Management

Whichever diet is chosen, it should be introduced in gradually increasing amounts over 4 to 7 days. It is best to feed *only* the chosen diet, frequently (e.g., 4 to 5 meals/day), and in small amounts.

Medications

ANTIPARASITICIDES

Used to eliminate occult parasites, such as *Giardia intestinalis* and helminth infestation. The main drugs used are:

- Fenbendazole 50 mg/kg Q 24 H PO for 3 to 5 days with food (e.g., Panacur—Intervet)
- Metronidazole 20 mg/kg Q 12 H PO for 7 days

Other possible drugs include albendazole, oxfendazole, and a combination of febantel with pyrantel. The author has limited experience with oxfendazole and albendazole; however, occasional adverse effects (e.g., bone marrow toxicosis) are reported with the latter, so its use is not recommended. A 2- to 3-day course of a combination wormer, such as Drontal Plus (Bayer Animal Health), has been shown to be effective against *Giardia* in dogs (febantel 30 mg/kg and pyrantel 30 mg/kg Q 24 H PO). A single oral dose of the same product is also effective against most enteric helminths (febantel 15 mg/kg and pyrantel 15 mg/kg Q 24 H PO).

ANTIBACTERIALS

Can be used for the following:

- Documented bacterial infections of the gastrointestinal tract (e.g., *Salmonella, Campylobacter, Clostridia*, enteropathogenic *Escherichia coli*)
- Idiopathic antibiotic-responsive diarrhea
- Secondary small intestinal bacterial overgrowth (e.g., secondary to partial obstructions, exocrine pancreatic insufficiency)
- As an adjunct to therapy for IBD
- As a therapeutic trial when the exact cause of clinical signs is not evident on diagnostic testing (see below)

The choice of antibacterial depends upon the indication. When a recognized bacterial pathogen is identified, an effective drug should be chosen (e.g., erythromycin for *Campylobacter jejuni*, metronidazole for *Clostridium perfringens*). For idiopathic ARD, opinions differ:

- Oxytetracycline (10 mg/kg Q 8 H PO) is effective in many cases and is still the first choice for many clinicians, although some clinicians prefer to avoid it because of concerns over antibiotic resistance.
- Tylosin (10 to 15 mg/kg Q 12 H PO) is a suitable alternative. However, it is only available as a powder, making dosing more problematic.
- Metronidazole (10 mg/kg Q 8 H PO) can also be used. For IBD, metronidazole is usually chosen as first-line therapy, and it has been suggested that metronidazole has immunosuppressive effects in addition to antimicrobial activity. Many cases of IBD can be controlled with a combination of dietary modification and metronidazole without the need for other immunosuppressives.

GLUCOCORTICOIDS & IMMUNOSUPPRESSANTS

Glucocorticoids are the primary treatment for IBD, and prednisolone (or prednisone) is the agent of first choice. Initially, the drug is normally administered at the high end of the dose range (e.g., 1 to 2 mg/kg per day PO in divided doses). Doses can be gradually tapered (over weeks to months) once remission is achieved. Therapy can sometimes be discontinued altogether, although lifelong therapy may be required.

If traditional glucocorticoids are poorly tolerated, budesonide is a viable alternative. This is an enteric-coated, locally active steroid that is 90% metabolized during the first pass through the liver. However, it is expensive and efficacy has not yet been shown in companion animals.

Patients with severe hypoproteinemia should be hospitalized and treated with parenteral therapy (to avoid concerns over suboptimal drug absorption).

If response is poor, azathioprine can be added (2 mg/kg Q 24 H PO initially). The main side effect is bone marrow suppression, and hematologic variables should be monitored regularly. *For safety reasons, clients should not break or crush the tablets.*

The main alternative immunosuppressive agent is cyclosporine. The drug is expensive, but may be effective in some cases.

Sulfasalazine (and related drugs) are often used when IBD is limited to the large intestine (e.g., Salazopyrin EN Tabs—Pharmacia). Side effects include keratoconjunctivitis

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sicca; therefore, tear production should be monitored regularly.

ADJUNCTIVE THERAPY

Additional therapies include probiotics, prebiotics, cobalamin supplementation, protectants and adsorbents, and motility modifiers.

- Probiotics can directly antagonize pathogenic bacteria, and they modulate both innate and specific mucosal immune responses. Recent studies have suggested that humans with IBD benefit from probiotic administration, but little evidence supports their use in dogs.
- Prebiotics are selective substrates for a few "beneficial" species, thereby causing alterations in luminal microflora. Most are nondigestible carbohydrates (e.g., inulin and fructooligosaccharides). Prebiotics are now incorporated into many veterinary diets and although they may assist in the treatment of IBD, more work is required before their use can be justified.
- Serum cobalamin concentrations (e.g., Anivit B12—Animalcare Limited) should be measured in all dogs with chronic gastrointestinal disease, and parenteral supplementation may be required when hypocobalaminemia is documented.
- Symptomatic therapy might be required to control acute bouts of clinical signs or flare-ups. If vomiting and diarrhea cause severe dehydration, IV fluid therapy may be required.
- If vomiting is severe, antiemetics (such as metoclopramide) can be used.
- Some clinicians favor the use of protectant adsorbents (e.g., bismuth, kaolin), although their benefit in chronic cases is questionable.
- Similarly, some clinicians use anticholinergics and opioid analgesics as potential motility and secretion-modifying agents. However, the author does not recommend routine use.

THERAPEUTIC TRIALS

The exact cause of chronic gastrointestinal disease is not always clear, despite a full diagnostic work-up. In such cases, a staged approach to therapy is recommended (**Figure 1**). The owner should be advised to maintain an event diary to monitor frequency of clinical signs, and various therapies should be added in turn. This approach allows such cases to be classified as diet-responsive, antibacterial-responsive, immunosuppression-responsive, or complex.

Patient Monitoring & Follow-up

- Patients with hypoproteinemia need hospitalization because laboratory values (e.g., serum albumin) need to be measured daily.
- Most other cases can be monitored on an outpatient basis.
- Dogs on immunosuppressive therapy should be reassessed every 2 to 3 weeks. Dogs receiving azathioprine should have hematologic variables assessed at least Q 14 D when the highest dose of medication (2 mg/kg) is being given; thereafter, monitoring frequency can be reduced.
- Most other cases can be assessed less frequently, such as every 3 to 4 weeks.
- Telephone follow-up is possible in some cases, although some revisits to the clinic are recommended.

In General

RELATIVE COST

- Antiparasiticides usually only need to be given as a single course unless infection recurs ($).
- Antibacterials are usually given as a 4- to 6-week course, and most recommended drugs are relatively inexpensive. Some cases of ARD require longer term (occasionally lifelong therapy) ($$–$$$).
- When immunosuppressants are required, long-term (potentially lifelong) therapy is usually necessary. Oral prednisolone (or prednisone) is inexpensive, even when long-term therapy is required ($–$$). Parenteral prednisolone is expensive, even when used only early in the course of disease ($$–$$$); azathioprine is expensive ($$–$$$); and cyclosporine is very expensive ($$$$–$$$$$).
- Sulfasalazine is relatively inexpensive ($–$$), but alternative drugs (mesalazine, olsalazine), although safer, are more expensive ($$$–$$$$).

Cost Key

$ = <$100
$$ = $100-250
$$$ = $250-500
$$$$ = $500-1000
$$$$$ = >$1000

PROGNOSIS

Depends on the cause. For intestinal disease, the prognosis is poor for lymphoma, guarded to good for ARD and IBD, and good for food sensitivity.

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