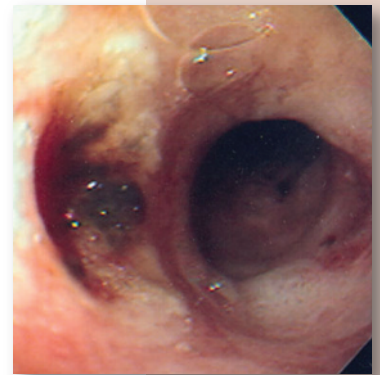


Peer Reviewed

Feline Inflammatory Bowel Disease

When addressing feline inflammatory bowel disease (IBD), the key to effective treatment is starting with the correct diagnosis.

Feline IBD is the *histopathologic* diagnosis of an *idiopathic* condition; therefore, before initiating potentially lifelong treatment with immunomodulatory drugs that may incur significant adverse events, several important causes of chronic enteropathy must be ruled out.



Endoscopic image of duodenum showing a large ulcerated area of mucosa in a 10-year-old spayed DSH presented for chronic diarrhea and weight loss. Histopathologic diagnosis was severe inflammatory bowel disease with necrotic ulcerated tissue.

How I Treat Feline IBD

- | | |
|--|--|
| <input type="checkbox"/> Make diagnosis | <input type="checkbox"/> Adjust vitamin intake |
| <input type="checkbox"/> Initiate a stepwise approach to treatment | <input type="checkbox"/> Administer medical treatment |
| <input type="checkbox"/> Initiate dietary intervention | <input type="checkbox"/> Assess therapy; readjust if necessary |

Make diagnosis

Rule Out Common Causes

- Rule out common causes of chronic enteropathy
- Consider differentials for chronic enteropathies in cats:
 - Food sensitivity, food allergy, or food-responsive disease
 - Intestinal parasitism
 - Medication effects or adverse events
 - Plant or toxin intoxication
 - Extraintestinal disease (eg, hyperthyroidism, chronic kidney disease, cholangitis, triaditis, infection)
 - Alimentary neoplasia
 - Antibiotic-responsive enteropathy
 - While this is recognized in dogs, whether it occurs in cats is unclear
 - Exocrine pancreatic insufficiency (rare)

IBD = inflammatory bowel disease

CONTINUES

IBD requires a histopathologic diagnosis, which may necessitate expense, anesthesia, and referral.

Pursue Histopathologic Diagnosis

- Note that IBD requires a histopathologic diagnosis
 - This may take considerable effort and expense, anesthesia, and referral
- Determine whether signs result from idiopathic IBD or a neoplastic condition (eg, lymphoma, adenocarcinoma)
- Expect (and inform clients) that the pathologist may use technologically advanced diagnostics and extract all available information from the biopsy sample
 - If client constraints preclude histopathologic diagnosis, initiate treatment after ensuring the client understands the potential pitfalls of treating without a definitive diagnosis

Perform Histopathology or Refer to a Pathologist

- Perform the following, or see that a pathologist can perform:
 - Histopathology
 - Mucosal/submucosal (endoscopic biopsy) or full-thickness (surgical biopsy)
 - Villus blunting or fusion, edema, lymphatic dilation, cryptal hyperplasia, fibrosis
 - Lymphocytic infiltration (intraepithelial, submucosal, muscularis, serosal)
 - Immunohistochemistry (T cells, B cells, CD3e, CD79a)
 - PCR for clonality by PCR antigen receptor rearrangement (PARR) and flow cytometry

☑ Initiate a stepwise approach to treatment

- Let the patient’s clinical condition dictate

urgency of treatment decisions

- Start with basic intervention and advance to more powerful treatment combinations
- As each component of treatment may have an individual effect, judge efficacy with a brief period of observation and assessment at each stage before adding to the therapeutic mixture
 - Poor prognostic indicators (eg, hypoalbuminemia, weight loss) may dictate a more aggressive initial approach

☑ Initiate dietary intervention

General

- Initiate hydrolyzed or hypoallergenic diets to decrease antigenic stimulation of the GI tract
 - Although idiopathic IBD is not a food allergy or food-responsive disease, dietary intervention remains an important treatment component
 - Antigenic stimulation by dietary components, most likely the protein portion, may contribute to the abnormal immune-inflammatory environment of the intestinal tract
- Match diet with patient (ie, palatability, wet/dry, client preferences)
- Assess effect after a 1–2 week trial; adjust accordingly
 - May require multiple adjustments
- Inform client that numerous commercial diet options are available
- Advise clients who prepare their own pet food to use careful, consistent attention for a complete and balanced diet that provides a single-source protein and single-source carbohydrate

IBD = inflammatory bowel disease, PARR = PCR antigen receptor rearrangement



READY, AIM, FIRE!

Proceed with conclusive diagnosis

- Start with basic intervention and continue to more powerful treatment
- Brief periods of observation and assessment after each treatment plan are beneficial

Proceed without conclusive diagnosis

- Client constraints may prevent histopathologic diagnosis
- Treatment can be initiated with client understanding of potential complications

Fiber

- Add fiber to patient's diet
- For large bowel diarrhea, add both soluble and insoluble fiber in moderation (eg, canned pumpkin, psyllium)
 - Fiber, both soluble and insoluble, appears to have several beneficial properties and is most frequently used in cases where large bowel diarrhea is a prominent sign

Prebiotics & Probiotics

- Institute prebiotics, which are included in most specialized commercial pet foods
- Institute probiotics from a reputable veterinary source
 - The product chosen must contain billions of live organisms when ingested, and the formula must survive GI passage
 - Probiotics appear beneficial for many cats with chronic enteropathies of various causes, including idiopathic IBD
 - Probiotics are generally safe and unlikely to cause harm
 - It is unclear whether different probiotics are needed for different conditions

✔ Adjust vitamin intake

- Measure cobalamin (ie, vitamin B12) and folate levels
- Administer cobalamin at 250 µg SC q7days for a month before tapering
 - Studies have demonstrated that many cats with chronic GI disease have suboptimal levels of cobalamin
 - Feline cobalamin levels are measured in a fasted sample
 - Although cobalamin supplementation is often instituted based on assumption, the actual number is still important
 - It appears that the lowest cobalamin levels usually appear in either severe cases of IBD or in cases of GI lymphoma
- Administer folate supplementation, 0.5–1.0 mg PO q24h, if indicated

✔ Administer medical treatment

Corticosteroids

- Administer prednisolone at 1–3 mg/kg q24h before tapering

Tx AT A GLANCE

- Rule out common known causes of chronic GI disease *first*.
- Idiopathic IBD is a histopathologic diagnosis.
- Dietary intervention is the first order of treatment.
- Measure and supplement cobalamin as needed.
- Prednisolone is the pharmaceutical foundation of treatment.
- Dietary intervention, cobalamin, and prednisolone are generally sufficient.
- Therapeutic failure may suggest poor compliance, inadequate workup, GI neoplasia, or other concurrent diseases; biopsy is then necessary.

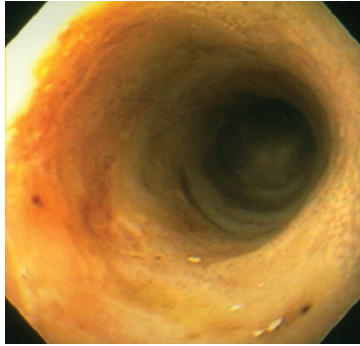
- Prednisolone, preferred over prednisone in cats, remains the pharmaceutical cornerstone of treatment for feline idiopathic IBD
- Cats are less prone to adverse events caused by corticosteroids side effects than dogs, but it is still a powerful corticosteroid and long-term use can have deleterious consequences in this species
- Maintain contact with the clients and patient
- Once signs have remained absent for 1–2 weeks, taper prednisolone dose 25% every 2–4 weeks until administration is q48h; it is rarely discontinued

Consider Corticosteroid Alternatives

- Consider budesonide (corticosteroid alternative) at a 0.5–1.0 mg/cat PO q24h starting dose
 - Theoretically, budesonide has a high first-pass removal by the liver with minimal systemic consequence
- Note that some cats appear to respond differently to different glucocorticoids; if prednisolone is not effective, dexamethasone or betamethasone is worth trying
 - Evidence is anecdotal and mixed for budesonide, dexamethasone, and betamethasone

CONTINUES

Dietary intervention, vitamins, and corticosteroids are generally sufficient for IBD treatment.



A 7-year-old spayed DSH was presented for chronic diarrhea, intermittent vomiting, and weight loss. Although endoscopy revealed some mucosal irregularities, there were no marked gross abnormalities. Histopathology revealed moderate lymphoplasmacytic IBD, and the cat responded well to a hypoallergenic diet, prednisolone, and cobalamin supplementation.

Assess therapy; readjust if necessary

Assess & Readjust: 1

- Assess the patient
 - Dietary intervention, vitamins, and corticosteroids are generally sufficient
- If necessary, reconsider diagnosis
 - Therapeutic failure at this point suggests poor client compliance or inadequate workup
 - This makes biopsy imperative
 - This may be indicative of an inaccurate diagnosis, such as GI lymphoma, low-grade alimentary lymphoma or other GI neoplasia, or other concurrent diseases
 - The potential causes of enteropathies may not have been adequately ruled out
- Consider other immunomodulatory drugs in IBD cases refractory to traditional therapy
- Consider chlorambucil (for low-grade GI lymphoma; 2 mg/cat q2–3days)
- Monitor CBC
- Consider cyclosporine (5 mg/kg q12–24h)
- Monitor for anorexia and vomiting
- If necessary, administer an antibiotic (eg, tylosin at 10 mg/kg PO q8h)

Assess & Readjust: 2

- Consider concurrent diseases
 - Cats are notorious for concurrent disease; the most relevant in cases of feline idiopathic IBD are chronic pancreatitis and cholangitis, forming the triad termed *triaditis*
- Treat for chronic pancreatitis
 - Includes analgesia, adequate calories +/- appetite stimulant, and maintaining perfusion by optimizing ongoing hydration
- Treat for cholangitis (neutrophilic, lymphoplasmacytic)

See Aids & Resources, back page, for references & suggested reading.

Therapeutic failure at this point suggests poor client compliance, inadequate workup, or concurrent disease.

IBD = inflammatory bowel disease

RILEXINE®
(cephalexin) Chewable Tablets for Dogs

Antimicrobial for Oral Use in Dogs only

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

BRIEF SUMMARY: Please consult package insert for complete product information.

INDICATION: For the treatment of secondary superficial bacterial pyoderma in dogs caused by susceptible strains of *Staphylococcus pseudintermedius*.

CONTRAINDICATIONS: RILEXINE Chewable Tablets are contraindicated in dogs with a known allergy to cephalexin or to the β-lactam (any of the penicillins or cephalosporins) group of antibiotics.

WARNINGS: For use in dogs only. Not for use in humans. Keep this drug out of the reach of children. Antimicrobials, including penicillins and cephalosporins, can cause allergic reactions in sensitized individuals. Sensitized individuals handling such antimicrobials, including cephalexin, should avoid contact of the product with the skin and mucous membranes in order to minimize the risk of allergic reactions.

PRECAUTIONS: Prescribing antibacterial drugs in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to treated animals and may increase the risk of the development of drug-resistant animal pathogens.

The safe use of RILEXINE Chewable Tablets in dogs intended for breeding and in pregnant or lactating bitches has not been evaluated.

Positive direct Coombs' test results and false positive reactions for glucose in the urine have been reported during treatment with some cephalosporin antimicrobials. Cephalosporin antimicrobials may also cause falsely elevated urine protein determinations. Some antimicrobials, including cephalosporins, can cause lowered albumin values due to interference with certain testing methods.

Occasionally, cephalosporins have been associated with myelotoxicity, thereby creating a toxic neutropenia¹. Other hematological reactions observed with cephalosporin therapy include neutropenia, anemia, hypoprothrombinemia, thrombocytopenia, prolonged prothrombin time (PT) and partial thromboplastin time (PTT), platelet dysfunction, and transient increases in serum aminotransferases².

ADVERSE REACTIONS: The most common adverse reactions in dogs include diarrhea, vomiting, anorexia and lethargy. To report suspected adverse reactions call Virbac at 1-800-338-3659.

ANIMAL SAFETY: RILEXINE Chewable Tablets were administered orally three times a day to 12-week-old healthy Beagles at 0 mg/kg (placebo), 22 mg/kg (1X), 66 mg/kg (3X), and 110 mg/kg (5X) for 12 weeks, and at 22 mg/kg twice a day for 12 weeks. The most common clinical findings included epiphora, salivation, vomiting and diarrhea among all the dose groups. Three dogs had decreased activity (1 in each from the 22 mg/kg twice a day, 22 mg/kg three times a day, and the 66 mg/kg three times a day groups). These observations were mild and sporadic.

There were increases in alanine aminotransferase (ALT) in the 110 mg/kg three times a day group and in the 22 mg/kg twice a day group that increased in a dose-dependent pattern. There was an increase in sorbitol dehydrogenase (SDH) in the 110 mg/kg three times a day group compared to the controls. These changes were minimal and the values remained within expected historical control ranges. There were several decreases in total protein (in the 110 mg/kg three times a day group) and/or globulin (in the 22, 66, and 110 mg/kg three times a day groups) compared to the controls. These changes resulted in occasional increases in albumin/globulin ratios. Although a drug effect cannot be ruled-out, these changes were not clinically relevant.

A mild prolongation in prothrombin time (PT) was observed in the 22 mg/kg three times a day group. This was not considered clinically relevant due to the small change that remained within the reference ranges.

One dog in the 110 mg/kg three times a day group had moderate amounts of bilirubinuria at the Week 8 and Week 12 samplings. No clinical significance was noted.

Cephalexin was not present in any Day 1 samples prior to dosing or in any control animals. After dosing, cephalexin was well absorbed into systemic circulation of the treated dogs. Within gender and dosage level, Week 8 mean trough concentrations were generally higher than the Week 4 and 12 mean trough concentrations (between a 0.9 and 3.6-fold difference). The geometric mean plasma cephalexin trough concentration following three times daily administration of the 110 mg/kg dose was 11.2 µg/mL compared to 2.6 µg/mL and 8.7 µg/mL following 22 mg/kg and 66 mg/kg, respectively at Week 12. Geometric mean plasma cephalexin trough concentrations following administration of 22 mg/kg twice daily were 0.7, 1.3, and 1.0 µg/mL at Weeks 4, 8, and 12, respectively.

STORAGE INFORMATION: Store at 20°C-25°C (68°F-77°F), with excursions permitted between 15°C-30°C (59°F-86°F).

HOW SUPPLIED: RILEXINE (cephalexin) Chewable Tablets are supplied in 75 mg, 150 mg, 300 mg, and 600 mg tablets packaged in bottles of 100 and 500 tablets or boxes of 28 blister-packs, 7 tablets per blister pack.

NADA 141-326. Approved by FDA.

Distributed by: Virbac Animal Health, Inc. Fort Worth, TX 76137 USA

Revision date: 08/2011

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