

Small Intestinal Diarrhea in a Wheaten Terrier

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Skipper, an 8-year-old, castrated soft-coated wheaten terrier (SCWT), presented for marked weight loss, poor appetite, and distended abdomen.

History

Skipper had a history of recurrent mild GI upset consistent with small intestinal diarrhea characterized by large, voluminous stool with decreased appetite, weight loss, and occasional vomiting. The referring veterinarian's management included a novel protein diet, prednisone at 0.5 mg/kg PO q48h, and metronidazole at 12.5 mg/kg PO q12h with minimal resolution of clinical signs.

Physical Examination

Skipper was quiet, alert, and responsive with normal vital parameters. Abnormal findings included distended abdomen, poor coat, generalized weakness, and decreased BCS (2/9).

Diagnostics

CBC, serum biochemistry profile, and abdominal ultrasonography were completed. Serum biochemical abnormalities included panhypoproteinemia, hypocholesterolemia, and hypocalcemia (Table). CBC and urinalysis were within reference ranges. Abdominal ultrasonography revealed diffusely thickened small intestine with hyperechoic mucosal layer and preservation of wall layering. A moderate amount of aspirated anechoic peritoneal fluid was evident. The remainder of the abdomen was unremarkable.

BCS = body condition score, SCWT = soft-coated wheaten terrier

Table Abnormal Serum Biochemistry Results

Variable	Result	Reference Range
Albumin (g/dL)	1.1	3–4
Calcium (mg/dL)	7.1	8.2–12.4
Cholesterol (mg/dL)	67	112–328
Globulin (g/dL)	1.3	2.1–4.5
Total protein (g/dL)	2.4	5.1–7.8
Total protein–effusion (g/dL)	1	

Ask Yourself



1. What are the differentials for abdominal effusion characterized as a pure transudate, and how can biochemistry profile findings narrow the differentials?
2. What diagnostic and screening procedures should be used to evaluate a SCWT with suspected protein-losing disease?
3. What treatments are available to manage potential protein-losing nephropathy differentials in a SCWT?

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Diagnosis

Protein-losing enteropathy (PLE)

Preliminary Diagnosis

Preliminary diagnosis of PLE is based on GI signs and free abdominal fluid that is a direct result of the significant panhypoproteinuria. Common causes include lymphatic abnormalities, inflammatory bowel disease (IBD), and neoplastic conditions. Breed-specific enteropathies have been identified. Protein-losing nephropathy (PLN), meanwhile, refers to any glomerular disease of the kidney that results in excessive protein loss.

SCWTs are predisposed to familial PLE and PLN; middle-aged bitches are most frequently affected. Mode of inheritance is complex and unclear. Concurrent PLE–PLN is occasionally (ie, uncommonly) seen in other breeds. Affected patients can have PLE or PLN in isolation. Both conditions may affect 5% to 15% of the breed and have many more suspected carriers.

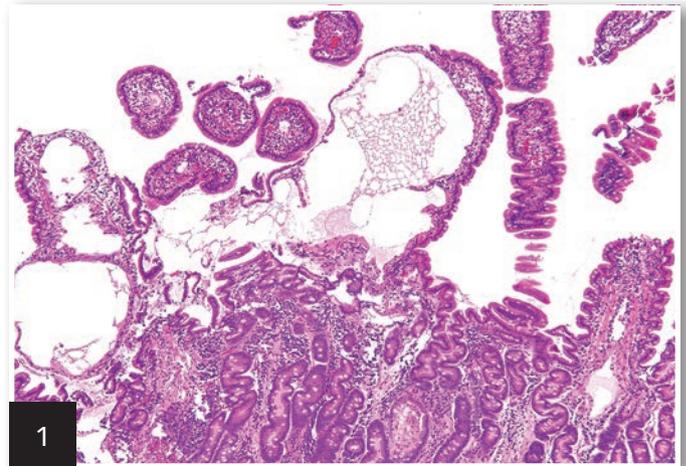
There is a high prevalence of food hypersensitivities in SCWTs with PLE, but whether these hypersensitivities have a primary or secondary role is unknown. Affected patients can have lymphangiectasia with or without concurrent IBD (**Figure 1**); both can be patchy and missed on biopsy sample analysis. A functional-structural change in glomerular permeability, specifically a podocytopathy, has been identified in SCWTs with PLN. Glomerular lesions are generally characterized by focal and segmental glomerulosclerosis (**Figure 2**) secondary to the podocytopathy, although immune-complex-mediated glomerulonephritis is sometimes reported.

Prognosis

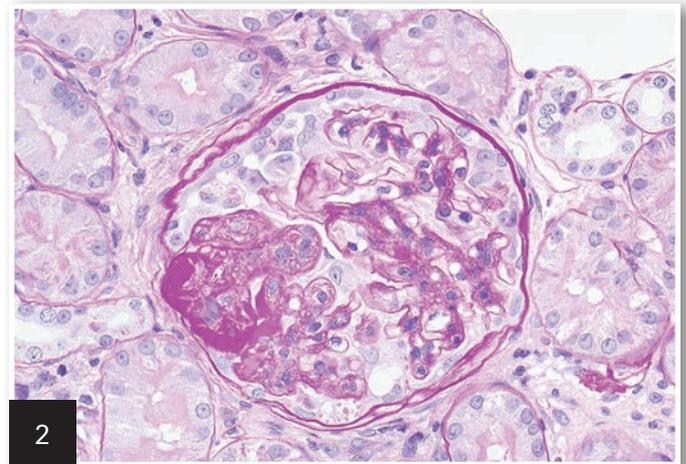
PLE or PLN prognosis may be poor if either condition is detected late in disease course; however, detection before serum protein concentrations decrease offers the best chance that treatment may slow progression. Because of genetic predisposition, affected dogs should not be bred.

Treatment

Lymphoplasmacytic enteritis with lacteal dilation was diagnosed by endoscopic biopsy. Medical therapy before diagnostics does not affect obtaining a diagnosis. Immunosuppressive therapy was fortified (prednisone 2 mg/kg PO q24h; azathioprine 2 mg/kg PO q24h for 7 days, then transitioned to q48h long-term). Additional treatment included spironolactone (2 mg/kg PO q24h) and cromolyn sodium (100 mg q8h, off label), along



1 Intestinal lymphangiectasia with lacteal dilation.



2 Glomerular lesion of glomerulosclerosis.

with a hydrolyzed protein diet. Skipper's ascites resolved, but total serum protein levels remained low.

Outcome

Skipper's PLE was well controlled with this treatment, although recurrent urinary tract infections and an episode of sepsis occurred, likely secondary to prolonged immunosuppression. Skipper developed proteinuria after resolution of the urinary tract infections (urine protein:creatinine 0.85; range, <0.5) which was within 1 year of PLE diagnosis. The proteinuria was responsive to enalapril at 0.5 mg/kg q12h; however, Skipper was euthanized because of unrelated illness. ■ **cb**

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

Topical Parasiticide For Dogs and Cats

BRIEF SUMMARY:

See package insert for full prescribing information.

CAUTION:

US Federal law restricts this drug to use by or on the order of a licensed veterinarian.

INDICATIONS:

Revolution is recommended for use in dogs six weeks of age or older and cats eight weeks of age and older for the following parasites and indications:

Dogs:

Revolution kills adult fleas and prevents flea eggs from hatching for one month and is indicated for the prevention and control of flea infestations (*Ctenocephalides felis*), prevention of heartworm disease caused by *Dirofilaria immitis*, and the treatment and control of ear mite (*Otodectes cynotis*) infestations. Revolution also is indicated for the treatment and control of sarcoptic mange (*Sarcoptes scabiei*) and for the control of tick infestations due to *Dermacentor variabilis*.

Cats:

Revolution kills adult fleas and prevents flea eggs from hatching for one month and is indicated for the prevention and control of flea infestations (*Ctenocephalides felis*), prevention of heartworm disease caused by *Dirofilaria immitis*, and the treatment and control of ear mite (*Otodectes cynotis*) infestations. Revolution is also indicated for the treatment and control of roundworm (*Toxocara cati*) and intestinal hookworm (*Ancylostoma tubaeforme*) infestations in cats.

WARNINGS:

Not for human use. Keep out of the reach of children.

In humans, Revolution may be irritating to skin and eyes. Reactions such as hives, itching and skin redness have been reported in humans in rare instances. Individuals with known hypersensitivity to Revolution should use the product with caution or consult a health care professional. Revolution contains isopropyl alcohol and the preservative butylated hydroxytoluene (BHT). Wash hands after use and wash off any product in contact with the skin immediately with soap and water. If contact with eyes occurs, then flush eyes copiously with water. In case of ingestion by a human, contact a physician immediately. The material safety data sheet (MSDS) provides more detailed occupational safety information. For a copy of the MSDS or to report adverse reactions attributable to exposure to this product, call 1-888-963-8471.

Flammable - Keep away from heat, sparks, open flames or other sources of ignition.

Do not use in sick, debilitated or underweight animals (see SAFETY).

PRECAUTIONS:

Prior to administration of Revolution, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. Revolution is not effective against adult *D. immitis* and, while the number of circulating microfilariae may decrease following treatment, Revolution is not effective for microfilariae clearance.

Hypersensitivity reactions have not been observed in dogs with patent heartworm infections administered three times the recommended dose of Revolution. Higher doses were not tested.

ADVERSE REACTIONS:

Pre-approval clinical trials:

Following treatment with Revolution, transient localized alopecia with or without inflammation at or near the site of application was observed in approximately 1% of 691 treated cats. Other signs observed rarely (0.5% of 1743 treated cats and dogs) included vomiting, loose stool or diarrhea with or without blood, anorexia, lethargy, salivation, tachypnea, and muscle tremors.

Post-approval experience:

In addition to the aforementioned clinical signs that were reported in pre-approval clinical trials, there have been reports of pruritus, urticaria, erythema, ataxia, fever, and rare reports of death. There have also been rare reports of seizures in dogs (see WARNINGS).

SAFETY:

Revolution has been tested safe in over 100 different pure and mixed breeds of healthy dogs and over 15 different pure and mixed breeds of healthy cats, including pregnant and lactating females, breeding males and females, puppies six weeks of age and older, kittens eight weeks of age and older, and avermectin-sensitive collies. A kitten, estimated to be 5-6 weeks old (0.3 kg), died 8 1/2 hours after receiving a single treatment of Revolution at the recommended dosage. The kitten displayed clinical signs which included muscle spasms, salivation and neurological signs. The kitten was a stray with an unknown history and was malnourished and underweight (see WARNINGS).

DOGS: In safety studies, Revolution was administered at 1, 3, 5, and 10 times the recommended dose to six-week-old puppies, and no adverse reactions were observed. The safety of Revolution administered orally also was tested in case of accidental oral ingestion. Oral administration of Revolution at the recommended topical dose in 5- to 8-month-old beagles did not cause any adverse reactions. In a pre-clinical study selamectin was dosed orally to ivermectin-sensitive collies. Oral administration of 2.5, 10, and 15 mg/kg in this dose escalating study did not cause any adverse reactions; however, eight hours after receiving 5 mg/kg orally, one avermectin-sensitive collie became ataxic for several hours, but did not show any other adverse reactions after receiving subsequent doses of 10 and 15 mg/kg orally. In a topical safety study conducted with avermectin-sensitive collies at 1, 3 and 5 times the recommended dose of Revolution, salivation was observed in all treatment groups, including the vehicle control. Revolution also was administered at 3 times the recommended dose to heartworm infected dogs, and no adverse effects were observed.

CATS: In safety studies, Revolution was applied at 1, 3, 5, and 10 times the recommended dose to six-week-old kittens. No adverse reactions were observed. The safety of Revolution administered orally also was tested in case of accidental oral ingestion. Oral administration of the recommended topical dose of Revolution to cats caused salivation and intermittent vomiting. Revolution also was applied at 4 times the recommended dose to patent heartworm infected cats, and no adverse reactions were observed. In well-controlled clinical studies, Revolution was used safely in animals receiving other frequently used veterinary products such as vaccines, anthelmintics, antiparasitics, antibiotics, steroids, collars, shampoos and dips.

STORAGE CONDITIONS: Store below 30°C (86°F).

HOW SUPPLIED: Available in eight separate dose strengths for dogs and cats of different weights (see DOSAGE). Revolution for puppies and kittens is available in cartons containing 3 single dose tubes. Revolution for cats and dogs is available in cartons containing 3 or 6 single dose tubes.

NADA 141-152, Approved by FDA

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Kalamazoo, MI 49007

www.revolutionpet.com

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Did You Answer?

1. Pure transudate is a clear fluid with low protein level (<2.5 g/dL) and nucleated cell count (<1,000/μL); decreased oncotic pressure from hypoalbuminemia is the primary cause. Decreased serum albumin is most frequently caused by decreased production as occurs in synthetic liver failure (>70% loss of functional parenchyma) or protein loss via the GI tract or kidneys. Protein loss via the GI tract is nonselective and results in decreased albumin and globulin.

Exceptions include some breed-specific (eg, Basenji) and infectious (eg, histoplasmosis) enteropathies, in which globulin is normal or increased. Other abnormalities associated with PLE include hypocholesterolemia, hypocalcemia, and hypomagnesemia. A definitive diagnosis of IBD, other infiltrative disease (eg, infectious, neoplasia), or lymphangiectasia requires intestinal biopsy. Ideally, a full-thickness biopsy specimen can be obtained; however, given the severity of disease and patient serum albumin, endoscopic biopsy may be safer. PLN and liver failure generally cause hypoalbuminemia only. If severe, PLN can progress to azotemia and/or nephrotic syndrome characterized by hypercholesterolemia and edema. Animals with synthetic liver failure often have additional markers of dysfunction (eg, reduced BUN, jaundice, hypoglycemia, hypocholesterolemia). Total serum bile acids should also be performed to assess liver function.

2. ANNUAL screening to identify protein loss is recommended. An ideal protocol includes CBC, serum biochemistry profile, urinalysis, urine protein:creatinine ratio, and fecal α-1 proteinase inhibitor test on 3 naturally voided samples. A DNA test at University of Pennsylvania (scwtca.org/health/dnatest.htm) can identify dogs at risk for podocytopathy. Definitive diagnosis and characterization of intestinal and/or glomerular lesions require histopathology.

3. Therapy for PLE includes probiotics, antimicrobials (eg, metronidazole, tylosin), cobalamin supplementation, antiplatelet therapy (eg, low-dose aspirin, clopidogrel), immunosuppressive agents, and gluten-free hypoallergenic diet. Cromolyn sodium (cost restrictive) can be beneficial in refractory cases.

PLN management involves inhibition of the renin-angiotensin-aldosterone system, control of systemic hypertension, diet therapy with protein restriction and omega-3 supplementation, and antiplatelet therapy. If immune complex deposition is confirmed via renal biopsy with electron microscopic analysis, immunosuppressive therapy may be indicated.