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.

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

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?
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 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. 

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

IBD = inflammatory bowel disease, PLE = protein-losing enteropathy, PLN = protein-losing nephropathy, SCWT = soft-coated wheaten terrier
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 hypercholesterolemia, 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, creatinine, protein:creatinine ratio, and fecal α-1 proteinase inhibitor test on 3 natural voided samples. A DNA test at University of Pennsylvania (scwcta.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.

**Topical Parasiticide For Dogs and Cats**

**BRIEF SUMMARY:**

A 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 or older for the following parasitic and indications.

**Dogs:**

Revolution kills adult fleas and prevents the eggs from hatching for one month and is indicated for the prevention and control of the infestations (Ectoparasites): control of flea biting lice, prevention of dermatitis caused by Dirofilaria immitis, and the treatment and control of ear mites (Otodectes cynotis) and the treatment and control of ear mite (Otodectes cynotis) and intestinal hookworm (Dirofilaria immitis) infections in cats.

**Cats:**

Revolution kills adult fleas and prevents the eggs from hatching for one month and is indicated for the prevention and control of the infestations (Ectoparasites): control of flea biting lice, prevention of dermatitis caused by Dirofilaria immitis, and the treatment and control of ear mites (Otodectes cynotis) and intestinal hookworm (Dirofilaria immitis) infections in cats.

**WARRNINGS:**

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

In humans: the use of Revolution in humans is not currently approved. Use of the product with caution and consult a health-care professional. Revolution contains isopropyl alcohol and the preservative butylated hydroxytolene (BHT). Wash hands after use and wash off any product in contact with the skin immediately with soap and water. It contains alcohol which, 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 the product, call 1-800-326-0471.

**UN利亚RMAL USE:**

Pottasial - Keep away from hair, 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 treated for existing heartworm infections. Administration of the antiparasitic, anthelmintic, or antibiotic should be tapered to eliminate the use of the product with caution and consult a health-care professional. Revolution contains isopropyl alcohol and the preservative butylated hydroxytolene (BHT). Wash hands after use and wash off any product in contact with the skin immediately with soap and water. It contains alcohol which, 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 the product, call 1-800-326-0471.

**FORMUALBLE - Keep away from hair, sparks, open flames or other sources of ignition.**

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

**SAFETY:**

Revolution has been tested only in 100 different pure and mixed breeds of healthy dogs and over 15 different pure and mixed breeds of healthy cats. Although the birds were not exposed to live heartworms, they were observed for 12 months. In addition, the number of circulating microfilariae may decrease following treatment. Revolution is not effective against microfilariae in vitro. Hypersensitivity reactions have not been observed in dogs with patent heartworm infections administered doses 5-10 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 dogs treated. Other signs observed in 1.5% of treated dogs included alopecia, dermatitis, pruritus, 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, anaphylaxis, hyperventilation, vomiting, anorexia, ataxia, tremors, salivation, seizures, and muscle tremors.

**WARNINGS:**

Assess the risk to benefit ratio prior to treatment of animals with the following pre-existing conditions or concurrent use of other drugs:

- Cats: Revolution is not recommended for use in cats (1) with a history of cardiovascular disease (eg, hypertrophic cardiomyopathy), (2) with chronic or recurrent lameness, (3) with a history of asthma or anaphylaxis, (4) during the management of shock, anaphylaxis, or acute cardiomyopathy, (5) with a urinary tract infection, (6) with chronic kidney disease, or (7) with a history of reactions to other oral anthelmintics.

- Dogs: Revolution is not recommended for use in dogs with a history of chronic cardiac, renal, or hepatic disease, or with a known sensitivity to selamectin.

- Cats and Dogs: Revolution is not recommended for use in cats or dogs with a history of a seizure, a history of encephalitis, or a history of a severe allergic reaction to any of the ingredients of this product.

- Cats and Dogs: Revolution is not recommended for use in cats or dogs with a history of immune-mediated disease, including but not limited to myasthenia gravis, polymyositis, autoimmune disease, dermatomyositis, and rheumatoid arthritis.

- Cats and Dogs: Revolution is not recommended for use in cats or dogs with a history of a previous reaction to Revolution, or in cats or dogs with a history of a previous reaction to selamectin.

- Cats and Dogs: Revolution is not recommended for use in cats or dogs with a history of a congenital or hereditary disease, including but not limited to heart block, conduction defects, and congenital heart defects.

- Cats: Revolution is not recommended for use in cats with a history of epilepsy or a history of a previous reaction to Revolution.

- Dogs: Revolution is not recommended for use in dogs with a history of immune-mediated disease, including but not limited to myasthenia gravis, polymyositis, autoimmune disease, dermatomyositis, and rheumatoid arthritis.

- Dogs: Revolution is not recommended for use in dogs with a history of a previous reaction to Revolution, or in dogs with a history of a previous reaction to selamectin.

- Dogs: Revolution is not recommended for use in dogs with a history of a congenital or hereditary disease, including but not limited to heart block, conduction defects, and congenital heart defects.

- Dogs: Revolution is not recommended for use in dogs with a history of epilepsy or a history of a previous reaction to Revolution.

**SAFETY:**

- Cats: Revolution was applied at 1, 2, 5, and 10 times the recommended dose to six-week-old kittens. No adverse reactions were observed.

- Cats: Revolution was applied at 1, 2, 5, and 10 times the recommended dose to heartworm infected dogs. No adverse reactions were observed.

- Cats: Revolution was applied at 3 times the recommended dose to heartworm infected dogs. No adverse reactions were observed.

- Cats: Revolution was applied at 2, 5, and 10 times the recommended dose to cats infected with cyrtosporidium. No adverse reactions were observed.

- Cats: Revolution was applied at 1, 2, 5, and 10 times the recommended dose to cats infected with Toxoplasma gondii. No adverse reactions were observed.

- Dogs: Revolution was applied at 1, 2, 5, and 10 times the recommended dose to dogs infected with Dirofilaria immitis. No adverse reactions were observed.

- Dogs: Revolution was applied at 1, 2, 5, and 10 times the recommended dose to dogs infected with Ticks (Rhipicephalus sanguineus). No adverse reactions were observed.

**STORAGE CONDITIONS:**

Distributed by:

Zoetis Inc.

250 Valley Road, Parsippany, NJ 07054

Call 1-888-963-8471.

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For a copy of the MSDS or more detailed occupational safety information. For a copy of the MSDS or to report adverse reactions attributable to the product, call 1-800-326-0471.

**DISCLAIMER:**

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**This product contains selamectin, the active ingredient in Revolution.**

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