Hookworms are among the most commonly encountered parasites in routine veterinary practice.

In the United States, the prevalence of hookworm (Ancylostoma caninum) infection in dogs has been reported as ranging from 2.5% to 10%, depending on study, region, and whether dogs are well cared for (i.e., owned pet).1-5 One U.S. study has reported an increase in hookworm prevalence,3 and this development has been speculated for Canada as well.6-8 While clinical signs of hookworm infection in adult dogs and cats are typically mild or subclinical, there can be severe outcomes for infected puppies and kittens. Disease (and degree of clinical signs) is related to hookworm numbers and feeding appetites, which can cause fatal anemia in animals with heavy parasite burdens.

Hookworms also pose a zoonotic risk. As such, while the emergence of resistance to anthelmintics presents a new veterinary management challenge, this development has implications for public/human health, where some of the same medications are used for hookworm treatment.

**CHALLENGES IN PREVENTING HOOKWORM INFECTION**

Historically, veterinary management of hookworm infection has been challenging for 3 key reasons. The first is that infective hookworm larvae (L3) are often present and can be plentiful in the environment.9 As a result, dogs can be readily infected (or reinfected) by L3 larvae through multiple routes, including skin penetration and ingestion of infected prey (FIGURE 1).

Abstract

Drug-resistant hookworms (Ancylostoma caninum) are increasingly common in North America. Originally confined to greyhounds in Florida, they are now widespread in dogs across the United States and have been described in Canada. Veterinary attention to antimicrobial (anthelmintic) use and stewardship is needed to prevent further development of resistance to remaining drugs and potentially in other parasites. Drug-resistant hookworms are a One Health concern that necessitate stringent communication on prevention and fecal clean-up to pet owners.
Second, puppies can be infected while nursing through transmammary larval transmission. The third challenge is “larval leak,” a term that has been used to describe the ability of hookworm larvae to exist in an arrested stage within a canine host (usually within the muscle tissues). These arrested-state larvae can become reactivated after anthelmintic treatment has ceased and during pregnancy.

EMERGENCE OF DRUG RESISTANCE
Unfortunately, a fourth hookworm management challenge now exists: emerging (and rapidly evolving) hookworm drug resistance. This relatively novel type of antimicrobial resistance is believed to have originated in Florida racing greyhound kennels under typical conditions leading to antimicrobial resistance: that is, widespread drug use and selection pressure. Regrettably, hookworm anthelmintic resistance is no longer limited to a single antimicrobial. It has been documented for several common deworming drugs, including fenbendazole and febantel (benzimidazoles), macrocyclic lactones, avermectin/milbemycin, and pyrantel (tetrahydropyrimidines). Similarly, greyhounds are no longer the only breed reported, with studies finding treatment-resistant hookworms in other breeds, and a recent study describing detection in more than 70 different breeds.

Further, in the spring of 2023, a case series of dogs with hookworms resistant to benzimidazoles was reported in Canada. The appearance of drug-resistant hookworms in Canada is believed to have occurred initially through canine importation (i.e., movement of infected dogs from the United States to Canada); however, resistance is now endemic within the country and may be a concern outside North America as well (e.g., in Brazil).

DIAGNOSIS OF HOOKWORM INFECTION
North American endoparasite guidelines, such as those from the Companion Animal Parasite Council (CAPC) and Canadian Parasitology Expert Panel (CPEP), advise routine fecal testing and deworming in dogs and puppies. These preventive care practices assist with the detection of hookworms and other gastrointestinal (GI) parasites and subsequent veterinary management of infection.

Hookworm infection is diagnosed through either routine veterinary fecal screening of well (subclinical) pets or testing of dogs with GI signs (e.g., diarrhea) as part of an infectious disease assessment. The currently available fecal test methods for detection are fecal centrifugal flotation (ova and parasite [O&P]), coproantigen testing in combination with O&P testing, and quantitative polymerase chain reaction (qPCR) testing. One recent publication compared a commercially available fecal qPCR test to traditional O&P test using zinc sulfate and described an overall (and statistically significant) detection superiority of qPCR. This same study observed a 1.4 times greater detection rate for *A caninum* with qPCR compared to O&P, and the qPCR parasite panel provided concurrent detection of the hookworm benzimidazole treatment marker.
In dogs with *A caninum*, if infection persists despite appropriate therapy (and larval leak and environmental infection are unlikely), presence of drug resistance should be considered. If resistance is suspected, additional fecal testing is now indicated with 1 of the following tests: a pre- and post-treatment fecal egg count reduction test (FECRT), molecular marker testing for resistance (fecal qPCR), or in vitro drug bioassays.11,12

**HOOKWORM RESISTANCE PREVALENCE**

Testing (fecal surveillance) can inform prevalence data. Based on recent research involving large sample sets in the United States and Canada, the prevalence of the hookworm benzimidazole treatment resistance marker (F167Y) has been reported as 11.2% in the United States and between 4% to 5.9% in Canada.4,5,8 In the United States, the benzimidazole treatment resistance marker F167Y is widely distributed and has been described with the highest frequency in the West (>13%), with several focal clusters (“hot spots”) observed.4,5 The detection rate was highest in nongreyhound dogs, peaked in June (but was reported in all 10 study months), and did not appear to be influenced by season, as for *A caninum*. The same study reported a higher frequency of hookworm infections (and the occurrence of the resistant marker) in young dogs and puppies compared with adult dogs.4,5

**FIGURE 1.** Sources of hookworm infection in dogs and the potential for zoonotic infection.
In addition to the F167Y genetic marker, a second genetic marker, Q134H, has been recently described to confer benzimidazole resistance in *A caninum*.\(^1\)\(^2\)

**Treatment of Drug-Resistant Infections**

Triple-drug combination treatment has been recommended for dogs with hookworm infections resistant to treatment and, together with environmental hygiene (i.e., telling owners to *pick up that poop please!* to avoid reinfection, is still considered appropriate for many dogs.\(^1\)\(^2\) However, due to evolving drug resistance and failure of these protocols in some dogs, the drug emodepside is now being used in certain U.S. cases for its potential efficacy against multianthelmintic resistance (MADR) cases.\(^1\)\(^2\) This drug should only be used after consideration of individual patient (and owner) factors and available algorithms for decision-making\(^1\)\(^2\) and in consultation with an infectious disease specialist or parasitologist.\(^1\)\(^2\) Emodepside is not currently labeled for use in dogs in North America, may pose a risk of adverse effects, and should not be used in heartworm-positive dogs, with the recommendation that dogs are tested (heartworm antigen and Knott’s) prior to emodepside administration.\(^1\)\(^2\) Additionally, there are anecdotal concerns regarding emodepside resistance in some hookworm-infected dogs, which will likely further decrease available treatment strategies for these pets.

**ONE HEALTH AND ANTIMICROBIAL STEWARDSHIP**

Hookworms are zoonotic, and as many of the same drugs (e.g., benzimidazoles) are used to treat human infections, rising *A caninum* resistance has implications for people as well. Diagnostic and antimicrobial stewardship, as well as rapid veterinary detection of resistance through routine fecal screening, will be critical for One Health, surveillance, and raising awareness with the hope of slowing this rapidly evolving drug resistance concern.

**SUMMARY**

While hookworm MADR may currently be the “poster child” for parasite drug resistance, anecdotal reports indicate that parasite anthelmintic drug resistance may encompass more than hookworms. Further research and veterinary fecal surveillance efforts are indicated to provide information that assists veterinary teams in their day-to-day practice, in improving pet health, and in counseling clients. **TVP**

**References**

**VETORYL® CAPSULES**
(Trilostane)

5 mg, 10 mg, 30 mg, 60 mg and 120 mg strengths
Adrenocortical suppressant for oral use in dogs only.

**BRIEF SUMMARY** (For Full Prescribing Information, see package insert.)

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

**DESCRIPTION:** VETORYL Capsules are an orally active synthetic steroid analogue that blocks production of hormones produced in the adrenal cortex of dogs.

**INDICATION:** VETORYL Capsules are indicated for the treatment of pituitary and adrenal-dependent hyperadrenocorticism in dogs.

**CONTRAINDICATIONS:** The use of VETORYL Capsules is contraindicated in dogs that have demonstrated hypersensitivity to trilostane. Do not use VETORYL Capsules in animals with primary hepatic disease or renal insufficiency. Do not use in pregnant dogs. Studies conducted with trilostane in laboratory animals have shown teratogenic effects and early pregnancy loss.

**WARNINGS:** In case of overdose, symptomatic treatment of hypoadrenocorticism with corticosteroids, mineralocorticoids and intravenous fluids may be required. Angiotensin converting enzyme (ACE) inhibitors should be used with caution with VETORYL Capsules, as both drugs have the potential to inhibit aldosterone, impairing the patient’s ability to maintain normal electrolytes, blood volume and renal perfusion. Potassium sparing diuretics (e.g. spironolactone) should not be used with VETORYL Capsules as both drugs have the potential to inhibit aldosterone, increasing the likelihood of hyperkalemia.

**HUMAN WARNINGS:** Keep out of reach of children. Not for human use. Wash hands after use. Do not empty capsule contents and do not attempt to divide the capsules. Do not handle the capsules if pregnant or if trying to conceive. Trilostane is associated with teratogenic effects and early pregnancy loss in laboratory animals. In the event of accidental ingestion/overdose, seek medical advice immediately and take the labeled container with you.

**PRECAUTIONS:** Hypoadrenocorticism can develop at any dose of VETORYL Capsules. A small percentage of dogs may develop corticosteroid withdrawal syndrome within 10 days of starting treatment. Mitotane (o,p’-DDD) treatment will reduce adrenal function. Experience in foreign markets suggests that when mitotane therapy is stopped, an interval of at least one month should elapse before the introduction of VETORYL Capsules. It is important to wait for both the recurrence of clinical signs consistent with hyperadrenocorticism, and a post-ACTH cortisol level of < 9.1 µg/dL (< 250 nmol/L) before treatment with VETORYL Capsules is initiated. Close monitoring of adrenal function is advised, as dogs previously treated with mitotane may be more responsive to the effects of VETORYL Capsules.

The use of VETORYL Capsules will not affect the adrenal tumor itself. The safe use of this drug has not been evaluated in lactating dogs and males intended for breeding.

**ADVERSE REACTIONS:** The most common adverse reactions reported are poor/reduced appetite, vomiting, lethargy/dullness, diarrhea, elevated liver enzymes, elevated potassium with or without decreased sodium, elevated BUN, decreased Na/K ratio, weakness, elevated creatinine, shaking and renal insufficiency. Occasionally, more serious reactions, including severe depression, hemorrhagic diarrhea, collapse, hypoadrenocortical crisis or adrenal necrosis/rupture may occur, and may result in death. Owners should be advised to discontinue VETORYL Capsules and contact their veterinarian immediately in the event potential drug intolerance is observed.

Approved by FDA under NADA # 141-291

Manufactured for:
Dechra Veterinary Products
7015 College Boulevard, Suite 525
Overland Park, KS 66211 USA

Method of use covered by US patent No. 9,263,235.

VETORYL is a trademark of Dechra Ltd.
© 2019, Dechra Ltd
F1612 Rev. January 2019

VETORYL Capsules are an orally active synthetic steroid analogue that blocks production of hormones produced in the adrenal cortex of dogs. Studies conducted with trilostane in laboratory animals have shown teratogenic effects and early pregnancy loss.

**Christian M. Leutenegger**
Dr. Leutenegger graduated from the University of Zurich School of Veterinary Medicine, Switzerland, in 1992. He completed a doctoral thesis on the development of recombinant vaccines for feline immunodeficiency virus. After a postdoctoral course in medical science, he completed a PhD degree testing the first DNA vaccines in veterinary medicine. He developed a strong interest in molecular immunology and virology and founded the Real-time PCR Research and Diagnostics Core Facility at the UC Davis School of Veterinary Medicine in 1999. After 13 years at IDEXX Laboratories introducing standardized molecular diagnostics in the veterinary industry, he joined Antech Diagnostics to expand the molecular testing portfolio. He has an extensive network of collaborators and has published over 200 peer-reviewed papers and book chapters.

**Michelle Evason**
Dr. Evason serves as global director of veterinary clinical education for Antech. She has worked in veterinary general practice, academia, specialty clinical practice, and the animal health industry. Dr. Evason has published on numerous infectious diseases, antimicrobial stewardship, nutrition, spectrum of care, and veterinary and pet owner education-related topics. She enjoys ferrying her 2- and 4-legged children to various activities and fulfilling most “Canuck” stereotypes.