DEALING WITH THE INVISIBLE THREAT

AN INTERNAL PARASITE PREVALENCE REPORT

Boehringer Ingelheim

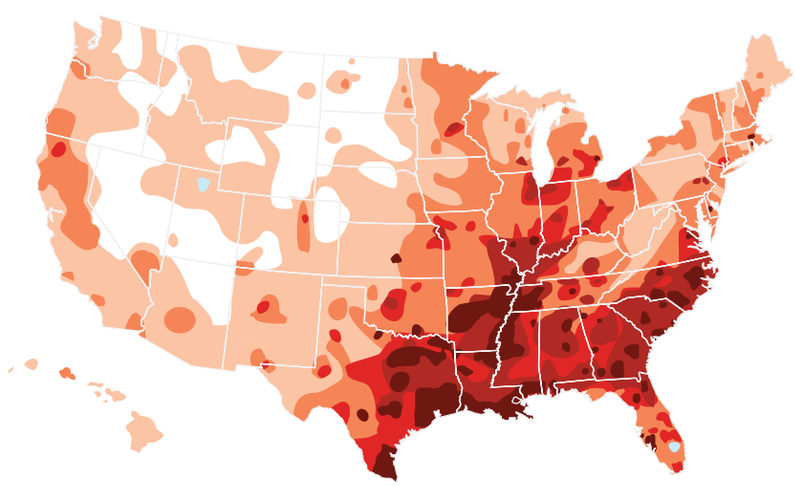
U.S.A. 2021

Heartgard® Plus (ivermectin/pyrantel)

HEARTWORM DISEASE IS A YEAR-ROUND RISK. EXPERTS AGREE ON THE NEED FOR YEAR-ROUND PROTECTION.

The American Heartworm Society (AHS), American Animal Hospital Association (AAHA), American Veterinary Medical Association (AVMA), and Companion Animal Parasite Council (CAPC) all recommend year-round heartworm disease prevention.[1,2,3]

U.S. HEARTWORM PREVALENCE MAP[4]



Average number of cases per reporting clinic

- < 1 case/clinic
- 1-5 cases/clinic
- 6-25 cases/clinic
- 26-50 cases/clinic
- 51-99 cases/clinic
- 100+ cases/clinic

HEARTWORM INCIDENCE

The severity of heartworm incidence as shown in this map is based on the average number of cases per reporting clinic. Some remote regions of the United States lack veterinary clinics, therefore we have no reported cases from these areas.

2019 Heartworm Incidence Survey
© American Heartworm Society

AMERICAN HEARTWORM SOCIETY
EST. 1974

EVEN DURING WINTER MONTHS, THE RISK OF HEARTWORM TRANSMISSION NEVER REACHES ZERO.[4]

Urban "heat islands," i.e., the masses of buildings and parking lots that retain heat during the day and radiate it at night, can protect mosquitoes and extend heartworm transmission season.[2]

1,000,000

Dogs are estimated to be heartworm positive in the United States each year.[4]

THE MOST COMMON DOG OWNER MISPERCEPTIONS ABOUT HEARTWORM DISEASE:

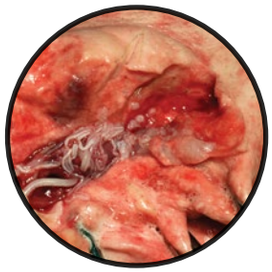
1. **MYTH:** Heartworm disease is easy to treat.
   TRUTH: Treatment is expensive and can be painful for the dog.

2. **MYTH:** My dog is not at risk.
   TRUTH: All dogs are at risk.

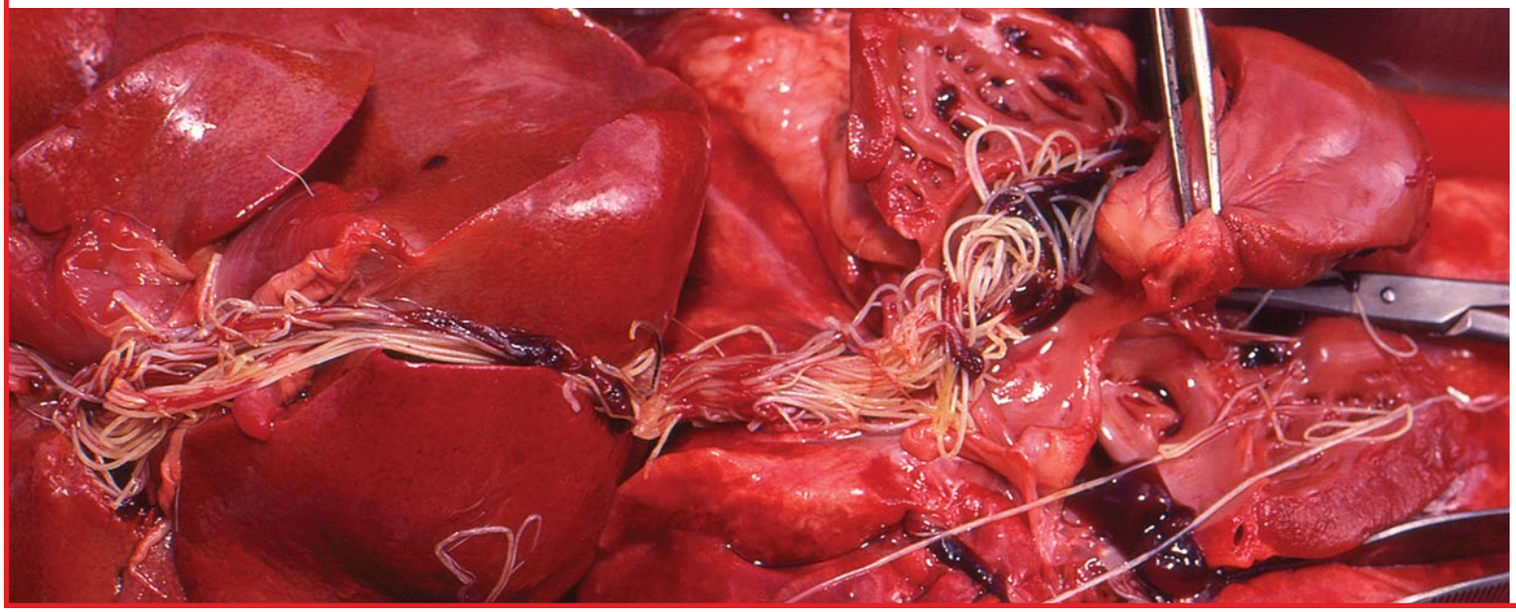
3. **MYTH:** I would notice if my dog had it.
   TRUTH: Clinical signs can develop so slowly that infection can go undetected, or occur so suddenly that emergency treatment is necessary to save the dog's life.

4. **MYTH:** Dogs fully recover after heartworm disease treatment.
   TRUTH: Once a dog has heartworm disease that requires treatment, the damage to the lungs and pulmonary arteries remains for the rest of its life.

HEALTHY ARTERY

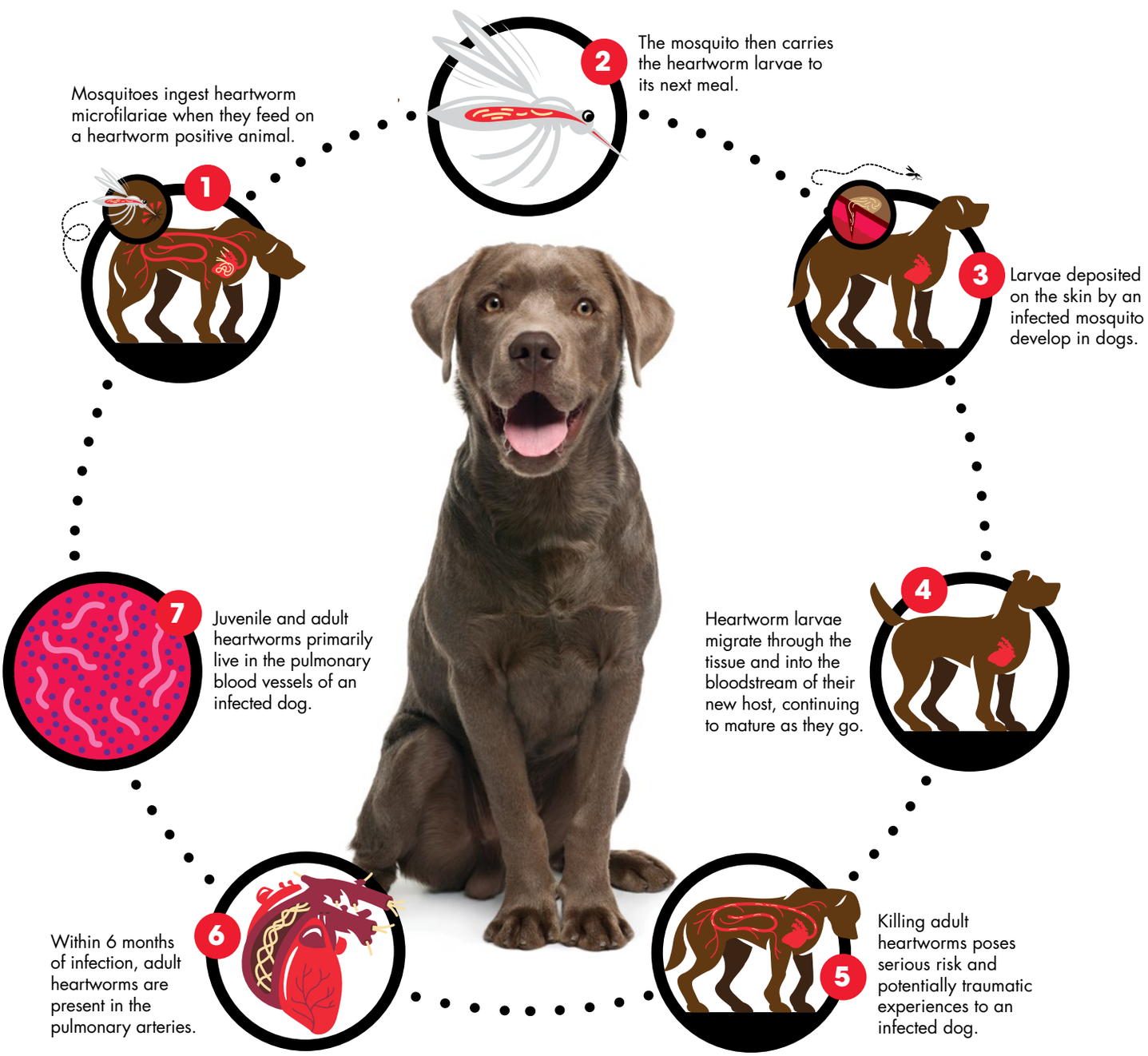


DAMAGE CAUSED BY ADVANCED HEARTWORM DISEASE



THE HEARTWORM LIFE CYCLE IN DOGS: ONE MOSQUITO BITE CAN CAUSE LIFE-LONG DAMAGE.

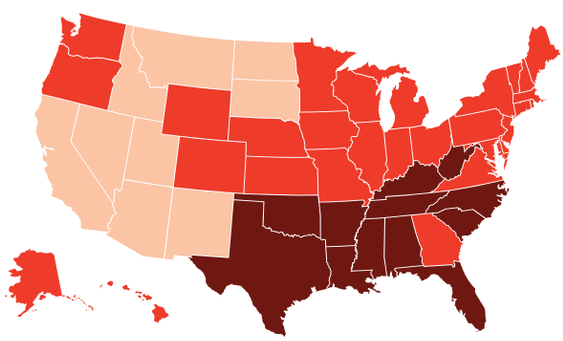
The Heartworm Life Cycle in Dogs



THE MOST PREVALENT INTESTINAL PARASITES* OF DOGS IN THE UNITED STATES ARE HOOKWORMS AND ROUNDWORMS.[5]

2020 INTESTINAL PARASITES PREVALENCE MAPS[6]

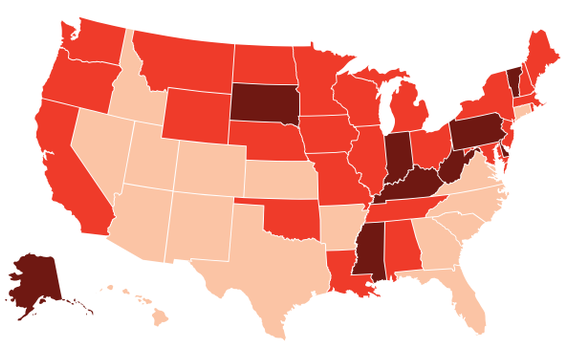
In addition to infecting dogs, hookworms and roundworms are zoonotic.



HOOKWORMS

Tested Positive: 3.08%

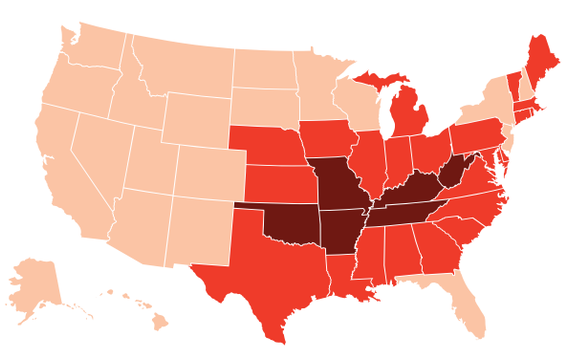
Tested Positive: 282,077



ROUNDWORMS

Tested Positive: 1.94%

Positive Cases: 177,365



WHIPWORMS

Tested Positive: 0.55%

Positive Cases: 50,445

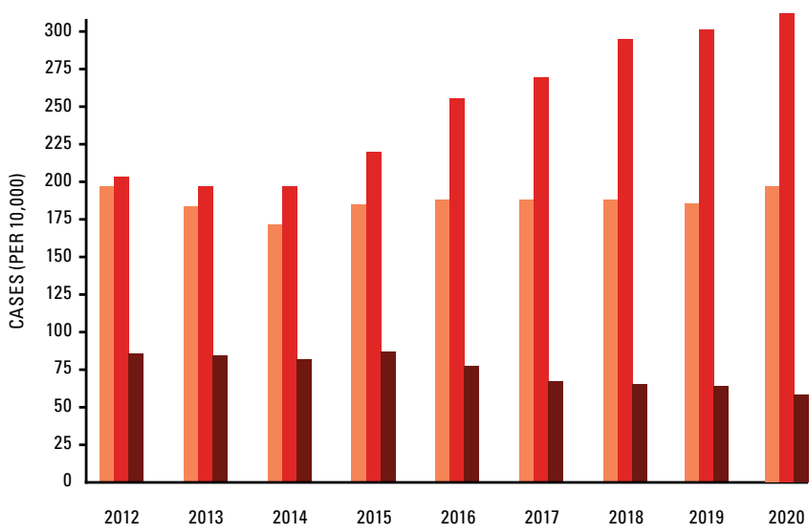
Infection Risk

Low Risk — High Risk

* GI nematodes only.

YEAR-AFTER-YEAR, INTESTINAL PARASITES CONTINUE TO BE A THREAT FOR DOGS THROUGHOUT THE COUNTRY.

Intestinal Parasites | Dog | Annual Totals[6]
Number of Cases per 10,000 Dogs



KEY TAKEAWAYS:

1. Hookworms and roundworms are more prevalent compared to whipworms.
2. Hookworm cases are on the rise, year over year.

Roundworms | Hookworms | Whipworms

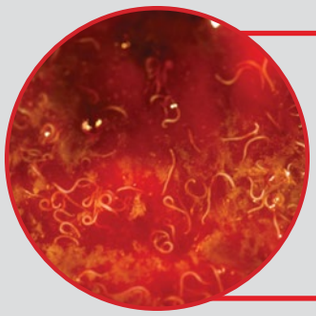
IT IS IMPORTANT TO REMIND PET OWNERS THAT ROUNDWORM EGGS CAN SURVIVE IN THE ENVIRONMENT FOR YEARS,[7] WHICH RAISES THE RISK OF REINFECTION.

Be sure your clients know that hookworm larvae and roundworm eggs can often be found in fecal matter and contaminated:

- Blades of grass
- Dirt and soil
- Dog and children's toys/balls left outside

YOUR CLIENTS MAY NOT REALIZE THAT HOOKWORMS AND ROUNDWORMS CAN CAUSE SERIOUS HEALTH PROBLEMS IN DOGS.

Treating severe infections is more expensive than using a monthly heartworm preventive to treat and control them.[8]



HOOKWORMS

RECOMMEND A PRODUCT THAT PREVENTS HEARTWORM DISEASE AND TREATS AND CONTROLS HOOKWORMS AND ROUNDWORMS.

WHAT CLIENTS NEED TO KNOW ABOUT HOOKWORMS AND ROUNDWORMS

1. Year-round, monthly parasite control that targets hookworms and roundworms means less fecal testing – as little as once a year, versus four times a year or more for dogs that don't receive year-round protection[9,10]
2. Monthly treatment and control helps reduce environmental contamination
3. All species of hookworms and roundworms can cause serious health problems and lasting damage in dogs
4. Hookworms and roundworms are zoonotic threats that can infect people, too
5. By the time a hookworm or roundworm infection can be diagnosed, parasite eggs and larvae have already been spread into the pet's surrounding environment where they can infect other pets and people in the home

Roundworm belly in a puppy

Roundworm obstruction on necropsy

OVER 90% OF PUPPIES UNDER 3 MONTHS OLD ARE INFECTED WITH ROUNDWORMS.[11]

HOOKWORMS

Transmission to Dogs

Hookworm larvae can be transmitted through:

- Ingestion of contaminated soil or grass
- Larvae on soil and grass that penetrate the skin
- The milk of infected mothers nursing their pups

Signs of Infection

- Weakness
- Diarrhea
- Pale gums
- Weight loss

ROUNDWORMS:

Transmission to Dogs

Roundworms can be transmitted through:

- Ingestion of infective ova from soil or hair coat
- Transplacentally
- Rarely, via the milk of newly infected mothers nursing their pups

Signs of Infection

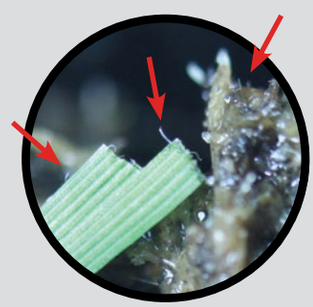
- Diarrhea
- Weight loss
- Worms in feces
- Swollen abdomen
- Vomiting
- Malnutrition
- Weakness
- Lack of appetite

ALMOST 73% OF U.S. PEDIATRICIANS REPORTED A CASE OF PARASITIC INFECTION IN CHILDREN.[12]

Control of hookworms and roundworms is essential because of their zoonotic potential. Parasite eggs and larvae exist in contaminated yards. In fact, hookworm larvae can actually climb up blades of grass with the morning dew, to be more available to infect passersby.

HOOKWORMS

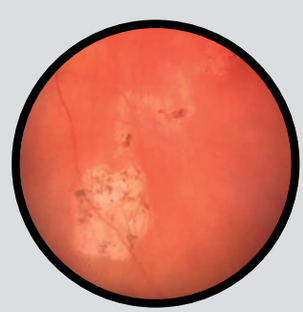
Infective hookworm larvae can pass through a person's skin after contact with contaminated grass, soil or sand. Hookworm larvae migrate under the skin causing extreme irritation and itching.



Three species of hookworms that commonly parasitize dogs are ***Ancylostoma caninum***, ***Ancylostoma braziliense***, and ***Uncinaria stenocephala***. Their habitats are so diverse that dogs anywhere in the United States are at risk.

ROUNDWORMS

It is easy for roundworm eggs to be accidentally ingested by touching dirty hands to the mouth. Roundworm larvae hatch out in the stomach, and can migrate throughout the body. Larval infections of the retina (right) cause damage in humans and affect vision, potentially causing blindness.



Regardless of where you practice, hookworms and roundworms can be a threat, and dogs deserve reliable, year-round protection.

TO HELP PREVENT HUMAN CASES, OWNERS SHOULD[13]:

For information about safe and healthy pet ownership, visit the Centers for Disease Control and Prevention (CDC) website at www.cdc.gov/healthypets

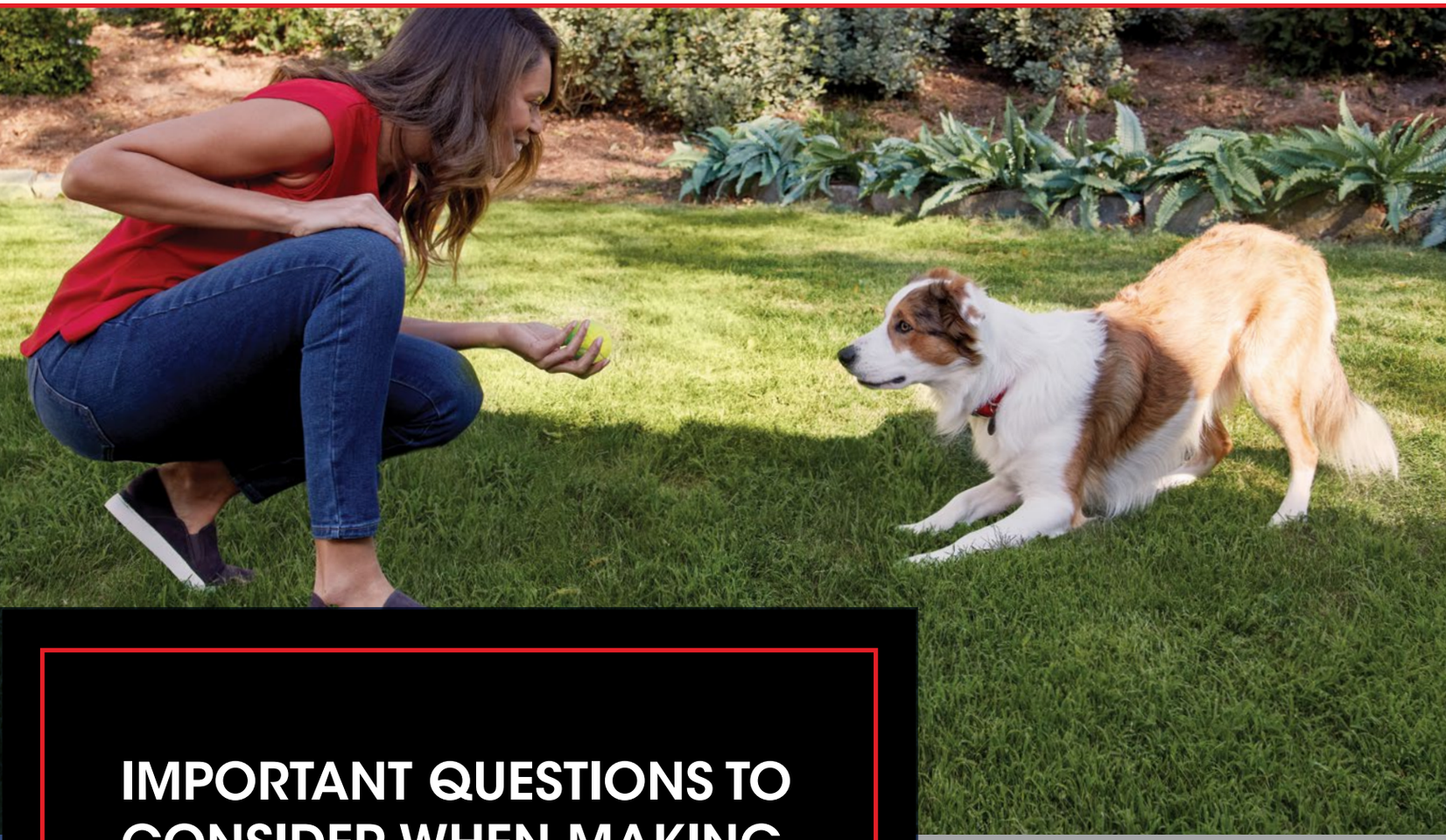
1. **WASH HANDS FREQUENTLY**
2. **KEEP YARDS FREE OF FECES**
3. **PREVENT CHILDREN FROM PLAYING IN UNCOVERED SAND BOXES**

HOOKWORMS IN HUMANS:

- Hookworm larvae migrate under the skin, causing severe itching and irritation.
- Hookworm infections can actually migrate to the lungs of humans, causing pneumonia.
- Pruritis associated with cutaneous migration can persist for years.

ROUNDWORMS IN HUMANS:

- Approximately 5% of the U.S. population has antibodies to ***Toxocara***, suggesting tens of millions of Americans may have been exposed to the ***Toxocara*** parasite.[13]
- Roundworm infections can cause permanent visual impairment or loss of vision.[13]
- Can enter the body via accidental ingestion.



IMPORTANT QUESTIONS TO CONSIDER WHEN MAKING YOUR RECOMMENDATION

- ✔ Do your clients understand the cost difference between treatment and prevention of heartworm disease?
- ✔ Do your clients understand the threat of zoonotic parasites?
- ✔ Does the product you're recommending regularly treat and control roundworms and the 3 most prevalent species of hookworms?
- ✔ Is the product you're recommending safe to give a puppy during their first visit?

Heartgard® Plus
(ivermectin/pyrantel)

PREVENTS HEARTWORM DISEASE, PLUS TREATS AND CONTROLS

3 SPECIES OF HOOKWORMS* AND 2 SPECIES OF ROUNDWORMS.†

THE BRAND THAT PET OWNERS KNOW, LOVE AND ASK FOR

HEARTGARD® Plus (ivermectin/pyrantel) is the heartworm prevention product that pet owners trust. Pet owners ask for HEARTGARD by name more than any other brand.[14]

FOR EFFECTIVE PREVENTION, FORM MATTERS

HEARTGARD Plus is the #1 dog-preferred, real-beef chew that makes compliance enjoyable for pets and pet owners.[15]

PROVEN EFFICACY AGAINST HEARTWORMS FOR OVER 34 YEARS

In three decades, more than 2 billion doses of HEARTGARD® have been dispensed, preventing heartworm disease in millions of dogs.[16]

PROTECTION STARTS IN PUPPYHOOD

HEARTGARD Plus is the only heartworm disease preventive that comes in a Real-Beef Chewable safe to give to puppies as young as 6 weeks!

HEARTGARD Plus has tools available to help you educate your clients.

Heartgard® Clinic.com

Important Safety Information: HEARTGARD® Plus (ivermectin/pyrantel) is well tolerated. All dogs should be tested for heartworm infection before starting a preventive program. Following the use of HEARTGARD Plus, digestive and neurological side effects have rarely been reported. For more information, please see full prescribing information or visit **www.HeartgardClinic.com**.

* HEARTGARD Plus is indicated for the treatment and control of *Ancylostoma caninum*, *Uncinaria stenocephala*, and *Ancylostoma braziliense*
† HEARTGARD Plus is indicated for the treatment and control of *Toxocara canis* and *Toxascaris leonina*

Heartgard® Plus
(ivermectin/pyrantel)

CHEWABLES

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

INDICATIONS: For use in dogs to prevent canine heartworm disease by eliminating the tissue stage of heartworm larvae (*Dirofilaria immitis*) for a month (30 days) after infection and for the treatment and control of ascarids (*Toxocara canis, Toxascaris leonina*) and hookworms (*Ancylostoma caninum, Uncinaria stenocephala, Ancylostoma braziliense*).

DOSAGE: HEARTGARD® Plus (ivermectin/pyrantel) should be administered orally at monthly intervals at the recommended minimum dose level of 6 mcg of ivermectin per kilogram (2.72 mcg/lb) and 5 mg of pyrantel (as pamoate salt) per kg (2.27 mg/lb) of body weight. The recommended dosing schedule for prevention of canine heartworm disease and for the treatment and control of ascarids and hookworms is as follows:

Dog Weight	Chewables Per Month	Ivermectin Content	Pyrantel Content	Color Coding On Foil Backing and Carton
Up to 25 lb	1	68 mcg	57 mg	Blue
26 to 50 lb	1	136 mcg	114 mg	Green
51 to 100 lb	1	272 mcg	227 mg	Brown

HEARTGARD Plus is recommended for dogs 6 weeks of age and older.
For dogs over 100 lb use the appropriate combination of these chewables.

ADMINISTRATION: Remove only one chewable at a time from the foil-backed blister card. Return the card with the remaining chewables to its box to protect the product from light. Because most dogs find HEARTGARD Plus palatable, the product can be offered to the dog by hand. Alternatively, it may be added intact to a small amount of dog food.The chewable should be administered in a manner that encourages the dog to chew, rather than to swallow without chewing. Chewables may be broken into pieces and fed to dogs that normally swallow treats whole.

Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes after administration to ensure that part of the dose is not lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

HEARTGARD Plus should be given at monthly intervals during the period of the year when mosquitoes (vectors), potentially carrying infective heartworm larvae, are active. The initial dose must be given within a month (30 days) after the dog's first exposure to mosquitoes. The final dose must be given within a month (30 days) after the dog's last exposure to mosquitoes.

When replacing another heartworm preventive product in a heartworm disease preventive program, the first dose of HEARTGARD Plus must be given within a month (30 days) of the last dose of the former medication.

If the interval between doses exceeds a month (30 days), the efficacy of ivermectin can be reduced. Therefore, for optimal performance, the chewable must be given once a month on or about the same day of the month. If treatment is delayed, whether by a few days or many, immediate treatment with HEARTGARD Plus and resumption of the recommended dosing regimen will minimize the opportunity for the development of adult heartworms.

Monthly treatment with HEARTGARD Plus also provides effective treatment and control of ascarids (*T. canis, T. leonina*) and hookworms (*A. caninum, U. stenocephala, A. braziliense*). Clients should be advised of measures to be taken to prevent reinfection with intestinal parasites.

EFFICACY: HEARTGARD Plus Chewables, given orally using the recommended dose and regimen, are effective against the tissue larval stage of *D.immitis* for a month (30 days) after infection and, as a result, prevent the development of the adult stage. HEARTGARD Plus Chewables are also effective against canine ascarids (*T. canis, T. leonina*) and hookworms (*A. caninum, U. stenocephala, A. braziliense*).

ACCEPTABILITY: In acceptability and field trials, HEARTGARD Plus was shown to be an acceptable oral dosage form that was consumed at first offering by the majority of dogs.

PRECAUTIONS: All dogs should be tested for existing heartworm infection before starting treatment with HEARTGARD Plus which is not effective against adult *D. immitis*. Infected dogs must be treated to remove adult heartworms and microfilariae before initiating a program with HEARTGARD Plus.

While some microfilariae may be killed by the ivermectin in HEARTGARD Plus at the recommended dose level, HEARTGARD Plus is not effective for microfilariae clearance. A mild hypersensitivity-type reaction, presumably due to dead or dying microfilariae and particularly involving a transient diarrhea, has been observed in clinical trials with ivermectin alone after treatment of some dogs that have circulating microfilariae.

Keep this and all drugs out of the reach of children.
In case of ingestion by humans, clients should be advised to contact a physician immediately. Physicians may contact a Poiso Control Center for advice concerning cases of ingestion by humans.

Store between 68°F - 77°F (20°C - 25°C). Excursions between 59°F - 86°F (15°C - 30°C) are permitted. Protect product from light.

ADVERSE REACTIONS: In clinical field trials with HEARTGARD Plus, vomiting or diarrhea within 24 hours of dosing was rarely observed (1.1% of administered doses). The following adverse reactions have been reported following the use of HEARTGARD: Depression/lethargy, vomiting, anorexia, diarrhea, mydriasis, ataxia, staggering, convulsions and hypersalivation.

To report suspected adverse drug events, for technical assistance, or to obtain a copy of the Safety Data Sheet (SDS), contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS, or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth.

SAFETY: HEARTGARD Plus has been shown to be bioequivalent to HEARTGARD, with respect to the bioavailability of ivermectin. The dose regimens of HEARTGARD Plus and HEARTGARD are the same with regard to ivermectin (6 mcg/kg). Studies with ivermectin indicate that certain dogs of the Collie breed are more sensitive to the effects of ivermectin administered at elevated dose levels (more than 16 times the target use level) than dogs of other breeds. At elevated doses, sensitive dogs showed adverse reactions which included mydriasis, depression, ataxia, tremors, drooling, paresis, recumbency, excitability, stupor, coma and death. HEARTGARD demonstrated no signs of toxicity at 10 times the recommended dose (60 mcg/kg) in sensitive Collies. Results of these trials and bioequivalency studies, support the safety of HEARTGARD products in dogs, including Collies, when used as recommended.

HEARTGARD Plus has shown a wide margin of safety at the recommended dose level in dogs, including pregnant or breeding bitches, stud dogs and puppies aged 6 or more weeks. In clinical trials, many commonly used flea collars, dips, shampoos, anthelmintics, antibiotics, vaccines and steroid preparations have been administered with HEARTGARD Plus in a heartworm disease prevention program.

In one trial, where some pups had parvovirus, there was a marginal reduction in efficacy against intestinal nematodes, possibly due to a change in intestinal transit time.

HOW SUPPLIED: HEARTGARD Plus is available in three dosage strengths (See DOSAGE section) for dogs of different weights. Each strength comes in convenient cartons of 6 and 12 chewables.

Marketed by
Boehringer Ingelheim Animal Health USA Inc.
Duluth, GA 30096

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Rev. 08-2018

1050-1999-04.

[1] The American Animal Hospital Association-American Veterinary Medical Association Preventive Healthcare Guidelines Task Force. Practice Guidelines: Development of new canine and feline preventive healthcare guidelines designed to improve pet health. *JAVMA*. 2011;239(5):625-629.

[2] Heartworm Guidelines. American Heartworm Society. https://www.heartwormsociety.org/veterinary-resources/american-heartworm-society-guidelines. Accessed February 17, 2021.

[3] Heartworm- Control and Prevention. The Companion Animal Parasite Council. https://capcvet.org/guidelines/heartworm/. Accessed February 17, 2021.

[4] Heartworm Incidence Map 2019. American Heartworm Society. https://www.heartwormsociety.org/veterinary-resources/incidence-maps. Accessed February 17, 2021.

[5] Drake J, Carey T. Seasonality and changing prevalence of common canine gastrointestinal nematodes in the USA. *Parasites Vectors* 12, 430 (2019). https://doi.org/10.1186/s13071-019-3701-7. Accessed February 17, 2021.

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[9] Companion Animal Parasite Council. Parasite Guidelines: Hookworms. https://capcvet.org/guidelines/hookworms. Accessed March 26, 2021.

[10] Companion Animal Parasite Council. Parasite Guidelines: Ascarid. https://capcvet.org/guidelines/ascarid/. Accessed March 26, 2021.

[11] Schantz PM. Zoonotic ascarids and hookworms: the role for veterinarians in preventing human disease. In: *Emerging Vector-Borne and Zoonotic Disease, The Compendium Suppl.* 2002;24(1):47-52.

[12] Thomblison P. Pets, worms and little people. *Contemporary Pediatrics.* September 2003.

[13] Toxocariasis FAQs. Centers for Disease Control and Prevention website. https://www.cdc.gov/parasites/toxocariasis/gen_info/faqs.html. Accessed February 17, 2021.

[14] Data on file at Boehringer Ingelheim.

[15] Data on file at Boehringer Ingelheim.

[16] Data on file at Boehringer Ingelheim.

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