

IMPORTANT NEW UPDATE

**INTERNAL
PARASITE
PREVALENCE
REPORT**

Heartgard[®]
(ivermectin/pyrantel) **Plus**

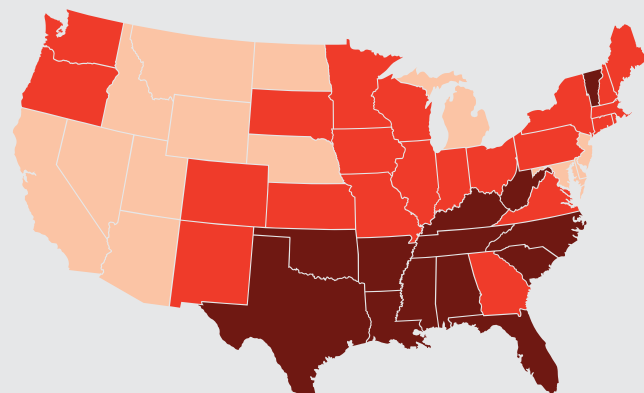


U.S.A. 2019

THE MOST PREVALENT INTESTINAL PARASITES* OF DOGS IN THE UNITED STATES ARE HOOKWORMS AND ROUNDWORMS.¹

2019 INTESTINAL PARASITES PREVALENCE MAPS²

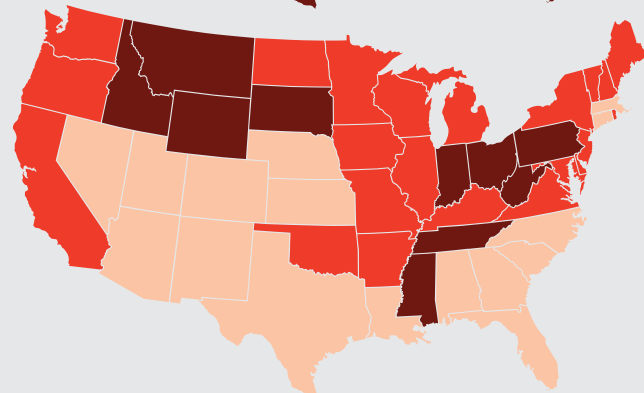
In addition to infecting dogs, hookworms and roundworms are zoonotic.



HOOKWORMS

Tested Positive: 2.91%

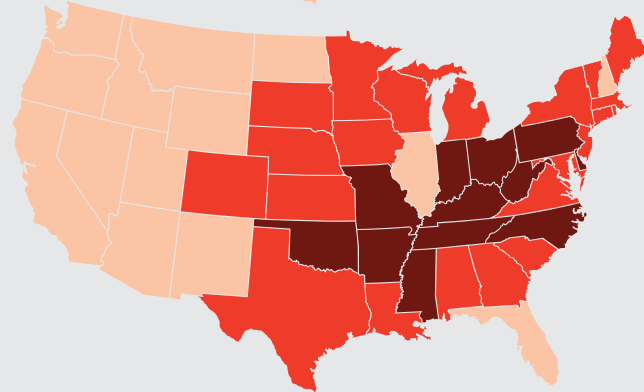
Positive Cases: 75,650



ROUNDWORMS

Tested Positive: 1.91%

Positive Cases: 49,792



WHIPWORMS

Tested Positive: .7%

Positive Cases: 18,116

Infection Risk

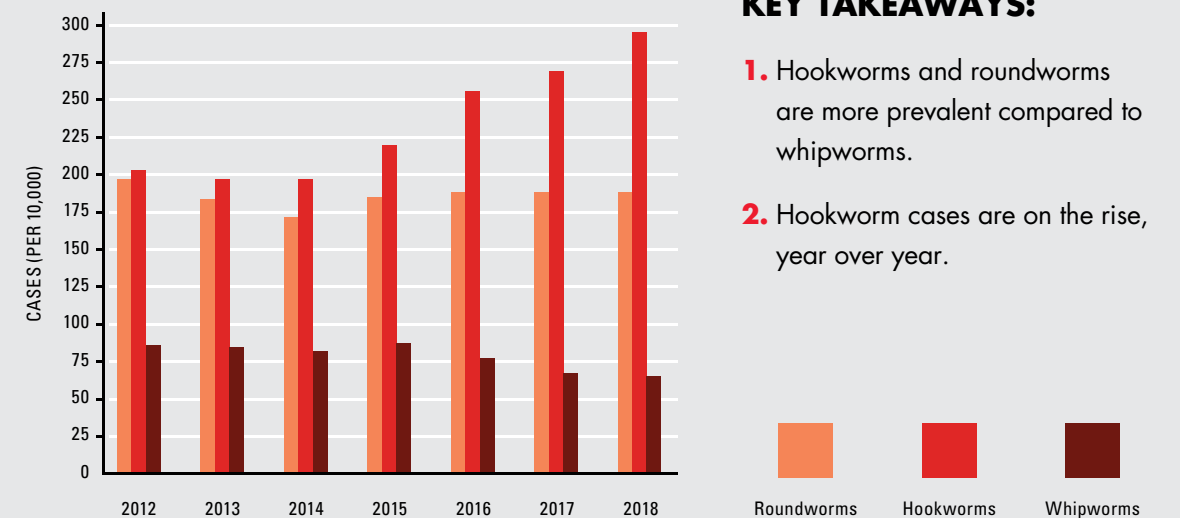
 No date High Risk

* GI nematodes only.



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

Intestinal Parasites | Dog | Annual Totals²
 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.

IT IS IMPORTANT TO REMIND PET OWNERS THAT ROUNDWORM EGGS CAN SURVIVE IN THE ENVIRONMENT FOR YEARS,³ 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 these infections is more expensive than using a monthly heartworm preventive to treat and control them.⁴

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

WHAT CLIENTS NEED TO KNOW ABOUT HOOKWORMS AND ROUNDWORMS

1. Hookworms and roundworms can cause serious health problems and lasting damage in dogs
2. Hookworms and roundworms are zoonotic threats that can infect people, too
3. 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
4. Monthly treatment and control helps reduce environmental contamination



OVER 90% OF PUPPIES UNDER 3 MONTHS OLD ARE INFECTED WITH ROUNDWORMS.⁵



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

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

ALMOST 73% OF U.S. PEDIATRICIANS REPORTED A CASE OF PARASITIC INFECTION IN CHILDREN.⁶



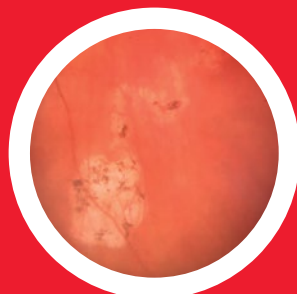
Parasite eggs and larvae exist in contaminated yards. Hookworm larvae actually climb up blades of grass with the morning dew, to be more available to infect passersby.



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.



Roundworm eggs are often accidentally ingested, dirty hands to mouth. Roundworm larvae hatch out in the stomach, and can migrate throughout the body. Larval infections of the retina (right) cause damage and affect vision, potentially blindness.



TO HELP PREVENT HUMAN CASES, OWNERS SHOULD⁷:



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

For information about safe and healthy pet ownership, visit the CDC website www.cdc.gov/healthypets



HOOKWORMS FACTS:

- Hookworm larvae migrate under the skin, causing severe itching and irritation.
- Hookworm infections can actually migrate to the lungs of humans, causing pneumonia.
- A single female hookworm in an infected dog can lay up to 20,000 eggs per day.⁸



ROUNDWORMS FACTS:

- The CDC reports 10,000 people in the US are infected with roundworms each year⁹
- Can cause impaired or loss of vision⁹
- Enter the body via accidental ingestion
- A single female roundworm in an infected dog can lay up to 100,000 eggs per day³

HEARTWORM DISEASE IS A YEAR-ROUND RISK.

Experts Agree on the Need for Year-Round Protection

- The AHS, AAHA, AVMA and CAPC all recommend year-round protection for heartworm prevention.^{10,11,12}

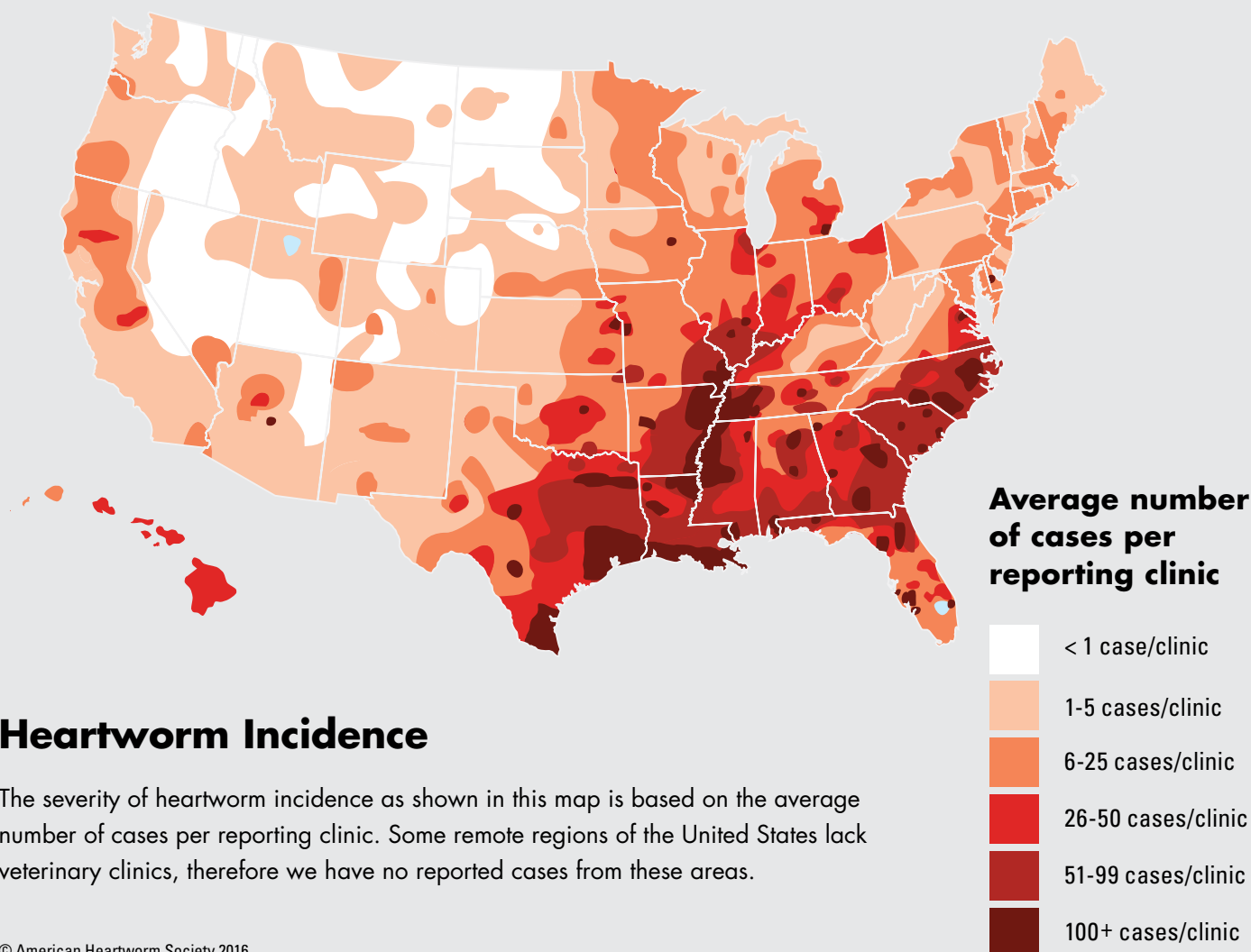


EVEN DURING WINTER MONTHS, THE RISK OF HEARTWORM TRANSMISSION NEVER REACHES ZERO.¹³

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 transmission season.¹³

1,000,000 DOGS ARE ESTIMATED TO BE HEARTWORM POSITIVE IN THE UNITED STATES EACH YEAR.¹³

U.S. HEARTWORM PREVALENCE MAP¹³



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.

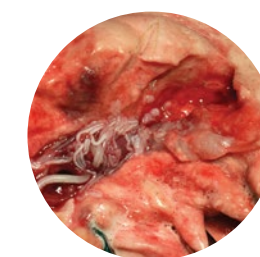


The most common dog owner misperceptions about heartworm disease:

- 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 surgery 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



IMPORTANT QUESTIONS TO CONSIDER WHEN MAKING YOUR RECOMMENDATION

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



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.¹⁵

FOR EFFECTIVE PREVENTION, FORM MATTERS:

HEARTGARD[®] Plus is the dose that gets in the dog and stays in the dog to prevent heartworm disease. Plus, it's the Real-Beef Chewable that dogs prefer.¹⁶

PROVEN EFFICACY AGAINST HEARTWORMS FOR OVER 32 YEARS

In three decades, more than 2 billion doses of HEARTGARD[®] have been dispensed, preventing heartworm disease in millions of dogs.¹⁷



Visit HeartgardClinic.com for staff training and client education resources.



 **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.HEARTGARD.com.

Heartgard® (ivermectin/pyrantel) Plus

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 Poison 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.

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.

For customer service, please contact Merial at 1-888-637-4251.

¹ Little SE, Johnson EM, Lewis D, et al. Prevalence of intestinal parasites in pet dogs in the United States. *Veterinary Parasitology*. 2009;166:144-152.

² Parasite Prevalence Maps. Companion Animal Parasite Council website. <https://capcvet.org/maps/>. Accessed May 06, 2019.

³ Lloyd S. Toxocarosis. In: Palmer SR, Soulsby L, Simpson DIH. *Zoonosis*. New York:Oxford University Press, 1998;842.

⁴ Vital statistics for your veterinary practice. In: Landeck E, ed. *The Veterinary Fee Reference*. 6th ed, Lakewood, CO: AAHA Press, 2009;57, 200, 213, 226, 259, 333.

⁵ 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.

⁶ Thomblison P. Pets, worms and little people. *Contemporary Pediatrics*. September 2003.

⁷ Parasites – Toxocarosis (also known as Roundworm Infection), Prevention & Control. Centers for Disease Control and Prevention website. <http://www.cdc.gov/parasites/toxocarosis/prevent.html>. Accessed January 23, 2012.

⁸ Kolkofen UP. Hookworm of dogs and cats. In: *The Veterinary Clinics of North America Small Animal Practice*. Philadelphia: W.B.Saunders Co., 1987;1341-1354.

⁹ Roundworm infection, Toxocarosis, FAST FACTS. The Center for Food Security & Public Health website. http://www.cfsph.iastate.edu/FastFacts/pdfs/toxocarosis_F.pdf. Accessed December 16, 2014.

¹⁰ 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.

¹¹ Current Canine Guidelines. American Heartworm Society website. <http://www.heartwormsociety.org/veterinary-resources/canine-guidelines.html>. Accessed January 25, 2012

¹² Controlling Internal and External Parasites in U.S. Dogs and Cats. The companion Animal Parasite Council website. at <http://www.capcvet.org/recommendations/guidelines.html>. Accessed January 25, 2012.

¹³ Heartworm Incidence 2016. American Heartworm Society website. <http://www.heartwormsociety.org/veterinary-resources/incidence-maps>. Accessed May 15, 2019.

¹⁴ Weyenberg K. Have a heart. *Pet Quarterly*. 2009;6(4):8-11.

¹⁵ Data on file.

¹⁶ Data on file.

¹⁷ Data on file.