RACE-Approved, 1 Hour CE Course

Mosquitoes and Heartworm Disease: The Forgotten Culprit (in a Deadly Disease)

Chapter One

A New Way to Fight a Common, Potentially Fatal Infection

Mosquito-borne diseases are more top of mind for the public than ever before because we are now dealing with the new "normal", outbreaks of West Nile virus and the introduction of other viruses like the Chikungunya and Zika viruses. As long as mosquito-borne infections exist, mosquito control matters.

Heartworm Disease

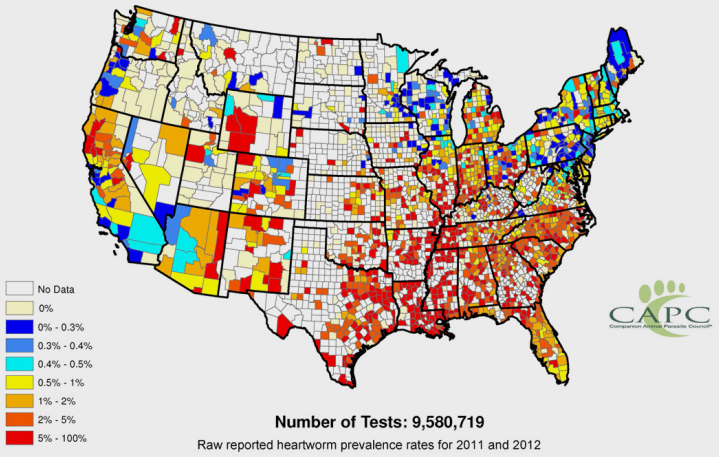
Heartworm disease is a serious and potentially fatal parasitic infection in pets in the United States and many other parts of the world. Heartworm infection is considered the most important vector-borne disease of pets in the United States and, as such, it remains of utmost importance to add new research and learning to the existing knowledge base and to look for new solutions and approaches to stop the increasing prevalence.

Heartworm Disease "Hot Spots"

Heartworms have been found in all 50 states, although certain areas have a higher risk of heart-worms than others. Some very high-risk areas include large regions, such as near the Atlantic and Gulf coasts, and along river tributaries. Most states have "hot spots" where the heartworm infection

Heartworm Disease "Hot Spots" Continued

rate is very high compared with other areas in the same state (CAPC, 2016)[1]. Factors affecting the level of risk of heartworm infection include the climate (temperature, humidity), the species of mosquitoes in the area, presence of mosquito breeding areas, and presence of animal "reservoirs" (such as infected dogs, foxes or coyotes).



Dirofilaria Immitis, the Parasite

Heartworm disease or dirofilariasis is caused by a blood-borne parasite known as Dirofilaria immitis (Bowman, 1999)[2]. While we refer to the Dirofilaria parasite as a heartworm, this is actually a misnomer since the adult heartworms do not actually live in the heart but rather live in the great vessels around the heart and in the lung tissue of affected pets. The parasite can cause severe lung disease, heart failure and damage to other organs in the body.

The Hosts

Dirofilariasis, unlike many other parasite infections, is invisible to the veterinarian and pet owner until the pet is very sick. Heartworm disease affects dogs, cats and ferrets, but heartworms also live in other mammal species, including wolves, coyotes, foxes, sea lions and, in rare instances, humans.

---

[1] *https://www.capcvet.org/capc-recommendations/canine-heartworm accessed October 16, 2016.*

[2] *Bowman, Dwight D. Georgis' Parasitology for Veterinarians. Philadelphia :W.B. Saunders Co., 1999. Print.*

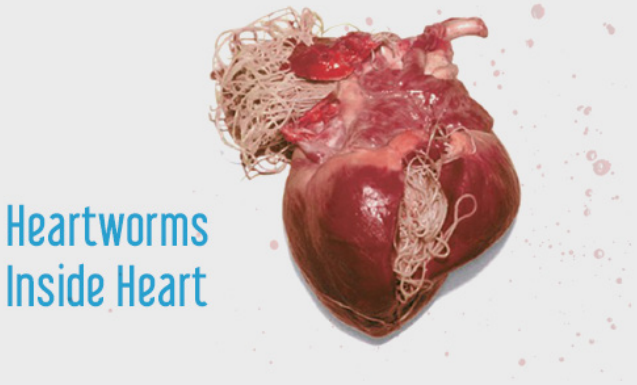
The Hosts Continued

Because wild species such as foxes and coyotes live in proximity to many urban areas, they are considered important carriers of the disease.

Dirofilaria immitis nematodes require both vector (mosquito) and host (dog) to complete their life cycle. The life cycle of the heartworm is complicated; the parasite requires the mosquito as an intermediate host before it can complete its life cycle in the dog.

As many as 70 species of mosquitoes can transmit heartworms; Aedes, Anopheles, and Culex are the most common genera acting as vectors. Mosquito species capable of transmitting heartworms can be found in most geographical areas (AHS, 2016)[3]. Transmission can occur anytime infected mosquitoes are active and feeding. In companion animals, infection risk is greatest in dogs and cats housed outdoors, although any dog or cat, indoor or outdoor, is capable of being infected.

The Heart



Adult heartworms are normally found in the large vessels that bring blood to the heart from the body and the right heart of infected dogs. Rarely, worms may be found in other parts of the circulatory system and even the chest and abdominal cavities of infected pets. The female worm is 6 – 14" long (15 – 36cm) and 1/8" wide (5mm). The male is about half the size of the female. One dog may have as many as 300 worms present when diagnosed.

[3] *https://www.heartwormsociety.org/ accessed October 16, 2016.*

Microfiliaria and Wolbachia

Adult heartworms may live five to seven years and, during this time, the female produces millions of offspring called microfilaria. These microfilariae live mainly in the small vessels of the bloodstream. Many pathogenic filarial worms are also infected by Wolbachia pipientis, an intracellular, gram-negative rickettsial bacterium, in an endosymbiotic relationship. The role of Wolbachia which live intracellularly within the filarid parasite, is not completely understood but it is thought that these organisms assist the metabolism of the worm and may even assist in keeping the host's immune system from attacking the heartworms. However, these bacteria have been implicated in the pathogenesis of filarial diseases, possibly through endotoxin production (MERCK Manual, 2016)[4] and the severe inflammation they cause when adult heartworms die.

For veterinarians, the most important aspect of Wolbachia is its symbiotic relationship with D immitis. This bacterium is necessary for normal maturation, reproduction, and infectivity of the heartworm.

Wolbachia and D immitis – A Symbiotic Relationship

Studies have demonstrated that a primary surface protein of Wolbachia (WSP) induces a specific IgG antibody response in hosts infected by D immitis. For veterinarians, the most important aspect of Wolbachia is its symbiotic relationship with D immitis. This bacterium is necessary for normal maturation, reproduction, and infectivity of the heartworm. If Wolbachia are eradicated from inside the heartworm, the heartworm gradually dies, after first becoming sterile. This can be accomplished with doxycycline therapy (MERCK Manual, 2016)[4].

---

[4] *http://www.merckvetmanual.com/mvm/circulatory_system/heartworm_disease/overview_of_heartworm_disease.html accessed October 16, 2016.*

Wolbachia and D immitis – A Symbiotic Relationship Continued

We will discuss in depth in a later module how the heartworm infection, once established in the vessels and lungs, may be considered curable, yet the pathology of the disease cannot be reversed in most cases.

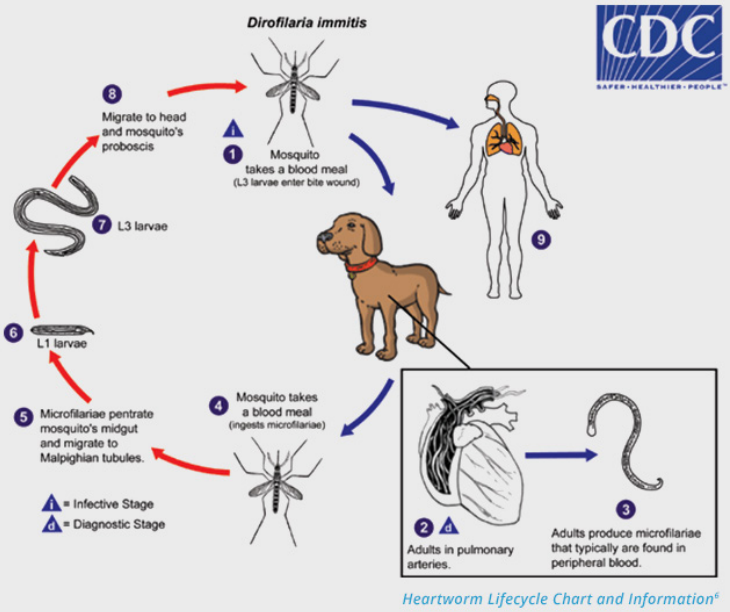
Chapter Two

The Heartworm Lifecycle

The life cycle of a heartworm begins when a female mosquito bites an infected dog and ingests the Dirofilaria microfilariae during a blood meal. A single dog can be bitten dozens of times by mosquitoes in a single 24 hour period (Capelli, 2013)[5]. It only takes one mosquito to transmit a heartworm infection from one dog to the next (AHS, 2016)[3].

The microfilariae develop further for about 14-16 days in the mosquito's gut and kidney organs and then enter its mouthparts. At this stage, they are infective L3 larvae and can complete their maturation to adulthood once they enter a dog.

Infective larvae enter the dog's body when the mosquito bites the dog. They migrate through the animal's tissues and then into the bloodstream and eventually find their



Heartworm Lifecycle Chart and Information[6]

[3] *https://www.heartwormsociety.org/ accessed October 16, 2016.*

[5] *Capelli et al., Risk of canine and human exposure to Dirofilaria immitis infected mosquitoes*

[6] *http://www.cdc.gov/parasites/dirofilariasis/biology_d_immitis.html*

The Heartworm Lifecycle Continued

way to the lungs and adjacent blood vessels where they mature to adults; mating and reproducing microfilariae within 6 – 7 months after the bite of the infected mosquito. The target host of interest to us is the dog or cat, but a wide variety of other animals can also be infected, including wild felids, mustelids, pinnipeds, beaver, horses, and humans.

Chapter Three

The Mosquito Vector

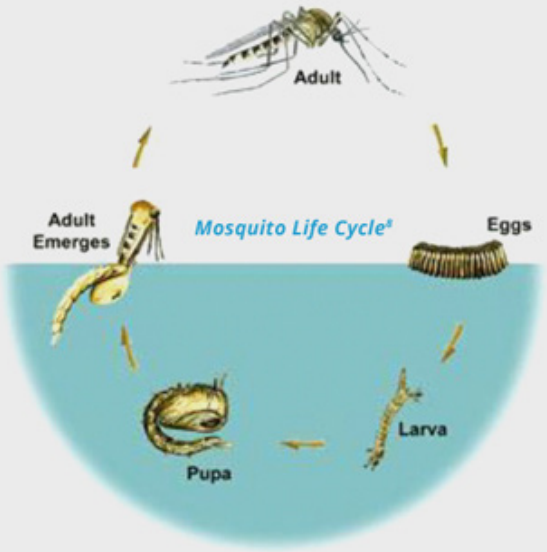
Vector-borne diseases account for more than 17% of all infectious diseases of humans, affecting more than 1 billion people and causing more than 1 million deaths annually, globally (CDC, 2016)[7].

Distribution of these diseases is determined by a complex dynamic of environmental and social factors. Globalization of trade and travel, unplanned urbanization and environmental challenges such as climate change are having a significant impact on disease transmission in recent years. Some diseases, such as Zika, Dengue, Chikungunya and West Nile virus, are emerging in countries where they were previously unknown.

Mosquitoes are the best known disease vectors for mankind rendering them the deadliest animal family in the world. Not only are these pesky insects devastating to human health, they also affect companion animals and livestock, carrying parasites and viruses that spread disease in the hosts they infect.

[7] *http://www.cdc.gov/features/stopmosquitoes/ accessed October 16, 2016.*

The Insect



Mosquitoes are members of the family Culicidae in the order Diptera (true flies). Mosquitoes are insects that develop through four distinct life stages – egg, larva, pupa and adult. Adult mosquitoes are distinguished from other flies by the presence of a long proboscis and scales on the margins and veins of the wing. Female mosquitoes' mouthparts form a long piercing-sucking proboscis. Their mouthparts are needle-like, and their saliva is both anesthetic, so you can't feel the bite, and anti-coagulant, which keeps the blood flowing. Males differ from females by having feathery antennae and mouthparts not suitable for piercing skin. A mosquito's principal food is plant nectar or similar sugar source. Only adult females feed on blood which is a required source of protein and iron for egg development.

The Problem

Because mosquitoes are such a problem, one that is potentially getting worse with warmer temperatures, larger cities (and their inevitable water-sources, in which the insects lay their eggs), and ease of global movement, these insects are seriously studied by experts across a variety of scientific, healthcare and government groups.

---

[8] *http://www.mosquito.org/ accessed October 16, 2016.*

The Problem Continued

Mosquitoes cause more human suffering than any other organism, over one million people worldwide die from mosquito-borne diseases every year.

Not only can mosquitoes carry diseases that afflict humans, they also transmit several diseases and parasites to which dogs and horses are very susceptible. These include dog heartworm, Eastern equine encephalitis (EEE), and West Nile virus (WNV). In addition, mosquito bites can cause severe skin irritation through an allergic reaction to the mosquito's saliva. Mosquito-vectored diseases include protozoan diseases, like malaria, filarial diseases such as dog heartworm and human lymphatic filariasis, and viruses such as Chikungunya, Dengue, St. Louis Encephalitis, LaCrosse Encephalitis, Zika and Yellow Fever.

Chapter Four

Vector-Borne Disease Control in Human Medicine

When experts in human health face a mosquito-vectored disease like malaria (the single greatest killer disease of humans), Yellow fever, Dengue or Zika, they seldom have any drugs or vaccines to use to protect humans from infection.

In most cases, the primary, sometimes the only, approach to prevention of these diseases has been vector (mosquito) control. The primary emphasis is almost always on preventing the vector from reaching the host therefore breaking the cycle required for their survival (CDC, 2016)[9].

[9] *http://www.cdc.gov/malaria/malaria_worldwide/reduction/index.html accessed October 16, 2016.*

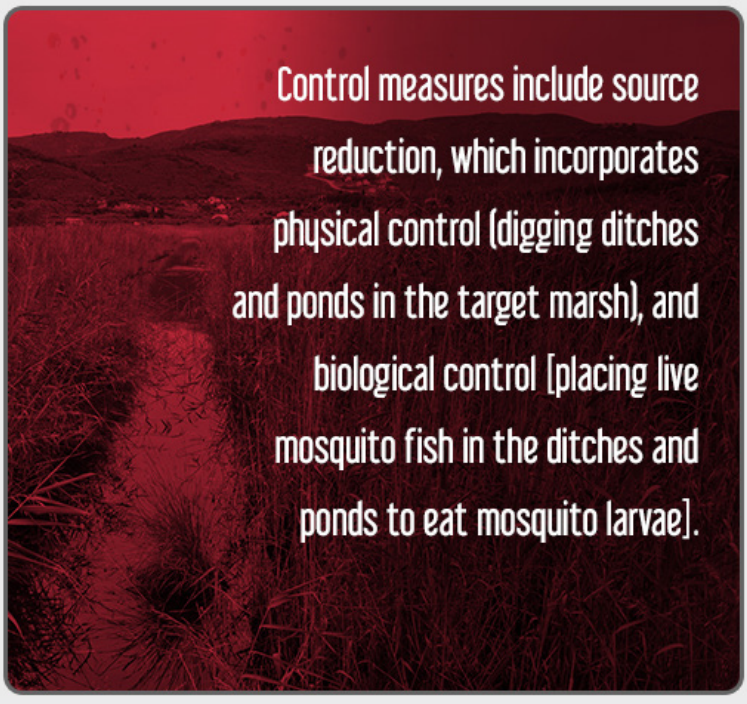
Vector-Borne Disease Control in Human Medicine Continued

In most cases, the primary, sometimes the only, approach to prevention of these diseases has been vector (mosquito) control. The primary emphasis is almost always on preventing the vector from reaching the host therefore breaking the cycle required for their survival (CDC, 2016)[9].

The IMM Approach

Mosquito control can be divided into two areas of responsibility: individual and public. Most often it is performed following the Integrated Mosquito Management (IMM) concept (Mosquito.org, 2016)[8]. Integrated mosquito management is a multi-modal approach that blends the use of both chemical and non-chemical control measures. IMM is the preferred approach for governmental mosquito control programs.

IMM is based on ecological, economic and social criteria, and integrates multidisciplinary methodologies into pest management strategies that are practical along with ongoing Larval surveillance to protect public health and the environment and improve the quality of life. The control measures include source reduction, which incorporates physical control (digging ditches and ponds in the target marsh), and biological control [placing live mosquito fish (Gambusia) in the ditches and ponds to eat mosquito larvae].



[8] *http://www.mosquito.org/ accessed October 16, 2016.*

[9] *http://www.cdc.gov/malaria/malaria_worldwide/reduction/index.html accessed October 16, 2016.*

The IMM Approach Continued

Other non-chemical control methods include using invertebrate predators, parasites and diseases to control mosquito larvae. Adult mosquito biological control by means of birds, bats, dragonflies and frogs has been employed by various agencies. However, supportive data is anecdotal and there is no documented study to show that bats, purple martins, or other predators consume enough adult mosquitoes to be effective control agents.

The Perfect Approach

Modern mosquito control programs in the U.S. are multifaceted and include surveillance, source reduction, and a variety of larval and adult mosquito control strategies (EPA, 2016)[10]. The perfect control for mosquitoes would protect us immediately from bites and mosquito-borne diseases, and it would be simple, inexpensive, and safe for the environment. Initially, when modern pesticides were first introduced for control of public health pests in the middle of the 20th century, some thought the perfect control had been discovered. Unfortunately, despite some early successes, pesticides applied across large geographies ultimately proved to be the less-than perfect solution for long-term mosquito control.

Chapter Five

Vector-Borne Disease Control in Veterinary Medicine

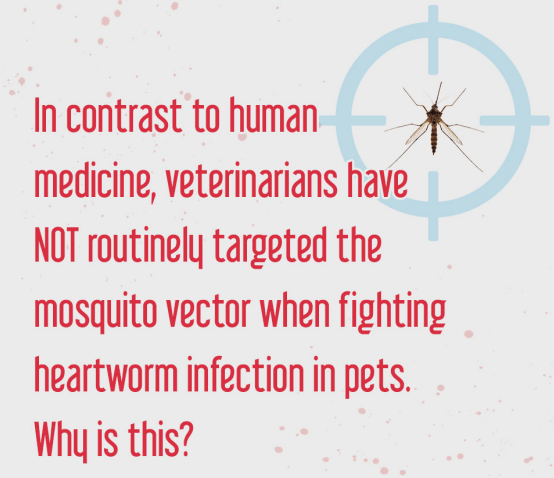
In contrast to human medicine, veterinarians have NOT routinely targeted the mosquito vector when fighting heartworm infection in pets. Why is this?

In veterinary medicine, an unusual thing happened. At almost the same time that veterinarians became aware of how serious infection with heartworms was for pets, some very effective drugs

[10] *https://www.epa.gov/mosquitocontrol/joint-statement-mosquito-control-united-states accessed October 16, 2016.*

Vector-Borne Disease Control in Veterinary Medicine Continued

were introduced by the pharmaceutical industry. These drugs, called macrocyclic lactones, or heartworm preventives, are designed to be given to pets orally or by injection (in a time-released product) on a regular basis to kill the young worms after they have entered the pet's body but before they have developed to the stages that cause harm.



For over 25 years these drugs seemed to be doing a good job, as long as pet owners used them absolutely according to their label instructions, year-round. Because these drugs did such a good job under ideal circumstances, the veterinary profession had little reason to worry about vector control, as human medicine did when it lacked any good drugs or vaccines.

The Resistance

Unfortunately, we now see an alarming increase in the number of heartworm infection cases in pet dogs and cats over the past several years. This increase is believed to be the result of owners not using the oral (or injectable time-release) preventives as compliantly as they should but also because strains of heartworms that are resistant to the preventives have now been detected in a large area of the mid-US. Even when pets receive their preventive medications perfectly compliantly, these strains are able to evade the drugs and develop to adults in the great vessels and lungs of the pet.

Most experts agree that it will be many years before we have new preventive drugs to fight the resistant strains of heartworm that may continue to emerge and spread during that time. Until recently, we have not had the kind of data showing that commercial topical ectoparasiticide

The Resistance Continued

products can effectively repel and kill mosquitoes and, thus, block the transmission of heartworm organisms from mosquitoes to pets and from pets to mosquitoes. But, in the past couple of years, studies have been conducted to assess the effectiveness of such products as repellents and insecticides for mosquitoes of many species. These studies show promise for a multi-modal approach that includes use of macrocyclic lactones in combination with repellent insecticidal topical products (McCall, 2015)[11]. We will discuss in depth the science behind the preventive synergy of macrocyclic lactone drugs in combination with repellent insecticidal topical in a later module.

Chapter Six

The Future of Vector Control

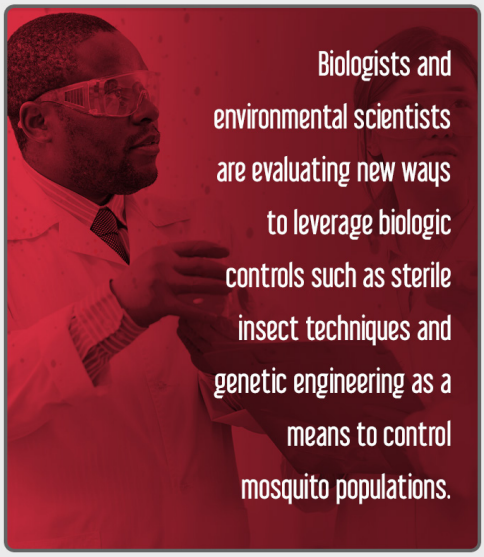
The integrated mosquito management methods currently employed by organized control districts and endorsed by the Center for Disease Control (CDC) and the Environmental Protection Agency (EPA) are comprehensive and specifically tailored to safely counter each stage of the mosquito life cycle. Larval control through water management and source reduction, where compatible with other land management uses, is a prudent pest management alternative – as is use of the environmentally friendly EPA-registered larvicides currently available. When source elimination or larval control measures are clearly inadequate, or in the case

---

[11] *McCall JW, Hodgkins E, Varloud M, et al. Inhibition of the transmission of Dirofilaria immitis to mosquitoes by weekly exposure of microfilaremic dogs treated topically with dinotefuran-permethrin-pyriproxyfen to uninfected Aedes aegypti, in Proceedings 60th Ann Meet Amer Assoc Vet Parasitol 2015; Abstract No. 7; 60.*

The Future of Vector Control Continued

of imminent disease, the EPA and CDC have emphasized in a published joint statement the need for considered application of adulticides by certified applicators trained in the specialized handling characteristics of these products (EPA, 2016)[10].



Additionally, biologists and environmental scientists are evaluating new ways to leverage biologic controls such as sterile insect techniques and genetic engineering as a means to control mosquito populations. These efforts, while effective in controlling the mosquito population, are receiving a great deal of scrutiny due to the lack of safety and environmental studies to show that introducing biologically altered or genetically modified mosquitoes into nature is a safe alternative for mosquito control.

The Oxitec Method

One particular group, Oxitec has applied a method developed by Luke Alphey, a British geneticist specializing in vector control. Partially supported by the Bill & Melinda Gates Foundation, Oxitec has applied the method in Brazil, Malaysia and Panama, and claims to have reduced the A. aegypti population in small test areas by at least 90 percent (Alphey, 2013)[12]. That's a far better percentage than spraying, which usually hits about 50 percent and has a tendency to breed resistance, requiring more and more spraying to get the same low result. Recently, the U.S. Food and Drug Administration approved an experiment commissioned by Oxitec in an unincorporated area of South Florida. The locals in the area have

---

[10] *https://www.epa.gov/mosquitocontrol/joint-statement-mosquito-control-united-states accessed October 16, 2016.*

[12] *Alphey, L., McKemey, A., Nimmo, D., Neira Oviedo, M., Lacroix, R., Matzen, K., and Beech, C. (2013). Genetic control of Aedes mosquitos. Pathog Glob Health 107, 170-179.*

The Oxitec Method Continued

protested and are scrutinizing the ethics and handling of such experiments. Their primary concern being the unproven effect of genetically modified mosquitoes that could further concerns about drug resistance and other unintended consequences. (Oxitec, 2016)[13].

The Future of Vector Control for the Veterinary Profession

As the human and pet populations continue to expand and our world continues to shrink, mosquito control in the United States will assume a more critical public health function, well beyond its quality of life role. While new ways to control mosquito populations may take years to research and fully understand both efficacy and safety, today the veterinary profession has an opportunity to embrace a new way to control mosquito-borne diseases through effective multi-modal protocols. Because mosquitoes are the only known vector of Dirofilaria immitis, controlling mosquitoes through the use of an on-pet, mosquito repellent insecticide should help control heartworm transmission in much the same way that targeting vectors has been used successfully to control vector-transmitted diseases in people.

End of Course Content

Are you ready to take the quiz?

Congratulations, you have finished the content for this CE course.

LAUNCH QUIZ

[13] *http://www.oxitec.com/ground-florida-oxitecs-derric-nimmo-part-2/ accessed October 16, 2016.*