Recently, a group of veterinary practitioners and parasite researchers gathered together to discuss the problem of heartworm disease in dogs and a new multimodal approach that may help to solve it.

New research suggests that a multimodal, Double Defense approach—administering Vectra® 3D (dinotefuran/pyriproxyfen/permethrin) plus a macrocyclic lactone—to target both mosquitoes and heartworms provides an additional measure to protect dogs against heartworm disease transmission.

THE SPREAD OF HEARTWORM

Dr. Elizabeth Hodgkins (moderator): Monthly oral heartworm products have been around since the 1980s. The incidence of heartworm infection has been rising and spreading—in spite of really good products and really good veterinary care. Why do you believe this is the case?

Dr. C. Thomas Nelson: We are a mobile society, moving across the country, moving to areas that were typically not endemic. When I graduated in 1979, the heartworm map showed a few dots out west. Now California ranks tenth in the nation for number of heartworm cases.

Dr. Nancy Soares: Veterinarians are doing a good job, but we are not making enough headway with this disease. A lot of it falls on the veterinarian in the examination room, talking to owners. As a practitioner myself, I know there is always a lot to talk about with owners, but preventing heartworm disease should start there.

Dr. Nelson: As practitioners, we need to be sure owners understand the importance of giving heartworm preventives every month. I give a lot of talks to veterinarians across the country, and I tell them that my own dog got heartworm disease. I switched from the daily product to a monthly product, and a year later, my dog was positive. I always ask the room—full of veterinarians and technicians—how many of them give their dogs’ heartworm prevention every month, never missing a dose and never late by more than a week. Maybe 10% to 20% raise their hands. We know better, and we are not compliant. Yet, we expect owners to be compliant.

Dr. Susan Little: Compliance is a major challenge and one of the key reasons that we still have a high prevalence of infection in dogs. Another concern is that many dogs are never seen by a veterinarian. Those dogs become infected with heartworm and serve as reservoirs to mosquitoes, which go on to infect other dogs. So infection is a constant risk.

ROLE OF MOSQUITOES

Dr. Little: With changing climate patterns, we have a lot of mosquito activity. And we are confronting more mosquitoes than we did before. More than 70 species of mosquitoes have been confirmed to vector heartworm, with as many as 25 species confirmed to harbor infection in the United States. Although not all are considered critical, this creates a greater risk for dogs.

Dr. Robert Wirtz: That represents about 40% of the approximately 180 mosquito species recognized in the United States. Usually only one or two mosquito species are the primary vectors of a specific infection of humans in a geographic region.

Dr. Little: It is also clear that while coyotes are a growing concern, domestic dogs are still the main reservoir for heartworm. We see extremely high prevalence rates in dogs in urban areas, which is surprising to many people. Some veterinarians think of heartworm as a rural disease, but it is more efficiently transmitted when dogs are close together because then the mosquito does not have to carry the infection far. Lots of mosquitoes equal lots of efficient transmissions. The prevalence rate of heartworm in shelter dogs in some areas in the South is very high.
exceeds 50%, so there is always an opportunity for a mosquito to find microfilariae and then transmit larvae to another dog just a few weeks later.

**Dr. Nelson:** Most mosquitoes travel only about 2 km. If you have a heartworm-positive dog in a neighborhood, then 33% of the mosquitoes in the area are infective. That makes a big difference.

**Dr. Little:** Yes, if we look at a community-wide survey of mosquitoes, the infection rate may only be 1% or 2%. But around infected dogs, 50% to 75% of the mosquitoes are carrying larvae and creating a risk of infection.

**Dr. Wirtz:** We see that with malaria, too. It can be very focal, based on the human reservoirs, vector behavior, and topography. If we can recognize that, then we can focus our resources on those higher-risk areas.

**VECTOR CONTROL**

**Dr. Hodgkins:** It sounds like there are a variety of challenges that contribute to the spread of heartworm, and many of them seem to focus on the mosquito vector. From a One Health perspective, perhaps it is prudent to consider what we are doing with human vector-borne diseases.

**Dr. Wirtz:** Vector control has always been at the heart of limiting vector-borne diseases.

**Dr. Nelson:** The multimodal approach used in human medicine is something we need to embrace more in veterinary medicine. We need to look at how we can decrease exposure to the infection.

**Dr. Wirtz:** Yes, I think that is the only way forward. The more transmission there is, with parasite exposure to the treatment drug, the quicker resistance is going to develop. One way to reduce the development of drug resistance is to control the vector.

**Dr. Little:** There is a natural attraction to vector control that focuses on protecting the dog from mosquitoes. A vector control product with permethrin can help protect a dog from the misery of being fed upon by multiple vectors, including, of course, mosquitoes, thereby making the dog more comfortable and contributing to its overall well-being. But beyond just repelling these vectors, an insecticide that has the ability to kill 95% of the mosquitoes that come in contact with a treated dog would reduce the population of mosquitoes available to transmit heartworm.

Mosquito-borne diseases are more top of mind for the public than ever before because we are now dealing with the new normal of endemicity 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.

**DOUBLE DEFENSE DATA**

**Dr. Hodgkins:** Dr. McCall, can you speak a bit about your recent research that is the foundation of the new Double Defense standard of care in heartworm control?

**Dr. John McCall:** Well, I think everyone intuitively knows that if you prevent an insect from biting or if you kill that insect, then you will not have disease transmission. But the main reason we have not taken advantage of that and incorporated it into our veterinary recommendations is that, in the past, we have not had this kind of data showing that a product actually repels and kills mosquitoes and, thus, blocks the transmission of heartworm microfilariae. But, in the past couple of years, we have conducted studies with models to assess the effectiveness of products as repellents and insecticides.

Recently, we conducted a study with two groups of dogs that had circulating Dirofilaria immitis microfilariae. We treated one group with Vectra 3D, and the other group was the untreated control. We exposed these dogs to mosquitoes weekly for four weeks. And we found more than 95% repellency with Vectra 3D for the entire month.

**Dr. Hodgkins:** Can you define repellency for us?

**Dr. McCall:** Repellency is preventing mosquitoes from biting—so anti-feeding. And in our study, Vectra 3D was 95% effective. But, more importantly, it was also effective.

> Vector control has always been at the heart of limiting vector-borne diseases.”

—Dr. Robert Wirtz
SUSAN LITTLE, DVM, PhD, DACVM (Parasitology)
Regents Professor and the Krull-Ewing Chair in Veterinary Parasitology, Center for Veterinary Health Sciences, Oklahoma State University
Dr. Little is active in veterinary parasitology teaching and oversees a research program that focuses on zoonotic parasites and tick-borne diseases. She is recognized as an international leader in parasitology and vector-borne disease with an emphasis on One Health. She is past-president of the American Association of Veterinary Parasitologists, President of the Companion Animal Parasite Council, and a founding director of the National Center for Veterinary Parasitology. She was instrumental in securing recognition for the subspecialty of veterinary parasitology through the AVMA’s American Board of Veterinary Specialists. She has received two Excellence in Teaching Awards from the national Student American Veterinary Medical Association.

JOHN W. McCALL, MS, PHD
Professor Emeritus, Department of Infectious Diseases, College of Veterinary Medicine, University of Georgia
Dr. McCall was a member of the faculty in the College of Veterinary Medicine at the University of Georgia from 1970 to 2006, retiring as Professor Emeritus of Veterinary Parasitology. For more than three decades, he has been President/Chief Operations Officer of TRS Labs Inc., a contract research laboratory. He is past vice president and editor of the American Heartworm Society and currently serves as associate editor. He was the UGA Director of the National Institutes of Health-funded Filariasis Research Reagent Resource Center from 1973 to 2006. He has published more than 250 peer-reviewed research articles, 50 non-refereed research articles, and 11 book chapters, presented more than 300 lectures, and co-written more than 250 scientific papers and abstracts for scientific meetings.

C. THOMAS NELSON, DVM
Past President and Executive Board Member, American Heartworm Society and Owner and Medical Director of Animal Medical Center, Anniston, AL
Dr. Nelson has been in private veterinary practice for nearly four decades, and he has served as an executive board member of the American Heartworm Society (AHS) since 2001. He was elected AHS president in 2004. He is the co-author of the AHS guidelines for the prevention, diagnosis, and management of heartworm infection. He has also served on the board of Companion Animal Parasite Council. Dr. Nelson has written or co-written several papers and contributed to several textbooks on the subject of heartworm disease. He is considered a pioneer for his clinical work in the study of heartworm disease in cats.

NANCY SOARES, VMD
2016–2017 President of the American Animal Hospital Association and Owner and Medical Director of Macungie Animal Hospital
Dr. Soares is AAHA’s 2016–2017 president. In 2007, Dr. Soares established her own practice, Macungie Animal Hospital, where she serves as owner and medical director. Her practice was presented with the AAHA-Accredited Practice of the Year Award in 2013, and has grown to include five full-time veterinarians. Macungie Animal Hospital offers an educational lecture series, youth activities, and shadowing opportunities for those interested in animal medicine. Dr. Soares has been published in the Journal of the American Veterinary Medical Association and has served as a lecturer for multiple veterinary conferences.

ROBERT WIRTZ, PHD
Retired Chief of the Entomology Branch, Centers for Disease Control and Prevention
Dr. Wirtz has spent a distinguished career in researching and developing solutions to mitigate the impact of insect-transmitted diseases, especially by mosquitoes, on the world’s population. In 1997, he began an 18-year career at the CDC, where he directed activities to reduce the threat of arthropod-borne diseases to humans. He also supervised work on insecticide resistance, analysis of insecticides and anti-malaria drugs, and evaluation and implementation of long-lasting insecticide treated bed net and indoor residual spray programs. His commitment to vector control spanned the globe and touched many countries and worldwide organizations, including the World Health Organization. Dr. Wirtz is also an accomplished author and co-author, with his work appearing in more than 275 publications, including nine book chapters, on worldwide parasite-related health issues. After retiring from the CDC in 2015, Dr. Wirtz continues to assist at the agency as a volunteer guest researcher and also works as an independent consultant.

ELIZABETH HODGKINS, DVM, ESQ.
Director, Veterinary Services, Ceva Animal Health, LLC
After earning her DVM degree, Dr. Hodgkins served an internship at the Animal Medical Center in New York City and an oncology residency at University of California-Davis. Following her residency, she taught veterinary parasitology at UC-Davis. Dr. Hodgkins then attended law school at the University of Kansas and became a member of the Kansas Bar. She developed and patented a currently marketed food for the management of feline diabetes. In 2003, she built and opened her own cat-exclusive private practice in Yorba Linda, California. In 2009, she joined Summit VetPharm’s Veterinary Services group for the Western Region. Currently, she is Director of Ceva Animal Health’s Veterinary Services group. She is also the author of Your Cat: Simple New Secrets to a Longer, Stronger Life (Thomas Dunn Books, 2007) and co-author of Not Fit for a Dog (Quill Driver Press, 2012).
A mosquito that is killed through its contact with Vectra 3D on a treated dog is no longer available to bite any other dog or any other person or any other pet in the area. So it is a form of insecticidal treatment, as well as a repellent.”

—Dr. John McCall

as an insecticide. So if a mosquito touches the dog, the mosquito is not going to survive. In our study, we found that the insecticidal activity was greater than 95% for the month, and none of the mosquitoes exposed to Vectra 3D-treated dogs developed infective larvae (L3). These exciting results show that we can actually block the transmission of the infection to mosquitoes. This type of product can both repel the mosquito and kill it before any infective larvae develop.

Dr. Hodgkins: And that would have an impact on the local environment of that dog? Say of the household?

Dr. McCall: A mosquito that is killed through its contact with Vectra 3D on a treated dog is no longer available to bite any other dog or any other person or any other pet in the area. So it is a form of insecticidal treatment, as well as a repellent.

Dr. Wirtz: There is a similarity here with the large bed net and indoor residual spray programs we use for malaria control. We get the most effective control when we have a community effect. We try to make sure that all the villagers get their houses sprayed or use a bed net. Not only are they protecting themselves, they are also protecting their neighbors.

Dr. Little: When we talk about controlling intestinal parasites, we talk about fecal pickup and fecal monitoring and making sure the dogs at the boarding kennel are free of parasite infection. We want to reduce transmission as much as possible. For some reason, we have managed heartworm differently over the years. I find the data that Dr. McCall has generated on preventing heartworm transmission to be incredibly compelling and powerful.

What is so exciting about this research is that it says there is more we can do to help prevent heartworm. We still have to administer the preventive—that is foundational and critical—but we can also reduce the number of mosquitoes feeding on treated dogs. The multimodal approach brings a higher level of care and protection to dogs.

Dr. Soares: It is compelling research. It is new, and the numbers are exciting. Honestly, we have not had a

The severity of heartworm incidence as shown on these maps 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.
whole lot of new data to talk about on this topic in the examination room in a long time. Dr. McCall’s research gives us the opportunity to talk about heartworm prevention and parasite control again. Patients should be receiving an oral heartworm preventive—that is key. They should also receive flea, tick, and mosquito control. But now we can talk about the importance of repellency in heartworm control.

**DRUG RESISTANCE**

**Dr. McCall:** In the study, I chose a particular *Dirofilaria immitis* isolate—the JYD-34 strain, which is resistant to macrocyclic lactones.

**Dr. Little:** It is the strain we are all afraid of.

**Dr. McCall:** One of my goals over the past several years has been to come up with a way to help reduce the rate of selection for these resistant strains. To me, this multimodal approach is one way of doing that because the mosquito that has the resistant heartworm parasite is going to be repelled and killed just the same as the mosquito that has the susceptible one.

**Dr. Little:** When I first saw you present these data, I was reassured by the fact that you chose JYD-34 because it is something veterinarians are concerned about. We know how to protect dogs from heartworm. We prescribe preventives as early as the label allows, and we do everything we can to support compliance throughout that dog’s life. We can implement this multimodal approach and administer something that repels and kills mosquitoes in addition to the heartworm preventives, and that could be effective as an additional layer of protection.

**ADOPTING THE DOUBLE DEFENSE PROTOCOL**

**Dr. Hodgkins:** It sounds like you see real scientific and medical value in moving to a Double Defense multimodal heartworm protocol. How do we change behaviors—both dog owners’ and the profession’s—to adopt this new approach?

**Dr. Wirtz:** Changing human behavior is a tremendous challenge in public health. Major portions of the Centers for Disease Control and Prevention’s programs focus on behavior change and communication.

*I think there is a unique opportunity to educate the local news media.*

**Dr. Soares:** Yes, consumer awareness is huge. Owner communication, education, and support are all key. Owners care that the product is efficacious and affordable, and they want to know that it is something that I, their veterinarian, would administer to my pet.

**Dr. Little:** Another way to raise awareness is to make the data about the prevalence of heartworm local and timely. The Companion Animal Parasite Council provides a tool that can tell you how many cases of heartworm disease have been diagnosed in your county, and you can get monthly updates. Technicians can put that information on a whiteboard next to the reception desk. That lets owners know it is a risk to their dogs. It underscores the need for heartworm prevention and also the need for mosquito control.

**Dr. Wirtz:** You might be able to capitalize on the public interest in the chikungunya and Zika viruses by explaining that vector control and personal protection, such as using insect repellents, are the only methods we currently have of reducing these diseases in humans. Similarly, by treating their dogs with Vectra 3D, owners are directly addressing the vector of heartworm transmission.

**Dr. Soares:** That is a powerful message that we can relay to owners.

**Dr. Little:** Veterinarians and other team members are already getting questions about Zika virus because there is concern and understandable curiosity about whether dogs are at risk. We do not have any evidence that pets are at risk, but those questions are getting asked. Those questions are a lead-in to the mosquito conversation—an opportunity for team members to say, “We are concerned about mosquitoes, too. Here is what we recommend…”

“We still have to administer the preventive—that is foundational and critical—but we can also reduce the number of mosquitoes feeding on treated dogs. The multimodal approach brings a higher level of care and protection to dogs.”

—Dr. Susan Little
The research is compelling, and we are not asking owners to change what they are doing. We are just adding the fact that we want owners to reach for a product that has repellency and is mosquitocidal.”

—Dr. Nancy Soares

Dr. Nelson: You have to piggyback on the focus on addressing vector control in humans.

Dr. Wirtz: Yes, there is a lot of public education on mosquito control in general. Again, it is a multicomponent approach. It is a matter of using all of the resources available to kill mosquitoes.

Dr. Little: We have all experienced mosquito pressure firsthand. We all know just how horrible it is, not just for health reasons but also for the lifestyle that people have. People want time in their backyards and their communities. They want their kids outside. There are even data linking childhood obesity to the introduction of Aedes albopictus because it is difficult for children to play outside when mosquitoes swarm them. So, for veterinarians, the mosquito concern can serve as a catalyst to start a conversation with dog owners. Educating about the risks mosquitoes create and the steps pet owners can take to reduce those risks is one more way veterinarians can serve their community.

Dr. Soares: I think that is a good way to position it. The research is compelling, and we are not asking owners to change what they are doing. We are just adding the fact that we want owners to reach for a product that has repellency and is mosquitocidal.

Dr. Little: And we are not asking veterinarians to recommend an additional product. If pet owners just administer a flea and tick control product that also repels and kills mosquitoes, then their dogs get another layer of heartworm protection and another layer of comfort.

HEARTWORM PREVENTIVE REMINDERS

Dr. Wirtz: It also sounds like reminders could be valuable for pet owners.

Dr. Nelson: There are practice management systems now that can text reminders. We send reminders for heartworm testing—which has higher compliance—but many practices do not send reminders for the monthly preventive.

Dr. Little: There are veterinary pharmacy systems in which heartworm preventive is delivered to an owner once a month and he or she administers it to the pet when it arrives.

Dr. Nelson: So the technology is there. People just need to use it.

Dr. Soares: Our goal is prevention all year long. If an owner purchases six or 12 months of preventives, once it is time that he or she should be running low, we send a reminder, same as we would for an examination or vaccine. We also offer free delivery; anything we can do to make owners’ lives easier.

THE VETERINARY TEAM

Dr. Hodgkins: Affecting positive change is going to require a lot of voices talking about Double Defense as a multimodal approach to heartworms. Talk a bit about the role of the veterinary team.

Vectra® 3D was over 95% effective in anti-feeding and in killing mosquitoes up to 28 days after administration.

Source: See Reference 8.
In this study, the anti-feeding and insecticidal activity of Vectra® 3D in mosquitoes was **over 99% effective** in blocking the development of infective larvae.

Source: See Reference 8.

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**Dr. Soares:** Each department has to be involved, and everybody has to care about it. My team cares about our patients—we want these dogs to be happy and healthy. Heartworm disease is a huge problem that we sort of pushed to the side, but we now have the opportunity to open the discussion with owners again. And there are many good talking points, especially with One Health and what is in the news and how people are being affected by their own mosquito-borne disease risks.

**Dr. Little:** Technicians are key to this conversation. They are already familiar with the heartworm life cycle and with the risk that mosquitoes pose. I think it’s important that they reinforce to dog owners that using a product that kills and repels mosquitoes reduces the risk of those mosquitoes feeding on their dogs. This could make a huge difference.

**Dr. Hodgkins:** What would you want team members to do when an owner comes in to purchase a refill of heartworm preventive?

**Dr. Soares:** This situation is an opening for a conversation. If we, as veterinarians, have done our job and educated team members about the products and what is best for patients and their families, then there is going to be a dialogue: “I know you are here to refill the heartworm preventive. What about the topical flea, tick, and mosquito preventive? I see that you have not refilled it.”

**Dr. Nelson:** That is an opportunity to review the patient’s record. Instead of just refilling the preventive, team members should ask when was the last time it was refilled? And how many doses has the patient received in the past 12 months? What other products is the owner giving the patient? Is the patient up to date on its immunizations?

**Dr. Hodgkins:** And would Double Defense become part of that checklist for dog owners?

**Dr. Nelson:** Definitely.

**Dr. Soares:** As a veterinarian, I think my job is to offer whatever the standard of care is. Pet owners are seeking answers from us, and they listen to our recommendations. I think the Double Defense message is compelling and would be well received. So I would want my team to reiterate this message.

### BEYOND PREVENTION

**Dr. Little:** What about when we have an infected dog that has been diagnosed with heartworm infection? If the dog is microfilaremic, in addition to receiving a heartworm adulticide, doxycycline, and a macrocyclic lactone, shouldn’t this dog also be administered a product that repels and kills mosquitoes so that any microfilariae in the dog do not get ingested by a mosquito, which a few weeks later feeds on that same dog or another dog? It may be that this strategy should become a primary component of the treatment of every heartworm-infected dog.

**Dr. Wirtz:** It is actually a no-brainer.

**Dr. Nelson:** It makes sense, and I support anything we can do to reduce the numbers.

**Dr. Little:** So would you change the way you treat a heartworm-positive, microfilaremic dog, making sure that it receives a product that repels and kills mosquitoes?

**Dr. Soares:** I will, absolutely.
The multimodal approach used in human medicine is something we need to embrace more in veterinary medicine. We need to look at how we can decrease exposure to the infection.”

—Dr. C. Thomas Nelson

Dr. Little: Some pet owners just want to protect their own dogs and are not worried about their neighbors’ dogs. So it might be good to reinforce to owners that the mosquitoes that feed on their dogs and ingest microfilariae could come back a few weeks later and reinfect that same dog. There is a cycle of infection.

Dr. Nelson: It is as simple as that, thinking about all the dogs that are at risk.

Dr. Little: Yes, the dog that is infected with heartworms also has to be protected from mosquitoes. Otherwise, the whole community is at risk.

A STRATEGIC MOVE

Canine heartworm disease is a life-threatening parasitic infection that veterinarians and dog owners continue to battle. Heartworm infection is considered the most important vector-borne disease of dogs 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.

Ceva Animal Health would like to thank Dr. John W. McCall for his groundbreaking study and all of the practitioners and parasite researchers that participated in this roundtable for sharing their expertise and views on the new Double Defense multimodal approach.

REFERENCES


LEARN MORE

Be sure to visit FightHeartwormNow.com for additional information about heartworm disease and mosquitoes. See Dr. McCall’s most recent research results and the new Double Defense heartworm protocol. You can also view video segments from this roundtable and interviews with these roundtable participants.