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An Eco-Friendly Ending

Aquamation Gaining Popularity as Alternative to Cremation **24**

AAHA 2022 Pain
Management Guidelines
for Dogs and Cats

Executive Summary of the Latest
Guidance from AAHA **35**

Keeping Up with the Bugs

Innovating to Meet the Challenges of Pet Parasites

by Maureen Blaney Flietner

Parasites aren't the most pleasant part of veterinary practice work. Not only must veterinary teams identify and treat for parasites and educate clients, they must also stay vigilant to protect themselves from zoonotic diseases. To make matters more concerning, parasites are spreading, migrating, and showing resistance to certain treatments.

Intestinal parasites continue to be on the rise in the United States, according to Craig Prior, BVSc, CVJ, a board member and past president of the Companion Animal Parasite Council (CAPC). "Every year on CAPC maps, we see more parasites showing up in areas they shouldn't," Prior said. "A lot of this is because parasites are dynamic, ever changing, and on the move. We're also seeing parasite rates go up."

Prior noted a 2019 study by Jason Drake, DVM, DACVM, that revealed increasing prevalence for roundworms and hookworms, and, for the first time, apparent seasonality to canine whipworms.

"We're also seeing resistant hookworms. It started in the greyhound population in Florida and now has moved to the general dog population," said Prior. "The conversation changes when you have resistant hookworms because we don't need to be helping to further that resistance. We as veterinarians should be practicing preventative medicine, preventing

"Every year on CAPC maps, we see more parasites showing up in areas they shouldn't."

—CRAIG PRIOR, BVSC, CVJ, VETERINARY CONSULTANT

disease in not just animals but in humans.”

Ticks also are on the move.

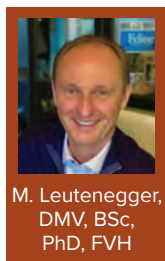
The Asian longhorned tick was reported for the first time in the United States in 2017 in New Jersey. Able to reproduce without mating, it spread rapidly. According to the Centers for Disease Control and Prevention (CDC), the tick is now found in 17 states from Arkansas to New York, and discovered on pets, livestock, and wildlife.

The lone star tick also continues to expand its range and numbers, according to the CDC. It is now found as far north as Maine and as far west as central Texas and Oklahoma. It can transmit several bacteria and other disease-causing agents that can cause, for examples, cytauxzoonosis in cats and ehrlichiosis in dogs.

What can be done? *Trends* reached out to several sources who shared how they are innovating to meet the challenges.

Molecular Diagnostics

In January, Antech Diagnostics launched a molecular testing platform for parasites called KeyScreen GI Parasite PCR.



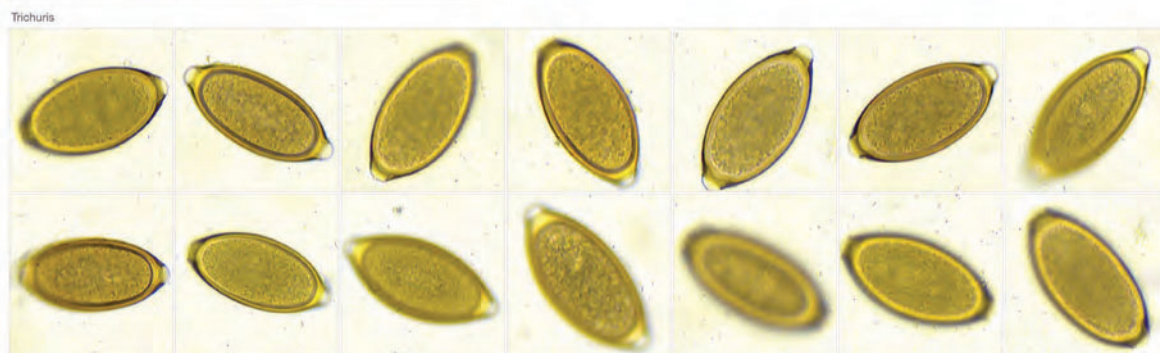
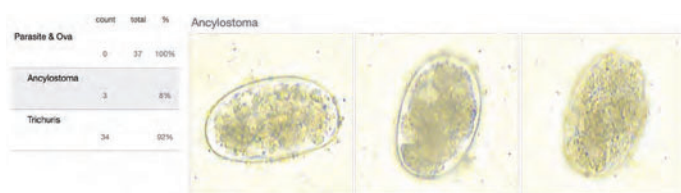
PCR (polymerase chain reaction) offers the most sophisticated diagnostic modality for the COVID virus. Antech’s molecular testing modality for parasites is essentially the same, offering the most sensitive test for parasites, explained Christian M. Leutenegger, DMV, BSc, PhD, FVH, director of molecular diagnostics at Antech Diagnostics.

“Molecular testing is fundamentally different and more sensitive than any other kind of diagnostic testing. It can detect a much broader range of parasites from one small sample. Our test currently detects 20 parasites. It accomplishes this by reading the genetic material, or the DNA/RNA, of a parasite,” said Leutenegger.

The testing platform identifies zoonotic and anthelmintic drug-resistant parasites that have evolved to become a more serious concern, a hallmark being multidrug-resistant hookworms, he explained. It also is the most sensitive test for parasites in veterinary medicine, differentiating round- and tapeworms and identifying important parasites such as *Toxoplasma*, whipworms, protozoa, and coccidia.

Leutenegger said Antech is investing heavily in molecular technologies, which are key for fast and affordable parasite screening in wellness exams. He expected that the most important cost and efficiency benefits for veterinary practices would be:

- Rapid access to highly actionable information that will allow practices to provide effective treatment from the first visit instead of having the pet return months later because they “still aren’t 100%.”
- The ability of veterinarians to practice pharmaceutical stewardship because there is no risk of overtreatment if they



Ancylostoma Trichuris

“Molecular testing is fundamentally different and more sensitive than any other kind of diagnostic testing.”

—CHRISTIAN M. LEUTENEGER, DMV., BSC, PHD, FVH, ANTECH DIAGNOSTICS

know exactly what's there and how to treat it.

- Saving time and resources as the molecular test requires a very small sample—0.15 grams—which can be stored for 10 days after collection. Practice staff can submit the sample without any special preparation and send it refrigerated to the Antech laboratory.

“Veterinary practices are having to serve more patients with fewer resources so the time and resource benefits of the more sensitive test can't be understated,” he explained.

Leutenegger said this innovation will provide a broader database of the prevalence and spectrum of gastrointestinal parasites in pets, a level of differentiation that current diagnostic modalities do not have.

Other than for COVID PCR testing, molecular testing for parasites isn't widely used in human medicine, explained Leutenegger. And while there are more and more PCR tests, turnaround time is often weeks.

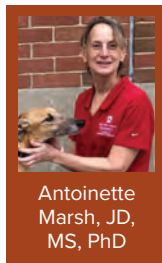
“You could argue that veterinary medicine is once again ahead of human medicine.”

A Hierarchy of Protocols

At Ohio State University, a study of drug-resistant hookworms is innovating by bringing information learned from other areas to companion animals.

“Resistant nematodes are not new. It's not something that sporadically just happened in dogs. We have seen it coming through our understanding of the treatment of livestock and horse parasites. Livestock practitioners

used one anthelmintic, determined lack of efficacy, and then used a combination of different anthelmintic classes with appropriate follow-up testing,” explained Antoinette Marsh, JD, MS, PhD, associate professor of parasitology at Ohio State University. She also chairs the American Association of Veterinary Parasitologists Hookworm Task Force.



Antoinette Marsh, JD, MS, PhD

“Just because a dog is infected with hookworms doesn't mean it is drug resistant. It really means the owner and veterinarian need to work

together to identify if it could potentially be drug resistance or something else because there are effective treatments for GI parasites, including hookworms,” she noted.

“We are seeing treatment successes at Ohio State by following dogs that are initially hookworm fecal positive. We document treatment success through subsequent fecal examinations. Dogs are treated and then, 12 to 14 days later, we get a follow-up fecal. If it cleared, we have success. If it did not, then we check what dewormer was used and if we need to provide additional treatment.”

“There's a hierarchy of protocols we are currently using,” said Marsh, “such as if we need to use a combination therapy of three different classes of dewormers or an alternative treatment. Pablo Jimenez Castro, DVM, associate chair of the task force, provided laboratory-based studies to support this approach.”

If a dog is positive for hookworm

egg shedding, it needs to be monitored and rechecked, she said. Veterinarians also need to learn whether their clients are buying dewormers off the internet and whether they are being sourced from reputable outlets.

Marsh said she sees more challenges ahead. Appropriate health and diagnostic screening need to be done for dogs involved in cross-country or international trips or rehomed after natural catastrophes since some places have parasites other areas do not. In addition, climate change is allowing endo- and ectoparasites to become established in new areas, she noted, pointing out that Ohio now has nine fewer frost days.

Artificial Intelligence

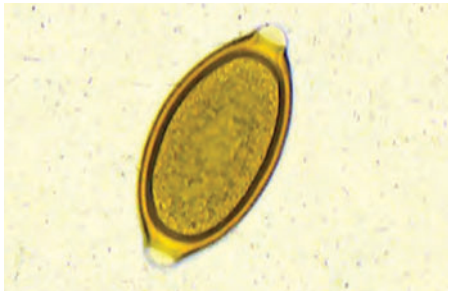
Zoetis' Vetscan Imagyst uses the deep learning of artificial intelligence as its innovation to meet parasite challenges. The first-of-its-kind technology allows for quick identification of specific parasite eggs in fecal samples, thus saving time and effort for technicians.



Richard E. Goldstein, DVM, DACVIM (SAIM), DECVIM-CA

“One of the things we have learned from COVID is that time is everything for technicians and veterinarians. And now there is such a shortage of technicians,” said

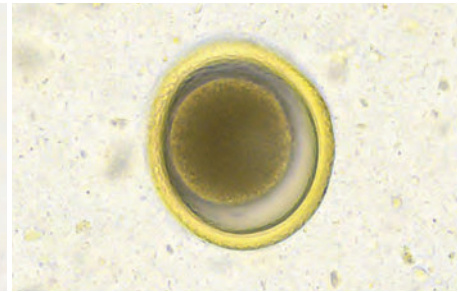
Richard E. Goldstein, DVM, DACVIM (SAIM), DECVIM-CA, vice president and chief medical officer at Zoetis Global Diagnostics, Medical Affairs. “This deep learning algorithm gives us real-time results and saves an estimated 15 minutes for a technician on every sample.”



Trichuris Parasite



Double Cystisospora Parasite



Toxocara Parasite

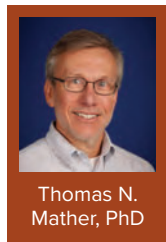
With AAHA recommending frequent testing for parasites, it's a lot for veterinarians to accomplish, said Goldstein. The Vetscan Imagyst can do the fecal at the level of a parasitologist within 10 minutes at the veterinary hospital. It uses a contained sample, with one gram put in a tube for two minutes and one drop put on a slide into the device.

“Five to seven minutes later, the results are in, and you can talk to the owner in real time. If the pet is negative, that's great. If it has giardia, hookworms, roundworms, and such, you can take care of that at the time, helping with compliance issues and giving you back tech time.”

The algorithm lives in the cloud, not on the device itself. Upgraded periodically and taught by board-certified parasitologists, the algorithm reviews thousands of identified images to learn to differentiate. It can identify 99% of the parasites seen in the US, said Goldstein.

Just-in-Time Learning

Flipping tick-bite prevention education from a just-in-case approach to a just-in-time approach is the inspiration behind innovative tick efforts this spring.



Thomas N. Mather, PhD

“What we've learned from TickSpotters, our nationwide crowd-sourced tick survey, is that while most people learn about ticks and

tick-bite prevention using just-in-case approaches such as lectures, brochures, and media reports when they actually have a tick encounter, it can be difficult to accurately recall that information,” explained Thomas N. Mather, PhD, professor and director of the Center for Vector-Borne Diseases, University of Rhode Island.

He said TickSpotters is a good example because there is never going to be someone more interested in potentially taking action than the person who has just taken a tick off their pet or child. With TickSpotters, a person who encounters a tick, snaps a photo, and submits it then receives the identification and best next actions to take.

The first venture launched this spring is a tick warning sign with a twist—a QR code, a bar code that can be scanned by a smartphone for information.

“Before the pandemic, I would have said that this is stupid because no

one is going to scan a QR code,” explained Mather. “Well, we have all learned how to scan a QR code because we were buying takeout food or looking at drink menus. It seems like the timing is right.”

A typical tick warning sign may include such unactionable items as wear light-colored clothing.

“Then the person looks down at his blue jeans and says ‘Aw, crap. I'm sunk.’ Or the sign advises to apply repellants, but no one has brought any along. These are not in-the-moment actions one can take,” said Mather.

On the other hand, a QR code on a sign can link a person to the BeReadyForTicks landing page containing prioritized, regionalized information.

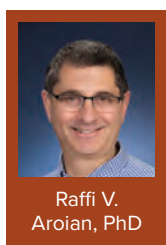
Another just-in-time innovation the team is working on is customizable dog ID tag blanks already etched on the back with a high-resolution BeReadyForTicks QR code. It links owners with best next actions for their most likely scenario—just finding a tick on their pet.

The QR on the tag will guide the owner to confirming the tick's identification but also link the pet's

tick protection with a message for the owner. “You protect me once a month. Now, protect yourself by spraying your shoes with permethrin once a month.”

Paraprobiotics

Safety concerns prompted studies into a new avenue of attack against gastrointestinal nematodes that affect humans and animals—paraprobiotics.



Cry5B IBaCC offers a potentially new product to address the growing threat of gastrointestinal worms in animal and human health.

The engineered

bacterium that safely treats hookworms in animal models now just needs veterinary and human health pharmaceutical development partners to push it forward, according to Raffi V. Aroian, PhD, professor of molecular medicine at University of Massachusetts Chan Medical School.

Aroian, who developed this technology with his colleague and partner Professor Gary Ostroff, PhD, explained that this paraprobiotic is not a small-molecule or chemical anthelmintic but a crystal protein from *Bacillus thuringiensis*, a natural soil bacteria family. Proteins like it from this bacterium have been used for more than 60 years in environmental applications against insects.

Studies of the bacterium show it is nontoxic, effective, stable at room temperature, and easily delivered, and it can be mass produced by a scalable process that can be made inexpensively anywhere in the world, he noted.



Shridula Hegde, first year veterinary student (left); Antoinette Marsh, associate professor (center); and Cristina Iazbik, blood bank staff; who are part of an OSU CVM team investigating drug-resistant canine hookworms, along with Caroline, a recently retired racing greyhound, who is being evaluated for parasite shedding.

Unlike drugs, Cry5B IBaCC works by a different mechanism and has been shown to attack a wide variety of gastrointestinal worms, said Ostroff. He explained that the benefits are provided as a result of worm-selective interactions between the paraprobiotics, the crystal protein payload, and nematode parasite gastrointestinal system.

“While a probiotic is a live microorganism that confers a health benefit when you take it, a paraprobiotic is a dead microorganism that confers a health benefit when taken,” said Aroian. “Even though probiotics are considered safe, within any given population there’s always a population of humans or animals that will adversely react to a live bacterium. Even for the safest probiotics, that’s true. So a paraprobiotic, a dead probiotic, removes that concern.

“When you kill bacteria, you also greatly reduce any concerns about a shelf life. You put a probiotic on a

shelf and it rapidly loses its vitality. If you give a paraprobiotic, it’s already dead. It can’t lose its vitality. It’s a much more stable product on the shelf.”

Another reason for choosing this avenue is because of environmental contamination issues, he noted. “Because the bacterium is dead, it can’t replicate in the environment so you’re not contaminating the environment with live bacteria. You minimize concerns about an avenue of resistance developing, which is always an issue with deworming drugs because they’re excreted into the feces. There’s always a chance with a drug in the environment at suboptimal concentrations that it helps to develop resistant parasites.” ✨



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