Treating Heartworm Disease in Shelter Dogs: 500+ Cases (and counting!)

Dr. Natalie Isaza

Video Transcript

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[Beginning of Audio]

Facilitator: I want to remind everyone about silencing the cell phones, and since we still are recording all the sessions please hold your questions till the end of the presentations and present your questions to the speaker using one of the microphones in the center aisle so we can capture your question.

And, all of these videos and materials will be available online in a week, and we'll also send you an e-mail informing you of their availability as well as an evaluation form that we really do depend on getting your feedback to help us move forward with planning for future educational events, even though it won't be as the Maddie's Shelter Medicine Conference anymore, as we all move forward to our specialty conference.

So, our first speaker this morning is Dr. Natalie Isaza. She is the clinical service chief and founding faculty member of the Merial Veterinary Community Outreach Program at the University of Florida.

The Veterinary Community Outreach Program was formerly known as the Merial Shelter Medicine Clerkship for our advanced veterinary students, and since its beginning in 2003, she and her students have spayed and neutered over 20,000 animals, and these are animals belonging to local rescue groups. She has treated over 500 dogs for heartworm infection and that is the topic of her presentation this morning. Her service has performed over 1,000 additional surgeries, such as repair fractures and even more exotic surgeries that would have resulted in euthanasia of the dog or cat and all of these efforts have prevented the euthanasia of homeless animals in Alachua County and surrounding counties of Florida.

So please help me welcome Dr. Natalie Isaza. *[Applause]*

Dr. Isaza: Hi everybody; can you hear me? Good, good. I am sorry I wasn't here for the beginning of the conference but could I get a show of hands of how many veterinarians we have here? Oh, most of you.

How about vet students? How about shelter personnel? Okay, so I'm assuming that all of you or at least some of you have treated heartworm in your shelters, correct?

So my talk today is going to be about the shelter heartworm treatment that we do, and it might be different than what you guys do and I want to kind of preface my talk by saying that, because we are in a university and we have sort of other issues that we have to deal with when it comes to treating dogs with heartworm. So, I'll get started.

You guys all know this: that the heartworm disease is a big, big probably in shelter dogs and cats. We are not going to be talking about cats today; I'm going to leave that to people that have better expertise with treating heartworm in cats, because I certainly don't.

But as you all know, especially if you're from Florida or from the South, there are a lot of rural shelters in our area that don't have the resources to treat dogs with heartworm, and some of them don't even have the resources to even test these animals. Because of that we have many, many animals that are euthanized every year in animal shelters just because of their heartworm positive status.

To sort of complicate all of that we have these new findings about resistance and I'm sure all of you have heard about that – I'm going to talk about that a little bit in my talk as well – and this is mainly seen in heartworms in the Mississippi Delta area of the country but the fear is that that is then going to spread to other areas of the country, particularly in the deep South, and again, most heartworm experts think that is due to the use of "slow-kill" therapies in shelter dogs, and I know a lot of shelter veterinarians use the slow-kill method. I'm going to talk a little bit about that at the end as well because I think that there's two different methods of "slow-kill;" one is a little bit more likely to have better outcome than the other.

So today in this lecture we're going to talk about heartworm disease, the incidence in the United States; we're going to talk about the heartworm lifecycle, refresh you guys' memories, I know my students have some difficulty remembering all of the little nuances of the heartworm life cycle.

We're going to discuss the recommendations for diagnosis therapy and prevention from the American Heartworm Society, so these are very brand-new guidelines that just came out in January of this year; we're

going to talk a little bit also about some of the strategies that shelters in the United States are using; we're going to talk about what we do, specifically, in our community outreach program at UF; and then, I'm going to just take some time at the end to talk about a few little cases that we've seen over the years that have been a little bit daunting and maybe a little bit confusing for me.

So, to get started we're going to talk a little bit about heartworm disease, remember that that is – that heartworm is actually caused by the filarial parasite, Dirofilaria immitis. It's transmitted by infected mosquitoes primarily of the genus Aedes, so this is like Aedes aegypti that spreads yellow fever and all of those other things – it's also spreading heartworm around.

There are two primary vectors in the United States but there are actually about 50 known vectors of heartworm in the United States; it's been found in all 50 states, but it is not known to be transmitted in Alaska. That just means that some dogs have shown up positive, but it hasn't completed the life cycle in the mosquito in Alaska.

So we know that dogs are the definitive hosts, and there are also some wild canids that serve as reservoirs, like coyotes and, of course otters, things like that, domestic wolves – if you're in that area of the country that actually – or, not domestic wolves, wild wolves, sorry – if you're in that area of the country that has wolves. Cats and ferrets are also considered potential hosts of heartworm but they aren't really perfect hosts of the disease and so they don't really have the classic signs that we see in dogs.

And then we do know that in shelter dogs, we can have prevalence as high as 70 percent in endemic areas. So you can see from this map, remember that – that incidence is, this is a – this is a prevalence map, so the prevalence is actually the number of cases in an area per 1,000 dogs, and incidence is actually the number of new cases. So this is our incidence map and this was just released this week.

I don't know if any of you guys are members of the American Heartworm Society? If you aren't, it's a really great resource for you. This map was just released, I think on Friday, and so this just shows the number of new cases in the United States since the last map they put out, which was in 2010.

You can see what we all know is in the South it's pretty bad because we have optimal temperature, climate, and the mosquito hosts to spread this disease around. We also have a lot of reservoir dogs, stray dogs and wild canids.

So, a little bit about the clinical signs. Remember that it's going to depend on the severity and the duration of infection, so if you have an animal that's been diagnosed and maybe has had heartworm for a long time, they may have more severe clinical signs, although I've seen dogs that have had maybe only a couple of years old that have Caval Syndrome. It really just depends on, you know, how many worms these animals have and the length of the time that the worms have been there. And also it really does impact the disease, if the animal exercises.

If you have an animal that's really active and they have a high worm burden, they are more likely to have more severe heartworm disease just because the pulmonary vessels are damaged every time that animal exercises. So you might find a heart murmur; I will tell you that most of the dogs that we see in our practice don't have heart murmurs, but that is a common finding in some practices and that's due to tricuspid insufficiency.

They may or may not have a gallop rhythm, so there's some electrical disturbances due to the heartworm. You might see if the animal is in right heart failure; you might see some jugular distension; you might see some cranial organomegaly; and they, sometimes, if they're going to be – and have Caval Syndrome – then they're going to have some ascites fluid built up so they're going to have this classic potbellied appearance.

Remember that even dogs that don't have, necessarily, severe clinical signs can still develop a Pulmonary Thromboembolism – so that's when a little piece of the worm breaks off and then lodges in the lung parenchyma, and that can cause Hemoptysis and it can also cause sudden death. So that's one of the reasons that we really, really stress exercise restriction in dogs that are undergoing heartworm treatment.

And remember this is really important: that the vast majority of dogs that we see are going to be asymptomatic; they're going to be young dogs; and I'm sure that's probably what's going on in your practices as well. And that's why – another reason it seems so heartbreaking to euthanize an animal simply because of a heartworm positive test especially when they're not clinical and they seem so happy and healthy otherwise.

The American Heartworm Society classifies heartworm disease in four different ways, so Class I is typically what we're going to see. And, I'm just going to go by symptoms here. We don't routinely do radiographs and blood work in our practice so you would include some of these lab findings also if you're classifying animals that way, if you're in private practice. But a Class I dog would be a dog that has a positive test but is totally asymptomatic.

A Class II dog would have a positive heartworm test but maybe have mild exercise intolerance and then the Class III dog is going to also have a positive test and have moderate to severe exercise intolerance and probably a cough as well.

And Class IV dogs are dogs that have Caval Syndrome so that's when they have worms that are blocking the vena cava essentially and they've developed ascetics and so these dogs are probably in heart failure and are really not candidates for being treated with immiticide therapy.

So back to vet school, everybody, and you guys that aren't in vet school… The heartworm life cycle, it does occur in two different animals. Obviously, it's going to occur in the mosquito and then also in the primary host of the dog, so the mosquito will bite the infected dog and they will ingest the microfilaria with their blood meal so that's the L1 form of the parasite.

In the mosquito the L1 will develop to L3, and that just takes anywhere from 10 to 17 days, and what happens is the L1 will then migrate back into the hind gut of the mosquito, which are the malpighian tubules. So just a little known fact about me, you guys, I was an etymology major in college before I went to vet school, so I know a little bit about insect anatomy; isn't that kind of creepy? *[Laughs]*

Anyway, the malpighian tubules is the hindgut of the mosquito and once they've developed to L3 they're going to migrate forward to the mouth parts, the mosquito is going to take a blood meal on the infected – on the dog, maybe not even infected dog, and the L3 or the infective stage of the parasite, and they're going to migrate through that puncture wound so they're not actually injected by the mosquito. They actually migrate in the blood through that puncture wound and go into the tissue of the dog.

So in the dog they go through L3 all the way to L5, and L5 can be a juvenile adult and it takes about 120 days for that animal, then, or for that worm, then, to become a reproducing L5 adult. And then the cycle starts all over again when that adult L5 starts producing microfilariae; then, again that mosquito is going to pick that up and the cycle continues.

So a couple of key points here is that the L1 to L3 stage of that life cycle is really very temperature dependent and so in colder areas that's just not going to happen and that's why a lot of people have gone to maybe just treating their dogs for six or eight months out of the year with heartworm prevention, and then in the wintertime they just stop it. We know from climate change that that's, you know, probably not the best way to do it because we had some really crazy weather this last winter and we know

that certainly the temperatures can be higher in cold areas when they're not supposed to be high.

So the other thing that's happened is that in large cities where you have lots of tall buildings it tends to trap heat and so although the climate might be cold in those little pockets of urban development you may have enough warmth and heat for that microfilariae to continue to develop to an L3 within the mosquito.

And then the other problem that we have is a lot of these mosquito vectors actually overwinter as adults so then they can resume that whole development and, again, like I said before, the development to the L3 within the mosquito usually takes about 10 to 14-17 days and that's only if you have ambient temperature and the correct humidity and so unfortunately here in the South we tend to have that year-round.

They have been – there had been studies that show that sampling of mosquitoes around kennel areas, around shelter areas, the infection rate can be as high as 70 percent in endemic areas. So as I mentioned before in the dog, the L3 larvae enter the puncture wound that's left by the mosquito and then in the dog the L3 will mature to L4 which is the precursor to the juvenile L5 and that takes about three to 12 days and both of these life cycles actually travel within the muscle fibers and so they're not really going into the vessels at this point and then L4s will become the L5, the young L5, about 50 to 70 days after the infection and the L5s are the ones that then penetrate through the muscle in the veins and enter the pulmonary circulation and that is about, you know, 67-85 days post-infection.

Then the L5s actually take a little time to mature; it takes them about four months post-infection before they are mature enough to mate and produce microfilariae, but the earliest that we can actually detect antigen in the heartworm positive dog with the current ELISA tests that are on the market now is about five months post-infection.

But the microfilariae begins circulation about six months after infection and, really and truly, it's probably more likely seven to nine months, so that's one reason we wait to test dogs because we wouldn't be able to detect it otherwise.

So a couple of interesting facts that I thought were kind of neat is that the adult heartworms, if left untreated, can actually live for five to seven years in the dog, and the microfilariae, which really surprised me, can live for one to two years, and that's without any kind of treatment.

In the cat, like I said, the cat is not really a normal host for heartworm – the adult heartworms only live for about two to three years and you very, very rarely see circulating microfilariae in cats.

So, how are we going to diagnose this? Well, these are the recommendations of the American Heartworm Society: they recommend both an antigen test and a microfilariae test. How many of you guys are doing both? How many of you are just doing microfilariae? How many of you are doing antigen? Okay.

We're just doing antigen, also, so I kind of learned something when I was going through these guidelines that maybe we need to step up and – and check for microfilariae, too, and I'll go into why that's important. So, first, a little bit about antigen tests.

Remember that these antigen tests that are currently on the market detect only the presence of female worms, so if you have an all-male worm infection you're not – you're going to get a negative test, okay? And the other thing that's important to know is that if you have low female numbers, so you have maybe a little Chihuahua that's maybe got one female worm and four female – four male worms – you may not have antigenemia so you may get a negative test because if there's not enough females, obviously, to produce antigen then you're not going to actually detect it.

And the other thing that's interesting: if you have a dog that's on a heartworm preventative like Heartgard® or Interceptor, one of these macrocyclic lactones that is actually going to also suppress antigenemia; so if you have a dog that you're treating with "slow-kill," and you've got them on these, just this particular drug and nothing else, then you may have a negative test that's maybe not really, truly negative.

So it's not necessary to test dogs until about seven months and that's because the microfilariae. Most of the adults are not really going to be producing any microfilariae or any antigen until about six months and so the Heartworm Society (and this also surprised me because we always test at six months) but they said seven months is really the optimal time to test if you're going to test a puppy, say. And then, there are many tests available: you guys, I'm sure, know the IDEXX Snap® test is really popular but there's also some other, you know, more up-and-coming tests that are maybe less expensive and also maybe a little bit more sensitive and specific.

So there's the ELISA test; the ELISA test that was first developed was the DiroCHEK® test *[Clears Throat]* and that was developed back in the boy, like I think it was the mid-'80s by actually Dr. Charlie Courtney who was

at UF for many, many years and now they've got some really fancy ones, these chromatographic immunoassay tests and these are all bench top tests.

These tests are actually designed to identify most of the occult infections and those are infections where maybe the adults are not producing microfilariae yet, so you might not necessarily have a microfilaremia, but you will have a positive test because of the presence of the adult female worm.

And most of these tests are nearly 100 percent specific and that means that if they're negative, they're really going to be negative. Okay? Most have a very, very high sensitivity and that's actually the true positive rate, so that just means if they're positive on the test – the likelihood that they're really positive is also really high. That sensitivity on these tests are actually going to vary depending on the amount of worms the animal has in their system.

And another thing that a lot of people do (at least I notice a lot of vets and some of the vet techs I work with have done) is look at the color change on the test to determine the worm burden. And you can't really do that because you may have three female worms that are making everything really bright blue or you may have one female worm and 10 male worms and it's very pale blue, so remember we're only looking at female antigens, so just because it's bright blue doesn't mean there's a ton of worms there.

Another thing I found really interesting when I was going through that AHS guidelines is that you should never record an animal as being negative. I guess this is just to cover yourself, right? Because you never really know; they might have a low worm burden, right, so you should always record it as "NAD," or "No Antigen Detected," okay, because none of these tests are 100 percent.

So, one of my colleagues at the University of Florida, Dr. Maureen Long, has done a lot of work lately with heartworm and actually looking at the different heartworm tests and this is some data that she presented at the American Heartworm Society Meeting in January of this year.

She actually took five of the most commonly used bench top tests and compared them, compared their sensitivity and specificity, so she looked at the Antigen Rapid One-Step, the Snap® Heartworm Test by IDEXX, the WITNESS® Test by Zoetis, VetScan, which is an Abaxis test, and then the Solo Step® test by Heska, and she actually compared them.

What you can see here? This is just the overall sensitivity (and sensitivity, remember, that's going to check, test the true positives) and you can see it's pretty high on all of them across the board. So 96 percent; that's pretty good, so you're pretty confident when you use these tests that if you get a positive you can almost for sure say that it truly is positive.

But when we looked at the sensitivity by worm burden and this is by, you know, the number of worms that the animal actually has, you can see that the favorite here, which is the Snap® Test – how many of you guys use Snap®? You can see the sensitivity goes way down on that. And so I would just caution you just to be extra careful because you may have a dog with a low worm burden and you may get a negative test.

This actually happened to us a couple of weeks ago with one of our heartworm treatments: we had a dog from the shelter that tested positive on the DiroCHEK® at the shelter, which is a microwell test, and I'll talk about that in a minute, and came in for heartworm treatment and she – the rescue group - had taken the dog to their veterinarian and tested with an IDEXX Snap® and it was negative.

So, you know, which one do you believe at that point? So I just want you guys to be aware that maybe, you know, if you have a young dog with a low worm burden you may get a negative test.
[Clears Throat] So these microwell tests were the ones that were first developed and how many of you guys are using DiroCHEK® or PetCheck? Any of you in your shelters?

So these, I think, are really a great idea for shelters because they – DiroCHEK® is actually considered the gold standard, although I think now, with some of these newer bench top tests, they're really sensitive and specific so they may be performing as well as DiroCHEK® but DiroCHEK® is a well test, so you can actually do a lot of dogs at one time.

I know at our shelter in Alachua County they use this test and, you know, it's a 96 well plate; so theoretically you could test 94 dogs because you have a positive control well and a negative control well. You could do 94 dogs at once and so that's pennies versus, you know, I don't know how much - $10.00 or so is what a Snap® test goes for?

But, you know, the problem with these tests is they do require a lot of steps, so there's some technical acumen that's a little that's necessary to run these, and so that might be a limiting factor if you're short staffed or if you don't have the expertise – the person that can actually run these. The techs at our shelter have been doing them for years and so they've got it down to a science.

So, as I mentioned before with microfilariae testing that the American Heartworm Society actually recommends that we test animals both with ELISA and also with a microfilariae test. Now there are less than 1 percent of infections that are patent and that just means that you're going to have circulating microfilariae without antigenemia, so it's really, really low probability that you're going to have a negative ELISA test and a positive microfilariae test.

So, because of this you don't want to just test for microfilariae alone, okay? Because you want to make sure that you do detect the adult worms if they're there. So, why do we want to test for microfilariae? Well, it's going to validate our test results, our serologic test results that we've done. It also identifies the patient as a reservoir, or potential reservoir, for infection to other dogs and then also if you have a very high microfilariae burden it's going to maybe impact the way you choose to treat those microfilariae or maybe what you choose to use for heartworm prevention in that particular dog.

Remember that certain heartworm preventions that we can use can actually precipitate a really severe reaction in dogs because it's going to kill those microfilariae very quickly and cause anaphylaxis. So, there's a couple ways for microfilariae testing: you can take a buffy coat and just look and sometimes you can actually just see those little things wriggling around in the buffy coat.

You can do a blood smear, but remember: just doing a blood smear is going to be insensitive for actually detecting very, very low numbers of microfilariae, so it's not really going to give you an accurate count on how microfilaremic your dog is.

And then it's also going to be confused with, and (I can't really pronounce that) I'm going to say *Dipetalonema* because that's what I'm used to, but *Dipetalonema* is the non-pathogenic filarial worm of dogs that lives in the cutaneous tissues. And so, this picture actually depicts the difference between *Dipetalonema*, which is the top worm, which is the really skinny filarial, microfilariae, and then dirofilaria, which is on the bottom.

So the modified Knott's Test actually allows you to differentiate those two because it's going to stain them and it's going to actually let you compare those species.

So as you guys all know it's really, really important to have all dogs especially in this area of the country, on heartworm preventative. The American Heartworm Society as you guys all know probably, they do recommend that dogs are on year-round heartworm treatment regardless of where they live in the United States. Puppies should actually be given

their dose – first dose – if you're in a shelter, no later than eight weeks of age.

Most of these heartworm preventatives are labeled for six to seven weeks, so make sure as soon as you get a puppy that you go ahead and give them that preventative dose. So if you give a dose after eight weeks of age, so say you have a 15-week-old puppy and you give that dose then you want to make sure that you test that dog six months after that initial dose because, remember, that dog may have been bitten by a mosquito and may have been infected before you gave him that heartworm prevention.

You want to make sure that you can detect that so if it's going to be adopted you might want to put in your, you know, handout to go home that you recommend that animal be tested six months after you gave that initial medication.

As you guys know, then, that have dogs and actually have your dogs on year-round prevention it's always a good idea to check your dog every year just to make sure that that prevention is working. And what's interesting is that if you reduce the reservoir population of heartworm in a community you actually decrease the prevalence of infection in unprotected dogs.

So it's sort of like kids that get vaccinated for flu in Alachua County: all of our school kids get vaccinated with intranasal flu vaccine and it's been shown even though the adults don't get vaccinated the incidence of flu is actually really, really low in our county.

So it's the same kind of thing; if you keep dogs on prevention and keep that reservoir population low it's going to actually protect dogs that aren't on any prevention at all. *[Clears Throat]*

So a little bit about some of the preventatives: macrocyclic lactones are what we typically use for all of our prevention and that's what's in probably every commercial preparation of heartworm preventative that we have, so the different lactones – macrocyclic lactones are ivermectin, milbemycin oxime, moxidectin and selamectin and you guys might remember or know these as Heartgard®, Interceptor, Advantage Multi and selamectin as Revolution.

What's interesting is this drug actually affects all stages of the heartworm life cycle, so L1 all the way up to the adults; it just affects them differently. Some stages are more sensitive than others to these drugs. These are extremely safe drugs when used according to label directions. Most of these, for instance, the Heartgard®, is about six micrograms per kilogram of Ivermectin in one, 51-100 pound cube – that's about 256

micrograms of Ivermectin; so it's still a very, very low dose, safe for collies and other herding breeds.

And then most of these also have a 30-day dosing interval for both oral and topical products. So for oral administration we have the Ivermectin, Heart products like Heartgard®. We have IVERHART MAX® and we have milbemycin, which is Interceptor. Topically, we have the moxidectin products, which are Advantage Multi and then selamectin, which is Revolution, and then we also have the parental drug moxidectin, which is ProHeart 6. Are any of you guys using ProHeart 6?

This was a drug that was available back in the '90s and was taken off the market because some dogs had some – there were some deaths associated with it, but it's been re-researched and more trials have been done and it's been re-released. So this is actually good for six months once it's been injected it's like a *[inaudible]* shot; it's been shown to be really effective.

So a lot of shelters are just going to use oral Ivermectin, so *[inaudible]* percent. How many of you guys are using that for heartworm prevention?

I don't think there's anything wrong with that, but just remember that it is off-label so – and you do need to be careful with it because the dose is so low, it's five to six micrograms per kilogram. It's really just such a miniscule amount. A lot of times you have to dilute that with something just to get enough volume in your syringe and you have to be really careful when you're dosing herding breeds with it. You don't want to – you know, you want somebody that knows what they're doing when they're figuring out these doses to go out in the kennel and give this. You don't want somebody just drawing up some indiscriminate amount of Ivermectin and sticking it in a collie's mouth.

[Clears Throat] So, as I mentioned before, all stages of the heartworm are actually susceptible to these macrocyclic lactones, but the L4 worm, which is the one that's hanging out in the tissue, and the juvenile worms, which are the young L5s, they have less susceptibility. So we have this window of susceptibility here that you guys probably know about and we're going to talk about strategies to try to trick the heartworm so that we can get the most out of our heartworm treatment by using this window.

So, a little bit about resistance: you guys have all heard about this, right? How the shelter vets are to blame for this because we're all using "slow-kill," right? Has everybody heard this? Yeah. Well, this is – actually in 2011 was first reported in "Veterinary Parasitology" by the group at Auburn and there was a dog that was treated with immiticide therapy. It was a dog – a Katrina dog actually, that was treated with immiticide therapy and then after that was – went through treatment to kill the

microfilariae. And this dog went through probably about 20 different treatments and was still microfilaremic, and so they did a little bit of further testing and they discovered that they had a resistant microfilariae on their hands and they called this "the MP3 Isolate."

So this particular microfilariae actually has an allele on the P glycol protein gene that actually differs from the general population of microfilariae and it has been shown to have decreased susceptibility to monthly doses of ivermectin, milbemycin, which is Interceptor and selamectin, which is Revolution.

But interestingly it is susceptible to three consecutive monthly doses of milbemycin or a single dose of moxidectin, so the single dose of moxidectin, Advantage Multi is moxidectin. So, if you guys are using that in your shelter then you're probably – and you're in the endemic area where this is a problem, in the Mississippi Delta, then you're probably going to be okay.

But it is resistant to our Heartgard® and Interceptor and just topical Revolution.

So what has AHS recommend for adult therapy if you have a heartworm positive dog? Well, they recommend, of course, that we use immiticide, which is melarsomine dihydrochloride and/or if you have Caval Syndrome they do recommend that you remove the worms.

How many of you have had the guts to remove heartworms from a dog in a shelter that's in Caval Syndrome?

You know I was reading this and I'm thinking, "I could do that." It's – it doesn't seem – you know I actually worked for Dr. Courtney for years after I graduated from undergrad, before I went to vet school, and Dr. Courtney was one of the gurus of heartworm. He actually worked for a guy named Ron Jackson in St. Augustine back when he first graduated from vet school, and Ron Jackson is the very, very brave private practitioner that first did this surgery.

So what it is is, like, they don't even – they're saying you don't even need to sedate the dog. I don't know, I think maybe sedation, but you don't need to put him under anesthesia; in fact you don't want to because then the worms get harder to grab.

They move, you know, and so he actually – this just blows my mind but I'm thinking I can do that. I see Kim says she could do it, too – you did it? Oh, but no, so what you do is you ligate the jugular so you do a cut down to the jugular, you ligate it, cranial to where you're going to make

your incision. Then you make your incision into the jugular and you feed an alligator catheter so – or alligator forceps, one of those long forceps with the little alligator things down into the thoracic then you just pull and you grab. And you do that until you don't get any more worms. After about three or four tries with no worms then you stop and then you ligate below where you made your incision, so they lose a jugular on that side, but they've gotten all the heartworms out.

So I don't know, I mean I think that if I were faced with that and the dog was going to die and I didn't have any other resources I might do it. I mean why not, you know? Give them a shot at life. Anyway, just a little digression there, sorry.

So there's some adjunctive therapies also that are recommended by the American Heartworm Society. Steroids, and that's kind of a new thing for people in endemic areas; they're recommending the use of steroids, NSAIDs and aspirin, aspirin not so much, NSAIDs for pain at the injection site.

Doxycycline – and we're going to talk a little bit more about doxycycline and equivalent drugs later on. And then macrocyclic lactones and then the combination of macrocyclic lactones with doxycycline, which is actually a really, really great combo.

So, first about immiticide. Remember from your vet school that immiticide is an arsenic compound and it's only delivered by deep IM injection. It's preferred, actually, it's only really recommended to be given between L3 and L5 in the epaxial muscles. If you give it elsewhere and you have a problem, Meriel's probably not going to help you out, but if you give it in this area and you give it correctly and you have an issue then they may be willing to help out with, you know, post-treatment if there's a problem.

Caparsolate was what we used when I was in vet school. I think in the middle-'90s was when immiticide came out, but caparsolate was nasty if you guys, you older vets out there, remember that. You had to give that IV and I remember reading at the time that actually the mortality rate was a lot higher than actually the morbidity rate when you used that and it doesn't surprise me because you're giving arsenic IV, so thank goodness now we have something that's a little safer.

So this drug is only going to kill the adult worms, it doesn't have any effect on worms – any of the worm stages under four months. You can use a two injection protocol, which is one injection 24 hours apart, or two injections 24 hours apart or three injections, which is one injection and you wait a month and then give two more 24 hours apart.

Of course the AHS recommends that you use a three-dose protocol for all positive dogs because it results in a little bit more gradual kill of the worms, so they don't all die at once and potentially have – create a big reaction and pulmonary thromboembolism.

So remember, these arsenic compounds are – they're arsenic – so they don't have a very great margin of safety. In dogs the dose is 2 ½ milligrams per kilogram but the LD50 in dogs so this is what kills dogs is 7.5 mg/kg so if you're doing multiple treatments at once make sure that your technician labels the correct dose.

You don't want to overdose a dog because you accidentally grabbed the wrong syringe if you're treating, you know, five or six dogs and that's what we do sometimes – we have to be really careful because we have all these students in there and they're grabbing syringes and so that's one of the big things, and I'm a real stickler about making sure everything is labeled, everybody double-checks, reads the dose before they actually inject it because we don't want to inadvertently give the wrong dose.

So, it is one of the only two "black label" drugs in veterinary medicine, and black label is like *[Clears Throat]* the 2010 equivalent of "skull and crossbones," so back in, you know, the 1700s we used skull and crossbones; now we use black label.

Now it's not the only black label drug that we use in veterinary medicine, because certainly we use chemotherapeutic agents to treat cancer and those are all black label, but these are the only – there are only two that are actually labeled for veterinary medicine that are black label.

One is Immiticide® and does anybody know the other one?

Metacam®, yeah, so meloxicam it came out with a new label last year because of the potential to cause kidney failure in cats. So the complications that you can see with this drug and probably by far the most common is pain and swelling at the injection site. You can also have ataxic hemiparesis or even paralysis of the pelvic limbs.

This is a CT of a dog that got an injection and I don't know if you guys can tell but the spinal cord is shifted over a little bit; this dog developed some severe neurologic problems following treatment with adulticide and I've actually not had – fortunately not had anything like this, but I did have one of my rescue groups whose own personal dog, the director of the rescue, her own personal dog was treated and developed a huge swelling at the injection site, about the size of a softball. This was a Golden Retriever and the injection was very, very close to the spinal cord and the

dog developed an ascending paralysis actually over about a week and it got to the point where the dog couldn't walk or move at all and the dog had to be carried outside and the bladder expressed.

They were just about to euthanize her and it started to resolve. So when I talked to Merial about this because I was, you know, oh my God, I can't believe, you know, this happened and they didn't seem surprised at all; they just said – they were actually surprised that the dog survived.

So just be really careful when you inject it. I'm very, very much a stickler with our students about injecting with a doctor watching and making sure that they are far enough away from the spinal cord, and some of those spinal nerves that come off – you'll know if you hit those spinal nerves and some of you probably have – those dogs will scream. You know the minute the needle hits, they'll scream and then you move it up maybe a half a centimeter and they're fine.

So if they do scream and start, you know, moving – don't inject it because that's when you get those big giant hard knots that form.

So, later, after the treatment things that can happen: fever, lethargy and inappetence is usually 24 to 48 hours after the initial injection. For this reason, sometimes we'll send dogs home with some NSAIDs just to make them feel more comfortable. They might develop a cough as some of those worms die and the pieces break off; they could develop a pulmonary thromboembolism and then the worst case scenario of sudden death, and that's usually if, you know, it can happen certainly when animals are exercising, but I've heard of it happening in dogs that are just sitting in a crate.

So, you know, that's something to warn people about especially if your dogs are going out to foster. Make sure that they understand the importance of restricting exercise and even if you do restrict exercise you still may have something bad happen.

So, this is a little bit hard to read but this is just a summary of some of the adverse reactions that were seen in clinical field trials. You can see the injection site reactions, coughing and gagging and then inappetence and anorexia were probably the highest or the most reported clinical outcomes of treating these, and then some of the others are much less.

So, this is, again, looking at the injection site reaction and what you're seeing, whether it's swelling or a seroma or some of these hard knots that form or tenderness and stiffness of the limb. All right, this is Riley. You want to run that? This was a dog that we treated about a month ago and

the student treated him without a doctor there, which they got yelled at and I cut that part of the tape out, sorry. *[Laughter]*

But this was less than 10 minutes after he was treated. He was treated on the right side, so hopefully –

[Begin Video]

Dr. Isaza: See how he's kind of dragging his foot there? This actually got worse, but I was yelling at the student; I didn't figure you guys want to hear that so but he actually had some CP deficits, like he was just totally dragging his foot and the injection site was about, I don't know, maybe – maybe 30 millimeters away from his – his dorsal spine *[inaudible]*. I just want to reiterate – he actually did fine; we gave him some pain meds, we gave him some tramadol, and he did okay, but, you know, I just – this could have gone the other way so just be really careful when you're injecting to make sure that you're far enough away.

Because then it's a really – it's a painful injection.

So the worst case scenario, of course, is if you treat a dog and they go off to foster and then they – the fosters let them run and play. I actually really tried to find – I had this great video of a dog that we treated and he went off to, he was actually in a kennel situation and they – the rescue happily posted on Facebook how great he was doing three days after his heartworm – his last heartworm treatment, and he's running and chasing a stick and you could see, like, the shaved spots and I just about died, and I just – I called the rescue and I'm like you guys seriously you have to keep this dog quiet.

And, you know, that's another thing: you've got to be really careful and make sure your fosters understand, make sure your clients understand this is super important because you don't want to go to all that time and effort and then have that dog die just because he's exercising and having fun. This is really really hard to do; don't get me wrong, I know. A lot of dogs we treat are really, really happy, young, pit bulls and they want nothing to do – they just want to play and have fun and it's so hard for some of the fosters to keep them quiet but it's so, so important.

So, some of the new therapies that are being advocated by the American Heartworm Society are the use of steroids, and we personally don't use steroids in our practice. How many of you guys are using steroids routinely?

This is particularly important I guess for dogs in endemic areas and the thought is that the dogs are going to have a higher worm burden,

potentially, and that the steroids, a tapering dose of steroids, prior to treatment is going to reduce some of that inflammatory response that you might see when those worms die. So, again, it's actually used to control some of the signs of pulmonary embolism. So, if pieces of worm break off and then you're giving it in a diminished dose, so it's a tapering dose, and again, highly recommended in endemic areas.

NSAIDs – now, aspirin is actually not recommended because a lot of people use it because it's anti-thrombotic effects, but it actually is contraindicated, but you can use NSAIDs like PREVICOX and Rimadyl if you have a really painful dog after injection that's – that's perfectly fine and, you know, we do use these and we use them just very sparingly. We just give them that day and maybe, you know, if they call and say the dog's really painful we may add in, give them another day or two but we don't give it long-term.

Doxycycline: now this is super important. Are you guys using doxy or its equivalent? I know you can't find doxy anymore. So, this is, you know, back in the day when I first started doing slow-kill, and that was when I was at Kansas State back in the '90s, we had a lot of dogs that were working dogs because there was a lot of ranches around and when you told a rancher that their dog wasn't going to be able to work, they didn't like that.

We didn't know a whole lot about what exactly was going on with heartworm – we didn't know Wolbachia even existed, but we used to put dogs on Heartgard® and just monthly, which we now know is probably not the greatest and I'll go into that in a minute. But doxycycline actually kills the obligate intracellular parasite, or bacteria called Wolbachia that lives symbiotically with all stages of the heartworm, with L3 and L4, and so because it's killing the bacteria it also kills L3 and L4 because they live in a symbiotic relationship.

So it also – if you have a dog that has an adult infection, so if there are adult worms present, it actually will suppress microfilariae. It actually kind of reduces their ability to produce offspring, and they actually showed that dogs that – or microfilariae from dogs – that were treated with doxycycline were not actually able to develop to an adult worm, so they might have looked normal as L3s but they never progressed and became adults.

So the recommended dose for doxycycline is 10 mgs per Kg twice a day for four weeks and it's suggested that that be done before you start your adulticide therapy.

We talked a little bit before about the susceptibility gap and I want to just reiterate that a little bit. If you have a dog that's asymptomatic and you have the space and maybe a foster home that can watch this dog it's really a great idea before you treat with adulticide therapy to just put them on the doxycycline regimen and also macrocyclic lactones like Heartgard® or Interceptor before you do the adulticide therapy.

The reason is it's going to give – these worms, these L4 early L5s that are not susceptible are very, very low susceptibility to some of these drugs – it's going to give those worms time to develop to adults. We know that the macrocyclic lactone and the doxycycline together are going to kill the L3s and it's going to suppress the reproduction in the adults, but we have that window, L4 to L5.

So, if you let these go for two to three months then these L3 or these L4-L5, immature L5s, are going to then become adults and you're not going to have any more L4s. When you do your adulticide treatment you're going to be killing all adults; you won't have any L4s left. So if you can do it, this is always recommended because you're going to have probably about – if you use the three-dose protocol you're going to have a 98 to 99 percent kill rate of your adult heartworm versus if you use – if you don't do this you're going to have about a 90 percent.

It does three things. It reduces the new infection, so obviously, if a dog is bitten by an infected mosquito you're giving it a macrocyclic lactone, it's going to take care of that; it's going to kill the susceptible larvae; and it's going to allow those older worms then to mature so that they're going to be more susceptible, then, to the adulticide therapy.

So, this combination – how many of you guys are using this for slow-kill? Anybody? Okay so, the macrocyclic lactones like Heartgard® and doxycycline: together these actually together suppress the production of adult or microfilariae by the adult worm and they also weaken the adult heartworm and then they also in combination actually provide more rapid adulticidal therapy, so it's going to kill the adulticide faster than if you're just using the macrocyclic lactones alone.

And, again, you're going to get rid of the Wolbachia for the reasons I talked about before. And you can use this method in cases where you have a shortage of immiticide, which we are probably going to have here again pretty soon, and also when you have cases where maybe treating is contraindicated. So, you want to go doxycycline, again, 10 mgs per Kg twice a day for four weeks and then concurrently keep them on monthly heartworm prevention.

So, this combination, again, just to reiterate, is more – has more rapid adulticidal therapy than just Ivermectin, so those of you that are using Ivermectin as a "slow-kill," I would suggest that you somehow combine with doxycycline or its equivalent and you're going to get a better outcome.

Oops, sorry about that.

So, there was a study in 2011 of – it was only 11 dogs but they actually showed that dogs that received macrocyclic lactones with Pyrantel, which was probably either IVERHART or Heartgard® - they were given it every 15 days rather than every month but they gave doxycycline at 10 mgs per Kg twice a day for a month. They actually killed 100 percent of the worms at day 300.

So this will kill the adults a lot faster than just the macrocyclic lactone alone, and remember, the life cycle of the adult without being treated is five to seven years.

So, if you look at the AHS guidelines they actually define slow-kill treatment as the use of only the macrocyclic lactones in heartworm positive dogs and remember that by using these drugs we're going to reduce the lifespan of the juvenile and the adults and then the older worms are going to be less susceptible and they're going to take longer to die.

And remember that one of the big issues about heartworm disease is even though you're treating monthly with Heartgard®, those worms are still there and they're still causing damage in the pulmonary vessels and they're, you know, the more the dog exercises, the more severe that damage is going to be.

So if you're treating that way, remember it might take up to a year according to this study, but the former study that was also a doxycycline – so – back in the day when I used to treat these dogs, it would take at least two years for the worms to clear with just using ivermectin products alone, and are you going to restrict a dog's exercise for two years because, really, that's what you would have to do.

That's going to be a really, really tough sell for, like, a new adopter to say well, you can't take your dog to a dog park for two years until we have a negative heartworm test.

The other problem with this is this is the reason why the American Heartworm Society thinks that we're developing resistance, because we're using just these alone without adding doxycycline or its equivalent in *[Clears Throat]* –

So, what do we do after the dog's gone through heartworm therapy, we should perform antigen testing six months after the treatment and for dogs that have been treated immediately after their diagnosis and they weren't given heartworm preventatives until the time of diagnosis or after the adulticide therapy, you want to make sure that you test those dogs about seven months after the initial dose of heartworm prevention.

And you, again, according to American Heartworm Society, you want to test for microfilariae as well as for antigen. So how do we get rid of the microfilariae? I will say in our practice we leave that up to the rescue groups. Fortunately, most of our dogs are on doxycycline or its equivalent and it's been shown that by using these together with macrocyclic lactones it actually eliminates the need for doing the microfilaricidal therapy post treatment, but if you don't use doxycycline, then you're going to want to treat the dogs about three to four weeks after the adulticide therapy and there's a few things that you can use. But remember that it might take a while to eliminate those, so you just need to retest them so it's not like you're going to kill them all with one, you know, the first time.

Remember that Katrina dog? It went through about 10 or 12 weekly treatments and still didn't clear those microfilariae. But this is very important to do if we're talking about eliminating reservoir hosts, so, you know, even though the dog is going to be negative he's still got circulating microfilariae that's potentially infecting, you know, other dogs in the community.

So some of the things that we can use to kill the microfilariae post-treatment is Interceptor, and that used to be an FDA-approved labeled drug to kill microfilariae, and that's just at the label dose, so whatever the dog weighs you just give it a – a dose of the minocycline and that's going to kill the microfilariae. It's really important, too, if you're going to do this, to make sure that you maybe keep the dog in your practice or your shelter for the day to look for signs of anaphylaxis, because that could potentially happen, still, especially if they're very highly microfilaremic.

You can also give Ivermectin at 50 micrograms per kilogram, so that's about 10 times the dose of what you would get in a Heartgard® and that's again the microfilaricidal dose. Be careful in collies – I know the dose is a little higher in collies, but you want to make sure your dose is accurate.

And – and then what's interesting to me, and – and this is actually the – the FDA-approved microfilaricidal drug now is Advantage Multi (or moxidectin) because moxidectin at the labeled dose – actually they've never seen an adverse reaction and it, again, it's the only FDA-approved, so if you guys are using that, then that's great; kudos, because that's going

to take care of the microfilariae without having that anaphylaxis that we see with the other drugs.

So you guys probably know – this has been a hot topic lately on how we treat shelter dogs. Certainly there's a lot of things to consider if you're treating a dog in a shelter. There's certainly financial considerations; it's not cheap to treat dogs for heartworm disease. Certainly the length of stay becomes a welfare issue if the dog has got to stay there a long time to be treated. You know you ideally would want to get them out to foster care, but then you have to trust your foster to make sure they're going to confine them and keep them, you know, from running and being crazy.

And then you have to decide who you're going to treat, so Dr. Polack and Dr. Blackmore, Smith-Blackmore at Animal Rescue League of Boston recently wrote this paper, just an overview, of how to do that and I will say the American Heartworm Society is sensitive to this and they are working on developing some recommendations for shelters and what – what you should do with your heartworm positive dogs.

So there've been a few studies that have looked at how shelters are treating dogs. This study was done in 2011 and this surveyed about almost 1500 animal shelters across the United States. Of those surveyed only about 30 percent even tested their dogs for heartworm infection. These were shelters, I want to point out, that are in the Deep South, so a lot of these shelters are very, very resource-scarce, so we're talking Alabama, Florida, Georgia and Mississippi.

So these are areas where we know heartworm is endemic, but yet only 30 percent of these shelters had the resources to even test the dogs for heartworm. Of the ones that they tested, 39 percent treated every infected dog and I would imagine that probably these – this 39 percent were probably Humane Society – people that had other resources because I know the open admission shelters, at least in our area around Alachua County, the resources are pretty slim and so, they're not going to necessarily be able to treat all the dogs or any of the dogs.

So, 49 percent of those shelters treated only some of the infected dogs and, again, that probably had to do with adoptability, and then 12 percent didn't treat any dogs. So, again, what they were looking at the protocols that were used, and of those 443 shelters that did treat in the Deep South, 43 percent of those used a two-dose injection of Melarsomine; 35 percent used a three-dose injection, and 22 percent used long-term low-dose Ivermectin and that's "slow-kill" and without doxycycline, I assume.

Recently Dr. Brian DiGangi, who's a colleague of mine at UF, sent out a survey, did a shelter vet LISTSERV (and some of you guys might have

answered this), there was actually 104 shelter veterinarians that responded to this survey. We were just trying to look at what shelter vets across the whole United States were doing for heartworm positive dogs.

And I will say that, you know, certainly shelters that probably have more resources, or veterinarians with more resources, were probably more likely to answer this survey than those that didn't because actually some of the results kind of surprised me. So we had 104 shelter veterinarians that responded to the survey and 43 percent of the shelters that we surveyed tested all dogs, 40 – about 49 percent – tested some of the dogs and about 10 percent didn't test any dogs at all.

And that might be, again, they might have been in an area that's not endemic. For heartworm prevention, the majority of the respondents to this LISTSERV survey indicated that they used oral Ivermectin, so just, you know, out of the bottle – oh, sorry, that – that's actually a prevention that's actually labeled for use and then 20 percent used off-label Ivermectin.

So, that was surprising to me, too, because I guess a lot of shelters are not able to afford, you know, some of the topical or the oral treatments. And most of the veterinarians indicated that they had at least some of their heartworm dogs were treated, and most of them made their decisions on whether the dog had behavioral problems, other behavioral problems, or maybe other medical problems that would not make them adoptable.

And interestingly most of the vets that responded used a three-dose protocol, which I kind of found surprising, because that's going to be more expensive and a lot of these shelters reserved the three-dose protocol for dogs under 25 pounds and that might be – and you'll see when I talk about it at the end maybe some of these smaller dogs tend to have more reactions than maybe some of the big ones.

Only 7 percent of the shelters just use Ivermectin alone without doxycycline and this other category indicated that they use doxycycline with monthly Ivermectin, which is actually very good. So some are using adjunctive therapy; 80 percent of the shelters use doxy or its equivalent as well as the macrocyclic lactone and other treatments that they used included non-steroidals and tramadol. Some used Benadryl prior to treatment to hold, you know, to fend off a reaction, and then some were using dexamethasone. And by the way, dexamethasone is not recommended; prednisone is, but dexamethasone actually will affect the ability of the Melarsomine to kill the worms, so prednisone is recommended, dexamethasone is not.

So, what do we do with elective surgeries? This is actually one of my students; he got a surprise. *[Chuckles]* We knew the dog was heartworm positive but when she opened her up – this is – she's holding onto the uterus – this is what popped out. We actually advocate for going ahead and doing those elective surgeries. How many of you are doing elective surgeries prior to treatment?

If the dog is asymptomatic it's probably a safer way to go because as my anesthesiologist, Dr. Pablo – you guys talked to him – I think he talked to you guys yesterday he says, you know, it's better to – to anesthetize an – a healthy worm than a non-healthy worm, so if the worm has been treated already, he's not going to be that healthy and he might break off into pieces and cause an embolism during anesthesia. So it's always better to keep the worms healthy until you spay them and then you can do the treatment.

We typically wait at least a week before we start with our adulticide therapy after surgery, but we always spay and neuter first. So, now what do we do with these shortages? So in 2011 this – this letter on the right is from the American Heartworm Society alerting all veterinarians to the shortage of immiticide, and that was, you know, we thought that was going to be horrible and actually it wasn't too bad.

We went for a few months without it, but then they were able to ramp up production in Europe, and we were able to get it and what's really nice about Merial is they do tend to – they're more willing to give it to shelters than they used to be, and I think they're recognizing they want to first, I think, get rid of this resistance thing. They want to encourage shelters to treat dogs rather than just do the "slow-kill," and we've not really had any difficulty getting this. Have any of you guys had trouble getting it, Melarsomine?

Well, this other letter here, this Merial letter from November, this is telling us that there's going to be a new shortage so I'm just, you know, holding my breath and hoping that we're going to still be able to get it and you know, this is, I think, going to be our life for a while with not just these drugs but a lot of veterinary drugs.

So the American Heartworm Society then came up with a new treatment plan that endorsed a slow-kill – now it's important to note that this is slow-kill using doxycycline and not just macrocyclic lactones alone. So, what they recommend in cases where you have a shortage of immiticide is you want to go ahead and start your heartworm preventative therapy; you want to start your doxycycline therapy, again, the same dose, 10 mgs per Kg twice a day for four weeks, and then you want to repeat this doxycycline once every three months, so one month out of every three

you're going to repeat that doxycycline until you have the availability of Melarsomine.

You want to make sure that you restrict all exercise, again, that's really important in not making the disease worse and you just want to treat the symptomatic dogs palliatively. If you have a dog with Caval Syndrome, get the guts and pull those worms out, and then you want to make sure to re-test before you administer the adulticide, because if you went a long enough time you may have cleared the infection.

So, now we have more shortages – doxycycline used to be free at Publix – breaks my heart – I used to just – we used to dispense it like candy to all of our heartworm positive dogs and now we can't get it anymore. I think I looked on the Publix website and I think it's like $300.00 for 60 days; I don't know, it's crazy. But now the FDA says the shortage has been resolved, but you read the fine print it says no supply, results – or no – no supply issue anticipated so they don't even – they know it's resolved but they don't know when we're going to be able to get it again.

The bottom line is there's probably one factory making it and they don't know when they're going to have enough to distribute it and it's probably never going to be free again, unfortunately.

So what do we do if we don't have doxy? Byron Blagburn, who is at Auburn, gave the *[inaudible]* two doses; we actually use minocycline, which is very, very similar to doxycycline, the disadvantages that we've seen it's the same dose as doxy – the disadvantages we've seen with this is it tends to cause a little bit more nausea and vomiting in our canine patients than maybe doxycycline.

It doesn't really help to give it with food – if they're going to get sick from it then, you know, sometimes we even have to stop the therapy. You can also use Azithromycin or rifampin, those are going to probably be more expensive because they're human drugs and rifampin is actually a drug they use to treat TB in people.

So how much does it cost to treat a dog? Well, at UF (and I'm not sure if at the shelter if our pricing is going to be the same as what you guys pay for Melarsomine through Merial), but our cost is about $10.00 a mL, roughly, so we get five boxes for $486.00, so it's around 10 bucks a mL, so if we do a three-dose protocol on a 22 kilogram dog that's going to cost us around $60.00 just in immiticide.

Again, Publix used to have free doxy. Now it's $342.00 for 60, 100 milligram tablets, so that's not even going to last very long, especially if you're doing that alternative slow-kill, if we run out of Melarsomine. If

we are – minocycline is a little bit cheaper – you can see, roughly, I don't know, it's like 16 cents a tablet or so for a 50 milligram tablet and then Heartgard® we actually get this for free. We're really lucky because we are the Merial Veterinary Community Outreach Program and so Merial provides us Heartgard® so we can then pass that on to our rescue groups, but if we were to buy it, it would be, you know, $53.00, roughly, for a six month's supply.

Ivermectin is by far the cheaper alternative and, you know, just remember to dose it carefully. I am perfectly fine with people using Ivermectin, I think it's probably really smart.

Okay so what are our problems with treating? Well, many of our shelters can't even afford to test the dogs as we've seen from some of this data, and much less treat them, and if they do treat maybe they're just going to use the "slow-kill," which is just the macrocyclic lactone.

Again, remember that they discourage – AHS discourages just the use of that alone. If you're going to do that, you want to make sure you use it with doxy and remember that development of resistance is real and we want to make sure that we don't contribute to that if we can help it.

So what are our choices, then? Well, we cannot treat at all, which really isn't very ethical, and also you're going to cause continuing damage to the pulmonary vessels if we don't treat – the slow-kill method with just the macrocyclic lactones. Again, we're going to have that resistance that we don't want and also the ongoing pulmonary damage. The slow-kill plus doxy is going to be better, but again, you're still going to have to restrict exercise and you're still going to have ongoing damage to the vasculature.

The two dose therapy is going to be much less expensive and it's probably a better choice for asymptomatic dogs and then the three dose therapy is probably going to be the better choice for dogs that are symptomatic. But what do we do, you know? We're damned if we do and damned if we don't, right? We're going to cause resistance if we use slow-kill and we don't have enough money to treat all the dogs with a three-dose protocol, which is what AHS wants.

So, I'm going to thank Julie Levy (and she's not here) for her clandestine attempts at getting this information for me from NAVC but she – this was a talk that was presented by Clarke Atkins and they actually looked at dogs at NC State University that had been treated for heartworm. It was 350 dogs and these were dogs that belonged to low-income families after Hurricane Floyd in 1999. None of these dogs had pre-treatment, blood work or radiographs – any of you doing pre-treatment blood work, radiographs?

So, we do a little bit, but not – we don't do radiographs. And they were using the two-dose protocol, and of the 350 dogs they only had two fatalities; one dog was in chronic heart failure and one had Caval Syndrome, so that's pretty good.

So when do you use the two-dose method? Well, when you have financial concerns, so if you're a shelter this is perfect, right? If you have a young and apparently healthy dog, again, that's shelter, too, right, because most of our dogs are going to be young. They're going to look healthy; they're going to be happy if we have a young dog that we know has had a short exposure. Dogs that have already undergone adulticide therapy, if you have a treatment failure, then you don't want to do a three-treatment protocol. Again, just a two is going to be sufficient.

And then dogs that you can restrict their exercise, so these are all good choices for use in two-dose. So, in that NCSU, this talk, this was pretty expensive. Their two-dose protocol is $360.00; two-dose protocol if they add doxycycline is $415.00. I think this is actually at the hospital itself and they give them a cut rate but still, this is crazy.

A three-dose protocol plus doxy plus a workup is $870.00, you know, most shelters can't afford this; I can't afford this, I couldn't afford to pay for this in my practice. And that doesn't include the heartworm preventative.

So, our program, we actually started in 2003 as the UF Shelter Medicine Program. We had one faculty, which was me; we had zero vet techs and we had five to seven depending on the whim of the Student Services Office how many they wanted to assign to me – five to seven very enthusiastic veterinary students.

We started treating the heartworm positive dogs in Alachua County in 2004, very late 2004, and then from 2004 until now we've treated 565 dogs, so these are just a pie chart of the rescue groups that we've worked with these larger pieces of the pie are Maddie's partners, our community got a grant in 2000 from Maddie's Fund and so these guys are really – we work really closely with them and we do the majority of their treatments for them.

We don't do routine pre-treatment blood work or radiographs; we sometimes do CBC and chemistries on older dogs but not always. Most of our patients, again, just like Heartworm Society says, are asymptomatic.

This is just a copy of our treatment sheet that we use and we do the three-dose protocol on most of our patients. So we actually, before 2006, we

did two-dose protocol – the reason we do three-dose, quite honestly, is because we're at a university and we have all these students and we want, we kind of want a lot of things – we do mimic what goes on in our hospital because we can get the drug fairly cheaply. We just feel more comfortable using this protocol although I used the two-dose protocol for about two and a half years and didn't have any problem.

I think that the two-dose protocol is fine. We transitioned to the three-dose protocol in 2006-2007 for all of our dogs and we've only had one dog that tested positive following treatment and had to be re-treated with two-dose.

So we recommend four weeks of Minocycline. Now, we don't provide this for our rescues. We will provide prescriptions for them, but we don't actually, you know, give it to them for free. We also recommend that they be on concurrent macrocyclic lactone – that they – they're going to get the three-dose protocol, one injection in four weeks and then four weeks later two injections 24 hours apart.

We routinely do give at least one dose of an NSAID at the time of injection and if they need additional pain medication like tramadol we'll prescribe that. We do sedate very, very rarely, very rarely. We actually had to sedate a dog the other day because he was trying to bite us but, we usually just use ACE butorphanol, sometimes Dexdomitor.

But this is how we distract our dogs who we don't need to sedate them – this thing in the middle, the Easy Cheese, that is the bomb. If you guys go to Target and get a deal on Easy Cheese, dogs love this stuff and they will – it's like crack– they will let you do anything to them if they get Easy Cheese. So, this works great – and Pup-Peroni® too, Pup-Peroni® slathered in Easy Cheese is great. *[Laughter]*

So this is our – this is the cost for treatment for a 25 kilogram dog, so for Minocycline for the rescue group has to pay for that; that's going to be out $50.00 for four weeks. It's still expensive but not near as expensive as doxycycline. Our cost for the Melarsomine for that dog would be $73.00 and for a two-dose protocol would be $48.00 and then Heartgard® Plus, if the rescue had to buy it would be about $9.00 a dose. So, if you're looking at adding everything up for a three-dose protocol would be about $130.00; for a two-dose protocol about $106.00.

Now we charge the rescues for a dog this big would be $85.00, so we don't make a lot on it, we lose money on it, but you know, it's worth it to us to be able to save these dogs from euthanasia. So this is just a graph showing our heartworm treatment; you can see in 2011 we really didn't miss a beat, so there was a shortage but we didn't really notice it.

Our average age of dog that we treated was about 3.2 years, but you can see most of them are around 2 – this is just estimated, our complication rate very, very low, about 5 percent complication rate. Again, I don't know if all of this is accurate because sometimes the rescues aren't going to report this to me if it's just mild pain or swelling they might not even tell me, so they're going to tell me if there's more, you know, if they need tramadol or if there's a big knot that formed.

We've had a 1 percent death rate – about five dogs out of the 565 and we have no statistical difference in complication rate, death rate for male versus female, two or three dose protocol or at the age of treatment and we've treated some older dogs also.

Just real quickly, I'm going to talk about three dogs that were a little vexing for us.

This is Duncan, he was a 3-year-old Min Pin: 4.3 kilogram dog, little, tiny guy. He presented to us with a Grade 3 murmur, and he presented for neuter, so we actually took him over to Cardio. He was actually in Caval Syndrome.

This dog had no – I mean he looked fine to us – he didn't have any ascites and they actually extracted 54 adult worms from him, which is a record at UFCVM. The record up to that point was 106 worms, but that was from a, like, a 50-pound boxer.

So, for weight – per weight range, this guy beats it and this is him, you know, proudly displaying his worms in a cup. This dog actually turned into a land shark; after we pulled these worms out. *[Laughter]*
He came back for immiticide, so he was actually feeling pretty bad – we thought oh, he's just a sweet little guy but yeah, he turned into a land shark because he felt so much better after we pulled those worms.

This is Bellamy. And Bellamy came in with a negative heartworm test using a DiroCHEK® from our local shelter. He did present with a heart murmur. He came in for a neuter, so our – what we normally do because cardio is really great to us and they'll just look at our dogs for free – so we sent him over and they said oh, yeah, well, the murmur is due to all the heartworms he's got in his heart.

We said what? He's negative. Like, no, he's not negative, and you can see – I don't know if you can see those little squiggly lines; those are some heartworms in the heart. So we re-tested him with IDEXX Snap® and he was still negative, so the conclusion we came to was this dog had – because he was a small dog – he had an all-male infection, which is

probably pretty rare but it does happen, so just make sure that you're aware of that.

And then finally we had Tiger. Tiger was a 3-year-old little Chihuahua a little, tiny guy, again, all of these dogs are little, this is a theme here, this is maybe why you want to do a three-dose on these. He actually had the three-dose protocol in February and March of 2009, was adopted by a really, really very conscientious owner, was kept on heartworm prevention, re-tested at six months following the treatment, which is what was recommended and he was still a very strong positive.

So we actually re-treated him with a two-dose protocol, so this can happen, you know; just be aware of that. This is the only one that I'm aware of that we've had to re-treat.

To conclude, remember that your treatment plans are going to vary among different shelters depending on your resources and if you don't have the funding for a three-dose, by all means do a two-dose, that's going to be a great outcome most of the time.

And if you have – are faced with a Melarsomine shortage like we probably are going to be faced with here in the next month or so, then make sure that you add your doxycycline or equivalent drug into your macrocyclic lactone therapy. Remember not to use those alone because that's going to induce resistance and also it's going to increase your length of treatment. And remember to exercise restrict all dogs undergoing heartworm treatment regardless of the method that you're using.

Here are my references and I just wanted to prove that we do more than pit bull heartworm treatments at ACAS: this is Elvis; he was treated about a month ago.

Thanks, I'll take any questions. *[Applause]*

[End of audio]