



# WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

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## 36<sup>th</sup> Annual Winn Symposium – June 26, 2014

### “Glimmers of Hope-HCM and FIP”

#### Transcript of Audio: Dr. Philip Fox, Questions and Answers

Steve Dale: While we do our little computer dance here and we have to switch computers and do all of that. I do have one more piece of business to take care of. By the way, I will tell you, the Winn Foundation, I am speaking for me, but I really think I am speaking for the board. We are determined to do everything we can to do what we can. Today we just had a grant meeting and I think I can talk about this. Zoetis said (essentially, they used to be Pfizer Animal Health for those who do not know), “Here’s a hundred thousand dollars and we want you to focus in on some things, but, essentially, spend the money wisely.” It goes very quickly. Every time we have our grant meeting, our annual grant meeting, unfortunately, we cannot fund nearly as much as we would like to. I am talking about cat health and behavior in general, but when it comes to FIP, as we just heard about, when it comes to cardiac disease that we are about to hear about, everything means a lot to us, but those two, we are determined to make a difference and to do something about, but we need your help to do that and we need the help of your friends to do that as well. For those on the board of the Winn Feline Foundation – put up your arms in the air – and please help me thank all the board members who do this stuff. [applause] Significant others of board members ... [laughter] Come on! Our camera guy over here and Otto is somewhere, maybe out of the room at the moment, but we thank them as well.

We have some announcements to make. The Winn Feline Foundation recently said, “You know what? ...” Because we have an executive director who is very wonderful, but she resigned, and our new executive director, I will say, I am so excited about. You may know her. She was the president of the board of the Winn Feline Foundation, a past president of the American Association of Feline Practitioners, and if I went through all of her credentials, all the things she has done in her career, I would be taking up Dr. Fox’s time, so just help me thank Dr. Vicki Thayer for accepting that position [applause] and Dr. Glenn Olah, who, unfortunately, just stepped out of the room. How about this for making an entrance? Dr. Glenn Olah, welcome back! The new president of the board of the Winn Feline Foundation. [applause] If you will help us to take a minute, we have something very special to do. Please help me again welcome Dr. Thayer, who is going to do that very special something for us. [applause]

Dr. Thayer: A number of people in the room probably realize that one of our long-time board members and CFA people is retiring this year and I would consider this individual kind of my guide star on board and that is our Betty White. We call her our Betty White and she is immediate past president and, as I say, retiring off the Winn board, but I did take some time to get something to recognize Betty’s number of years of involvement and dedication to Winn. [applause] We did something a little different this year. Oftentimes we give a Lenox crystal cat, that goes out with an award, but because Betty was a Siamese breeder, I went searching on eBay trying to find the right figurine that would fit and this says, “In appreciation to Betty White for years of dedicated service. Winn Feline Foundation.” [applause]

Betty White: Oh thank you! [applause] It has been a real privilege for me – and that is the only word – to sit on that board. You have no idea what those February board meetings are like, all these wonderful grants, all these wonderful proposals, but only so much money. For someone who has a liberal arts background who knows

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nothing about science, I would reach, I really reached at those meetings, but they are all so very, very wonderful, so thank you. [applause]

Steve Dale: Thank you all very much. I will say that – because I am going to talk for a minute until we get our computer issues dealt with here – I will say that being on the board of the Winn Foundation is wonderful. Part of my job is to go out and raise money and I have taken advantage of Betty a little bit because I have said, “Well, we have some amazing veterinarians on our board” because people will ask, “Well, who’s on your board?” and I will say we have some amazing veterinarians on the board. We have Betty White on our board and people will say, “Ooh, Betty White! Really?” [laughter] And I say, “Yeah!” In fact, once, Betty told me a story – this Betty told me a story – that she used to get mail from that other lady. I host a radio show and what I did was ... this Betty White, I am not sure that she knew, but the other Betty White did know, they knew of each other. Of course, everyone knows the other Betty White and I hooked them up and they had a conversation live on the radio. I said, “Betty White, meet Betty White.” It was a promotion for the Morris Animal Foundation, we are friends with them, which that other Betty White is involved in, and this Betty White has given so much to the Winn Foundation for so many years and I also am very grateful. Thank you very much. [applause]

Well, we do have the best of the best that come to the Winn Feline Foundation Symposium. Dr. Phil Fox is known among veterinary cardiologists, not only in America but all over the world. As I mentioned earlier, feline hypertrophic cardiomyopathy is something that means a heck of a lot to me. It means a heck of a lot to most of you because, as all of you know – bless you! – so many cats, too many cats die of this disease. Dr. Fox is among the long list of those who are doing something about it. Dr. Fox ... [applause]

Phil Fox: Thank you for the kind remarks. I appreciate those. That was really a wonderful talk preceding this on FIP. I do not know if you realize how hard it is to do that work when you are trying to get a DVM degree and a PhD. It is really a phenomenal effort, so, I am glad I did not have to do that. [applause] Thank you.

Dr. Thayer: There are 3 x 5 cards on the table, so if you want to write any questions for our question and answer session – I apologize to Dr. Fox for interrupting – go ahead and at the end we will pass them forward for a question and answer session.

Phil Fox: Thanks for the invitation. I have gotten money from this foundation over the years and it makes a big difference. You might say, “Well, it isn’t that much,” but it is enough to get you started and in this particular case, it combined with money from Morris and it made the difference. This was a large study that was very expensive to run and I think you will see how that turned out. We have had this disease ... I have been practicing for 35 years and nobody but nobody knows, or knew before this, what the incidence of hypertrophic cardiomyopathy was. So, how many people are veterinarians here? And then the others are bankers and stuff like that? [laughter] Lawyers?

Betty White: Beneficiaries.

Phil Fox: There you go. I have been privileged ... I went to Ohio State University – thank you – out of a PhD, so I did it reverse. I was working on a PhD and I had no clue what I wanted to do. The only reason I went for a PhD is ... I woke up one day. I was a senior in college. I had no plans. I went from a little college in Ohio to out of

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state because it was two hours away; that was the decision process. I cranked along without a plan until all of a sudden I was ready to defend my thesis, which I did not really want to do, and my cubicle mate was doing something. I said, “What are you doing?” He was a farmer from northwest Ohio. He says, “I’m filling me out an application for vet school” because Ohio State had a vet school. I said, “Why would you want to do such a stupid thing like that? After all the work we’ve put in, why would you want to do this?” and he said, “Do you think I want to do all my life being in a laboratory and looking for a fifth postdoc?” and in those days, money was real hard to get NIH had cut down and I said, “Well, that’s a pretty good idea.” So, he had a second application and I filled one out – it took me, like, an hour – and then we went on and I forgot about it. I got in vet school and he didn’t, so ... [laughter]

I have lucked out on a number of things. I had a job in Connecticut. Back then you could do ... it was very sexy to do small animal, equine. Gentleman farmers or gentlewoman farmers and you would do their Jack Russells and you would do their horses. I was really worthless for horses, but it was the macho thing to do. One of my professors at Ohio State said, “Why didn’t you ask me for a recommendation for an internship?” and I said, “I didn’t even think of it. Why would you want to do an internship?” He made a call to the Animal Medical Center in New York – things were very loosey goosey then – and he says, “I got a good student (maybe that’s what he said); fit him in” and they said, “Well, we closed. He’s a month late,” and he said, “That’s how he is ...” [laughter] I went and I had an interview... It was not even a process. I talked to one guy when he was operating, one guy in the cafeteria and one guy says, “I gotta go to the john.” I followed him in. That was the interview. [laughter] So, I was there one year and I said, “Gosh, how can you leave? How can you leave New York City?” So, I went on to an internship and residencies in those days were two years instead of three and then, all of a sudden, I blinked and here it is.

So, the point of all this is that we have been dealing with HCM and other CMs for ... I have been dealing with it for a third of a century and people I learned from have been dealing with it since it was invented because it was not until the early ’70s, mid-70s, that ... There was no recognition that cats had heart disease. It was FIP or whatever caused ascites with high proteins, it was mammary gland tumors in cats, which we hardly ever see. It was a whole bunch of stuff, but it certainly was not heart disease and when they could not breathe and died or dropped dead, well, you know, bad air, termites, the guy is spraying the lawn in Jersey, whatever it was, it was all that stuff.

When you listen to speakers – I mean, other speakers – you should really question what the basis is of what they are telling you because what happens is that inadvertently, speakers are at a tertiary care center and the cases they see are the worst of the worst and then they give you this, “Oh my gosh” and you go, “Oh, geez.” So, everything sounds like it is doom and gloom. Nobody had any data in the world as to HCM other than that came out with a few studies. One was NC State, Clarke Atkins; one was John Rush at Tufts; a couple came out of AMC, but they were pathology studies. These animals had no life, they all died and they all got blood clots. So, I got up one day and I said, “Geez, I’d really like to know more about that because that’s how I would lecture” and I had a study that all my buddies ... If you work this long, you have a lot of people hate you or they like you and I had half and half. I had enough that liked me that they all said, “That’s a great study, Phil. We will throw in with it.” I went to an agency – it wasn’t Winn and it wasn’t Morris; I am not going to say what other big branding agency there is – and submitted. They said, “Great study” because there were 25 collaborators, the best of the best, and they said,

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“We don’t give out ...” I guess this was about ... when? “We don’t give out money” for what I needed and what I needed was money to pay people to do telephone calls and telephone surveys and incredible database management and coordination. This is called an epidemiologic study and if you do not do epidemiologic studies in every disease, you will not have a clue what is going on because all you will know is what you hear from the guy or gal who comes out and tells you all these horror stories. You will not have a clue. And what is worse than that is neither will your veterinarians because then when a veterinarian sees an animal that has an echo-derived diagnosis of HCM, guess what happens? It is a real bad thing that has happened with ultrasound. Ultrasound is safe and effective. It is quick. The bad news is is that everybody has one, most people are not trained, and if the cat gets labeled as having HCM, you damn that cat forever and that whole family to chase it around once or twice a day, at least, and try to jam pills down the mouth, and you would like to know does that make a difference. I mean, wouldn’t you like to know that? So, I got up after 25-some-odd years and said, “I’m mad as hell. I’m not going to take it anymore.” It took me 25 years. Well, this agency said, “Well, we don’t do that.” I said, “What is it you don’t do?” They said, “We won’t fund that. That’s not what we do.” I said, “But I’ve got the best people on the continent.” “No.” So, if I would have bought a piece of equipment, they would say, “Oh yeah, sure, we’ll give you a hundred thousand dollars” because that is what the budget was. I said, “So, I need a hundred thousand for a full-time equivalent veterinary technician that’s really good and good with people” because she or he had to talk to people, call up veterinarians; those people are hard to find. “Oh, we don’t ...” So, that really pissed me off. I am not going to say who it is, but anyway, so I ended up getting a big chunk of money from Morris, who says, “That’s a great study. Yeah, we’ll give you this,” but it still was not enough. Winn came by and partnered up. It is nice for Winn to be able to do that and that has resulted in this initiative.

So, I am going to give you a little thumbnail course of what HCM is and I am going to talk about some data, try and focus generically on the data because you are not all researchers.

Here is the Animal Medical Center in the City of New York in 1909. We celebrated the 100th anniversary five, six years ago. The Animal Medical Center is a unique place. It was started by women; I mean, don’t they start everything? [laughter] Most of the people in this audience are women. And these people were women of education, means and grit. These women had money, at least this core group. They were married to the Mellons and the Carnegies and the Rockefellers and Vanderbilts, you know, blah, blah, and they wanted to make a difference because in New York City at that time, a lot of the foundations – well, you could not get on a foundation if you were a female. They would not take women. Up until maybe ... when I got to New York City, a couple of our board members ... I remember getting invited to dinner, it was an all-men’s club on 5th Avenue and 54th Street. Great club, you know, sorry you couldn’t go. Anyway, they started this and they called themselves the New York Women’s League for Animals. You should see these annual reports in those days. They really had it together. Here is a guy taking his dog on the transportation available to him at the time, there is a liaison or something going on in the corner we don’t know quite what, it is lost to history and here is the New York Women’s League for Animals. It was a dispensary on the Bowery and advice and treatment free. Horses, dogs, cats, you know, the hours. Well, we changed the free thing pretty well. [laughter] That is how that started.

Now, if you think a lot is known about hypertrophic cardiomyopathy, you will hit your head and never regret it because here is why that is. If you go on the National Institute of Health PubMed, you can do these free literature searches. Type in HCM man, human, type in HCM and echo, HCM and genetics, these are the numbers of articles published – and I did this a year ago – some 87,000 on cardiomyopathy, 13,000 on HCM in people, 2,700

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genetics. That is a lot of articles! But then if you put HCM and feline, 11 articles on genetics and they are the same three authors. I am not saying that in a bad way. I am just saying there is nobody doing work because there is no money. A 165 articles, feline and HCM, and if you put feline cardiomyopathy, 500; that is really not that many. This goes back to the early '70s when NIH started to do this. To give you a perspective of what is known and if you ask yourself, "Why would we blow your dough, which is hard to get, on HCM, on heart disease?" Not that it is the most important, but it has a level of importance and I want you to feel good to see that the reason why there is not much stuff is there is not much money for it, historically.

Now, heart muscle disease is heterogeneous and it is hard to diagnose correctly. One of the things I do on the side is pathology. I had a mentor. I kind of did a nonconforming pathology. He is a Chinese guy at AMC. He name is Sam Lo. He was the best of the best and he liked me for some reason and I hung out with him. He taught me a lot and the crazy thing is, I am almost the de facto veterinary and cardiology pathologist. It is the damndest thing. People send me hearts all the time If they have heart from sudden death. I am not going to dwell on this, but the important part is that it is not that easy to diagnose. So, if you have a heart with a ... I will get to that. I will get to that.

So, the clinical journal in the world with the highest impact factor, it is considered the most important journal that is read by the most important people is this journal called Circulation. This guy named Barry Maron, he is the mogul. He is the glue. He is an unbelievable guy. I met him in New York years ago and somehow he took pity on me or something like that and he has mentored me. I have had a chance to publish a few articles on HCM and actually, thanks to him, he and I and a couple of other colleagues published our first article on HCM in '95 in this journal. That silly article has turned out to be still quoted, particularly with the cutoff for what constitutes pathologic thickness. So, if you have got HCM in a cat, you have to have H, that is hypertrophy, that is thickness, and it is still 6 mm, the septum or free wall and the left heart is 6 mm when the heart is at the end of its relaxation. So, the reason I tell you that is if you are not a veterinarian and you are a client and someone echoes your cat and says, "Your cat has HCM," you should say, "What is your criteria for that diagnosis?" You should not just accept that. Why would you do that? If someone said you have got cancer, would you say, "Oh, thank you. I'm good with that." You would say, "No, give me some more information" and you would get another opinion. Six millimeters. Now, there is some controversy over that. There is a good friend of mine. I have had a beer with him any time of the day or night. I avoid him like the plague at meetings. Conflict resolution is conflict avoidance. He wants to make the cutoff 5 mm because he knows, he knows, he knows a lot. He is a good guy. He is a know-it-all. [laughter] And that is not the right value. Six millimeters is the right value because what that means is that some cats ... if you make the cutoff value 5 mm, you have crucified cats that are 5.2 mm forever. What 6 mm means is that you might miss some cats that have mild hypertrophy, but if they are 6, they got it. If I was a breeder, I would want to not miss the cats that got it because the truth is, you cannot tell with echo, you know, two tenths, three tenths of a millimeter? If someone says they can measure the same segment time after time and get 5.3 mm, they are full of crap. They cannot do that. There is too much variation and there is genetic variability that we do not even have a clue about. So, 6 mm is reasonable and you will miss some mild forms, but you know what? There is a relationship, which I will show you, between the magnitude of thickness of the heart and outcome. There are only three reasons, there are only three reasons to treat a cat. There are only three reasons to treat a pet with drugs, in my opinion. That ought to be: to increase quality of life, to reduce morbidity (meaning the number of times you have to go to the vet with that cat) and number three, it should make

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you live longer. Live longer, live the better and stay out of the hospital. Those are the only three reasons that all of us who are veterinarians should treat animals. So, when we go to treat, that is what I teach my interns and residents. They look at me like I have got two heads, yeah well he's got a thick wall, but will treatment make him feel better, live longer, have less morbidity. And if you do not know that, you still may decide to treat, you know, it could be any disease, but tell the owners, admit, 'fess up that here are the controversies, based upon the information we know – and we do not know a lot of stuff – and this is what I would do. They can believe you or not believe you or go for another opinion. So, that is the context that I believe is reasonable in cats with heart muscle disease. I mention this just as, you know, put it on your list of something to consider.

I am going to go over briefly what is feline HCM, how prevalent is it, what is the natural history – that is the data – how do you detect it, can you manage it and we will go with that.

Feline HCM is characterized and defined by hypertrophy, the thickened left ventricle, excluding all diseases that can result in the magnitude of hypertrophy that is designated greater than 6 mm. What are the things you have to rule out, therefore? You guys know what they are. What do cats get that we get in terms of, you know, if you get an IRS audit, what happens to your blood pressure? So, hypertension, right? Hypertension. So, if you got an older cat with mild-to-moderate wall thickness, got to get a blood pressure because if that cat is hypertensive, it does not have HCM, it is different drugs, totally different drugs; amlodipine for hypertension, not amlodipine for HCM. Then, what is that other disease that causes cats to lose weight and they have goiter in their throat? Hyperthyroidism. Nobody should miss hyperthyroidism today, but a lot of people miss it because they do not do a test. We are pretty good at diagnosing. I am really good at diagnosing hyperthyroidism. Guess why? I just run a T4 on any cat that is sick and older than 7 years of age. I do not even have to think about it. It does not occur in cats less than seven. It just doesn't. I have got a really good colleague in New York. Boy, she is way smarter than I am and she will get a 2-year-old cat and she will run a thyroid panel on it. I go, "Jesus, why are you doing that?" "Well, we want to make sure. I know it doesn't usually ..." Okay, well, is that cost effective? No. So, hyperthyroidism, hypertension has to be excluded. There are a couple of congenital things. You are not going to see them; they are really rare. So, if you have got an old cat that has got a thick heart that is not hypertensive and not hyperthyroid, then you probably have what would qualify for hypertrophic cardiomyopathy.

It is all over the place and you can see, here is a real thick septum. Here is a little focal region of thickness. You have got to be able to have a level of experience or training in order to sort through this. I truly do not mean to say this offensively, but if you are doing echoes, not people in this state but somewhere else and you are not trained, like you are self-trained, you should not be doing it. I mean, would you be doing brain surgery just because you have got, you know, someone dropped off a brain set? Not really. It is easy to make a mistake in these things. If you are a progressive veterinarian in echo, that is okay. If you have gone on courses, I mean, you know, I have taught one for years in North America and it is a good course. There are good ones in all the big names. If you go to those, then that is totally okay, but I get referrals from people all the time who are colleagues – and I appreciate the referrals – but the people come in with a diagnosis and then I have got to dance around and say no, he's just the most normal cat, you know, thank you, you know, try to make something up so that the vet looks okay. The point is it is a tough modality to use and it should not be used unless one is committed to getting the training. There are a lot of other ways to make a difference in practice than diagnostic ultrasound.

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If you use a consultant, some people use consultants, there are some really, really good consultants in every state, there are really some unqualified consultants, and here is the rub with that. Ultrasound is completely unregulated. You do not need a certificate. You do not need baloney. You do not need anything. You just buy a machine. They sell set-ups now that are PC-based. You put your probe in. It has got a USB port into your computer and that is your 5 MHz probe. It is software and the images are terrible. You can get them under twenty thousand. You can charge – just do the math – two hundred each; you can pay that off. It is unregulated. So, if you use people that ... Here are a few tips, in my opinion. You should look at the report and you should ask, before they go, tell me ... because the report is four fifths numbers; eight tenths of the four fifths, we do not even use them. The machine spits them out. The machine spits them out. I was in a lecture in Rome once; the best lecture I ever slept through. I woke up at the end and the guy says, “In conclusion, beware of putting reliance on machines that spit out numbers. That’s called an echocardiogram.” It is like a gun thing, you know; I’ll give up my echo when you pry my cold, dead hand off the probe. I use it, but it is not the first thing to do. Now, the bad news is in a cat, an x-ray isn’t very sensitive and specific. That is the problem. When you have a murmur or a gallop, you are forced to go to diagnostic ultrasound, largely. If you use a consultant who just handwrites ... Here are reasons to fire a consultant:

1. They write it by hand. You cannot even read it. You laugh, but that’s ... , I mean, come on.
2. Measurements are listed to the tenth of a centimeter. That person – I am sure I am pissing someone off here – but wake up if you are doing it. God did not make – or whoever you believe in – did not make the ventricular septum four possibilities. It is not 0.4, 0.5, 0.6 or 0.7 cm. It just isn’t. Nothing is like that. And those are the readouts you get because these machines are set to where they round up or round down and the people who do that do not even realize that and it makes a huge difference.
3. If the person does not listen to the cat’s chest and look at your x-ray, if you have one, out, done. You do not need that person. There is an enormous conflict of interest in diagnostic ultrasound. There are wonderful, incredibly good people, but conflict of interest is out there as well. What do I mean by that? So, if a cat has got a noncardiac cause of respiratory distress, that consultant should – and many do but some don’t – should say, “You don’t need me for the echo. I am not going to stress your cat out. Get a chest x-ray or something. Tap the chest.” But more often, they will do the ultrasound and then, you know what the recommendations are? What are the recommendations? You know them. Re-echo in three months, right? Re-echo in six months. How many people have you had that say, “You don’t need me anymore. You need ... ” whatever. It does not happen. That is a conflict of interest and that is really prevalent. That is an issue.

I had a dog yesterday – yesterday? – that came in for an echo and it was coughing. I did not do the echo. I got into it with the client and they said, “Well, my doctor said he needed an echo.” No, you don’t. Cough, you need a chest x-ray. And it had pneumonia. I did not know it had pneumonia, but I did not know what it had, and the echo would have missed it. So, just be careful about an ice pick focus of the database. There is a good place for an echo. You need good echo for a diagnosis of HCM, but it is a big world out there and pick and choose the people you use. If you have not gone to a meeting, you are doing your own echoes, I can tell you, there are five meetings that are really great that will help get you to the next level, if you are doing your own stuff.

Now, asymptomatic heart disease is the dominant thing that we see. It is those cats that have symptoms. Heart failure, arrhythmias, blood clots, fainting and occasionally sudden death are what gets our concern. Here is what

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the echo can do. You hear about hypertrophic cardiomyopathy and hypertrophic obstructive cardiomyopathy. Who can tell me what hypertrophic obstructive cardiomyopathy is? The new president said that the first person who gets it right gets a small ... gets a Prius. [laughter] Wayne will do this. Who said that? Okay ... Here is a cat. Now, intuitively, would you give me that this looks kind of thickish? Okay, it is thickish. It is a nice young cat and what happens in some cats, left atrium and then here is the left ventricle and we have a free wall and a septum. The septum divides the left ventricle from the right ventricle. That septum is the barrier between them. In hypertrophic cardiomyopathy you can have everything is thick or one portion is thickened and one variant of this, here is the mitral valve. The mitral valve has an anterior leaflet and a posterior. Anterior because the head is that way. Posterior because the butt is this way. So, sometimes this anterior leaflet gets sucked up into the outflow tract that feeds into the aorta. Not a good thing to have in people. Really a disaster in people because as the heart pumps blood, there is less blood going out because of this dynamic blockage, this dynamic blockage. So, that is called the obstructive form of HCM. We call it hypertrophic obstructive cardiomyopathy or HOCM. Now, it has been, for a long time, believed that that was worse, to have HOCM. The study that we did showed there was no difference. So, there was no difference in anything that we could measure, whether you were a hypertrophic obstructive cardiomyopathy cat or a hypertrophic cardiomyopathy cat. That is a huge finding and that came out of this study. Why is it a huge finding? It is a huge finding because the very presence of hypertrophic obstructive cardiomyopathy was a driver, a driver of therapy. In people, we all – I did it – we all said, “Jesus. Hypertrophic. He’s hypertrophied and he’s obstructed. Better treat him!” Now we know that you do not have to, it’s not worse, and it may make a difference in your choice to treat or not, particularly when the magnitude of hypertrophy is not that great. I do not treat these anymore just because they are HOCM and I think a lot of people probably do not do that as well. It is an emerging management development.

Here is the other interesting thing. You see this blood, this yellow and all those colors, so if you take a straw – there are no straws in here – and you take a straw and you take a mouthful of warm water and you blow it into the straw. The straw is the aorta, so you blow the water through the straw (blowing sound) and you can feel at the end, the velocity, you can feel some pressure against your hand. That is because the air or the blood, the velocity that goes through there has some energy against your hand and you can feel it. So, on the color flow echo, you know, there is echo ... Echocardiography shows us the walls and we can measure them. Color flow Doppler – half of you know this, half of you maybe don’t – color flow Doppler is when you press another button and it transforms blood flow into color, so if blood is going towards the transducer, it is looking like red. If it goes away from the transducer, it is blue, so color Doppler mapping. The Doppler helps us map the direction and magnitude of the blood flow. Very useful to us as well. So, we have echo, we have color flow Doppler echo and these high velocities ... so, you take your regular straw, now you go to the bar downstairs and you spend about \$28 for a glass of seltzer and you get this little mixing straw that has a little tiny hole in it. You get that mouthful of seltzer, blow through that and two things happen. One is you cannot blow so much seltzer through that and the seltzer that goes through hits you at a higher velocity, so you can feel it more. That increased velocity creates energy and that energy turns up as a murmur, as a murmur. So, when a veterinarian hears a murmur in a cat and it is different than a dog, one of the possibilities is that the genesis of the murmur is hypertrophic obstructive cardiomyopathy. So, it may be a surrogate marker of underlying heart disease and that is why, as veterinarians, we just cannot blow off a soft murmur like you can on Friday afternoon in a dog because dogs do not get hypertrophic cardiomyopathy, they get leakages, and a soft murmur means a small leakage and we can say probably not a big deal. You cannot say that in a cat. So, you are stuck having to pursue that. You need to pursue it with echo.

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We know that in a small number of cats, HCM cats, there is a genetic basis, particularly Maine Coons and ragdolls, and if you have got a Maine Coon, if you are a Maine Coon or ragdoll breeder, the good news is there is a nice test for this. Penn does it. NC State does it. If you are negative, though, it does not mean that your cat is okay; that is the problem because there are other genes, so it is a really limited utility. If you are a breeder ... and most breeders are really, really conscientious and they would like us to be able to state that this cat does not have this myosin heavy chain binding mutation, but it does not mean that the cat does not have HCM because of some ... or it might not get HCM. So, we are thankful for what we have, but it is not perfect yet.

How prevalent is HCM? Well, I will show you. Here is my ultrasound log from 1984. You see the green. The green is HCM and the other colors are other conditions. You can see that the preponderance of diagnoses that we make is HCM. So, it is clearly the most common disease. The blue was dilated cardiomyopathy; thankfully, we do not see much of that anymore because it was shown to be associated with a deficiency in what? Taurine. I'm preaching to the choir here. And guess when that was reported? It was reported by Paul Pion and his colleagues, incredibly excellent work at UC Davis. At first, Paul got a lot of pushback from pet food companies and they said, "Well, it's not our diets," and then mysteriously ... that article came out in '87 and by 1990, all of a sudden, all the big commercial diets were reformulated and look what happened to the blue bars, and it stayed that way. So, it was not them but somehow they changed their diets anyway and it did go away. So, happily, we do not have this because that is just a miserable disease that we do not have to deal with.

Natural history, I will talk about in this other ...

How do we best detect cardiomyopathy? We start with a stethoscope, right? Here is a little secret. The vets in this room know this because you are cat people. A lot of vets don't. If you take a dog, the dog is just going to sit there and you can put your stethoscope at the elbow and you are in the mitral valve area. The dog doesn't care, doesn't know, the vet doesn't care, doesn't know; it's a win-win. What do cats do? They squirm. They want to get away. They crouch down, they do all this stuff, and you need someone to help, not restrain a cat but keep it from jumping. The client wants to hold the cat and you tell them, "That's no good. That doesn't work." If you scratch your nose, the cat jumps off. So, what the problem is is that if you put your stethoscope down to a cat that is kind of bread-loafed, you are over the spine, and there are no murmurs that occur over the spine. So, you see what I am doing here, you guys, lift the cat up, so with my right hand I am picking it up. It does not like it that much. It is squirming around, but it allows me to put the stethoscope underneath the chest, which is where the valve areas are. You do that on the left and right side. It takes me a couple of times because I am there and the cat took a half step up, now I have got to repeat it, so you are actually painting from the left to the right side with your stethoscope, from the elbow up to the front. If you do that, you are going to hear a lot of murmurs. That is the secret; I mean, it is not a secret, but that is the secret.

The x-ray

A VD is the best x-ray to take because a VD will show you a big left auricle. Here is a big left auricle in a cat with cardiomyopathy. This was one of my best clients ever from New Jersey. She was a wonderful lady and a wonderful cat. I had treated this cat until the HCM got really bad and he got a blood clot to where we picked off one bad leg and the leg ... Rarely, these cats, if they survive, they get atrophy and then the paw heals in contracture. This woman made a little peg-leggy thing. It was great. This device was so good that the cat could

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still get birds, so she put a bell around it, but the cat figured out how to do that and then finally, the cat embolized again and she euthanized it and she donated this so that we could teach from it. This is a big left auricle, but it is the sensitivity. If you have a good echo and the cat is not dyspneic, then I would do an echo first. So, of course, the cat has respiratory disease, you have to do an x-ray first because you have to know if there is edema or not. ECG is a lost art. Hardly anybody does these anymore. They are really useful. If a cat has wide P waves or tall R waves its got heart disease. It takes about a minute or less to figure that out. It is cheap. Everyone has an ECG machine they got from their great-grandfather. So, it is paid off and you do not have to charge the Cardiopet or whatever it is called and I guess it is IDEXX. You do not have to quadruple it so it is \$400 to the owner. I fight with our administrators all the time and hide the ECG so that it's not ... you know, it's like 40 bucks. It's worth about 40 bucks and I do a lot of them. It is good information and it is quick and if it is normal, it doesn't mean anything, but wouldn't you hate to miss ... like, wow, look at the width of those P waves. It is a real strong clue.

## Auscultation

Gallop rhythms. What is a gallop rhythm? Yeah, it's an extra heart sound. So, here is a soap-boxy thing I have. How do people know we are veterinarians? It is because of our jewelry and what is the most common thing we wear – and it is not underwear – it is a stethoscope, right? That is how they know we are veterinarians. We have it around our neck all the time, from the second we get up to whatever. How much time do people spend learning how to use it? I have never seen anyone who says, “You know, I go to the Internet every week and I look ...” Nobody does that. There are some good commercial CDs. Gallop rhythm is really useful. So, if you have a cat with HCM and it has a presystolic gallop, you can make a cageside, bedside, in the booth diagnosis, largely.

Normally, your heart sounds are lub-dub, lub-dub, lub-dub. Lub is S1, dub is S2. Lub-dub, lub-dub. Now, if you have HCM, you usually have a fourth heart sound, which is presystolic, so lub-dub, it is buh-lub-dub, buh-lub-dub, buh-lub-dub. So, the buh is right before lub. Buh-lub-dub, buh-lub-dub. It is a timing thing. If you hear that, you probably have HCM. Probably. Very likely. So, a cat with a murmur and a gallop, well, the murmur is real common. A gallop is going to indicate that you probably have HCM if he has a gallop. An S4 gallop or an S3 gallop is a diastolic gallop, so lub-dub, lub-dub, lub-dub-buh, lub-dub-buh, lub-dub-buh and if you heard that in a cat, that cat has DCM; we still see that, or a doberman or dog if you do dogs. So, I would suggest to you, you have got to pay a little attention. Just go on the Internet. They are all free. Some of them are terrible and some are real good. You will train your ear. It will make a big difference. Make a big difference.

Now, what about BNP, biomarkers?

How many people use that? Okay. It is useful in a cat. IDEXX is coming out ... well, I think it now has a bedside SNAP test and I was one of the people in the group that investigated that. The advantage of that is that you will have it and you hear a buh-lub-dub and you go, “Oh, I heard this talk in Louisiana. It sounds like an S4 gallop. I think I ought to do a SNAP,” whatever they are going to call it. A SNAP test, if it is abnormal, the likelihood is that the cat probably has HCM. That is how that is going to work, so just keep your ears peeled for that. They also have a blood test that you can use. It is not as convenient. It is more accurate so you have to ... I don't know how these things are priced out. I think that if you use IDEXX, if you add a BNP, it is not much money. That is probably way cheaper than the other, but the other you get it quicker. So, keep aware of that.

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What are the strategies to manage heart failure? Well, this is easy. Here is a poor cat that is dyspneic. He is in an oxygen cage. Cats that are dyspneic with edema, I think, have a fairly characteristic affect and it is very different than dogs. This is as bad as you get with pulmonary edema before you are dead in a cat. These cats are almost fatigued. Their heads are generally down. They are sternal and they are panting. How many times do you ever see a cat pant? Rare, very rare or when it has got respiratory distress. Even if it got stepped on or injured, they do not pant. The other thing to do is you can look at their nostrils. Their nostrils will flare out. You have to look. They will dilate. They are sucking. They are sucking air in. That is a real dyspneic cat. Now, most of these will have crackles and we basically want to ... this will be ... I am not going to present this tonight. This is part of what this study will get us to is risk factor analysis because what you want to do is you want to put the highest category of risk those conditions that are markers for sudden death, increased morbidity and decreased quality of life. So, we will be in a position to significantly contribute to the literature based upon this that we have. The other thing is are there effective long-term therapies? We do not actually know that. And what about the asymptomatic cat? So, I think we want to bear in mind the fact that the potion has to be worth it in order to justify it.

So, I will spend a few minutes just showing you some of that data with this background and just hit the high points of it because there is lots of data and I don't want to make you convulse. This is the study. Let's see. I started this, like I said, with my best buddies at universities and once we hit a time to get the data, no one had done any of the work. It was one of these good ideas. It was like being good and going to church and loving your neighbor. Yeah, it sounds good, but no one is going to do it when it comes down to it and getting the data to Fox. I had a panic attack and I had to start to reach out to others and I started to tap some colleagues in Europe whom I had overlooked because I thought it would be easier to work with the Americans, and the Europeans are a lot easier to work with because they are Europeans. I got a 110 cases from Valérie Chetboul at Alfort in France and I got 85 cases from Gerhard Wess at Munich. The Italians were wonderful and they started to roll in and then I would use that as a lever with N-wide American colleague, got a big slug from Ohio State and it started on a roll. So, it has taken several years to get this data. We wanted to assess five-year outcome. Once you diagnose HCM in your cat, what happens in five years? That is the key. The cases we recruited were never in heart failure and they just had HCM. It's kind of like real-life stuff. So, we called it ... So, I am really delighted. Everyone's got an acronym. I don't have an acronym. My whole career, you know, about 100 publications I don't have a paper with an acronym. My kid actually did this for me when he was 14. He said, "Why don't you call it REVEAL?" and then he did it in his head and that is why he's got A's in physics and math. So, it is REVEAL and actually, it is pretty good. The international collaborative study to assess cardiovascular risk and evaluate long-term health in feline HCM. Bruce Keene and Dr. Motsinger-Reif for NC State. Bruce is a long-time buddy. He is a stellar cardiologist. He is head of cardio there and Dr. Motsinger-Reif is head of statistics at NC State, so these are real pros and I am delighted to have that. Again, thanks for the support.

Here is why: Science is a way of trying not to fool yourself. That is why we do this. The first principle is you must not fool yourself and you are the easiest people to fool. That is what this is about. That is what it is about for us as specialists. We think we know it. We are fooled and that is why we do these studies.

I am going to roar through this because I covered a bunch of it already.

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We wanted to basically identify and risk-stratify cats that were asymptomatic at the time of entry. We wanted to differentiate whether there was increased risk between HCM and HOCM. We wanted to know what was the actual incidence of heart failure and blood clots. If your cat had HCM, wouldn't you want to say how likely is it it's going to get heart failure and how likely is it it's going to get a blood clot because if it is likely, you might want to treat or monitor, and that is what it is about. This is what is cool about the study. It is a global study. I made every mistake you can in one's career, but I do want to take a little credit for this because it is a global study, and I would tell you that there are very few global studies in veterinary medicine. I am not aware of one. There are 60 investigators in 20 countries and these boxes indicate the countries. I could not get anyone from China that I could speak to and understand. I was dealing with a guy I know pretty well in Moscow. He is like a Mafioso guy and he kept on telling me that he was going to come through. So, he could not deliver a Russian and I got no Chinese, so I feel bad about that, but I got Taiwan; it is not really China but ... pretty much across the US. The green states are not Republican or Democrat or ... Western Europe and Scandinavia. I was delighted to get those groups as well. There is a long list of people. These were the best people in those countries. These are not schmucko people. These are people who teach, are board certified, teach cardiology or are recognized by peers.

There are a couple of ways you could diagnose HCM. Let's see if this shows. That's okay. That doesn't show. Okay, so let's look at some of the data. We statistically evaluated and compared sites; are the French data the same as the Hungarian data are they the same as the Danish data, and you have to do that. Now, since this, we now have 1,700 cases, so it is a real study; 1,700 is a real epidemiologic study. Most veterinary studies are small, clinical studies, they can be 12 cases, single site. We have over 700 normal cats and over 1,000 HCMs. I wanted a thousand. I wanted a few more than a thousand so I could say we have more than a thousand, which sounds a lot better than if we say we have damn near a thousand. We've got more than a thousand cats. It is marketing. So, there is good statistical power. You can largely believe that the statistical test differences that are revealed – no pun in REVEAL – are likely true versus various ... because most veterinary studies are underpowered and when you look at the limitations, they say studies are underpowered. So, these cats were an average of around five years of age when we started. They were about 5 kg of so, which is 11 pounds. That is the typical cat. HCM cats are more predominantly male, as we know. I am not going to go through these, so I am going to give you the broad brush strokes.

The first thing we found that there was no difference in anything between the obstructive and nonobstructive forms of this disease, so we combined HCM and HOCM and treated as one and compare that against normals. If you read a study that does not have a control, it does not mean it is a bad study, but it does mean that it is unsure that you can believe the conclusions because they are not compared to anything. So, the value of the study is we had 700 cats at least that did not have heart disease. These things are called survival curves. All you need to know about them. This is time. So, in the beginning, you start day zero and this is the percentage of cats alive. So, at the beginning, 100% are alive and they start to die. One wants to look at median 50% survival, so you draw a line and you see how many days, months or years and, obviously, the longer the survival, generally the better. Let's see.

There is another thing called hazards. It is called a Cox proportional hazards ratio. You will see it in the literature. It is very useful. Here is how it is useful and we will take this, for example. This is time to event for arterial thromboembolism. Let's see. If you were a cat that had hypertrophic or hypertrophic obstructive cardiomyopathy compared to normal, you had five and a half times greater chance of ... actually, that translates to

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an 85% greater chance of getting a blood clot every day you wake up. So, if you are a cat that has this, every day you wake up, you have an 85% greater chance of developing that than a normal cat. So, it is useful and it is valuable to say, "Wow, the magnitude of that change is a big deal."

So, what comes out largely is three variables that appeared to predict risk or to offer prognosis because that is what you want to know, whether it is you or your family or your dog or cat, what is the prognosis if I have X, what is the risk, and that is the thickness of the septum or free wall and the diameter of the left atrium. All these analyses, you will see these boxes turn up yellow. One of the things that we will do when the second paper that comes out of this is actually publish the risk factors that can be used by veterinarians to say, "Okay, does this cat that I've echoed have the parameters of thickness or atrial size within these categories that then puts it at risk?" If you remember that pyramid I showed you just a little bit ago, the high risk is where you want to focus, so you should be able to, as a veterinarian, say, "These are the top three things. You've got them or you don't got them." If you have them, what are the opportunities to manage? Basically, that is how this data will be used.

I am going to finish up with a summary. By the way, there was no breed difference in survival, even though some breeds are predisposed to HCM. It did not matter if you were a Sphynx cat or a Maine Coon cat or whatever for the numbers of cats we had. I think that there are certainly some cats that have malignant genotypes. I was working with a great Maine Coon cat breeder in New York and Mark Kittleson, who has done wonderful work at UC Davis, has this in-bred colony. If you are one of Mark's cats or this breeder's cats, all of this siblings, the parents would die and then the siblings would die, so that is called a malignant genotype and people have it too. That is why if we had that, you would be wearing an internal defibrillator, but it is not done in cats. But, anyway, we were not able to find a big incidence rate, so this is interesting. These numbers are not the numbers because the data has been redone and I do not have it yet with the higher number of cases; they will be proportionally the same. This really surprised me. If you are a cat that has any form of heart disease, you have a 3.4% chance per year of developing over five years, so five times three is 17%. It is a lot. It is way more than anybody thought. So, if you had 17% chance of going into heart failure in five years, I don't know what you'd think. It would get my attention. So, that suggests that maybe we ought to be monitoring these cats in a certain way and looking for things that might actually prevent it, which there are no known things to prevent it yet, but it shows you, I think it cries out for a need to look at these affected cats differently. That is the value of this. And then for blood clots. I was shocked with this. I thought that it was 1 in 500 cats that would get a blood clot, 1 in 1,000, and what it showed was that cats with HOCM or HCM had about an eight and a half chance over five years of getting a blood clot. That is like 1 in 12. That is way higher than I thought. That is pretty high. How high do you have to ... Once you get it, it is a disaster. So, I changed what I did, what I do. Now, I am more aggressive with aspirin or clopidogrel.

Here is the other interesting thing, lastly. We looked at the prevalence and cause of death of the HCM cats because they started dying, because that is what you do, and we looked at the control cats. For the first time that I am aware, this study has revealed the actual causes of deaths from the major causes of mortality. Now, these were not autopsy-performed. This is an epidemiologic study. If the vet said the cat had FIP, we said FIP. If the vet said he died of anemic or chronic kidney disease, so right there I am going to get crucified by the reviewers who are going to say, "Well, you didn't keep him in your lab around the world for five years," so I will have to deal with that, but this type of study has value with this number of numbers. Number one cause of death, noncardiac death, is cancer. The number two cause was chronic renal failure. Number three was what we

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lumped as GI disease, so if it was not cancer and you had weight loss or you had ascites or liver enzymes and it wasn't kidneys, we lumped that as GI disease. That is the first time that has ever been revealed and how that will be used will be interesting, but instead of maybe focusing just on flea and tick control, maybe the focus ought to include in a different way but I don't know what way that is, so a more aggressive way to monitor for cancer, which is the number one. That is how I would interpret this data.

Let's see if there is anything else. I think we are just about ...

In summary, we documented and compared the natural history and health outcomes in 1,700 cats. We found no difference if you were H or HOCM with regard to heart failure, cardiac death, blood clot formation. We found substantial hazard or risk if you have really thick ventricles or a big left atrium in terms of cardiac pathology. I have described the incidence. What is the difference between prevalence and incidence? Prevalence is a snapshot, so here I go – kachunk – and I can print it out, I can count out the number of men, number of women, so there are 68% women and the rest are men. That is the prevalence at this moment in time. If I photographed you all when you were 10 years of age and monitored your, whatever, until now, the new diseases would be the incidence. It is the development of a new disease. That data is hard to get because you have to do studies like this. This study identified the actual incidence of cancer, kidney failure, renal disease, heart failure, blood clot formation and, lastly ... oops, I'm sorry; I went back to the top.

Here is the last thing: survival curve. So, what does it mean, the number of days, percentage alive. Red is heart. Well, I just said what it is. This is noncardiac. If you are a cat with heart disease, you would drop off, you start to die a lot more quickly than if you are a cat that does not have heart disease. I think that suggests that we would take this – and I don't know the adjective – not more seriously, because we take it seriously, but we might look at it in a way not to freak out the owners but, instead, to identify the strategic monitoring opportunities that will have to be developed in order to identify hitting risk factors that might then trigger certain treatments.

Thanks again to Winn for your support. [applause]

Steve Dale: Maybe what I'll do is have you stay more or less put and share the microphone with Beth. You all have sheets of paper, pads, and we are going to have some volunteers, our wonderful volunteers, go around and retrieve the questions.

I have some exciting Winn Feline Foundation news for you while I wait for the questions to come to me. We have a single web address, but soon we will reveal a new website! Woo-hoo! So, we are updating our website, making it easier for people to give us money, but also offering new and different information and we will have a new and better look, still with feline health w-i-n-n – thank you, sir – [felinehealth.org](http://felinehealth.org).

Dr. Thayer: [Winnfelinefoundation.com](http://Winnfelinefoundation.com). I mean, .org. So, it is [winnfelinefoundation.org](http://winnfelinefoundation.org).

Steve Dale: Which makes sense, right? So, [winnfelinefoundation.org](http://winnfelinefoundation.org). So, about 15 minutes. Where's Beth? There you are. I want you to share a microphone with Dr. Fox because we need you to answer the questions also.

So, the first question is: What do you guys think of the US soccer game this afternoon?

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Audience member: Who won?

Steve Dale: Not the US. Germany did win.

Any updates on the use of polyprenyl to treat FIP? I don't know that you would necessarily know that. This question is about polyprenyl immunostimulant. That is the drug that Dr. Al Legendre is here talking about. Would you know if there is any update or not?

Beth Licitra: Steve and I spoke about this today. I am really not familiar with a lot of drugs that are out there to treat FIP, so I cannot answer that question for you.

Steve Dale: I can answer a little bit. What he is doing is looking for another drug, ideally, to use in conjunction with that is what he told me.

What is your experience with adult cats, 3 years old, with dry FIP? Do you see cats like this very often? And also, do you see senior cats? What's sort of the age range?

Beth Licitra: Most of the cats that come to us are younger animals, but certainly, especially in an outbreak situation or where catteries are having a problem, we do see older cats. I believe we do actually get a fair number of the dry FIP cases and I could go back in our records and look and maybe that would be some nice data for Winn to have and what we have in our foundation but, yeah, it is definitely something that we see and the dry cases are especially hard to diagnose, too. That is also a problem for us, so they don't go through necropsy. Sometimes it is a little bit challenging to diagnose this.

Steve Dale: This is an interesting question: Does the ultrasound - this is for Dr. Fox - does the ultrasound thickness of the wall of the heart vary in the size of the cat? So, would a Maine Coon cat, therefore, have a different thickness than, I suppose, a Singapura?

Phil Fox: I do not think it varies that much. I know I have colleagues who believe more strongly that it does. You take the extremes. You take a 4-pound cat, it is going to have a smaller heart than a big Maine Coon, but I think, by and large, the numbers, they seem to be pretty close, but it is unresolved and there is some controversy about that.

Steve Dale: If you have a cat that diagnosed with HCM, that is asymptomatic, young, is one option do nothing except watch?

Phil Fox: Yeah, one option is absolutely nothing. I am working on a manuscript with Dr. Carson Childer, Ohio State, for a special feline issue for the Journal of Veterinary Cardiology and this article is on what do you do for the asymptomatic cat. We talked back and forth a bit and in previous years, decades, people felt compelled to just review the literature, which is really human literature, and truthfully, there is no data in animals. We don't know. I think that it is a reasonable option not to treat many cats that are not severely affected and I think that many, many people would go along with that. I think this is an emerging area that as more data comes out that indicates prognosis or risk that that will force opinions one way or the other.

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Steve Dale: I have a quick question to add onto that of my own. Does aspirin really do any good? I am talking about for cats, not people.

Phil Fox: Dan Hogan at Purdue has done a wonderful job. You might have heard of it. It is called the FATCAT study, the feline arterial thromboembolism study. This was an issue that people had ... we would curse it every day because nobody knew if aspirin worked and then when clopidogrel came out, which is better? Clopidogrel is much more expensive and it is daily versus aspirin every three days, so what Dan and his colleagues showed was that clopidogrel is superior, quite superior. So, if you had a cat that had a blood clot, it is not that aspirin is useless, but you would want the best drug if they could afford it. Now, what nobody knows is what about the cats that never had a blood clot? Well, I think if you are at high risk, with a huge left atrium, I think you are compelled to discuss with the client the options. I just had a client last week who could not afford the clopidogrel, but she could get aspirin in every three days, so I felt okay about that. I have got others who want it. So, if you say if it works better in cats that had a blood clot and survived, it is not a big stretch to say maybe that is the best drug that probably has risen to the top.

Steve Dale: Is anyone working on doxycycline as an MMP inhibitor in FIP?

Beth Licitra: Not that I know of right now, but it's probably something that I think we would be interesting in looking at because FIP being that it is a disease that there is really no good treatment for, I think our ability to do clinical trials in animals would be a little bit better as when you think about cancer. It is sometimes easier to get drugs into clinical trials that way. It certainly wouldn't hurt to look at, and Gary and I are thinking about proposing a grant to do that through Cornell in collaboration with our hospital, but doxycycline is specific against MMP-1 and MMP-2 and we are looking for MMP-9, so it might not actually be something that would be ideal, but certainly, if we had a more specific MMP-9 inhibitor, it would be something to think about. I think with cats you always have to remember that; they do not really tolerate a lot of drugs as well and some of the protease inhibitors can be quite toxic, so it would be something to think about. But, yeah, for FIP with no treatment, it would be really nice to have something.

Steve Dale: So, let's say there is a cat with early suspected dry FIP. Is there a downside to trying doxy?

Beth Licitra: I don't know enough about doxycycline in cats to answer that question, but there are veterinarians in the room who could certainly answer that better than I. I am not any good at these treatment questions, I will admit that right off the bat, as a young veterinarian.

Steve Dale: I have a question for Dr. Fox, then. How can the pro-BNP test be used to weed out HCM in a breeding program or can it be used? And you might briefly – I don't know that everyone knows what that test is – explain.

Phil Fox: Sure. Great question. BNP is a biomarker. Biomarkers are chemicals that can be detected in tissue or fluids. It can be detected in urine, effusions, blood, serum --wise. So, if you could get an indication of a condition without doing a brain biopsy – I am making that up – wouldn't that be better? So, BNP stands for a thing called brain natriuretic peptide. It was first discovered in pigs in the brain, so it stayed like that. That test is an IDEXX test. ANTECH has another biomarker called ANP for atrial natriuretic peptide, so there are a couple

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of these out there. I am not sure in a dog or cat. ANP has not been looked at that much and more information is available for BNP, so I can talk about that more intelligently. I was always looking for a way to supplement the echo, which is expensive. If you have \$300 or \$200, whatever, for an echo, it is a lot of money, so we looked at BNP in cats with occult cardiomyopathy, it's published, and found that the BNP was pretty good at a certain sensitivity and specificity. I think it was 85% sensitivity, 84% specificity. So, it was not 100% but if you were a cat and you use the IDEXX BNP and the value was greater than 100, that test was, let's say, 86% sensitive and specific, which is not bad. So, it picks up a number of cats at a reasonable cost. Then, you should then go and do the echo. This is not a replacement for echo at all. It is to help people screen and that is how I think it should be used. I have got colleagues who do not like that notion for different reasons, but I think that that is reasonable. It is how it is in the human healthcare system. It is a reasonable screening.

Steve Dale: What if you have a Maine Coon cat or ragdoll cat or there are other breeds, too, that sometimes are associated with HCM, American shorthair and the Devon rex, etc. Are you more likely then to proactively even suggest to your veterinarian, maybe I should have the cat tested?

Phil Fox: If we had more time, that would be a great question for the audience to see what the practice and perspectives are. I am biased, so I am not going to do a BNP ever because I have an echo machine right here and I can do an echo pretty quickly and way quicker than I can get the result back and it is more reliable than a surrogate marker, but I think that anything that gets clients to pay attention to their pet's health when there is a reasonable – and here is the caveat and it is a good that you asked that, if you just add it to every cat you do ... like ages ago when I was moonlighting and Cardiopet was not IDEXX, it was Cardiopet. Cardiopet, which was a company then, marketed that every cat that breathes should get an ECG and it was a presurgical screen. Well, it was almost always unremarkable because if you select an unselected population, you are going to get false positives and you will not get a cost-benefit ratio that is reasonable. Same thing for biomarkers like BNP. It is best used in cats that you have an inkling, a gallop, a murmur, an irregular heart rate, a history of siblings, x-ray looks like the heart is a little big, then it is reasonable. Most people think it should not be used in complete absence of good clinical judgment or clinical database, so if you are just going to run it and add it on your profiles, you will get more false positives and you will have to describe to the owner why you ran it in the first place. So, just use your good clinical sense and select the best patients to run it on.

Steve Dale: Two final questions. Beth, for you first. You're young. I want to know if, in your lifetime, we are going to see an effective prevention or an effective treatment for this very mysterious disease called feline infectious peritonitis.

Beth Licitra: Maybe because I'm young, I'm also a real optimist, but I think so.

Steve Dale: That's a yes.

Beth Licitra: Yes!

Steve Dale: Okay, and maybe not as young but nearly as young, Dr. Fox. Same question, really, for you. HCM?

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Phil Fox: (Does not sound as optimistic so far). It depends when the horizon is. There is only a set number of drugs and they do not come along very quickly and people use them de novo without any data and then they get ingrained. I think the profession is getting very good at detecting HCM. The echo machines, by and large, except for that cheapo one I mentioned, are getting very good and any practice that wants to invest in an echo machine, you can get a pretty decent machine, way better than the high-end machines we had 15 years ago, for 50ish – I'm not trying to sell them – 40, 45, 55, you can get a really nice machine and with some training, you can make the diagnosis. So, we are better at that than knowing what drugs to treat. We know when something is effective in a multicenter clinical trial and they just do not come along very quickly. So, I think that, yes, we will not know for at least 10 years because I do not know anybody who is doing these studies and they will take at least five years to do.

Steve Dale: So, in five years there will be no HCM?

Phil Fox: I wish!

Steve Dale: That's not what you said?

Phil Fox: I think that things will emerge in dribbles and I think we will collectively get better. It is frustrating because we would all like to know right away and it is just unfortunately, it is just not that simple. I think, if anything, we will see somewhat of a trend away from treating mild-to-moderate cases because of the difficulty in getting people to jam drugs down for a benefit that is elusive.

Steve Dale: All right. Two stellar speakers once again – we couldn't do this without you as well – so thank you. [applause]

**END OF THIS AUDIO SECTION AND SYMPOSIUM**