



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

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2012 WINN FELINE FOUNDATION SYMPOSIUM TRANSCRIPT

Dr. John Rush: Feline Cardiomyopathy – More than Genes

Steve Dale:

Few have contributed as much to learning about cardiomyopathy in cats. Dr. Rush obtained his DVM and Master's degrees at the Ohio State University in 1984. He joined the Cummings School of Veterinary Medicine at Tufts in 1989. He has served as section head of the Emergency and Critical Care Services and as a clinical cardiologist and as an associate department chair. His research interest includes cardiac biomarker, cardiovascular drugs, dietary therapy for cardiac disease, and interventional devices for cardiac disease. We are going to hear a lot about that and in terms we can all understand. He has published over 115 peer-reviewed articles on cardiomyopathy, Dr. John Rush. Thank you.

Dr. John Rush:

Thanks for that introduction. It is wonderful to be here! It is just going to take me just a minute or two to switch computers around here and then we will get started.

Alright thanks again! It is wonderful to be here. It is wonderful to be invited to talk a little bit about Feline heart disease. How many people have actually had a cat with heart disease at some stage? Almost half of the people here have had a cat with heart disease. As we said before it is a pretty common issue. Happily though the Winn foundation has helped to support research in heart disease and they have supported us a little bit recently so hopefully we will be able to push this along.

This is the veterinary school at Tufts University, not far from here and of course there is always the rainbow that ends at Tufts University, a never ending pot over there. It is often appropriate at least in professional forums to tell you a little bit about who has sponsored the research that we are doing as there might be conflict of interest for instance if I am going to talk about a drug that is made by a company or something like that. There are a variety of different companies that have supported some of our research activities.

Think about heart disease and I am giving you kind of the approximate frequency of heart disease that we see in cats at Tufts.

We have seen a lot of hypertrophic cardiomyopathy and a relatively small number of dilated cardiomyopathy in these heart muscle diseases. We see a fair number of these that are either restrictive or unclassified cardiomyopathies. We see a number of cats that have arterial embolism, a clot to a limb. They end up being euthanized before anybody figures out what kind of heart disease they had because it is a very difficult disease. In the spectrum of seeing diseases that are heart muscle diseases, that is the vast majority of what we are going to see for feline cardiac disease. When we think about the most common form it is going to be this hypertrophic or thick walled heart muscle disease, so this just means thick wall heart muscle disease. This is sort of what the heart should look like in cross section with that red mushroom being the size of the cavity and this brown being the thickness of the walls. I think you can appreciate this cavity is

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very small and the walls of the main pumping chamber, the left ventricle are very thick. That is essentially the disease that we are interested in as the most common disease. What does this disease cause? It can cause congestive heart failure, clots often to the back leg, sometimes a front leg or someplace else. It can cause fainting and it can cause sudden death which is probably one of the more common causes of sudden death in cats.

When we see cats that seem to be healthy, but they go in under anesthesia and die suddenly under anesthesia it is probably one of the common causes that the cat had underlying heart disease and nobody knew about it. Then a bad thing happened under anesthesia, so the main feature is this probably is not that critical to know but the walls of the main pumping chamber are very thick. The cavity is small. If you were to look at this on a microscope, some people find that the fibers they just are not lined up. We would like them to line up and when the muscle contracts that they contract in a uniform fashion. They work with each other. If this one contracts and it is at odds with that one and so we are not going to get effective contraction and sometimes we see this green scar tissue in there fibrosis and certainly you would not want scar tissue in your muscle if you are hoping that it is going to contract. As a result of these changes, the upper chambers of the heart, the left atrium and/or the right atrium started to get enlarged and then pressure starts to build backup. So this is not a problem with the heart pumping. This is not a contractile issue. This is a problem of the heart filling, it happens during the filling stages, diastole; that thick heart makes it hard especially for the left ventricle to fill with blood and again a lot blood the is flowing through the heart muscle is going happen in a slower heart rate during the filing phase so when the heart starts to beat really fast, it is going comprise the heart's ability to fill. Again, we said the contractile function is usually okay, but problems in these lower chambers leads to enlargement of the upper chamber, the left atrium and the right atrium. That said, this left atrium we are going to concentrate on a little but because that tends to be the marker of whether we are getting in to trouble or not.

So what causes hypertrophic cardiomyopathy in the cat?

Well we just heard that genes are important and in the genes, this is kind of a little contractile unit, you may have heard things like actin, myosin, troponin, and tropomyosin which are all just different proteins that work together to allow the heart muscle to contract. It is the same sort of stuff that is in skeletal muscle, but they are just a little bit different in the heart. An abnormal mutation in any of these proteins can cause hypertrophic cardiomyopathy so there are abnormalities that are well defined in people and there are seven hundred different specific mutations that cause cardiomyopathy in people. In cats, we have identified two; one of them in Maine coon cats and one of them in ragdoll cats and that is it. It is likely the mutation that is in Maine coon cats is not the mutation that happens in domestic short hair cats or happens in any other breed, so we have got a long ways to go to try to identify these genetic mutations.

What is the relationship between the genetic test and development of hypertrophic cardiomyopathy?

How many people have done a genetic test on cat of any sort? A good number

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So okay, one of these things that is hard to get in your mind is how do these two relate to each other? So if we just look at when do cats present with signs of this hypertrophic cardiomyopathy? Then say they start out at age 0 and we are lucky they live to 20 or longer. Well, an average cat has no signs of hypertrophic cardiomyopathy. No problems until it is middle aged. We just have it at about eight but it could be at two years of age, it could be at 12 years of age and then after that point in time if they are positive, they have clinical signs of the disease. This may not be not exactly the sphere because if they have heart failure they are only going to live six months or year after that.

So if we were to do the genetic test, the question is when the genetics test is abnormal. Well again, the genetics test is going to be positive from birth, so while they do not necessary having a clinical signs of the disease, the gene is positive at birth. The next question would be well when is the echocardiogram? We are going to talk about the ultrasound exam of the heart, that is the main test that we do to try to sort out what kind of heart muscle disease is there, when is it abnormal? Well again at birth and at maybe the first six months of age, the echocardiogram looks perfectly normal and then somewhere between six months or a year of age and 10 or 12 years of age, some of the cats start to become abnormal. Then later in life most of them that are going become abnormal are abnormal. So that echo may not look abnormal until middle age or later and the other thing that is a little challenging is some of the cats with the genetic mutation never showed an abnormal echocardiogram. They never get the disease. So that is another major challenging thing for us in trying to decide how to tie this all together.

If we talk about this myosin binding C protein mutation in Maine coon cats and this is one of the ones that Dr Lyons talked about having identified as a clear-cut mutation. It pretty reliably picks up the cats at the University of California Davis cat colony where they have a Maine coon cat colony. Although they have seen a few of their Maine coon cats that are negative for this genetic mutation that still got hypertrophic cardiomyopathy. If we look at the tests about one-third of all Maine coon cats around the world carry the abnormal gene.

In the real world, it is a little bit more challenging. Some of the Maine coon cats with the mutation get hypertrophic cardiomyopathy. Some of these cats get really severe disease and some get mild disease. It is not clear why some get it really bad. Some cats with the mutation never get hypertrophic cardiomyopathy and some Maine coon cats without the mutation get hypertrophic cardiomyopathy. So I think this tells us that genes are not the entire story. So if we kind of look at this and we say well what is the population of Maine coon cats that do not have the gene, it is like this, it is about a third of the cats that have the gene. If we consider this group that has the gene, many of them but not all of them get hypertrophic cardiomyopathy but some are not going to get hypertrophic cardiomyopathy and if we consider the ones that do not have the gene, some of those get hypertrophic cardiomyopathy, but a lot of them, the majority of them will not. So we have to kind of find a way to explain this phenomenon that is sort of difficult to explain. So there are several options. There could be more than one genetic mutation or that other genes that are inherited at the same time bring on the hypertrophic cardiomyopathy or it may be that environment influences impact the expression of genes that cause it, things like drugs, vaccines, a stressful environment, exercise, nutrition,

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and/or early growth patterns, those all could cause it. Certainly it is possible that genetic play a very little role, but I think very few people think of that.

So we had some interest in the nutrition end of things and that was driven a little bit by the fact that when I see cats in our neck of the woods that have hypertrophic cardiomyopathy, a lot of them are the big boned, big headed cats and we thought that there might be something there. So we started to look at cats and measured their heads, measured the size of the vertebra, measured the length of their humerus and we identified that the cats who got hypertrophic cardiomyopathy were on balance bigger. They had bigger skulls and a long humerus than the cats that did not get cardiomyopathy. There seems to be some role for genetics in this and when we look at the Maine coon cats, we actually find a closer correlation with obesity and size of the cat than we do with genetic mutation. So that is sort of very tricky in trying to sort that out. Again, I am going to skip this and move right around here.

So what do cats with cardiomyopathy, how do they get into trouble? They can get into trouble with congestive heart failure. They can get into trouble with arterial embolism, fainting, or sudden death and unfortunately in cats the main clinical manifestation of heart disease is usually a crisis even. Cats do not do as much as say dog or people with regard to chasing balls and then kind of slowing down or getting short of breath. They kind of throttle themselves down so a lot of times, cats do not tell you they have a problem until it is nearly at the last minute, which can be very challenging. So indeed it can be any breed, although there are some predisposed breeds, it can be any age. There is about 2 to 1 predisposition for male and so there is despite the fact that probably you get the same genetic material, there is something bad if you are a cat about being male. It brings on hypertrophic cardiomyopathy or at least the clinical signs. We tend not to see coughing but we do see rapid breathing, difficulty breathing, and they tend to be like cats in that they become lethargic, they hide; they just do not interact with people as much. Again if there is a clot, we see sudden onset limb weakness or paralysis. Again things that might cause a fast heart rate in a cat like recent major stress from anesthesia, surgery, et cetera that seemed to be able to bring on the shortness of breath.

On exam, there is a variety of things we look for; altered pulses, altered things on listening to the heart. That may be one of those things that – well we will see if this will go through. I do not have dog picture, we do have the cat picture. Let's see if I can get this is to play here because, it is not going to play. Sorry it is not going to play loud enough. Well these are the heart sounds. A normal heart sounds is just lub-dub, lub-dub, lub-dub, lub-dub, and cats that have heart disease often have either a gallop, which is an extra sound so a-lub-dub, a-lub-dub, a-lub-dub, a-lub-dub or they have a murmur, lub-shhh-dub, lub-shhh-dub, lub-shhh-dub. Although they have to do it at cat heart rates which are up at 160 to 200 so it is tik, tik, tik, tika tck, instead of lub-dub, lub-dub, lub-dub, lub-dub. So those are some of the things you can pick up with stethoscope.

What is congestive heart failure?

To me congestive heart failure is fluid accumulation in or around the lungs so pulmonary edema if it is in the lungs, pleural effusion if it is around the lungs causing the lungs to collapse and that fluid accumulation causes poor oxygen exchange in the lungs which leads to rapid breathing, labored breathing and the other things we see in cats.

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How do we figure out whether it is heart failure or not?

Well certainly the history and the physical exam which as we talked about can help us. Chest x-rays are important in trying to figure out is there fluid in or around the lungs. The echocardiogram and there is a new test that is called the BNP test, NT-proBNP which is cardiac biomarker which actually looks pretty promising and very interesting for trying to figure out whether there is abnormal heart disease.

These are chest x-rays and again this is a normal cat, this is a cat with actually pretty darn bad hypertrophic cardiomyopathy, one of the things I want to point out is that especially on the lateral view the heart sometimes does not look especially big on a chest x-ray, so it is not always the best test for us for looking at the heart. Although to look at the lungs – that is what I want you to pay attention to – this black area here is the lungs, that is the heart, this is the lungs around it. Keep that in mind because I am going to show you fluid in the lungs in a minute. So you have to have that picture of what the lungs look like, so normal and a cat with hypertrophic cardiomyopathy. On the other view, again it is a little bit easier to pick out that heart as big on the other view. Still the lungs are nice and black because they are full of air. So now if we take a look here at heart failure, the heart is bigger and see this whiteness in the lungs? That whiteness is going to be heart failure fluid, pulmonary edema. You can imagine the lungs are going have trouble exchanging oxygen. That is going to cause rapid breathing and shortness of breath, difficulty breathing.

In another situation here, we have a cat that has fluid around the lungs so this is the air-filled lungs and this is all fluid around the lungs. We take a needle and we tap that off and the lungs are much better shortly after that. I think those are the two we think about with congestive heart failure, fluid in or around the lungs, that tends to be what we see in cats and this is the fluid that is in the lung. I am sorry that is sort of graphic, but this pink foamy fluid is what is accumulating in the lungs and that is what causes of the shortness of breath.

So that chest x-rays, how about echo? Because you know lot of times people say we should look at an echo on your cat to figure out if it has heart disease or not.

We use an echo to try to figure out are the walls thick or not, so what we are measuring is the walls of the heart, is the main pumping chamber thicker than our little cut off 0.6 cm and an echo also allows us to look at the size of the left atrium and are capillary muscles thick and a little bit on the right heart.

What does is this echo look like and how is it helpful. This is kind of a short answer. We are going to look at the size of the cavity of the left ventricle. The blue is the right ventricle, the brown is the muscle and here is a fairly normal cat echo. You can see it has a pretty good cavity size. The walls are not that thick and the heart can contract pretty well. So that would be a fairly normal echo.

Here is for comparison a cat with hypertrophic cardiomyopathy and it still has pretty good contractile function, but I think you can see the cavity is much smaller and the walls are much thicker. That is how we are identifying or defining, hypertrophic cardiomyopathy, it is dramatically thickened walls of the heart and a small cavity and it is really hard to get that muscle to stretch and fill with blood and sometimes it is the

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whole pumping chamber of the heart and sometimes it is just the free wall or just the septum. Here is just the free wall, see how thick and muscle bound that is? You can image that just does not work very well.

Then in the next picture we look at, we said if the heart does not fill well with blood, the left atrium gets big. The left atrium is the upper chamber where blood is coming back from the lungs to the left atrium down to the left ventricle. This little Mercedes Benz sign is the aorta and that is the left atrium and on this view in a normal cat, we could maybe take two or two and half of the aortic dimensions and fit in this left atrium, 1, 2, 2.5, 3. So here is a normal aorta and a normal left atrium in a cat and what happens is as the blood backs up because it cannot fill that thick chamber, the left atrium starts to get big and I think you could appreciate that this aorta and this is the left atrium that is dramatically enlarged left atrium and that is going to be associated with the heart failure. The other thing that we can look at on this particular one, which is another cat with a very big left atrium is you may or may not be able to see that little blush of smoke that shows up. That little blush of smoke, oops sorry, that is my bad. That little blush of smoke that shows up is a marker of cats who are at risk of getting a clot in their heart. The clot then breaks loose, goes down stream and lodges someplace else in the body. When we see a big flotation with that smoke we worry a lot about clot formation.

On an echocardiogram again we are going to measure the thickness of the septum and the thickness of the free wall and figure out if it is normal or if it is too thick. If it is too thick then we are thinking it is probably hypertrophic cardiomyopathy. One other thing that it does here which ends up being a challenge for treatment and this may be certainly in the more than you need to know category but if anybody has ever talked about an out flow tract obstruction or systolic anterior motion of the mitral valve, it is very confusing. So if you wanted to know about that the general idea is that this is the aorta and that is the main pumping chamber. This is the wall which is too thick and there is thickening up at the top of the intraventricular septum. This should be a straight shot right down into the ventricle and this thickening is causing an obstruction. So in order to maintain an arterial blood pressure of 120 like your arterial blood pressure, the left ventricle has to work harder. It has to raise the blood pressure up to 150 and as it does that we get turbulent flow here which causes a murmur and it pulls open the mitral valve which causes mitral regurgitation. At that end point we should not see any color on that echocardiogram and all that color is abnormal flow and that abnormal flow is what causes the murmur. The lub-shhh-dub, lub-shhh-dub, lub-shh-shh-shh is the abnormal blood flow that is in the heart as a result of this problem. When this happens if we do the drug that increases the vigor of contraction in the heart which is what you might want to think about doing in some cases and then we pinch that off even more – now the blood pressure goes even higher here and that might even lead to a low blood pressure, hypotension.

That is one of the challenges we have in cats that is different than dogs and different than most people's disease.

When think about clots in cats, this pad is nice and pink and this one is not because the cat threw a clot to that leg. Again pink and not pink because the clot went to the leg. These clots tend to go to the back legs. This is a clot that was pulled out of the main artery in a cat. It was pulled out of the aorta and you can see

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this vessel goes to one back leg and that vessel goes to another back leg. These are supposed to supply like the bladder et cetera. This clot problem happens in 20 to 40% of cats with cardiomyopathy and the bigger the left atrium is the more likely we are going to get a clot in the left atrium and then it breaks loose and goes down stream.

So, we can see them go anywhere but the majority of times they go to a back leg. If it goes to a front leg they are dragging their front leg. They cannot use it. If it is both back legs they cannot walk at all. It is kind of often a major crisis event because no cat has told anybody that they have a heart problem. They are just walking around being normal cats, doing what they are supposed to do and then you come home from the grocery store and they are crying and they cannot use their back legs and they are pulling themselves along with their front legs. It is kind of a catastrophe when that happens. They can go to other places in the body but this is the one we tend to see most often. So there is the aorta, there is the big left atrium. That is a clot that is floating around inside the left atrium and that is about ready to break loose and go down stream. You can also see a little bit of the smoke in there. That is a scary thing when we see that because we know this is a cat that is about ready to throw a big clot and that it might not survive that. Again as we said there are a lot of cats with arterial embolisms who that is the end of the game. They get a clot in their back legs and people say it is a bad deal, you should quit.

Let's talk a little bit about other forms of heart muscle disease.

Dilated cardiomyopathy, the cavity is dilated and the heart does not contract well. What you have in mind is that is a big cavity, the walls are thin and it just does not squeeze down very well. The contractile function is markedly reduced with dilated cardiomyopathy. Again this is one of the ones that was previously studied. Again taurine deficiency was identified to be a cause and as a result of figuring out that the diets were a little too low on taurine in part from I think Winn Foundation funds, this disease went from equal frequency to hypertrophic cardiomyopathy to now where it is very uncommon. That is one of the ways where supporting research can help things because we basically almost wiped this disease off of the map through research activities.

Restrictive cardiomyopathy, you may or may not be able to see this kind of scar tissue in here with little clots attached to the inner surface. This is another form of cardiomyopathy which we probably do not need to spend too much time on.

We are used to getting blood tests, blood tests help us for certain things. They are really helpful for kidney disease. They are really helpful for like is there an anemia or not? So are blood tests helpful for cats that have heart disease?

Well some of the main tests that we do like a complete blood count or CBC or a chemistry profile, we tend not to see major abnormalities in cats. In fact some of the sickest cats have pretty normal blood tests. If cats are over 6 years of age we recommend getting a thyroid test because high thyroid function, hyperthyroidism can affect the heart and cause it to get a little thick. Certainly in the cats that look like they have reduced vigor of contraction we want to get blood taurine levels. If they have a really big right heart we want to

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check for heartworm disease. But there is this new test, this NT-proBNP test that looks kind of promising for what it might be able to do and this is one of those tests that we have been studying so I am going to talk about it just a little bit.

It turns out that if you have a cat and it has a murmur or an irregular heartbeat or somebody hears a gallop that extra third sound, but it does not have any signs yet. It is a healthy cat that is taken in to the vet and the vet says 'Oh you cat has got a murmur.' Then you have to try to decide, do I want to do the echo or not? The echo is like; I do not know what it is costing for you but three, four or five hundred dollars for an echo. Do you want to go ahead and do that or not? Well this test might help us because if this BNP is above 100 the chance there is significant heart disease is much more likely. Whereas, if this test is like 25, the chance you are going to get some sort of useful information from an echo is pretty low. That may be helpful there. The second spot where this test might be helpful is a lot of times when cats come in with shortness of breath it is hard to tell if have heart failure or if it has asthma or FIP or pneumonia or pyothorax or some other disease process and this test differentiates heart failure from the rest of those shortness of breath diseases. This test is available in people. If you go in to the hospital and you have shortness of breath or difficult breathing they will do this test and if it is real high they think you probably have heart failure and go down that diagnostic pathway and if it is low they will look at something else.

This test is now here and if we kind of look here and we say well how high is this level? Well in healthy cats it is pretty darn low. In those who have cardiomyopathy but they are not telling anybody about it, occult cardiomyopathy, it is kind of middle range and in those that have heart failure it is way up here. Hopefully this is going to turn into a bedside test so that people can get this answer really quickly. It is a pretty good test for trying to sort that out. It is right nine times out of ten and so it might give you a little bit of the wrong information one time out of ten but still it turns out that veterinarians, if they only have a history, physical exam and ECG (the electrocardiogram) and a chest x-ray, if they do not have an echo for shortness of breath – they are correct about 70% of the time. The test is better than the veterinarians are on their own.

So, could it be useful either in an asymptomatic cat that has a murmur or gallop and you are trying to decide should I do an echo? Then, you can do that test and try to decide whether to do an echo. In a cat with shortness of breath and you are trying to decide is it heart or lung disease, especially if the client is kind of on the fence as to whether they want to spend money or not or they do not want to do an echo. The BNP might then be helpful. That is where that new blood test might work.

We have talked about congestive heart failure, arterial embolism, syncope in the asymptomatic cat.

Let's see what do we have loaded here next.

We have got these various diseases: - Heart failure - Clots (FATE) - Fainting (syncope) - The asymptomatic cat

Now we are going to think about what cardiac medications do we have available to try to manage these cats. So we have one FDA approved medication. From a perspective of what does the FDA say, yea the

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companies jump through the hoops and we are confident this works in cats. What medications do we have? We have one – furosemide also called Lasix which is a diuretic. If we take a peek at well what are the cardiac medications that we use with some frequency in cats it is actually a lot of them. I use these medications almost every month. We use furosemide, drugs called ACE inhibitors, pimobendan, nitrates and other diuretics. We use anticlotting drugs like aspirin, Plavix, clopidogrel and other heparins. We use drugs to try and control the fainting and even in asymptomatic cats we try to use some of these drugs. Then the question is well ‘How do we know to use these?’ Well as you already know there are not a lot of people that are plunking down giant amounts of money to study cats. We are kind of left on our own to figure out well what is the dose in dogs. What is the dose in people? Let’s figure out a dose that might work in cats and try and go from there. How many of these drugs have been reported in the literature to have been used in greater than 30 cats with heart disease?

Well, actually not very many of them and all that says is we gave this drug to 30 cats and this is how they tolerated it. It does not tell us anything about the effectiveness. So 30 cats are not a lot of cats, you know there are all sorts of fun reactions that can happen with drugs so we really do not know a lot about what are the best medications to treat cats. They can figure that out, you may have heard of a blinded, randomized placebo controlled trial which basically means you look at a drug versus a sugar pill and the owners are blinded and the investigators are blinded and once it is all done you get a feel for which one works better. Sometimes the drug works better and sometimes the sugar pill works better. So if we were to say well how many of these studies do we have, blinded, randomized control trials that we are confident that we know this drug works in cats with heart disease? None. There are no blinded, randomized control trials looking at cats with heart disease. That is where we are in the scheme of research and being able to answer, you know when you take your cat in to the veterinarian and they say you should give this drug or maybe this drug will work that is kind of where we are. We are not as far along as we would like.

If we get fluid in the lung, congestive heart failure; we have got a cat in the oxygen cage and we have got some chest x-rays that show a little fluid in the lungs. What might we use? We might use furosemide, Lasix which is a diuretic. We might use an ACE inhibitor like benazepril or enalapril. Everybody thinks furosemide works and a lot of people think ACE inhibitors are helpful. After that we kind of do not know which is the best way to go. So there are a couple other drugs we might use and certainly dietary modification because water, the body holds on to water by holding on to salt or sodium. We do not want to give them a high salt diet. Fish oil supplement might be helpful so you know that is kind of where we are at right now so we wanted to try to sort out well could pimobendan be useful to treat fluid accumulation in cats with cardiomyopathy. This is a drug that increases the vigor of contraction of the heart. It makes it a little bit easier for the heart to pump blood forward. We know in dogs that it improves survival time, in dogs that have heart failure and it results in improved clinical signs because somebody has paid to have these randomized blinded placebo controlled trials and/or comparative trials done. We do not really know very much about it in cats. So we went out with a couple of other places in this area, the Massachusetts Veterinary Referral Hospital and Angell Animal Medical Center and then Tufts and we put together all of

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the cats that we had treated with pimobendan which was 170 cats. They tended to be 11-year-old cats again mostly male, that is what we see. It is more often males that get heart failure and this is a reflection of just what we see in cats because a lot of you might be interested in a specific breeds but the majority of cats we see are domestic short hair and domestic long hair cats. They tend to be a little bigger than normal. About 40% of them had hypertrophic cardiomyopathy. A much smaller proportion had the dilated form of cardiomyopathy.

These are the medications they were already giving and then we looked at the addition of pimobendan. This is the dose we used. It seemed pretty safe. Pimobendan was only stopped by 5 of 170 owners. That actually seems pretty safe. That is not too bad. In two of those five cases the heart disease resolved and in one the owner could not afford the drug anymore, they stopped it for cost. In one they could not get the medication in to their cat so they stopped. We are all familiar with that game. It is amazing the owners deny they do it. Then one reason for stopping is they thought their cat was vocalizing and seemed agitated after getting the drug. So if we look at what is noted in the record for side effects, again only five cats had a side effect that might have been related to it. That vocalization and agitation was seen in two cats. One of them wanted to continue it because their cat felt better; then not wanting to eat, vomiting and constipation so not that many side effects so it seems promising from that. What we do not know is whether that actually translates into clinical benefit or not. We have greater comfort that this drug is safe but what we do not know is, is there a clear cut clinical benefit? Do they either live longer or do they feel better. The live longer, you can only sort that out with a randomized, blinded placebo controlled trial and the same sort of trial could also answer the question of do they have a better quality of life where there clinical signs improve.

We have one or two other studies with a couple other institutions especially the University of Pennsylvania trying to answer that question and it turns out that if you ask cat owners and dog owners the question of if you could have really good quality of life or a longer survival time, which would you pick? A lot of the owners say, like 90% say quality of life. They value quality of life over survival time. Then when we asked people, both dog and cat owners of animals with heart disease how much time would you trade, over 85% of those that would trade would trade at least six months of high quality time for improved survival time. So, this quality of life thing is another piece of the puzzle that is really hard to study but is highly valued by cat owners and so we need to be trying to sort that out.

We just published on a quality of life tool that we are hoping will be helpful to try and assess that. When we think about an active clot, you have got a cat and they walk in the door and they have a clot well potentially not a lot that we know of really works there. We can give oxygen. If they have fluid in their lungs we can treat that. We can warm them up a little bit. We want to give pain killers because these cats are often are very painful. Physical therapy might be helpful and then we can give anticlotting drugs. Drugs like heparin, Plavix, clopidogrel and aspirin. We can give drugs that try to break the clot apart although these drugs have not been proven to really result in any major benefit or we can go ahead and try and cut the clot out but these are cats with bad heart disease and they tend not to really tolerate the anesthesia. If we think about, you know a lot of people say well this sounds like a bad deal. How is this going to go?

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For those that have back leg clots about 30 or 40% will walk again. So that means that over 50% of those cats are never going to walk again. It is a bad deal. For front leg clots over 90% of them will walk again and so I think a lot of veterinarians on the basis of well it is the back legs, only 30 or 40% of them walk again and we are not sure what treatment is the best thing and they are very painful when this happens and they might get another clot. A lot of people decide to quit. I am a fan of treating it at least for a couple of days. I think a lot of veterinarians would say it is time to quit when this happens. The question is a lot of cats are put to sleep in the first 24 hours, what happens to the cats that are not put to sleep in the first 24 hours. Most of the cats with a front leg clot regain function and there are three or four studies that looked at somewhere between 60 and 184 days tends to be the average survival time for the cats that are not put to sleep. Some cats may live for a very long time. We had one cat in that particular study that had three clots over a nine year period of time. Recent studies suggest that cats after they get a clot are more likely to die from fluid accumulation in the lungs than from another episode of a clot.

The more that we can get good at trying to figure out how to prevent this the more likely that we will be able to help cats. These are drugs for not when you actually have a clot but in cats that you think might be at risk of a clot that you might use it to try to prevent it. So aspirin is used, we do not know the dose, we do not know the right frequency. It is, you know there are some other issues with. There are low molecular weight heparins. We will talk about that. There is Plavix or clopidogrel which look kind of promising. Then Coumadin or warfarin which is really hard to use, I will not use it because I have made too many cats sick with it. We tend to initiate it in cats that have a pretty big left atrium or those that have a prior clot or those that have that smoke in their left atrium, that is when we tend to use it.

These low molecular weight heparins; dalteparin, Enoxaparin – they have a longer duration of action than the regular heparin formulation that we use in the clinic all the time. They are pretty safe; they do not need any monitoring. The two main down sides are they require subcutaneous injections twice a day. It is a volume that you might give that would be similar to that for diabetic cats so it is a really tiny volume but is still an injection twice a day and they are expensive to use on a long term basis. Probably 400 to 500 dollars a month for a really big cat, 300 to 350 for a small or medium sized cat so it is kind of expensive. This is though currently my preferred anticlotting drug and that is just based on anecdotal stuff.

Most people would say they like Plavix or clopidogrel which is an antiplatelet drug so platelets float around in the blood stream; they canglom together and form a clot which is different than interfering with protein which we were talking about with the previous one. Plavix is kind of expensive but in the last month we have got generics available and so the cost is going to be much lower at this point in time. The main side effects we see are foaming at the mouth in maybe 15 or 20% of cats where it tastes really bad and then sometimes you can hide it in a capsule or a liver toxicity. An increase or elevation of liver enzymes with increased bilirubin and they turn yellow. The few cats we have seen with that have had that go away when we stopped the Plavix. So this is my second choice for an anti-clotting drug.

Then there is that cat that does not have any outward clinical signs. We just do an echo and they have a really thick heart, is there anything we can do for them? Well a lot of people think if you can slow the heart

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rate and improve filling that would be useful and drugs like beta-blockers Atenolol or carvedilol are probably used most frequently and some people use diltiazem. Those would be drugs that would help keep the heart rate slow and might improve that outflow tract obstruction but cardiologists are highly variable in their approach to say who needs it and who does not need it. Some use those very early in disease and some do not use them at all.

How long will cats with cardiomyopathy live? The asymptomatic cats are often going to live from three to eight years from the time of diagnosis. Those that have heart failure the various studies have said somewhere between 92 days and 1½ years. I would say on balance if we can get them six months to a year that is very good. The fainting cats are much less common and flat cats again the studies are sort of showing a much shorter period of time once they have a clot.

Who should you screen for hypertrophic cardiomyopathy and how should you do it?

That would be a very interesting question to be debated. You could have 10 cardiologists up here all with a different opinion. In my mind if you have a cat with a heart murmur or a gallop they may be hiding heart disease. That would be a cat that I would try to figure out if it has significant heart disease or not because the first sign of a problem is usually going to be a crisis event where they either have heart failure or a clot so if you find it earlier you can maybe do something about it. Cats with irregular heart rhythms, cats that have unexplained respiratory difficulties or a related cat has heart disease. Probably about half of the cats we have are you know in the same household and they have the two brothers or the brother and the sister. About half of the brothers or sisters that we see have heart disease when we have diagnosed heart failure in one of their other cats. Then sometimes people just like to know, 'My breed is disposed for cardiomyopathy, do they have it?' That might be a good enough reason to look.

How to do it; well the dogs are checked for shortness of breath and then in cats that does not work very well. You know how do we do the screening? We do the screening with echo. Maybe that anti-proBNP will play a role. Certainly listening is helpful but you know a solid 30 or 40% of cats have no murmur or gallop when they have big time disease so just an exam by a veterinarian is not going to do it because you are going to miss a whole bunch of cats that have significant heart disease. Cat disease is hard, it is not easy and those are some of the tools of the trade and I think we are learning more every year in part from various places that support the interest in cats like the Winn Feline foundation.

I was asked to maybe mention two of the things that they are supporting and we have in fact been studying. One of the things we are looking at is that pimobendan drug that we talked about for heart failure. We have seen a couple of cats with kidney disease and heart disease that seem to do better and their kidney values actually dropped a little bit. We are trying to do a study now to see if there is anything there. What I do not want you to do is start giving pimobendan to cats with kidney disease though because we are not anywhere near that. No place close to that.

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The other thing we are looking at is a treatment for cats that have active clot. It is called bosentan which is a new drug that is very expensive, like ridiculously expensive \$1000 a dose or more and it seems to help in people that have high pressures in their blood vessels to their lungs and we think there might be a chance that this could be helpful for cats that have clots and so we are starting a study to try and investigate that. You know those are just examples of us trying to get a little bit more information about it so that the rest of the veterinary world can hopefully learn from that and do a slightly better job.

That is all I have.

(End of Session)

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