



# WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

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**40<sup>th</sup> Annual Winn Symposium – June 28th, 2018**

**“Perplexing Paradigms of Feline Medicine”**

**Transcript of Audio: Introduction, Dr. Melissa Beall on “Feline Leukemia Virus – past, present and perpetually perplexing”**

**Mr. Steve Dale:**

You have at all of your tables some index cards and we will take questions at the end. I will run around the room and I'll have helpers run around the room to grab those. I failed to do some things. One thing I failed to do is our executive director cannot do everything herself. She is pretty amazing, she is a super hero to us but she cannot do everything herself. Sitting in the back of the room, often very quietly doing her work is our super assistant. Lisa, can you please stand up? We need to acknowledge you. [applause] See, she very quietly does things. You can tell.

Our next speaker is someone who I have had many times the pleasure of meeting. I don't remember, I think it was at NAVC (the North American Veterinary Conference) we got a super secret note and the note said there are some of you we would like to have come. The e-mail even whispered, you could tell. We'd like to have you come because there are some things about FeLV that we think people should know about. We are thinking about and we are not sure about and we want to bring some leaders in to talk about that. Dr. Melissa Beall has been a leader in veterinary medicine for some time. She received her veterinary degree at The Ohio State University. [applause] University of Wisconsin! I think I could mention any university here and have it get applause. But I guess not Wisconsin, University of Illinois! [laughter] Alabama! Auburn! Alright that worked!

Getting back to Dr. Beall, she then worked in small animal practice in a laboratory of animal medicine before entering a graduate program in comparative medicine which is a really cool thing, at Cornell University. Cornell University! [applause] That worked. Over the last 12 years at IDEXX she has contributed to the development and launch of vector borne disease, pancreatic, lipase and NT-proBNP diagnostic products and NT-proBNP. By the way you are not necessarily here to talk about that but that is something that truly is on the cutting edge and really important. Have you guys heard about – do you guys mind if I mention the D word? That is dog?

Dog flu has been around for a while, I think in 2005 it mutated from horses to dogs. It was an equine flu, that was H3N8 and then a couple years ago in the city I live in actually we saw H3N2 for the first time. No company does as good a job, as comprehensive a job at tracking exactly where the dog flu is. We are so dependent and grateful actually for IDEXX doing that. There is no CDC for pets and IDEXX picked it up and said we are going to include all the other labs that are testing for dog flu and we are going to then talk about this and we are going to show this on the website which helps veterinarians track dog flu and also communicates to people like me who communicate to millions of pet owners so we could track where the outbreaks are. Hopefully in my view more dogs get vaccinated as a result and that is all because of IDEXX. As a medical affairs veterinarian she currently supports Rapid Assay products and Cardiopet Pro-BNP at the reference laboratory at IDEXX. Please help me welcome my friend Dr. Missy Beall. [applause]



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## Dr. Melissa Beall:

Can you hear me in the back okay? Yes.

I want to thank the Winn Feline Foundation for inviting me today and making a difference in the lives of cats I think is really what it is all about. It is what I want to talk about tonight in terms of feline leukemia virus.

Before I started vet school I moved to Ohio and took up a job at the vet school working for Dr. Gary Kociba in his laboratory and as you know there was a lot of work on feline leukemia virus at the time at Ohio State. I had no idea when I did that, even before vet school that I would end up when I got to IDEXX spending the better part of 10 years looking at feline leukemia and trying to understand some of the very perplexing things that we were seeing coming from customers in the field and the results that they were getting. I would like to talk to you a little bit about the work that we have been doing on that.

How many in the room have ever had to deal with a feline leukemia positive cat or test results that didn't make sense? Lots of folks; so you'll be able to sort of sympathize with what is happening in this area. The one thing I would like you to walk away with from this talk is recognizing that feline leukemia while we talk about it as being one virus, it is not one disease. It is different in each cat in the way each cat handles that infection and a lot of that is based on its immune response to the virus.

Why FeLV?

Well it is not going away, it is still here. We are going to talk about the different types of infections that we see and these regressive infections which I'll talk about in a few minutes are probably more common than we recognize. There is a lot of new information available. I want to talk about some of that tonight and some of the things that are changing related to that. We want to make sure we are helping protect cats from this infection. We also want to make sure we are protecting cats from unnecessary euthanasia. Finally and most importantly, there is an opportunity to do more for these cats making a difference in the lives of these cats and really trying to give homes to FeLV infected cats placing them in homes safely because they can live, some of them at least a nearly normal lifespan.

To do this I have to start with the evolution of the cat. This is a great article from Scientific American and what I want to point out is that when you look at the evolution of the cat there was a point here where our domestic cats broke off from all the other cat species. That is important because at that time there was an ancestral cat, we don't know who. There was an ancestral cat that ate a mouse or some rodent species that had what we call a murine leukemia virus, mice and rodents can have these same types of leukemia viruses. This infected mouse ended up giving this ancestral cat this leukemia virus which integrated into the germ line of that ancestral cat. Today, all small cats that come from this lineage here, our domestic cat and related cats have what we call endogenous FeLV. It is inherited from cat-to-cat, they all have this. None of these other bigger cats do. That is important for a couple reasons we will talk about in a second. This slide also reminds me to remember that our cats today are still very much like those ancestral cats being predators. They are predatory species. These are cats that will hide their clinical signs or their symptoms to protect themselves because in a predatory



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these cats have maintained some of those early characteristics. One of the things that is interesting about cats having these endogenous copies of FeLV is that they may in fact be beneficial. I put the Winn note up here because Winn has just recently chosen to fund some research on endogenous FeLV. It is thought that the expression of these endogenous FeLVs and that they have been maintained over time are in some way protective for cats because they help protect cats from the exogenous or infectious form of the virus. One of the observations that we have is that it is very difficult to infect adult healthy cats with FeLV and show that they develop the progressive disease that we typically think of for FeLV. Younger cats are typically the cats that are more susceptible to infection with FeLV in terms of developing progressive disease or clinical signs that we typically think of.

All cats have an endogenous form of FeLV but it is the exogenous or this infectious form of feline leukemia virus that we have to worry about in terms of our cats contracting this illness. What is interesting is this exogenous form can come in and infect a cat and it will combine or mutate with the endogenous forms that exist within the germ line in the genome of the cat to make different viruses. It can change after entering the cat. That influences how that infection plays out. We typically see transmission of FeLV from the queen to the kittens, that is considered vertical transmission but we also see horizontal transmission. We worry about this in terms of bringing an infected cat into the household because that virus can be spread through close contact and these salivary or respiratory secretions can be spread through breeding, that close contact. Truth be told this virus is not very hardy. It is very susceptible to detergents, to drying, to variations in hot or cold temperature. For it to survive in the environment it really needs room temperature conditions and moist conditions. It is possible to clean and sterilize and prevent transmission because the virus itself is just not very hardy.

This disease was first studied and discovered at the University of Glasgow back in 1964. Dr. William Jarrett was working with a colleague in practice who discovered this amongst a group of cats in Scotland where they noticed basically an outbreak of lymphoma. At that time there weren't a lot of diagnostic tests available but they quickly developed an antibody test and they went out and did a seroprevalence study to find out how common is this infection in our domestic cats and our pets. At the time they were seeing about 40% of cats testing antibody positive. Over the years you can see that the number of cats that we find today and this is now testing for the protein or the viral proteins of the FeLV, it has dropped significantly. We have done a very good job of controlling the spread of this infection through vaccination and segregation and choosing which cats we put into households. If you look a little more closely at more recent times and this comes from studies of more than 80,000 patients. In the more recent years what we are seeing is a slight up-tick in the prevalence of both FeLV and FIV. Given the numbers of patients in these studies this is likely a significant increase from 2.3% FeLV in 2006 to 3.1% in 2016. In these studies they recognize that the cats that were at greatest risk were those that were male, had outdoor access, were older and more likely to be testing positive if they were sick. In the study what they saw was the adult cats were more likely to test positive even though I told you the young cats are more susceptible. In the juvenile population they saw 2.5% of cats test positive. Then 3.6% in the older cats. What does that mean? How can the young cats be more susceptible but the older cats test positive more often? It is just the likelihood that an older cat is going to test positive, it is not that they are necessarily acquiring the disease or they are at risk of acquiring the disease but we are recognizing the disease in these cats because they are older.



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that is because veterinarians were seeing sick cats. Up to 8% of cats with respiratory signs in this study tested positive for FeLV and we know these sick cats are the ones that are going in to see the veterinarian. That is why we think in this study veterinarians saw more positives than in the shelters. It is interesting to note that in healthy cats the prevalence of FeLV was 1.7%. If they had oral disease of stomatitis, gingivitis (bad teeth) 4.7% and 5.5% positive if they had abscesses or wounds meaning they were outdoors and they were fighting. Then 8% in those respiratory cats. This is going to be a common theme. We worry about FeLV and coinfections, comorbidities meaning they have another infection along with that FeLV which causes that cat some trouble in controlling their FeLV infection because their immune system also has to fight a respiratory infection and maybe a hemotropic mycoplasma infection. They are dealing with multiple things.

One of the things that we have to recognize about FeLV is that things are changing right now. I know I have some questions from Vicki about what is happening in the shelters. We know that the terminology that people use to describe FeLV has changed. We have seen a lot of different names and things used over the years. We know that there are some new guidelines coming out very soon from the American Association of Feline Practitioners and those recommendations will have some new guidelines in them. We think that the expected lifespan in FeLV infected cats is longer than we originally understood. The studies that were done originally many years ago looked at the life expectancy of cats when they were held in homes that held 20, 30, 40 cats and they lived for two to three years. We think there are populations of FeLV infected cats when put into a smaller household that can live 3, 4, 5, 6 years, 14 years, 16 years. These are the things that are changing and with these changes come an opportunity for us to do more to benefit these cats.

Has anybody ever heard of any of the words that are on this? This is just one of those words, but these words have been used interchangeably to mean different things or the same thing and it is very confusing, regressor, regressive, progressive, abortive, focal, latent, right? What do these things mean in relation to an FeLV infection. When I graduated from school we said, "Yea, FeLV positive cat, I know what to do with that cat," end of story. We thought it was all solved. It is much more complicated because it is not just a single disease. This is the description of what happens to an FeLV cat. This was published back in 1991. It is very easy to understand, right? Try explaining this on the telephone call where you have to tell someone what their test result mean. This is complicated. It is absolutely accurate based on the experimental infection studies but it is very, very complicated and we want to try to simplify this so that we can get everybody on a common understanding around FeLV. One of the big things that has been coming up and stirring up a lot of conversation is that more and more shelters are choosing not to screen their cats for FeLV. This is a letter that Vicki was kind enough to share with me. It is a newsletter that came from Oregon, their humane society talking about leukemia testing. I know you can't read this in the back of the room so I'm just going to read a little bit of this to you. They have been collecting data on about 6,900 cats for the FeLV virus beginning in 2016 through September 2017, of the cats tested they found 21 true positive. Then they say we verify a true positive by running an ELISA test on serum and then following up with an IFA to detect virus. This will rule out false positives which can occur. I'm going to talk about this in a minute. In addition to the 21 cats that tested positive on the SNAP test, that was 0.3% of the cats that they tested, that confirmed positive on the IFA there were five additional cats that tested positive but were negative on IFA and they considered those guys to be false positives. I'm going to talk to you about why that might not be a good answer



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Then down here they are saying because of the low prevalence of FeLV in our population we have decided that we can better serve our patients and community by targeting our FeLV screening program to high risk cats. There is nothing wrong with doing a screening program for high-risk cats; it is absolutely acceptable to do that. If shelters are moving in this direction, it is not just happening in Oregon, we know it is happening in Canada, we know it is happening in Florida and other places around the country. We can do this but there is an education component, a communication component that has to happen at that shelter with the adopter and to the veterinarians in their area so that they know that this cat has not been tested and needs to see a veterinarian and needs to be tested particularly if they are going into a multi-cat household. This is important, this is changing and we need to be aware of it and we need to talk about it. This is becoming an economic decision based on what the shelters can do, the cost of the testing and how they prioritize their funds. More shelters are moving these cats either out into foster or trying to get them adopted and asking for the owners now to have this testing performed through their veterinarian. Any time we have change we need to develop this common understanding. We have to make the communication and the terminology and all these things work together.

Some of the things that we are trying to do is come up with common terminology. We need to share the same language and communicate about the same things. We need to understand these diagnostic tests. It has been very confusing over the years the way things have been written in the literature. I want to talk tonight about what these different diagnostic tests are and what they mean. We need to have a better understanding of the disease. We do not have all the answers to this disease. We don't. That is the purpose of the research. There has been very little research on FeLV in recent years. It is now growing again. More funding is coming in and the research is what is going to help us answer the questions that we don't have answered today about the disease. This is all necessary, this common understanding if we want to do the very best for these FeLV infected cats.

As I said at the beginning if there is one thing that you take away from this it is please recognize that an FeLV infection is not the same in all cats. These are the three cats we are going to talk about tonight. Pretty much every picture of a cat you will see in this presentation is an FeLV positive cat. We have worked with a lot of different people who send me their pictures all the time so I have put them in here. These are all FeLV positive cats. The cats we are going to talk about tonight are Basil, Jasper and Zombie. I have their ages listed up here. We are going to come back to them in a minute but we have to start with some biology. As Dr. Katie said at the beginning, I know I have a pretty broad audience here so some of this I'm going to simplify but I think it helps just to get everybody on the same page so that you can understand. You have to understand these terms in order to understand the diagnostic tests. I'm copying these analogies because I thought they were really helpful and I think it helps explain this a little bit.

If you think about the cells in our bodies, the DNA in the cells is sort of like a cookbook. It contains all the information a cell needs to do what it needs to do. A cookbook is filled with what? Recipes. Each individual recipe, I kind of relate to that RNA molecule. If I pulled out one recipe, RNA, and that RNA, that recipe is what makes the product. The instructions to make a given product, let's say it is bread. In our case with the cell it is going to be a protein. Keep those in mind, DNA is the cookbook, RNA is the recipe. The protein produced is the product. This is what it looks like if you put those things



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the cookbook, the cell decides I need to make something. It goes to the cookbook and tears out the recipe. The RNA has to move out into the cytoplasm in order for it to be cooked into the protein. The DNA and RNA represent nucleic acid and the RNA gets translated into protein. Clear? Kind of a good analogy?

Here is what it looks like when FeLV infects a cell. Here is the virus. The virus contains an RNA genome. It contains a reverse transcriptase, again enzymes like Dr. Katie talked to you about. This is an enzyme that the virus needs to act on that RNA genome and it contains an integrase and I'll explain what the integrase does in a minute. When that virus comes upon a cell it binds to a receptor, we talked about that already tonight and it inserts what it contains, these three things. That RNA because it is a retrovirus has to be reverse transcribed into the DNA. It is like taking a recipe and making it back into and inserting itself into the cookbook. The way it does that is it reverse transcribes itself into the DNA, makes a double stranded DNA, sends it back into the nucleus and inserts itself into the genome of the cat. The genome of the cat, the cookbook of that cell now contains this exogenous FeLV genome for as long as this cell survives and if this cell divides and gives rise to new cells then those cells get that genome as well. The virus has now inserted its recipes into the cookbook of this cell and it will persist with this cell and any cell that comes from it as long as the cat lives. That is infection, you can't change it, it is there forever. Now this virus is very smart because it will use all the machinery of that cell to make what it needs, new viruses. New RNA, new proteins, new enzymes, it will package them and it will bud from this cell, not hurting the cell at all. This cell is going to go on and survive, divide and perpetuate this infection. This is why this virus is so tricky. It has just taken over this cell and any cell that comes from it.

How do diagnostic tests detect this infection?

We have two ways. We have talked about the nucleic acid and we have talked about the protein. Those are the two ways we detect the infection. Those two methods, we have protein tests and often refer to that as just an antigen test. These are ELISA tests. Those are the ones we think of and I will talk about the IDEXX test, or SNAP test or reference lab plate ELISA. There is also the IFA that is a fluorescent antibody assay which we will talk about as well. We also have nucleic acid tests. This is polymerase chain reaction or PCR and it can detect viral RNA or proviral DNA. The proviral DNA is that viral genome inserted into the cook book. If you think about just what that virus looks like, the RNA genome sits protected within this capsular core of the virus and there is a lot of this protein that is made. This p27 protein that is made and it is a soluble protein that is in abundance. That is what we screen for when we use the snap test.

The ELISAs that we talk about for this protein, if you have never seen a reference lab plate ELISA, this is what it looks like. It is a 96 well plate. You can run lots of different samples all at the same time. It takes some time to run this plate. It has at least six steps or more and takes at least 30 minutes or more to perform at the reference lab. The SNAP test basically takes what this plate does and it makes it into a



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pet side test that you can run with three steps in about 10 minutes. It uses some special technology to do that. The ELISA just stands for enzyme linked immunosorbent assay. I'll show you a diagram of how that looked for us in a minute.

I first want to tell you about a study that was done on the SNAP test, actually it was done on all the in clinic tests that are available currently. This study was done by Dr. Julie Levy at the University of Florida. If you are working in a shelter or you are working with a veterinarian or you are a veterinarian you have options today in terms of what type of retroviral test you use. If you haven't seen this study you should go look it up. It is in the Journal of Veterinary Internal Medicine right now. Basically the conclusion from this study was that the SNAP did have the overall best performance and the best sensitivity and specificity. These are the results of that study, again comparing a SNAP to the Witness, Antigen and VetScan, basically combo tests of FELV and FIV. You will see that for FELV in this study the SNAP came out at 100%. I will tell you unequivocally no test is perfect and no test is 100%, never. My job would be great if that was true. That would make my life so easy. What we have is you have to look at these confidence intervals. This is the performance. That is the certainty with which we can know that performance. If we did this study again and again and again we would expect to get results in this range so somewhere between 97 and 100%. That is very good and it was better than any of the other tests that were evaluated in this study. Good to know that we can use this test in a screening situation but keep in mind no test is perfect.

How does it work? Well these tests use very special antibodies. These antibodies were actually developed by Dr. Hans Lutz and they are two monoclonal antibodies. We draw antibodies in the shape of a Y and basically what they do in this assay is we have an antibody that sits on the solid phase of either the SNAP or that plate and it captures this protein in the cats blood. It has that soluble P27 antigen protein and it forms a sandwich. One antibody captures it, the antigen binds and the other antibody comes in and forms a little sandwich so think about a peanut butter sandwich; bread, bread with peanut butter in the middle. If you don't have any peanut butter those two pieces of bread don't stick together. The only way you get color is if that antigen is present. In that well or on the SNAP you get the blue dot. The reference lab ELISA that we offer has a confirmatory protocol so that when you do get a positive you can run that sample again and confirm that it is specific. That protocol basically uses two wells. The first well runs exactly like this but in that second well what we do is we take that patient's sample and we incubate it with an antisera, other antibodies against the feline leukemia virus. If that was holding those two antibodies together it is truly FELV related it will be bound by this antisera and it won't be available to stick between the antibodies. What we see is a reduction in color between those two wells. That tells us that what we are picking up is specific to FELV. Sometimes we will see cats that have something else that bridges these two antibodies, maybe it is jelly. Bread, bread and jelly are going to stick together but jelly isn't specific to FELV. In this situation that jelly would still stick, we would still have color but we don't see that neutralization. They we say "Huh, that is a false positive," some cats will do that, about 1:3000 I think. This is a great way to confirm an in clinic positive on a screening test that is truly derived from FELV and not something else.



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How about the IFA?

This isn't looking for soluble antigen, this is looking for cell associated antigen. You are looking for replication of that virus in infected cells in the circulation. How does it work? Well it starts with a blood smear from your patient and then you use these antibody reagents to look for those viral proteins that are being expressed in the cells and then you take that blood film and you put it on the microscope and you look for that immunofluorescence. You are looking for that apple green color of cells to call it positive. It is different than looking for soluble antigens. Sometimes we see that even though you could have a true positive soluble antigen protein you may have a negative IFA because there aren't enough cells or cells in the blood producing the proteins from the virus, the virus isn't replicating in the blood.

Last one.

PCR, polymerase chain reaction

PCR works exponentially amplify nucleic acid in your sample. Think about it like a copy machine. I take one piece of paper and put it into my copy machine. I can make many, many copies. Same thing with a piece of DNA, I stick it in there and I can make many, many copies. PCR works the same way. It is designed to take one small piece of nucleic acid and through primers and probes bind and amplify exponentially those copies so that you can detect them. After 30 or 40 cycles you are going to have 2<sup>n</sup>, 2<sup>n</sup> pieces of this DNA that you can now detect just like with a copy machine. These are the techniques that we use to diagnose FELV infections. In our lab we use real time PCR and this is a very handy tool because it gives us some additional information about that PCR. It doesn't just tell us positive or negative, we can actually look and see and get a sense of how much DNA was there to begin with by looking at what we call crossing points. Essentially how this works is that you start with your sample and as you go through all the cycles the graph goes in this direction. What we are looking for is for the fluorescence in this PCR reaction to exceed that threshold. This patient sample exceeds the threshold at around 20 while this patient's sample exceeds the threshold at about 30. I can tell you that this patient at 20 had more copies of that initial DNA, or that virus or that RNA than that patient at 30. A lower crossing point is associated with higher viral loads or proviral DNA within the cell. That gives us a feel for just where that infection is.

I just gave you a lot of information. (Nope, not yet!) I'm going to give your mind a little vacation to Italy. I know that was a lot of information so we are going to take a little vacation to Italy and I put this in just because I thought this was hilarious. We were fortunate enough last fall over Thanksgiving to do a little family vacation to an island off the Southern Coast of Italy called Ischia and, I don't know if you can see on the map up here, Ischia sits up here kind of off the coast of Naples. We were hiking Mount Epomeo with the family and I was amazed when we were in Italy. There were many cats, I'm not going to call them feral cats because I think they were cared for cats but they are free cats and they are everywhere. I thought it was really cute that these cats were sitting on the hood of this little car that was parked on this really narrow little road as we were coming down this mountain. You can see in the sky that it is starting to get a little grey in the day and it is starting to rain a little bit and I didn't realize but behind me, my son coming down had slipped on the pavement and was just flat out on the ground. It was just so funny because a caught the cats, and I love the expression on their faces. It was



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going to get him.” He jumped off the car and runs over to see, “Are you okay? Really?” I don’t know if you can tell but my son was a little bit nervous, he was why is this cat coming to see me right now? It was hilarious because the cat after checking out walked right up to me and looked at me and was like, “He is good to go, everything is fine. Please proceed on your way.” Believe it or not, clearly he needed an escort so these nice ladies helped him as we walked down the rest of the trail. It was amazing. It was just so cute and a true story! I’m not usually that good with a camera so I thought that was pretty cool.

Everybody feeling better now? [laughter]

Let’s go back to our three FELV positive cats that we are going to talk about. These cats are part of a study that we are doing with Dr. Julie Levy and a shelter called Austin Pets Alive. Julie came to us after that last study that I told you about and she said I want to use your test to look at cats in a shelter when they present the first time and they are tested and then I want to see what happens to them over the next six months. I want to see if they stay positive? Do they go negative? I want to know everything about these cats. We said “Okay, we think we can help with this study.” These cats when they come in, the first time they are seen, they have blood drawn. They get a SNAP, not just any test, they get a whole blood SNAP, a serum SNAP, a plasma SNAP. They get an ELISA plate just like we would run in a reference lab on serum and plasma. They get a PCR, they get an IFA and Dr. Hardy at MVL. Then they have two time points blood sent over to the University of Glasgow for virus culture and isolation, an antibody titer and on and on and on. This is a huge study. In this study they have enrolled and completed 130 FELV positive cats that go through the entire seven sampling events and 130 cats that are screening negative. We also get one time point of all of those events. This study was actually funded by Maddie’s Fund and we are just right now in the data analysis. I’m going to show you what happened for these three cats now that you understand the diagnostic tests.

These are the different tests that we will talk about and we will start with Basil.

Basil is positive across the board; positive with whole blood, positive with plasma, positive with serum, positive confirming on our ELISA plate and positive by PCR and positive with IFA. That is a pretty typical cat, FELV, and that is what we would expect.

Here is Jasper, positive on whole blood, negative on serum though when we test the plasma he confirms positive as P27, so that means it neutralizes and positive by PCR but negative by IFA.

Imagine if I cover up these two results and think back to that letter from the shelter in Oregon. I have a whole blood positive serum negative cat that was negative on IFA. I called that cat uninfected, was the cat uninfected? Nope, this cat is PCR positive. We have two methods by which we have confirmed that infection even though the IFA is negative. It is a different stage of the infection, it is a different way in which this cat has controlled or managed this infection.



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For Zombie, I'm going to show you two time points. This is time point zero, remember this was our youngest cat we had in the mix. Positive, we confirmed that positive from the SNAP on the plate and it neutralizes so it is truly FELV derived but is negative by PCR and negative by IFA. Six months later here is what Zombie looks like; negative for antigen on SNAP, negative for antigen on ELISA, PCR positive, IFA negative. It is real. FELV is not a single disease. It really depends on how that cat controls the infection and what they do. In our study we saw about 75% of the cats that presented to the shelter looked like Basil, positive, positive, positive. This may be biased by the cats that were coming in because they knew they were doing the study, because of everything else that was going on. This may be higher than what we would typically see in a general population, but 25% of the cats looked like Jasper and Zombie. That is one out of every four FELV screening positive, whole blood positive cats that could be giving you discordant results which don't necessarily mean an inaccurate test result and uninfected. The reason I say that and the reason I make a big deal about this and because I have been looking at this for 10 years. It is because I think those cats; those 25% of cats deserve more. They deserve regular checkups. They deserve monitoring. They deserve attention. It matters what home we put these cats in, all of these cats. Just because they are like Basil, doesn't mean they are not going to live six, seven, eight years. What is the prognosis for euthanasia? Grave. What is the prognosis for FELV? It is not that, it is better. It is better than that. For a lot of these cats it is a lot better than that.

Remember, I showed you that really complicated diagram from 1991 with the experimental infection studies? This how we have kind of navigated to simplify the outcomes of an FELV infection, you can see that from the data that I just showed you. We have basically three outcomes. One is those progressive cats like Basil. These cats appear to have that persistent viremia, they are going to be at higher risk of FELV related disease, the diseases that we typically think of, the opportunistic infections, cytoproliferative, immunosuppressive, those are our progressive cats. We also know that at the other end of the spectrum there are some cats that for whatever reason will not allow that proviral integration and will fight of the infection, they won't become infected. I can't tell you who they are because they always test negative on everything but they exist, we know they exist. They don't become infected.

Everything in between is a regressive infection. The regressive infections come in several flavors. We have latent and we have focal. The way we define a regressive infection and this is really important and I keep hammering people on this, is not be the test result – it is by this statement “In regressive infections the cat controls that infection either prior to or shortly after bone marrow involvement.” They control the infection, their immune system steps in and controls it at one of these two places and that is what helps dictate whether it becomes a latent infection or a focal infection. We are going to walk through this on the next video.

What we start with is out infected cat. FELV positive shedding the virus in either the saliva, urine, it could be through the milk for the kittens, in feces to an uninfected naïve cat. We know that the most susceptible cat is going to be a young cat. The next step is for that virus, through this oral contact, is then integration and replication at those lymph nodes in the oral pharynx. This is the place where it is going to start; it is here where they have picked up the virus. Then there is an initial viremia of



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lymphocytes and monocytes that will then spread this infection through the blood system to other organs in the body. This could be gut associated lymphoid tissues. It could be other lymph nodes, it could be spleen. Then it gets to the bone marrow as well where again we are going to see infection of progenitor cells like of the monocytic lines, granulocytic lines and platelets. In a progressive state we are going to see high viral and proviral DNA loads. That sets up for a secondary viremia which means that virus now goes back out into the blood a second time and goes in search of those epithelial tissues where the virus will now infect and that is it's source of shedding. That is how we get to the progressive cat. This is the cat that has that persistent viremia, higher risk of FELV associated diseases, higher likelihood of being infectious because it has made it to the epithelial tissues, salivary glands, gut and bladder where it is going to shed. We said there are some cats that have abortive infections. They don't allow that initial proviral integration. They stop the infection and then we have the regressive cats that control this infection prior to or shortly after bone marrow infection. If they stop it before it gets to the bone marrow, significantly we call them focal. If they infect the progenitor cells in the bone marrow and then shut it down we call them latent. This is our current thinking around illustrating and explaining the pathogenesis of FELV. I have now illustrated on here the different stages or the different test results you can get at each stage of the infection. As you saw with Basal, IFA positive, PCR positive, ELISA positive, typical for your progressive cat.

Abortive cat? We are going to see them as all negative on those three tests.

Your regressive cats, the latent cat is never going to be IFA positive because it has not made it to the epithelium. We don't have that secondary viremia, that secondary viremia is required really for that IFA to be positive. PCR negative because it hasn't infected the progenitor cells in the bone marrow that give rise to the circulating cells that would be infected in the blood, but they will be antigen positive because they have a source of the infection somewhere focally that is churning out this soluble antigen at a high enough level that we can detect it on the test.

In your latent cats this means that it has gotten to the bone marrow. It has infected the progenitor cells but the immune system has shut it down. Those progenitor cells with the proviral DNA in the blood cells will be out in the circulation and you can pick it up by PCR, but the immune system may work really hard and bring down all the antigen expression just like it was in Zombie where we can no longer detect antigen but they will still be PCR positive.

I added a second image; this is just a still with the results a little bit bigger if any of you want to take pictures of that. Keep in mind that this is a dynamic situation. I have the circle drawn going in one direction and always going in one direction. We know that there are some cats that can move basically from here back to here and will look like this. Some cats that will be ELISA positive here will eventually go negative. How do I tell that from an abortive cat? I can't today. We know that there are some regressive cats that will pop forward into a progressive state at some point in their life. We don't know exactly why or how or who. We think stress, other infections, things that disrupt that immune control of that infection will change what a cat does if they are infected. It is dynamic, this is where the research is needed. We don't have all the answers to say who is infectious in this group. Who is going to progress, when are they going to progress and why? We don't know that yet.



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In terms of a protocol that we follow for screening, what do we recommend?

Screening for that soluble antigen using whole blood is going to be the most sensitive tool that you have to identify these cats that are infected. If you get a negative in a healthy cat on a screening population that is a very good indicator that cat does not have a FeLV infection. However, if you are a breeder or you are using a cat for a blood donor, you should really be using PCR with your serology. You can see how some of these cats may be negative for antigen but be PCR positive. Any cat that is used for breeding or used as a blood donor it is really recommended that you use those two tests together. We do this for leptospirosis, we do this for some of our vector borne diseases. You will get the best information by using those two tests together.

If you get a positive on a cat it is recommended that you confirm that positive using that reference lab ELISA so we know it is a specific positive. We want to see that and we want to make sure that is a true positive.

Once you get that we know that cat is infected. There has been proviral integration and that cat is infected. Now the question is what stage is this cat? How is this cat managing his infection? That is where the PCR and IFA come in. If you run a PCR and it comes up negative well then that is a good indication that the cat has the focal form of the regressive infection. If the cat comes up with a positive but negative on IFA it is a good indication that cat has the latent form of the regressive infection. If the cat is positive right through to IFA, it is highly likely that cat has the progressive form of the infection.

Let's go back to our three cats and make sure we can classify these okay. We said Basil, with all three tests positive we would consider Basil progressively infected. For Jasper and Zombie we are going to consider them to have a latent regressive infection because of that PCR positive status. These two cats again don't have quite the same FeLV disease because they are managing it differently but they deserve to be monitored. We need to keep an eye on these cats throughout their life and we need to manage them appropriately because we want to reduce their stress, we want to make sure that they have good husbandry. We will talk about how we want to treat these cats and what we want to do for these cats throughout their life and how we want to pair them in a multi-cat household. One of the reasons I recommend that we monitor these regressively infected cats is because we will see and this is a study published in the journal of feline medicine and surgery from 2010 showing that in cats with lymphoma and this is not limited to just GI lymphoma but a variety of types of lymphoma in cats; two thirds of these feline lymphomas had evidence of FeLV proviral DNA. The age range, the most common age at which these cats were diagnosed with lymphoma was 9 to 14 years. That is well beyond the two to three years that we expect an FeLV infected cat to live. Most of these lymphomas by immunohistochemistry they could not find antigen. They didn't test the blood so I don't know if they were antigen positive in the blood but this suggests that some of these regressive cats that have focal infections may be predisposed to lymphoma. Well if we didn't test for it we wouldn't know it. These cats are going on; they had cats that were 17 years old in this study. I consider that a nearly normal life for a cat. We want to monitor these cats because we want to think about testing a cat that we suspect has some sort of a lymphoma. Sometimes those cats don't get tested because they are tested as a



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kitten and they have lived indoors all their life and they were never tested again, sometimes these cats get missed. FeLV vaccination, should we vaccinate? I think currently the AAFP Guidelines recommend vaccinating kittens through their first series and again at a year. That is really important because it does help prevent kittens from developing the progressive form of the disease. Please recognize that vaccination does not prevent infection in cats. There are lots of old studies out there that show basically what happens is it prevents the progressive form of the disease. The cats are able to control that infection prior to or shortly after bone marrow involvement. It prevents progressive disease. We think it is helpful in these cats that go outdoors. In the study that I showed you originally out the University of Florida, out of 967 cats with bites or abscesses if they had been FeLV vaccinated only 2% had FeLV versus 14% if they were unvaccinated. It is helping protect them from the progressive form of the disease.

The other thing I think is really important is how we pair these cats. We know that if we put a FeLV positive cat into a household with a young cat there is that risk that the FeLV positive cat can transmit the FeLV to the kitten who is naïve and at risk. We don't really want to put an FeLV infected cat in with a kitten. Typically they come in with, if they come from a shelter, some respiratory infections and other things that in a cat that might be immunocompromised would make them more susceptible to those opportunistic infections. Knowing helps us pair cats appropriately. This wouldn't be an ideal pairing. I also learned very recently that while it may be fine to put a positive cat with another adult healthy cat, the risk of them developing progressive disease is very low, it is not a good idea to put an infected cat with an adult cat that has a chronic illness who may be sick, who may be immunocompromised. It is really no different than sticking it in with a young kitten that is essentially immunocompromised who doesn't have that immune control that an adult would have. This situation even though they are two adult cats and it is unlikely for an adult cat to acquire the infection and develop progressive disease, if that adult cat is in any way compromised, old chronic disease, immunocompromised they are at risk of not only being infected but developing progressive disease. We need to know the status of the cat so that we can pair them correctly.

How do we keep FeLV positive cats healthy?

Basically three things: Husbandry, we need to keep the immune system strong. What do we do for ourselves to keep our immune system strong? We try to eat right. We try to get enough sleep. We try to reduce stress in our lives. Diet, husbandry, all of these things are important for keeping these cats healthy. We want to minimize their risk of opportunistic infections. We want to pair them correctly, minimize any fighting in the household. We want to make sure they get regular veterinary care. A lot of times these cats will have oral disease that might put them off from eating and then that starts a whole cascade that is very difficult to manage so keeping up with regular dentistry, keeping their mouths healthy. Then there is a question of are there treatments, we will talk about that in just a second. I was taught cats should be kept indoors. If you have an FeLV positive cat it should be kept indoors. These are pictures from FeLV sanctuaries. These cats go outdoors. They go outdoors in a controlled fashion and it makes them healthy and happy to have not only the outdoor access and the fresh air but I am



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going to call climbing trees exercise, right? Exercise is important for maintaining a healthy immune system. I think it is important and even if they can't get out in a fenced yard to have access to a controlled out space with outdoor access, whether that is a little patio or porch or fenced in area. That is very effective. It doesn't take a lot to keep these cats in. What you are doing really is keeping other things out. Most of these cats once they recognize where they are they don't try to escape. This is nothing more than, I think it is five or six feet of just sold fence poll with a nice arched plastic fence that goes around the perimeter that leans in. These cats love having access to this space.

What about treating FeLV cats?

There is no cure, there is no treatment that will prevent or stop this infection. We know there are great things on the horizon for FIP so that gives us a lot of hope for FeLV. Mostly what we need to do is keep their immune system strong, manage any underlying conditions that they have, treat infections aggressively once they are recognized and then experiments are still underway around antivirals and whether or not they are helpful. Maybe in certain situations but there are side effects so really it is at the discretion of the veterinarian in the situation to decide whether that is warranted. There are a number of folks that are using immune modulators. There are no good peer reviewed studies, placebo controlled studies that show us that those immune modulators are making a difference. I know there are some people out there that really, really believe in them and like them and use them and they may be helping. We just don't have the studies today to be able to go out and say "Yes indeed this is how you want to do it and what you want to do." We need to kind of keep that in mind. Again, we need more research there.

Just to wrap up, our goal is to understand that things are changing and that we need to work toward a common understanding working through all these things about the disease, the terminology, the diagnostics and continued research. I want to take a moment and thank all the folks who have helped me over the years in our studies with Austin Pet's Alive! Ralphy's Retreat is a sanctuary for FeLV cats in Maine that we have worked with. Dr. Levy and the Maddie's fund for that APA study where again working with Dr. Margaret Hosie over at the University of Glasgow and then all the folks at The Cat House on the Kings and then all the folks at IDEXX who have contributed to the projects that we have done.

I will thank you again. Here is another calico cat in Italy hiking. I didn't know these cats hiked but they do and that is my daughter.

Thank you very much. [applause]

**Mr. Steve Dale:**

Perfectly on time. We are going to take some questions. You have the index cards at your table, I and my trusted assistants will walk around grabbing the index cards and speakers, first of all come on back up because we are putting you back to work, Dr. Tolbert. You will have to share a hand held mic or one of you can use this one. Can you hear me okay? Can you all hear me in the back of the room?



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Dr. Beall, “Do you still recommend the vaccine for feline leukemia for cats or kittens in a cattery with no outside experiences ever in their life?”

**Dr. Melissa Beall:**

In terms of recommending vaccination for cats in a cattery, I think it is something that you need to work with your veterinarian on deciding if that is appropriate for your situation. Risk based, unlikely, if the risk is very low then perhaps not. I have dealt with situations in catteries in the past where someone brings in a cat that based on the testing and records that were shared with them and not based on re-doing that testing themselves and maybe doing the tests a couple months apart and they have introduced FeLV into their cattery. Then it is only found out when a kitten goes out, is sold and then tested. It is hard to say never under any circumstance and it is an opportunity cost, you kind of have to weight the risks against the benefits. I think it has to be made on a case by case basis. My feeling is that the young cats really benefit from having that initial series of vaccines. We expect the older cats will have some resistance to developing progressive disease even if they are infected but those younger cats may not.

**Mr. Steve Dale:**

About 30% of show cats have the parasite, that is you. Where do they get this from?

**Dr. Katie Tolbert:**

Well that is a great question. The answer is we don't know. Originally we thought with *T. foetus* they may have somehow developed *T. foetus* from cows and there was some change in the parasite and it just developed this ability to kind of adapt to a new host but there have been some really good studies out of Auburn that suggest that may not be exactly the case because when you take the parasite from the cow and put it into the cat, you don't mimic the same disease and when you take the parasite from the cat and put it into the cow again you don't mimic the same disease. I'm sorry, we don't know. That is a bad answer but that is the truth.

**Mr. Steve Dale:**

As our cats are living longer and longer we are seeing more lymphoma in cats. How about cats that have never been, likely, exposed at all to another cat with feline leukemia? A cat that has indoors its whole life. A cat who's parents have been indoors their whole lives, their parents have been indoors, their parents have been indoors their whole life... What is the relationship?



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**Dr. Melissa Beall:**

Not all cats that have lymphoma that is due to feline leukemia virus. We will see lymphomas develop because of other things. It is just that in about two thirds, in that study of the lymphomas that they looked at, they found proviral DNA from feline leukemia. That means that at least a third of them are due to some other cause not related to FeLV. We expect to see both, not all will be due to feline leukemia.

**Mr. Steve Dale:**

What is the status of the ELISA test for tritrich?

**Dr. Katie Tolbert:**

To my knowledge there is not an ELISA for tritrich unless IDEXX has developed something that I am unaware of. Are you guys aware of something?

**Audience member:**

I heard that North Carolina State had developed one.

They have developed a PCR for tritrich and that is the most sensitive and specific test that you can do for the diagnosis of *Tritrichomonas foetus*.

**Audience member:**

That is from an anal wash or from something else?

It is from a fecal sample. Usually what we try to do is you can submit just literally voided feces. The best sample is what you just described is actually a colonic flush. Inject saline into the proximal colon, pulling it back out and spinning that down and submitting that to NC State or TAM U, I think IDEXX does one too. That is the best way to do it.

**Audience member:**

Do you have any idea why IDEXX is not doing them anymore?

Because I got there, [Laughs] and we are not doing them as well as some of the other laboratories that had been doing them because what they would do is they would do the PCR on the culture pouch instead of doing the PCR from the feces. You have to have viable organisms. You have to have a lot of organisms in order to PCR test it from the culture pouch so it wasn't as sensitive and specific as a test. Since there were so many other good laboratories that were already offering it, it didn't make sense for us to invest in doing that sort of diagnostic.



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**Audience member:**

You know we always ask that [\_\_\_]

I know, we could do it, it is just you know we don't. [Laughs]

**Mr. Steve Dale:**

What is the value of using FortiFlora pre-emptively, which you did talk about, and do you see *E. hirae*, did I say that right? *Enterococcus hirae*. Easy for you to say! Do you see that coming onto the market in any commercial way?

**Dr. Katie Tolbert:**

That is a really great question, and think it is possible. That was actually something that Dr. Jody Gookin at NC State was able to isolate. She is the one that did the study that I mentioned where they looked at healthy kittens that were euthanized from overpopulation compared to kittens that died because of diarrhea and so she cultured the *E. hirae* from those cats. I do believe that she has actually approached a few companies to see if they have interest in developing that. I'm not involved in that, I don't get any money from that unfortunately. I'll keep you posted.

**Mr. Steve Dale:**

The other question regarding FortiFlora?

**Dr. Katie Tolbert:**

Oh, sorry, remind me of the question again. (Using it pre-emptively.) Yea, our research again would be (I suspect no downside). Cost would be the only downside and getting it into a cat with a cat that doesn't want to eat it. Many cats do, although if the cat has a severe IBD, I have had a lot of trouble. I don't know if you guys have in getting a cat to take FortiFlora or any probiotic really. Yea, the other cats that don't have intestinal disease or have acute diarrhea, absolutely they love the taste. Do I see a benefit? I think it is very possible. I want to be really careful about completely translating what we have done in the laboratory and saying 100% that is going to work in every intestinal infection case, we are just not sure. The nice thing about the Winn Feline Foundation is I think this is a stepping stone towards, "Hey, this looks really cool and this looks like something we do need to chase down. Now let's take it to the next step." For the next step my question is we have done this in a model where we present the bacteria where the infection is. If you give the bacteria orally and it has to get all the way into the late part of the small intestine and the first part of the colon, will it still work? If not, could you do like once a week, not ideal, but once a week sort of like a retention enema with said probiotic. You



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might think that sounds crazy! But I have dealt with a lot of people who have *Tritrichomonas foetus* infected cats and let me tell you what, they would do it. I think that is what we have to figure out. Yes I think there could be a benefit, but what dose? What concentration of bacteria? How should you administer? How frequently do you have to give it? For how long do you have to give it? The short answer is yes, I think there could be a benefit. The long answer is it is not that easy.

## Mr. Steve Dale:

This is my favorite question. Who is the guy speaking? Meaning me. [laughter] My name is Steve Dale, I'm on the board of the Winn Feline Foundation. I suppose I did not, thank you. (I'll take you home with me.) [laughter] I suppose I did not identify myself, I'm sorry. I even could answer that question!

Besides specific adhesion sites produced by T. f what about identity of specific adhesion sites on the host. If you understood that...

## Dr. Katie Tolbert:

This person has a PhD or should have one. That is a really great question. What we have studied has really been from the parasite side. The question is could you identify something on the host side that you could potentially hide or remove that wouldn't affect the host. The answer is yes, absolutely, that is likely. We haven't explored that but that is definitely something that should be explored, that is a great question.

## Mr. Steve Dale:

Should we test for lymphoma for a cat both PCR and ELISA, Dr. Beall?

## Dr. Melissa Beall:

I have to ask, is that testing, we don't have a lot of screening tests for lymphoma today. (Do we have any?) No, (I didn't think so) that I know of. I don't know if someone can rephrase that question or clarify for me?

## Audience member:

I think what I meant to say was should we test lymphoma cats for FeLV PCR...



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## Mr. Melissa Beall:

Yea, I think that is something that we probably don't do enough of today. Again, I don't expect all of them to be FeLV positive but what I hear from feline practitioners and a number of them have said this to me is "I have this patient, Susan Little was one, I cared for this patient its entire life, FeLV negative and now has GI disease. I'm going to test for FeLV and low and behold it is FeLV positive. (What?) Yea, again, it is something that I think because we think we have tested them when they are a kitten or they are young and they come up negative and they don't have any risk factors we kind of assume that they are uninfected. They can have these regressive infections that we just can't pick up maybe by antigen or maybe they are discordant between sample types and they get forgotten about over time. Now they come in later in life 14, 12, 16 or whatever it is and they have some signs of maybe IBD, lymphoma, GI lymphoma or some other lymphoma and they end up testing positive. You are not going to change what you do for that patient but I think it is important to understand exactly what you are dealing with as you try to manage that patient.

## Mr. Steve Dale:

I have a question and it is my question! How many here have known a cat over the age of 15?

There are a couple hands not raised which is really interesting. How many have seen a cat or have had a cat with kidney disease? It is really common right? Can you explain SDMA and why Steve Dale, incidentally, thinks SDMA has been a game changer truly to help us with earlier diagnose of these cats and what that difference has made.

## Dr. Melissa Beall:

SDMA stands for symmetric dimethylarginine, (notice I made her say that!). It is not that easy to say. It is a small molecule, it is a biomarker that really represents glomerular filtration rate. We don't have a lot of great ways to measure glomerular filtration rate noninvasively in either cats or dogs. SDMA is fantastic in the cat because it will pick up changes in that glomerular filtration rate earlier than what we see with creatinine. For those of you who are veterinarians in the room, remember we see changes in creatinine after 75% loss of functional nephrons. With SDMA we can pick that up maybe after 40% loss so a lot earlier.

## Mr. Steve Dale:

Explain what that means, sort of in English?

In English, we are losing the lights. (Whoop) And we are done, thanks very much. Let's go get a drink. [laughter]



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## **Dr. Melissa Beall:**

In English what that means is that as the kidney becomes compromised we have to lose more of the kidney before we see a change and elevation in creatinine. In the case of SDMA that loss can be less and we will detect that something is happening. The other thing that is great about SDMA versus creatinine is that it is not effected as much by muscle mass. You know a lot of these older cats that are developing chronic kidney disease become skinny. They lose muscle mass over time. As you lose muscle mass your creatinine becomes a less reliable indicator of your kidney function. SDMA is less affected by that so it is another way we can pick up changes in kidney function in those situations and it will be better than what we see with creatinine.

## **Mr. Steve Dale:**

That was a great answer and thank you for turning on the lights, whoever did that. A great answer indeed, I really do think that having that test available is a huge game changer because of the information it gives us. Now I want the next step and that is something to do, if not solve, better treat kidney disease. The Winn Feline Foundation will be making an announcement in that regard. We don't have the answer but we do have an announcement to make in that regard that will be coming soon to a web site near you!

Can Pepcid be given orally to treat gastric issues?

## **Dr. Katie Tolbert:**

Yes is the, again, short answer. The bummer about a lot of things in cats is we don't really know the benefit of acid suppressant therapy in cats because it has not been studied. We did the first study a couple years ago to look to see if Pepcid and Prilosec could actually serve as an acid suppressant in cats. That was really the first time that anyone had looked at those therapies in cats. Anecdotally, I would say from my own practice, yes of course I feel like Pepcid helps in certain situations and I am sure the veterinarians and the veterinary technicians and probably owners in the room can say, "Yea, when don't give my cat Pepcid it doesn't eat or it vomits. The problem right now that we have is that we don't really know which condition it is going to help with. For example there is a lot of debate about should Pepcid or Prilosec be used in chronic kidney disease. There is some pretty good evidence that we shouldn't be using it in chronic kidney disease in cats but people are still doing that. The answer is yes, the long answer is we have got to study that more to determine is Pepcid helpful in feline inflammatory bowel disease? Is Pepcid indicated in chronic kidney disease, or Prilosec or whatever? Is Pepcid helpful in mast cell tumors in cats? All of these things we don't know the answers to and the trouble is that we base everything on human studies and as you guys know cats are not humans. That is very problematic.

## **Mr. Steve Dale:**

Even if we based it on dog studies, would that be problematic?



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Just as a comparison would be tramadol. You guys know that tramadol is a very effective pain medication in cats because cats metabolize tramadol. Dogs do not metabolize tramadol so tramadol is not an effective pain medication in dogs. We can't use studies in dogs to say "Yep, that is going to work in cats." Similarly, we can't use studies from cats to say "Yea, that is going to work in dogs." All of those things need to be separate which is why it is so good that we have the Winn Feline Foundation so that we can actually dedicate money to do these studies that need to be done in cats.

## Mr. Steve Dale:

Just a couple more and we don't have time to go through all of them but the good news is in the after party these guys will be hanging out with their party hats on. [laughter]

The role of dietary management for *T. foetus*, and they mentioned Royal Canin diet, HP, and I want to add to that are there any other therapeutic diets that you would recommend.

## Dr. Katie Tolbert:

That is a great question. Here is the problem with parasites which you guys probably know. Just because you get a positive infectious disease test does not mean that is the cause of the disease. For example, you can have a dog that has giardia and has diarrhea but you clear up the giardia and dog still has diarrhea. The same thing happens in cats. I think sometimes when we see *Tritrichomonas foetus* and they respond to diet for example, like their diarrhea responds to diet, it is possible that helped with the *T. foetus* because as I told you the microbiota, the resident bacteria is so important and maybe you have changed the resident bacteria and no longer favors the *T. foetus*. The other possibility is that maybe that cat just had food responsive disease and the diarrhea was from food responsive disease and then you gave it a diet and the cat got better. Any time that I have a cat that has chronic diarrhea, I always consider infectious disease but I also consider the possibility that just because it is there does not mean that it is the whole story. Yes, absolutely, I think diet can play a role in the treatment of feline trichinosis, but not in every cat.

## Mr. Steve Dale:

This question I'm going to add to a little bit. Essentially it is, how do I know what probiotic to purchase? That is the nature of the question. I think there was a study done on a whole bunch of probiotics and the study was, what is really in the probiotics? There were two probiotics used among many others, others that we might buy for ourselves I think in this study and Provable and FortiFlora were the only two probiotics, both veterinary products that actually what is in them is on the label. It speaks well of veterinary medicine but still the question is, "How do I know which probiotics to get and should I go over the counter?"



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## **Dr. Katie Tolbert:**

Yep, that is a loaded question. I'll do my best not to piss anybody off. Yes, the study that you mentioned, there were several studies that have investigated both human and veterinary specific probiotics. Basically in these studies they said, were they appropriately labeled, did they contain what they said they contained, did they have the appropriate dose or the concentration of the bacteria that they actually contained and were they viable organisms. It was pretty scary to read some of these studies because a large number of them were not appropriately labeled, they had something else besides what they said that they contained or basically they had something besides what they said they contained and sometimes that was actually a pathogen which is kind of a bummer. Sometimes the numbers of organisms were extremely, like on the order of 10 fold less or more 100 fold less than what they said they contained. I just told you how important it is for the dose for example to potentially play a role in fighting infectious disease. A couple things about that is one I would always go with a reputable company that invests in research. I think you know who those are. That is Provable, that is Purina FortiFlora, that is Visbiome so I always recommend those because, one, I believe that they actually contain what they say they contain based on studies, two, they actually invest in veterinary research to help us understand what role probiotics can play in health and disease. Hopefully that was answered.

## **Mr. Steve Dale:**

I think so and it speaks well of the veterinary products Provable and FortiFlora.

Dr. Beall, do you consider, and you could chime in on this too actually. Do you consider a 17-year-old cat old? I have always heard, it's an interesting question though, that a 15-year-old cat is what is the average life span. How old do you think cats should live? Perhaps as long as Larry King? That is my guess.

## **Dr. Melissa Beall:**

I don't know what the AAHA Life Stage Guidelines are for senior and geriatric but I'm pretty sure 17 is in the geriatric category and so I am sure you will have much more experience in terms of age and how long cats... I have heard of cats living into their 20s too.

## **Mr. Steve Dale:**

Let's find out, 15, anyone here or if you are a veterinarian have clients with 15-year-old cats? Sure. How about 16? I'll jump to 20, 17, 18, I'll go slower, 19? 20? 21? Do I hear 22? 23? We lost Dr. Vicksman. 24? Dr. Holub, Dr. Holub wins! You win the opportunity to give a donation to the Winn Feline Foundation! [laughter] Dr. Holub does generously all the time as it turns out.



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First of all, for you guys I have one more question. Isn't this audience great! Oh, yes very good! Please help me thank our speakers. [applause] This is interesting to me, this is the most intimate crowd I think we have had for one of these in the 5, 6, 7, 8, 9, 10 years that I've been standing here sort of moderating these but this is one of the best. You guys are great and I mean that. They listen to every word you guys were saying and there were great questions. I thank you very, very much really. Now for those of us who want to do it we can go next door and we can party all night long! One more thing, these books, the Winn Foundation Books, they are for you. They are available free in a PDF form online where you can order more. All we ask is that you pay for postage, that is all we ask. Take some with you. Thank you!

**Transcript provided by Veterinary Information Network (VIN)**

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