



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

37th Annual Winn Symposium – July 2, 2015

“What’s New Pussycat – Advances in GI Therapy”

Transcript of Audio: Dr. Craig Webb on Stem Cell Therapy and GI, Q and A

Beginning of Dr. Craig Webb Audio

Steve Dale:

Before I introduce Dr. Webb, how many of you are cat breeders that belong to a breed club that have been previously, well not so previously. I will just leave it there. How many of you are cat breeders that belong to a breed club? A lot of you in the room. So I have got something, a scoop for you. I know we were talking about number two earlier and litter boxes. I don't mean that kind of scoop, I have a real scoop for you, and our president is going to talk more about this to all of you tomorrow. We want to make it easier for you, and we want to celebrate you as breeders. So the Winn Feline Foundation, at next year's symposium...oh my gosh [COUGH] sorry about that, I guess I ought to start smoking... So for breeders, what we are going to do is, next year at this symposium, you can just come in. We will welcome you if your breed club contributes throughout the year, to the Winn Feline Foundation. We will also recognize you in special ways, and all of that will be talked about tomorrow, but personally, and I know my colleagues on the board feel this way, we are fans of what you do, and we want to support in ways that at least we can support, what you do.

I am just such a fan personally of pedigreed cats. They are absolutely wonderful, and I try to in what I do for living, spread the word about pedigree cats. In fact I just wrote a story for my National newspaper column, about the most popular cat breeds, and received e-mails back about, what is an exotic, what is that? So I love talking about cat breeds to people. We love trying to help you out, and to support you in what you do, but we want to help educate you as well. We happen to have the best, and I am about to introduce one of the best.

Stem cells in human medicine, and I have talked on the web about this before, it's controversy in ways it is not in veterinary medicine, which we will talk about. Our scientific advisory board, when Dr. Webb's studies and other studies regarding stem cells came along, our veterinarians just looked at the science of it. There is no emotion behind it, there is no controversy behind it. Sometimes physicians, I hope there aren't any in the room, confuse me, because there really isn't. It should be about what good medicine is about, and that should be about all. Review of the current therapies of dietary intervention, vitamin B12 supplementation, and probiotics, how fat derived stem cells work in treating chronic intestinal disease, and that word that we heard a lot about today, diarrhea, a pilot research study in the use of stem cells as a therapeutic approach to chronic inflammatory bowel disease, here is Dr. Craig Webb, from Colorado State University.

Dr. Craig Webb:

So let me start by thanking Vicki, and thanking Steve, and thanking the Winn Feline Foundation for inviting me here to gorgeous Toronto Canada. I was in Toronto once before, probably 20 or 25 years ago. I usually get invited to places like Nebraska. Nobody from Nebraska I hope, or Ohio, so to come to a place like this is actually really wonderful. You from Ohio? I love it, my wife, half of her family... She said she can't



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

hear you. Oh you can't hear me. Oh, I thought you were about to start throwing things at me because I said something bad about Ohio. Does that help? You are from Ohio. Half of my wife's family is from Ohio, which is the only reason I am not really that anxious to go to Ohio. Nebraska, other reasons. So anyways, just thrilled, and the weather has cooperated, a beautiful place. So thanks so much just for having me here, regardless of what I need to do as far as thanking the Winn Feline Foundation for supporting research in cats. There just are very few outlets for people such as Dr. Gookin and myself, and any of us who want to try to research cats, and research things that will help cats, we have so few options, as far as places to go to try to get funded, that the Winn Feline Foundation is really a unique and very critical part of the future of the health and happiness of these little guys.

So, my talk is on the use of stem cell therapy in feline chronic enteropathy. I will start with a disclaimer slide. None of the kitty cats you will see in this talk were my own, or members of my family, nor would anybody pay me for what you are about to see, but again the one disclaimer, and I refuse to disclaim, you are supposed to disclaim your funding sources, I refuse to disclaim the Winn Feline Foundation. I embrace them, just as Dr. Gookin does. Thank goodness for us and for our cats that they are here to help us out. So they have funded everything I will talk about today.

The last time they actually had me talk, not that long ago, about this, I had with me my wife Dr. Tracy Webb, and that's important for this audience, and important to me for many reasons, but the most important being that she is the smart half of our combination. She is the brains of the organization and the brains of the operation. She knows what the heck she is talking about, and what she is doing. I am just trying to help cats with poop and diarrhea. That is about the level, I am honestly a clinician, but I work at an academic institution, so I have to convince them that I am doing some kind of research, and so thank God I have my wife to actually do that stuff for me. So that is important to you, and those little white cards that you are going to write down your questions on if you have them, please feel free to do that. You are welcome to do that, as long as I am welcome to take them home with me and have somebody smarter than myself help me with the answers. You can e-mail me, and I will provide you with that answer.

So I would like to start with what an ideal world would be for us, as both people, and then in particular as gastroenterologists and veterinarians worried about diarrhea in kitty cats. For me then, that starts or is exemplified by this particular case. This is how GI cases in cats should go. We have got presented to us, as a 6-year-old female spayed domestic longhair, that may actually be a particular breed. I graduated from of a vet school that did not make us memorize breeds, and I am sure everybody in the audience is much sharper than I as far as picking out breeds in cats. So if this is something more specific than a domestic longhair, please write that down on a card and let me know, so I can be more accurate.

The problem that this owner brought the kitty in for was chronic intermittent vomiting. This was a great owner, as many cat owners are. Some of them are crazy, some of them are great, some are crazy and great. This owner gave a wonderful description. He said yeah, this has been going on for about a year, so right away you get some feel for the immediacy of the problem, not so bad, it has been going on for about a year. He said yeah, oh about once a week, maybe every other week, my cat, and it always happens about 2 in the morning, my cat starts making these noises. She wakes me up, kind of upsets me, and starts making these noises, and they actually do the noise for you, it sounds like this, augh, augh, augh, and I swear to God the cat is bringing its entire gastrointestinal tract up and depositing it on my carpet.

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • info@winnfelinefoundation.org
Phone 201.275.0624 • Fax 877.933.0939 • www.winnfelinefoundation.org



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

So after I get woken up by this, I fall back to sleep. Much to my surprise, the following morning my cat is still alive, and sure enough I have to carefully try to find where its gastrointestinal tract is, on what part of my carpet before I step on it. It doesn't seem to have affected my cat otherwise all that much, the cat still wants breakfast. That is the history you get, and again this is an outstanding owner. Not only do they give you a great history, they bring with them a sample of what happened. This is what they brought off the carpet, so they have given you the history, they have given you the problem, maybe even given you the diagnosis. This is a cat vomiting up hairballs. Ideal. I haven't had to do a thing yet. I have just sat in the room. So I have the cat, I have the problem, I have the diagnosis, and because of that, because this is an ideal case, I have the treatment.

Sure, now I run into occasionally a few owners who are not all that compliant, and I am looking for an alternative treatment, well I even have some of those. Maybe it's diet, maybe it is a little oil, maybe you have got a grease up the intestinal tract a bit in this cat, and this is, this is a big deal, maybe not so much for the health of the cat, were not sure about that, but this is a common feline problem, right. Since the beginning of time, since the beginning of ownership of cats, we have been aware of hairball vomiting.

In fact, and I didn't notice till rather recently, there is a National Hairball Awareness Day. It happens, and my father was a physicist, it happens in the fall also on the National Physics Day, so throw the two of them together and that's exactly what my father would do at breakfast, if you were ever silly enough to ask him, well what happens when a cat vomits up hairball. He would show me, because he is a physicist. So that is how big a deal this is in our cat population, and yet we do not know anything about it, I mean next to nothing.

Quite a recent article by a wonderful vet from across the pond, and basically Dr. Cannon is telling us, in these studies, or in any studies, the few that you could find, we still have, although there are a range of possible hairball diets or treatments, there is no objective information in the public domain regarding the efficacy, in fact studies to evaluate the success of other recommended, they just don't exist, highlighting that even in an ideal GI case, with a case or a problem that is so prevalent and so common in the feline population, we know almost nothing about it, and when I say no, I mean we have so little evidence to support what we are doing to try to help these cats. This is both highlighting where my own study is going, but again highlighting what I said at the very beginning, about the importance of people like the Winn Feline Foundation, because they are the people that are trying to solve this problem.

So how do we make decisions if we do not have the evidence? We do not have the studies, how do we decide how to treat these guys. Well unfortunately in veterinary medicine the most frequent strategy for making that kind of decision is anecdotal, anecdotal evidence. I tried it in the last cat and it worked so I am going to try it in the next cat or my buddy down the street talked to me about it and said, they tried this and it worked so I am going to try it. Of this I want to give you an example just to bring home again the strengths and or weaknesses of anecdotal evidence.

This is my favorite example. Vitamin E in inflammatory bowel disease, we have some vague appreciation for vitamin E as an antioxidant and so a few laboratory animals running around with a little less diarrhea because they were given some vitamin E. There is a dose we pulled out of our own diarrhea and came up



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

with, it does not seem to have any side effects that are untoward so that is at least one good thing but there are actually no clinical studies in dogs and cats.

What I do have, though, is solid anecdotal evidence. This is a picture, there in the middle, that is Dr. David Twedt, one of the grandfathers of gastroenterology in veterinary medicine and just one of the guys. That is me on his left, and Dr. Ugo Lotti on his right. Dr. Twedt is so famous that frequently we have people coming from all over the world who want to spend time with him, just kind of trying to suck stuff out of him, just by being next to him you get a little smarter. Dr. Ugo Lotti came from Italy to spend a summer doing some research with Dr. Twedt, a great project. This happened to be the summer before Dr. Twedt starting taking vitamin E. Dr. Ugo Lotti spends the summer, he leaves. Dr. Twedt, realizing he is getting a little on in years, slowing up just a bit, says 'Well, I had better do something to reverse those effects, I am going to start taking vitamin E,' which he does.

The next summer we have another Italian come to spend the summer with us doing research with Dr. Twedt. Now, I want you to pay close attention. Although Dr. Twedt's expression has not changed much at all, in many ways, the quality of the visiting Italian veterinarian has changed significantly. Anecdotal evidence that many of us, especially as we are getting a bit older, should consider taking vitamin E. Right, I mean what else would have made the difference? Perhaps not the most satisfying, I am certainly taking vitamin E now by the way, not the most satisfying way to get evidence. Let us take a look at another case and see if we can do just a bit better.

This is an 8-year-old female spayed domestic shorthair with chronic diarrhea. This is the cat we see all the time. Why is it? Because we will do all of those tests, Dr. Gookin mentioned a number of them, including, with the fecal exam, we will do our minimum database, our CBC, biochem profile, urinalysis, and you cannot get to the receptionist at CSU without having that done. Total T4, checking for some of those bad viral diseases, we do the Texas A&M GI panel which I will touch on briefly in a bit. We do all of this and that is a considerable investment, and boom, nothing, negative, nada, within normal limits, nothing, and yet I still have an adult cat who is having diarrhea. What do we do next? Well, let us spend some more money. It is a cost centered thing. Medicine will throw him to ultrasound because they are pretty confident ultrasound will tell medicine to go ahead and take them to endoscopy. We do just that, we get all the way into the cat with the scope, and grab some pieces of actual tissue, those things that Dr. Gookin would have loved to be able to do before the cats are dead, we can do them in adult cats, we can get scopes in them, grab some pieces while they are still alive. We do that, and in the majority of these kinds of cases, you already know the answer, you are going to be told if you are an owner or you are going to be doing the telling if you are a veterinarian, this cat has inflammatory bowel disease. I could do it at half-price, just give me the cat, I will give it back to you and give you the histopath even before you go through all of this stuff, it will be inflammatory bowel disease.

Critical part of this diagnosis is that we almost always forget the real name, which is idiopathic inflammatory bowel disease. Why is that important? Well, idiopathic in the Greek's world comes from idios (one's own) pathos (suffering), it is an adjective (whatever that is, my high school kid could tell me) arising spontaneously from obscure or unknown cause. Now stated that way, it sounds almost comforting to be able to walk back into the exam room and say, 'well Ms. Smith, your cat has idiopathic inflammatory bowel disease,' sounds Greek, right? Well, in the modern day, Dr. House reminds us that in fact it just



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

means we do not know what the hell we are talking about, we do not really know what is going on, so we throw idiopathic on there. All of that effort and all that money, and we have gotten to the very same place we were when the client and the cat first walked in the door.

How might we treat, now that we have spent all of this money to put that diagnosis on the cat, how might we treat it? Well, it is not surprising that since we have very little idea of what is really going on, that we would have little idea or little evidence as far as what to effectively treat that cat with. We have a half-dozen things we will try, and half-dozen things we will put into that kitty cat, or try to put into that kitty cat, or hell, we do not do it at all, do we, we sign the script and then we say, 'good luck'. So it is not surprising that either because the medicines are not the right medicine for the right disease or because the owner simply cannot afford the prescription diets and they cannot continue to try to slam two or three medications down their kitty's mouth two or three times a day, that treatment fails. Again, even for one of the most, besides hairballs, for one of the most common GI diseases our kitty cats suffer from, idiopathic inflammatory bowel disease, we have little idea of what we really should be treating with and often not enough success in our treatment efforts. That motivates a number of us, whether we are clinicians or researchers, to try to take the next step, to move off anecdotal and try to find some actual evidence for what might work in these guys, and what could we reliably and confidently prescribe to owners of these kinds of cats.

How can we move from anecdotal to evidence? Well one of my favorite ways is to look at the human model of our patient's disease. The whole world tries to look at our patients as models of their disease; I prefer to do it in reverse.

What human models are out there for the diseases that my patients are suffering from? Well, if you look at inflammatory bowel disease in humans, it is a much better and much more specifically and clearly defined syndrome than, 'Well, it is an adult cat who has some diarrhea and I cannot figure it out.' They have categorized these into several very specific forms, one of which is Crohn's disease, and in many ways, or at least in some ways, Crohn's disease looks reasonably similar to what our adult cats might be suffering from. Let us take a look, how does our human model deal with their version of inflammatory bowel disease, Crohn's disease.

That is when I ran across this, and as soon as you run across one, many others, at least in the human field of research, study on stem cell therapy in inflammatory bowel disease. I highlighted the key line which I will read for you: "Mesenchymal stem cells have immune regulatory and regenerative properties and low immunogenicity. Based on these properties, these mesenchymal stem cells have been used in the systemic route in inflammatory bowel disease with promising results, even though it is still too soon to draw firm conclusions." I thought, well, now that sounds pretty intriguing and there are a variety of important properties that we will touch on very briefly that might make it a pretty dang ideal treatment for these kitty cats.

Now, first to touch on very briefly, these stem cells are a particular kind of stem cell. They are not the embryonic stem cell that the various political administrations have made political livelihoods off of, they have nothing to do with embryos and all of that emotional and religious and those kinds of concerns. These are not them at all. So we get, whew, shove those right off the table. They also are not the stem cells that



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

we might have learned about in high school biology that are actually in the gastrointestinal tract and in many other tissues. Resident stem cells are fascinating and absolute critical for the function of the GI tract. As Dr. Gookin pointed out, when those villi are effaced, the GI tract does not work at all, it is awful. It turns out the GI tract effaces itself even without the help of bugs, oh every two days you basically poop out almost all of your mucosa and you have to replace that or you are going to die, like those kitties, and who does that, it is the stem cells that are residents of those villi, the crypts, and regenerate themselves. So wonderful cells full of all sorts of critical properties, these are not those cells either. These are mesenchymal stem cells that in fact we can pull out of a piece of fat. Unlike the controversies that might happen when you get stem cells from embryos, who in this room would have any problem donating a little piece of their own fat, right? We would be happy to get rid of some of that. So boom, all of those issues, again, go by the wayside.

Mesenchymal itself means that it has something to do with connective tissue and that is where these cells enter the veterinary profession. You can see from this, mesenchymal stem cells here are shown (the dang toolbar still is not working; that is okay with me, as long as it goes away about now...good) so these mesenchymal stem cells are shown as being able to help or even regenerate connective tissues in bones and muscles, skin, tendons, ligaments, and so these stem cells first enter the veterinary field in a horse's joint. That is still a huge area of research and effort is the use of mesenchymal stem cells in joint diseases in athletes, athletic horses, now making its way in to dogs, trickling a little just into kitties, but joint disease, whether it be tendon ruptures, tendon repairs, or osteoarthritis, more chronic stuff, that is really where they hit the veterinary profession first. But you will notice the gut is not on here. So, I mean, Dr. Gookin goes off on some potentially crazy tangents that Winn funded for, but this is nuts, right?

This makes no sense at all, until you look a little closer at more of their what you call biochemical properties. All of a sudden, all these black lines on the mesenchymal stem cells having some sort of impact or effect on almost every process in our immune system. If there is one thing we know about inflammatory bowel disease in adult kitties, we know that the immune system is messed up. It is probably reacting to the wrong thing, or it is overreacting, it is overstimulated, it has just become a very bad immune environment. Here we have a single little cell that, again, I will not bother you with these at all, the acronyms and names for cytokines and interleukins and effecting all these B cells and T cells and it goes on, the language of it is just overwhelming, but take my word for it, this is the immune system almost in total and the mesenchymal stem cell is affecting or can have an effect on each and every part of that system. So boy, if there ever was at least potentially a silver bullet that you might use if you have an immune system problem, the mesenchymal stem cell is one that it looks like it is raising its hand.

Then they found just that when they have used it looking at human disease, Crohn's disease, and what mesenchymal stem cells (stromal is just another word for mesenchymal stem cells) can do and again, it is just a laundry list of impacting the immune system of that patient. Importantly, and I would have to come sit back where you are, they are, I think it is, yes, the very first, they are immunologically inert, so not only do you have a silver bullet but you have a silver bullet that you can shoot into an animal and it will not do any harm, it will not be recognized or thought of as foreign and 'I have got to get rid of you', so a critical component to this potential treatment. So, all of that inspired us or motivated us to think about using this in cats with chronic enteropathy. At CSU we are already doing some research with this with cats with kidney disease, and in Missouri, Dr. Marino is doing work on this in asthmatic cats, so there was certainly some



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

background to the use of this in various feline diseases. We wanted to look at it in cats with GI disease, and we called it a proof of concept study, meaning, it means a couple things, but meaning for us that before we got crazy, we wanted to start and see is there any reason that we might go forward with this. Does giving this to some cats give us any hope that it might make a difference and motivate us to again put in, again, research dollars are so hard to come by, we wanted to get some idea in a small number of cats that at the very least this was safe, and then potentially effective. So that is kind of what we call a proof of concept study.

Now, again, I started out by reminding you, I am a clinician. I am interested in cat poop, and the owners of cats with diarrhea, and I want to make both of those people feel better. I have some science behind me just because I married well. So, unlike the Dr. Gookin studies which are done correctly, do not tell everybody who is from Winn, put their fingers in their ears now, I rarely do this nearly as correctly as I should. So what I did, I said, well, instead of making all sorts of entry criteria, and maybe getting one cat every six months, I want to open my clinic door to the cats I actually see. I say, if your cat has chronic diarrhea, come be in my study. So I added a little bit about, well, we have got to make sure that it does not have a significant other disease that is still causing problems, so if the cat is gasping because it has cardiac disease, maybe not. Or, if it has got asthma that is bad, or if it's total T4 and thyroid hormone level is 12 or something, maybe not. But how many of you have ever seen or know of an older adult cat who only has one problem, please raise your hand...yeah, one, and she even took her hand back. These are not the kinds of cats we see in the clinic, so it made no sense to me. So we opened the door. The one thing we did that helped in my mind tremendously is we also had a placebo group, and these owners were blinded to what their cats were getting. Too pretty for us, pretty critical because again, any owner that you say, 'Yeah, I am going to give your cat something that is going to make him feel better; I need you to come back in two weeks and tell me it made him feel better', that does not work. Hence the blinded owner and the placebo group being critical parts of this.

Here is our study design. We have the cat come in and again, we did as much as was feasible or financially feasible to make sure the kitty did not have other bad diseases, it was not in bad chronic renal failure, so we did the bloodwork, we did the Texas A&M GI panel I mentioned earlier, mostly for cobalamin or vitamin B12 which is, at least in some studies, a great indicator of the severity of your GI disease, and we had owners because again, I am a clinician, and what the owner thinks is a pretty critical part of what is going on with their cat, so we had questionnaires that then would help us put various scores on their poop, everybody has seen the chart, number your poop. That day, if they met the grade, they got the first injection of adipose-derived mesenchymal stem cells, so stem cells that have been pulled out of a piece of another cat's fat. We culture and do various things behind the scenes, and we have a syringe ready to give the cat a certain number of these stem cells. Then two weeks later the cat gets injection number two, because we wanted to see if these cats could do well with multiple treatments.

Now remember, the placebo cats would get injections with just basically sterile saline, and the owners are not told which their cats receive. Then two weeks after that, we have them return, we repeat some of the bloodwork, we have them fill out that questionnaire again. These times are coming from again, just wisp and whims from human studies, so little is known, that most of this we are making up, how many should we give, how often, those are all open questions, but we took our best guess. Then, because again we had no idea really what time frame we should be looking at, we kept the owners, and this is critical, we kept the



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

owners blinded, although we were not treating them anymore, we kept them blinded for at least a month, sometimes 2 or 3 months, for follow-up later, and that is indicated here for those of you who are younger than I am, this is what a phone used to look like, and this is just meant to represent usually it was actually email contact, but some kind of contact with owners still blinded to what their cat had received. So that very simply is the study design. Let us meet some of the stars.

Very first cat to enter our study was Kiff, owned by Knut, and I am not making that up. You have no idea how many times I walked into that lobby going, damn, is the cat Kiff, or is the cat Knut, or is the owner Knut or Kiff. Fortunately super guy, he did not care what I called him or his cat, and I am sure I frequently got it wrong. Seven-year-old male castrated orange tabby, chronic vomiting for years, it had gotten progressively worse, that is what attracted this guy to our study. He had tried so much stuff. He had given up, the cat was on nothing and clearly this kind of last straw for this poor guy. He was on a natural balance diet but no meds for some period of time. He had been losing weight, his appetite was off, this is sick cat not feeling good. Stool was soggy and here is that little scale, so the owner considered the stool soggy. Turned out this guy did have a concurrent problem. He had a heart murmur that got worked up. He had obstructive cardiomyopathy, but everything seemed to be well-controlled on Atenolol, so doing fine, although we noted the murmur. He had previously had ultrasound and histopath, and sure enough, got his kitty diagnosed with the classic diagnosis, moderate lymphocytic plasmacytic enteritis, otherwise known as inflammatory bowel disease. It was a great first study cat for us, just what we wanted.

It turns out, thank goodness, the research gods were smiling on us, this cat actually got stem cells. So, we start with a CBC/chem; that was all unremarkable, kind of the baseline stuff. He was not hyperthyroid. His cobalamin or vitamin B12, this is a very low number, 166. This guy had serious gastrointestinal disease. He was vomiting up to three times a day, his stool was soggy, had diarrhea at least once a day, pretty miserable. Got his first injection, at two weeks got his second injection, and then two weeks after that, and having had nothing but stem cell therapy, those two injections, his cobalamine had gone from 166 which is kind of in the toilet to 528 which is great, normal and plenty. From vomiting much more frequently, he is now only vomiting about once a day, and when asked on the questionnaire 'is your cat having diarrhea', the answer was 'no', and the number put to that answer was 3.5, so 3 being normal, and the cat's appetite has increased. So Knut was going to take us to Stockholm. This is Noble prize, we are feeling so good about ourselves at this point, we are figuring, n of 1, that is all we need, let us end the study now.

So, just when we were about to follow up with Knut about a month later, we learned that the little guy had had an acute onset of dyspnea unresponsive to medical therapy and was euthanized. I mean, this close to our final follow-up, and we thought, we just went from Stockholm to I am looking for another job, because of course although we had all the reason to believe this was a safe therapy and would never do anything else to this cat, this raised the specter of oh, what if something has gone terribly wrong. Again, I told you this guy was a fantastic owner. He was. He allowed us to necropsy, which Dr. Gookin highlighted the importance of that. Our pathologist, the one working this cat, they knew of the previous histopath, they knew nothing of this cat's entry into any study. They found, thank goodness, I mean it is still awful for little Knut or Kiff, he died of basically heart failure, and clearly classic heart failure. But then what was particularly fascinating for us, the histological evidence, remember previously it had been moderate lymphocytic plasmacytic enteritis, IBD, was not identified in sections of the small intestine, perhaps due to treatment or resolution. Who has ever heard of resolution of inflammatory bowel disease? So again, we are booking our flight.

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • info@winnfelinefoundation.org
Phone 201.275.0624 • Fax 877.933.0939 • www.winnfelinefoundation.org



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

A couple other examples. This is Sesame and Pilar, because of course who owns only one cat, it is almost unheard of. Wonderful owner brought both of them in. They were I think just siblings in family only as opposed to birth. Both were, they were phenomenally similar to each other, both were 13 year olds, chronic diarrhea with intermittent vomiting. This owner was treating them with prednisolone every other day, FortiFlora that probiotic Dr. Gookin mentioned, but the stools were still moist and soggy and having diarrhea four to five times a week. These guys had no histopathic diagnosis, but I tell you right now it was IBD, it just did not cost as much. Here is classic treatment for these problems in these two cats, and it clearly is not working, so she was motivated to bring them to our study.

To make a long story short, neither of them were hyperthyroid, their cobalamin was ok, but they were, again, having lousy diarrhea, they were vomiting some. They get our first injection, they get our second injection two weeks later, two weeks after that, eh, it is not looking great, did not seem to have much impact. We said okay, well, she remained blind, and the owner remained blinded. We will get a hold of you in about a month, two months from now, who knows, we will just see, but again the enthusiasm is a little bit dampened at this point. Well it turns out, just about a month later, Pilar came back in for what the owner presumed to be a urinary tract infection, inappropriate urination outside of the box, so we wanted to do a cystocentesis and grab some urine for a sample for culture. Our nurse made the first mistake at this point, she had me restrain the animal. Never have the doctor restrain the animal, they suck at it. I was trying to restrain and this cat was wiggling and squirming, and I said, “Ah, I am not doing a very good job, am I, I am sorry...” and lo and behold the cat pooped, so who would not be straining if they have to poop. Then we laughed just fine, got the urine no problem. I pick up Pilar, okay can you handle the samples and I am going to take Pilar back to the lobby to mom. This happens with age, I had this delayed response because just as I am going to hand Pilar back to mom in the lobby, it dawns on me, ‘Jeepers, that was the most normal cat stool I have ever seen.’ I ran back into the exam room to make sure I could get a hold of it, and sure, it was beautiful, fully formed. So I asked the owner, so, how has it been going, right? Diarrhea now a full month or might have even been a bit more after we kind of had lost, after we had taken our last samples, diarrhea now is only once or twice a week, otherwise all stools were normal, had only vomited once in the past 2-4 weeks. So way out here at a time point that we had almost written off, boom, this cat was a new cat.

Another example, Nora, how many of you have cats show up your clinic, or I guess I won’t even ask, how many of you do this with your cat? Right, this is how Nora shows up, shows up with chronic diarrhea of six months’ duration. A little bit of again the kidneys are not working as well as they should but that had been stable for quite some time. No specific meds but using again a probiotic and a little slippery elm. Moist, soggy diarrhea once or twice a day. This is one of those owners who is heavily into the diet stuff, various different diets, no histopath done on Nora. Boom, Nora’s cobalamin was just fine, but the stools are soft and yucky, and we are having diarrhea way too frequently. We get our second injection, and then two weeks after that, stools eh, not a whole lot going on there either, but now with our previous experience we are thinking, well let us now give up hope yet, and sure enough, by the time we got out to between one to three months, no diarrhea, normal stools. This is one of those cat owners that you do not have to email, right, you can just sit at your desk and the emails will come, and they came quite frequently. No change after first treatment, but since the second treatment, completely normal stool with no cling-ons, has not happened since January. Nora is doing great, one episode when there was stress in the house, but otherwise firm and formed.



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

Now, at this point, you could certainly argue, well, all these cats would have gotten better anyways, had nothing to do with the stem cells, they just finally got better, their disease resolved, but...oh and I am sorry, the owner was so happy that she brought me a stool sample just to prove that the emails were not lying. That brings up the importance of the blind placebo control. There were 7 kitty cats that ended up getting stem cells, 4 that ended up getting the placebo which was just saline, went through everything, was the same process, but they got saline. Again, unsolicited, this was 1 of the 4, I just got to say I hope she is in your control group, still battling with all of the problems, trying to work with food, little to no change and that was the recurrent theme. In fact 1 of the 4 cats got quite a bit worse. Adding strength to our claim that since the only thing that was different between the two groups and the only thing that was changed, so even if they came in on treatments already or diets already, they were told do not change anything during this three-month period that we are trying to see what the stem cells or the placebo are doing, so nothing else was changed, adds to the strength of our trying to claim that, well, at least these stem cells are something worthy of study. From this group of about 11 cats, we got the proof or proof enough to continue. We found no adverse reactions at all, either during the giving or with time, because they were getting these stem cells, and so we are ready then to now take the next steps study-wise to advance this possible treatment.

You might think that, well, obviously now there are all sorts of clinical things we can do in our next studies, so we can demand that the cats have the histopath, we can bring uniformity to their treatments, etc, etc, but in fact, what we are doing is, I would not call it a big step backwards, but we are now catching our breath. We have the proof to say, okay, this has promise, it is worthy of further study, but think about the huge number of questions that we could answer even before we get to the cats again, and that is what we are doing now at this period of time. These cats all received stem cells, and another important part of the study, from the same donor cat, a specific pathogen-free donor cat who happened to be getting spayed, and that is also important it was a female, and they took a piece of her fat and through again the magic of my wife, that produces enough stem cells to treat about 7, 8, 9 different cats. So all of those numbers worked out, but it begs the question, well who would be the best donor? Is it a boy, is it a girl, is it a healthy cat, should it be from another cat who is having diarrhea because those cells are jazzed up ready to go...all of those questions, even just to kind of come up with who should be the best donor.

Then there are questions, once you take it out of the donor, this little piece of fat, are there things you should do or could do to that fat to make it even better or more specialized or more prepared for the job you are going to ask it to do when you put it into a cat with diarrhea. Those are just some of the things for instance, it turns out that fat you get from a female cat, stem cells you get from a female cat, are distinctly different in a number of potentially important ways then the stem cells you get from a male cat, and so right away, just from the benchtop research we are now doing, you lean toward, well, I think we had better get it from Fred instead of Ethel. Then pre-treating these with various cytokines or putting them into a little well with a little bit of funny stuff sure enough influences what they are more likely to do or not do to the immune system. Again, there are all sorts of possibilities and questions to be answered now before we even get back in to more cats. And, they are highlighting that actually. It turns out there are some viruses, or this particular virus which otherwise has no consequence on a cat, they do not care, has no clinical consequence if they have got this foamy virus rolling around your kitty cat, but oddly enough, it does seem to affect the properties of the stem cells you would get out of that cat. Right there you are saying, well just like in a blood donor program, there probably needs to be some kind of prescreening process for kitties that are going to be donors of stem cells.



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

The same individual, Dr. Borjesson from UC Davis, her group has done this with stem cells, how phenomenal. This is a kitty cat with this chronic gingival stomatitis; you just look at that and you cringe. Injection of adipose-derived feline mesenchymal stem cells, and this is what that cat becomes. It is amazing. So if there were any veterinarian in this country who should be yelling for the use of stem cells as a treatment for kitty cats, it should be Dr. Borjesson, right? I mean, she has seen this, she has done this, she has seen stem cells do this, she ought to be standing on the top of the Westin yelling, 'stem cells, stem cells, stem cells,' and yet what is she telling us. She is telling us whoa, be careful now, slow up. Veterinarians offer stem cell therapies to satisfied demanding customers because your clients have seen these pictures. So clinicians are sucked into giving treatment even in the absence of research to support such treatment, taking us right back to the very beginning of all of this, where so many things are unknown, so many things about this treatment need further research before we start throwing it out there and that is where people like the Winn Feline Foundation come in to help us out and fill in many, many important gaps because as it is now, you can go on the internet and find stem cells for your cat, no problem, piece of cake. Any client who wants to can get their cat injected with some stem cells. There are 2 or 3, but 2 major stem cells companies, right? Boom, boom. So it is a no-brainer to get; if you got the money, you can get stem cells into your cat. But, is that the right thing to do, is it an effective thing to do, and perhaps most importantly of course, is it a safe thing to do.

We had no side effects in our kitty cats, but what I will tell you is that again, it was my wife who prepared those, and it was my wife who handed me the syringe that I was then going to spend the next 20 minutes injecting into the cat, because you do not want them to clump, and I was standing there at the cat cage doing this with the syringe for 20 minutes. But if my wife, you would have to know my wife which I do quite well, if my wife hands me a syringe of something to inject into a cat, I know I would have no problem injecting that into myself, because I know my wife. What you have to ask yourself, and what we as a profession have to ask ourselves, and what we have to ask our clients, you send a piece of fat off to company X, they send you back a syringe, would you inject that into yourself because you are about to inject it into your cat. So, again, huge number of questions that need to be researched to make this truly, hopefully, potentially a silver bullet and it is the Winn Feline Foundation that undoubtedly will continue to take our field forward in just that direction, so thank god for people like them and thank you for joining them at a symposium like this, and again, going on to support them in the future. So, thank you, thank you Winn, and I will turn it back to Steve. Thanks very much. [applause]

Beginning of Question & Answer Audio

Steve Dale:

Our board members get to get some exercise in lieu of joining a health club and run around from table to table to grab questions. Dr. Thayer just read my mind, but then she knows that is very light reading. There is a photo contest that we have ongoing right now, so for those of you who have a cat, how many, raise your hands again, I just wanted you to move around so you are awake, okay keep those hands up, how many of those who have a cat, raise your hands if you have a cat, right, dress up your cat for the Fourth of July? I do not see quite as many hands going up, but if you can think of a way in which your cat is patriotic, or you know one of those cat owners that Dr. Webb was talking about, that do things that might be a little different, we do have a photo contest going on. It is WinnFelineFoundation.org. If nothing else, it is entertaining to see some of the submissions of these cats, but you can enter the photo contest as well. We also have a



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

newsletter that goes out with information that is the kind of information that you just saw, information from scientists, so I am going to call Dr. Webb and Dr. Gookin back up here, and I will ask you to share the microphone perhaps, and I will ask these questions; thank you.

The first question goes to you, Dr. Webb. I do not quite understand this, but I will read it as it is. This person wants to know if, in the study that you did, “Were you blinded as well as the cats?”

Dr. Craig Webb:

That is a great question, and yes I was.

Steve Dale:

So I think you referred to that actually, so you did not know.

Dr. Craig Webb:

When I was handed the syringe, I did not know what was in it.

Steve Dale:

“Did the stem cell cats, did they stay well, those that got well?” So that was a while ago, how are they doing now?

Dr. Craig Webb:

That is a great question. Again, being cat owners, I do not have to elicit opinions, they come on in, and so I am aware of at least three of the, so 7 got treated, 3 of the 7 have continued to do very well, but a number of the 7 have developed other problems and other conditions. But the GI signs, although we have not formally followed them up long term, the GI signs from what we have informally gathered have continued to do quite well.

Steve Dale:

When you showed that slide from the human medical community, of stem cells and all of that, there was, the way I read it, in fact there was a red star next to it, I do not recall the exact wording, but essentially it said there may be side effects in people we just do not know enough. Right, can you talk about that?

Dr. Craig Webb:

Right, one of the biggest concerns, because they are stem cells which means they have all the potential to do all sorts of stuff, one of the overriding big concerns is cancer, or neoplastic processes. If you are putting an ignorant cell that just wants to divide into a body, that is basically the definition of a cancerous cell. So, that is a concern where longer term follow-up will be critical, and it is an absolutely critical, unanswered question.

Steve Dale:

I am going to try to pronounce this, and also read the handwriting, this is for Dr. Gookin, “Treating a kitten with diarrhea and suspected sepsis and epithelial translocation, what antibiotic would you recommend?”



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

Dr. Jody Gookin:

Wow, I should not say it, my veterinary colleagues would kill me, but if I had a septic kitten, I would treat them with the best stuff I had, because you just do not have any time to waste, and you cannot culture and figure out what you should be using, so if a kitten came into my clinic and it was septic I would give probably something like, well, Clavamox, but in IV formulation, and a fluoroquinolone. What do you do, Dr. Webb?

Dr. Craig Webb:

Yes, Unasyn and injectable Baytril. [Audience: We cannot get Unasyn in Canada, I believe, I have not been able to find it...]

Steve Dale:

“Would you ever recommend antibiotics as a preventive or prophylaxis?” Controversial question I suppose, but a good one.

Dr. Jody Gookin:

For bacterial diarrhea, no I would not recommend preventing with antibiotics, because there are so many players involved, there is so much bacteria in the GI tract, the antibiotics are very promiscuous, they are not going to just take out the one thing that you want to kill. They are going to take out the good guys too. So for example if the enterococcus we are looking at is a good guy, and you give it an antibiotic to kill the E. coli, and that antibiotic also kills the enterococcus, you could make it worse. So, no, I would not do that. You will also actually select for that cat to have intestinal bacteria that are resistant to that antibiotic that you gave it.

Steve Dale:

By the way, I caught your Fred and Ethel, yes, yes, it is the reruns, I am not that old to personally remember, but I caught that. We had a fish named Fred, and he did not make it very long. He is buried in our back yard, though, it is true.

“Do you ever think there is a relationship between the progression of HCM and stem cell therapy?”

Dr. Craig Webb:

No, I think the two were unrelated, to be honest.

Steve Dale:

Some cats though before they succumb with HCM, so they are doing okay, they are doing okay, they are doing okay, and for a few weeks before they die, they do have GI issues, and/or other issues as well.

Dr. Craig Webb:

Absolutely, yeah, cardiac diseases are on the rule-out list for vomiting and diarrhea, for sure, so that is not surprising.



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

Steve Dale:

That is a good question. “How do I find out about studies that my cat could be in? She is a domestic shorthair, she has food allergies, seasonal allergies, diabetes, asthma, ear infections, bowel problems (laughter). Her poop goes from black to...(well, I won’t even, I will stop there)...vomiting 3, 4 times a week”

Dr. Craig Webb:

So, yeah, it may require a little bit of searching, but places I would start would be whatever veterinary teaching hospital is closest to you, and I would just ask them, or dive onto their websites. Winn Foundation publishes the studies that they are funding, not just the ones they have funded, but the ones that are receive current funding that will list the researchers as well, so that is a potential route. It is somewhat difficult. I get emails all the time from people living all over the country who want to be a part of that study, that unfortunately often cannot happen just because being in the house is an important part of making the study work, so it is certainly worth you searching for it, but do not be too disappointed if your cat just cannot be helped because of the logistics of it.

Steve Dale:

“Can you provide more detail about what the Texas A&M GI panel does and provides?”

Dr. Craig Webb:

The Texas A&M GI panel has a TLI, trypsin-like immunoreactivity, that is looking for EPI, which is exocrine pancreatic insufficiency. It has PLI, which is pancreatic lipase immunoreactivity, which helps you look for pancreatitis. Then it has cobalamin and folate, two important basically vitamins that give you a measure of what might be going on, either the GI tract is not working well or as Dr. Gookin mentioned, a measure of dysbiosis potentially in the GI tract.

Steve Dale:

So I asked about antibiotics as a preventive earlier. Dr. Gookin, I need your help in saying this again, it is *E. hirae*, so do you ever envision the day, this is my question kind of, but I will get to this one which is similar, sort of, follows it...envision a day where as a prophylactic, I asked about antibiotics earlier, that *E. hirae* might be used?

Dr. Jody Gookin:

I think it will be...can I envision that day? Sure, but I also am a scientist, and I need that evidence. With the right evidence, if things progress the way they could, then absolutely. I think that probiotics are a really, really hot topic. People are using them. What we really lack is hard-core evidence for their efficacy, and when should we use them, how do they work. So I think that that is growing exponentially right now, and I do see a future where probiotics will have specific indications and maybe even specific contraindications as our understanding of what they are doing grows.

Steve Dale:

So speaking of which, is *E. hirae* (notice I pronounced it every time differently, I figured I will hit it right eventually), is it vulnerable to antibiotics? Healthy cats did not have antibiotics, sick cats did have antibiotics, therefore perhaps sick cats did have *E. hirae* prior to medicine.



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

Dr. Jody Gookin:

Yeah, that is a great question. So the E. hirae is pretty susceptible to antibiotics, and correctly, some of the kittens that were in the sick group had received antibiotics. We did look statistically to see if there was a relationship between those kittens having had received antibiotics and them being more likely to have gotten that EPEC and we could not find any relationship. The thing I do not know, though, is specifically do we have enough kittens to actually answer that question, because once you look at subsets of the data, like just the kittens that got the antibiotics, or did not, and then just the kittens that had the EPEC, and did not, you are talking about small numbers of cats. So with large numbers of cats, could it be that antibiotics predispose to colonization by pathogenic bacteria? I think that that could be possible, yeah.

Steve Dale:

So that cat that I mentioned that is the domestic shorthair that has food allergies, seasonal allergies, diabetes, asthma, ear infections, bowel problems, as well as vomiting, could one day stem cells be used for that cat? And could that cat that you are treating for problem A among the fifteen problems there, could it treat 14 of the 15 just because it is stem cells?"

Dr. Craig Webb:

Right, it is certainly possible, because many of those that you rattled off clearly have an immunological or immune system basis, kind of as the final common pathway, and so, yeah, that may be very well a treatment you would consider.

Steve Dale:

Similarly, most felines have multiple issues it says, along with IBD, concurrent problems such as stomatitis, coronavirus maybe, herpes, those are the ones listed here, same thing, could stem cells then miraculously, or are we putting too much faith in the stem cells, putting the cart before the horse or the mouse before the cat.

Dr. Craig Webb:

Right, and that is what we are specifically trying not to do, for sure, and so, no, will I start kind of willy-nilly offering these injections to any concurrent disease-riddled cat that comes in the clinic, absolutely not. But is it certainly a possibility and therefore worthy of further study? Yes, absolutely yes.

Steve Dale:

Did any cats get cobalamin?

Dr. Craig Webb:

No, so any changes in cobalamin were not because they started receiving supplementation. We did not allow owners or have owners change the treatment, any treatments the cats were already on.

Steve Dale:

So you said that, I think you said one of the cats in the control group died...

Dr. Craig Webb:

Got worse.



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
Toll Free 888-9MEOWIN (888-963-6946) • Local Phone 201-275-0624 • Fax 877-933-0939

Steve Dale:

Got worse. So were those cats given stem cells after the study?

Dr. Craig Webb:

Right, one of them, when everything was unblinded, one of them came back and asked for stem cells. That cat did receive stem cell therapy, and did not get any better, which is, again, in a client's world is unfortunate, you feel bad, as a clinician you feel bad. As a researcher, you are thrilled, really, because to have 100% response to any treatment is just unrealistic and something is not right. So in fact 2 of the 7 that received stem cells, they did not get any worse, they got moderately better, 5 got significantly better, and then the 1 who was unblinded did not get much better and that is exactly what we would expect and in fact hope for in a complicated biological system like that.

Steve Dale:

“Dr. Gookin, does the timeframe after death greatly affect bacteria distribution, number, etc.”

Dr. Jody Gookin:

I think it would, absolutely. The question is, how long does it take for that to happen. So I think that has to be a consideration and one of the reasons why we specifically kept track of whether there were differences in the amount of time between death and us looking at these bacteria. It is also one reason why now the studies we are transitioning into are in live kittens. So having made the observation in dead kittens, and needing to see that GI tract to make that distinction, whether those bacteria are there or not, now that we can find them by other means like PCR and culture, we can study live cats and remove that death variable. Are they dying for some other reason and then the EPEC adheres, so that is a very legitimate question. We did look at that in the study. The study that I showed today is actually published, and we looked at whether there was any relationship between the time between death and the necropsy, and the bacterial populations present, and we could not find any.

Steve Dale:

That was actually the last question. So I have one more thing to do, and I want to ask you to help me do it, and that is thank our great speakers [applause]. I hope you consider learning more about the Winn Feline Foundation, like our Facebook page, as they say, that is what the kids say, right, but do like our Facebook page, and I also I do hope you check out the website. Thank you very much for attending another Winn Feline Foundation Symposium.

The End of the Audio