



## Update on FIV: What Every Shelter Needs to Know Webcast Transcript

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*Lynne Fridley:*

Good evening. I'm Lynne Fridley, Program Coordinator for Maddie's Institute<sup>SM</sup>. The topic of our webcast is, "Update on FIV: What Every Shelter Needs to Know." At Maddie's Institute<sup>SM</sup> we are committed to helping you find innovative, humane and effective ways to keep animals happy and healthy, while preparing them for placement in a new home. Our speaker tonight is Dr. Annette Litster. She is originally from Australia and has a really cool accent. She is the Director of Maddie's<sup>®</sup> Shelter Medicine Program at Purdue University's College of Veterinary Medicine where she is an Associate Professor. Dr. Litster holds a Master of Medical Science in Clinical Epidemiology and is a registered specialist in Feline Medicine. Through her evidence-based research into FIV (feline immunodeficiency virus), she is passionate about establishing greater understanding and clinically useful approaches to this disease. Before we get started, there are a few housekeeping items that we need to cover.

First, 10 audience members will be chosen in a random drawing for a door prize. Each will receive a copy of Maddie's<sup>®</sup> Infection Control Manual for Animal Shelters. We will contact the winners via email, so good luck. Next, please take a look at the left hand side of your screen where you will

see a Q & A window. That's where you will ask questions during the event. Dr. Litster will answer as many as she can at the end of the presentation, but please submit your questions early. Questions submitted in the last few minutes will not be processed in time for a response. If you need help with your connection during the presentation, you can click on the question mark, which is the help icon at the bottom of your screen. There are other little images along with the help button; these are called "widgets." The green file widget will take you to the resources that our presenter wanted to share with you, as well as some from Maddie's Institute. The resources will also be available on our website after this presentation, so don't worry if you do not get a chance to review them during the event. Before I turn things over to Dr. Litster, I want to say a few words about Maddie's Fund<sup>®</sup>.

We are the nation's leading funder of shelter medicine education and it is our goal to help save the lives all of our nation's healthy and treatable shelter dogs and cats. The inspiration for that goal was a little dog named Maddie who shared her unconditional love with Cheryl and Dave Duffield. They promised her that they would honor that love by founding Maddie's Fund and helping to make this country a safe and loving place for all her kind. Please use what you learn here tonight to make the dream she inspired a reality. Dr. Litster, thank you for being here tonight.

*Dr. Annette Litster:* Thank you very much, Lynne. I'm very pleased and thank you for giving me the opportunity to speak tonight about a topic that I am really passionate about, FIV. And, it's a very interesting topic – one that has attracted a lot of audience interest, as well. So, let's get started.

I [would] just like to give a run through of the presentation – how it is laid out. To me, thinking about FIV, there is a lot that we know about FIV and I would like to update the audience about that – about the prevalence and risk factors, transmission, diagnosis, clinical science, vaccination and treatments that are available. There is a lot of evidence in the veterinary literature from both naturally infected cats and experimentally infected cats about those aspects of FIV.

However, there is a lot of really good practical information that we need still to gather about FIV-positive cats so that we can look after them well in shelters, so that we can make good decisions for their care. One of the main ones is the markers of disease progression. And, what I mean by this is, how we know when the disease is going to progress from the so called “asymptomatic stage,” where there is really not much outward sign that the cat has FIV infection? How do we know which ones are going to progress into symptoms [and] clinical signs of disease and which ones are not? What things should we be looking for? We also want to know how to manage these cats optimally – how to look after them the best way we

can for shelters, adopters [and] foster homes, as well. We would like to be able to give some prognosis. These types of things are very difficult to study in the field with naturally infected cats. We know that we get slightly different information from naturally infected cats to experimentally infected cats, so we really want to focus on naturally infected cats. And, because most of the time this disease does not cause much in the way of clinical signs, you need really long study times to do that. When I partnered with the Maddie's Fund for the Purdue Maddie's<sup>®</sup> Shelter Medicine Program, I was really able to make a dream come true, because through Maddie's Fund I had long-term, secure funding for shelter medicine research. I have been able to do a long-term study of naturally infected cats and this is something that has been really a lifelong career goal of mine that Maddie's Fund has made possible. I would like to present what we are learning from the Maddie's<sup>®</sup> Purdue FIV study, which I think is the most exciting part of all.

Firstly, we will go through what we know about FIV. You will see, as we go through the presentation, that it is peppered with lovely slides of cats that are enrolled in the FIV study. We start off with a beautiful photo of Tank from Georgia and he has FIV. His main problem is that he's a bit too tubby. He's enrolled in the Maddie's<sup>®</sup> Purdue FIV study. We are just waiting for the next slide to load up. It is a little slow.

Let's talk about prevalence and risk factors. Worldwide, the prevalence estimates vary between 1% and 14% of healthy cats around the world. There are some areas, such as Japan, where there seems to be a higher prevalence. We know that the prevalence is higher in sick cats. But really, it depends on the study design, the kind of information that you are able to collect. It depends on the entry criteria, whether all cats are tested – just healthy ones, just sick ones, that kind of thing.

Dr. Julie Levy, the Director of the University of Florida, Maddie's<sup>®</sup> Shelter Medicine Program did a really large, very useful study of over 18,000 cats in 2004 in the USA. She collected specimens from cats attending veterinary clinics and animal shelters. She found that about 3.1[%] cats presented at veterinarian clinics were positive for FIV and about 1.7% of cats presented at animal shelters were positive for FIV.

In Canada, Dr. Susan Little performed another study and she found about 4.3% of the cats that she tested were positive for FIV. A statistical breakdown of Dr. Levy's study showed that the cats that were positive for FIV were more likely to be adult. They were more likely to be male and intact. They were more likely to be free roaming or have at least outdoor access and if they came through a shelter, the ones that were most commonly affected with FIV-positive status were feral cats. There are about the same number of stray and relinquished cats [1.6% and 1.4%, respectively].

You can see there as well. Cats were more likely to be FIV-positive if they had current signs of illness.

There was another study done in the USA that looked at strains of FIV and this virus has a number of different strains. There have been seven identified so far. I am confident that there will be more as the years go on. The seven identified so far as A, B, C, D, E, F and U. In the USA, you can see [that] there is A, B, C and F. I am going to also present some information later about what we found in the Maddie's<sup>®</sup> Purdue FIV study.

I find transmission [to be] a really interesting part of my work because it is hard to know when you co-house cats if the disease going to be transmitted or not. Bite wounds are a really important part of the transmission. You can see a lovely photo there of Domino and his lovely teeth. He has FIV and he is another cat from the Maddie's<sup>®</sup> Purdue FIV study. The most common, by far, is bite wounds for FIV transmission, and these have usually got to be deep bite wounds. They are not the kind of wound that you can't really find after that cats have looked like they have had a bit of an argument with one another, but look serious at the time, but you can't find the wounds – they look like they were biting, but there is no broken skin. Those ones do not seem to be all the dangerous. Also documented, but much, much less commonly, the infected mother

can pass the infection to the kittens during pregnancy, birth or lactation. It is a risk for blood donor cats. There are also very rare transmission events just under laboratory conditions where there is mucosal transmission across the oral, rectal or vaginal mucosa. These are so rare, because with FIV a mucosal infection – just casual transmission across a mucus membrane – requires up to 10,000 times more virus than other routes. We know that fomite transmission is not important. So, in shelters, as long as you use your regular disinfectant routines that should be enough to prevent fomite transmission. Also, there can be differences between strains. We know that from the laboratory. We don't have too much information from natural infections. What we know from the literature published studies of natural infections and experimental infections, when you mix non-infected cats with infected cats? Here is a table where across the top we have columns for: FIV-positive cats; FIV-negative cats that were in contact; any cats that became infected by being in contact with FIV-positive cats – whether it was a study done in a laboratory or a home; and, how long the observation period was. There have been five studies in the literature. You can see [that in] the first three, the FIV-negative cats that were in contact did not become infected. The next one was a laboratory study, and it is not recorded how many FIV-positive cats were, but 20 negative FIV-negative cats became infected over a period of 2 to 4 years. There was another study in a home with 9 FIV-positive cats and 17 FIV-negative cats at the beginning of the study, and by the end of 10 years, 6 of those 17

FIV-negative cats had become FIV-positive. So, this really inspired me to do a study on FIV transmission when I was contacted by somebody that had a large multi-cat household. They, in fact, had 138 cats in a closed household – so mixed FIV-positive and negative. Our aim was just to document the FIV status of these cats living in this mixed household. My hypothesis was that in a stable household, where the cats pretty well got a long and were used to one another, that feral transmission would not occur.

So, just to explain about the cats, as I said, there was a stable multi-cat household of 138 cats. Those cats had completely unrestricted access to one another. All of them were indoor-only except for just one FIV-positive cat who also was quite aggressive, apparently, with his housemates. There was one FIV-negative cat that did escape for a 12 month period. There was testing done on intake or close to the time of intake. We are going to call that the FIV SNAP Test 1, and that's the normal SNAP test that many of you do in shelters that detects antibodies against FIV. What we found was that in that population of 138 cats, there were 8 of them that were FIV-positive. That is 6 male neuters and 2 female spayed. They were all spayed and neutered, these 138 cats. Their average age was about 28 months. Of the FIV-negative cats, the 130 of those, there were 71 males and 59 females, [with an] average age of four months and, [again] all of those cats were FIV-negative. Then, we



followed up later with FIV SNAP [Test] 2. We were able to do that in 50 of the cats, 50 of the 138. [In] those 50, there were five FIV-positive and 45 FIV-negative cats from the SNAP Test 1 results. That SNAP Test 2 was done an average of about 28 months after SNAP Test 1 for each of the cats – in the range was anywhere between 1 month and about 11 years. So, what were our results? The FIV SNAP test results in all 50 cats were completely unchanged over that period. There were still 5 positives and 45 negatives. [Of] the FeLV (feline leukemia virus) test results, 1 cat had an FeLV-positive result. We even tested 5 of those 50 cats a third time and found exactly the same results. One of them at SNAP Test 2 was FIV-positive and 4 were FIV-negative. At SNAP Test 3, same deal. Of those 5 that had a third test, they were all FeLV-negative. I like playing around with spreadsheets and doing some arithmetic, so what I did was I looked at those 50 cats that we were able to get the second SNAP test results on, after a range of time anywhere from a month later after SNAP Test 1 to 106 months later. I did some calculations. Looking at the entry date, when I had the first test results for them and when they came into their household, for all FIV-negative cats and the number of days that each of the FIV-negative cats was exposed to an FIV-positive cat. So, for instance, if you are looking at an FIV-negative cat on one day and on that one day there happened to be 3 FIV-positive cats in the household, then that represents three days' worth of exposure on that one day, because that one cat is exposed to 3 FIV-positive cats.

What I found was [that] the average cumulative exposure duration that each of those FIV-negative cats to FIV-positive cats was almost 12 years (11.98 years). They had had all of that exposure in a closed household with unrestricted access to one another. They did not change their FIV status, which I found very reassuring. My conclusions were that even with mutual grooming or perhaps mild aggression – one of the FIV-positive cats did like to groom all of the rest and another one as I have mentioned liked to fight with the others. They shared food bowls, litter boxes, etcetera, but they did not transmit FIV over many years of cumulative exposure in a mixed household. It could be that how much virus they are carrying in their body and the type of virus. The strain of virus could be important factors there. We are not sure about that. It is really a complicated mix of feline behavior, virology and immunology that explains what's going on. But, I think that this study really has got some really reassuring conclusions. When I tell you about the FIV study that we are doing prospectively, there are a few other messages that I am going to give you that FIV transmissions can occur. I am not saying it does not ever occur, but we will talk about that a little bit later.

*Lynne Fridley:* We have our first poll question. This is your chance as the audience to chime in here, “Does your shelter test cats for FIV on intake?” Your answer [choices] are: “Yes,” “No,” “Don’t know” or “Not applicable.”

Please click on your choice and we will look at our answers here in just a second. I see everybody is still answering, but let us go ahead. Wow. Dr. Litster, what do you think of that?

*Dr. Annette Litster:* Wow. That is very impressive, yes. And, you will see [what] the recommendations are, later on in the presentation. I will tell you that you should be testing on intake and it looks like we are really preaching to the choir here. That is great. So, thank you. Well, let's get on. We will talk a little bit about pathogenesis – how the virus works in the body to produce signs of disease. This is a lovely photo of Clarence from Memphis. He does not have FIV, but he is enrolled because he is a match for Ace. He also lives with Booth and Booth is also enrolled in the Maddie's<sup>®</sup> Purdue FIV study. Thank you Clarence, Booth and Ace. So, the FIV infection has a number of different stages. Those stages are not really clearly defined or completely agreed upon, but I will go through them for you. There is the acute infection stage, which is soon after the initial transmission of the virus. It's often silent. There are no clinical signs to be seen at all. There are large amounts of virus circulating in the blood stream at this time. You will have heard, perhaps, about this term CD4 and CD8 from human HIV infection

*[Audio Disruption]*

Now, CD4 and CD8 cells are particular types of immune cells. They form the basis of many parts of the immune response. CD4 are also called helper cells. CD8 are also called cytotoxic cells and both of those classes of cells decline. You will hear me mention those terms CD4 and CD8 immune cells during the presentation a little bit. The response to the initial infection is that there are antibodies produced and then, that brings the amount of circulating virus down. There is also an increase in CD8 count. The ratio between the CD4 and the CD8 count is reduced, because that CD8 number is larger. That brings the ratio down. We know from HIV that that CD4:CD8 ratio is an important indicator, or marker, of the progression of infection.

Then, most cats enter a long asymptomatic period after the acute infection. There can be progressive dysfunction of the immune system. While there is progressive dysfunction, there are not always clinical signs of disease. Luckily, as with most body systems, cats have more of the immune system than they may need under particular circumstances, like being well looked after in a small household. While the immune system may decline progressively, it does not always result in clinical signs. The CD4 count declines, so again, there is even further reduction in that CD4:CD8 ratio. There can be non-regenerative anemia. The total lymphocyte count, those are more immune cells, that goes down and neutrophils, another type of immune cell, that also goes down in the CBC, the complete blood count.

It is mainly the cell-mediated immunity – the type of immunity where cells are mainly involved in responding to infection. That is the main arm of the immune system that is infected. The antibody-mediated immune arm can be stimulated, because there is usually a balance between cell-mediated immunity and antibody-mediated immunity. That balance can get out of kilter because cell-mediated immunity is reduced. Because of that imbalance, there can be an increase in the amount of antibodies or globulins in the blood. There can be an increased serum globulin concentration. We do know from previously published work that FIV-positive cats can respond adequately to vaccination, unless they are in an advanced stage of disease. We know that it is not only cell-mediated immunity that responds to vaccination, but it is also antibody-mediated immunity.

Here is Athena. She has FIV and you can see she is another tubby FIV-positive cat. All the more to love her partner Apollo with. Apollo does not have FIV. They are both living together and both enrolled in the FIV study. Thank you, Athena and Apollo. We are just waiting for that next slide to load. [I] want to take you through some clinical signs. As I said earlier, clinical signs may take years to develop, if at all. In fact, when we were enrolling FIV-positive cats in our study, we found that 41 of the 89 FIV-positive cats had no clinical signs at all on a physical examination performed by me. This asymptomatic period can last for years. The

clinical signs, of course, by their very nature, if they last for years, they are more likely to be seen in older cats. Common ones tend to be chronic inflammation of the mouth and the skin. There can be an increase susceptibility to various kinds of secondary infections. There can even be signs associated with cancer, especially lymphoma. Signs of dysfunction of the nervous system or the kidneys have also been reported and slow progressive weight loss is something that is often seen. Just a few photos here from the FIV study. We can see at the top right there, there is hair loss without any inflammation, where the cat seems to have just licked hair from its skin. It can be quite red, itchy and inflamed, as well. We see that fairly commonly in FIV-positive cats. As you can see with one of the cats there on the bottom left. Chronic wounds were certainly a problem for the cat whose leg is in the photo there, on the bottom right. Interestingly, we have had a number of cats that are FIV-positive in the FIV study that have had operations or have had wounds and there doesn't seem to have been a real problem with wound healing. This one really stood out in our memory, because this cat has particular problems with wound healing that can occur.

Chronic upper respiratory track disease. If you really, if you have got a big screen, you might see that this cat at the top left of the screen has mild signs there. There is a small amount of discharge from the eyes and the nose and that can be quite chronic. Chronic oral inflammation also can be

seen, especially at the corners of the mouth there. That is so called  
faucitis. That responds well, often to a full mouth extraction done by a  
veterinarian. That is quite a common thing, to get dental disease and oral  
cavity inflammation in cats with FIV.

We will talk a little bit about diagnosis. There is a lovely photo of  
Huckleberry. He does not have FIV, but he is a match for Orangello Mac.  
Huckleberry lives with Menuchin, who also enrolled in the FIV study.  
Thank you to Huckleberry, Menuchin and Orangello. We will start with  
antibody tests. These are the ones that probably you are most familiar  
with in shelters. There is a SNAP test, which there is a photo there; you  
would be very familiar with the dots on that snap test. It is highly  
sensitive and specific. There are reports of it being up to 100% sensitive  
and 100% specific, in some studies. We are lucky. It is a really, very  
accurate test and it detects antibodies. It does take time for those  
antibodies to develop after initial infection. They may not occur for up to  
60 days, sometimes even a year or longer. So, it is generally advised that  
the testing occurs perhaps 60 days after infection. You must use the test  
within two hours of opening the foil pack. Then, once you have put the  
blood in the test, you need to read that in ten minutes. So, you time it and  
read it in ten minutes. You should always keep that refrigerated. There is  
another kind of antibody test and that is called the Western Blot test. It is  
a send-out test offered by IDEXX, and it used to be thought to be a more

specific test. But, there has been a study done by Dr. Julie Levy from University of Florida that, in fact, found that the regular SNAP test was more sensitive and specific, in the study population that she had, than the Western Blot test. Perhaps, there is not as much need to send-out as you might think. As I said earlier, usually antibodies will be detectable within 60 days of exposure, but it could take much longer – 12 months or perhaps even longer, if the viral exposure is low.

There can be false-positive results though and I think a lot of you are aware of those. That is because these antibody tests just detect antibodies. They do not know where the antibody has come from. It may be that there are antibodies produced in response to vaccination, rather than infection. So, if a cat has had an FIV vaccination, then that cat can have a positive antibody test result that will persist for at least a year after full vaccination. We have a cat enrolled in the FIV study that is still testing faint positive nine years after the last FIV vaccination. Also, if young kittens are born to FIV-positive queens, they are not always infected by their mother. In fact, most of the time, they are not. They can be, but most of the time the infection does not pass from mother to kitten. But, the antibodies do pass from mother to kitten. The antibody test can pick up maternal antibodies and again, that kitten may not be infected; they may just have maternal antibodies.



We will talk a little bit about antigen tests, which are tests that are designed to detect viral proteins. There is a PCR test and because it detects virus rather than antibodies, it can potentially distinguish cats that are vaccinated, by FIV-uninfected from FIV-infected cats. The vaccine virus is killed. It is not picked up by the PCR test. So, if a cat is vaccinated but uninfected, it can be, it should be negative on the PCR test. If it is positive and the test picks up viral protein that means that it is infected. Now, you should also bear in mind that this vaccine will not protect all cats from infection. It is possible that a cat could be vaccinated and also infected subsequent to being vaccinated. It can end up being quite tricky to tease out all of these results. I am going to present an algorithm on the next slide to try and help us do that. The test does rely on adequate amounts of the virus being present in the blood for it to register a positive result. As part of the Maddie's<sup>®</sup> Purdue FIV study, we did do some follow up on this IDEXX PCR test. We found that both sensitivity and specificity were approximately 94%. The test will also provide you with strain information – whether it's A, B, D, or whatever it is.

There is virus isolation – and we certainly use virus isolation in the Maddie's<sup>®</sup> Purdue FIV study that's performed with our friends and colleagues at the University of Glasgow – but it really is a reference technique. It is not available to shelters and veterinarians, in general. There is a lot of work involved. It takes at least 28 days to perform, as

well. We need it for back up, so that we have absolute assurance of what we are talking about with our FIV study, but it really is a reference technique.

I would like to present this algorithm, here, that has been provided by IDEXX and also has been based on information from Dr. Levy and her colleagues with the American Association of Feline Practitioners' Retrovirus Management Guidelines. We start off here with this orange box, at the top left, and just say we get a negative result on our SNAP test. We can really, pretty well assume that that is going to be an uninfected animal. If it is a positive test, then we might want to just check by repeating the SNAP test. You could try Western Blot, but as Dr. Levy found out, it probably will not get you much further. So, you might want to use just another SNAP test for confirmation. If the cat is negative on the follow-up test, which perhaps you might have performed later on—maybe you have performed the initial test on a kitten and it's over six months old by the time you perform the follow up test. If it is negative, you can say, "Well, probably, the initial test might have been from maternal antibodies." But, the cat now, it is free of infection. It always was, it was just maternal antibodies. Also, a positive test [result] could be from vaccinated animals. If we want to really follow-up on that, [whether] it could be positive from vaccine or not, we might want to follow up using a PCR test. If that PCR test is positive, then that test has detected viral

protein [and] we know the cat is infected. We are pretty sure that it is. As I said, the test has 94% sensitivity and specificity, in our hands. We are pretty sure that the positive PCR result coupled with the positive ELISA test result denotes an infected animal. If the PCR test is negative, that is inconclusive. It may well be that the particular strain of infection is not being picked up by the PCR test. There might not be enough virus for the PCR test to pick up. Unfortunately with a negative result, we do not get too much further in our diagnostic process with PCR. So time for another poll question, over to you, Lynne.

*Lynne Fridley:* Yes, another poll question. I would like everybody to answer the poll question in the poll area, not the Q & A area. The next question is, “Which test does your shelter use to identify FIV-infected cats?” [Answer choices are:] “SNAP test,” “Western Blot test,” “PCR test,” “We do not test for FIV,” “Don’t know” or “Not applicable.” Please answer in the poll area and we will look at the results in a few seconds. “Which test does your shelter use to identify FIV-infected cats?” Let’s look at our results. Well, it is an overwhelming majority, Dr. Litster.

*Dr. Annette Litster:* Yes, and they are using the most accurate test as well. As we know, the SNAP test is the one that has the highest rates of sensitivity and specificity and [is] the one that is recommended as an initial test. It sounds like this audience is really switched on to their FIV diagnostics. Well done. Okay,

now, we are going to talk about which cats to test. I have made a list here of all of the cats that really, if your resources are limited, you cannot test all of them, you want to know which ones to target for SNAP testing. Here is the list. Sick cats. Cats and kittens that are going to be group housed – and that’s because of the possibility of transmission through bite wounds. If you are going to adopt cats out, and then if it is a negative test result, just to be on the safe side, you want to retest a minimum of 60 days later just in case there was a subsequent infection event. Cats that have had a recent exposure to an FIV-positive cat or perhaps a cat that you do not know what the FIV status is, especially if there is a bite wound that you can see and it has broken the skin. Again,, follow up a minimum of 60 days later. If a cat is co-housed with an FIV-infected cat, it is a good idea to get that cat tested annually. We know from the study that I presented earlier that the high-risk cats are outdoor, free roaming cats and cats with bite wounds. Those are good ones to test. Of course, if you are considering vaccination against FIV, you need to know the FIV status of the cat because after vaccination they are going to test positive. You might not know whether they are testing positive because they have been vaccinated or because they are in fact vaccinated and infected. Blood donor cats should be tested because as we have seen earlier, blood donation from an infected cat can transmit the infection.

Here is Menuchin. You heard about Menuchin earlier who lives with Huckleberry. Menuchin is enrolled in the Maddie's<sup>®</sup> Purdue FIV study not because he has FIV, but because he is a match for Rocky. Thank you very much, Huckleberry, Menuchin and Rocky. I would like to talk about treatments for FIV and basically they work on two different aspects of the disease. One is targeting the immune response to the disease and then we will go on and talk about targeting the virus. Now, there are many of these new therapies coming out all the time, and especially in conjunction with HIV. Then if treatments have proved useful for HIV, people are often wondering whether they will be useful for FIV. There is a lot of work to be done in good, well-designed clinical trials in cats. I am going to present a couple of therapies that target the immune system that we do have some evidence for. One is interferon therapy. This [is] recombinant feline interferon. This is interferon that is synthetically made and it is an immune protein that is the same as a cat's own immune protein, called interferon. Unfortunately, it is not available in the US, but it is widely available in Europe, the UK and Australia, for those of you who are listening from those locations. There was a study done from naturally infected cats, 7 naturally infected cats. Three were healthy at the beginning of the study and 4 [were] unhealthy. They had 5 untreated FIV-positive cats as controls. [It was] just an 8-week treatment period. They found that if the cats were healthy or mildly unhealthy, they just remind stable, there wasn't much change. And, that was 4 of the cats. The

remaining 3 cats were unhealthy at the start of treatment and they did have improved clinical scores.

There was another study done with oral human interferon that is available in the USA, and it was a particular low dose regimen that was used. There were 30 naturally infected cats, 24 treated and 6 placebo over a total of 14 months this time. They noticed most of the improvement occurred in the first 2 months. Also, over the 14-month treatment period, treated cats did survive significantly longer than those cats that were just on placebo.

There were not changes noticed in that CD4:CD8 ratio, which I mentioned earlier, or other parameters on a complete blood count (CBC). Those did not seem to differentiate between cats that had effects of disease and those ones who did not.

There is also anti-viral therapy. I just wanted to show you this cartoon. Here, in the center, we have the blue dome [which] represents the cat's cell and you can see here there are these other virus particles that have these green spiky projections from them. You can see that the virus enters that blue dome, the cat's cell. It goes through the entry point of the cell membrane. You can see, here, I have mark this step number three with a red star because as it turns out, that is where some of the treatments that we use as anti-viral therapy target. They target this stage where the virus has entered the cat's cell and it is integrating into the cat's own DNA so

that it can use that to help the virus reproduce. You can see at the other end that it reproduces itself and then leaves the cell. That is how the virus spreads in the body and reproduces. We will just present a couple of the anti-viral agents. They are called PMEA and AZT (Zidovudine) and that is because they have long, unpronounceable chemical names. As I said earlier, they work on that step three in the cartoon. The first one [that] we have some information about was AZT. That is the one that a lot of people with HIV, that are living with HIV, use regularly. They did do a placebo-controlled study in cats with FIV and they showed that the stomatitis, or inflammation of the mouth, did definitely improve using AZT. They also found that the CD4:CD8 ratio improved. They used a 3 week treatment period. However, there were some side effects of treatment, depending on the dose used. The higher the dose used, the more chance there was that the cats would become anemic. But, that anemic condition did usually resolve in the first 3 weeks of treatment. It is possible, they found in HIV, that AZT-resistant strains of virus can arise. If the AZT was used on a chronic basis, it is possible that viral resistance could happen. It is not really suitable for cats with signs of bone marrow suppression because of the dose dependent anemia that can occur. The other study that was done used PMEA. It was a placebo-controlled study with a 3 week treatment period and there was some clinical improvement noted, but there was more severe anemia than with using AZT.

We are going to talk a little bit about vaccination against FIV and here is “Crommy,” Cromwell. He has FIV. He is quite the character from Chicago and he is enrolled in the Maddie’s<sup>®</sup> Purdue FIV study.

Vaccination, the FIV vaccine, is classified as non-core by AAFP Vaccine Guidelines. So that means, it should only be administered to cats in specific risk categories, where you feel that there is a particular reason that a cat is at particular risk of coming into contact and fighting with an FIV-infected cat. The AAFP Vaccine Guidelines do not recommend this vaccine for shelter use.

Outdoor cats that fight, or cats living with FIV-positive cats in unstable relationships, or perhaps you might consider that for after adoption, but certainly not for shelter use. As we said earlier, we cannot distinguish between vaccinated and infected cats using the SNAP test. What we want to do is make sure [that] if FIV vaccination is performed that microchipping is also [being] done at the same time, so those cats can always be identified as cats that have been vaccinated against FIV, rather than known to be infected with FIV. As far as the effectiveness of the vaccine goes, it is only made to be effective against subtypes A and D, but field trials have shown some protection against subtype B. Different challenge studies have shown anywhere between 0% and 100% preventable fraction – that is the proportion of cats that would be protected by vaccination over and above the proportion that might be naturally



resistant. The effectiveness of the vaccine has been very difficult to gauge in field trials so far. For shelters, as I said earlier, it is not recommended for use in shelters or free roaming cats. I was talking with Dr. Levy about this earlier in the week and really, shelter resources are better used elsewhere, such as spay/neuter or rabies vaccination programs. It is quite an expensive vaccine to use, because it requires at least three doses to be effective and the protection is strain-dependent, as I said earlier. There are strains here, such as strain B in the USA that it does not necessarily protect against. Reduced aggression, once they have been spayed or neutered, should hopefully decrease their risk for being infected with FIV. Also, if these cats are then presented later on, at veterinary hospitals and shelters, and they are FIV-positive on a SNAP test, then disposition decisions might be made that are not really based on fact. People might assume that they are infected rather than knowing that they are vaccinated. That is why microchipping is so important. Over to you Lynne, with the next poll question.

*Lynne Fridley:*

We have another poll question here. Please answer in the poll area – in the slide area of your browser and not in the Q & A section. “Does your shelter adopt out FIV-positive cats?” Your choices are” “Yes,” “Yes, but only if they are healthy on a physical exam,” “No,” “Don’t know” or “Not applicable.” Please answer in the slide area, in the poll area, and we will look at the results in just a few minutes. Well, a few seconds. “Does your

shelter adopt out FIV-positive cats?” Let’s see what we have here. Wow. Thirty-six point eight percent said “Yes” and 26% said, “Yes if they have been deemed healthy on a physical exam? What do you think, Doctor Litster? That’s pretty good.

*Dr. Annette Litster:* That is great, yes. There are some shelters [that] are doing wonderful things, with finding homes, good homes, long-term homes, for healthy FIV-positive cats. Congratulations to all of you who are involved in that. Now, the next part of the presentation – what we need more evidence about for the cats naturally infected with FIV. Here is Daddy. He is one of the sweetest cats I know. He has FIV and he is enrolled in the Maddie’s<sup>®</sup> Purdue FIV study. Hi, to Daddy. We are just waiting for that next slide to load. Here is Newt. We are going to talk about markers of disease progression. Newt lives in Memphis and he is a match for TJ. Newt does not have FIV. Hi, to both Newt and TJ.

We do not know too much about clinical staging exactly – about when the disease is going to progress or if it is going to progress in which individual cats. That was most of my motivation for starting the FIV study, because I really wanted evidence to base practical decisions on. There is some information in the literature that CD4:CD8 ratio declines in the terminal stages. There are also immune proteins called interleukin 2 (IL-2) and tumor necrosis factor alpha (TNF- $\alpha$ ). They are proteins that are part of

the immune system. They decline in the terminal stages. There can also be a change in viral proteins. Our friends and colleagues at the University of Glasgow have done a lot of work with our FIV study on this. What happens is [that] these viral proteins [that] the virus reproduces over and over again over the lifetime of a cat that is infected with FIV, that virus evolves over many replications and generations of the virus. There can be a natural selection of certain types of virus that seem to be able to resist the immune response of the host. That is why they are still hanging around after many generations. They may lead to progression of disease. We are working on that to see if we can use changes in viral proteins to predict whether some cats will develop disease and other cats will not.

Viral load, the amount of virus on the blood, has also been shown to be connected with progression of disease. There was one study of 33 naturally infected cats. They were divided into cats with high viral load [and] cats with low viral load at enrollment. It was found that the ones on enrollment that had a high viral load, had a significantly reduced survival over the next 4 years, and that viral loads did increase just prior to the cat's passing away.

Let's talk about prognosis, something else that is a practical problem that we need more information about. I thought this was a really fun photo of Amos. He does not have FIV, but he is a match for Stormy. Hi, Amos

and Stormy. I think Amos is quite the bad boy in Memphis, Tennessee. We just are waiting for the next slide to load. What we know about published evidence of survival in naturally infected cats is really not very much at all. Certainly no prospective studies such as the Maddie's<sup>®</sup> Purdue FIV study.

There have been a couple of retrospective studies. One was in a closed household, where there were cats that had FIV, some with FeLV, some with Feline coronavirus (FCoV), over 10 years [on] 26 cats. Nine of the 26 were initially infected with FIV. Six additional cats were infected at the end of the 10 years, but FIV did not seem to adversely affect life expectancy when they did some statistics of the survival of those cats. There was also a retrospective study done in Canada, with 39 FIV-positive cats. [There were] 22 FIV-negative cats studied over 8 years and there was not a difference in the survival time of FIV-positive and FIV-negative cats over that study period. There have been some experimental studies that have shown that subtype B might be more host-adapted and therefore, less pathogenic. There really needs to be more work done on that.

We want to talk about optimal management for FIV-positive cats for shelters and adopters. This is a lovely photo of Tac, who is also from Memphis, Tennessee. She is an FIV-negative cat who is a match for Wrigley. Hello, to both Tac and Wrigley. What should we be doing in a

shelter with respect to testing? We should test all cats before adoption or before group housing, as we said before, and follow up the testing 60 days later. Always use tests individually. You should not be just testing a few out of a group or pooling specimens. That is an unreliable way to test. With trap-neuter-vaccinate-return (TMVR) programs, testing is optional. If you are going to spend the resources on testing, you really have to have a plan in place for what you are going to do when you receive the test results. Not everybody is actually going to change the management of their TMVR colony in response to test results from FIV SNAP test. If that is the case, if you know that you are not going to change your management plan for whatever reason, perhaps resources would be better spent elsewhere, than to spend them on a test where you are not going to really take much notice of the results. You also need to make sure, if you are adopting out cats that are FIV-positive, that you advise prospective adopters or foster parents about what they are taking on and that FIV-positive cats may need some extra care. We are going to talk about that very soon and talking about integrating them into a household perhaps with FIV-negative cats, as well. Again, follow-up testing [should be] performed after 60 days.

Shelter management considerations. Of course, we always want to spay and neuter all shelter cats, especially all FIV-positive cats. I think that is a given. We need to display the FIV status of all cats prominently in our

shelter records and on the cage or the room where FIV cats are housed. You should really house FIV-positive cats away from kittens and sick cats, because we know that their immune system may not be able to respond to disease as well as a cat without FIV. For their own protection, it is best to house them away from kittens or sick cats. These are the things, really, that adopters and foster parents should know. They should really have FIV-positive cats indoor only.

Monitor these FIV-positive cats carefully for clinical signs of disease, especially if there are multiple FIV-positive cats in the same household. They should see a veterinarian for a six-monthly wellness check and if there are signs of FIV related disease, perhaps consider antiviral therapy in conjunction with your veterinarian. You need to explain the possible risks of transmission to FIV-negative cats in the same household and we had a bit of a talk about that in this presentation. There is no evidence that FIV will infect humans, so we do not have to worry about that side of things. So, it looks like there is another poll question, over to you, Lynne.

*Lynne Fridley:* Yeah, there is another poll question. I understand that a few of you are having difficulty in answering the polls. If you will refresh your browsers, if you will do that now, maybe that will take care of the problem. The next poll question is, “If you adopt FIV-positive cats, what kind of housing do you use for them in the shelter?” Your answer [choices are:]

“Single housing,” single cat housing, like cages, “Room housing, but only with other FIV-positive cats,” “Room housing with FIV-positive and FIV-negative cats,” “Don’t know” or “Not applicable.” Please answer in the poll area. “If you adopt FIV-positive cats, what kind of housing do you use for them in the shelter?” Please submit your answers. We’re going to look at the poll results in just a second. [I will] give you all a reasonable amount of time to answer this time. And, let’s look at the results, Dr. Litster.

*Dr. Annette Litster:* Okay, so we have got mostly “Single cat housing” or “Room housing, but only with FIV-positive cats.” And, that’s what we recommend. There are some people room housing with FIV-positive and FIV-negative cats and that can work out as it did in that study that we did, if it is a very stable household where everybody gets along. Thanks for that information; it is really interesting.

Just move to the next slide. Here is Fiona. She is FIV-positive. She lives in Georgia and she is enrolled in our study. Hi, to Fiona. I like to think of the Maddie’s<sup>®</sup> Purdue FIV study as a tale of two cities because it has really been based in Memphis, Tennessee and Chicago. There are some, quite some, differences between the study populations in each of the centers, as you’ll see. Just to go through the study protocol with you. It is a 5 year study. It is a controlled-study because there are FIV-positive cats

matched with FIV-negative cats. They are all naturally infected FIV-positive cats. The study started on January 1, 2010. We collect data every 6 months for the FIV-infected cats and FIV-negative cats have data collected every 12 months. They are all age and sex matched to each other. At each data collection point, we collect information on a clinical history, general physical exam, a gingival score – so a score that tells us about the amount of inflammation in the mouth. We do blood testing for a serum by chemistry and complete blood count. We are interested in the CD4:CD8 ratio and also perform urinalyses.

Then, that generates a report that we give the cat owners and they can take those written reports to their regular DVM to discuss them. We also will send samples from all the FIV-positive cats to the University of Glasgow Retrovirus Research Laboratory and to IDEXX West Sacramento. If there are any necropsies, they are performed by the one pathologist at Purdue. As you will see, we have a lot of cats in one household, in Memphis. Those FIV-positive cats are all weighed every month and that cat owner provides that information for us every month. We will check in every 3 months with every cat in the study by email and phone, just to see how things are going. We remind all the cat owners that they should contact us the moment anything happens. We like to hear, as often as possible, from all cat owners in our study. So far, with the study enrollments, we had the first 2 years, during which time we were able to enroll cats. The



enrollment period has finished now. And, that was from January 2010 to January 2012. At the time of enrollment, all cats were classified as “healthy” or “not healthy.” By “healthy,” I mean that there were absolutely no abnormalities found on a physical examination by me. I am not talking about any laboratory testing. I am talking about just the physical examination that I can do with my eyes, ears and hands. [Cats were noted as] “not healthy” if they had even one abnormality found on a physical examination. They were classed as “not healthy” and that was done at the time of enrollment. All controls had to be “healthy.” We in our group discussed this a lot and decided that if any control cats, because there was matching to the FIV-positive cats, if any control cats were “not healthy,” then we would have to match them on the type of disease, as well. That would just be too difficult, so we made it just one rule: all control cats must be “healthy.” Then we will be able to group all of our cats into different categories and do different types of comparisons over different categories when we get all the results in.

FIV-positive cats can be “healthy” or “not healthy” at the time of enrollment. Here is a little cartoon that tells us about numbers. We have 89 pairs of cats enrolled. Thirty-eight [are] from Chicago and 51 [are] from Memphis. Now, we will look at the Chicago arm of the studies. There were 21 “healthy,” FIV-positive cats and 17 “not healthy” FIV-positive cats. Three of the 21 “healthy” cats were from one particular

shelter that did have FIV-positive cats room-housed together. There were only FIV-positive in a room. They were not co-housed with FIV-negative cats. There were 7 of the “not healthies” that were from that shelter. All of the rest of the FIV-positive and negative cats were originally from shelters in Chicago, but now with single-cat owners or maybe an owner that had 2 or 3 cats.

We will look at the black arm on the right from Memphis. There were 51 pairs of cats, of their 89 pairs enrolled from Memphis. Twenty of the FIV-positive cats were “healthy” on enrollment and 31 “not healthy.” I mentioned earlier that many of the cats came from the one household in Memphis. There were a lot of them from that one household that had FIV, where there were many cats housed together that had FIV, and some cats also co-housed that did not have FIV. Eighteen of the 20 “healthy” FIV-positive cats were from household one. Twenty-nine of the 31 “not healthy” FIV-positive cats were from household one. You can see there is some mix there of cats grouped in large households and cats that are kept in smaller groups or even single-cat households.

Some results so far. The mortalities for FIV-positive cats in Chicago, there have only been 4 out of 38 FIV-positive cats [that] have died. Three of the 4 were from the “healthy” group. One looks like the death was FIV-related, but the other 2 were not FIV-related. One cat died from what looked like FIV-related

disease from that shelter, where there were room-housed FIV-positive cats. That cat was in the “not healthy” group at the time of enrollment. In Memphis, by contrast, 34 of the 51 or 2/3rds of the cats that were FIV-positive have died. Twenty cats from the “healthy” group and 31 cats from the “not healthy” group [are enrolled]. Most of these were from this large multi-cat household, household one. Now, let’s look at the mortalities in the FIV-negative cats. [In] Chicago, none of the FIV-negative cats have died. In Memphis, 4 of the FIV-negative cats have died. Two of the 4 were accidental deaths; two were illness-related. One was from that large multi-cat household X and one from another large multi-cat household that has enrolled some cats in the study.

Here is a table where we compare the FIV-positive cats in Chicago and those in Memphis. You can see that I have done some statistics. Looking at the age at enrollment, the average age in Chicago was 4 years old and in Memphis it was 5 ½ years old. The number that were enrolled in the “healthy group,” it was 55% of Chicago cats; whereas, only 39% of Memphis FIV-positive cats were enrolled in the healthy group. [Of] those enrolled in the “not healthy” group then, 45% [are] in Chicago, but 61% [are] in Memphis. The time from the first known FIV-positive diagnosis until the time they ended the study, on average, was about 6 months from Chicago, but 2 years in Memphis. We don’t know when these FIV-positive cats actually had their infection first, were infected with FIV.

What we have got to do as a surrogate marker is have the time from first FIV diagnosis – that is as close as you can get with a naturally infected study, almost all of the time. The length of time enrollment was also longer in the Memphis group: an average of 3.2 years, whereas it is only 1.9 years in the Chicago group. [As per] multi-cat housing 10 of 38 were in the Chicago group, but in Memphis, of those 51 cats enrolled with FIV in Memphis, they were all (51) enrolled from a multi-cat household. You can see that there are some statistical differences. So, in summary, FIV-positive cats enrolled in Memphis are older. They have been known to be FIV-positive for longer. They have been enrolled in the study for longer and they are housed differently than FIV-positive cats from Chicago. This may well explain some of the differences we are finding in outcomes so far from the study. A few more results. We found it interesting that there were quite a few of the cats that have died in the study [that] did have lymphoma on necropsy – 13 of 38 or just over a third of them.

Lymphoma was always found in the bone marrow, often in other sites, as well. A lot of these cats, if they did die, they had a period of weight loss for at least 3 months and it was severe weight loss, over 10% a month.

You might be interested, after the other study that I presented, that 3 of the cats that were originally enrolled in the FIV-negative group have become FIV-positive, because they were co-housed with FIV-positive cats. Now, interestingly, all 3 of those cats had very significant bite wounds. They

had to go to a veterinary hospital to have treatment. Some of them were hospitalized and 2 were from a large multi-cat household, with mixed population. One was a territorial outdoor cat that was always fighting, so FIV transmission does occur under those circumstances. If there is going to be co-housing, it has to be a stable household.

Clinical and laboratory results. We have found sub-types A, B, D, and F identified in our population. There has not really been any association that we could draw between health status and the subtypes. We found those clinical findings that I presented pictures for earlier. Also, we have found that the CD4:CD8 results are lower in the FIV-positive cats at the time of enrollment and over the study period so far. So, Shelter Medicine to the rescue. We are solving practical problems for FIV-positive cats. What we really want to know is early information about which naturally infected cats are going to become affected with clinical signs of disease, so we can advise potential adopters and foster parents. Are there particular kind of morbidities such as say upper respiratory track disease for instance, which is very common in shelter cats? Does that seem to be a particular risk factor for argument sake, for the progression for FIV disease? Changes to the immune response and viral loads, the cores or the result of clinical progress, which came first, the chicken or the egg? We hope to find these things out in our FIV study. We really want to know what the best possible management plans are for FIV-infected cats in shelters, so we can

give them long healthy lives in adoptive homes. This study is the work of a large group of very dedicated, hard-working people and I would like to thank many people that are in these acknowledgements, here. I thank you all so much. It's been wonderful working with each and every one of you.

I also want to acknowledge, my husband was saying to me the other day, that I am really standing on the shoulders of giants. These wonderful women have all laid the foundation for the Maddie's<sup>®</sup> Purdue FIV study and have contributed to it. Dr. Jules Beatty, Dr. Cynda Crawford, Dr. Margaret Hosie from the University of Glasgow and of course, Dr. Julie Levy. Thank you to these giants in the field who paved the way for me to come along with the Maddie's<sup>®</sup> Purdue FIV study. Here are a couple of useful resources you should be able to download. These full articles [are] from these links. I think we are ready for questions. Wrigley is going to lead us in. There is a beautiful photo of a beautiful cat. Wrigley has FIV and she is enrolled in Maddie's<sup>®</sup> Purdue FIV study.

*Lynne Fridley:* Oh, Wrigley looks like my cat, Itty Bitty Kitty.

*Dr. Annette Litster:* Oh lovely.

*Lynne Fridley:* She's beautiful. The resources that Dr. Litster just mentioned are also in your resources, so if you didn't get to write them down, don't worry; they're there.

*[End of Audio]*