{Pre-Audio transcript, Steve Dale, Master of Ceremonies}: Dr. Niels Pedersen joined the faculty of the School of Veterinary Medicine at UC-Davis in 1972. He spent the first 25 years in clinics, small animal internal medicine, specialty medicine with a special interest in infectious diseases of cats and dogs. Teaching now for 30 years, he has been active in research throughout his career. More that 40 publications in peer-reviewed journals and 40 publications related to FIP. He has had a special interest in feline infectious peritonitis since 1964. Some of us might not be that old. He has received numerous national and international honors. Supported research, particularly with cats. He has written 2 classic textbooks. I have often introduced him as having written the book on feline infectious disease. This guy literally wrote the book on infectious disease in cats. Dr. Pedersen was the first recipient of the CFA's annual award for contributions to the health of cats, and remains active in consultations. His work with SOCK FIP, he is still working to TKO FIP. Please help me welcome Dr. Niels Pedersen.}

Dr. Niels Pedersen: Thank you. No coat but I have a tie. It's quite an accomplishment. So okay, I'm going to have to reveal a little of what we've done with some of the things that's been said. Maybe between Al and myself, we've made a little bit clearer because FIP is the most complicated disease that I had personally studied. Believe me, I've studied FIV, I've studied FeLV, I've studied calicivirus, I've studied herpes virus. You name it I've studied it. But this is the first disease, the start of the study and it's the last one that I'm going to study. I've told myself, I will not retire until I have some solution to this disease. But I have to tell you that every time that I thought that I've had it figured out, it's thrown me a curve ball. So I was... what I called a worthy opponent. Unlike FELV and FIV which were as predictable, as predictable, this disease is totally unpredictable. Now, I'll probably bring some of that out. Okay. So, it's already been mentioned that this is one of the most common infections causes of death in younger cats, 1 to 300 in the nationwide survey of cat vets are responsible. Mortality is between two and five percent and seen those figures in shelter adopted kittens and purebred kittens as well. And mortality, I would like to think that there… mortality is virtually 100% with caveat once the clinical signs are appearing, okay.

So, I will tell you there are apparently a lot of cats that do get the infection but never get sick, okay, or at least apparently get sick. So we will talk about that. And the other thing that I want you to know is that the death can occur over weeks, months and even years now. So if I have to say that this disease is like something, it's most like tuberculosis and that many of these cats get it at a very young age and they can have it in their bodies for all of their life. And then have it pop out when they're 10, 12, 14 years of age or some stress or something that occurs at some point in life that it pops out. So this virus, once it gets in to the tissues in the body, it can hang out there for long periods of time just like tuberculosis. Many of us have TB or mycobacteria in our lymph nodes tucked away here and there and many of us are immune because we have that little infection and for most of us, that's a lifetime infection but you don't realize that. As we get all get older and our resistance goes down, we have other diseases that the rate of tuberculosis goes back up. Most of that TB is a part of when we're younger in life. So, this is something that we need to think about.

I will talk about disease in Burmese and Birman cats where virtually all the FIP is of the dry form and these cats with dry FIP can live for a long time and we have seen a

number of cats that are five to seven years of age where they go through that terminal slide that Al was talking about. And if you look back at those histories, there's no doubt that they have been sickly for all of their life, okay, and finally the virus gets ahead of them. I don't need to tell you that this is a tremendous emotional as well as financial drain on people. So we have the different groups of cats and we are working with the SF SPCA on the disease in shelter cats… and where did these slides comes from, whoever recognizes these, I didn't steal it, I borrowed it from Leslie Lyons for a bit, borrowed it from somebody else. So if you see this and it's your picture, you come up and put a name on it for me and we will talk begin about Birmans towards the end. And there are other places that I'd like to mention with too many young cats and these are -- especially kitten rescues. Kitten rescues have become very popular with the no-kill movement which basically takes cats away from the shelters and puts them out in various places all over the place and many of these kitten rescues are perfectly good. They do a good job of holding animals until moms are going to be adopted or they can move them back into the, into the shelters for adoption.
But many of these kitten rescues are basically hoarders. They're excuses for people that are hoarders to legitimize a serious obsessive-compulsive disorder. So when we look at these areas, these are important areas that we need to consider. We also recognize that FIP or coronavirus infection does occur in kittens from the field as well. At least in the Sacramento SPCA, 40% of the kittens that are relinquished at the SPCA are already exposed to coronavirus. So this is a very common infection out in the wild.

Now, let's just take some historical perspectives and the first description of this disease was in 1963 by Jean Holzworth, who I consider the greatest feline medicine person that ever lived and probably ever will live and that she described it in Cornell Veterinarian and it… this disease I'd like to say is not, it is a disease that is of relative recent appearance. It has come out about in the 50s; it appeared in cats for the first time. So this did not exist a hundred years ago or thousands of years, or 10,000 years ago or 10,000 years ago like FeLV and FIV. So relatively new infection which would explain in part why the mortality is so high. It's because these cats have not a lot of time to evolve a protective mechanism as they've have for FeLV and FIV and a lot of the other infections that we have in cats.

Okay. So the viral etiology is by Wolf and Griesemer from Ohio State, again, a great home for veterinary pathologist of that era and even today. And this is just a picture. So pictures with that first article, again, you see the fluid in the abdomen, you see the peritonitis… this doesn't show it very well. But I don't want it to be too graphic, I have some very graphic pictures but it's not really good to show those graphic pictures at meal-time but anyway, this is Jean Holzworth when she was young, how many of you actually knew Jean Holzworth? And not very many out here. Jean was the greatest lady that I've known. And here she is in her younger days and she knew more about cat diseases when nobody knew about cat diseases. This is me, obviously when I first started out, maybe I had comparable time in our two careers and this was the last picture that I had, the pleasure of having with Jean and she died about two years after this picture was taken. So I decide to mention some of the pioneers in the field and Jean Holzworth is certainly one of the great pioneers. Okay. Let's just talk about where FIP comes from. There's been a lot of controversy over the last few years and that controversy has been really quite straightened out. So I can tell you, the story I'm telling you is the truth, okay? This is the medical explanation for where

FIP comes from based on our knowledge… from our lab and from Utrecht, the Utrecht group, who I consider to be one of the outstanding FIP research groups in the world.

Okay. So, FIP results from a mutant form of a virus called feline enteric coronavirus. A lot of people use the term feline coronavirus. The problem with the term, feline coronavirus, is that it's not correct because this virus, this FIP virus, the enteric coronavirus were named before that terminology came along. And the term feline coronavirus is… it's generic for any coronavirus of cats, okay? And the virus that causes the enteritis in cats is a coronavirus and the mutant form that causes FIP also is a coronavirus. So I prefer to use the term feline enteric coronavirus than FIP virus, because then you can understand a little bit more about where these viruses come from and what they do. Now, feline enteric coronavirus is ubiquitous to all multi-cat environments, indoors and outdoors throughout the world.
There are two strains of the virus, strain one which is called cat-light is 95% or more of the strains in Europe and the United States. In Asia, dog-like strains are about 20% of the isolates. So we have two basically, two basic serotypes of enteric coronavirus.

And, this virus is spread by the fecal-oral route. And I don't need to tell you that there is no beast known, other than… well, more at to transmit agents by the fecal-oral route than cats, okay? Especially when you put them in multi-cat environments because you put litter boxes in there and they share those litter boxes. Litter boxes throw up dust, it gets on your clothes, and it's all over the place. And then it drops off in the environment and anything that gets in the environment, you know, goes on the cat's fur, anything that gets on the cat's fur goes into the cat's mouth. So, this is a normal thing. So, when you have an environment where you start allowing cats to use litter boxes, then you really up the infection rate. And now I mention that in their area, in Tennessee, which is more rural than our area, that the infection rate… the feral cats are the one… or the outdoor cats, was relatively low, probably lower than 40% which is the Sacramento area, the urban area. And that's again just as Al says, because cats go out there burying their feces. And the young are usually kept around their mother in the same territory until after they're weaned. And so, their contact with other cats… another cat feces is fairly limited. So, when you bring them into a shelter within a week, that 40% infection rate goes up virtually to 100%. So within a week's time in a shelter, that infection rate goes up. Now, what about catteries? You guys can… a lot of you can say, "My cattery is free of coronavirus, or free of FIP." I have never tested a cattery that has more than six cats that raises more than several litters, that goes to shows, that's swapped kittens back and forth that hasn't had enteric coronavirus, and I've never, never saw… I've never seen that cattery. So, they may insist out there, I don't doubt that they do, but those of you that feel that you don't have FIP in your cattery, you may well not have FIP, but you probably have enteric coronavirus. Especially if you take the young cats from other sources, you go to shows and that type of thing.

Okay, spread by fecal-oral route… primary infection usually occurs around nine weeks of age. It's almost imaginable somewhere around nine weeks is when they first start shedding the virus in their stool after the primary infection. And the primary infection is either non-apparent. Mostly it's clinically silent. You don't see anything… or you might have a mild diarrhea, sometimes with vomiting for a day, diarrhea for two days, nothing serious, and it's gone. Usually you see nothing. So

then after they recover, they shed this virus in their feces for weeks, months, and sometimes years as I'll show you. And even after they recover from this infection, most of these guys can be reinfected if they're exposed again to the… even the same strain that infected them the first time, so they lose their resistance when they lose the infection, many times. So they could be easily reinfected.

Okay, so what are some of the strange things that go on here? FIP viruses and FECVs are not too different species of viruses. This is -- this has come out by a paper by Brown et al a couple of years ago, where they claim that these two virus… these were two different species of viruses that were being passed independently of each other in the environment. I can tell you that the work of -- our work and the work of Utrecht come out and refuted that fairly strongly. Now, FIPs always arise from the infected strain of FECV, so if you do a genetic mapping, you sequence the FIP virus that comes from a cattery that has enteric coronavirus in it, that FIP virus will be virtually identical to the enteric virus that's in that particular cattery. For another cattery that has another genetic type, those FIPs in that cattery will arise from that genetic type.

So you can literally track by genetics a strain of FIP back to its source, we can do that. You can track it, if you want to spend enough money, you can find out exactly where it all started just by doing a genetic mapping. Because the genome of these viruses is just like our genome. It has all these little differences in it that are… make each of us individuals, okay? So we can tell the individual strains of viruses very easy.

The other thing is that… excuse me….. the remote is hair-triggered. Okay, FIPs arise by simple mutations. Now, from the enteric virus, so during… and I'll show you this in more detail. During this primary replication in the gut of this enteric virus, this particular class of viruses has this what we call RNA viruses, in that the way they mutate or that they replicate themselves, they're very error-prone, so they're always producing variants, mutants, occurring all the time. Continuously they're mutating, all the time mutating. And you know, we've heard about mutation of viruses when we talk about influenza and HIV strains and all sorts of things. We know that these… that viruses are always mutating.

And so, during this primary infection, there's… these mutations occur. Now, if the mutation occurs in a certain gene of the virus, a certain area of the virus that causes the virus to change where it likes to grow. Now, as I'll show you, the enteric virus likes to grow in the specific cells of the epithelium in the intestine. Now, if it mutates in a certain way, that mutant virus then goes into the body and grows not… no longer in the intestinal epithelium, but in what we call macrophages, which, I don't know if you know what a macrophage is, but it's a cell that gobbles up things. It is the most primitive cell in the immune system. It is the basic cell of the immune system. It's a cell that cleans up debris, gobbles up things, and it's the first thing that initiates the immune response.

So here then, if this mutation occurs, we have a virus that is just a gut virus, that doesn't do anything. And if a certain mutation occurs and it goes into the body, infects another cell type altogether, which at the basis of the entire immune system, the macrophage. And macrophages wander all over the body, so this just spreads the virus all over, and then the immune response against those infected macrophages is what causes the disease that you know of, of FIP. Now, what are macrophage-loving

pathogens? Tuberculosis, mycobacteria, loves to grow in macrophages. HIV loves to grow in macrophages. The deep mycotic infections loved to grow in macrophages. So there are a lot of infections that love to grow in macrophages.

Okay, so… and once this mutation occurs, as I said, it no longer is able of replicating in the intestine, and it's found only internally in the diseased tissues, those tissues of that cats that have FIP. And cats -- and this is important to remember, cats with FIP do not transmit FIP virus to other cats. So, a cat that has FIP does not infect other cats, it isn't cat-to-cat transmission. The only way another cat can get FIP is to start the cycle all over again, start with enteric coronavirus, mutate, have a mutation, and then there's other factors that kind of come into plays that we'll or I'll talk about in a little bit.

Okay, what is enteric coronavirus? So this is… if you don't… you got to understand the basic virus that is that's out there that's ubiquitous, that's everywhere. And here it is, this is the enemy, and it is called a coronavirus because it has its little projections on the surface which look like crowns, corona means the corona… the crown of the sun, the crown, you know, that corona is a very common term and very appropriate for this particular group of viruses.

Now, this is a just a little cartoon showing you that these are the intestinal villi. Remember your the intestines are lined by little fingers, right. Little finger-like projections which is surface area, and right at the tip of your finger is what you call the mature epithelium. That's where all the absorption of fluids and the nutrients and so forth, occur, right at the tips, and if you, this virus, this enteric virus has a trophism extremely, just for that cell type. In fact, no enteric coronavirus that has ever been grown in tissue culture, because you can't replicate this specific cell, mature cell type in tissue culture.

Okay, here is what we call fluorescent antibody staining. So the green is where we see virus, and here's one of those fingers, and the finger goes down here like this and this is the tip of the finger where the mature epithelium is, and you see there's where the virus is. It just likes that one little cell right on the tip of the intestinal epithelium. Okay, and if you look at what happens after the cat is infected, I'll show you three courses.

So the blue, don't forget the… just forget the value. So this means that after they are infected, they start shedding. So the blue virus, you can see very high levels of virus. That's 10^{15} particles per part of the milligram. So it's like unbelievable how many particles come out in the feces of these cats. It's like; it's unbelievable when you talk about billions of viral particles in just a little bit feces. So here they're shedding, and then this cat stopped shedding after a few weeks, and it recovers, and I noticed that the antibody titer goes up and it goes up to about 1 to 400. And usually if you have a titer around 1 to 400 and it is accurately done, in the cat, that usually means shedding enteric coronavirus for sure, okay. And then you see that antibody titer disappears as the infection clears, okay, and so that will go down very low, and then they'll become… a lot lose their immunity and they could be reinfected again.

So titers do have some value if you have other information to go with it, okay. So if you were to do, if you were to have a small cattery of let's say six or seven older cats

and they all had titers of 1 to 25 and low, you probably don't have any shedders. If you have a lot of cats in your cattery and a lot of them are shedders or have titers up around 1 to 400 or 1 to 100, you got it in your cattery even though you will not need to measure the virus, but there are some really neat cheap tests, relatively cheap, that will measure fecal virus shedding. It's not as helpful as you think when you figure that in your catteries up to 80% of your cats are shedding at any given time. So it gives you… it doesn't give you much helpful information because you could guess already that if you have a large cattery and you have a lot of young cats, a lot of kittens, then you probably have 60-80% or more of your cats shedding. You can just guess that without spending any money.

Okay, here is another cat that's shedding persistently for a long period of time. And then they can shed for many months or even years, you notice that as long as they continue to be infected or shed, that titer will stay up around 1 to 400, 1 to 100, 1 to 400. So the infection keeps stimulating the immunity. The infection that goes away, then the antibody drops down. And here's one that lost the infection very early, titer went up, titer went down, then it got reinfected. And then reinfection looks exactly like primary infection. So in some cases with… some people have asked, "I haven't had a cat in my household for years. I have, I have one old cat that's nine years old, hasn't had any other exposure to cats and then six months ago or eight months ago, I got a young cat because I figured he needed a mate… a partner." Cats, you should never second guess whether a cat wants a mate or not, you know. That's a… I have two cats that are unrelated and they're the most loving cats that absolutely adore each other, but then my kids have each had two cats and all three of those homes the two cats hate each other. So it's all in a draw.

So anyway, never… then in the situation, the older cat will develop FIP. And so then they'll say "Where did it come from? How did they get FIP," …you know. Well, there are plenty of sources but the one source is probably that younger cat that came in. It got reinfected again, this type of immune virus occurred and we're off and running.

Okay, so what is FIP or what is FIPV, FIP virus? Okay, the FIP virus as I said is greater than 98% related to the same virus that's found in the feces of those individuals that have died of FIP or dying of FIP and litter mates and other healthy cats in the same environment. Now not greater than 98% is very related I tell you that. Genetically that's a very strong relationship. And I've also mentioned that FIP is a relatively new infection in cats against which they have very little natural resistance. And you can tell natural resistance. The wet form of the disease is the cats that are not being part of any immune response at all. So they are the least immune-responsive of them all. The cats that have dry FIP are mounting a partial immune response, so that's why it's granulomatous and it's spread out as type course and everything, and we know that in the history of FIP, most of the FIP in the past was wet. Now we're seeing progressively more dry FIP in many of our cats and in some breeds like the Burmese and the Birmans, most of the FIP is now dry, indicating that there is an evolution of resistance as time goes on in these cats. And so at the end, genetics are important and I'll talk about that a little bit more.

Okay, so here we have the cartoon where we have the little viruses or… and then we have just black virus… this are mutant viruses that have the mutation that causes FIP,

and these mutant viruses can escape from the bowel because they no longer can infect these cells but now they could gain the ability to infect these macrophages which then take them all over the place. And now, because they're macrophage pathogens, the disease that they cause is entirely different than the initial disease. So here you have two closely related viruses causing entirely different diseases. Where have you heard that story before, with influenza? Different strains much more virulent than others, the SARS coronavirus where we had virus that almost went from civet cats into humans and almost made it. Scared the hell out of us, didn't it? That killed a few hundred people; it didn't quite adapt itself enough to survive, almost did it. Maybe the next time it will, so these viruses are doing this to us all the time.

Okay, so this is to tell you that cats have a very short bowel, okay, maybe not that short but anyway… so these cats have had this macrophage trophic virus, they will often go ahead and continue to shed enteric virus from their stool, but this virus here that is in these macrophages is not shed to the outside of the body. It's all in the body and the lesions, so the only infection that this cat can cause another cat is another enteric virus infection. And if you look at the fluorescent antibody staining of the lesion of the cat that has wet FIP in this case, and this is a whole cluster of macrophages, within one of these inflamed lesions and you can see how bright green they are. They are just chockfull of virus. Every macrophage is just stuff full of virus. This is a characteristic of feline infectious peritonitis.

Okay, I'm not going to do many graphic pictures, but I do not understand why veterinarians have so much trouble diagnosing it like me, okay. I do not understand it because there are just the two forms. There is the wet form and the dry form and sometimes there is a little intermediate as they can switch from one to another and you can catch them in that transition stage, but people seem to have a hard time making this diagnosis, and like Al said, if you have a young cat from a shelter cattery that has a distended abdomen and has this yellowish, mucinous fluid that contains the right kind of inflammatory cells, high protein… gee, what else is this? What else can we call it? And the problem that we have is that because the diagnosis of FIP as I said, once they become clinically apparent, they're going to die, okay, and I tell you right now, they're going to die. There is no treatment. Okay… that I know of, that has been successful to reverse this thing. Okay, so basically because it's a fatal disease, people especially veterinarians, and especially owners and especially pathologists; do not want to tell you that this is a fatal disease. They say, just as Al says. You get tired of seeing a path report that describes, there's a clinical history just like FIP, lesions that cannot be anything but FIP and then they say, characteristic of FIP, typical FIP. What does that mean? You tell me, does it have FIP? Just tell me.

And so, the problem is that in any of these kinds of diseases where there is a 100% mortality and believe me, owners are just as guilty because owners will push that risk, and is there a chance that it is this, or it is that, toxoplasmosis is one million, you know, is it the mycosis, one in a million, you know, all of these things, and so, they are always grasping for stuff and they are pushing it, and the more they push you, the more diagnostic tests that you ask for, and the problem is that hardly any of those diagnostic tests are 100% correct. And so, even the PCR test maybe only 80%. Immunohistochemistry might be 70-80% depending on what you do. The blood work is not 100%. They are all just little things that help you make the diagnosis, but there is not a single test that's simple, short of taking a biopsy or taking some fluid, and

doing a specific test by a lab that knows what they are doing, which is another problem, okay, to get a decent result back. And then, you know, then there are still veterinarians refusing to believe that antibody titers are not necessarily diagnostic, so they will continue to do the FIP virus serology on a whole bunch of cats. One cat will die of FIP in the cattery. They will test every cat for $30 or $40 a cat, and then they'll get the results back and then they will say, "Well, I don't know what they mean." So then they'll call me up. Well, I didn't order 50 serologies at $50 a piece, you know, and so they wanted a free consult, you know, as far as I never charge for consults, but they want a consultation as to what that test means, well, no veterinarian should ever ask for a test that they do not know how to interpret it.
If the results come back [Applause] if the results come back and they can't interpret it, why the hell did they ask for it in the first place?

Okay, so anyway, so much for my bandwagon, and… okay, so now the other form of FIP is the dry form of FIP and in the wet form you can also get it in the chest cavity as well. The dry form is granulomatous lesions and in 60% of the cats, they are in the abdomen. The main lesion is the mesenteric lymph nodes, the kidneys, hepatic lymph nodes, liver, spleen, and those types of organs. And then it can spread from there to the central nervous system and then, eyes are part of the central nervous system, so usually when they have ocular involvement, as this one cat has uveitis in one eye, which is a fairly typical form. Often will be in the brain and then it can involve the brain and the spinal cord, so you can have the whole spectrum of neurologic signs. ataxia, incoordination, some kind of seizures, a lot of different kinds of clinical signs associated with this neurologic spread. Just some typical lesions.

And again, those are called keratic precipitates which are little accumulations of macrophages out there. Remember, macrophages, again, when the virus likes to grow. And this is a younger… and this is a young cat with uveitis with keratic precipitates, that's like 99% or 98%. But again, don't blame your vets because I have had owners come to me who "The vet said you cat has FIP with 98% certainty," but 98% certainty is still not good enough for those people, so they want me to add the other 2%. And I'll usually look at them and say, "Hey believe your vet," you know, "in this case, your vet is absolutely right." Now it does… it isn't always that case but a lot of times, I'll just say, "Listen, we can't do much better than this." And I used the term with my students calling every little laboratory data piece that points to the direction to the certain disease as being another nail in the diagnostic coffin, okay. This is a human term and it's the coffin, death, okay, so if you get enough nails on that lid, the person in there is dead, okay? And they have whatever, you know, you know what that is, and so, we call that, if you give enough indicators, you can get there without being 100%.

Okay, so risk factors for FIP virus. Okay, the biggest risk factor is you got to be exposed to the enteric coronavirus which is again ubiquitous and largely asymptomatic. You have to have a mutation in that virus. Now, how frequent does that virus mutate to cause an FIP virus? Interestingly, some studies have been done indicating that up to 20% of the cats that are undergoing a primary enteric coronavirus will generate a mutant that can cause FIP. Now, it doesn't too much mathematical thing to know that where there is a difference between the 2% to 5 % that die than 20% that get the mutation, right? So that's the difference between those that have the ability to mount an immune response to this new macrophage trophic pathogen. So

only about one in five cats that get the mutants actually develop the clinical disease that die. The rest of them seem to be able to control it relatively well. So remember I said, the mortality is 100% when they become clinically sick. Okay, so what are some risk factors of the host… let me go back I maybe missed something. Okay, no. Okay, we know that the age of initial exposure plays into this. Now in the shelter in the cattery environment, this initial infection occurs around 9 to 10 weeks of age. This is at a time when the immune system is not fully mature. Remember kittens are not born within a mature immune system. That starts to really… some of it is mature effort, some types of immune system but remember that their ability starts to grow around four weeks and around sixteen weeks it starts to reach adult levels but it still continues to mature on until a year or even four years of age. Like for instance, I told you about the little ringworm. A lot of infection is herpes in a lot of infections of cats. Some of those cats take several years before they get enough immunity to keep those things, you know damped down. So if you deal with older cats or older queens, you're going to have a lot less problems than you do when you deal with young queens, you know, for a lot I can name dozens of diseases where that's the case.

So anyway, so, the fact that this virus in these types of environments, the shelter and the cattery environment occurs at a young age when the immune system is not fully mature, that does I'm sure play a role into it. Stress, any stress especially in cats. Remember, cats show stress in two ways. They defecate, they pee on things they shouldn't, they bite you when you don't expect them to and do things like that. And then the other stress thing is that their resistance needs to all other infectious agents go up. So herpes becomes clinical, their calicivirus becomes clinical, much of these diseases start to become clinical, but in a normal kitten, they are under no stress, they would be not clinical or that they are relatively mild.

Okay. So we have then stresses of all kinds. And I'm not going to… there are stresses of excess ammonia odors, there are the excesses of diet that are too high in energy causing bacterial overgrowth. And we can talk about situations that occur in catteries and shelters that have to do with the environment. Other infections that are occurring at the same time, the herpes and all the other things that are lowering their resistance, so all of these things play into this whole thing. But also we have the FIP as we do with all the infectious diseases. Remember now even with HIV, do you realize that the first human known to ever survive has been seen, and that 16% of humans, especially European are resistant to HIV infection naturally.

So the genetics plays a role and many people can get HIV and live a lifetime and then others get it, they're dead within several months. So you know, there's… immunity does play a role, or the genetics does play a role and when we look at one study in a Persian cattery, we could calculate the heritability to be about 50%, which means that 50% of the incidents of disease can be explained by heritable factors. And the other 50 percent are environmental factors and all these other things. And how important genetic factors are in a random bred, we don't know, we know they're important in purebreds but we don't know in random-breds, they're probably there, they're probably at work, but they may not be as much.

Okay. In conclusion, that is the status of the immune system as the ability to respond rapidly and strongly to this mutation, this mutant virus is key to the outcome. It determines whether they're going to live or die. Now, risk factors for husbandry, we

mentioned that. So, we know that increased incidence of virus carriers and magnitude and duration of fecal shedding are increased. We did a study where we put these cats into shelters and we can tell in the shelter environment that their virus shedding levels went up when they went into the shelter. Those cats that were shedding at the time went into the cat shelters showed more malnutrition, others stressors we talked about before… again, anything that decreases the ability of the immune system to overcome the mutant virus is going to tip the balance from the host to the virus. There are other things too that we need to look into. Early spaying and neutering and all of these other things can tip the balance. Remember I said it's like TB. So you get a cat that got this mutant virus and it's fighting it, and it's kind of successful.
You don't see any clinical signs. And then you do something to stress that animal. You tip its immune balance away from resistance to susceptibility. So you take it and you spay it or you'll do some other procedure, and so forth and so on and you tip that balance away that they can become clinical. That also explains why many cattery people will say, "I don't… I've never had a cat with FIP in my cattery." Yet cats they're given to other people or sold to other people have developed FIP and most of those cats develop that first exposure in the cattery that they originated in. We can track the virus back to those catteries and those places. And you think, well, that person is just fibbing you, you know, they're not telling the truth that they never had FIP in their cattery. If they let that cat, those cats in that cattery, maybe they would never have gotten FIP, but then they take it, they sell it, they ship it across the country. They put it into another shelter or another cattery in that…all of that environment, and again, could tip the balance away and Diane Addie did a study. And I liked Diane a lot because Diane likes these studies with field material. Admittedly, I would use some field material but I also have to use experimental animals as well, and people ask me how I did that. Diane will not use experimental animals. You're limited with what you can prove but it can prove a lot of things. One of the things that she showed was that that it didn't really matter the history of the cattery as far as the FIP incidents did not affect the incidents of FIP in cats that were sold or taken from the, those environments. So she showed that you could have an environment that never had known FIP cases and then will get that at where their kitties went and what happened to them, and you could see that many of them would develop FIP.

Okay. Approaches to FIP prevention. Okay, so how are we going to prevent this? One of the main things that people have talked about is to isolate the pregnant queens prior to parturition, wean kittens as early as possible, remove queens from kittens and raise kittens in isolation. Okay, this is Diane's method of doing this. Now, theoretically this should work good, right? Or well, because the… I told you that they don't get infected until they're about nine weeks of age. Okay. So isolate the queen whether they're shedding or not, pull the kittens off at four weeks of age, or as young as you can, take the queen, remove her from the environment, raise the kittens in isolation and voila, they're free, right? No. Because isolation means full quarantine with facilities that are completely quarantined. You're cleaning and suiting up going in and out of the rooms, you know, because this virus is so easily transmitted. Isolation doesn't mean queen in bedroom A and another queen in bedroom B, you know. That's as hopeless as anything; I'll show you just what we mean by that.

So if you're going to do this, then, I just have to tell you that you need isolation facilities that are far beyond the scope and isolation quarantine techniques, they are far beyond the scope. And here's a study that was done in Switzerland where they,

they early weaned this group of cats and then conventionally raised this group of cats. This is the percentage of the cats that were shedding in their feces and this curve is not statistically different. These people who thought they were doing something… that they were doing absolutely nothing, okay, and so they're doing a lot of effort but wasn't accomplishing anything. And so if you're using this technique, at the very least, you need to test your cats after they're 16 weeks of age, test their feces or test for antibodies. If they're antibody-positive, they've been exposed. If they've got virus in their feces, they've obviously been exposed. And then moreover, once you get your cattery free of enteric coronavirus, what are you going to do with it?
You guys show, you show people, you want to trade cats around, you want to buy cats, you want to send your cat some other place, you want to go to shows. Yeah, you can either… you can get rid of it. Then you can sit there with your cats for the next 20 years in total isolation, you're getting it to work. And maybe, if you do it right. But you're not going to be breeders and showers, I don't think anyway.

Okay. Approaches to FIP. Effective vaccine. There's one vaccine on the market, it's safe, okay? That's all I can say. It's not efficacious but it's safe. Okay. And it is unlikely… it is highly unlikely that there ever will be a vaccine for this virus. Because the truth is, you cannot vaccinate for disease against which the host cannot vaccinate itself in the majority of cases, okay, that's why there'll never be an HIV vaccine. Knock on wood, I hope there will be, but I don't think so. And the treatment of HIV is drugs, antiviral drugs, and will probably continue to be that way. Okay, so I don't think we're going to have an effective vaccine but I wish there would be but I doubt it.

Okay. The bottom line, there is no effective prevention. We can change our breeding practices. We do suggest breed away from affected individuals and bloodlines. If you have toms especially… we made a point that toms that throw kittens, not to use those toms in your breeding and it's not because toms have... it's a sex-linked susceptibility factor. The females have the same resistance and susceptibility factors. It's just that if the females have susceptibility factors and you have resistant toms in there, you won't see much disease, but it's when you have… you put in a susceptible tom in there. Remember toms can breed a lot of things to produce a lot of kittens so their genetic effect is much greater especially if they're passing on a defect. So it's just like any genetic disease. Any simple Mendelian genetic trait. If you keep breeding away from homozygous or having both alleles of the genetic trait, if your toms are always sound you know, and don't carry the gene, you're not going to have a problem for most of those traits unless it's a dominant trait.

Okay. So changes in husbandry practice. I can tell you the most important thing that you can do other than breed away from individuals is, for God sake, reduce the number of cats that you have in your house. You know, be smart breeders. You know, if you have 5 or 6 queens, especially there are older queens, there are proven blood lines, you choose your breedings very close and you're not willi-nilli breeding everything to everything in the hopes of getting something that is going to win at the show. That you do it, thinking. Joan Miller taught me that a long time ago, if you think about your breeding plan, you won't need near as many cats, you won't be producing near as many kittens, they're going to be show winners, you're going to have a better reputation and so forth. And it's the young breeders that end up with too

many cats and can't turn anything down, they can't get rid of anything and pretty soon, you're just in big trouble and so be smart about that.

The bottom line, no effective treatment, no effective antiviral drugs. Now, I have to tell you that it is doable. Now, this virus, these coronaviruses have the same replication mechanism that HIV has. They have an enzyme that converts their RNA to DNA just as HIV. Remember those are above the reverse transcriptase inhibitors in HIV and some of those… and those drugs, "nuke" drugs are being used on hepatitis A and B cases very effectively, okay, which are also RNA viruses and we've actually screened a couple HIV viruses that have antiviral effect against coronaviruses, but the problem is they're just too toxic.
You know, they're also too toxic to the cats themselves but there are literally thousands of drugs sitting in depositories that have been developed by many drug companies with all different prototypes of drugs for HIV and those… if you screen those, you would find so many drugs that could work against this disease. And then from those, you could even fine tune those that will make it a safer and more effective just as what they've done to HIV. What does it cost? It costs millions of dollars… tens of millions of dollars to develop one of those drugs. And moreover, you're not going to cure with these drugs, so you got to do exactly what you do with HIV and that is to treat the disease just as it were diabetes with insulin, all right? You'll never going to get rid of HIV, you're just going to keep the virus levels down.

So if we did have the antiviral drugs, which I think you can, okay, you can do this. Now, with non-specific immune modulators. Dr. Legendre talked about this. polyprenyl immunostimulant is still under evaluation. I'd like to comment on… I will comment on interferon… omega and other interferons. They do not work, okay? The biggest waste of money that anybody can do is to use these human and cat interferons for the treatment of FIP. They do not work. And so basically, that's what I have to say. Antiviral drugs, I mentioned the AIDS… the anti-AIDS drugs can work there.

Genetic approach to FIP prevention now in the future. Okay, avoid bloodlines that… especially, males, not because males carry… just carry, females can too, but that's the most effective way to handle things that may be done in the future as they determine the genetic factors that increase or decrease the susceptibility and then apply them to breeding. Okay, in other words, we think that we can identify genetic markers that will tell you which cats are most susceptible to disease and which are most resistant, that's going to cut the incidence down dramatically if we can do that and we do have… we just had a grant funded to do that. I'll talk about that now.

The reality I'm going to tell you, guys, FIP is not a model for human disease and receives no support from NIH. NIH supports human-related diseases and animal diseases that are related. You can make a weak case that this is a lot like SARS or it's a lot like dengue fever and this… but these are weak cases. You're not going to get much money from NIH and so that means that all of your money for this has to come from private sources and it will be costly. A lot of you think that $5,000 is going to buy you a cure or a cause. Research is extremely expensive and to run a laboratory, a good research program with good research people is going to cost one lab $300,000 to 400,000 a year. Is that right, Al? If you have post docs and all that other stuff, technicians and everything. So you're talking about a lot of money to do that and

funding for FIP research will come largely from private sources. These will be individuals who have lost cats, to organizations and foundations.

And then you say, "How can individuals and private organizations make a difference?" I'm going to tell you about Save Our Cats and Kittens, the original Save Our Cats and Kittens, which had been SOCK it to feline leukemia, which… this organization existed between 1976 and 1992. This organization took itself out of existence because it was so instrumental in basically eliminating FeLV as infectious disease of importance to pet cats. Okay, how did we do that? They raised money. They raised hundreds of thousands of dollars, this organization, over that period of time. All went to Davis. I'm not telling you that you need to send it to Davis, but you need to support people who are doing research. They decided they want us in.
But out of this pain, those simple diagnostic tests that you all use to diagnose FeLV, that you do it in your home, in your labs and all those little snap tests and all that were developed at UC Davis with this money and it was that test and we were also the first lab to show that you could make FEoV vaccines based on whole viruses. A lot of vaccines now are based on whole viruses. Vaccines that we developed are now being used by Intervet and other companies. But to make the long story short, it wasn't the vaccines that cured… that took leukemia out of nature. It was the tests, the rapid ability to test for carriers and to get rid of them, isolate them or get rid of them from the environment and we literally pushed FeLV out.

In 1960s and 70s, early 70s, 30% of the sick cats had FeLV. Now, we hardly ever see it in our cats. It's way out of nature. We beat it out back into nature where it's not an important pathogen. We put it back out of nature. So again, these things can be highly successful, but they take…they have to be targeted and they require support. So SOCK FIP is a volunteer group that's again, working with us. Some of the members of SOCK FIP are here and have a booth out there. They're raising money for research. Right now, we're doing the genetic study as well as the study with SF SPCA, with their financial support and with the support of Morris Animal Foundation, Winn Feline Health and this cat consortium. And I'm not telling you to send your money to Davis. Send your money to where ever it is being used, the Bria Fund (Winn), Diane Addie funds, whoever, Cornell—Dr. Whittaker's, all... find a place that's doing research and give them support. It's going to take a little bit of money to do this. The more researchers that are working on it, the faster this thing is going to get solved.

Okay. So the Cat… my final thing, the Cat Health Network has been created recently where they're producing… these are the groups that are working on that and these are working on these high... what we call high-density genetic arrays. These are 80,000 genetic markers across the whole genome of the cat, which we can use to identify genetic traits within cats.

I just want to end with one last thing. I'm going to tell you about just the Birman breeders of Denmark. Maybe it's my Danish ancestor or my Danish blood. I don't know what, but the people of Denmark have been outstanding to me and they introduced 500 samples from their Birman cats in the last year and a half for me for this genetic study. So I'd like to thank Susanne Wehnert and Anne Sorensen from Denmark and Susan Little and I…

Susan Little and I and Leslie Lyons had the privilege of going to Denmark a few months ago to talk with those people and they're a great bunch. So that's all I have to say. Thank you. I'm sorry if I have gone over time.