

Disease Du Jour Podcast Episode 53 Equine Herpesvirus

Transcript Dr. Gisela Hussey

Kim Brown Welcome to this episode of Disease Du Jour the topic of equine herpesvirus with Gisela Hussey, DVM, MS, PhD, an associate professor in pathobiology and diagnostic investigation at the Michigan State University College of Veterinary Medicine. Dr. Hussey's research focuses is on herpesviral diseases.

I'm Kim Brown publisher of EquiManagement.

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With the outbreak of neurologic herpes in Europe and multiple neurologic, abortogenic and respiratory cases reported in North America, we wanted to bring our listeners an update on equine herpesvirus.

So, Dr. Hussey, why do you think this is happening? Are we getting better at recognizing and testing for equine herpesvirus, or do you think we're actually seeing a global upswing in disease?

Dr. Gisela Hussey So I think that's a good question. I think the answer is probably somewhere in the middle.

I think we are getting better at recognizing it. We are getting better at diagnosing it. Um, herpesviruses have been around for a very long time, and that is true for the equine herpesviruses as well.

Now I think there is the perception that the incidents of neurological disease or EHM, um, has increased in the past decade, but I'm not aware that anybody has done any particular studies in this ... investigating this question, um, in specific.

Um, I do know that, you know, when they are in neurological outbreaks, um, there are multiple labs that tend to sequence these viruses. And, um, I think with that perception comes to the idea that, um, there has been some changes in the, um, circulating strains and that that may contribute to the increased incidents of neurological disease.

But again, it, um, EHM is a multifactorial disease, um, that depends on viral factors as well as host factors and environmental factors. So it's really difficult to truly answer that question.

Kim Brown And we know that most of the cases when they, when they are tested are equine herpesvirus type one, but there are a few reports of EHV type 4 infections.

So how do veterinarians explain the difference to horse owners when they're doing this testing.

Dr. Gisela Hussey So I think that is actually a really important distinction. So EHV-1 and EHV-4 are both, um, members of the same family, the alpha herpesviridae. And, um, they both

cause respiratory disease that really is clinically indistinguishable, um, when you see it in the horse.

Now clearly, if you submit a diagnostic sample, that would give you a diagnosis of whether you're dealing with EHV-1 or EHV-4.

The big distinction between the two is that each before does not really cause a substantial viremia. There is a little bit maybe of EHV-4 viremia, but there isn't really a substantial viremia. And because when we are talking about the pathogenesis of neurological disease or abortions, um, the viremia is really central and getting the virus from the respiratory tract to those sites, we don't really see, um, neurological disease with EHV-4. And we don't see abortions, um, to the same degree as we would with EHV-1 either.

So really, if you have an outbreak or, you know, lots of horses was respiratory disease and it's diagnosed as EHV-4, you would worry much less about neurological disease.

And this is also reflected, um, where in most of our states, um, if you have an EHM outbreak or neurological disease, that is actually a reportable disease, EHV-4 is not a reportable disease.

And so I think the distinction between EHV-1 and EHV-4 is really critical. I think the distinction of whether, um, an EHV-1 strain as a neuropathogenic or an abortogenic strain is certainly interesting from an epidemiological point of view and just, you know, um, doing research on the disease, figuring out what's going on there. Do we have strain changes?

But as far as how you deal with, um, an outbreak or what you do in the barn or what you tell your owners, it would be exactly the same, whether you have a neuropathogenic strain or a non-neuropathogenic strain. But what you tell your owner um, if you have EHV-1 versus EHV-4, if the ... because you could basically tell them if EHV-4 the worry about EHM, um, is really, um, negligible.

Kim Brown Well, and that's a, that's a good distinction that veterinarians should bring up to their owners. That's a good point.

So when you, you were just talking about how veterinarians should concern themselves ... So if they have EHV-1 or EHV-4, what is their level of concern? What should they do depending on what is diagnosed?

Dr. Gisela Hussey Well, again, if it's diagnosed EHV-1 and there are neurological cases, it's a reportable disease. So, um, that would get the state vet involved. I think there would be mandatory quarantine and all of those things. With EHV-4, that is not the case. However, I mean, if you have EHV-4 in the barn, you probably also don't want to spread that to everybody and everywhere.

So in terms of, you know, some biosecurity measures and all of those things, I would still recommend that you stick to those because while you wouldn't worry about neurological disease and horses necessarily dying, you also don't want a whole barn full of horses with respiratory disease. Especially if you have a lot of youngsters, um, there.

Kim Brown And why is that? Why do you say that? Especially if you have a lot of youngsters.

Dr. Gisela Hussey Um, so both EHV-1 and EHV-4 respiratory disease is really common in young horses, but as horses age, they've been infected with the virus, both these viruses establish latency in their hosts. And there is probably regular reactivation.

So they will have some level of immunity that will protect them from the respiratory disease as they get older. So this is why, when we are looking at older populations, we rarely see respiratory disease, but we do see neurological disease to a much higher degree.

So there is an age factor in what disease manifestations we see with EHV-1.

Kim Brown That's very interesting. So why do some horses that get EHV-1 develop neurologic signs and some don't. And I'm sure that you could retire tomorrow if you can answer this question.

Dr. Gisela Hussey Yeah, sure. That is the million-dollar question. And what we do know it is, is that it is a multifactorial disease.

So, you know, there are host factors that, um, determined whether a horse does get EHM or not. There are viral factors. So we all know about the point mutation and the premonorase gene that makes a viral strain more likely to cause neurological disease or less likely to cause neurological disease. Although, as I've mentioned before, both, um, strains can cause neurological disease.

So in terms of what you do was your horses, it'll be the same.

Um, but then of course, you know, the host and environmental factors really are very important too, because even if you have a whole herd of horses infected, let's say it was a highly neuropathic strain of EHV-1, some of these horses will get EHM and some won't get EHM.

Now some of the factors that predispose or make it more likely that a horse gets each and we know, so we know that if you have mares over 20 years of age, they are much, much more likely to come down with EHM. Um, we also know that middle aged horses of certain breeds are more likely to get EHM than others. And there's a few other factors. But, um, you know, what exact immunological mechanisms and, um, all of those fun things, or, you know, other genetic, um, components that are very host specific will predispose horses to each EHM or not. That is, uh, an area of research that I'm actually very interested in and that we are studying, but clearly we don't have, you know, all the answers to that.

And if we had all the answers, then we could do a lot more to prevent EHM. Um, so that's the goal clearly.

Kim Brown And you mentioned this. I had not heard before that there are middle-aged horses of a certain breeds that are more prone to this. Could you elucidate on that? Just a little?

Dr. Gisela Hussey So, yeah, I mean, so what we also know is that ponies, um, don't really get EHM while, you know, if you're talking about warmbloods for example, um, they are more likely to get EHM. And this is just one example. I think there are some studies out there that look specifically into braids. So there clearly are some genetic factors that predispose or are protective, um, from the disease.

But again, The specifics. Yeah, we don't really know. Um, but generally speaking, if you, you know, were to have, you know, a herd of one-year-old horses, um, that become infected with EHV-1, they would be less likely to get EHM than if you have, let's say, um, a group of horses that are between 10 and 20 years of age.

Kim Brown Well, that's a good point to make for our veterinarians. So as they're walking into their clients, they can, they can help them understand the risks better.

Um, so how can veterinarians help protect their patients from disease caused by herpesvirus? And we're talking not just neurologic, but the respiratory, the abortogenic.

Dr. Gisela Hussey So I would say, um, again, you know, there are vaccines out there and I know that that's always a big question of interest. And these vaccines, um, they do have some efficacy for preventing the respiratory disease. I mean, again, as horses age, they are also less likely to get respiratory disease. So vaccines are typically fairly successful at inducing immunity that can protect from respiratory disease. There are also some vaccines that, um, are marketed for, um, at least reducing abortion, but none of the vaccines can prevent EHM.

So, you know, if you have a big group of horses that are, let's say, less than five years of age, um, where you are a little bit more worried about the respiratory disease, or if you are running a big breeding operation, or there are horses that travel a lot to shows, um, you know, or there's a lot of traffic in, in trafficking, in and out of the premises.

That's where the AAP guidelines would recommend vaccination. And I, you know, always sort of stick with that.

And I think, you know, again, just in terms of trying to reduce the total virus that's replicating in the herd and, you know, was that reducing the amount of virus that there to infect horses? There is certainly a value in vaccination. But I do think because vaccination really doesn't prevent EHM, biosecurity in my opinion, is at this point even more important.

And that really just means common sense.

So, you know, when you're introducing new horses into a herd, which is a stressful situation for them, you want to make sure you're quarantine them. Um, and you maybe monitor their temperature twice daily. If you go to a horse show, you know, you don't share what a buckets or a feeding, um, trays or things like that. You try and stay away from horses that are not, um, you know, horses that your horse is commonly exposed to.

You know, anything that you touch, um, could carry the virus that you could then bring back to your horse. You want to make sure you wash your hands regularly. It's really common sense.

And you don't necessarily, house them all together in close quarters with bad ventilation.

So, you know, when we are talking about viruses, you know, we all very aware of how to prevent a COVID, you know, it's, um, it's kind of very similar in many ways, except for that clearly we are not, you know, putting little masks on all our horses these days.

But I would say that's general, just common sense, um, measures that I would take, clearly if you have an outbreak, then we are talking more about, you know, increased, um, you know, physical exams every day, taking daily temperatures. Um, if you are in an outbreak situation, you may want to, um, do some diagnostics where you collect nasal swabs and blood for testing or viraemia that you then submit to a diagnostic lab, um, and a lot of those sort of things.

But on a day-to-day base, you have to be, um, you know, aware that these viruses are around. Most horses have been infected with the virus, they are latently infected. So, you know, just use common sense, I would say, and use vaccinations, um, according to AAEP guidelines in many ways in specific risks groups where it's indicated.

But don't vaccinate your horses and think that they are now wonderfully protected and you all good and don't need to worry about anything else anymore.

Kim Brown Yeah. You had mentioned earlier that depending on whether you're running a breeding farm or you have a lot of young horses, or you've got horses that are traveling, that there are different vaccines that are marketed for those particular purposes. Can you explain to the veterinarians maybe in a way they can help their owners understand why there are different vaccines for those and how they work?

Dr. Gisela Hussey So for one, not all vaccines work equally for prevention of abortion. So if you have a breeding operation, you probably want to pick one that's marketed for that particular purpose. And then on the other hand, you know, pregnancy, um, does present a time in the horse's life where the immune system is, I want to say altered because people always talk about pregnancy as this, you know, highly immunocompromised state, but that is not entirely true like that too. It really depends on what trimester the horse is and other things. However, because there is the risk of immunocompromise, we don't really recommend the use of modified live vaccines in, um, pregnant horses.

And a modified live vaccine that's out there, um, on the market, which is Rhinomune, is actually not licensed for prevention of abortion anyway. So that is a vaccine that's used for prevention of respiratory disease, mostly in young horses.

In my opinion, there are advantages to using modified live vaccines because you're really dealing with the whole virus that's just attenuated in many ways. But of course there's also risks associated.

And interestingly enough, when we look at the inactivated vaccines that are commonly used, which are Prodigy and Pneumabort, Provenza, there's a few others. Um, they've actually shown to work better at reducing viremia and, um, are, you know, Pneumabort and Prodigy are the ones that are licensed for prevention or at least reducing abortion.

So those would be the ones that you use in a pregnant mare or in a breeding operation in many ways.

And, you know, they have adjuvants that stimulate the immune response specifically. And so that's, in my opinion, probably why they may be more geared towards developing, not just an antibody response, but also cellular immunity, which is really important, and the protection from the secondary disease manifestations of EHV-1.

Kim Brown Right. Okay. So now we're going to ask the other million-dollar question. So why do you think that manufacturers, why have researchers not been able to create an anti-neurologic vaccine against equine herpesvirus?

[musical intro to commercial break. Music plays during commercial]

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[music fades out after commercial ends]

Dr. Gisela Hussey So, I mean, so, you know, let's take a step back here and let's look at herpesvirus vaccines in general. They are notoriously really difficult viruses to develop vaccines for, and, you know, the two main reasons for that would be because they do establish latency in their hosts. And that happens usually at a very early age. They also are known to have many viral proteins that function as immunomodulatory or immunosuppressive proteins. So they basically directly work against the immune system. So that makes it really tricky to develop good vaccines that can get around that.

Now, the other thing that's unique to EHV-1 is that this is a virus that goes from the respiratory tract in individual, um, you know, blood cells and establishes viraemia there and sort of hides out in these cells and that's how it gets transported to the spinal cord vascular endothelium. Um, so that's the blood cells up the spinal cord. And then you get, you know, infection of those cells and, you know, um, the neurological disease. And you get, you know, um, an inflammatory and immune response at the spinal cord to that all contribute to the pathological, um, image that we see.

And so there is this unique feature off EHV-1 and the viremia that really gives the virus an ideal way to hide out and to modulate. Because again, we got to remember these blood cells. Those are the cells that really mount the immune system too. So the virus can hide out

in this location to get to the secondary sites, but it also can really alter the, um, induction of immunity.

And then on top of it, and this is sort of, you know, more what I study when I do my research too. I think for me, it's really intriguing that, um, what happens early on at the respiratory tract seems to have a big effect on the induction of immunity that we see downstream. And in my opinion, also on whether we EHM or not.

Now, those are not, you know, usually we don't have the numbers to really make this claim, but it's certainly something that I've observed many times.

And so, you know, we've recently actually had a study where we compared old horses and youngsters in terms of what clinical disease we saw in them following, you know, infection with a neuropathogenic strain of EHV-1. And then of course, we also wanted to study the immune system, that immunological responses that went along with it.

And what I found fascinating, you know, was the same virus, exact viral strain, same viral strain in the youngsters, which were one to two years old. Um, all of the horses had significant respiratory disease accompanied by fever, but only one of them had a very mild form of neurological disease.

Now in the old mares, which were all 17 years old or older, none of the horses had any respiratory disease, but all of them had some level of neurological disease and seven out of 10 actually had significant, um, you know, a neurological disease that resulted in, um, euthanasia.

So there definitely is this, um, you know, discrepancy between how much respiratory disease we see and the risk for, um, the EHM I think, and I think that is a very interesting, um, phenomenon and one that's very worthwhile looking into further.

Kim Brown That is. Has that been published?

Dr. Gisela Hussey Um, the, some of that has been published. Some of that we're in the process of publishing.

Kim Brown Okay. Well, we look forward to reading that and, and, uh, for our listening audience in the article on EquiManagement.com, we'll, uh, talk to Dr. Hussey and see if we can get a link back to any of the published research so that you can go back and read that cause that. I want to go read that. That sounds very interesting.

Um, so. There have also been some questions out in the public that vaccinated horses might be at higher risk for neurologic disease. What are your comments on that?

Dr. Gisela Hussey Well, I would say I would be cautious, um, because you know, there are studies out, well, there are some reports out there that certainly indicate that; there are also some reports out there that sort of say, that's not true.

And I have yet, um, to find a study that inconclusive or conclusively actually affirms that. So well, while there may be some truth to it, I also think it may depend on what type of

antibody is in use. Um, you know, there's different subclasses of antibody and all of that, but, um, I would be very cautious with this claim.

Um, it's it's a difficult one to really answer because yeah, there may be some truth to it, but I'm not convinced. So not quite sure what to say. I mean, I would say, you know, if, as I'm studying this virus and trying to learn more about the immune system and what all goes on, um, it's certainly always something that's in the back of my mind, and I wouldn't just dismiss these reports either because there are certain days probably you know, some information in there, but what it exactly means and what the mechanism is, or, you know, if the statement that vaccination increases each EHM is true, that I would be highly doubtful of.

Kim Brown Yeah. And some research you had just mentioned may lead people to look at those horses a different way based on age or exposure and, and yeah, so that, that's a good point. Thank you for clarifying that point.

Dr. Gisela Hussey And there are so many confounding factors too. You know, and also when, when I was just talking about, so, you know, I'm by heart, probably more of an immunologist than I'm a hardcore virologis. And what we do know is, you know, there is the innate, um, arm of the immune response, which is really immediate early on, and then there's the adaptive arm of the immune response, but the two, of course, are linked.

So what type of early, you know, in the first few hours, first 24 to 48 hours, what type of immune response you get early on at the respiratory track, will really determine the type of adaptive immune response. Meaning is it more cellular or cell-mediated? Is it more antibody mediated immune response you get. So really, you know, if you don't have any or very little replication, uh, at the respiratory track, no respiratory disease, then maybe that's going to alter the immune response that we'll see, um, you know, down the road too.

And this is the same as the vaccination. Maybe depending on what vaccine you use or how you use it. It might alter, you know, the type of immune response that is induced. So you can't just have a blanket statement where you say, Oh, all vaccination predisposes horses to EHM. I think that that would be a disservice.

So it's much more difficult and differentiated really than that.

Kim Brown Yeah. So I guess for, for veterinarians, it's still let's follow AAEP guidelines. Let's protect them, watch them, biosecurity. So, I mean, just the logical things that we can help with our, our clients.

Dr. Gisela Hussey Exactly.

Kim Brown I'm going to go off on a little bit of a tangent here and just to be perfectly clear, we have a Merck Animal Health is our sponsor for this. So, um, but I wanted to ask you, because I had become aware that you have done some research recently looking at the modified live equine influenza vaccine, Flu Avert, how it might protect a horse against equine herpesvirus infection. So, what's going on there.

Dr. Gisela Hussey So, I mean, this actually is a perfect follow-up question on what I just talked about. You know, clearly, um, you know, so there are some historical it's that horses that are vaccinated with this vaccine, you know, might be, tend to be better protected from EHV-1 as well. But those are sort of more, you know, word of mouth reports.

But the whole idea behind this really is that if you use another virus vaccine, respiratory virus, um, that may not suppress the immune system or induction of immunity the same way herpesviruses do. So equine flu would be a perfect example here. And you use a modified live vaccine that is able to really stimulate strong, early innate immune responses at the respiratory tract, that that actually might be beneficial for guiding or inducing the adaptive immunity to EHV-1.

Now, I mean, clearly, um, if you just give the flu vaccine, you can't expect to come back three months later and have great protection from herpesvirus, you know, unless you vaccinate against that as well.

And we haven't done any studies where we've, you know, sorta kind of done, you know, the vaccination with Flu Avert at the same time as we vaccinate with, um, let's say Prodigy, if we are talking about, um, Merck, and use it, so to speak, as an adjuvant to guide the immune system.

But we've done some preliminary studies and these are in vitro studies where we've just looked at the effect of inducing, you know, early cytokine and interferons and chemokine responses in respiratory epithelial cells and would that reduce viral infection with EHV-1 in these respiratory cells.

We did find that, yes, that is true, because the Flu Avert does stimulate, you know, cytokine and chemokine responses, interferons, and those are typically beneficial for prevention of EHV-1 as well.

So the value of Flu Avert, um, for protection from EHV-1 is likely by inducing strong innate immune responses.

Kim Brown Which goes right along with the research you talked about earlier that the horses that got the stronger respiratory response early on seemed to not develop the neurologic disease.

Dr. Gisela Hussey Right. And, you know, and when you are thinking, and this is sort of more as, um, you know, how could this be applicable to, you know, horses in the field, but, you know, if you're thinking about, oh, you know, I'm going to go and take my horses to a horse show there, you know, there's likely going to be a more stressful situation. There may be more exposed, you know, let's just vaccinate them before we go.

So let's say you give these horses, um, you know, the flu vaccine to boost for, um, you know, a protection from influenza at the same time. If you do it at the right timing, it actually might help against, um, fighting off any EHV-1 that they may be exposed to that show there as well.

So that would be, you know, a practical approach to sort of, you know, killing two birds with one stone.

Kim Brown There's so much, you know, so many, so many places require you to have the flu vaccine on board at a certain time. So hopefully that, that may be something that we can learn more about that would benefit our horses in more than one way.

Dr. Gisela Hussey Right. And I mean, clearly, I'm using a vaccine like Flu Avert, which is an intra-nasal vaccine. It's a modified live vaccine, that's known to stimulate mucosal immunity, um, is what we would want because it's the mucosal immunity that's really important early on. I mean, clearly if you use an inactivated vaccine that you give sub-q IM, that's not going to do the same thing for mucosal immunity.

So the sort of thought behind using Flu Avert was really that this is the vaccine that's known to produce strong antiviral mucosal immunity, which we know would also be really important in the protection from RHV-1.

And, you know, clearly you could also use other immune stimulants, you know, and other things, but in this particular instance, it may be, um, just, you know, an easy and simple thing that could be very useful to do.

Kim Brown Well, I have learned a lot in just these few short minutes we have been talking, and I recognize that you do this on a day-to-day basis. Is there anything else that you would like to share with the veterinarians about equine herpesvirus and perhaps the, the increased concern they're getting from their horse owners at this time when we're just seeing so many more reports of herpes?

Dr. Gisela Hussey Well, I mean, I think the, the main point that, um, I like to make and that I try and get across to all veterinary students as well, who are the future of veterinarians clearly is that, you know, clearly we are trying to develop better vaccines that will protect from EHM as well.

But in the absence of such a vaccine, what we are really left with is good biosecurity. And I really try and bring this home that it is critical to follow those guidelines.

And so really think about, you know, what you're doing with your horses, you know, are you introducing new horses to her and what are sources, um, you know, off, um, infection.

As I said, um, EHV-1 is a virus that, um, is usually transmitted, can be transmitted by aerosol, but it's much more likely to be transmitted by fomites, which means anything that touches you know, and nasal secretions. You know, the, the gear that caretakers used to clean the horse stalls, feeding equipment, stuff like that. You know, use common sense, clean things regularly. Don't just introduce new horses into the herd. Um, you know, good ventilation, um, is also a good idea. And, you know, clearly you do have horses maybe coming into the barn new, but maybe keep them separate from the other horses.

You know, there's really good virus security guidelines out there and use them, stick to them. I mean, I wouldn't, you know, be in a huge panic on a daily base. I mean, these viruses

have been around for a long time. But using common sense and I'm following these guidelines would be prudent in my opinion.

Kim Brown Well, thank you very much, Dr. Hussey, for joining us today. Your, your students are very fortunate to have someone who is not only got an inquisitive mind in the research lab, but has very practical tips. And thank you for sharing those with us this morning.

Dr. Gisela Hussey Happy to do so.

Kim Brown And thank you to our audience for listening to Disease Du Jour today, and a special thanks to our 2021 sponsor Merck Animal Health.

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