

# EQUINE LEPTOSPIROSIS

Current Insights Into Disease Pathogenesis,  
Risk Factors and Prevention



A ROUNDTABLE DISCUSSION

Sponsored by Zoetis

# EQUINE LEPTOSPIROSIS

Current insights into disease pathogenesis, risk factors and prevention

## PARTICIPANTS



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Leptospirosis is an acute and, sometimes, chronic bacterial infection in horses caused by pathogenic spirochetes belonging to *Leptospira interrogans*. Recent serological evidence indicates that equine exposure to *Leptospira* spp. is more prevalent across the nation than previously believed.<sup>1,2</sup> This roundtable discussion explores the current knowledge about equine leptospirosis, including:

- Pathogenesis of infection
- Disease incidence and prevalence
- Risk factors for infection
- Clinical disease syndromes and their economic impact
- Disease prevention

## INTRODUCTION TO EQUINE LEPTOSPIROSIS



**Dr. Jacquelin Boggs:** Can you describe *Leptospira interrogans*, the organism involved in equine leptospirosis?



**Dr. Craig Carter:** It's an obligate aerobe, which means it needs oxygen to grow and replicate. The bacterium is a spiral-shaped organism about 6 to 12 microns in length with a little hook on the end. It likes moist environments; neutral to alkaline pH; and will not survive long in dry environments. It invades the host through direct contact with mucous membranes or through abrasions in the skin, enters the bloodstream and lymphatics, and finally reaches the rest of the body.



**Boggs:** And the portal of exit?



**Carter:** It's generally urine.



**Boggs:** What clinical disease entities are associated with *Leptospira* infection?



**Dr. Thomas Divers:** I've always looked at its association with recurrent uveitis, abortions and renal failure.



**Boggs:** How do these diseases or conditions affect the life, life expectancy and quality of life of a horse?



**Divers:** I think recurrent uveitis is the most debilitating because it's chronic, and there's often a progressive loss of vision.

The renal failure cases are sporadic and often treatable.



**Dr. Terry Blanchard:** It's usually characterized by late-term abortions, sometimes sporadic, and it can recur on the same farm. In rare instances, abortion storms can result in tremendous economic losses to the horse breeder, as well as the farms.



**Dr. Brian Gilger:** Uveitis has a huge impact on the horse population. In a recent study,<sup>3</sup> about 30% of horses that had recurrent uveitis never went back to their previous activities and 30% of those horses didn't perform at the high level they did before. So it's quite a devastating disease.

**Boggs:** So there is both an economic and an emotional impact?

**Blanchard:** That's correct.

**Carter:** I can remember a farm in Texas that I went out on, there were about 30 horses. A young couple was raising these horses, and about seven of them were affected and two or three were already blind. They were just devastated. Unfortunately, the treatment didn't improve the situation much. It was extremely emotional and impactful for the family. But it can be rough on the veterinarian, too, because you feel like you don't have many tools in your toolbox to help the situation. It's a very helpless feeling.

## EQUINE LEPTOSPIROSIS: PATHOGENESIS

- In North America, *Leptospira interrogans* serovar Pomona, or *L. pomona* is the primary pathogen associated with disease in horses.<sup>4</sup>
- Urine from infected animals serves as the source of infection.
- Spirochetes penetrate mucous membranes or abraded skin, enter the bloodstream and can cause horses to become septicemic.
- The organism can colonize in the kidneys and be shed in the urine.
- Infection may lead to equine recurrent uveitis (ERU), abortion or acute renal failure.

## INCIDENCE, PREVALENCE AND SEROVARS

**Boggs:** What is your understanding of the prevalence or incidence of leptospirosis?

**Carter:** We recently did a national survey to look at serological titers to *Leptospira* in horses.<sup>1</sup> Twenty-nine

states participated, as well as Ontario, Canada.<sup>1</sup> The incidence of positive titers for various serovars was pretty evenly distributed across the country geographically without any major statistical difference.<sup>1</sup> The leptospiral organism is out there, it's everywhere and animals and people are at risk.

**Boggs:** What was the seroprevalence in this study?

**Carter:** Our cutoff was a 1:200 titer on microscopic agglutination tests, and for the 1,495 animals in the titer study, the overall seroprevalence was 45%, which is much higher than we expected.<sup>1</sup>

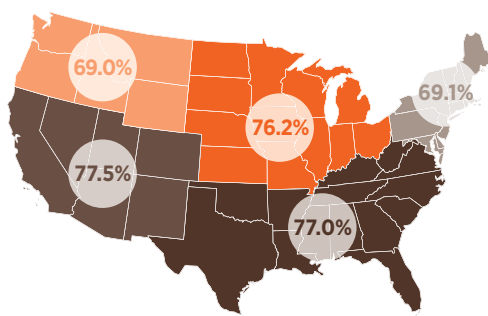
**Boggs:** That means exposure to leptospire may be more prevalent across the United States than what was previously believed.

**Carter:** Yes.

**Blanchard:** Was there a regional distribution for different serovars?

**Carter:** There were some differences, but as far as the overall seroprevalence there really was no geographic difference.

**Boggs:** Zoetis just did a similar study across the United States.<sup>2</sup> We used a 1:100 cutoff, which resulted in a 75% seroprevalence.<sup>2</sup> So our results probably would have been fairly consistent with yours if we had used that 1:200 cutoff.



**Boggs:** Is leptospirosis geographically specific, or can it be found anywhere?

**Carter:** When I speak to practicing veterinarians, there's a perception that leptospirosis is really not a national problem. I think what we're seeing in the epidemiological data is that there's a great likelihood that this is a national problem. So we need to add prevention, management and treatment tools to our toolbox.

**Boggs:** When there's a perception that it's not a national problem, are these veterinarians assuming it's isolated to Kentucky or more of a regional problem?

**Carter:** Sometimes yes, I'll hear that the only place in the country with a lot of leptospirosis is Kentucky. But I think we have tremendous laboratory support for leptospirosis here in the horse capital of the world because of the density and value of horses where we are. Whereas when veterinarians around the country build their differential diagnosis list, I don't think leptospirosis pops up on that list very often. Many regions of the U.S. do not have access to laboratory support to confirm a diagnosis of leptospirosis.

**Divers:** I receive a lot of phone calls from veterinarians having outbreaks of infectious disease that may be associated with *Leptospira*. I assumed that most of the problem was in Kentucky, the Northeast, the Southeast and occasionally Texas. When I saw Dr. Carter's serology data, I was really surprised that many horses were seropositive in parts of the United States that I considered low risk for leptospirosis. Leptospiral infection and seroprevalence may be much higher throughout the country than I had ever realized.

**Boggs:** What is the most clinically relevant *Leptospira* serovar in the horse?

**Carter:** The one that always comes to the top of the list is *Leptospira interrogans* serovar Pomona.

**“The leptospiral organism is out there, it's everywhere and animals and people are at risk.”**

— Dr. Craig Carter



## CLINICAL SIGNS AND DIAGNOSIS

- Clinical signs associated with acute infection are generally nonspecific, such as fever, depression, anorexia and generalized pain.<sup>5</sup>
- Definitive diagnosis usually requires a fourfold rise from baseline titer to convalescent titer on the microscopic agglutination test (MAT).<sup>6</sup>
- A single high titer does not differentiate between exposed and infected animals.<sup>7</sup>
- Because of the localized and chronic nature of ERU, serum titers can be low negative.<sup>4,7</sup>
- With no pathognomonic signs of acute infection and difficulties with diagnostic testing, leptospirosis is likely underdiagnosed in horses.



**Boggs:** In some farms, *Leptospira* is almost endemic on the property. That speaks to the fact that it may be difficult to completely eradicate it from a population or an environment.

**Carter:** That's correct. In our area I know of one farm where it is almost an annual event. Then there are other farms around the area that just don't seem to get hit. So I don't think it's predictable. Exposure to *Leptospira* is an almost ubiquitous risk with the number of species that harbor and shed the organism along with the other domestic animals that can carry it. You know it's the perfect model for a vaccine because, truly, it'd be impossible to prevent exposure to this organism.

**Boggs:** So it would be potentially difficult to identify which farms are going to be at high risk versus which are not?

**Carter:** Correct.

**Boggs:** What are the best ways to manage these risks and help prevent a *Leptospira* infection?

**Carter:** There are some management changes that are helpful, such as not feeding on the ground, and trapping and removing wildlife, but you're never going to totally eliminate the risk.

**Boggs:** Are there different risk factors for uveitis or are they pretty similar?

**Gilger:** No, it's very similar. In my experience, the farms that have had lots of uveitis, some of them have standing water and some of them don't. Some of them have lots of wildlife or livestock nearby. I don't think you can predict which ones are going to have *Leptospira* and which ones will not.

## RISK FACTORS AND DISEASE PREVENTION

**Boggs:** What are the risk factors for horses contracting leptospirosis?


**Carter:** *Leptospira* prefers a moist environment; it seems to thrive in rainfall. In Kentucky, the frequency of abortion increases during the years where we have high rainfall! That always leads to standing water and this is where the organisms congregate. There are also factors such as wildlife in the area. Raccoons, opossums, skunks, red and gray fox, whitetail deer and rodents harbor the organisms.<sup>8</sup> Some of these animals house themselves in the barns and can urinate in the feed or bed down in the hay, and then the feed, grounds and surface water are contaminated. So you have this almost ubiquitous potential for exposure.


**Blanchard:** If you have a mare that aborts in the pasture due to leptospires, the likelihood of other mares being exposed to the organism from the passed placenta and abortus is pretty high, at least in the short term.

**Boggs:** So it's going to be challenging to prevent or completely eliminate some of those risk factors, although with abortion some care and caution may help.

**Blanchard:** Is the clinical progression of the disease more rapid or more severe in certain breeds?

**Gilger:** There are two breeds in which the progression of uveitis is particularly severe. One is the Appaloosa and there's definitely a genetic component to that.<sup>3,6</sup> The second is the Warmblood.<sup>3,6</sup> We used to think that the Warmblood uveitis was mostly a European disease, but it's clearly something we see in the United States also. Keep in mind that all horses are at risk, not just these two breeds.

 **Boggs:** So what would your recommendations be in terms of preventing leptospirosis?

 **Divers:** Attempts should be made to improve feeding procedures such as not feeding hay or grain on the ground, and keeping rodents and wildlife out of the barn. I think it's going to be very difficult to totally prevent exposure, since the serologic survey demonstrates that so many horses in the United States have antibodies against *Leptospira*. So hopefully a vaccine will be helpful in preventing infection.


“I think it's going to be very difficult to totally prevent exposure, since the serologic survey demonstrates that so many horses in the United States have antibodies against *Leptospira*.”


— Dr. Thomas Divers


## RISK FACTORS FOR EQUINE LEPTOSPIROSIS


- Stagnant, slow-moving water and ponds
- Increased rainfall, flooded horse pastures
- Skunks, white-tailed deer, raccoons, opossums or other wildlife sharing horse pastures
- Keeping feed or hay in open containers, feeding horses on the ground
- Horse(s) on the premises diagnosed with ERU, leptospiral-associated abortions or acute renal failure


## LEPTOSPIRAL-ASSOCIATED UVEITIS

 **Boggs:** How familiar do you think equine veterinarians around the country are with uveitis in general?


 **Gilger:** Equine recurrent uveitis is the most common cause for blindness in horses worldwide, so I think most veterinarians are very familiar with this disease.


 **Boggs:** Can you help me define the difference between uveitis and equine recurrent uveitis?

 **Gilger:** Uveitis is just inflammation of the eye and there are lots of different causes for it. What's unique about ERU is the recurrent nature of the uveitis, which means that it occurs over and over again for literally the life of the horse. One of the most common things that actually sets the uveitis off is a leptospiral infection.

 **Boggs:** So *Leptospira* would be one of the key triggers for that cascade of events?

 **Gilger:** Absolutely.

 **Boggs:** Would you say veterinarians across the country are familiar with how closely linked the *Leptospira* organism is with causing uveitis or ERU?

 **Gilger:** Yes, I think that most veterinarians understand that there's a link between *Leptospira* and uveitis. I think what is underrepresented is the percentage of horses that truly have leptospiral-associated chronic uveitis. There have been several recent studies that suggested 40% to 70% of horses get recurrent uveitis from initial infection with *Leptospira*.<sup>9,10</sup> So I think that most veterinarians don't understand the high risk of developing uveitis from leptospiral infections. Especially over the last couple

of years, it's been so wet in the eastern United States. We've had a lot of farms that have had these outbreaks of uveitis that I don't recall seeing before.

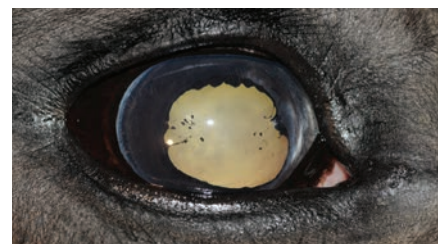







Photo courtesy of Dr. Brian Gilger


 **Boggs:** What types of horses are at risk of uveitis caused by *Leptospira* and why?


 **Gilger:** All breeds are susceptible but certainly two breeds are more prone to develop uveitis: the Appaloosa and the Warmblood breeds.<sup>3,6</sup> Not only are they susceptible to uveitis but they also tend to go blind much faster than other horses.<sup>3,6</sup> So when they get leptospiral-associated uveitis, the prognosis is much worse.


 **Boggs:** What treatment options are available for uveitis from *Leptospira* and what do they cost?

 **Gilger:** Treatment of equine recurrent uveitis is very challenging. Most veterinarians do a very good job of controlling an active bout of uveitis using topical corticosteroids, atropine and systemic nonsteroidal medications. The problem is, those episodes will recur over and over again and each time there's more damage to the eye. Prevention of these recurring episodes is almost impossible. Cyclosporine implants, vitrectomy and other procedures have been done but they're very expensive. Most people spend \$1,000 to \$3,000 for the diagnosis and up to \$5,000 per horse on therapy over two to three months. If you add that up over 10 years of a horse's life, the costs can be considerable.

 **Boggs:** What is the economic impact of leptospiral-associated uveitis?

 **Gilger:** The economic costs are very challenging to get a handle on because there's the cost of treatment and surgery, but also it's the loss of value of the horse. If you've got a horse that's blind in one eye or has multiple recurrent painful episodes, he doesn't perform, you can't show that horse, and it's very difficult to sell the horse. So the economic value of those horses will drop off substantially. Most horses that develop recurrent uveitis won't go back to their previous performance level. You have to either buy a new horse or do different things with that horse, so that impacts the economic value of that horse substantially.

 **Boggs:** Anybody else have any experience with uveitis in terms of the economic or emotional impact?

 **Gilger:** I think one of the shocking things about our most recent study was that of the horses that came into North Carolina State University with the diagnosis of recurrent uveitis, about a third of them were already permanently blind on initial presentation.<sup>3</sup> Even with the best of care from the university, about another 25% of those horses over the course of the next two to three years went blind.<sup>3</sup> So it's a very poor prognosis even with the best of care. Anything we can do to prevent this disease or decrease the incidence and prevalence is going to be fantastic for horse owners. If you look at the fact that between 40% and 70% of recurrent uveitis is caused by *Leptospira*, if we can prevent leptospiral infections, it's going to decrease the prevalence of the disease.<sup>9,10</sup>


“Most horses that develop recurrent uveitis won't go back to their previous performance level. You have to either buy a new horse or do different things with that horse, so that impacts the economic value of that horse substantially.”


— Dr. Brian Gilger


## EQUINE RECURRENT UVEITIS: STATISTICS


- ERU is the most common cause of blindness in horses.<sup>11</sup>
- Leptospire are the most commonly identified etiologic agent in ERU.<sup>3,4,12</sup>
- More than 400,000 horses in the U.S. suffer from leptospiral-associated ERU.<sup>13</sup>
- Leptospiral-associated uveitis is estimated to cost the industry \$561 million from loss in horse value due to visual impairment and blindness.<sup>9,10,13-16</sup>
- Leptospiral-associated uveitis has been estimated to cost U.S. horse owners \$2.1 billion, including the cost of diagnosis, treatment and loss in value of horses that become visually impaired or blind.<sup>3,9,10,13-16</sup>


## LEPTOSPIRAL-ASSOCIATED ABORTION


 **Boggs:** How frequently is the seovar *L. pomona* the cause of abortion?


 **Carter:** It's almost entirely Pomona.<sup>4</sup>


 **Boggs:** How would you determine if a breeding farm should vaccinate their broodmares against leptospirosis?


 **Blanchard:** If you have a confirmed leptospiral abortion then there's a problem on that farm. It's likely to persist because it's probably in the environment and the wildlife, so the source would be there. To me, that would provide justification for using a vaccine.


 **Boggs:** What is the potential economic impact for a breeding farm if they lose a foal to abortion?

 **Blanchard:** It's quite frustrating to the mare owner or the farm owner to have a horse suffer a late-term abortion. It's quite costly in terms of veterinary and maintenance fees. They not only have to carry that foal to term but it has to survive and be salable or trainable for it to be a profitable venture. The University of Kentucky recently did a study using a stochastic model to look at how long it took to pay off a mare bought as a maiden broodmare in the November sale.<sup>17</sup> On average, for the majority of those mares, it took seven years for that mare to become profitable to the owner.<sup>17</sup> So to skip a year because of a late-term abortion is quite costly in terms of lost stud fees and veterinary fees.

 **Boggs:** Dr. Carter, do you want to comment on your serologic study where you actually did some financial analysis in terms of the economic impact of abortion?

 **Carter:** Yes, absolutely. I'm running a diagnostic lab, and we only have the benefit of material that the veterinarians and the farmers bring us. So we call this our “iceberg phenomenon,” and what that means is if we confirm a diagnosis, there is generally X number of diagnoses out in the field that we're missing because we're not seeing that material. It's anywhere from 10% to 50% of the cases we're likely not seeing. We found that over that 20-year period in and around eastern Kentucky, we had 541 confirmed abortions. Again, think of that iceberg phenomenon of what we're missing. Considering only the cases we saw in our laboratory, we estimated over \$100 million in losses in 20 years.<sup>18</sup>


 **Boggs:** A huge economic impact.


 **Carter:** These are rough numbers, based on some high-value animals. But any way you roll this, it adds up to a very high economic cost.


## LEPTOSPIRAL-ASSOCIATED ABORTION: STATISTICS


- The risk for leptospiral-associated abortion is 3.7 times higher during seasons of heavy rainfall.<sup>1,19</sup>
- A season of heavy rainfall can result in losses of up to \$4.2 million in Thoroughbred horses alone.<sup>1,19</sup>
- Because reliable abortion data is only available for breeds representing less than 15% of all U.S. horses, the actual number of leptospiral abortions may be five to 10 times higher.<sup>18</sup>


## A VACCINE SPECIFICALLY FOR HORSES


 **Boggs:** Why is it beneficial to have a vaccine developed specifically for horses instead of using an available cattle vaccine?


 **Divers:** It would be very important for equine practitioners. Cattle vaccines and occasionally swine vaccines have been used in horses, but whenever we do that, as veterinarians, we take a risk. There's always a chance for an adverse effect, and it makes us nervous. To have a *L. pomona*-specific, equine-licensed vaccine would be really important to go forward with vaccinating a larger number of horses for leptospirosis caused by *L. pomona*.


 **Blanchard:** There's really no safety data on using leptospirosis vaccines licensed for use in cattle, for instance, in a horse. It's quite risky. If there are any adverse reactions, it's difficult to defend your vaccine choices.


 **Carter:** A large segment of the horse population is comprised of very valuable animals, so any time we poke something into a muscle or under the skin, we want a high level of confidence that it's going to be not only efficacious but also safe. I think this vaccine will help provide a higher level of that confidence.


 **Boggs:** I hear many of you talking about safety and efficacy. You all have seen our safety and efficacy data that support the vaccine use in horses,\* so does that give you increased confidence versus using some product off-label?


 **Carter:** Yes, absolutely.


 **Boggs:** From a clinical perspective, does having an equine vaccine against leptospirosis seem like it would be beneficial?


 **Divers:** I've been a proponent of the vaccine for several years. One reason is that biosecurity alone probably is not going to prevent infection. Number two, we believe that the humoral antibody response is protective against the infection. Regardless of which organ system is involved, infection has to occur first. If we have protective antibodies, we will not have infected horses. If we don't have infected horses, we don't have the bacteria going to the reproductive tract, the kidneys and the eyes, and therefore we've stopped the leptospiral bacteria and the clinical disease associated with infection of those organs. I think we all agree that the vaccine should work. The safety data looks good. I think every horse owner should at least talk to his or her veterinarian about the possibility of using the vaccine on his or her horse and make that decision in consultation with the veterinarian.


 **Boggs:** Which horses should be vaccinated to help protect them from leptospirosis caused by *L. pomona*?

 **Gilger:** If horses have developed leptospiral-associated uveitis, the vaccine should not be used in those horses. It should be preventive for other horses that are at risk for leptospirosis caused by *L. pomona* in the same environment. I would recommend that the horses on the same farm be vaccinated against *Leptospira*, but that a horse with active uveitis is probably not a candidate for the vaccine.

 **Boggs:** So you wouldn't vaccinate the horse when he's having an actual active flare. What do we do with that horse a year down the road?

 **Gilger:** With recurrent uveitis, it's a lifelong event. So the information we have right now would suggest that they should not be vaccinated.

 **Divers:** Dr. Gilger mentioned not vaccinating horses with recurrent uveitis. On those farms, would you feel comfortable vaccinating the rest of the horses not knowing what their antibody level might be?

 **Gilger:** That's a good question. At least one study suggested that if you vaccinate horses that have active recurrent uveitis, you're not going to make those horses worse.<sup>20</sup> So that data would suggest that we're probably OK even vaccinating horses with recurrent uveitis; however, we need more data and more long-term studies to really qualify that. On the flip side, I think it's really critical that we vaccinate these additional horses that are at risk on that farm.

“There's really no safety data on using leptospirosis vaccines licensed for use in cattle, for instance, in a horse. If there are any adverse reactions, it's difficult to defend your vaccine choices.”

— Dr. Terry Blanchard



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\*Currently, there are no vaccines available with USDA-licensed label claims against equine abortions, uveitis or acute renal failure due to *L. pomona*.

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