

# Recurrent Uveitis



*Down on the Farm*

by HEATHER SMITH THOMAS

Recurrent uveitis is the most common cause of blindness in horses. Originally termed “moonblindness” because horsemen thought the recurring attacks were related to phases of the moon, this eye disease has also been called iridocyclitis and period ophthalmia, but the current term is equine recurrent uveitis (ERU). This eye problem has several causes, but the most common cause seems to be leptospirosis infection.

Dr. Rance LeFebvre (UC Davis, California) has been working with eye problems in horses for a number of years and was co-author of a study (published in the *Journal of Clinical Microbiology*, July 2000) in which the eyes of 30 horses with recurrent uveitis (eyes that were at that point having an inflammatory episode) were examined to detect whether leptospirosis bacteria were present in the eye. The eye tissues were cultured, tested to determine the serology of the bacteria, and checked for DNA of the leptospires. Leptospiral DNA was found in the aqueous humor of 21 out of 30 horses (70 percent), while only one of 16 control horses was positive. Six of 27 horses with uveitis (22.2 percent) cultured positive for *Leptospira* from the aqueous humor of the eye, and none of the 12 control horses tested positive.

“We tried to culture all of them, but it is very difficult to grow those organisms. So the DNA test was an absolute confirmation that they were there,” says LeFebvre. This showed that leptospirosis is indeed a very common player in this disease.

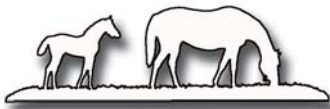
This was an interesting finding since, in the past, we were usually not able to detect the presence of leptospires in the eye itself. The eye problem generally occurs months after the active infection in the body, and veterinarians assumed that the organism was long gone from the eye by that time.

Traditional treatment has been use of anti-inflammatory drugs to reduce inflammation and pain, but now we realize there might also be value in giving antibiotics, to try to control the leptospirosis organism. The tricky part, however, is getting the antibiotic to the source of the problem, in the eye. “If you give the horse systemic antibiotics it doesn’t get into the eye itself very well, due to the blood-ocular barrier. Some people are putting time release strips of anti-inflammatories right into the eyeball, but whether this would work with antibiotics, we don’t know,” he says.

Recurrent uveitis is a very serious and devastating disease but it’s not one that has gained enough notoriety for there to be enough funding to adequately research it. “This is the limiting factor. We work on a shoestring here; there are not a lot of people willing to spend money for the research, to keep making progress. But now we know that leptospirosis is definitely involved. It may be the main player in causing uveitis in horses,” he says.

“We know that leptospirosis gets into the eye and infects it and causes an inflammatory response. Usually what happens is that the inflammation causes scarring. But what we don’t know is why there’s another flareup later when the inflammation dies down. We’d like to find out whether these animals are staying infected (and after the inflammation dies down, the bacteria come back) or are they becoming reinfected multiple times? I don’t think anyone knows the answer to that,” says LeFebvre.

“The inflammatory response probably knocks the leptospirosis down, but I doubt if it kills it entirely. Then once the inflammation goes away, the leptospirosis comes back—that’s my guess,” he says. So if there was some way to deliver an appropriate antibiotic to the eye that would combat the leptospirosis so it wouldn’t return, this might help.



## *Down on the Farm Cont'd.*

“The damage to the eye is not coming from the infection, but rather from the inflammatory response to the infection. If you could get antibiotics into the the eye, you could at least solve one problem by curing the current infection—and you probably would cure it if you could get antibiotics into the eye in high enough concentrations to kill the lepto. If the horse didn’t get reinfected on down the road, you could probably prevent subsequent occurrences,” he says.

“Most antibiotics work pretty well for lepto, including penicillin and streptomycin, but there is no guarantee of success unless you can get enough of it into the eye. Lepto is susceptible to these antibiotics. The other side of the coin is that animals who have lepto localized in the kidneys are hard to treat. We can run antibiotics through those kidneys at very high concentrations and still not clear the infection,” he says. This is one reason many animals keep shedding the leptospire in urine; the organism can live in the kidneys a long time (even for life, in carrier animals like rodents and dogs). In a test tube, lepto bacteria are very susceptible to antibiotics, but in some body tissues they must have a way of hiding, perhaps inside the cells. And if this is happening in the eye, there is no guarantee that you can get enough antibiotic in there to eliminate it.

“Leptospirosis has been with us a long time and in many ways we still are not very far down the road in combating it; these pathogens are very good at what they do. Even though some species continue to shed the bacteria, horses don’t seem to remain carriers for life, but we don’t have an absolute answer for how long they shed the bacteria after having an active infection. An educated guess would be that horses probably remain chronically infected for several weeks to several months. Cows, for instance, can be infected for a lifetime, but they have specific serovars of lepto that are adapted to cows. As far as we know, there are not any really good host-adapted servers for horses. Even though we sometimes see abortion storms in mares, I don’t think there is a strain that has adapted itself to horses so that they would stay infected for years,” he says.

“These are things we are working on now for treatment, but we’re a ways off; it’s hard to get absolute solid data that’s not equivocal or that has enough numbers that you really trust it. The most common treatment now is just an anti-inflammatory of some sort, but if you are not combatting the infection itself you are just putting a bandaid over the problem.” You are halting pain and inflammation, just marking time, because the problem may return. Knowing what’s causing it, but not knowing how to get at it is very frustrating.

There is work being done at North Carolina State University on time-release implants for anti-inflammatories (immune suppressing drugs that stop the inflammation), put into the eye. “I wonder if this might work with an antibiotic, delivering it into the eye over long term. This is technology we are still trying to figure out. These are great ideas but need a lot more work and study to see if they would be successful,” says LeFebvre.

### **Vaccination**

There’s been some work on an equine vaccine for leptospirosis but it may be awhile before it is in use to try to prevent ERU. “Even if the eye problem was caused by just lepto, I am not sure we know enough yet about the immune response or how these horses’ eyes become infected in the first place, to know if a vaccine would work. If the horse’s eye is becoming infected with a systemic infection, yes, a vaccine might work. But if it is getting infected due to urine splash or contamination of the eyeball itself, going straight to the eye (without the horse actually being sick with lepto), the vaccine may not help,” says LeFebvre.

“We have also isolated a couple of leptosporosis organisms from horses’ eyes that have not ever been classified before. They are brand new lepto that we’ve never seen. We don’t know where they came from or how they got there. We

sent them back to the National Leptospirosis Reference Center in Ames, Iowa, and they'd never seen these before either. These are absolutely different from all the other common leptospires that we normally see in North America," he says. The vaccine must be geared toward the actual pathogen that is causing the disease, or it won't work.

In areas where there's a high incidence of leptospirosis, some people are using the cattle vaccine to try to protect their horses, and this is somewhat controversial. "It's not approved for horses, but I don't think this is a problem. That vaccine is composed of dead leptospires; they are not alive, yet they elicit a pretty good immune response. The only concern I have is that even though the vaccine has five different leptospires serotypes, if those are not what are in the eye, it won't be protective. Of the isolates we found in eyes, four of them were pomona (which is in the vaccine) and two of them were yet to be identified and were brand new," says LeFebvre. So the vaccine might help in many cases, but not in all of them.

"I have heard some anecdotal responses back from horse owners who have gone ahead and vaccinated their horses with the cattle vaccine and seen the incidence of moon blindness drop in the horses who had had a couple of bouts previously, but until the research is done, we don't know if the vaccine is really effective in these instances or whether it was just luck," he says.

"I haven't heard of any mass vaccination of horses with the cattle vaccine, but in cases where they have used the vaccine in horses I have not heard of any adverse reactions, so I think it's probably pretty safe, but we don't know how protective it really is for the eye problem," he says. It may keep mares from getting leptospirosis and preventing abortions; some breeders have reported that vaccination halted leptospirosis abortions. Time will tell whether we can develop an effective equine vaccine that can help prevent recurrent uveitis as well as abortions in pregnant mares. 🐾