

# Equine Recurrent Uveitis (ERU) " Moon Blindness "

By Heather Smith Thomas

" Moon blindness " is a chronic, painful eye disease, and it's the most common cause of blindness in horses. It was so named during the 1600s because people thought recurring attacks were related to phases of the moon. This eye disease might be one of the first veterinary diseases ever documented. In the pyramids at Giza (Egypt), there are depictions of ocular problems in cavalry horses of that time, 4,500 years ago, showing uveitis or a disease very similar. This eye problem has also been called iridocyclitis and periodic ophthalmia, but the current term is equine recurrent uveitis (ERU).

During the past several centuries, horse owners thought the main causes were heredity, damp stables, bad feed, and marshy pastures. It was noted that land drainage reduced the incidence and that there was more moon blindness among horses on farms irrigated with town sewage. These factors pointed toward bacteria, yet the most popular theory a few decades ago was that moon blindness was due to lack of riboflavin (a B vitamin) in the horse's diet.

## Causes

According to Brian C. Gilger, DVM, MS, Dipl. ACVO, a professor of ophthalmology at North Carolina State University who recently published *Equine Ophthalmology*, ERU can be caused by several factors. One of the most common causes is infection with *Leptospira*, spiral-shaped bacteria, or spirochetes, that can be found in areas with stagnant water.

" It's not the infection that causes the uveitis, but the immune response to the initial infection," says Gilger. "Lepto is one of the initiators of this immune response."

Other causes include trauma to the eye, and bacterial infections such as brucellosis, *Streptococcus*, *Rhodococcus equi*, and *Borrelia bergdorferi* (the spirochete that causes Lyme disease).

Viral infections such as equine influenza, equine viral arteritis (EVA), and equine herpesvirus can also trigger an attack, as can certain parasites and systemic infections (septicemia, endotoxemia).

"Anything that causes breakdown of the blood-ocular barrier (the barrier between the body's blood circulation and the internal parts of the eye) can produce an immune response, so any type of virus or bacteria that can get into the eye may initiate the problem," says Gilger. "The tiny larvae of *Onchocerca* (*O. volvulus*, a parasitic worm) commonly induced uveitis in the past, but with use of ivermectin, we don't see this much anymore. But there are ocular parasites that have become immune to ivermectin, so I suspect that onchocerciasis-induced ERU may start reappearing in the next five years simply because of resistance to ivermectin."

The initial episode of ERU often occurs in horses four to eight years old. Not every horse that gets uveitis (inflammation in the uveal tract of the eye) will develop recurrent uveitis, but he or she is considered at risk until several years without relapse have passed, says Gilger. A horse is not considered to have ERU until two or more episodes have occurred.

The initial episode can affect one or both eyes, and recurrences can affect one or both. If just one eye is affected, the other might become inflamed later.

The recurring episodes of inflammation within the eye can develop weeks or months after the initial uveitis subsides.

## **The Disease**

Equine recurrent uveitis involves the entire eye, but most of the clinical signs, including inflammation, begin in the uveal tract--the iris and tissues that line the part of the eye behind the iris.

The uveal tract contains many blood vessels and most of the blood supply for the eye. Thus, diseases involving systemic circulation can also affect uveal blood circulation.

The blood-ocular barrier normally prevents large molecules or cells from entering the eye, helping keep the fluid within the eye clear. But disruption of this barrier by trauma or inflammation allows blood products and cells to enter the eye.

It also enables activation of certain immune responses in the body, resulting in the production of antibodies that attack some of the horse's own ocular proteins in the eye that are not normally targeted by the immune system. When foreign antigens from the bloodstream (such as bacteria) enter the eye through the ruptured barrier, antibodies against them also accumulate inside the eye, heightening the inflammatory response, says Gilger.

"Any injury to the eye, corneal ulcers, etc., have potential to set up immune response in the eye that may cause uveitis," says Gilger. "The reason things like leptospirosis and onchocerciasis cause uveitis is that their molecular makeup is very similar to some of the structures in the eye. When the body has a reaction against the lepto, the immune response also attacks the eye itself.

"Similarity between proteins of these organisms and the eye tissues is what makes those organisms bad for causing ERU because it sets up the immune response," he says.

Other organisms can cause the same problem, but not as frequently. There are several theories about why the eye has recurring episodes.

"One is that the horse is encountering similar types of things again, causing the immune response to reoccur," he says. "Generally, the eye has a big bout of inflammation, and how well the horse's body controls it will be a factor in future episodes. Once the eye gets back to normal, the inflammatory receptors will then express themselves again, and the immune response will recognize those proteins, then another episode will occur.

"Another thing that makes it complicated is that we are probably calling several different diseases the same thing," he adds. "One horse that has recurrent inflammation may have a completely different type of disease causing it than another horse. Our research is attempting to characterize these different causes."

He explains there is a difference between inflammation in the eye (uveitis) and recurrent uveitis. If your horse gets hit in the eye with a branch or gets an infection in the eye, he'll get uveitis, and it can be very severe, but this is not recurrent uveitis, says Gilger.

"We see a lot of horses here in our hospital, and about half the cases referred to us by veterinarians for evaluation of ERU end up being something else."

Tim Cutler, MVB, MS, Dipl. ACVIM, ACVO, a veterinary ophthalmologist at Animal Eye Specialty Clinics of South Florida in West Palm Beach, says initially the diagnosis is uveitis, and it might not be recurrent.

"It has some similarities to arthritis in a joint," he says. "ERU may be likened to rheumatoid arthritis in the same analogy. We diagnose ERU when it happens the second or third time (just as arthritis isn't considered rheumatoid until it becomes chronic)."

Cutler advises horse owners to keep a record of eye problems and hang a pen on the barn calendar, then mark any days the eye is red, tearing, or squinting and requires treatment. If this happens several times, the eye should be evaluated more closely. Another thing that helps in diagnosis is to measure the pressure within the eye, which can be done by a specialist.

"If it's not normal, and there's a difference between the eyes, you've established the diagnosis (as ERU)," says Cutler.

A horse with ERU is at risk for episodes during times of stress, which can include vaccination, deworming, a trailer trip, or a heavy show schedule.

"Stress compromises immunity and activates the body's response to challenges," says Cutler. "The eye with ERU is always on alert. That eye's immune surveillance can be compared to a paranoid security guard. When there's an upgrade in perceived danger, it starts 'shooting,' and uveitis occurs essentially every time any warning signal is perceived in the eye."

## **Signs of ERU**

The uveal tract has many blood vessels. Signs of early inflammation include dilation of the vessels and redness. Congestion and inflammation cause fluid and protein to leak into surrounding tissues as the blood-ocular barrier is disrupted.

Eye membranes are red and swollen, the eye waters, the pupil constricts, and the horse holds the eye closed; it is painful and sensitive to light. The cornea (front cover of the eye) might become cloudy.

Each episode further damages the eye. The lens might become opaque or dislocated and cataracts can occur. The retina at the back of the eye might be impaired or detached, and optic nerve function becomes disrupted, causing loss of vision.

Some eyes develop corneal ulcers and secondary complications that require removal of the eye (enucleation). Glaucoma (a possible complication characterized by an increase in intraocular pressure that causes defects in the field of vision) is responsive to therapy, according to Cutler, but cataracts are not.

Removal of a cataract does not solve the problem because in this instance, the cataract is secondary to the uveitis.

## **Treatment**

The main goal is to try to preserve vision, control inflammation in the eye to halt further damage, and relieve pain. The earlier treatment is begun, the better chance for a good outcome.

"In most cases, we treat the eye non-specifically with medications like steroids and non-steroidal anti-inflammatories to reduce inflammation," says Gilger. "This works in about 90% of horses. In others, the disease is just too severe.

"In the last 10 years we've developed drug implants that deliver cyclosporine (a drug used to suppress the immune system, as for treating a human kidney transplant recipient to keep the immune system at bay)," says Gilger. "These implants can deliver the drug over a three- to four-year period and have proven very successful. We're now in the process of getting this commercialized and having FDA approval."

The implant is put beneath a flap of tissue on the outside of the eyeball, a procedure that requires the horse be anesthetized. The sustained-release delivery produces a constant level of the drug directly into the eye, bypassing the blood-ocular barrier that hinders systemic application.

Systemic treatment with cyclosporine is very costly (as well as less effective) and can produce serious side effects since it can be toxic to kidneys, the liver, and the nervous system. Implants also work better than topical administration because most drugs do not penetrate the eye when applied topically. The implant eliminates the need for horse owners to continually medicate their animals, says Gilger.

In recent studies, Gilger and his colleagues found the implant and slow release of cyclosporine over time decreased the duration and severity of inflammation, tissue destruction, and other damage in the eye.

They determined that horses with chronic ERU that have little or no active inflammation, but are experiencing frequent recurrence of episodes (or early relapse after traditional medications are halted), are the best candidates for the implants.

Horses with active inflammation that can't be controlled by anti-inflammatory medication are not as likely to benefit from an implant.

Cutler says that the earlier treatment is begun, the better: "There is no miracle for ERU, but this implant is very close. Once you realize that medication alone is not resolving an eye problem, this implant can often make a huge difference. I've had a few horses that didn't respond well, but there are many that I don't even see anymore because they are so much better."

There is also speculation that antibiotics delivered into the eye might be beneficial, since leptospirosis seems to be a common cause of ERU.

Tom Divers, DVM, Dipl. ACECC, ACVIM, a professor of medicine at Cornell University's College of Veterinary Medicine, says lepto is the only well-documented cause.

"An important finding which we've only learned in the last five years is that the lepto organism is still present in the affected eye of horses with ERU," he says. "For many years, we thought the infection was long gone by the time the eye problem develops." This is not true in most cases.

In the past, antibiotics were rarely considered for treatment.

Divers says his group is studying a potential antibiotic treatment and its expected levels within the eye. It is currently being used to treat horses at Cornell's clinic for ERU, but a couple years of clinical experience are required to evaluate its efficacy.

"We've done sensitivity tests to see which antibiotic would be most effective, and this one seems promising," says Divers. "Our goal is to develop both a vaccine and a treatment."

Rance LeFebvre, PhD, professor of microbiology at the University of California, Davis, says some clinicians are putting time-release medication right into the eyeball, but whether this would work with antibiotics, he doesn't know.

"Most antibiotics work pretty well for lepto, including penicillin and streptomycin, but there's no guarantee of success unless you get enough of it into the eye," says LeFebvre. "On the other hand, animals with lepto localized in the kidneys are hard to treat. We can run antibiotics through the kidneys at high concentrations and still not clear the infection."

Many animals continue shedding leptospores in urine; the organism can live in the kidneys a long time, even for life in carrier animals such as rodents and dogs.

In a test tube, the bacteria are susceptible to antibiotics. However, in some body tissues they have a way of hiding from the same antibiotics, perhaps inside the cells.

If this is happening in the eye, there's no guarantee you can get enough antibiotic in there to eliminate it.

Recurrent uveitis is a serious and devastating disease, but it hasn't gained enough notoriety to spur the funding needed to adequately research it.

"This is the limiting factor," says LeFebvre. "We know that lepto is definitely involved and may be the main player (in ERU). We know it gets into the eye and causes an inflammatory response, and the inflammation usually causes scarring. But what we don't know is why there's another flare-up 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 irritate the inflammatory receptors again) or are they becoming reinfected multiple times?"

LeFebvre says if you could get antibiotics into the eye, you could at least solve one problem by curing the current infection, "and you'd probably 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 (perhaps he's protected by vaccination), you could probably prevent subsequent occurrences."

"There are things we're working on now for treatment, but it's hard to get solid data that's not equivocal or that has enough numbers you can really trust," LeFebvre says. "The most common treatment now is just an anti-inflammatory of some sort, but that's not combating the infection itself."

### **Take-Home Message**

Horses can have eye infections that aren't equine recurrent uveitis. Any horse with eye pain, squinting, sensitivity to light, and/or excess tearing should be examined by a veterinarian and possibly by a veterinary ophthalmologist to determine the exact cause.

Equine recurrent uveitis is a painful condition for your horse, and it needs treatment.