No Definites Exist In Diagnosing Lyme Disease

This tick-borne illness gets plenty of publicity, but when it comes to sick horses, there's a lot we don't know.

BY GLENYE CAIN OAKFORD

It's a universally dreaded diagnosis: Lyme disease. Caused by the *Borrelia burgdorferi* bacterium and transmitted through tick bites, Lyme disease was formally identified in humans in the mid-1970s and is one of the nation's most publicized illnesses. But decades after its identification in Lyme, Conn., it remains little understood in horses.

Because public awareness of Lyme disease is high, people take precautions to prevent tick bites on themselves and their horses. But a number of veterinarians and researchers say scientific knowledge hasn't kept up with public awareness—and fear—of Lyme disease, and they worry that the infection, with its often vague and variable symptoms, is being over-diagnosed and possibly over-treated.

"I certainly don't think there's intentional over-diagnosis," said Nora Grenager, VMD, Diplomate ACVIM, of Grenager Equine Consulting in Warrenton, Va. "There's more awareness of it, so more and more horses are being tested. Owners are certainly very well-informed these days, between getting a lot of media information and choosing to do their own research about horses, which is easier to do now. So it comes up frequently now as a question: Could this horse have Lyme disease?

"And because the signs are nonspecific, and tests aren't always yes-or-no definitive, and the treatment is relatively benign and often helps with other issues, all of these things make over-diagnosis understandable," she continued. "It's truly very hard to definitively diagnose it. It's probably not as prevalent as we're diagnosing it, but right now we don't have a great alternative. It's complicated."

Becky Harcleroad, who manages Snowberry Farm, a Thoroughbred breeding facility in Livingston, N.Y., has seen several cases of Lyme. Two horses at Snowberry displayed vague, hard-to-explain symptoms: A gelding seemed unusually docile and a bit depressed, and a retired broodmare had intermittent hind-end lameness. A third horse, her daughter's hunter mare, had a slightly arthritic neck with no other overt symptoms but had a high Lyme titer on a blood test.

Science hasn't kept up with the publicity when it comes to Lyme disease, and there's still a lot we don't know about this tickborne illness when it comes to horses. *DUSTY PERIN PHOTO*

"I can't say that the Lyme has caused the arthritis," Harcleroad said, "but it may very well have contributed to it, so we treated her when we first bought her."

Getting a firm Lyme diagnosis can be difficult because the symptoms are often vague and sometimes can be attributed to—or, in fact, caused by—other problems. Individual horses might show different symptoms. Lyme disease can appear as a lameness or stiffness, but it also can cause uveitis (moon blindness) or even neurologic symptoms.

Another complicating factor in diagnosing the disease is that horses can test positive for exposure to the bacteria without actually becoming sick. That likely means that at least some of the horses that test positive for Lyme in blood tests have been exposed to the bacterium but are not actively ill, which can inflate the number of horses reported as actually having the disease.

"We know that there is a very significant proportion of horses that are infected with *Borrelia,* the organism that causes Lyme disease," said Amy Johnson, DVM, Diplomate ACVIM and assistant professor of large animal medicine and neurology at the University of Pennsylvania's New Bolton Center. "There's no doubt. If you check their blood test, they will have developed antibody levels against this organism, showing that they've been exposed to it, and the only way they can get exposed is to be bitten by a tick and infected with this bacteria. Those horses are all infected at some point in their lives, but the vast majority of them show no clinical signs whatsoever.

"Then there is another population of horses that do have something wrong with them," she continued. "They're lethargic, or they have behavior changes, or they're lame, or they're losing weight, or some other issue which is often somewhat vague, in terms of clinical signs. They're just not doing as well as they should be, and their blood tests are positive for antibodies against Lyme disease. But proving that the infection with *Borrelia* is the cause of their clinical problem is exceedingly difficult, and that's where this disease gets frustrating."

So What Do We Know?

Proof that the bacteria implicated in Lyme disease actually causes the disease has been surprisingly elusive.

Probably the best-known study of Lyme infection in horses took place at Cornell University (N.Y.) more than a decade ago. Researchers infected eight previously pathogen-free ponies with *Borrelia burgdorferi* by placing infected ticks on them.

"All the ponies did get high blood titers, proving that the ticks had attached and given them the Lyme bacteria, but none of them got any of the typical signs we call Lyme disease," said Grenager. "So even though they were infected with it and had the official diagnosis based on lab work—which is how we currently can diagnose it—none of them showed any of the signs. When they euthanized the ponies, they were able to find some evidence of the Lyme bacteria in places where we think of it causing a problem, like the lining of the joints and the nerve sheaths, and a little bit in the muscles. But only barely, just minimal evidence of it in a few ponies."

These kinds of results make it more difficult to study Lyme disease in horses, as researchers can't recreate the disease in an experimental setting.

That's not to say that *Borrelia burgdorferi isn't* the cause of Lyme disease.

"I fully believe that horses get Lyme disease and that there is a syndrome of Lyme disease," said Grenager. "Certainly, we've proven it in some horses in different ways, like the ones that have the neurologic form or eye problems like uveitis. But I don't think we've been able to prove it yet in a nice research setting. That doesn't mean that it's not a syndrome we see. We need to continue to address it and research further, for sure."

What is known so far about *Borrelia* bacteria is intriguing, but also discomfiting to the average horse owner.

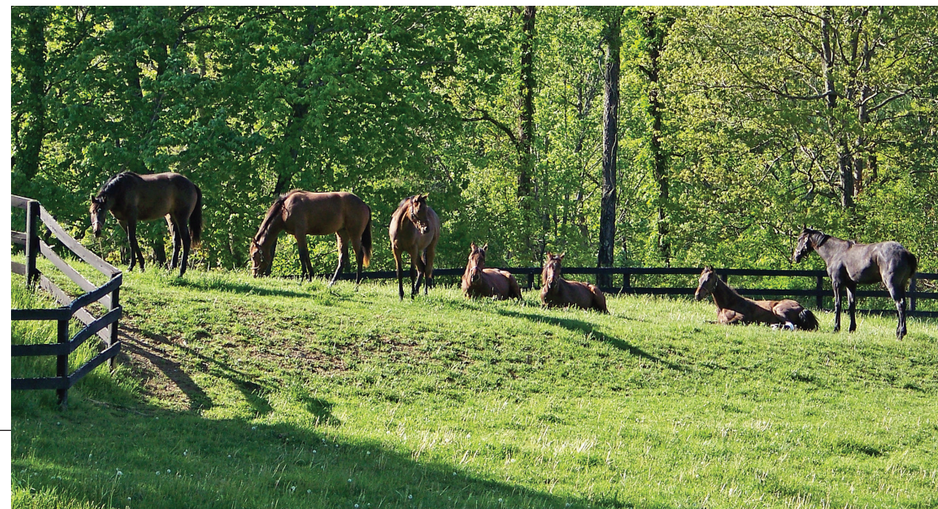
"The bacteria is really smart and evasive," Grenager said. "Once it enters the body, or even before it enters the body, it's able to change in a variety of ways. It's able to change the outer-surface proteins, the things that stick out from the bacteria. Those can modulate in various ways how well the body's immune system can 'see' the bacteria, as well as allow the bacteria to 'sneak' through areas that normally would invoke a huge response to eliminate the bacteria in normal situations. So it ends up lurking in places like the eye, the joints, the spinal cord—places where once it is able to get there, the body isn't as equipped to handle it."

The Diagnostic Dance

So what are horse owners to do? For a start, don't worry too much about Lyme disease if your horses live in areas of the country where it is rare. There isn't a public national database of Lyme disease's occurrence in horses, but the U.S. Centers for Disease Control and Prevention reports that Lyme disease in humans occurs most frequently in the Northeast, the mid-Atlantic region and in the northern central states.

According to the CDC's website, 95 percent of last year's confirmed U.S. Lyme cases occurred in just 14 states: Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia and Wisconsin.

To diagnose the disease, veterinarians take a number of factors into consideration. The first is clinical signs such as stiffness or lameness in more than one leg, sore or hyper-responsiveness to touching their muscles, lethargy, or behavior changes. The horse may be running a fever, or it might be something as vague as "sore



Because Becky Harcleroad manages Snowberry Farm in the "epicenter" of Lyme disease territory—"Columbia and Dutchess Counties in New York have some of the highest rates of Lyme in people and dogs and horses," she says—she and her veterinarian have made an aggressive plan for prevention and treatment. *PHOTO COURTESY OF BECKY HARCLEROAD*

While researchers can infect horses with the *Borrelia burgdorferi* bacteria that causes Lyme disease by placing infected ticks on them, it's difficult to study the disease because the horses don't necessarily show any symptoms. *ZILLI/ISTOCKPHOTO.COM PHOTO*

hocks." If the horse is located in an area known for Lyme disease, then the next step is lab work.

"The most commonly used 'best test' is to send it to Cornell, where they measure three different types of antibodies," said Grenager.

She also noted that while antibody levels are useful information, even that isn't fully understood in the Lyme context. "Even horses that we really think have it and that we treat, it can take a long time for the antibody levels to come down, and in other horses it doesn't," she said. "We just don't yet understand very well what those numbers mean, but as more and more horses get tested, we know what signs they're showing and whether or not they're responding to treatment. We'll learn more as time goes by."

Johnson hopes research will provide both a better understanding of antibody levels and lead to improved diagnostic tests.

"We can document exposure to the organism, but we can't say, based on the antibody levels, whether the horse still has living spirochetes in its body somewhere or whether the horse has effectively killed all of the spirochetes but is still producing antibody because that's what the immune system does—it produces antibody for longer than the disease is actually there," she said. "If we had a test that would reliably detect the presence of living organisms in the body, that would be a start."

But He Got Better After I Treated Him...

Response to treatment can provide a hint as to whether Lyme was the culprit, although that isn't clear-cut, either. Standard treatments for Lyme, like tetracycline drugs, have an anti-inflammatory effect, which can help symptoms not caused by Lyme, too. And while treating a horse presumptively for Lyme may sound like a safe option, it can be counter-productive if the symptoms are actually being caused by another problem that goes unaddressed.

In addition, there are risks to antibiotic use. Horses treated with intravenous oxytetracycline may develop phlebitis (inflammation of the blood vessel where the catheter is placed) or an intermittent fever from the treatment. Using antibiotics needlessly can contribute to drug-resistance, and antibiotics can kill off good, healthful bacteria, too, which might allow more damaging bacteria to flourish and cause, for example, diarrhea.

So a proper diagnosis, followed by proper treatment, is important—but not always simple.

"It's very challenging to comfortably diagnose a horse with Lyme disease," Grenager said. "Sometimes it seems like a slam dunk: You see a horse that's stiff and tired, losing some muscle along its topline and sensitive to touch, the titers are high, the owner takes it trail-riding through woods all the time, and it gets better after a month of treatment. But others are tricky, because they have rather non-specific clinical signs."

In Harcleroad's case, testing titers for Lyme exposure and treating the disease made sense to her and her veterinarian, because she and her horses live in what Harcleroad called "an epicenter" of the disease.

"Columbia and Dutchess Counties in New York have some of the highest rates of Lyme in people and dogs and horses," she said. According to statistics from the CDC, New York ranked third by the number of confirmed human cases last year, behind Pennsylvania and Massachusetts.

In the three cases Harcleroad suspected, she sought blood tests, and all three horses' samples came back with relatively high titers.

The gelding recovered fully after 31 days' treatment with doxycycline. The retired broodmare was treated twice, most recently for 40 days, and her symptoms resolved. And the hunter mare also seems fine, Harcleroad says.

"She was high again when we did another blood test last year, and then over the winter we had it checked again, and she was in good shape," she said. "The titer was nice and low."

Treatment for Lyme disease generally runs between 30 and 60 days, and the illness appears to be an acute, rather than a long-term, problem in horses.

Should You Vaccinate?

Given the Lyme-prevalent area they operate in, Harcleroad said Snowberry Farm is especially vigilant about the disease. She doesn't hesitate to pull a blood test when she's suspicious of a horse's symptoms, and the farm implements a thorough tick-control protocol.

"We've also started vaccinating our own horses for Lyme disease," said Harcleroad. She doesn't think the vaccine, which is produced for dogs, is 100 percent effective, but it seems to have worked on a daughter of the infected broodmare, a filly vaccinated for much of her life.

"She has no Lyme titer to speak of, even though it seems like ticks are attracted to her," says Harcleroad, who had that mare tested after she spiked a fever.

There's no equine vaccine yet, and use of the canine version is considered off-label, but it has been used in horses for some time. In the Cornell pony study some of the ponies were vaccinated with it.

"And it was preventive for them getting the high titers," Grenager said. "But they were ponies that started with no titer whatsoever, then they vaccinated them, then tried to give them Lyme disease. The ones who had been vaccinated did not develop the high blood titers, so it seemed like it might have been protective in that group, but, again, it's hard to say, because none of them showed symptoms.

"But we only have that one study, which is a good start, but the questions for a vaccine are how efficacious it is, how long the vaccine lasts, and what the risks are," she continued. "So far, at least, it doesn't seem any riskier than others. But you also have to think about that you are administering something to your horse for a disease that potentially isn't all that common. It seems like it is, but we don't really know."

And, she added, so far there's no data on whether the vaccine would protect against the most fearsome of Lyme cases, the neurologic ones (see sidebar).

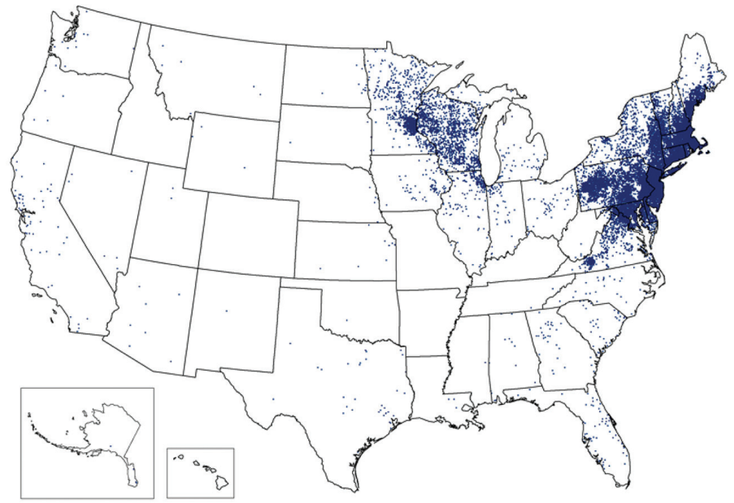
The bottom line: Horse owners should consult with their veterinarians about whether their horse should be vaccinated, giving thought to the likelihood of the horse being exposed to Lyme disease and any potential risks associated with an off-label use of the vaccine.

For horse owners who suspect Lyme disease, Grenager offered some common-sense advice.

"Take the time to really talk with your veterinarian, and have a thorough examination done," she said. "Carefully take into account all the signs, where you live, and make it an in-depth discussion so that the diagnostics we have available are as helpful as they can be. And, generally, if horses do get diagnosed with Lyme disease, at this stage they're the typical cases, which do respond fairly well to treatment. While it is a scary thought that your horse could have Lyme disease, make sure that's what's going on to the best of everyone's ability to diagnose it, and go in with as much knowledge as possible."

Reported Cases of Lyme Disease—United States, 2012

One dot is placed randomly within the county of residence for each confirmed case. Though Lyme disease cases have been reported in nearly every state, cases are reported based on the county of residence, not necessarily the county of infection.



Of the U.S. Lyme cases reported last year, 95 percent occurred in just 14 states: Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia and Wisconsin. *MAP COURTESY OF THE CDC*

A Deadly Deviant Of Lyme Disease

For horses, Lyme disease usually manifests in acute symptoms that resolve with treatment. However, in a handful of reported cases, the problem was still life-threateningly severe, with neurologic symptoms. That manifestation of Lyme disease appears small, as of today, with just six cases published since 1987.

"It's rarely reported, though it probably happens more frequently than it is reported, because not every veterinarian that has a case will write a journal article about it," said Dr. Amy Johnson, who specializes in equine neurological issues. "We've probably collected 10 or so cases here at New Bolton Center. That's an estimate, but there is maybe one a year that we feel confident making a diagnosis of neuroborreliosis, or the neurologic form of Lyme disease."

It's not clear why *Borrelia* affects some horses' nervous systems. "It probably is a difference in the function of the immune system," Johnson said. "That's a theory: that those horses' immune systems aren't as efficient at protecting their central nervous system from this bacteria. Could it be a more virulent strain that these horses were exposed to? Absolutely. Could it be a bunch of different factors, maybe the horse had a fairly normal immune system but was very stressed or in an environment where it got exposed to a large number of organisms? Those are all things that would be great to know, but we don't have enough documented cases where we could even look at the contributing factors leading to neurological disease."

Neurologic signs are always an emergency situation, and, if your animal lives in or has come from a Lyme-prevalent area, it's worth considering the disease among the possible culprits.