

Neurologic Herpes

Dr. Christine King

Neurologic herpes has been making the equestrian news lines lately. Although this disease occurs only sporadically, several horses at a barn may become affected, creating a mini epidemic. Usually, these outbreaks are very well contained by quarantine measures (see below), so the disease does not get to spread much beyond the epicenter (the facility in which the first cases appeared).

But typically, at least a couple of horses per outbreak die or are euthanized, so news of a neurologic herpes outbreak sends people into a panic, and it spawns all sorts of misinformation. I thought I'd try to dispel some of those misconceptions and share with you what we do know about this disease and where current research is focused.

Neurologic herpes is one of several viral diseases in horses that affect the central nervous system (brain and spinal cord). It is caused by infection with equine herpes virus type 1 (EHV-1). This virus can also cause mild respiratory disease, abortion in pregnant mares, and death in newborn foals. There is enough genetic difference between the various strains of EHV-1 that typically in an outbreak one sees either abortion and neonatal deaths (the abortigenic strains) or neurologic disease (the neuropathic strains).

Neuropathic strains of EHV-1 have always been with us. But in recent years we've seen an upswing in both the number and severity of outbreaks of neurologic herpes in horses. Research indicates that at least some of the recent outbreaks have been caused by a mutant strain of EHV-1, a strain that is more virulent—more infectious and more pathogenic (damaging)—than earlier strains. It is speculated by researchers that vaccination pressure (i.e. widespread and frequent use of EHV-1 vaccines) forced this mutation, as occurs with other viruses in animals and humans.

In my opinion, another contributing factor is that, as a population, our horses have become less healthy and resilient over the generations. Today's horses are much more heavily vaccinated and cosseted than were horses even 20 years ago. Breeding for color, speed, and other self-serving attributes over health and longevity has, I believe, further weakened the genetic pool. We've seen an increase in all sorts of diseases in horses over the past couple of decades. Mutant viruses cannot be blamed for all of them.

Anatomy of an outbreak

Although some strains of the virus may have changed a bit over the years, the pattern of neurologic herpes outbreaks has remained the same. The outbreak typically originates in a big, busy barn such as a large boarding farm or the barn at a show ground or race track. Not only is there a lot of horse traffic coming and going through these places, but many of these horses are under stress from travel, training, competition, etc. (See the January 2006 issue of *Horses Inc.* for an article on stress and the performance horse.) Stress is a huge factor in susceptibility to herpes virus infections, as I'll explain in a minute.

The outbreak typically begins with the introduction of a horse who is shedding a neuropathic strain of the virus. That horse may be new to the facility or he may be returning home from an event where he picked up the virus from another horse. The infective horse may be showing signs of a mild respiratory infection or he may just have a mild fever; in some cases, though, he may seem completely normal.

The herpes viruses, including EHV-1, have a habit of latency, meaning that a horse can harbor this virus in his body for years, without showing signs of infection. EHV-1 likes to hide out in white blood cells, lymph nodes, and even in the trigeminal nerve (one of the major nerves that supply the head)—places where it is out of reach of virus-neutralizing antibodies. Replication and renewed shedding of the virus can occur during periods of stress, the same as with cold sores (Herpes Simplex type 1 infection) in people. Stress is a trigger because it interferes with immune function, lowering our resistance to infection.

So, another possibility for transmission of EHV-1 is that a resident horse who has been harboring the virus all along gets stressed and starts shedding virus and infecting his barn mates. This process is how EHV-1 and EHV-4 persist in the horse population. Recent studies have shown that foals are infected by their mothers, or by other foals and broodmares on the farm, in the first few weeks or months of life.

These studies have also shown that vaccination of pregnant mares does not prevent this transmission.

Back to the outbreak in progress: the incubation period, or the time between infection and onset of illness, for this virus is only a few days (2–8 days). So, within a day or two of the virus being introduced to the barn, a couple of the horses will begin showing signs of illness. The horse who introduced the virus often is the first one affected, but he may not become ill at all.

The first signs of illness with EHV-1 are fairly vague: lethargy, picky appetite, mild watery nasal discharge, mild fever (in the 102–103°F range), and with this new strain of virus, reddish mucous membranes (gums, lining of the nasal passages, lining of the eyelids, etc.).

The giveaway that you may be dealing with neurologic herpes is the onset of neurologic signs in one or more horses who have/had a fever. Neurologic signs can include incoordination (ataxia), stumbling, weakness, and perhaps severe lethargy or sleepiness. In years past, the damage was mostly confined to the lower part of the spinal cord, so signs would mostly relate to the hind end (weak and wobbly hindquarters, progressing to dog-sitting because the hind legs are too weak to stand; loss of tail tone; loss of bladder and anal control). The horse would usually remain fairly bright and have a good appetite. With this new strain the rest of the system can be affected, too, including the brain, so the horse may be weak and ataxic in all four limbs and may show abnormalities of behavior as well as gait.

When neurologic signs develop in a horse who has or recently had a fever, the veterinarian will have a strong suspicion of neurologic herpes and recommend that the facility be closed to all horse traffic while diagnostic tests are run. The vet may also recommend isolating the horses who already have neurologic signs and even those who just have a fever, to avoid further spread of infection among the other horses in the barn. That precaution is not always possible, though, so sometimes the inhabitants just have to ride it out with good hygiene, frequent monitoring of all at-risk horses, and use of antiviral drugs, anti-inflammatory drugs, and supportive care as needed.

The good news is that not every horse in the barn will necessarily become infected; and of those who do, not every one will necessarily become ill. Of those who become ill, most will recover. The prognosis for recovery is correlated with the severity of the neurologic signs. While recovery may still be possible for horses who go down and cannot rise unaided, they are more likely to die or be euthanized than the horses with neurologic signs who remain standing.

Unless infected horses had already left the facility before the red flag went up about neurologic herpes, the outbreak ends there. The facility remains quarantined until repeat testing indicates that all infected horses have stopped shedding virus, and then life starts getting back to normal.

Mandatory EHV-1 vaccination of all at-risk horses has been practiced in some of the recent outbreaks, but the results have been poor and even the premise is questionable. Here's why.

The role of vaccination

There are two basic types of EHV-1 vaccine on the market: killed virus (KV) and modified live virus (MLV). The KV vaccines do stimulate EHV-1 specific antibody production in most vaccinated horses, but their efficacy is not that great, and boosters need to be repeated frequently to maintain high antibody levels. Of particular importance here, *these vaccines do not protect against neurologic herpes*. They don't stop virus shedding (and thus spread of infection) by infected horses, either.

The immune system uses two basic mechanisms to combat invading pathogens, including viruses:

1. antibody production, also called humoral immunity, meaning something pertaining to the body's fluids, (the "humors" of medieval times)
2. destruction or removal of pathogens by the cells of the immune system, called cellular or cell-mediated immunity

The KV vaccines can stimulate a good humoral response (i.e. measurable increase in circulating antibodies), but they don't stimulate the kind of cell-mediated immune response that MLV vaccines and actual viral infections do. The more we study EHV-1 infection in horses, the more we realize the importance of the cellular arm of the immune system. This is an active area of current research.

There is one study, published last year, which showed that the currently available MLV vaccine against EHV-1 prevented neurologic signs in ponies experimentally exposed to a neuropathic strain of

EHV-1. However, that study was funded in part by the vaccine manufacturer, and it is not clear whether the challenge involved the new virulent strain of EHV-1. The virus used in that study was obtained from a horse with neurologic herpes, but as I've already said, neuropathic strains of EHV-1 and neurologic herpes have always been with us. The value of this MLV vaccine against the new neuropathic strain of EHV-1 needs to be investigated further and validated in independent studies.

Not only do the KV vaccines not protect horses against neurologic herpes, there is some evidence that frequent or recent vaccination can increase a horse's risk for succumbing to neurologic herpes when exposed to one of the neuropathic strains of EHV-1. That certainly appears to be the case in the outbreaks we've seen in recent years. On the one hand, the horses most at risk (i.e. those in big, busy barns or who travel a lot) also are the horses who are vaccinated most heavily against EHV-1 and other respiratory pathogens, so there is that simple coincident aspect. However, there's more to it than that.

EHV-1 has a predilection for the cells that line the blood vessels (endothelial cells). In the process of replicating within these cells, the virus damages the cells; blood clots then form within the vessel, blood leaks out of the damaged vessel into the surrounding tissues, and the tissues downstream may lose their blood supply. With the neuropathic strains, it is the endothelial cells of the central nervous system that are most severely affected. (The abortigenic strains are more drawn to the placenta and the fetus.)

In addition to direct viral damage of the endothelial cells, particles of virus stuck to virus-neutralizing antibody (called antigen-antibody complexes) can also damage the endothelial cells and cause the same tissue-destructive effects. So, at least in theory, high levels of EHV-1 specific antibody in the bloodstream when there also are high levels of virus in the bloodstream may make endothelial damage, and neurologic disease, even more likely.

Thus, vaccination in the face of an outbreak doesn't make sense to me for at least three reasons: (1) the current vaccines do not effectively protect against neurologic herpes; (2) specific immunity following vaccination takes several days (probably more like 2 weeks) to peak, and much longer than the incubation period for EHV-1 infection; and (3) high circulating levels of antibody may actually contribute to this disease.

A lot of research is being done in the field of EHV-1 vaccine technology. Of particular interest to researchers is the development of vaccines which stimulate specific, protective, and long-lasting cell-mediated immunity against all neuropathic strains, including this new one. In the meantime, quarantine, good hygiene, frequent monitoring, and antiviral drugs are serving us fairly well when instituted early in an outbreak.

Action plan for neurologic herpes

If you are a barn owner or manager and you suspect a horse at your facility has neurologic herpes, call your veterinarian immediately. Let her know you may have a case of neurologic herpes in the barn. While awaiting the results of the diagnostic tests, here are some initial steps to follow, to limit the spread of the virus through your facility and beyond:

1. Implement a complete quarantine order immediately. Err on the side of caution, risk being very unpopular for awhile, risk being wrong, and put your foot down; for the good of all, *no horses in or out* until diagnostic tests for EHV-1 have been completed. No exceptions.
2. Separate the infected, suspect, and already-exposed horses from the unexposed horses as best you can with the facilities you have. This virus, while highly infectious, doesn't get very far on its own, as it cannot live for very long outside the body. Respiratory secretions (e.g. nasal discharges) are among the most infectious of materials. Fortunately, coughing is uncommon with EHV-1 infection, so transmission by air is limited to just a few feet. This virus is primarily spread through direct horse-to-horse contact and by human hands, shared halters, feeders, water troughs, etc. Quarantine and good hygiene practices generally are enough to limit its spread.
3. Instruct every member of your barn staff and all boarders on good hygiene practices. No sharing of anything between horses, avoid unnecessary contact with horses, and cleanse your hands with warm, soapy water or one of those waterless hand sanitizers after touching an infected or exposed horse. Make sure all of the horses are well care for, particularly the sick ones, who may need extra

- nursing care; just be careful about spreading infective material to other horses.
4. Monitor all horses on the premises for fever at least once a day, preferably morning and night. (The normal rectal temperature for an adult horse at rest is in the range of 99–101°F. Anything above 101.5°F is suspicious, unless the horse recently exercised, in which case you should take the temperature again a couple of hours later.) Call your veterinarian for any new cases with fever or neurologic signs.
 5. Follow your veterinarian's directions regarding quarantine and management within your facility. Do not lift the quarantine until your vet gives the all-clear.

In closing, neurologic herpes can be a very bad deal for the horses affected and the people involved. But as newsworthy as these outbreaks are, they tend to be very well contained through prompt action and common sense. Remember, too, that the best defense against any infectious disease is a healthy, happy horse.

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