

Merck Animal Health Equine Respiratory Update

IN COLLABORATION WITH THE UNIVERSITY OF CALIFORNIA, DAVIS SCHOOL OF VETERINARY MEDICINE

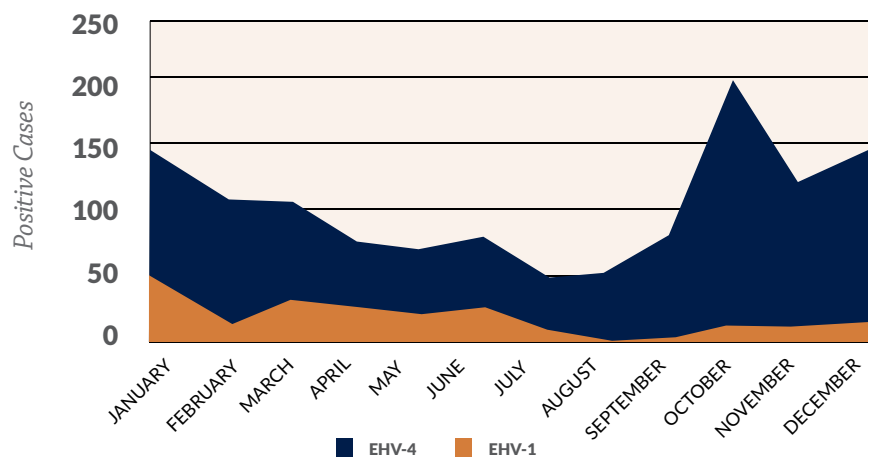
Discerning differences between EHV-1 and EHV-4

There's no question the herpesviruses are among our most challenging infectious respiratory diseases of the horse. More than 80% of horses are exposed to equine herpesvirus-1 (EHV-1) or equine herpesvirus-4 (EHV-4) in the first two years of life.^{1,2} And once infected, always infected. Subclinical or 'silent' shedding of these viruses presents an ever-present threat to our equine populations.

EHV-1 sparks urgency and concern because of its infectious respiratory nature and potential to cause abortions in breeding herds, as well as the risk of equine herpesvirus myeloencephalopathy (EHM). Approximately 10% of EHV-1-infected horses develop neurological signs during EHM outbreaks.³ EHV-4, on the other hand, seems to run rampant behind the headlines, telling a story of its own as the most common infectious upper respiratory disease of the horse (Figures 1 and 2).⁴ Both diseases have been monitored since the Biosurveillance Program began in 2008, allowing us to keep a close eye on the frequency of disease cases.

If you are a Biosurveillance Program participant, you've likely received a report from the UC Davis Equine Infectious Disease Research Laboratory with a positive diagnosis for EHV-1 or EHV-4. If

FIGURE 1: EHV-1 and EHV-4 Seasonal Disease Incidence⁴
Monthly Cumulative 2008-2020
EHV-1, EHV-4



the horse was vaccinated in the last six months, frustration abounds—an assumption of vaccine failure despite best preventive efforts. Let's look at why this may have happened.

Managing key characteristics: Latency and reactivation

EHV-1 and EHV-4 are closely related alpha herpesviruses but are antigenically and genetically different. They may enter a cell through a lytic cycle, leading to an infection, or a latent cycle, which leads to establishment of long-term infection. Each can occur in parallel or independent of one another. Latency provides a mechanism for maintenance of a virus in an infected herd/individual or a reservoir of infection through reactivation to a

new herd/individual. Reactivation is triggered through periods of stress like transportation, weaning, housing changes and major life events, to name a few.

Recrudescence (reactivation) is commonly asymptomatic and often results in 'silent' shedding of the virus. Upon reactivation, latent virus translocates to respiratory epithelium, leading to viral shedding and/or establishment of a new infection—with or without viremia—that can lead to reproductive or neurologic impact through endothelial cell infection. Viremia is a common event for an EHV-1 infection, which may lead to virus dissemination to the uterus and/or the central nervous system.

Merck Animal Health Equine Respiratory Update

Viremia is NOT a common event for an EHV-4 infection, except for a rare highly virulent strain. Therefore, EHV-4 is less likely to lead to an abortion or neurologic case.

Sterile immunity is not a reasonable expectation for a herpesvirus vaccination program, unlike tetanus and rabies. Biannual vaccination will aid in the reduction of disease severity and viral shedding, but due to the nature of the equine herpesvirus, vaccination will most likely not eliminate disease. Timing of the biannual booster vaccination may be beneficial in disease reduction when anticipating stress-triggering events. EHV-1/4 are commonly diagnosed from October to January.⁴ EHV-4 is particularly prevalent in October and December. In fact, EHV-4 represents 21% of all October positive disease cases since the Biosurveillance Program began (Figure 3), and 39% of those October EHV-4 cases occurred in weanlings (6 months to 1 year of age). Of all EHV-4 cases, 60% occurred in horses 5 years of age and younger.⁴

Considering increased seasonal disease incidence, moving biannual vaccination for EHV-1/4 to December/January and August/September may be advisable to get ahead of spikes.

Did you know?

Nine equine herpesviruses are characterized worldwide in domestic and wild equid populations. Only EHV-1, EHV-2, EHV-3, EHV-4 and EHV-5 are found in domestic horses.

In addition to biannual revaccination, biosecurity measures become paramount to disease management, with the following goals:

- Prevent entry of disease on premises through isolation of new/returning arrivals;
- Limit disease spread and severity of clinical signs;
- Limit disease spread to adjoining premises.

Knowledge is power

Equine herpesvirus is a frustrating disease and it's unfortunately not something we can eliminate from our horse populations. But we have the tools to keep it in check, and properly timed biannual vaccination could be one of the best lines of defense when coupled with proper risk mitigation strategies. *With rapid diagnostic testing available through the Biosurveillance Program, you know specifically what disease you're dealing with and can adjust and modify management practices accordingly.* ●



REMINDER: SAMPLE LABELING IS CRITICAL

Before submitting your next sample, **please confirm the nasal swab and blood tube samples are properly labeled.** The name on the label should be consistent with the name on the accompanying paperwork. A first and last name is preferred to help distinguish two horses with the same name. This will help us more readily identify samples to ensure you get timely lab results. Thank you!

From our friends at the UC Davis PCR Laboratory

¹Slater J. Equine herpesviruses. In: Sellon DC, Long MT, eds. *Equine Infectious Diseases*. 2nd ed. Saunders Elsevier; 2014:151-168.

²Pusterla N, Hussey GS. Equine herpesvirus 1 myeloencephalopathy. *Vet Clin North Am Equine Pract*. 2014 Dec;30(3): 489-506. doi: 10.1016/j.cveq.2014.08.006. Epub 2014 Oct 7

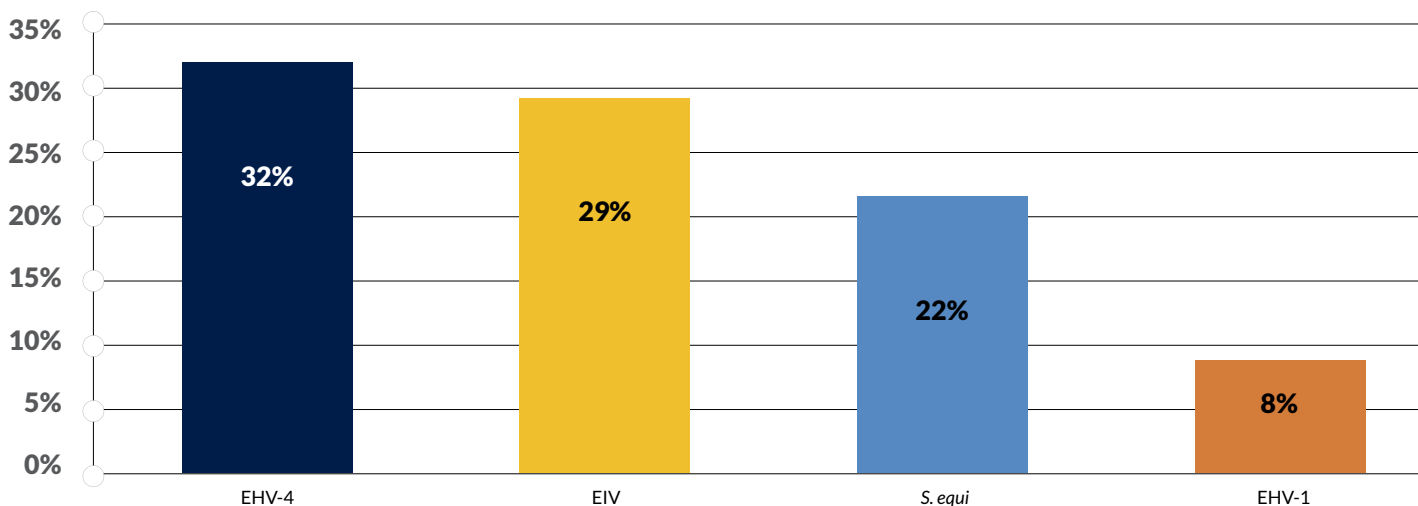
³Equine Herpesvirus-1 Consensus Statement. *J Vet Intern Med* 2009; 23:450-461.

⁴Merck Animal Health and University of California, Davis School of Veterinary Medicine (Nicola Pusterla). Infectious Upper Respiratory Disease Surveillance Program. Ongoing research 2008-present.

FIGURE 2: Biosurveillance Program Disease Incidence March 2008-December 2020⁴

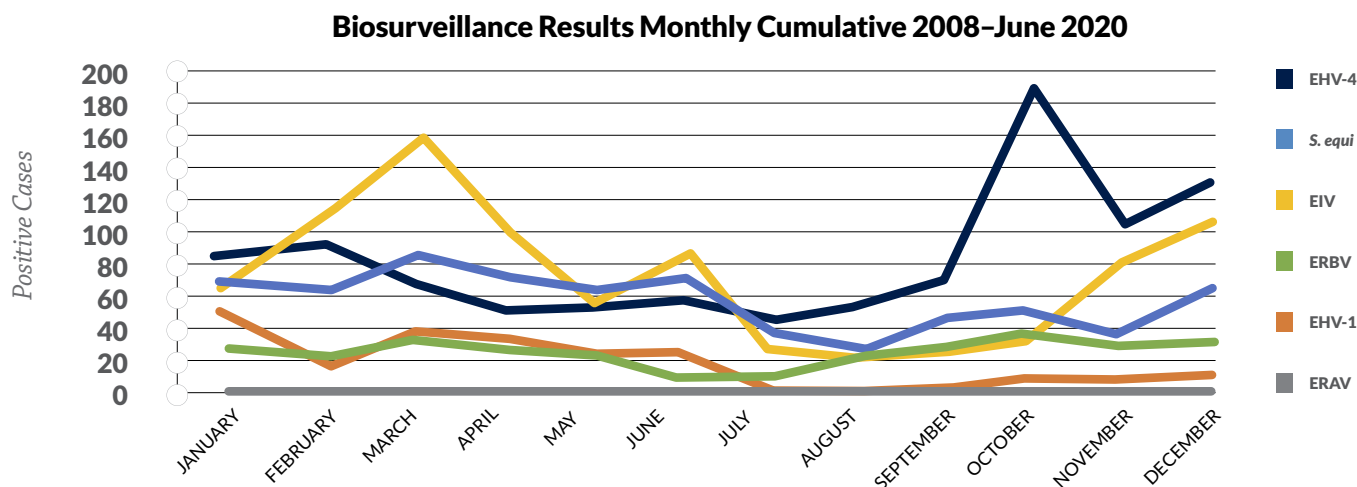
More than 9,700 samples have been collected since the Biosurveillance Program began nearly 13 years ago. Of those, 32% have returned positive for one of six pathogens tracked, including equine herpesvirus types 1 and 4 (EHV-1, EHV-4), equine influenza virus (EIV) and *Streptococcus equi* subsp. *equi*, which have been tracked from the inception of the program, and equine rhinitis A/B viruses (ERAV/ERBV), which were added in 2012.

Disease Incidence 2008–2020¹
(As a percentage of total positive samples)



Through December 2020, EHV-4 was the most diagnosed infectious upper respiratory disease, comprising 32% of all positive samples, followed closely by EIV at 29% and then S. equi at 22%.

FIGURE 3: Seasonal Incidence of Equine Infectious Upper Respiratory Disease⁴

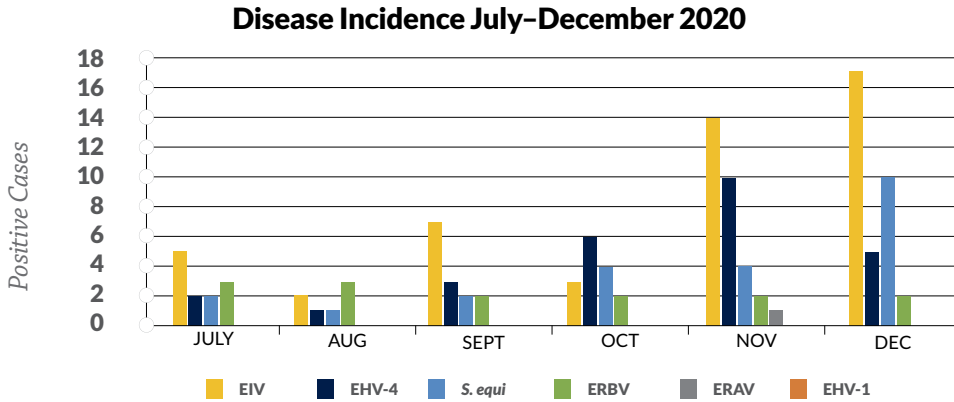


The monthly cumulative depicts the seasonal effect of respiratory pathogens spanning 148 months—nearly 13 years—of surveillance. EHV-4 continues to be more prevalent in the fall months, in contrast to the other respiratory pathogens (especially EIV) that are more prevalent in the winter and spring months.

⁴Merck Animal Health and University of California, Davis School of Veterinary Medicine (Nicola Pusterla). Infectious Upper Respiratory Disease Surveillance Program. Ongoing research 2008-present.

FIGURE 4: Six-Month Disease Trends July to December 2020⁴

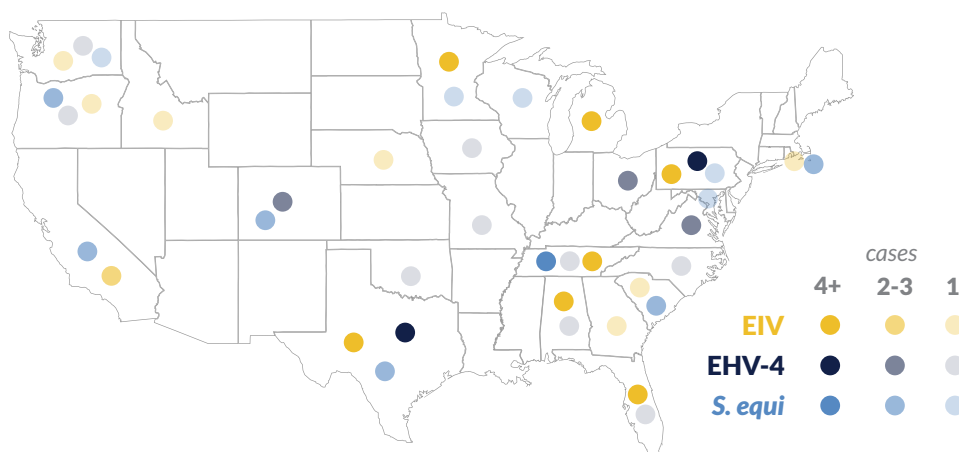
A total of 328 samples were submitted from July to December 2020. Overall, 34% of total samples submitted tested positive for one of the six primary pathogens (*S. equi*, EHV-4, EIV, ERBV, EHV-1, ERAV).



The most recent six months of data (July to December 2020) identifies EIV as the most prevalent infectious upper respiratory disease reported, followed by EHV-4 and *S. equi*.

TABLE 1: Primary Demographic Parameters for the Three Major Pathogens (July–December 2020)⁴

Demographic Summary	EIV (48 cases)	EHV-4 (27 cases)	<i>S. equi</i> (23 cases)
Median Age	7 years Range: 1 month – 22 years	4 years Range: 5 months – 23 years	10.5 years Range: 2.5 years – 21 years
Predominant Breed(s)	Quarter Horse	Quarter Horse	Quarter Horse Pony/Mini
Travel	Yes 48% No 44% Unknown 8%	No 63% Yes 30% Unknown 7%	No 65% Yes 22% Unknown 13%
Primary Discipline	Pleasure 44% Show 31% Other/Unknown 25%	Show 40% Pleasure 30% Other/Unknown 30%	Pleasure 74% Show 9% Other/Unknown 17%

FIGURE 5: Geographic Representation of the Three Major Pathogens July–December 2020

Map represents states with positive cases of EIV, EHV-4 and *S. equi*. During the reporting period (July–December 2020), EHV-1 cases were not represented. During ensuing months, EHV-1 cases were noted in the U.S. as well as other international venues. EHV-1 remains an important pathogen monitored through the Biosurveillance Program.

⁴Merck Animal Health and University of California, Davis School of Veterinary Medicine (Nicola Pusterla). Infectious Upper Respiratory Disease Surveillance Program. Ongoing research 2008–present.

The Art of Medicine

By **Fairfield T. Bain, DVM, MBA, DACVIM, DACVP, DACVECC**

Working up a febrile horse provides a fundamental reminder of the most basic—and important—diagnostic tool: The physical exam

Sight, hearing, touch. We've been gifted with these powerful senses and put them to use every day examining horses. This artful combination of sense and skill is one of the things I love most about equine medicine. There are times, however, when time is not on our side and the ability to put our hands on the horse and perform a thorough physical exam is limited. When we're in a hurry, it's easy to overlook things or jump to diagnostic tools too quickly. Yet, I would argue the greatest diagnostic method at our disposal is the physical exam. Let's play this out in working up a suspected febrile horse.

SENSE

1. **Sight.** What clinical appearance would lead you to consider the horse has a fever? Does the horse have a runny nose or eyes? What kind of runny nose is it? What do you notice about the horse's demeanor?
 - a. Don't forget that some of the encephalitis diseases (especially EEE and WNV) cause fever and initially have no specific clinical signs other than vague signs like depression or somnolence.

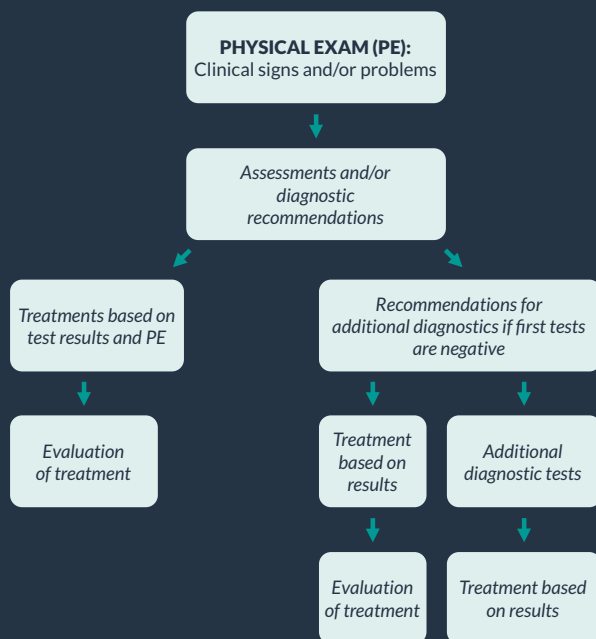
2. **Touch. Hearing.** Perform a complete assessment of physical exam features, including lung and abdominal sounds. Does the horse have an easily induced cough or labored breathing? Are the lymph nodes swollen?

SKILL

3. Regardless of whether you suspect a fever, taking a horse's temperature should always be part of the physical examination. It is the most valuable aspect of the exam.
4. What is the pathophysiology of fever? A stimulus has triggered a response—in this case, elevated temperature. A fever usually tells us the horse is fighting an infection of some kind. Our task is to find the cause.
5. Based on clinical assessments, a likely next step is a complete blood count to hunt down common ailments first.

- a. Ultrasound has become a critical rapid diagnostic evaluation of body cavities (chest and abdomen).
 - b. Traditionally, fibrinogen has been the standard laboratory measurement to indicate some evidence of active inflammation, but its time-course to rise above reference range concentrations is at least 12-24 hours.
 - c. Serum amyloid A (SAA) is a relatively newer test that can detect onset of an inflammatory stimulus as early as six hours. SAA is available as a point-of-care test so it can be a useful on-the-scene tool. The profession is still learning how to apply SAA in disease detection and management.
6. With a fever detected and other clinical signs identified, using the diagnostic algorithm (Figure 6), what specific tests should be chosen to detect specific pathogens?
 - a. Depends on site of disease (chest versus gastrointestinal tract), then age groups and situations. Occasionally, cancer can cause fever—usually advanced cancer that is invading the intestinal tract, like lymphoma.

Figure 6: Basic Diagnostic Algorithm



The Art of Medicine (continued)

7. Molecular diagnostics generally offer more rapid respiratory and gastrointestinal (GI) infectious disease detection.
8. Certain bacterial pathogens, particularly respiratory, may require bacterial culture via tracheal wash. This culture is valuable for antimicrobial agent selection.
 - a. Do not overlook the value of cytology as an on-the-scene evaluation of tracheal wash samples for detection and characterization of bacterial agents. This is important when the horse is febrile and not demonstrating easily detectable respiratory signs.
9. In younger foals, *Rhodococcus equi* is an important pathogen. Cytology and culture are very valuable in guiding therapy.
10. GI disorders, particularly *Salmonella* and enteric viral diseases (rotavirus in foals and coronavirus in both foals and adults), can be rapidly detected by molecular panels. This is especially important when the animal is febrile and has not developed signs of diarrhea.
11. Keep regional considerations in mind. For example, a febrile horse in Florida in early spring or summer may be more of an encephalitis concern than a respiratory concern.
12. Lastly, there are some situations where elevated body temperature is an issue—thermoregulatory problems like anhidrosis (predominantly in the hot South) and drug reactions (more common when earlier erythromycin and related drugs were used for *R. equi* in foals), so the difference between true fever and hyperthermia can occasionally be something to recognize and understand mechanistically. ●

New ways to detect fever: More than a microchip

Newer microchips, like Bio-Thermo®, have a built-in temperature monitoring system that makes regular body temperature readings easier and safer for the owner or barn manager. When partnered with the **EquiTrace™ app**, the horse's temperature is instantly recorded, allowing rapid identification of disease and daily health monitoring. Contact your Merck Animal Health sales representative to learn more about the unique combination of the Bio-Thermo microchip and EquiTrace app.

Client Reminder:

Temperature should be monitored at least twice daily if the horse is showing clinical signs or at an event/show.

Owner Tips

Equine herpesvirus has been in the news lately. To help answer questions and educate clients, don't forget our downloadable equine herpesvirus Quick Facts. Download and share or link directly to them from your social media or other digital client communications:

- [EHV-1](#) and [EHV-4](#) Quick Facts (one for each)
- [EHM](#) Quick Facts

EQUINE HERPESVIRUS TYPE 4 (EHV-4) QUICK FACTS

Equine herpesvirus type 4 (EHV-4) is the most common infectious equine respiratory disease in the horse. It is endemic in many equine populations.

Watch for These Signs:

- Respiratory distress
- Stress-induced abortion
- Neurological signs
- Edema of the lower limbs
- Colic
- Diarrhea
- Urticaria
- Neurological signs

Diagnosis:

- PCR
- ELISA
- Immunofluorescence
- Immunoblotting
- Immunohistochemistry
- Antigen detection
- Antibody detection
- Antigen detection
- Antibody detection

Treatment and Recovery:

- Supportive care
- Fluid therapy
- Antibiotics
- Antiviral drugs
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Corticosteroids
- Anticoagulants
- Antithrombotics
- Antispasmodics
- Anticonvulsants
- Antiepileptics
- Anticholinergics
- Antidysrhythmics
- Antidysrhythmics
- Antidysrhythmics

REMEMBER: Vaccination + Biosecurity is Best!

VACCINATION IS THE #1 WAY TO PROTECT YOUR HORSE AGAINST EHV-4

REMEMBER: Vaccination + Biosecurity is Best!

VACCINATION + BIOSECURITY IS THE BEST WAY TO PROTECT YOUR HORSE AGAINST EHV-4

Additional information:

- Equine herpesvirus type 4 (EHV-4) is a member of the Herpesviridae family.
- EHV-4 is a DNA virus.
- EHV-4 is a single-stranded DNA virus.
- EHV-4 is a member of the Herpesviridae family.
- EHV-4 is a DNA virus.
- EHV-4 is a single-stranded DNA virus.

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EQUINE HERPESVIRUS MYELOENCEPHALOPATHY (EHM) QUICK FACTS

Equine herpesvirus myeloencephalopathy (EHM) is a neurological disease of horses caused by equine herpesvirus type 1 (EHV-1).

Risk Factors:

- Stress
- Immune suppression
- Close contact with infected horses
- Transportation
- Large group housing
- Stable dust
- Stable flies
- Stable flies
- Stable flies
- Stable flies

Watch for These Signs:

- Neurological signs
- Ataxia
- Paralysis
- Colic
- Diarrhea
- Urticaria
- Neurological signs

Diagnosis:

- PCR
- ELISA
- Immunofluorescence
- Immunoblotting
- Immunohistochemistry
- Antigen detection
- Antibody detection
- Antigen detection
- Antibody detection

Treatment and Recovery:

- Supportive care
- Fluid therapy
- Antibiotics
- Antiviral drugs
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Corticosteroids
- Anticoagulants
- Antithrombotics
- Antispasmodics
- Anticonvulsants
- Antiepileptics
- Anticholinergics
- Antidysrhythmics
- Antidysrhythmics
- Antidysrhythmics

REMEMBER: Vaccination + Biosecurity is Best!

VACCINATION + BIOSECURITY IS THE BEST WAY TO PROTECT YOUR HORSE AGAINST EHM

Additional information:

- Equine herpesvirus myeloencephalopathy (EHM) is a neurological disease of horses caused by equine herpesvirus type 1 (EHV-1).
- EHM is a DNA virus.
- EHM is a single-stranded DNA virus.
- EHM is a member of the Herpesviridae family.
- EHM is a DNA virus.
- EHM is a single-stranded DNA virus.

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EQUINE HERPESVIRUS TYPE 1 (EHV-1) RESPIRATORY AND REPRODUCTIVE DISEASE QUICK FACTS

Equine herpesvirus type 1 (EHV-1) is a member of the Herpesviridae family. It is a DNA virus. EHV-1 is a single-stranded DNA virus. EHV-1 is a member of the Herpesviridae family.

General Facts:

- Equine herpesvirus type 1 (EHV-1) is a member of the Herpesviridae family.
- EHV-1 is a DNA virus.
- EHV-1 is a single-stranded DNA virus.
- EHV-1 is a member of the Herpesviridae family.
- EHV-1 is a DNA virus.
- EHV-1 is a single-stranded DNA virus.

Watch for These Signs of Respiratory and Reproductive Disease:

- Respiratory distress
- Stress-induced abortion
- Neurological signs
- Edema of the lower limbs
- Colic
- Diarrhea
- Urticaria
- Neurological signs

Diagnosis:

- PCR
- ELISA
- Immunofluorescence
- Immunoblotting
- Immunohistochemistry
- Antigen detection
- Antibody detection
- Antigen detection
- Antibody detection

Treatment and Recovery:

- Supportive care
- Fluid therapy
- Antibiotics
- Antiviral drugs
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Corticosteroids
- Anticoagulants
- Antithrombotics
- Antispasmodics
- Anticonvulsants
- Antiepileptics
- Anticholinergics
- Antidysrhythmics
- Antidysrhythmics
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REMEMBER: Vaccination + Biosecurity is Best!

VACCINATION IS THE #1 WAY TO PROTECT YOUR HORSE AGAINST EHV-1 RESPIRATORY AND REPRODUCTIVE DISEASE

REMEMBER: Vaccination + Biosecurity is Best!

VACCINATION + BIOSECURITY IS THE BEST WAY TO PROTECT YOUR HORSE AGAINST EHV-1 RESPIRATORY AND REPRODUCTIVE DISEASE

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About the Newsletter

This biannual newsletter provides information generated through and related to the Biosurveillance Program. Merck Animal Health is passionate about this program and is providing this newsletter to customer veterinarians to help them stay up to date on the latest trends and historical information the study has yielded to date. Technical veterinary advice, interpretation and case management support will be provided by Merck Equine Veterinary Professional Services and Nicola Pusterla, DVM, PhD, DACVIM, Department of Medicine and Epidemiology, UC Davis.

If you have questions about the program or **to request past issues of the newsletter**, please call our team at (866) 349-3497, or email us at the addresses listed below.

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Relevant Supporting Research

For more information on the latest respiratory disease published research from Merck Animal Health, click on the links below.

- 1) [“Prevalence Factors Associated with Equine Influenza Virus Infection in Equids with Upper Respiratory Tract Infection from 2008 to 2019.”](#)
 Vaala W, Barnett DC, James K, Chappell D, Craig B, Gaughan E, Bain F, Barnum SM, Pusterla N. *AAEP Proceedings*. 2019 Vol 65.
- 2) [“Prevalence Factors Associated with EHV-2/5 Among Equines with Signs of Upper Respiratory Infection in the US.”](#)
 James, K., Vaala, W., Chappell, D., Barnett, D.C., Gaughan, E., Craig, B., Bain, F., Pusterla, N. *ACVIM* 2017 Abstract.
- 3) [“Prevalence factors associated with equine herpesvirus type 1 infection in equids with upper respiratory tract infection and/or acute onset of neurological signs from 2008 to 2014”](#)
 Pusterla, N., Mapes, S., Akana, N., Barnett, D.C., Mackenzie, C., Gaughan, E., Craig, B., Chappell, D., Vaala, W. *Vet Rec*. 2015; doi: 10.1136/vr.103424.
- 4) [“Voluntary Surveillance Program for Equine influenza Virus in the United States from 2010 to 2013”](#)
 Pusterla, N., Kass, P.H., Mapes, S., Wademan, C., Akana, N., Barnett, D.C., Mackenzie, C., Vaala, W. *J Vet Intern Med* 2015; 29:417-422
- 5) [“Surveillance programme for important equine infectious respiratory pathogens in the USA”](#)
 Pusterla, N., Kass, P.H., Mapes, S., Johnson, C., Barnett, D.C., Vaala, W., et. al. *Vet Rec*. 2011 July 2;169(1):12. doi: 0.1136/vr.d2157.
- 6) [“Voluntary surveillance program for important equine infectious respiratory pathogens in the United States”](#)
 Pusterla, N., Kass, P.H., Mapes, S., Johnson, C., Barnett, D.C., Vaala, W., Gutierrez, C., et. al. *AAEP Proceedings* 2010.

About the Program

Since March of 2008, Merck Animal Health has been conducting an ongoing, voluntary equine biosurveillance program to study the prevalence and epidemiology of relevant viral and bacterial respiratory pathogens. More than 9,700 samples from U.S. equids of all ages, genders and breeds presenting with fever and signs of acute upper respiratory disease and/or acute neurological disease have been collected since the study began. Samples are submitted by participating Merck Animal Health customer clinics and tested via quantitative PCR at the University of California, Davis School of Veterinary Medicine (UC Davis). **To be eligible for testing, horses must have an unexplained fever (T ≥ 101.5°F) AND one or more of the following signs: Depression, nasal discharge, cough, and/or acute onset of neurologic disease.** The results are then returned to the Merck Animal Health customer within 24 hours and provide invaluable diagnostic and treatment information.

Four-Fold Purpose:

- 1) To provide a valuable diagnostic tool to participating Merck Animal Health customers to assist in obtaining an accurate and timely diagnosis during an acute respiratory disease outbreak so they can provide optimal treatment, quarantine and vaccination strategies to their clients and patients.
- 2) To provide the horse industry with a better understanding of the prevalence and epidemiology of these respiratory pathogens.
- 3) To identify and monitor the current circulating strains of major equine respiratory pathogens.
- 4) To evaluate the efficacy of current vaccination protocols.



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