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Merck Animal Health Equine Respiratory Update

In Collaboration with University of California, Davis School of Veterinary Medicine

EHV-4's Hidden Threat to Young Horses

Biosurveillance Program research presented at the 2024 AAEP Convention suggests EHV-4 may not be restricted to the respiratory tract

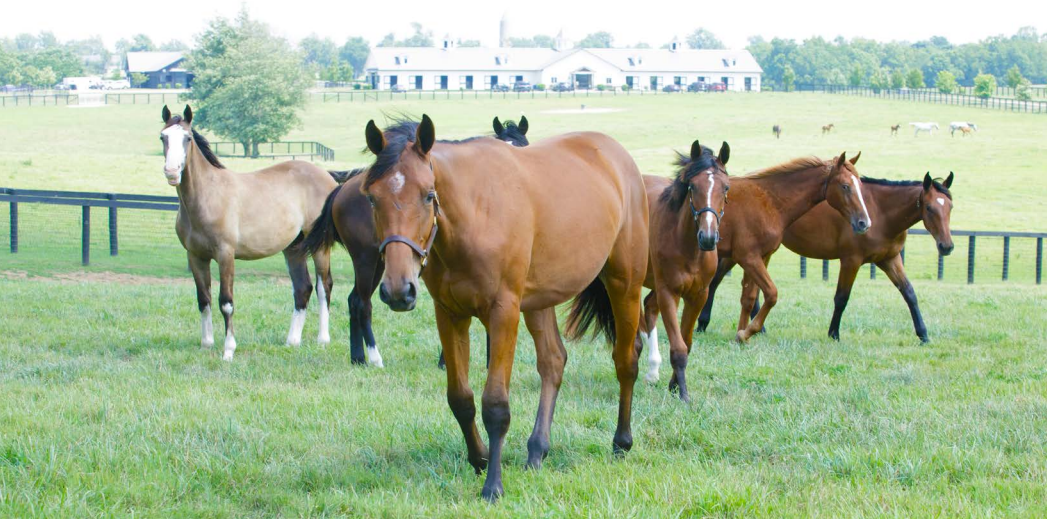
Equine herpesvirus-4 (EHV-4) has long been recognized as a common cause of respiratory illness in young horses, often resulting in mild symptoms like fever, nasal discharge and occasional lethargy. However, recent research led by Dr. Nicola Pusterla of the University of California, Davis, sheds new light on how this virus may occasionally behave more aggressively than previously thought.

In a study of 183 horses with acute fever and respiratory signs, only 13.7% of those who tested positive for EHV-4 in nasal swabs also had the virus detected in their bloodstream (viremia)[1]. This is a stark contrast to equine herpesvirus-1 (EHV-1), where viremia is expected in nearly all infected horses. "EHV-4 just doesn't have the same ability as EHV-1 to invade the bloodstream," explains Dr. Pusterla. "This likely accounts for why we don't see EHV-4 causing complications like abortion or myeloencephalopathy."

EHV-4 viremia was only found in horses already shedding the virus through nasal secretions. None of the control horses tested positive for EHV-4 in their blood. This indicates that viremia is closely tied to active viral shedding, reinforcing that blood testing may only be relevant in confirmed shedding cases.

Why viremia matters

Although rare, the detection of EHV-4 in the blood raises important clinical considerations. Viremia suggests the virus can move beyond the respiratory tract, potentially affecting other organ systems. Notably, younger horses were more likely to be viremic and showed a higher incidence of distal limb edema—a finding that surprised researchers. "We observed that young, viremic horses were more prone to developing limb edema," says Dr. Pusterla. "While the exact cause is speculative, it may be due to viral replication in endothelial cells."



Clinical takeaways

This research offers a few practical insights:

1. **Monitor young horses closely:** Younger horses with fever and respiratory signs should be watched carefully for signs beyond the respiratory tract, like limb swelling.
2. **Consider blood testing in severe cases:** While routine blood testing for EHV-4 isn't necessary, it could be informative in young horses showing more severe or unusual clinical signs, especially when nasal shedding is confirmed.
3. **Watch for co-infections:** Horses with EHV-4 may also be battling other respiratory pathogens, which could worsen clinical signs. Comprehensive diagnostic testing might be warranted in more severe cases.
4. **Biosecurity still matters:** Even though EHV-4 complications are rare, biosecurity measures and vaccination protocols should remain a priority, especially in facilities housing young stock.

[1]Pusterla N, Barnum S, Lawton K, Craig B, James K. (2024). *Investigation of the frequency and selected prevalence factors of EHV-4 viremia in horses with acute onset of fever and respiratory signs.* Proceedings of the American Association of Equine Practitioners, 70, 325-326.

Co-infections complicate the picture

The study also found that over a quarter (27.3%) of EHV-4-positive horses were co-infected with other respiratory pathogens, including equine influenza virus (11%), *Streptococcus equi* subspecies *equi* (10%), equine rhinitis B virus (9%), and even EHV-1 (2%). "Stress and latent infections likely play a role in these co-infections," Dr. Pusterla notes. "And when multiple pathogens are at work, the clinical signs can be more severe."

TAKE HOME MESSAGE

While EHV-4 viremia is uncommon, understanding its potential impact helps veterinarians provide more comprehensive care. "Our findings reinforce that EHV-4 typically causes mild disease, but on occasion, it can cross into the bloodstream and contribute to more complex clinical presentations," says Dr. Pusterla. "Being aware of this can improve how we manage and support affected horses."

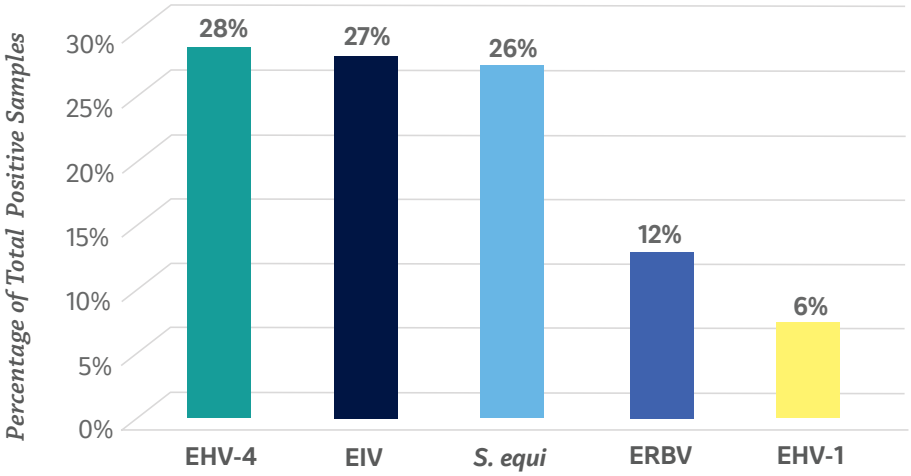
This study offers a timely reminder that even familiar pathogens like EHV-4 can surprise us, underscoring the importance of ongoing research and vigilant clinical observation.

Click to view the AAEP abstract here.

Respiratory Biosurveillance Program Cumulative Disease Trends

More than 12,580 samples have been collected since the Biosurveillance Program began 17 years ago. Of those, 35% 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* subspecies *equi* (*S. equi*), which have been tracked from the inception of the program, and equine rhinitis A/B viruses (ERAV/ERBV), which were added in 2012.

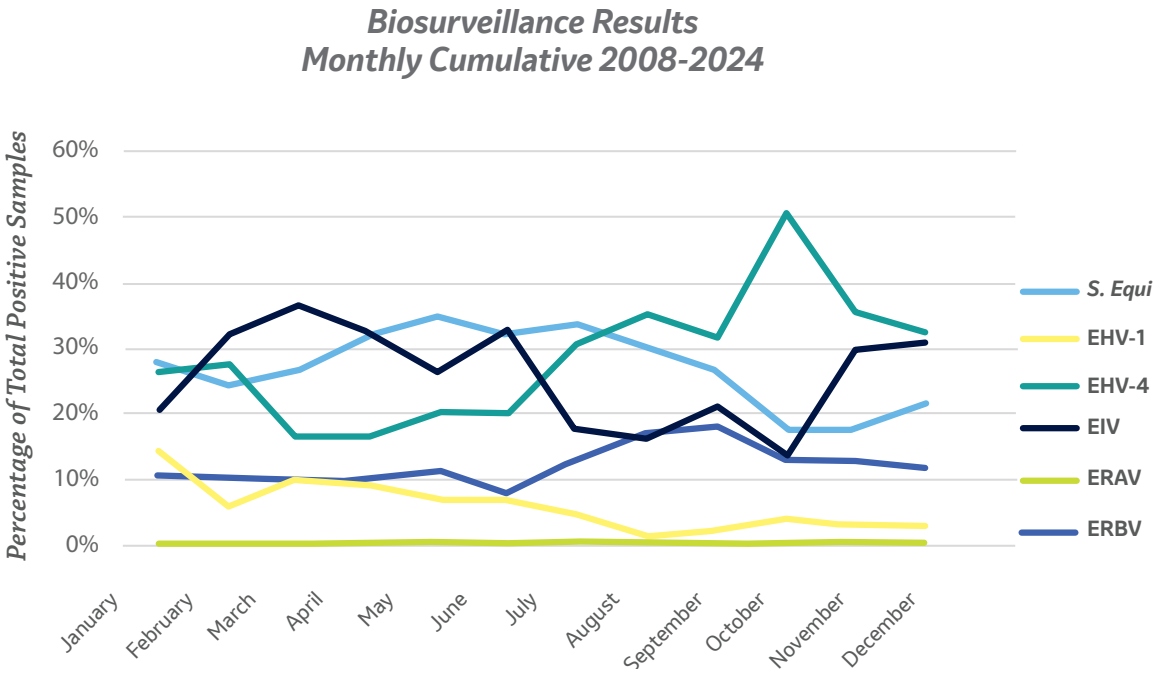
FIGURE 1: Biosurveillance Program Disease Incidence: March 2008-December 2024[2]



Through December 2024, EHV-4 has edged out EIV and S. equi *as the most diagnosed infectious upper respiratory disease, accounting for 28% of all positive samples. Note, only 0.1% of cases came back positive for ERAV.*

[2] Merck Animal Health and University of California, Davis (Nicola Pusterla). Infectious Upper Respiratory Disease Surveillance Program. Ongoing research 2008–present.

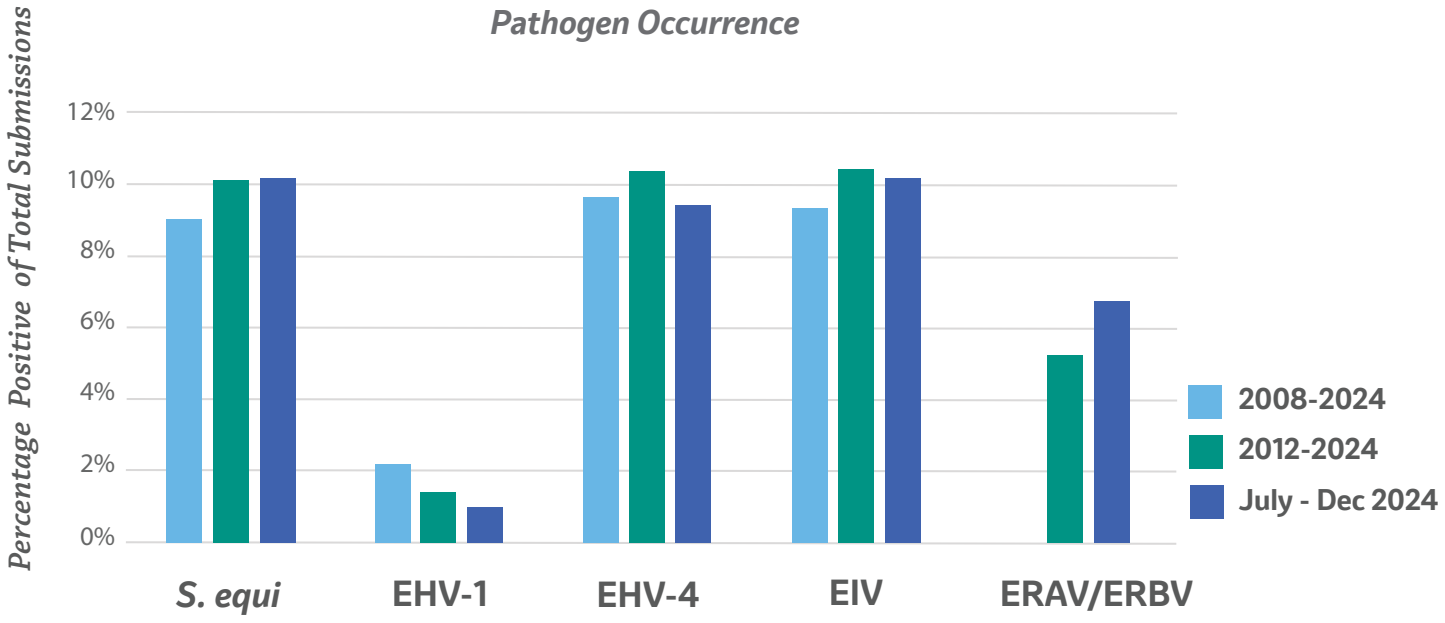
FIGURE 2: Seasonal Incidence of Equine Infectious Upper Respiratory Disease[2]



The monthly cumulative depicts the seasonal effect of respiratory pathogens spanning 17 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.

FIGURE 3: Comparing Long-Term and Recent Disease Patterns[2]

A unique view of pathogen occurrence since the Biosurveillance Program began (March 2008-December 2024), since ERAV/ERBV were added to the panel (October 2012-December 2024) and the last six months (July-December 2024). The "big three" (EHV-4, EIV, *S. equi*) continue to dominate with near equal presence, while ERBV is surging.



Current Six-Month Update

A total of 325 samples were submitted from July to December 2024. Overall, 38% of total samples submitted tested positive for one of the six primary pathogens (*S. equi*, EIV, EHV-4, ERBV, ERAV, EHV-1). During this timeframe, *S. equi* and EIV were the most prevalent upper respiratory diseases reported, followed closely by EHV-4.

FIGURE 4: Disease Incidence July to December 2024[2]

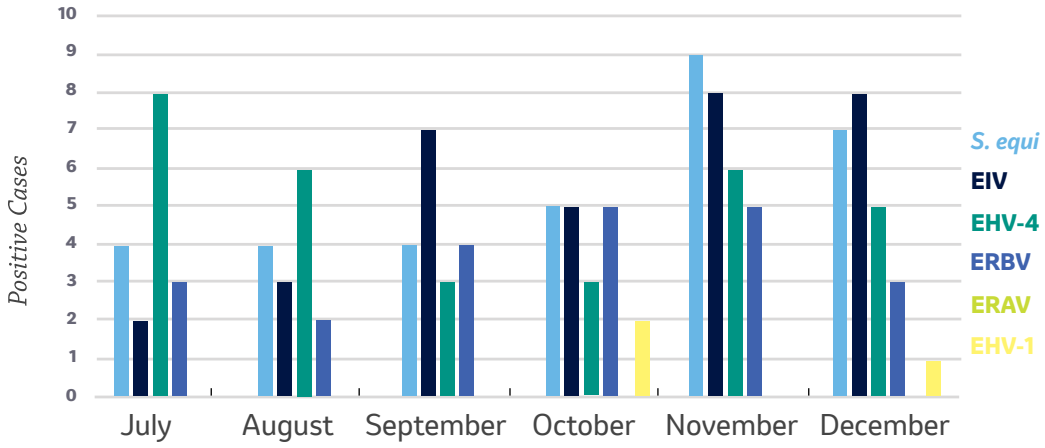


TABLE 1: Primary Demographic Parameters for the Four Major Pathogens (July-December 2024).[2]

Demographic Summary	*S. equi* (33 cases)	EIV (33 cases)	EHV-4 (31 cases)	ERBV (22 cases)
Median Age	**9.5 years** Range: 6 months – 24 years	**6 years** Range: 1 – 24 years	**1 year** Range: 4 months – 22 years	**1 year** Range: 4 months – 25 years
Predominant Breed(s)	**Quarter Horse**	**Quarter Horse**	**Quarter Horse**	**Thoroughbred**
Travel	Yes 39% **No 58%** Unknown 3%	**Yes 58%** No 33% Unknown 9%	Yes 39% **No 61%**	Yes 36% **No 55%** Unknown 9%
Primary Discipline	Show 25% Pleasure 33% **Other/Unknown 42%**	Show 42% Pleasure 12% **Other/Unknown 45%**	Show 39% Pleasure 13% **Other/Unknown 48%**	Show 14% Pleasure 23% **Other/Unknown 63%**

PRACTICE TIPS

Respiratory Pathogen Refresher: EHV-4

As the most common infectious upper respiratory disease in the horse,[2] EHV-4 should be on your radar and that of your owners. Here's a quick review of EHV-4, including links to resources you and your clients may find useful.

EHV-4 typically occurs in younger horses (<5 years of age) but can affect horses of any age. It is highly contagious and spreads via coughing horses, direct and indirect contact, and nasal secretions. Most horses are exposed to the virus at a young age and become latent carriers for life. Disease can be reactivated by stress.

EHV-4 and EHV-1 are of the same family of viruses, but each can cause disease independent of the other. Existence of a carrier state compromises efforts to control EHV-4 and explains why outbreaks of EHV-1 and EHV-4 can occur in closed populations of horses.

- **Seasonal occurrence:** EHV-4 infections typically peak between October and February but can occur year-round.
- **Virus shedding** can occur silently and last for more than 10 days.
- **Incubation period** may be as short as 24 hours, but is typically 4-6 days or longer.
- **Clinical signs** to watch for include fever ranging from 102°F to 107°F, nasal and ocular discharge, lethargy and loss of appetite.
- **Vaccination recommended** every six months for horses at higher risk, including those that travel frequently, interact with large groups or have compromised or immature immune systems. Choose a vaccine that has been shown to be effective against virus shedding of EHV-1 and EHV-4, such as PRESTIGE®.
- **Good biosecurity** is critical to reduce risk of disease spread.

For more information, visit the AAEP guidelines on EHV-1/4.

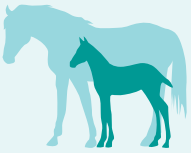
OWNER TIPS

EQUINE HERPESVIRUS TYPE 4 (EHV-4) QUICK FACTS

Equine herpesvirus type 4 (EHV-4) is the most common infectious upper respiratory disease in the horse.[1] It is endemic in many equine populations.

- Disease varies in severity
- Typically occurs in younger horses, but can affect horses of any age
- **Highly contagious** – spread via coughing horses; direct and indirect contact; nasal secretions
- Most horses are exposed to the virus at a young age and become latent carriers for life
- Disease can be reactivated by stress
- Virus shedding can occur silently (without clinical signs) and last for more than 10 days
- After exposure, incubation period may be as short as 24 hours, but is typically 4-6 days or longer
- EHV-4 and EHV-1 are of the same family of viruses, but each can cause disease independent of the other

EHV-4 is a tricky disease. As with EHV-1, existence of a carrier state seriously compromises efforts to control EHV-4 and explains why outbreaks of EHV-1 or EHV-4 can occur in closed populations of horses.



Watch for These Signs

- Fever (102°-107°F)
- Nasal and ocular discharge
- Lethargy
- Anorexia

Diagnosis

- Diagnosis is often performed with a nasal swab that is submitted to a laboratory for polymerase-chain reaction (PCR) testing

Treatment and Recovery

- Supportive care and rest. Non-steroidal anti-inflammatory products such as Banamine® (flunixin meglumine) may be prescribed by your veterinarian
- Recovery depends on severity of disease

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

- EHV-4 typically peaks from October to February, but can occur any time of year[1]
- Horses at risk should be revaccinated at 6-month intervals [2]
  - Horses that travel and are in frequent contact with large numbers of horses
  - Horses at home exposed to traveling horses
  - Horses with compromised or immature immune systems
- The benefits of vaccination:
  - Reduced risk of infection
  - Reduced shedding of virus by infected horses so less virus is circulating in the horse population
  - Reduced severity of clinical signs
  - Less time off exercise, training, competing
  - Lower cost of veterinary treatment

REMEMBER: Vaccination + Biosecurity is Best!

1. **EHV-4 is highly contagious and spreads rapidly**
2. Avoid nose-to-nose contact with other horses
3. **Isolate** all new entries or horses returning to the stable from travel
4. **Check temperatures** at least once and preferably twice daily (Normal = 99°F – 101°F)
5. Isolate any horse with elevated temperature and/or occurrence of unprovoked coughing
6. **Do not share** tack, water buckets, feed sources, etc.
7. Practice **good hand hygiene** (hand sanitizers in absence of soap and water)
8. **Clean and disinfect** hauling equipment like trailers after each use
9. **Contact your veterinarian immediately** to schedule a comprehensive examination

ADDITIONAL INFORMATION

www.equinediseasecc.org/disease-information
www.AAEP.org/guidelines
www.aphis.usda.gov

Talk to your veterinarian today to see if your horse is at risk for EHV-4 and determine the appropriate vaccination program. For more information on the PRESTIGE® line of EHV vaccines, visit www.PrestigeVaccines.com.

[1] Merck Animal Health and University of California, Davis (Nicola Pusterla, DVM). Infectious Upper Respiratory Disease Surveillance Program. Ongoing research 2008–present.
[2] AAEP Risk-Based Vaccination Guidelines (www.aaep.org)

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Click to share these EHV-4 Quick Facts with clients.

About the Newsletter

This biannual newsletter provides information generated through and related to the Biosurveillance Program. Driven by an Unconditional commitment to the horse and those who serve them, Merck Animal Health is providing this newsletter to veterinarians to help them stay up to date on the latest trends and historical information the study has yielded to date. Merck Animal Health Equine Veterinary Professional Services and Nicola Pusterla, DVM, PhD, DACVIM, AVDC-Equine, UC Davis, will provide technical veterinary advice, interpretation and case management support.

If you have questions about the program please call our team at (866) 349-3497, or email us at the addresses listed below. For more information and to access past issues of the newsletter, visit www.Merck-Animal-Health-USA.com.

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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. Investigation of the Frequency and Selected Prevalence Factors of EHV-4 Viremia in Horses with Acute Onset of Fever and Respiratory Signs Pusterla N, Barnum S, Lawton K, Craig B, James K. (2024) Proceedings of the American Association of Equine Practitioners, 70, 325-326.
2. Characterization of Equine Rhinitis B Virus Infection in Clinically Ill Horses in the United States during the Period 2012-2023 Schneider C; James K, Craig BW; Chappell DE; Vaala W; van Harreveld PD; Wright CA; Barnum S; Pusterla N. *Pathogens* 2023, 12, 1324. https://doi.org/10.3390/pathogens12111324
3. Voluntary Biosurveillance of *Streptococcus equi Subsp. equi* in Nasal Secretions of 9409 Equids with Upper Airway Infection in the USA. Jaramillo-Morales, C.; James, K.; Barnum, S.; Vaala, W.; Chappell, D.E.; Schneider, C.; Craig, B.; Bain, F.; Barnett, D.C.; Gaughan, E.; et al. *Vet. Sci.* 2023, 10, 78. https://doi.org/10.3390/vetsci10020078
4. Voluntary Surveillance Program for Equine Influenza Virus in the United States during 2008– 2021. Chappell DE, Barnett DC; James K; Craig B; Bain F; Gaughan E; Schneider C; Vaala W; Barnum SM; Pusterla N. *Pathogens* 2023, 12, 192. https://doi.org/10.3390/pathogens12020192
5. Voluntary Surveillance Program for Equine Influenza Virus in the United States During 2008-2021. Chappell DE, Barnett DC, James K, Craig B, Bain F, Gaughan E, Schneider C, Vaala W, Barnum SM, Pusterla N. *AAEP Proceedings*, 2022, Vol. 68.
6. Frequency of Detection and Prevalence Factors Associated with Common Respiratory Pathogens in Equids with Acute Onset of Fever and/or Respiratory Signs (2008-2021). Pusterla N; James K; Barnum S; Bain F; Barnett DC; Chappell DE; Gaughan E; Craig B; Schneider C; Vaala W. *Pathogens* 2022, 11, 759. https://doi.org/10.3390/pathogens11070759
7. 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.
8. Prevalence Factors Associated with EHV-2/5 Among Equines with Signs of Upper Respiratory Infection in the US. James K, Vaala W, Chappell DE, Barnett DC, Gaughan E, Craig B, Bain F, Pusterla N. ACVIM 2017 abstract.
9. 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 DC, Mackenzie C, Gaughan E, Craig B, Chappell D, Vaala W. *Vet Rec.* 2015; doi: 10.1136/vr.103424.
10. Voluntary Surveillance Program for Equine Influenza Virus in the United States from 2010 to 2013 Pusterla N, Kass PH, Mapes S, Wademan C, Akana N, Barnett DC, Mackenzie C, Vaala W. *J Vet Intern Med* 2015; 29:417-422.
11. Surveillance programme for important equine infectious respiratory pathogens in the USA Pusterla N, Kass PH, Mapes S, Johnson C, Barnett DC, Vaala W, et. al. Vet Rec. 2011 July 2;169(1):12. doi: 0.1136/vr.d2157.
12. Voluntary surveillance program for important equine infectious respiratory pathogens in the United States Pusterla N, Kass PH, Mapes S, Johnson C, Barnett DC, Vaala W, Gutierrez C, et. al. AAEP Proceedings 2010.

About the Biosurveillance 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. Nearly 12,580 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: Lethargy, nasal discharge, cough and/or acute onset of neurologic disease.** The results are returned to the Merck Animal Health customer within 24 hours of laboratory receipt of sample 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 recommendations 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.

UC DAVIS VETERINARY MEDICINE

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Subject Line: Spring 2025 Equine Biosurveillance Program Update
Pre-Header: *Learn about new research on EHV-4 viremia and practical tips for managing*

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Equine Professionals Network
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New Insights on EHV-4 Viremia in Young Horses

Novel study documents the frequency of EHV-4 viremia in horses presented for acute onset of fever and respiratory disease. Dr. Nicola Pusterla shares practical tips for managing the disease.

SEE THE FINDINGS

Current 6-Month Infectious Disease Trends

- Disease incidence
- Seasonal effects of respiratory disease
- Demographic patterns for the top four pathogens
- Respiratory disease on the map

Practice Tips: Respiratory Pathogen Refresher

EHV-4 is ever present. Dive into this quick refresher to get a jump on disease management and client education.

Client Education Tool: EHV-4 Quick Facts

An easy-to-share client resource with important takeaways to help keep EHV-4 in check.

READ THE COMPLETE UPDATE

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