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Merck Animal Health Equine Respiratory Update

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

Getting to Know the "Other" Herpesviruses

For some time, we've suspected more than one pathogen at work in the equine respiratory disease complex, among them are the gamma herpesviruses – equine herpesviruses type 2 and 5 (EHV-2, EHV-5). While the clinical importance of EHV-2 and EHV-5 is less clearly defined, there is some evidence suggesting that EHV-2 and EHV-5 may be clinically important as respiratory and ocular pathogens in some situations. It has been speculated that these viruses may downregulate the immune system, making the horse more susceptible to other viral and bacterial infections.

Evaluating data collected from the Merck Animal Health Respiratory Biosurveillance Program, a retrospective study was conducted from September 2012 to May 2016 to characterize associations between demographic factors, clinical signs and potential co-infections with EHV-2/-5 infection amongst a group of 3,030 horses that presented with acute onset of fever and/or respiratory signs. Findings were recently presented by Dr. Wendy Vaala at the 2017 ACVIM Forum, "Prevalence Factors Associated with EHV-2/-5 Among Equines with Signs of Upper Respiratory Infection in the US."

Study Results and Observations

Findings indicate neither EHV-2 nor EHV-5 alone were significant in terms of producing clinical signs. However, co-infection with EHV-2/-5 was more frequently associated with overt signs of respiratory disease. In addition:

- Nasal discharge was only associated with EHV-2/-5 versus infection with EHV-2 or EHV-5 only
- Young horses less than 1 year were less likely to be PCR (+) for EHV-5 alone, yet more likely to be PCR (+) for EHV-2/-5
- Older horses were less likely to be PCR (+) for EHV-2, EHV-2/-5, but more likely to be PCR (+) for EHV-5 alone
- Thoroughbreds were more likely to be dual infected; Warmblood and Draft horses were less likely to be co-infected
- Increased risk of co-infection when multiple animals affected

Infection rate (n=3030):

- EHV-2 only infection: 11%
- EHV-5 only infection: 21%
- EHV-2/-5 co-infection: 28%
- Negative for both EHV-2/-5: 39%

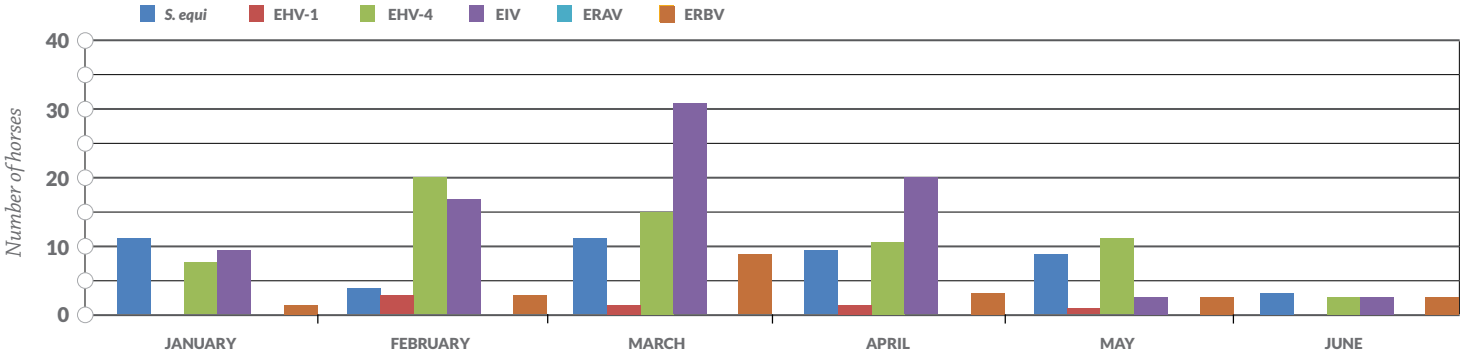
Fast Facts: EHV-2 and EHV-5

- Host-adapted, gamma herpesviruses
- Ubiquitous in horse populations worldwide
- Speculative role as primary pathogens in horses of all ages
- EHV-2 was identified in 1963
  - Implicated in keratoconjunctivitis, upper respiratory tract (URT) disease, fever, general malaise, pharyngitis, and lymphadenopathy in youngsters
- EHV-5 was identified in 1970
  - Implicated in URT disease, equine multinodular pulmonary fibrosis (EMPF)
- Immunomodulatory role: Predisposing or reactivating role for EHV-1, EHV-4 or *R. equi* infections
- EHV-2 and EHV-5 genomes share sequences with human herpesvirus-4 (Epstein-Barr virus)

Disease Trends from January to June 2017[1]

A total of 549 samples were submitted from January to June 2017, as compared to 422 samples submitted during the same timeframe in 2016. Overall, 38% of total samples submitted tested positive for one of the six primary pathogens (*S. equi*, EHV-1, EHV-4, EIV, ERAV, ERBV).

The infection rate from February to April was significantly higher at 50%, as compared to 33% during the same 2016 timeframe. This increased infection rate is likely a result of several factors, according to lead researcher and UC-Davis professor, Nicola Pusterla, D.V.M., Dipl. ACVIM. "We see an increase in infection rates during the colder months of the year, which has to do with a greater number of young horses on the ground, as well as changes in husbandry practices — more horses being kept indoor rather than on pasture."

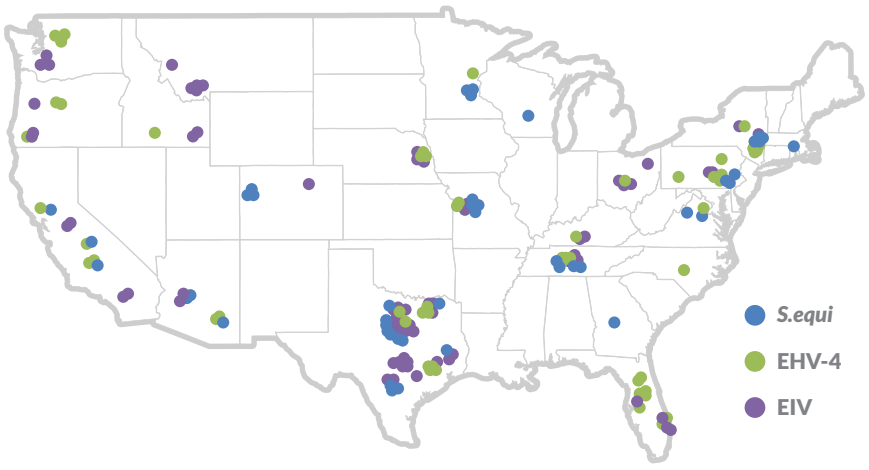


From January to June 2017, ***EIV was the most prevalent infectious upper respiratory disease reported,*** *followed by EHV-4 and* S. equi.

Demographic Summary	EIV (81 Cases)	EHV-4 (67 Cases)	*S. equi* (50 Cases)
Median Age	6 years Range: 6 months – 24 years	6 years Range: 2 months – 27 years	8 years Range: 2 months – 26 years
Predominant Breed	Quarter Horse	Quarter Horse	Quarter Horse
Travel	Yes 48% No 44.5% Unknown 7.5%	Yes 24% No 66% Unknown 10%	Yes 34% No 50% Unknown 16%
Primary Discipline	Pleasure; show	Pleasure	Pleasure; show

This table provides a summary of primary demographic parameters for the three major pathogens (January-June 2017).[1]

This map shows positive EIV, EHV-4, *S. equi* cases from January to June 2017.[1]



Practice Tip

Tips for Improving Quality of Nasal Swab Samples

While collecting nasal swab samples for diagnostic testing may seem routine, there are a few things to keep in mind to ensure a diagnostic-quality sample.

- Swabs affect sample quality — cotton contains pesticide and herbicide residues that act as inhibitors. It is also more difficult to extract cells from cotton. For these reasons, **a synthetic swab with a plastic shaft is ideal.** Remember to collect nasal secretions using **two,** 6-inch rayon swabs.

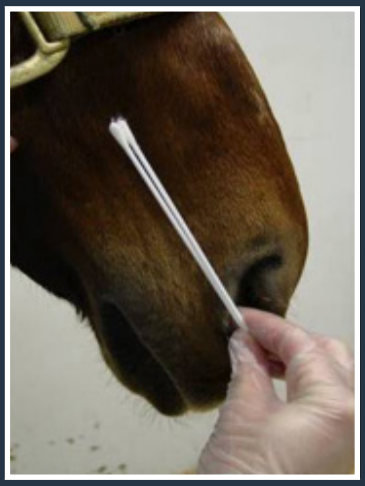
- Any kind of organic material – such as dirt, especially during dry conditions – may also act as an inhibitor. If the nostril or swab looks dirty, you may need to clean the nostril and collect another sample.

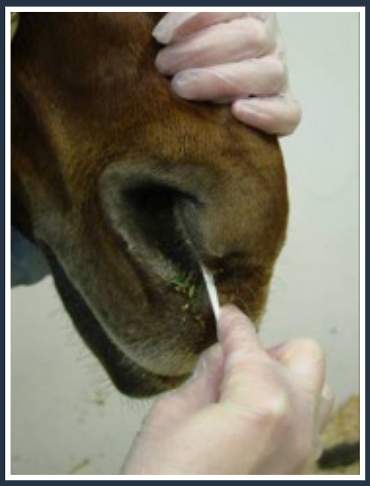
- Sampling from one nostril is sufficient. Insert two swabs at one time. Remember to **allow swabs to soak for 5 to 10 seconds,** while gently rotating swabs.

- Nasopharyngeal swabs generally yield better results for EIV and *S. equi*, whereas there is no difference between nasal and nasopharyngeal collection technique in detecting EHV.

- To optimize the sensitivity of the testing procedures used, it is important to **sample only those horses that are symptomatic. Criteria for inclusion:**
  - **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.**
    Please refrain from sampling asymptomatic horses or chronic cases. Unless indicated, a maximum of 5 samples (from symptomatic horses) per location is encouraged.
    This service should be used as a diagnostic aid and not a screening tool.

All samples should be labeled with date, name of horse and owner. Also, please complete the sample submission form and questionnaire before submitting. The information you submit with each sample is critical to helping our industry better understand and manage current and emerging infectious respiratory disease in the horse.





Infectious Disease and Biosecurity Resources

Equine infectious disease awareness and management cannot be emphasized enough. There are several resources available to help monitor and manage infectious disease, as well as provide valuable information and tips for owners.

- Equine Disease Communication Center (EDCC), equinediseasecc.org, which provides real-time information about disease outbreaks. Sign up to receive disease notifications via email or by following @EquineDiseasesCC on Twitter.
  - The EDCC website also includes information on reportable diseases by state. This link can help discern which diseases should be reported to state animal health authorities.
- American Association of Equine Practitioners (AAEP) infectious disease guidelines (www.aaep.org), providing guidance on respiratory, gastrointestinal, neurologic and vesicular infectious disease control.
- United States Animal Health Association (www.usaha.org), through its Infectious Disease of Horses Committee (IDOHC) provides information on testing procedures, risk assessment, quarantine protocol, as well as a guidance document on the neurologic form of equine herpesvirus.
- Biosecurity Toolkit for Equine Events, California Department of Food & Agriculture (www.cdfa.ca.gov).
- Equine Biosecurity Risk Calculator – a self-quiz for horse owners provided by the University of Guelph (www.equineguelph.ca). A unique tool geared to the horse owner, and developed in partnership with Colorado State University and the AAEP.
- Worms & Germs Blog, also a service of the University of Guelph, providing information on equine infectious disease.

Equine Coronavirus Testing Discontinued

Effective July 31, 2017, the equine coronavirus (ECoV) fecal testing program was discontinued. Please note, **the upper respiratory biosurveillance testing program will continue unchanged.** Your support and participation in the additional ECoV program has been appreciated and we look forward to sharing a synopsis of ECoV testing results in an upcoming biosurveillance newsletter.

What Participating Veterinarians are Saying About the Program

"The Merck biosurveillance program has been of tremendous diagnostic value to our clinic. The ability to get a firm diagnosis on fevers of unknown origin has helped us rule out possible respiratory issues, or something like anaplasmosis, which is common in our area. We've also been able to definitively uncover suspected recrudescing EHV-1 in retired racehorses.

The program has given us the opportunity to get ahead of the curve on some of these respiratory viruses and get an answer. It has armed us with important information to help handle and manage disease spread, as well as assisted in educating owners on the importance of vaccination. I can't underscore enough its importance as a management tool."

- Steve Naile, D.V.M., Equine Clinic at OakenCroft, Ravena, N.Y.

Quick Tips For Clients

The following tips are provided to help you share information with clients on common infectious respiratory diseases in horses. Click the link to download and use this on your website or through your social media properties. Don't forget to ask your Merck Animal Health representative about the biosecurity infographic poster — a great resource on biosecurity for in-clinic use and as an educational giveaway for your clients.

Click to download and share the tips to the right.

MERCK Animal Health

Getting to Know the Other Equine Herpesviruses — EHV-2 and EHV-5

Researchers continue to study some of the lesser-known equine herpesviruses – specifically, EHV-2 and EHV-5. The significance of each is not well understood, as these viruses can be found in horses with respiratory signs as well as healthy horses. Experts believe these viruses may play a complicating role in other respiratory infections, as they may suppress the horse's immune system. Here are a few facts about EHV-2 and EHV-5:

- *Known as gamma herpesviruses*
- *Ubiquitous in horse populations worldwide*
- *A direct link to disease from either virus (alone) is yet to be established*
- *EHV-2 is often implicated in inflammation of the tissues around the eyes (keratoconjunctivitis), upper respiratory tract disease, general sickness, pharyngitis – commonly seen more in young horses*
- *EHV-5 is often implicated in upper respiratory tract disease, and a condition known as equine multinodular pulmonary fibrosis*
- *Co-infection with both EHV-2 and EHV-5 may be more frequently associated with overt signs of respiratory disease*

About the Newsletter

This bi-annual newsletter is being sent as a value-added service to clinics enrolled in 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 Technical Services (Drs. Barnett, Vaala, Gaughan, Craig, Bain and Chappell) and Nicola Pusterla, D.V.M., Department of Medicine and Epidemiology, UC Davis.

If you have questions about the program, please call our technical services team at (866) 349-3497, or email one of the technical services veterinarians 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 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., Pusteria, N. ACVIM 2017 Abstract.

2) "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.

3) "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

4) "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.

5) "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.

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

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 7,000 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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