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Equine Herpesvirus Myeloencephalopathy: Mitigation Experiences, Lessons Learned, and Future Needs



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Executive Summary

In January 2007, the Center for Emerging Issues (CEI) at USDA-APHIS-VS-Centers for Epidemiology and Animal Health (CEAH) issued an Emerging Disease info sheet which suggested that the neurologic manifestation of equine herpesvirus-1 (EHV-1) met the criteria for an emerging infectious disease based on: (1) the occurrence of a more virulent strain of EHV-1 than previously seen in the United States, and (2) increased recognition of outbreaks of disease at equine events with associated high case fatality rate. The neurologic manifestation of EHV-1 is also referred to as equine herpesvirus myeloencephalopathy (EHM). Equine herpesvirus (EHV) was a focus of presentations at multiple equine industry and veterinary meetings in 2007, illustrating concern within the equine industry related to EHV.

Much remains to be discovered about EHV-1 and the neurologic manifestation of the disease that could help prevent or mitigate outbreaks. The objective of this report is to provide information—from interviews conducted with selected scientists and researchers concerning EHV, including EHM, and those involved in mitigation of recent outbreaks or trace-outs related to EHM—that may be useful in mitigating future outbreaks and developing research needs, response plans, and communication materials related to EHM.

Response to a contagious disease situation begins with recognition of clinical signs and identification of the disease agent, thereby allowing the private veterinary practitioner to determine the optimal care for the sick horse or horses. Response efforts then progress to mitigation efforts at the population level, to prevent spread of disease to other horses at the facility or to horses at other facilities. Along with information related to EHM in the individual horse, this report contains two broad aspects of EHM outbreak prevention and control: (1) disease specific aspects, primarily at the population level, and (2) the regulatory framework needed to respond efficiently to EHM outbreaks. Not only is there still much to learn about the disease, but also much discussion needs to take place regarding what is known about EHM, what is not known, and how that affects recommendations for disease prevention and control. Interviewees emphasized the need for preplanning regarding information resources, identification of and contact information for disease experts, defining and clarifying roles and authorities of various entities potentially involved in a response, and determining when action will be taken and by whom.

The interviewees expressed the need for:

- Critical evaluation of existing literature;
- Vaccine development and study of the efficacy of currently available vaccines for the prevention of EHM;
- A rapid horse-side test that detects EHV-1 and distinguishes the neuropathogenic strain of the virus from the wild-type (non-neuropathogenic strain);
- Individual animal risk factors, transmission characteristics, latency studies, and prevention options;
- Clinical trials of treatment efficacy to determine appropriate treatment options; and
- Preplanning to facilitate the effectiveness of outbreak response efforts.

Dr. Peter Timoney, Professor, University of Kentucky, Gluck Equine Research Center and Chair of the Infectious Diseases of Horses Committee of the United States Animal Health Association (USAHA), pointed out that "...within the past few years, a mutant of the wild-type of EHV-1 has been identified which evidence would indicate is very frequently associated with outbreaks of EHM. Also, this mutant has been identified among isolates of EHV-1 made prior to 2000. As the distribution of this virus mutant becomes more widespread in the equine population, the frequency and severity of outbreaks of EHM is likely to increase further unless measures to control its spread and occurrence of the disease can be developed." Although this mutant strain of EHV-1 has been frequently associated with EHM, the wild-type EHV-1 also has been known to be associated with EHM cases. One of the interviewees stressed that "...we are missing an opportunity to advance the knowledge of EHM by not gathering observational data during outbreaks." To address that issue, CEAH has developed an Example Study Design and Survey Instrument for Collection of Epidemiologic and Cost Estimate Data from Future EHM Outbreaks (Appendix C) that is available for use by those responding to future EHV-1 outbreaks.

Telephone interviews, using open-ended questions (Appendix A), were also conducted with those who had been involved in mitigation of recent EHM disease events, to gather information that could describe the identification of EHM cases and methods used to mitigate the outbreaks, and to gather comments related to lessons learned, and need for additional educational materials and further research related to EHM. Interviews were conducted from July through October 2007 relating to 16 EHM disease events—13 outbreaks and 3 trace-outs.

Results of these interviews demonstrate the variation of settings, persons responsible for initial recognition, authorities responsible for taking action, level of response, and approaches in mitigating EHM disease events. In some States, EHV-1 was reportable; in others it was not. In some it was reportable, but not actionable—that is, the State veterinary regulatory officials did not consider it a disease for which they would take regulatory action in response to the disease report, but they did want to be aware of the situation, and in some situations offered advice. Action taken ranged from State mandatory quarantines to a voluntary “stop-horse-movement” action recommended by a university clinician to a private riding stable owner and the attending private veterinarian. The criteria for release of quarantine and approaches to testing in-contact horses varied among outbreaks. Nine laboratories were used for polymerase chain reaction (PCR) testing during the outbreaks. A few mitigators said it would be beneficial to understand how results from the laboratories compared and that validation of testing by a reference laboratory or protocol would be beneficial. Several mitigators indicated it would be beneficial to develop a consistent approach across States to address future EHV-1 neurological disease events.

Although biosecurity and disease containment measures were implemented in the face of the disease events, it wasn't until someone with disease control experience evaluated the situation on-site that some breaches in containment practices were discovered. These observations demonstrated the need for someone with a critical eye and attention to detail to verify adherence to recommended biosecurity and disease containment measures.

Few respondents tracked all the costs associated with mitigating the EHM disease events, but indications are that outbreak mitigation can be quite expensive. Mitigators reported that associated categories of cost included human resources, loss of income due to cancellation or reduction in scope of events/ racing, disrupted training schedules, diagnostics, treatment of horses, and biosecurity procedures (supplies and, in some instances, personnel required to assure compliance with protocols).

This report contains a comprehensive description of research, education, and other needs expressed by mitigators related to EHM.

Next steps include:

- Discussion among veterinary regulatory officials (State veterinarians, racing commission veterinarians, etc.) to determine areas of consensus regarding case definitions, outbreak definition, and best management practices related to EHM disease events. The USAHA Infectious Diseases of Horses Committee meeting would be a logical venue for such a discussion.

- Establishment of validation criteria for PCR testing for EHV-1 and distinction between the neuropathogenic strain and the non-neuropathogenic strain. The American Association of Veterinary Laboratory Diagnosticians (AAVLD) would be a starting point for dialogue regarding guidelines or oversight of such validation.
- To identify potential risk factors for EHM, consistent data will need to be gathered across outbreaks. Compilation of data from multiple outbreaks will be necessary due to the small number of EHM cases associated with individual outbreaks. Data from EHM outbreaks collected by those in the field will need to be submitted by outbreak responders to one entity to be stored. When sufficient data are compiled, analyses can be performed.
- Evaluation of the efficacy of currently available commercial vaccines through challenge models and detailed epidemiological studies.
- Development of new vaccines that are efficacious in preventing EHM by research institutions and commercial interests.

Background and profile of disease emergence

Equine herpesvirus type 1 (EHV-1) is primarily a respiratory pathogen associated with a variety of clinical manifestations in horses. In addition to being a significant cause of respiratory illness and abortion in horses, EHV-1 is responsible for neurological disease, called equine herpesvirus myeloencephalopathy (EHM). EHV-1 is enzootic throughout the world and almost all horses older than 2 years of age have been exposed. Following initial exposure, EHV-1 has the ability to develop into an inapparent, latent infection. It is this ability to reside as a silent and persistent infection in horses which provides a reservoir of virus for continual transmission. The incubation period of EHV-1 is 1–10 days; typically signs are seen within 1–3 days. Viral shedding usually occurs for 7–10 days, but can occur up to 28 days from the onset of signs. The neurologic signs include ataxia, urinary bladder atony and reduced tail tone. In severe cases, horses will be unable to stand; these cases have a very poor prognosis. Foals are rarely affected with the neurologic form of EHV-1, and no sex predilection is seen. Treatment is supportive and tailored to the specific case. Antivirals such as acyclovir, valcyclovir, famciclovir and penciclovir have been used, but efficacy of these drugs has yet to be determined in equids.

Excerpt from: USDA-APHIS-VS-CEAH-CEI info sheet: "Equine Herpes Myeloencephalopathy: A Potentially Emerging Disease."

In January 2007, CEI released an Emerging Disease info sheet which suggested that the neurologic manifestation of EHV-1 met the criteria for an emerging infectious disease, based on: (1) the occurrence of more virulent strains of EHV-1 than seen previously in the United States, and (2) increased recognition of outbreaks of disease at equine events with associated high case fatality rate. In this same summary, CEI indicated that many data gaps existed, and more investigations were needed to better understand the disease and to identify factors playing a role in this possible emergence. In addition, CEI suggested that identifying such factors would assist with control of future outbreaks. The CEI info sheet indicated that the general ecology of this disease is not fully understood; additional research is needed. A standard case definition and standardized reporting requirements for EHM would be good starting points for further study, with subsequent studies comparing cases to controls to determine risk factors for individual horses to develop EHM. The info sheet is included as Appendix B in this report and is also available at: http://www.aphis.usda.gov/vs/ceah/cei/taf/emergingdiseasenotice_files/ehv.pdf

Several recent reports (Allen et al., Goodman et al., Nugent et al.) describe a point mutation in the equine herpesvirus-1 polymerase. Terms that have been used in the scientific literature to describe the strain of the virus that contains this point mutation are “neuropathogenic or mutant strain.” Terms used to describe the strain of the virus that does not contain this mutation are “the non-neuropathogenic or wild-type.” Both are field strains of EHV-1. The mutant, or neuropathogenic, strain of the virus was found to exist as early as 1970, based on testing of archival samples. The frequency of paralytic outbreaks appears to be increasing, especially in the period 2000–05. Outbreaks of EHM investigated during this period were predominately associated with the mutant neuropathogenic strain of the virus; however, the wild-type non-neuropathogenic strain has been implicated as a cause of two EHM outbreaks (Appendix B).

Further clarification of the terminology used in recent scientific literature related to the EHV-1 virus includes that the mutation has been reported to be a single nucleotide polymorphism (SNP) within the EHV-1 gene encoding for the viral DNA polymerase (open reading frame 30, ORF30). This point mutation has been reportedly associated with neuropathogenicity and higher levels of viremia in horses. A PCR test was developed that allows for differentiation of the non-neuropathogenic (wild-type) from the neuropathogenic strains (mutant) of EHV-1 by detecting the SNP genetic marker (ORF30 A₂₂₅₄ wild-type to G₂₂₅₄ mutant). An SNP in the EHV-1 polymerase gene results in a single amino acid sequence

difference in the DNA polymerase protein. The N752 Pol variant (Asparagine=N or Asn) has been referred to as the non-neuropathogenic or N752 sequence variant of EHV-1 DNA Pol. The D752 Pol variant (Aspartic acid=D or Asp) has been referred to as the neuropathogenic variant or the D752 variant.

There is speculation about the evolutionary origin of the D/N752 sequence variation of EHV-1. Goodman et al. suggested that the N752 variant arose from the D752 progenitor and that the prevalence of the N752 variant is higher. These authors suggested that the N752 variant may have selective advantage over the D752 variant.

EHV was a focus at several meetings in 2007, including the American Horse Council, the Infectious Diseases of Horses Committee of USAHA, the American College of Veterinary Internal Medicine (ACVIM), the National Institute for Animal Agriculture (NIAA) and the American Association of Equine Practitioners (AAEP), illustrating the heightened interest in EHV.

The purpose of this report is to serve as a source of information and as a basis for further discussion by veterinary officials and those in the equine industry regarding the prevention and mitigation of EHM outbreaks. In addition, the report highlights some of the research needed to provide information that would provide scientific evidence on which to base best management practices for EHV-1, and specifically EHM. The compilation of information obtained from interviewing mitigators of recent EHM disease events also was undertaken in the hope of providing lessons learned to benefit those responding to future EHM outbreaks.

References related to EHV-1 terminology:

- 1) Allen GP: Brief communications: Development of a real-time polymerase chain reaction assay for rapid diagnosis of neuropathogenic strains of equine herpesvirus-1. *J Vet Diagn Invest* 19, 69–72, 2007.
- 2) Goodman LB, Loregian A, Perkins GA, Nugent J, Buckles EL, Mercorelli B, Kydd JH, Palu G, Smith KC, Osterrieder N, Davis-Poynter N: A point mutation in a herpesvirus polymerase determines neuropathogenicity. *PLoS Pathogens* 3, 1583–1592, 2007.
- 3) Nugent J, Birch-Machin I, Smith KC, Mumford JA, Swann Z, Newton JR, Bowden RJ, Allen GP, Davis-Poynter, N: Analysis of Equid Herpesvirus 1 Strain Variation Reveals a Point Mutation of the DNA Polymerase Strongly Associated with Neuropathogenic versus Nonneuropathogenic Disease Outbreaks, *J Vir* 80, 4047–4060, 2006.

Part I: Interviews with Selected Scientists and Researchers Concerning Equine Herpesvirus

Based on the emergence of EHM as a more virulent disease than previously considered and interest from the equine industry, interviews were conducted with selected scientists and researchers concerning equine herpesvirus infections and, specifically, EHM. Interview topics included the current status of knowledge related to EHM, need for EHM research, and actions to control the disease. The individuals interviewed were: Dr. Lutz Goehring, Assistant Professor in Clinical Sciences, Colorado State University; Dr. Paul Lunn, Professor and Department Head of Clinical Sciences, Colorado State University; Dr. Barry Meade, USDA:APHIS:VS Veterinary Medical Officer and Ph.D. candidate in equine infectious diseases at the University of Kentucky; and Dr. Peter Timoney, Professor, University of Kentucky Gluck Equine Research Center and Chair of the Infectious Diseases of Horses Committee of the USAHA. Each person interviewed was given a draft of his comments to review and edit prior to finalization of the interview. Comments from those interviewed are organized under several key headings addressed in the interview. The interviews with these four people were conducted and finalized from July to September 2007.

General Observations and Comments Related to EHM

Dr. Peter Timoney:

1. EHM is not a new disease. For example, in 1972, the Irish Department of Agriculture created an Equine Diseases Section at the Central Veterinary Research Laboratory to work on equine diseases following a series of major outbreaks of EHM that affected the Thoroughbred breeding industry that year.
2. This led to the establishment of an Irish Liaison Committee on Equine Diseases with representation from various sectors of the horse industry, government laboratory service, and university and equine veterinary professions; so, historically, it can be said that outbreaks of EHM have been the stimulus behind advancements in efforts to control not only EHM but also other equine diseases, especially those that are contagious.
3. Since 2000, there has been an increase in the frequency of reported EHM outbreaks in the United Kingdom, Western Europe, and also in the United States, in a variety of settings including racetracks, show grounds, breeding farms, and riding schools. This disease does not respect any venue.
4. Within the past few years, a mutant of the wild-type of EHV-1 has been identified which evidence would indicate is frequently associated with outbreaks of EHM. Also, this mutant has been identified among isolates of EHV-1 from prior to 2000. As the distribution of this virus mutant becomes

more widespread in the equine population, the frequency and severity of outbreaks of EHM are likely to increase further unless measures to control its spread and occurrence of the disease can be developed.

Dr. Paul Lunn:

1. ACVIM formed a task force to develop a consensus statement related to equine herpesvirus. In March 2007, Dr. Brad Smith, president of the Large Animal Specialty for ACVIM, selected the members of the task force, which includes Drs. Nick Davis-Poynter, Julia Flaminio, David Horohov, Klaus Osterrieder, Nicola Pusterla, Hugh Townsend, and myself. In the consensus statement, we plan to address nine different areas related to EHV and fully reference each section. The statement, expected to be released in fall 2008, will address all aspects of EHV, not just the neurologic form of the disease, and will include the following topics:
 - Outbreak response—What are the key things I need to know as I plan for, and respond to, an outbreak of clinical EHV-1 infection?
 - Diagnostic testing—What kinds of viral detection tests should I select for diagnosis, prognosis, and screening of horses for EHV-1 and its strains?
 - Identification of the D752 SNP—What are the clinical implications of the DNAPol SNP for veterinarians and horse owners?*
 - Vaccination—How and when should I use current commercially available vaccines to control EHV-1 infection and disease?
 - Risk factors for disease—What are the risk factors for respiratory, abortigenic, or neurologic disease caused by EHV-1?
 - Pathogenesis—How and why does EHV-1 infection target the pregnant uterus and CNS? Why do some horses but not others get neurological disease?

*The difference between the non-neuropathogenic (wild-type) and neuropathogenic (mutant) EHV-1 field strains has been reported to be based on identification of the single nucleotide polymorphism (SNP) within the EHV-1 gene encoding for the viral DNA polymerase (open reading frame, ORF30) that is highly associated with neuropathogenicity for horses. A PCR test has been reported to distinguish between the non-neuropathogenic (wild-type) and the neuropathogenic strain (mutant) of EHV-1 by detecting the SNP genetic marker (ORF30 A₂₂₅₄ wild-type to G₂₂₅₄ mutant). This SNP in the EHV-1 gene results in a single amino acid sequence change in the DNA polymerase protein from an N (Asparagine=Asn) to D (Aspartic acid=Asp).

References:

- 1) Nugent J, Birch-Machin I, Smith KC, Mumford JA, Swann Z, Newton JR, Bowden RJ, Allen GP, Davis-Poynter, N. Analysis of Equid Herpesvirus 1 Strain Variation Reveals a Point Mutation of the DNA Polymerase Strongly Associated with Neuropathogenic versus Nonneuropathogenic Disease Outbreaks, *J Vir* 80, 4047–4060, 2006.
- 2) Allen GP. Brief communications: Development of a real-time polymerase chain reaction assay for rapid diagnosis of neuropathogenic strains of equine herpesvirus-1. *J Vet Diagn Invest* 19, 69–72, 2007.

- Disease control—Beyond vaccination, what are the key factors to consider in controlling disease caused by EHV-1?
 - Epidemiology—What, if anything, has changed about EHV-1 epidemiology?
 - Treatment—What treatments are useful for EHM, beyond supportive care?
2. It is likely that the ACVIM task force also will provide a description of limitations of the current knowledge of equine herpesvirus in the concluding remarks of the consensus statement. These would be presented in general terms and would not be considered as a list of recommended research priorities.

Research and Investigation Needs

1. Critical evaluation of existing literature:

Dr. Peter Timoney: It would be worthwhile to compare EHM with herpesvirus infections in other species with reference to risk factors, control methods, and treatment (if any).

2. Vaccine development and study of impact of use of currently available vaccines:

Dr. Barry Meade: While there are some data that would indicate the abortion rates have gone down with the introduction of EHV vaccines, the current available vaccines do not appear to stop viral shedding in animals with respiratory disease. There is only limited evidence that vaccination is effective against the neurologic form of EHV-1 and no commercial EHV vaccines are currently labeled for prevention of this clinical condition. To my knowledge, they cannot prevent the establishment of latency. Development of a vaccine that could prevent latency and the neurological form of EHV should be a top priority for research related to this disease.

Dr. Peter Timoney: A vaccine is needed to prevent or reduce the frequency of latency as well as occurrence of EHM. Such a vaccine should stimulate the appropriate cellular and humoral immune responses needed to control the cell-associated viremia.

Dr. Lutz Goehring: There is a need to evaluate the impact of previous vaccination against EHV-1 and occurrence of EHM. This would require collection of detailed vaccination history on both EHM cases and non-cases (controls) in naturally occurring outbreaks of disease.

3. Diagnostics:

Dr. Barry Meade: A rapid horse-side test similar to heartworm testing or the Directigen test for equine flu—maybe something based on the nasal swab PCR done at the University of Kentucky Veterinary Diagnostic Center or at least a commercial version that can be done at other laboratories would help manage outbreaks.

4. Epidemiology:

Dr. Barry Meade: We need to have a better handle on the EHV-1 neurological events that occur yearly. They are probably handled fine from a regulatory sense—such that I do not believe there has been documented spread from one racetrack to another—but we are missing some good observational data. There is more to an outbreak than when it starts and when it is over. In general, there are benefits to be gained epidemiologically in developing best practices for investigation and management of EHV-1 outbreaks. Specifically, I think there are opportunities to determine risk factors that contribute to disease spread, to gain a better understanding of dynamics of virus transmission in natural populations, to evaluate the efficacy of response activities of regulators, and to increase our response capacity to animal disease outbreaks.

Comments related to epidemiological research needs from the interviewed EHV scientists and researchers are grouped into the following categories: risk factor determination, transmission characteristics, response by regulatory veterinary medicine to contain or limit the outbreak, latency studies, and prevention and/or treatment options.

- Risk factor determination

Dr. Barry Meade: Gathering of information during disease outbreaks would allow investigators to evaluate factors involved in EHM, such as recent training, sales, EHV-1 vaccine use (date or type), whether acyclovir

decreases viral shedding, whether continued training increases the isolation period, and the role of direct and indirect contact on spread of a disease—grooms, tack, etc.

Dr. Peter Timoney: Determine risk factors for disease occurrence in individual horses in order to generate ideas for future research on prevention and treatment. If aged horses were to be at higher risk for EHM during outbreaks, then investigation into the reasons for this predisposition would be warranted.

Dr. Lutz Goehring: We need basic risk factor information related to EHM. It seems that previous studies lacked large scope or were limited by geographic occurrence of the outbreaks. Since there is currently no reliable challenge model for EHM, study of naturally occurring EHM is our best hope of gathering information regarding risk factors for the disease. My EHM studies were conducted in Holland and were based on a small number of cases of EHM, thus limiting their generalizability. However, these studies do suggest potential risk factors to evaluate including age, breed, and seasonality. The only other published field-based study looking at risk factors for EHM was based on a single outbreak in Ohio—again, limiting the application of the findings to other outbreaks. The study of multiple outbreaks with collection of information on both cases of EHM and non-cases (controls) could allow for determination of associated risk factors for occurrence of EHM. If multiple outbreaks could be studied then some comparisons across outbreaks could be made. There is a need to evaluate the impact of previous vaccination against EHV-1 and occurrence of EHM. This would require collection of detailed vaccination history on both EHM cases and non-cases (controls). There is also a need to collect information regarding transport or movement as this has been proposed to be associated with EHM occurrence.

Dr. Paul Lunn: There is a need to understand why some horses get EHM and others do not during an outbreak of naturally occurring disease. It would require many different fields of expertise to investigate this. The pathogenesis of EHM is still not well understood. Does EHM occur due to an immune response? Why does the immune response not prevent this disease or does it? It is difficult to study the pathogenesis of this disease as there is not a good experimental challenge model for EHM. It is hard to study EHM in a controlled challenge study setting when there is not a way to reproduce EHM that is of equal severity as that observed in naturally occurring outbreaks. Potential identification of risk factors for this disease

as determined through epidemiologic studies of natural outbreaks may allow us to control the disease without knowing the exact mechanism or pathogenesis of the disease. In addition, there is a need to understand the epidemiology of the virus better than we do now. Are there strain differences that occur during an outbreak? Collection of samples during outbreaks that would allow for strain typing of multiple isolates would be of value. This would require sampling multiple horses during an outbreak. Strain typing would require funding and someone with knowledge of the technique for strain typing.

- Transmission characteristics

Dr. Barry Meade: How do we estimate transmission parameters? What is the likelihood of contact between infected and susceptible animals? How do we estimate the proportion of infection that is transmitted prior to symptom onset and what role does this play in disease persistence or spread?

- Response by regulatory veterinary medicine to contain or limit outbreak

Dr. Barry Meade: For those involved in regulatory veterinary medicine, there needs to be some means of evaluating risk for a specific set of circumstances so they can decide on an appropriate level of response. As an example, what is the minimum length of time that horses will need to be prohibited from moving and how do you evaluate your success in stopping viral spread prior to resumption of movement? Should these criteria be applied under all circumstances or is there a threshold for the number of in-contact horses, the type of event, time of year, type of premises, etc.?

- Latency studies

Dr. Barry Meade: Does a productive immune response prevent latency and can we easily identify latent carriers?

Dr. Lutz Goehring: Evaluation of the role of latency in EHM is needed.

Dr. Peter Timoney: It would be interesting to know if the two types of EHV-1 (wild-type and mutant)* can coexist in the same horse and if they can, what the impact of one on the other may be, with regards to reactivation and recrudescence.

- Options for prevention and treatment

Dr. Lutz Goehring: There is a need for evaluation of treatment and/or prevention of EHM. Although not all horses that develop viremia go on to develop EHM, viremia is necessary for EHM to occur. A method of treatment, or a preventative that could limit viremia, may be protective against the occurrence of EHM. Studies designed to test drugs in prevention or treatment would be of value. In addition, drugs that may alter coagulation could also be of benefit in prevention of EHM and might be worth evaluation in treatment/placebo format in naturally occurring outbreaks.

Dr. Peter Timoney: More needs to be known about the efficacy of various treatment options (antiviral, aspirin, other) on the outcome of cases of the disease in the field. We need to explore the options of treatment and prophylaxis that hopefully could reduce shedding of virus and thus limit spread of the virus once the disease has been identified. A vaccine capable of preventing or reducing the cell-associated viremia is a critical need. We must not close our minds off to any approach that might reduce the impact EHM is likely to have in the future.

*The difference between the non-neuropathogenic (wild-type) and neuropathogenic (mutant) EHV-1 field strains has been reported to be based on identification of the SNP with the EHV-1 gene encoding for the viral DNA polymerase (open reading frame, ORF30) that is highly associated with neuropathogenicity for horses. A PCR test has been reported to distinguish between the non-neuropathogenic (wild-type) and the neuropathogenic strains (mutant) of EHV-1 by detecting the SNP genetic marker (ORF30 A₂₂₅₄ wild-type to G₂₂₅₄ mutant). This SNP in the EHV-1 gene results in a single amino acid sequence change in the DNA polymerase protein from an N (Asparagine=Asn) to D (Aspartic acid=Asp).

References:

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- 2) Allen GP. Brief communications: Development of a real-time polymerase chain reaction assay for rapid diagnosis of neuropathogenic strains of equine herpesvirus-1. *J Vet Diagn Invest* 19, 69–72, 2007.

Miscellaneous Comments and Suggestions

Dr. Lutz Goehring: In addition to collecting questionnaire data on both EHM cases and non-cases (controls), there may be some benefit in collecting and banking sera for future studies [such as]:

- Determination of EHV-1 titers at the onset of an outbreak and subsequent occurrence of EHM;
- Determinations of some deficiency or factors in those horses that go on to develop EHM. The lesion in the central nervous system of EHM cases is compatible with vascular injury and coagulation. In humans, factors that are risk factors for coagulation include age, ethnicity, and geographic location.

Dr. Barry Meade: There should be some kind of mechanism for investigation of EHV-1 events nationwide. In the past, APHIS has provided assistance to State veterinary regulators to investigate a variety of disease situations. As an example, I was asked to investigate the first occurrence of West Nile virus among horses in New York in 1999. At that time, it would have been helpful to have access to content experts on equine neurological disease or questionnaire design. We probably could have learned more had these types of resources been available at that time. There are several things that must be taken into consideration before assistance is offered: (1) What would be the structure and framework of support? (2) Would these investigations be done by Federal personnel? (3) Can the Centers for Epidemiology and Animal Health provide personnel to be used in an investigation? (4) How could such a service be marketed?

Needs Other Than Those Specifically Related to Research

Dr. Peter Timoney: There is a need for communication about what we know of EHM and our current knowledge on control of the disease. This communication needs to occur with and between all sectors of the horse industry, inclusive of horse owners, trainers, breeders, racetrack personnel, and equine event management staff. We must also admit to limitations in our current knowledge of this disease. For example, we have limited scientific knowledge of the impact that vaccination, with the variety of available EHV-1 vaccines, would have in a field setting, in terms of restricting occurrence of this disease. To reduce losses from occurrences of EHM, we need to work across multiple areas and look at a variety of different approaches to achieve greater control of the disease.

Summary from Interviews with Selected Scientists and Researchers

It is apparent that those who were interviewed agree there is still much to learn about EHM. These EHV scientists and researchers advocate gaining more information about strategies for prevention of EHM and evaluation of treatment options. They also suggest it would be beneficial to share, across various levels, what we do know and what we do not know about the prevention and treatment of EHM.

The need to evaluate strategies for prevention of EHM is one area that all interviewees appear to agree upon, particularly as some of the interviewed scientists and researchers indicated that, in their opinion, there was an emergence of a more severe form of EHM during recent outbreaks. Two areas suggested for further examination in EHM prevention are the impact of the use of available vaccines and determining risk factors associated with EHM.

In addition to evaluating the efficacy of available vaccines in reducing the risk for EHM, scientists and researchers suggested investigating the development of new vaccines that may reduce the occurrence of latency, viral shedding, and onset of EHM. Several interviewees mentioned the challenge of developing such a vaccine and the fact that there is currently no challenge model that parallels the severity of naturally occurring disease. Testing of such a vaccine will be difficult, except through field trials, unless appropriate challenge models are developed.

All those interviewed indicated the importance of determining risk factors associated with EHM. Some indicated there would be a benefit in collecting epidemiologic data related to the risk for EHM outbreaks and the risk of development of EHM at the individual horse level during outbreaks. The information could be gathered through a survey related to factors in both cases and controls during an outbreak. To evaluate some of the suggested factors, sample collection with subsequent laboratory testing would be required.

Other points made included:

- We are missing an opportunity to advance the knowledge of EHM by not gathering observational data during outbreaks.
- A horse-side test would be advantageous in mitigating an outbreak.
- Can the two types of EHV-1 (wild-type and mutant) coexist in the same horse and if they can, what is the impact of one on the other with regard to reactivation (recrudescence)?

- Evaluation of treatment to prevent neurologic signs in EHV-exposed horses, as well as the efficacy of treatment of horses with EHM, is a priority for further investigation.
- There is need for discussion of the options for involvement of APHIS in gathering needed epidemiologic data related to EHM.
- ACVIM is developing a consensus statement on EHV-1, addressing multiple key areas and supported by extensive scientific references, that is expected to be posted on the ACVIM Web site by fall 2008.



Photo by Chad Mendell

Part II: Summary of Interviews with Mitigators of Recent EHM Disease Events

Interviews were conducted with those who had been involved in mitigation of recent outbreaks of EHM to gather information that could describe the identification of EHM cases and methods used to mitigate the outbreaks, and to gather comments related to lessons learned, and need for additional educational materials and further research related to EHM. A set of open-ended questions (Appendix A) was used for the telephone interviews. Notes from this interview were then prepared and provided for each person to review for accuracy. Interviews were conducted from July through October 2007. Sixteen interviews were conducted relating to 16 disease events—13 outbreaks and 3 trace-outs.

1. Dr. Rick Arthur, the California Horse Racing Board Equine Medical Director, was interviewed related to his experience with two EHM situations: the Los Alamitos Quarter Horse and Golden Gate Fields Thoroughbred racetracks EHM outbreaks (started late December 2006). [n=2 outbreaks, n=1 interview]
2. Drs. Kent Fowler and Tim Boone, California Department of Food and Agriculture, provided comments related to their experience of receiving a horse that had been recently imported to the United States and developed EHM after arriving in California (December 2006). [n=1 trace-out, n=1 interview]
3. Dr. John Madigan, Professor, University of California at Davis, provided comments on his experience with an EHM outbreak at a riding stable in Pacifica, California (started in fall 2006). [n=1 outbreak, n=1 interview]
4. Dr. Paul Morley, Director of Hospital Biosecurity for the James L. Voss Veterinary Teaching Hospital at Colorado State University, provided comments related to an EHM outbreak that occurred in the veterinary teaching hospital (started end of October 2006). [n=1 outbreak, n=1 interview]
5. Drs. Alfredo Sanchez (Tufts University Equine Ambulatory Veterinarian) and Mary Lis (State Veterinarian in Connecticut) provided comments related to an EHM outbreak among polo ponies at the University of Connecticut (started early January 2007). Dr. Lis also provided general comments related to mitigation, for comparison purposes, about an EHV-1 disease event at a private veterinary practice in Connecticut that occurred within several weeks of the University of Connecticut outbreak. [n=1 outbreak, n=2 interviews]

6. Dr. Mike Short (Veterinarian with the State Veterinarian's Office in Florida) provided comments related to an EHM outbreak at multiple venues including show facilities and veterinary clinics in the West Palm Beach area of Florida (started mid-December 2006). [n=1 outbreak, n=1 interview]
7. Dr. David Fitzpatrick, Chief Veterinarian for the Illinois Racing Board, provided comments related to his experience with the EHM outbreak at Balmoral Park racetrack among Standardbred horses in Illinois (started in early April 2007). [n=1 outbreak, n=1 interview]
8. Dr. Robert Stout, Kentucky State Veterinarian and Rusty Ford, Equine Program Manager with the Kentucky Department of Agriculture, provided comments related to an EHM outbreak that occurred at Turfway Park Thoroughbred racetrack (started December 21, 2005). [n=1 outbreak, n=1 interview]
9. Dr. Don Hoenig, State Veterinarian in Maine, provided comments related to an EHM outbreak at a boarding facility in Maine. (started mid-March 2007). [n=1 outbreak, n=1 interview]
10. Dr. Guy Hohenhaus, State Veterinarian for Maryland, provided comments about his involvement in tracing out horses that had left the Marion DuPont Scott Equine Medical Center and returned to premises in Maryland. [n=1 trace-out, n=1 interview]
11. Dr. Steve Halstead, State Veterinarian in Michigan, provided comments related to an EHM outbreak that occurred at Northville Downs Standardbred racetrack (started mid-December 2004). [n=1 outbreak, n=1 interview]
12. Dr. Nancy Halpern, State Veterinarian for New Jersey, provided comments related to an EHV outbreak with an epidemiologic link to EHM cases that occurred at Monmouth Park Thoroughbred racetrack (started October 20, 2006). [n=1 outbreak, n=1 interview]
13. Dr. Steve Reed, a faculty member at The Ohio State University at the time of the outbreak, provided comments related to an outbreak of EHM that occurred at the veterinary hospital at The Ohio State University (started January 2003) that had an epidemiologic link to the EHM outbreak at University of Findlay Equine Center. [n=1 outbreak, n=1 interview]

14. Dr. Nat White, director of the Marion DuPont Scott Equine Medical Center (EMC), provided comments related to the EHM outbreak that occurred at the EMC in Virginia (started February 20, 2007). [n=1 outbreak, n=1 interview]
15. Dr. Don Hopson, a veterinarian with the Virginia Department of Agriculture and Consumer Services, provided comments related to tracing out of horses that had left the Marion DuPont Scott Equine Medical Center and returned to premises in Virginia. [n=1 trace-out, n=1 interview]

Case Recognition and Person Responsible for Mitigation

Who notified you of the first case of EHM?

Those involved in the recognition or reporting of the first or index case varied by outbreak. In addition, the position of the person who eventually managed the outbreak varied. In some situations a State veterinary official was notified and took action to investigate and/or manage the outbreak; in other situations the racing commission or racing board veterinarian was notified and managed the situation; and in yet other situations, the director of hospital biosecurity, an equine infectious disease specialist, or chief of equine services was notified of the index case and managed the outbreak.

Those who identified the index case and then notified the State Veterinarian, racing commission or racing board veterinarian, biosecurity director, or equine infectious disease specialist were primarily private veterinary practitioners or university veterinary clinicians. In one situation, the stable owner, along with the attending veterinarian, contacted the State Veterinarian's office. In some situations, the State Veterinarian was notified of the situation but was not the one to take action in managing the outbreak. For example, in three different outbreaks on racetrack sites (two in California and one in Illinois), it was the veterinarian working for the racing commission or racing board who managed the outbreak. In two of the university clinic outbreaks, although the State Veterinarian was notified, the management of the situation was left to the director of hospital biosecurity or equine medicine faculty and hospital directors.

Quarantines

Was quarantine imposed as part of mitigation and, if so, who imposed it, what criteria were used to lift the quarantine, and what were the dates for placement of quarantine and lifting of quarantine?

A “stop-horse-movement” action was implemented in all outbreaks discussed by interviewees, but the persons or authorities responsible for stopping movement varied greatly. Official quarantines were imposed by the State Veterinarian’s offices of Connecticut, Florida, Kentucky, Maine, Maryland, Michigan, New Jersey, and Virginia. The Connecticut State Veterinarian described an alternative approach used to respond to an EHV-1 situation at a private veterinary clinic. The veterinary clinic personnel notified Dr. Lis of the diagnosis and the actions they were taking (voluntary quarantine). Based on these actions, Dr. Lis communicated with the Vermont State Veterinarian (the State from which the index case originated) and the Connecticut Veterinary Medical Association regarding the management of the situation. Dr. Lis provided this comparison in order to illustrate her flexibility in applying management strategies depending on the situation. Educational and outreach meetings included discussion of both the private veterinary practice EHV-1 situation and the EHM situation at the University of Connecticut. Veterinary teaching hospitals at Colorado State University and The Ohio State University quarantined their equine facilities. The California Horse Racing Board and the Illinois Racing Board quarantined the affected racetracks in their States. In some instances, initial responders, such as private veterinarians or university faculty, who suspected an EHV case recommended a stop-horse-movement order prior to official action being taken.

Although most States considered equine herpesvirus reportable, some, such as California, did not consider the disease as being actionable. The California Horse Racing Board placed “voluntary” quarantines at the racetrack, and the owner of the California riding stable voluntarily stopped horse movement. At the time of the outbreaks, interviewees indicated EHV-1 was not reportable in Illinois or Ohio; however, mitigators of both of these outbreaks informed the State Veterinarian’s office.

The impact of the quarantines varied due to the length of time they were in place, the number of facilities and horses affected by the quarantines, and whether or not events/admissions were cancelled. The length of quarantines (stop-horse-movements) varied, from 14 days to 3 months. Mitigators of outbreaks at racetracks tried to restrict the quarantine to the affected barn/s as long as the disease was contained; in a few outbreaks, as the disease spread, the entire track was quarantined. This quarantine strategy was implemented in order to

maintain racing and economic stability while managing the risk of spread of the disease. At Golden Gate Fields, the transport of clinically normal horses was restricted, but allowed to occur, between three tracks (Golden Gate Fields, Bay Meadows, and Pleasanton) in order to keep an adequate number of horses in the races. Some outbreaks and quarantines were limited to 1 or 2 facilities with as few as 19 horses, whereas others, such as the Florida outbreak, involved quarantine (or partial quarantine) of 2 show facilities with approximately 1,000 horses. Other quarantines consisted of portions of 3 private equine veterinary clinics, and 5 other premises with fewer than 40 horses on each premises. The Colorado State University Veterinary Teaching Hospital, The Ohio State University Veterinary Teaching Hospital, and the Marion DuPont Scott Equine Medical Center closed their teaching hospitals to equine admissions and quarantined horses in the hospital.

The criteria for release of quarantines were not consistent among outbreaks. A majority of mitigators (Lis, Short, Stout/Ford, Hoenig, Halstead, Halpern, Reed, and Hopson) reported that they waited 21 days after all quarantined horses appeared clinically normal and then required a negative test on all exposed horses to release the quarantine. One mitigator (Madigan) indicated the voluntary stop-horse-movement on the premises was in place for 21 days after no fevers were detected, and then all previously EHV-positive horses were retested by PCR to confirm negative results. At Golden Gate Fields, the California Horse Racing Board required horses to be afebrile for at least 14 days followed by two negative PCR tests (on both whole blood and nasal swabs taken 2 days apart). At the Los Alamitos racetrack, all horses in exposed barns had to be afebrile for 7 days, then two tests (on both blood and nasal swabs) were taken 48 hours apart, with negative results required in order to release quarantine; many of the test-positive horses had been moved off-site as part of the mitigation. The Colorado State University Veterinary Teaching Hospital and the Marion DuPont Scott Equine Medical Center waited 14 days after any horse had clinical signs (after all were afebrile for 14 days and no new neurologic cases were identified), then required negative PCR tests on nasal swabs from all horses in the hospital on samples collected on 4 consecutive days at the Colorado State University Veterinary Teaching Hospital, and 3 consecutive days at the Marion DuPont Scott Equine Medical Center. The State of Maryland tested all horses with an epidemiologic link to the Equine Medical Center; if no horses were febrile within 7 days, they tested all horses that had been at the Equine Medical Center and a subset of in-contact horses twice, by nasal swab and blood PCR, in order to release hold orders. The State of Virginia's criteria to release quarantine for trace-outs to premises with horses with contact with Marion DuPont Scott Equine Medical Center were: (1) 21-day period after the date of

detection of the last febrile horse (with no history of nonsteroidal drug treatment); and (2) all horses on the premises were then tested for EHV on blood and nasal swabs with all test results negative on PCR.

Case Definition/Categorization

Did you have a case definition at the outset or eventually develop one and if so what was it?

Across outbreaks different criteria were used to define a “case.” More specifically, several of those interviewed made a distinction between a case of EHM and a herpesvirus infection with and without clinical signs, such as fever. Several of those interviewed indicated that their case definition for EHM evolved over the course of the outbreak. The case definition initially used or that evolved for EHM for most of those interviewed was “clinical signs of neurologic disease along with laboratory confirmation of EHV infection or a horse with neurologic signs that was part of an outbreak where at least one other horse had laboratory confirmation of EHV infection.” Several of those interviewed indicated the need for further case criteria beyond EHM during an outbreak, such as for categorization of: (1) horses with fever and laboratory confirmation of EHV infection; (2) horses that had laboratory evidence of infection without clinical signs of disease; (3) horses with clinical signs of disease that were not tested, but had an epidemiologic link to confirmed cases; and (4) horses with fever and laboratory confirmation of EHV-1 infection that had an epidemiological link to EHM cases on another premises.

Testing or Monitoring Performed

Once you recognized the first EHM case(s) how did you identify subsequent cases?

Divergent approaches were taken at the onset of the outbreak regarding identification of infection beyond the index EHM case. In all situations, enhanced surveillance for clinical disease was implemented. Another approach was to test all potentially exposed horses for EHV as soon as the index case was identified in order to determine the scope of exposure/infection. A second approach was to enhance surveillance through monitoring of body temperature and observation for neurologic signs, but to test only those horses on the premises that developed signs consistent with EHV, including fever and/or neurologic signs. In some of the outbreaks, testing of exposed horses for exposure to EHV was

conducted after all signs of disease had resolved in order to lift a quarantine or a stop-horse-movement order. The specifics of this approach are discussed under the quarantine section of this report.

Once the index case was diagnosed in the majority of the outbreaks/disease events or for trace-outs, monitoring of body temperature was conducted as part of surveillance for fever. When asked what defined a fever, eight of those interviewed indicated that it was a temperature above or equal to 101.5°F; five indicated a temperature of greater than or equal to 102°F; one indicated greater than 101°F in the morning; one indicated greater than or equal to 101°F; and one indicated 1°F above the horse's normal temperature. All those interviewed indicated action was taken if a fever was detected in exposed or at-risk horses which included those horses being tested for EHV infection.

For some outbreaks a single laboratory was used for PCR testing, whereas other outbreaks used multiple laboratories to perform PCR testing. Interviewees reported nine different laboratories involved in PCR testing during the outbreaks: California Veterinary Diagnostic Laboratory, the Lucy Whittier Molecular and Diagnostic Core Facility, Colorado State Veterinary Diagnostic Laboratory, Cornell Animal Health Diagnostic Center, University of Florida Emerging Disease and Arbovirus Research and Test Program Laboratory, University of Kentucky Livestock Disease Diagnostic Center, Michigan State University Diagnostic Center for Population and Animal Health, Gluck Equine Research Center, and the Ohio Animal Disease Diagnostic Laboratory.

For three of the EHM outbreaks or trace-outs in California, samples were tested either at the California Veterinary Diagnostic Laboratory or the Lucy Whittier Molecular and Diagnostic Core Facility. In the situation with the index case that was necropsied at the San Bernardino Veterinary Diagnostic Laboratory, tissues were examined histologically and with immunohistochemistry, and further testing on the spinal cord was performed. The California Animal Health and Food Safety Laboratory tested some collected samples as part of the outbreak at a boarding facility in Maine (used multiple laboratories). Testing was done at the Kentucky Livestock Disease Diagnostic Center, and/or the Gluck Equine Research Center at the University of Kentucky for the outbreaks that occurred at the racetrack in Kentucky, the outbreak in Florida (used multiple laboratories including the Kentucky laboratory), the outbreak at the Standardbred track in Illinois, the trace-out of horses that left the Marion DuPont Scott Equine Medical Center and returned to facilities in Virginia and Maryland, the outbreak on a boarding facility in Maine (used multiple laboratories), the outbreak at Monmouth Park racetrack in New Jersey, and the outbreak that occurred at The Ohio State University

Veterinary Hospital (used multiple laboratories). The Michigan State University Diagnostic Center for Population and Animal Health performed the testing done as part of the management of the outbreak at the Standardbred track in Michigan and for the outbreak in Florida (used multiple laboratories). The Animal Health Diagnostic Center at Cornell was used for testing of samples from the Florida outbreak (used multiple laboratories), the outbreak at the University of Connecticut, and the boarding facility in Maine (used multiple laboratories). The Colorado State University Veterinary Diagnostic Laboratory tested samples from the outbreak at the Colorado State University Veterinary Teaching Hospital and also the Marion DuPont Scott Equine Medical Center outbreak.

Across outbreaks, the method used to diagnose a case of EHV infection varied and included one or more of the following: clinical findings consistent with EHV infection (fever and/or neurologic signs); necropsy and testing of tissues with presence of EHV detected; positive testing of nasal swabs for EHV by PCR; positive testing of whole blood for EHV by PCR; virus isolation on tissues, swabs and/or whole blood; and seroconversion or a fourfold rise in titer based on testing of paired sera samples. As indicated earlier, the approach to management of some outbreaks entailed sampling of all exposed horses at the onset of managing the outbreak while others tested only horses that developed fever or neurologic signs. Across outbreaks, the majority of testing of clinical or exposed horses occurred once the index case was identified, and entailed the collection and testing of nasal swabs and whole blood (in 12 of the outbreaks and/or trace-out situations) by PCR at 1 or more of the laboratories listed in the preceding paragraph. In two of the outbreaks (2004 in Michigan and 2006 in Colorado), only nasal swabs were collected and tested by PCR as a means of managing the outbreaks.

Testing for the neuropathogenic variant of EHV was reported to have been done as part of the investigation of all four California outbreak/disease events or trace-outs (testing done at California laboratories), the outbreak in Florida (testing done at the Kentucky Livestock Disease Diagnostic Center and/or Gluck Equine Research Center), the outbreak in New Jersey (testing done at Kentucky Livestock Disease Diagnostic Center), the outbreak in Illinois (testing done at the Kentucky Livestock Disease Diagnostic Center and Gluck Equine Research Center), the outbreak at the boarding facility in Maine (testing done at a California laboratory, the Kentucky Livestock Disease Diagnostic Center and Gluck Equine Research Center), and the trace-out of horses in Virginia (testing done at the Kentucky Livestock Disease Diagnostic Center and/or Gluck Equine Research Center). In all situations in which testing for the neuropathogenic strain was reported to have been conducted, positive results were obtained on at least

some of the horses tested. Several of those interviewed indicated that the outbreaks they were summarizing (Michigan racetrack, The Ohio State University, and Kentucky Turfway racetrack) occurred prior to the availability of the test for the neuropathogenic strain of EHV, while others indicated the result of such testing was not critical to their management of the outbreak (Colorado State University Veterinary Teaching Hospital).

Some mitigators indicated that during the testing they received results from the laboratory indicating that the sample was suspect (neither negative nor positive). Most responded to this result by assuming the horse was positive for EHV and implementing whatever biosecurity practices were used for test-positive horses to prevent disease transmission. The horse was then retested to determine its test status. One mitigator indicated conflicting results from two different laboratories on the same horses for EHV PCR positive or negative status; another reported that two different laboratories reported different results related to the neuropathogenic variant of the virus on the same horses. Yet another mitigator indicated that one type of sample (blood or nasal swab collected at the same time) was positive while the other was negative on PCR test for EHV.

Scope of the Outbreak or Investigation

When asked, why did you consider the situation an outbreak?

In the California situation, in which a horse that was recently imported to the United States was the index case, those interviewed were not sure they would call this an outbreak since there was only one case of EHM (for this report, classified as a trace-out situation).

For Golden Gate Fields, Dr. Arthur was not sure he would call this an outbreak, in the traditional clinical usage of the term, with only one clinical EHM case. Only with extensive monitoring of temperatures and the use of PCR testing was there any sense of an outbreak at Golden Gate Fields. However, he did consider the event at Los Alamitos to be an outbreak, as there were multiple EHM cases, multiple febrile EHV-infected horses, and a spread from the original or index case barn.

At the boarding stable in California there were multiple horses with EHM, two horses that tested positive for EHV, and the detection of additional febrile horses after the identification of the index case that tested positive by PCR for EHV.

At the University of Connecticut polo facility there were three acutely neurologic horses on same premises within a short period of time. This was considered an outbreak because of multiple cases of EHM in a public venue and the concern that it needed to be contained.

At Balmoral Park there were several horses with fevers and two with EHM, all within one barn at the racetrack over a short period of time; PCR tests were positive for EHV in the initial neurologic case and in additional cases of EHV infection.

For the boarding stable in Maine, Dr. Hoenig said, "...there were three neurologic cases on this one private boarding stable premises, which was not normal in the equine population in our State [Maine]."

At the Michigan racetrack, Dr. Halstead stated "...[he] did not initially consider this an outbreak but when they recognized additional EHM cases beyond the index case, based on heightened surveillance that was implemented after recognition of the index case, they considered it an outbreak. In other words occurrence of multiple cases of EHM at the racetrack over a short period of time made us consider it an outbreak."

Monmouth Park was considered an outbreak because there were multiple febrile horses with a positive PCR test for the neuropathogenic variant of EHV, following a direct epidemiological link to a confirmed neuropathogenic EHV outbreak in Canada.

During the Florida EHM situation, Dr. Short indicated "...we considered this an outbreak because there were two cases of severe neurological disease, one with confirmed contagious disease [that is, EHV-1] and there was a lot of risk for extensive exposure based on the situation we were facing."

Nosocomial spread of EHV occurred within the three veterinary hospitals reporting outbreaks (Colorado State University Veterinary Teaching Hospital, the Marion DuPont Scott Equine Medical Center, and The Ohio State University).

Dr. Hopson indicated concern because horses had returned to Virginia farms after having potential exposure to the index case of EHM at the Marion DuPont Scott Equine Medical Center.

Dr. Hohenhaus indicated he considered one case of EHM as an outbreak and EHM is reportable in his State (Maryland).

How many EHM cases occurred and what was the outcome for these cases?

All the outbreaks except one had one or more horses with neurologic signs and with laboratory confirmation of EHV infection. The exception was an EHV outbreak with an epidemiologic link to cases of EHM and confirmation of EHV infection with the neuropathogenic variant of the virus in febrile horses with no neurologic disease. For several of the outbreaks, trace-outs of potentially exposed horses resulted in identification of additional horses with infection, some of which showed signs of fever and/or neurologic signs. The number of EHM cases per disease event/outbreak or trace-out ranged from one to seven for those that had any EHM cases as part of the outbreak. The median number of EHM cases was three per disease event. Of the initial outbreak sites and trace-outs, all but two identified one or more horses with fever and laboratory-confirmed EHV infection, but without neurologic signs. Across the outbreaks and trace-out situations, the case fatality rate among the horses with neurologic signs (EHM cases) ranged from 0 to 100 percent. In one outbreak with five laboratory-confirmed EHM cases, no animals died; in another outbreak with seven EHM cases, six animals died or were euthanized. In one outbreak there was concern whether the cause of death or reason for euthanasia was actually due to EHM in horses that tested positive for the virus. This made calculation of a case fatality rate across all reported outbreaks/disease events and trace-outs difficult. Seven of those interviewed who had been involved in outbreaks with more than one EHM case were asked if the severity of disease was consistent across the entire outbreak: two indicated that the severity had been consistent across the outbreak and the remaining five indicated that the more severe cases occurred early in the course of the outbreak.

General Biosecurity Procedures and Other Control Strategies

What biosecurity or control procedures were used?

The table below summarizes responses to an open-ended question related to methods used to control the outbreak including biosecurity procedures implemented.

General management and biosecurity procedures reported in response to open-ended question related to procedures that were implemented as part of control	Data relates to 16 disease events: n=13 outbreaks and n=3 trace-outs
Quarantine of individual barn or entire facility or voluntary stop-horse-movement	State Veterinarian imposed quarantine, n=9 Mandatory quarantine other than State Veterinarian imposed, n=1 Voluntary stop horse movement, n=6
Trace-out or some form of contact or notification of those who may have had horses exposed through contact with the EHM case	n=16
Guard to enforce quarantine or stop-horse-movement	n=4 (all were at racetrack venues: two at Thoroughbred tracks and two at Standardbred tracks)
Monitored body temperature to detect new cases	n=16
Number of times temperature was taken per day on horses in quarantine or restricted area	Daily, n=1 Twice per day, n=9 Three times per day for horses in quarantined barn n=2 (horses outside of the quarantined area but on premises, temperatures taken twice per day)
Required log of body temperatures	n=11
Temperature logs inspected by regulatory authority	n=6
Used biosecurity precautions in quarantine area	n=16
Footbaths at entry point of quarantined barn or facility	n=12
Restricted persons entry to quarantined/restricted facility to only those necessary to care for horses	n=13
Allowed normal but potentially exposed horses from restricted/quarantined area to exercise but with protocols to reduce risk of them spreading disease	n=8
Moved <u>all</u> of the clinical cases (neurologic as well as febrile horses) off-site	n=2
Moved EHM cases off-site or into isolation facility	n=6
Moved all or some of the EHV test positive horses off site	n=4
Moved test positive or clinical cases to a separate quarantine facility/barn on-site	n=2
Wore gloves when working with horses in quarantined or restricted site (for some or all of the personnel)	n=7

General management and biosecurity procedures reported in response to open-ended question related to procedures that were implemented as part of control	Data relates to 16 disease events: n=13 outbreaks and n=3 trace-outs
Wore dedicated clothing or disposable coverall in quarantined area	n=10
Stop sharing of equipment including tongue ties, tack, buckets, feeders	n=12
Vaccination against EHV as part of management of outbreak	Advised against vaccination of exposed horse, n=2 Not addressed one way or other by those interviewed although private practitioners may have implemented vaccination, n=10 Recommended for horses that commingle, n=1 Required for new arrivals to venue where cases had been identified, n=3 Required for horses at venue but not in direct contact with cases of EHM/EHV, n=1 Required for both new arrivals and those already at venue, n=1
Tested potentially exposed horses for EHV as part of initial management of outbreak at onset	n=6 (two of these were trace-out situations)
Tested potentially exposed horses for EHV as part of research project but not for purposes of managing outbreak	n=2
Tested only clinical cases (neurologic or febrile horses) for EHV in order to manage the outbreak	n=10
Tested both clinical cases (neurologic and febrile) and exposed as part of quarantine or stop horse movement release process	n=12
Had feed deliver truck park outside quarantine barn to unload feed	n=3
Recommendation to work with horses with clinical signs of disease last for service providers or other personnel	n=4
Starters or horse identification personnel wore gloves and changed between each horse examined	n=4 (This was at racetrack venues and applied to contact with horses outside of the quarantine area)
Used disinfectant wipes to clean off hands of the rider of pony horse and surfaces of tack on pony horse between horses ponied	n=2 (This was at racetrack venues and applied to pony horses used outside of the quarantined area)
Implemented special protocols for handling of manure and soiled bedding for quarantined barns/horses	n=3
Spray vehicle tires with disinfectant when leaving the premises or quarantine area	n=2
Periodically cleaned and disinfected common areas, such as starting gate, warm-up area, test barn buckets, etc.)	n=6 (This applied to areas outside the quarantine as a general biosecurity practices begun because of outbreak)

Identified Needs

What would have been helpful for you to have that you did not have at the time of the outbreak?

Responses regarding what would have been helpful in addressing the outbreak or disease event fell into four primary categories: Planning, Disease Control/Biosecurity Measures, Diagnostics, and Communications.

Planning

Several respondents said it would have been helpful to have consistency between States and to have disease program standards. One respondent indicated that it would have been good to have discussed outbreak response in advance of the outbreak and to have a pre-existing plan. Some States had case definitions prepared; in other States, the case definitions evolved during the outbreak.

Dr. White said, "We needed clearer guidelines from the State regarding what they were going to do about containment of the problem on farms where horses that had left the hospital were now housed (trace-outs). Owners were really concerned and confused what criteria would be used by the State to contain the problem. It would be good for those in a role with the State to meet with experts on the disease and come up with best management practices and how those will be implemented and enforced." Another respondent indicated that it would have been beneficial to have clearer State lines of authority and explanation of how outbreak response measures would be executed at the racetrack.

Three of the respondents said that having designated isolation barns or a separate facility where infected horses could be moved would reduce the impact of the quarantines and the potential spread of disease. One person indicated he would like to have an isolation area with equipment available to sling neurological horses, if necessary.

Knowing which supplies are needed and having them on hand to respond to an EHV-1 outbreak would enhance the timeliness of response. Interviewees commented that the following items should be readily available:

- Disinfectant and footbaths to get started on the containment of the disease to a given barn;

- Appropriate swabs for collection of nasal samples from suspect cases; and
- Supply of quarantine orders in the hands of State field veterinarians.

Communication needs expressed by mitigators that could be addressed in advance planning include:

- Rapid, confidential communication system among States and between States and Federal regulatory officials;
- Private practitioner awareness of EHV and sampling methods;
- Access to EHV researchers to answer questions about test methods and interpretation of results; and
- Submission forms for the laboratory and all the contact information for the laboratory.

Mitigators also emphasized the need for both human and financial resources. One respondent indicated that instituting an Incident Command System (ICS), specifically tasked with logistical aspects of the response, would have provided additional resources. However, since no emergency was declared, resources available through ICS were not an option. Availability of funding to assist with testing was another concern.

Disease control/biosecurity measures

Much is yet to be understood about EHV-1, particularly the neuropathogenic variant. One respondent said it would have been beneficial to have information regarding the duration of virus shedding in a field setting—to know a mean and maximum for number of days of virus shedding, as much of what we know now is based on experimental challenge studies. A better understanding of the distance that the virus might spread via aerosol transmission would help mitigators identify likely exposure risks. Other issues to be addressed include: (1) the meaning of an EHV-1-positive test in a clinically normal horse, and (2) the implications of detecting the neuropathogenic variant of the virus via testing of nasal swab from a clinically normal horse.

Scientific validation for recommended biosecurity and containment measures was highlighted by one respondent who asked the following questions: “What recommendation should we give to manage the basic things on the farms where exposed horses then went? For instance, what precautions should be taken for feed delivery vehicles and personnel at farms? Is it acceptable for the farrier to come to the farm that was quarantined and then go to other farms? What precautions should be taken? Should they wear dedicated clothing? Do truck tires need to be sprayed with disinfectant? If we cannot give detailed guidance on these topics then we should say so.”

Diagnostics

Issues regarding diagnostics for EHV-1 were also raised by mitigators. “Is there a reference laboratory for validating tests for EHV-1? For example, which PCR is the best one to use and should we be doing the testing for the neuropathogenic variant?” One respondent indicated that the availability of a rapid test, such as a stall-side test, would allow for more prompt management decisions. Others felt that having the ability to run the test in their home States and having additional funding to assist with testing would have been beneficial.

Communication materials and plan

Although a few respondents indicated that they had developed some guidelines prior to the outbreak, several others indicated that having information prepared in advance for veterinarians, equine owners, and the general public would have been advantageous. In addition, implementation of communications early in the outbreak would have facilitated the outbreak response. When asked what would have been beneficial to have that they did not have when addressing their outbreak, respondents commented on the need for:

- “Clear concise communication points to try to alleviate panic,”
- “Earlier implementation of communication system to reduce rumors and expedite communication. We were capable of implementing this; we just did not do it as early as we should have. It is hard to know how things will evolve and this situation escalated and evolved more quickly than we anticipated.”
- “Clearer guidelines from the State. It would be good for those in roles with the State to meet with experts on this disease and come up with best management practices and how those will be implemented and enforced.”
- “Private practitioners to be more aware of EHV and sampling methods.”

Educational material developed or needed

Several sources of information were cited by respondents when asked about the need for and availability of educational material. Some materials had been developed prior to outbreaks and others were developed during outbreaks.

Sources of existing information that proved beneficial were:

- California Center for Equine Health (CEH) (n=3¹);
- AAEP infection control guidelines (n=3): one person indicated that the “AAEP Web site information was very helpful. It gave me a clear idea of how to go about testing and initial actions to contain the disease. It was step by step helpful guidelines that I could immediately use to help me manage this outbreak.”

¹ Refers to number of respondents who mentioned this resource.

- “Dr. Long at University of Florida helped a lot with good educational info.”
- *The Horse* magazine (n=2); EHV backgrounder;
- University of Florida Web site;
- “An article in Equine Veterinary Education by Dr. George Allen.”
- Journal articles;
- Material Safety Data Sheets on disinfectants used;
- “USDA Biosecurity brochure for equine owners, but it does not specifically address EHM containment...” and
- Marion DuPont Scott Equine Medical Center Web site.

Information developed in response to outbreaks included:

- A biosecurity handout for trainers and horseman (n=2);
- “An educational program through the University of Connecticut. The AAEP infection control guidelines were very helpful; included EHV info from AAEP on the U of Conn Web site.”
- “Information for track management about EHV; the University of California at Davis equine owner information was a very good start on this type of material.”
- Information for grooms in both English and Spanish regarding basic hygiene protocols and infection control methods; and
- “Question and Answer sheets” on EHV (n=2); one with assistance from Dr. Hal Schott at Michigan State University.

When asked what educational material they would have liked for EHV and EHM, some respondents indicated that they had the information they needed; however, others said it would be beneficial to have some information prepared in advance of an outbreak and to have an organization, like AAEP or USDA, develop a consensus on best management practices for EHV. In addition, a few respondents said they would like to have equine owner-level best management practices specific for EHV, as well as general biosecurity practices, such as keeping horses isolated for a period of time after they return from events or veterinary hospitals.

Another person said that having information on EHV in one fact sheet would be beneficial as he had to consult several sources to compile appropriate information for equine owners. Respondents identified a couple of points that should be highlighted in fact sheets:

- The horse with the neurological form of EHV poses a contagious disease risk to other horses, and
- Clarify that the virus type does not correlate 100 percent with clinical disease manifestation, e.g., neurological variant can be associated with abortion and vice versa.

In fact, one respondent said, “It would be good to have educational material on all likely equine contagious diseases but it’s difficult to predict which we will need next.”

Communication Efforts

What communication efforts did you carry out?

Respondents provided several pointers related to communication efforts in the face of an outbreak, including the use of press releases, Web sites, e-mails, equine practitioner meetings, owner/trainer meetings, meetings with workers at outbreak sites, racing commission meetings, and conversations with animal health authorities in other States.

A key point is to have clear, open communication to minimize anxiety and confusion. Two respondents highlighted the value of having a public relations (PR) person involved from the beginning of an outbreak. One of these said that PR personnel were involved about 1 week into the outbreak, but should have been involved sooner. The other respondent indicated that a PR person was involved in meetings, worked with media contacts, reviewed press releases, and updated the Web site with communication points.

Several of the respondents reported that designated spokespersons, many with prior media training, served as communication contacts during the outbreak. Most of these spokespersons had predetermined talking points. One person stressed that responding entities work together to ensure that everyone communicated the same message.

Media relations efforts ranged from interviews with local newspapers to national equine publications. Respondents issued press releases and posted outbreak information on Web sites, some with daily updates.

Face-to-face communications with equine veterinarians, trainers, owners, and facility managers proved to be important in several of the disease events. One respondent said that the combination of media interviews and a public meeting seemed to bring people together and help them understand the plan of action, convince them that the disease could be controlled, and helped control rumors. Personnel involved with one of the disease events held three meetings with equine veterinarians, and three separate meetings for owners, trainers, and anyone else who wanted to attend. Those addressing an outbreak at a racetrack held weekly meetings with trainers to discuss progress and plan of action. One neighborhood stable meeting drew 100 attendees.

One respondent used the outbreak as an opportunity to improve relations with two major racetracks in the State. “We also went to the two major racetracks and spoke to them about EHV and the need to have a control plan. We never had any EHM cases there, but we were able to use the outbreak at a boarding stable as a teachable moment, to come up with an emergency response plan for the tracks not just for EHV but any contagious disease outbreak. It allowed us to meet the track administration and come up with a workable plan and do a walk-through and identify an isolation barn and response plan, including monitoring for clinical signs of disease, so we can make a rapid response if need be. We discussed if there is an outbreak we might need to suspend activities at the track for a few days to get a handle on the situation, so if we ever need to take this action we have laid the ground work to make this a more likely successful plan.”

Communication with veterinary peers and equine advisory groups was another important aspect of outbreak management, both in gaining information on how to best address the outbreak and to inform others about the plan of action to control the outbreak. Most respondents communicated with State Veterinarians, horse councils, equine advisory groups, event and track management personnel, racing commissions, and State veterinary and equine practitioners associations. In addition, some held veterinarian meetings to share information about outbreak control, included lessons learned from the outbreak in subsequent continuing education seminars, and conducted a seminar for veterinary students, faculty, and graduate students regarding the outbreak. Some mitigators also provided updates on the equine industry monthly conference calls facilitated by Dr. Tim Cordes of USDA:APHIS Veterinary Services.

Web sites, e-mails, and a toll-free telephone hot line were used to provide information to horse owners and the general public. One respondent indicated that they did get information onto their Web site but were late doing so; it would have been good to have it up sooner to reduce the rumors and misinformation that occurred early in the outbreak. The Marion DuPont Equine Medical Center used a toll-free telephone hot line that equine owners could call in and ask questions. This was for individuals, not the media, and the resident veterinarians answered these calls.

The key message conveyed by a majority of respondents was to explain the plan of action and biosecurity measures so people understood the actions being taken by authorities and measures they could take to control the disease. Sharing this information helped to relieve anxiety and decrease rumors and misinformation. Two other key messages were to: (1) detect cases by finding

horses with fever or neurologic signs and moving these horses to an isolated site for care, and (2) explaining that the disease did not pose a risk to humans. Opinions about the use of vaccine in the face of an outbreak were mixed. Some respondents recommended vaccination in the face of an outbreak, whereas others did not.

Cost of Outbreak and Management Issues

Do you have any estimate of costs associated with the outbreak or trace-out?

- a. Testing, cost per test, number of tests, cost of shipping samples, cost of collection of samples for testing;
- b. Closure or lost business;
- c. Number of days of stopped-horse-movement and per-day estimate of loss number;
- d. Type of personnel involved in mitigation of outbreak and number of days each contributed to this outbreak situation;
- e. Cost of treatment of cases and number of cases treated; if there is a range of treatment cost, then supply: (1) the dollar amount of the highest cost of treatment and number of cases, (2) the dollar amount of mid-range treatment and number of cases, and (3) the dollar amount of mild-case treatment and number of cases;
- f. Cost of deceased horses due to this disease outbreak;
- g. Cost of biosecurity procedures, PPE supplies, disinfectant, hand hygiene products, barriers, and signage; and
- h. Other costs: specify what this cost was and the amount.

Few of the respondents had tracked costs of mitigating their outbreaks or trace-outs in detail. However, in some of the interviews various categories of costs were delineated. These included human resources costs, loss of income due to cancellation of events/racing, diagnostic costs, cost of communication and education efforts, and supply costs. The source of funding for outbreak response varied.

Dr. Arthur reported that the testing involved in mitigation for the Golden Gate Fields and Los Alamitos EHM outbreaks cost \$20,000 in laboratory fees alone, and was paid for by the racing associations. This included a reduced cost per test from the laboratory.

Connecticut has funds to investigate any sudden death or neurological cases, and helped with the cost of testing horses. In Florida, Illinois, and New Jersey, samples were collected by private veterinarians and the horses' owners paid for testing. One respondent indicated an individual trainer at a quarantined outbreak site had a \$12,000 bill for laboratory testing.

In Kentucky, where the cost was \$14,700 to perform approximately 420 PCR tests, the testing was performed at the Kentucky Livestock Diagnostic Laboratory at no charge to the Kentucky Department of Agriculture or the horses' owners. This was provided by the laboratory as a service to the equine industry of the State of Kentucky. In addition, due to the stopped movement, equine owners incurred additional board for 50 horses from December 21 to January 10, and an additional 50 horses from January 6 to February 1, with board costing \$50-\$100 per day per horse.

Dr. Hoenig: "IDEXX paid for some of the testing in Maine because they were working on a new test and they wanted samples to work with and to use in validation of their test."

Dr. Halpern: "There were 24,962 rectal temperatures taken at Monmouth Park during their outbreak. So the time for personnel to do this monitoring is only part of the cost of this outbreak."

Dr. Reed: "All testing was paid by The Ohio State University, which paid for deceased client horses. Estimated board costs for horses kept in the hospital as part of self-imposed quarantine and drugs used to treat some of EHM cases were approximately \$20,000."

Dr. White: "Hospital budget person estimated cost of lost income due to hospital being closed, treating horses, testing, etc., was \$755,000. No horses died from EHV at the Marion DuPont Scott Equine Medical Center."

Dr. Hohenhaus: "If the State Veterinarian of Maryland ordered the test, the State paid for it. Approximately \$3,500 in test costs. There has been lots of disruption to Maryland and Virginia equine sporting events associated with EHM situations."

Dr. Short: "[In Florida]...we tracked the time our Division employees spent on the outbreak and it was just over 4,000 hours."

Several respondents indicated that there were several days of loss associated with stopped or limited horse movement, but accurate estimates on those costs were not provided by respondents. Additionally, in multiple outbreaks, some

horses died or were euthanized, but the value of such horses or the cost of treatment given was not provided by these respondents—in part because they were not the veterinarians in charge of the medical treatment of these cases, but instead were the people involved in mitigation of the outbreak or trace-out.

One respondent indicated it would have been good to collect detailed information related to the various costs for the EHM outbreak.

Lessons Learned

What were lessons learned from your experience in mitigating the outbreak or trace-out?

Responses are grouped in the following categories:

- Planning for Disease Detection and Response;
- Biosecurity and Disease Containment;
- Information about EHV-1 and EHM; and
- Education and Communications.

Planning for disease detection and response

Several respondents stressed the importance of being prepared for an outbreak by having a response plan and guidelines worked out prior to an outbreak. One person said, “Have a plan for how you will manage such an outbreak, from being prepared to collect samples appropriately to how to contain the situation and having the supplies on hand to do this.” Other key planning needs mentioned by respondents were to:

- Have case definitions and quarantine criteria ready before an outbreak or within the first 1–2 days of an outbreak and stick with the quarantine criteria once they are established;
- Know what you are going to do with results before testing. Specifically, this person said, “Do not test till you know what you will do with the result if it comes back positive on a normal horse”; and
- Determine who will be paying for the testing.

The need for planning was summarized by one respondent: “It is important to have a plan for how we will manage the next EHM case or outbreak, as there *will* be another one.”

The lack of consistency in how different States addressed outbreaks was problematic for several respondents and created confusion among horse owners. One respondent suggested that regulatory officials work together using sound science to come up with a consistent response to EHM management.

The various options for testing for EHV-1 and the neuropathogenic variant of the virus led to some result discrepancies among tests. Two respondents suggested that the National Veterinary Services Laboratories or some other official laboratory criteria be established that would certify or validate the testing methods.

Biosecurity and disease containment

The implementation of additional day-to-day biosecurity practices at a racetrack was the result of one of the outbreaks. This was carried out in cooperation with racing commission and track management.

The early recognition of signs consistent with EHM along with a proactive approach in treatment and containment efforts are important strategies in responding to an EHM outbreak. Dr. Paul Morley, Director of Biosecurity at the Colorado State University Veterinary Hospital, who managed an EHM outbreak at the Veterinary Hospital, said: "The Findlay outbreak information was a great resource for me. The implementation of measuring rectal temperature in all potentially exposed horses once a suspect case of EHM occurs was very important in our management of this outbreak. We plan to implement an electronic medical record system that will flag any animal with a fever in our hospital and this will alert me, the director of biosecurity. We would then institute barrier precautions and work up the patient to determine cause of fever. This is not only important in control of EHV but of all contagious disease events."

Several respondents indicated that it is important to be able to remove EHM cases from the population to reduce viral challenge to other horses on the premises. The removal of an EHM case from the population requires having the ability to isolate the horse and provide necessary care for that horse while complying with biosecurity procedures. Those who addressed outbreaks at racetracks agreed that having an off-site facility or a quarantine barn on the track would facilitate management of the outbreak.

Although some respondents also believed it was important to segregate EHV-1 test-positive horses from potentially exposed but test-negative horses, others believe there is no reason to test clinically normal horses, even if they have been exposed, since some of these may test positive for EHV and it may be difficult to

then determine how to manage them. One respondent said, “We do not believe horses that are normal—no clinical signs of disease—should be tested for EHV, as it is challenging to know how then to interpret a positive test in a normal horse. In other words, what action should be taken based on such testing?”

One of the respondents who dealt with an outbreak at a racetrack acknowledged the need to be very aggressive in response to the first EHM case(s) and put control measures in place, but said it is important to try to have racing continue, even if on a limited basis.

Several lessons were learned by respondents in regard to biosecurity and disease containment. After trying to use private practitioners to implement control efforts at a racetrack, one respondent concluded: “It is best to have veterinarians who are not employed by the trainers in charge of the control efforts, such as those that work for the track management.” Respondents reported that some of the common practices that have been in place for years at racetracks were re-evaluated and changes made as follows:

- “We minimize commingling of horses at the detention barn as much as possible. We have done away with the common-use urine collection stall at the detention barn; this stall was reused to collect urine from horses. Now we pick the stall and spray it down when done with each horse. We recommend trainers bring their own water buckets to the detention barn.”
- “We have the ID person not touch the horses, but have the handler show them the ID on the horse’s lip.”
- “The person checking tattoo on lip changes gloves between horses.”

Implementation of biosecurity and disease containment measures at racetracks proved challenging as evidenced by the respondents’ comments below:

- “The workers live like the 1930s, in that the backside of the track is their life. They live there and have very little in the way of change of clothes and footwear, so we need to take this into consideration when trying to implement biosecurity and restrict access to the barns.”
- “The trainer in [a quarantined barn] had the coffee pot on all the time so people would come in for a cup and to chat—as that is what they always did—yet we were trying to limit access to this barn, so it is hard to get the message across in this setting.”
- “The racetrack management putting people in charge of being sure protocols were followed really helped, but it took multiple cases of EHV infection to convince them this was necessary. As we identified more infected horses based on testing in-contact horses, we got more buy-in from trainers for the control protocols we were putting into place.”

Information about EHV-1 and EHM

Another category of lessons learned from these EHM outbreaks centers around the herpesvirus itself and the neurological presentation of the disease. Although we have learned a lot from those who mitigated EHM outbreaks, there still is much to learn.

Perhaps one of the most important lessons learned regarding EHM case management was recommended by one of the respondents: “If a horse or horses have a history of neurological disease that was preceded by fever, EHM is high on the differential list and these horses should be managed as though they pose a risk to other horses.”

Another mitigator pointed out that this disease agent can spread rapidly with a few less-than-optimal control efforts, such as the pony horse leaving the quarantine barn at a racetrack and having contact with horses in other barns. This respondent pointed out that the trainer did not understand that the pony horse was part of the quarantine as the trainer simply did not think of the pony horse as a “horse.”

Dr. Steve Reed, faculty clinician at The Ohio State University Veterinary Hospital during an outbreak in 2003, reported that EHM, as observed during this outbreak, was a much more severe disease than he had observed in the past. Some cases experienced ascending paralysis with progression to encephalitis.

Since there is still much to learn about this disease, such as risk factors, vaccine efficacy, and treatment, one respondent recommended the archiving of samples for future study. [Note: The suggested research needs will be addressed in more depth later in this report.] “The equine industry wants to know when they can safely move their horses and we as regulatory officials need to have the answer if we are involved,” one respondent emphasized. “The owners are very cooperative the first time around, but the next time around they expect us to have more answers.”

Education and communication

Much was learned about communication needs and efforts during these EHM outbreaks. Several mitigators emphasized the importance of open and timely communication through multiple venues, such as meetings, Web sites, and media interviews, to minimize rumors and give people confidence that the situation is being handled effectively. One respondent learned that they should

have implemented the communication system earlier to share current facts and the plan for managing the situation. He said, “We found that not giving timely, accurate and complete information will cause rampant speculation, rumors, and panic.” Another respondent confirmed that “you can’t please everybody,” reporting that “...some people thought we overreacted in our control efforts, and others thought we should have quarantined all test-positive horses even if they did not have clinical signs of disease.”

Other respondents used their outbreak as a teachable moment to share information about disease control and vaccination in general. “We saw this as an opportunity to educate horse owners and event organizers about importance of disease monitoring and having a plan in place to isolate ill horses,” commented one respondent. “This disease event provided a planning and educational opportunity.”

Another communication initiative that resulted from an EHM outbreak is the development of e-mail lists and a phone tree. “We are currently working on an e-mail list so we can do alerts and share info, and then in some situations there is a phone tree that we would call or alert designated people, and then they would contact others in their group or organization,” said one State Veterinarian. “I have always had an open-door policy, so if people are wondering what the situation is on any given disease they can call my office and they will get to speak to someone or get a prompt call back.”

Research Needs

What would you say are needed areas of research related to EHM?

Several research needs regarding EHV-1 and EHM were identified by respondents. These research needs have been grouped into three categories:

- EHV-1 epidemiology;
- Diagnostics; and
- Vaccine development and treatment options.

EHV-1 epidemiology

Several research needs were identified regarding epidemiology of EHV-1 and EHM as illustrated by the respondents comments listed below:

- Conduct surveillance to determine if this disease really is getting worse or is it just heightened awareness and concern about it. (Hohenhaus)

- Identify non-horse reservoir of EHV. “I think there may be some reservoir of the EHV that can somehow modify it, either in number of viral particles or pathogenicity—some kind of cytokine promoter gene phenomenon. In several outbreaks I have dealt with, mules have visited or been moved onto the premises in the proceeding 21 days. I do not think they are carriers of the virus but somehow they might modify the virus or shed high numbers for a short time.” (Madigan)
- Why recent outbreaks have been occurring. (Sanchez)
- “What is the percent of horses that, in a stressful situation, would shed EHV and of those, which shed the neurological form of the virus?” (Short)
- Epidemiologic studies to determine the percentage of horses that shed EHV-1 at shows and other equine events, both the neurologic variant and the wild-type as determined by PCR testing of nasal swabs. (Madigan)
- “We need to understand this virus better and understand the role of latency in the outbreaks of EHM.” (Arthur)
- “Are the isolated single EHM cases a result of reactivation of a latent infection or due to exposure to another horse that is shedding?” (Arthur)
- Test interpretation of “garden variety” EHV versus the mutant strain; risk posed by horses that have one type versus the other. (Hohenhaus)
- “What is the significance of the neuropathogenic variant of the virus being shed by a normal horse?” (Hoenig)
- More epidemiologic studies from outbreaks to identify risk factors for EHM and impact of vaccination on outcome of cases and controls. (Morley)
- “We need more research on risk factors for EHM so collection of case-control study info during naturally occurring outbreaks would be valuable.” (Morley)
- “It would be good to know if there are biosecurity practices that could reduce the risk of this disease or not.” (Lis)
- “How far can virus be spread via aerosol mode of transmission?” (Fowler and Boone, Morley)
- “What is the incubation period in naturally occurring cases and how virus spreads?” (Halpern)
- Duration of shedding of EHV-1 from field-based situations. (Morley)

Identification of risk factors associated with the development of EHM is one of the primary areas for epidemiologic research mentioned by a majority of respondents:

- Which horses are at risk for EHM, versus those that only develop a fever or exhibit no signs of disease despite being exposed?

- Correlation of positive PCR test with virus isolation results and if there is a way to predict the risk test-positive but clinically normal horses pose to other horses;
- What are risk factors for reactivation of EHV?
- Is there a risk posed by certain types of horses as carriers? Determine if there is a way to identify the horses that are going to pose a risk before there is an index case or outbreak.
- What is the risk posed by a PCR-positive, EHV-shedding horse that is clinically normal?

Diagnostics

Some of the suggestions regarding research needs for EHV diagnostics were to:

- Have the National Veterinary Services Laboratories or some other standardizing system recommend or validate the tests that are being done to identify EHV and the neuropathogenic variant;
- Develop a rapid test/stall-side test for the variant that causes the neurological form of the disease;
- Establish a better description of the immunopathology of the central nervous system lesions; and
- Determine the most appropriate diagnostic samples to test: nasal swabs versus blood in naturally occurring outbreaks.

Vaccine development and treatment options

Vaccine development and treatment options were other areas in which additional research was deemed necessary by respondents. Two respondents indicated that a study of the efficacy of the available vaccines in prevention of EHM would be beneficial. A majority of respondents stated that development of a vaccine to prevent the neurological form of the disease should be a priority. Three respondents stated that the efficacy of treatment options needs to be assessed, particularly the efficacy of antiviral drugs.

Summary and Conclusions from Interviews with Mitigators of EHM Disease Events

Mitigators of each of the EHM disease events stopped horse movement, either through voluntary cooperation or mandatory restrictions; however, the approach taken by mitigators, and the positions of authority of the mitigators, was quite varied. Several of the respondents mentioned a need for more consistent guidelines from State to State on how best to contain EHM once an index case is identified. Perhaps a “Best Management Practices” document could be prepared using the current state of knowledge about EHV-1 and more specifically EHM, but acknowledging that much dialogue and research is needed to determine where consensus exists and to fill existing information gaps.

If a consensus regarding best management practices were developed, it would provide a starting point for mitigators of future outbreaks, as well as eliminate some of the confusion among those involved in the equine industry about why outbreaks were managed differently. Although guidelines would potentially provide consistency and add credibility to mitigators’ actions, it is important to note that criteria for release of quarantines or other stop-horse-movement actions can be assured through different approaches. Shortening the quarantine period (e.g., from the AAEP-recommended 28 days after there is no evidence of disease), would require more testing than would basing the status on disease detection only.

Nearly all respondents mentioned the need to develop a vaccine that is efficacious in preventing EHM. In addition, they stressed the need to identify risk factors for EHM and transmission capabilities of EHV-1 in order to apply scientific knowledge to the development of best management practices. Several respondents indicated that they believed it ideal to move EHM cases to a barn or facility separate from other horses. Efficacy of biocontainment procedures also needs to be evaluated to make recommendations for best management practices. Few of the respondents had tracked all of the costs associated with the EHM outbreaks. To better document the financial impact of EHM outbreaks, and to prepare for the financial costs of mitigating EHM outbreaks, costs need to be tracked in future outbreaks.

Part III: Recent Publications That Address Needs Suggested in Interviews

The purpose of Part III is to provide information from a few selected recent publications that address some of the questions posed by those interviewed for this report. This section does not provide an extensive and all-inclusive review of the literature regarding EHV-1 or EHM, as multiple reviews are presently available and the ACVIM will have fully referenced responses to nine key areas related to the understanding of equine herpesvirus available in fall 2008 on the ACVIM Web site.

1) Recent Advances in Our Understanding of Equine Herpesvirus-1 (EHV-1) Myeloencephalopathy. Allen G, Timoney PJ. Report for the Infectious Diseases of Horses Committee of the U.S. Animal Health Association, 2007.

This proceedings paper contains as-yet unpublished information from these authors as well as cited published information and is available on the USAHA Web site at <http://www.usaha.org/committees/reports/2007/report-hd-2007.pdf>

Disease emergence:

Evidence of recent increase in EHV-1 myeloencephalopathy (EHM) in assemblages of horses in the United States and discovery that the majority of these outbreaks were caused by a mutant hypervirulent strain of the herpesvirus suggests that EHM is an emerging disease.

Molecular characterization of 450 archived EHV-1 isolates recovered from equine fetuses in Kentucky that were aborted over a 50-year period (1956-2005) revealed a statistically significant increase in herpesviral isolates with the genetic marker (ORF30 A₂₂₅₄ to G₂₂₅₄ mutation) for the neuropathogenic strain of EHV-1.

Enhanced pathogenicity:

Mechanistic basis for such increased virulence of the ORF30 mutant strain of EHV-1 lies in the enhanced replicative capacity of this mutant strain to result in tenfold higher levels of leukocyte-associated viremia, relative to those generated by the wild-type EHV-1 infections.

Recent experimental inoculations with the mutant strain of EHV-1 resulted in a higher attack rate and neurologic mortality rate than did challenge with the wild-type, abortion storm isolate of EHV-1.

Diagnostic testing:

The laboratory test that yields the most rapid and sensitive diagnostic results for EHV-1 is the PCR and the equine samples of choice are nasal swabs and buffy coat leukocytes collected from whole blood samples. Since the post-exposure, temporal profiles of the presence of EHV-1 in nasal secretions and circulating leukocytes of the horse do not completely overlap, the collection and testing of both clinical specimens is necessary to achieve the maximal diagnostic sensitivity. Facilitation of EHV-1 genotyping in diagnostic laboratories has recently been achieved with a real-time PCR-based test procedure.

In the context of an ongoing epizootic of EHV-1 neurologic disease, positive PCR test results on horses associated with the epizootic by physical proximity, a history of exposure, and/or clinical signs consistent with EHV-1 infection can reliably be interpreted as evidence of active infection by herpesvirus. The interpretation of positive PCR results on nasal swabs or blood samples from horses not linked to an outbreak of EHV-1 infection and tested only for purposes of general screening, health certificate requirements, or pre-transport monitoring for virus shedding is more problematic and carries less certitude. A part of the interpretative uncertainty derives from lack of any information on positive and negative predictive values of EHV-1 PCR tests. There is strong evidence to suggest that latent virus does not circulate in blood leukocytes. These authors thus suggest that horses whose blood leukocytes test positive for EHV-1 DNA by PCR are most likely to be actively infected by the virus.

Immunologic requirements for vaccine-induced protection from EHV-1 myeloencephalopathy:

These authors reported having developed an equine disease challenge model for evaluation of the efficacy of vaccines for protection of horses against EHV-1 myeloencephalopathy. These authors suggested that to protect against EHM, a vaccine would need to induce an immune response toward production of cytotoxic T-lymphocyte precursors. They conducted proof-of-concept studies using a virulent, wild-type EHV-1 intranasal vaccine that produced full protection against challenge inoculation (90 days after vaccination) with a highly neuropathogenic, mutant strain of equine herpesvirus.

2) Prevalence of latent, neuropathogenic equine herpesvirus-1 in the Thoroughbred broodmare population of central Kentucky. Allen GP, Bolin DC, Bryant U, Carter CN, Giles RC, Harrison LR, Hong CB, Jackson CB, Poonacha K, Wharton R, Williams NM. *Eq Vet J* 40:2, 105–110 (6), 2008. The abstract below was excerpted from the Web of Science.

Abstract:

Reasons for performing study: An emerging problem of equine herpesvirus-1 (EHV-1) infection in horses in the USA is a high-mortality myeloencephalopathy that commonly occurs where large numbers of horses are stabled. EHV-1 isolates recovered from recent neurological outbreaks represent a mutant virus strain that possesses enhanced neuropathogenicity. A central question of EHV-1 myeloencephalopathy is the latency carriage rate for these mutants of EHV-1 in USA horse populations.

Objective: To estimate the prevalence of neuropathogenic strains of EHV-1 as latent infections in the Thoroughbred broodmare population of central Kentucky.

Methods: Submandibular lymph nodes (SMLN) were collected during *post mortem* examination of 132 Thoroughbred broodmares. Total DNA purified from SMLN tissue was tested for the presence of latent EHV-1 DNA by an ultrasensitive magnetic bead-based, sequence-capture, nested PCR method. Differentiation of active from latent infections by EHV-1 was achieved by detection of transcripts of EHV-1 glycoprotein B by reverse transcription PCR.

Results: Latent EHV-1 DNA was detected in the SMLN tissues of 71 (54%) of the 132 mares submitted for necropsy. Thirteen (18%) of the 71 latently infected horses harbored the neuropathogenic biovar of EHV-1. Of the 13 horses latently infected with an ORF30 mutant strain of EHV-1, 11 also carried a latent, wild-type strain of the virus in their SMLN tissues.

Conclusions: Neuropathogenic strains of EHV-1 have established a significant presence in the Thoroughbred broodmare population of central Kentucky as latently infected carrier horses. The data also indicate that a highly sensitive DNA detection method is required to identify many instances of EHV-1 latency.

3) Equine Herpesvirus Type-1-Associated Myeloencephalopathy in The Netherlands: A Four-Year Retrospective Study (1999–2003). Goehring LS, van Winden C, van Mannen C, Sloet van Oldruitenborgh-Oosterbaan M. *J Vet Intern Med* 20:601–607, 2006.

These authors described nine confirmed outbreaks of EHV-1-associated myeloencephalopathy (EHM) in the Netherlands. The authors stated that the typical presentation of EHM in The Netherlands is: (1) an index animal with

neurologic signs; (2) fever occurs in horses other than those with signs of neurologic dysfunction; (3) signs of mixed neurologic myelopathy; (4) seasonality of outbreaks (late fall, winter, and early spring); and (5) specific risk factors (breed, age, and sex) were associated with presence of neurologic signs in horses. In this study, factors individually associated with severe neurologic dysfunction included increasing age, horses having been febrile, and being female. After adjusting for premises, breed, and fever, age, and sex were no longer significant risk factors, suggesting that fever was the most important factor related to the chance of developing severe neurologic dysfunction. Neurologic dysfunction was never encountered in Haflingers, Fjords, Icelandic horses, the archetypical pony breeds, and horses less than 3 years of age. Most index cases in this study had a history of transportation or exercise under stressful conditions. Most EHM outbreaks in The Netherlands occurred on premises with unvaccinated horses and the authors conclude that today's vaccines are an unlikely risk factor for development of EHM.

4) Comparison of the efficacy of inactivated combination and modified-live virus vaccines against challenge infection with neuropathogenic equine herpesvirus type 1 (EHV-1). Goodman LB, Bettina W, Flaminio MJB, Sussman KH, Metzger SM, Holland R, Osterrieder N. *Vaccine* 24, 3636–3645, 2006.

These authors described a challenge infection using aerosolized virus that had been isolated from a fatal case of EHV-1 myeloencephalopathy in Findlay, Ohio (strain OH03, kindly provided by Dr. G.P. Allen). Healthy female mixed breed horses ages 3–10 years were randomly assigned to one of three groups for this study: (1) the control (placebo) group received minimal essential medium, n=5; (2) inactivated virus vaccine group (FluVac[®] Innovator 6 combination vaccine, Fort Dodge), n=5; and (3) modified live virus (MLV) vaccine group (Rhinomune[®], Pfizer), n=5. All vaccinated horses received two intramuscular injections of vaccine per manufacturer recommendation at 30-day intervals and were challenged with OH03 virus (5×10^6 plaque-forming units of cell-free virus supernatant) 59 days after initial injection.

The authors designed this study to compare the efficacy of two commercially available vaccines used to protect horses against the respiratory form of EHV-1 disease. The immunization regime was that recommended by the manufacturers' instructions and the challenge was with a recent, neuroinvasive EHV-1 isolate. Fever occurred in horses in all three groups but duration of fever was statistically different among the groups. The mean duration of the fever in the modified live vaccine group was 1.2 days; the mean duration in the controls was 3.4 days; and

the mean in the inactivated vaccine group was 2.25 days. Induction of EHV-1-caused neurologic disease was observed in three of the five horses in the control and inactivated vaccine groups while no neurologic signs occurred in the modified-live vaccine group.

Nasal shedding peaked on days 3–5 in both control and inactivated vaccine groups; in contrast, only marginal shedding was detected in one of the five horses in the modified-live vaccine group. Comparable levels of viremia, up to 10^6 genome copies per million lymphocytes, were detected in all three groups of horses. On days 6-8, fewer of the modified-live vaccine group horses had detectable viremia when compared to the other two groups, although the difference was not statistically significant. When the data on viremia were compared to development of neurologic signs for the horses in all three groups there was a suggestion that the duration of viremia was more important than the number of infected lymphocytes.

These authors suggested that neutralizing antibodies are not correlated with protection from abortion and extend those findings to clinical presentation as it pertains to the neurological form of EHV-1. They indicated that an EHV-1 specific serum IgG isotype assay may be predictive with respect to protection against EHV-1 infection with the immune response in the modified live vaccine group being characterized by IgGb antibodies after the second dose of vaccine and horses vaccinated with the inactivated vaccine having a high proportion of IgG(T) antibodies. These authors proposed that high IgG(T)/IgGa or IgG(T)/IgGb ratios as induced by the inactivated vaccine seem to be unfavorable with respect to protection against EHV-1 clinical disease while the EHV-1 specific responses dominated by IgGb antibodies seemed to be correlated with protection.

In conclusion, these authors suggested that the quick recovery from fever and the protection from neurological signs, despite the high challenge induced viremia, indicate that the RaCH-based MLV vaccine (Rhinomune®) is apparently effective in protecting horses from EHV-1 disease, at least under conditions of a relatively short interval (29 days) between the booster dose of vaccine and the challenge infection. It is important to note that the results of their study related to the “poor performance” of the inactivated vaccine evaluated in this study may not be indicative of all inactivated vaccines and that other inactivated vaccines with proven immunogenicity and efficacy in prevention of abortion and respiratory disease in EHV-1 studies should be tested in future studies.

5) Outbreak of Neurologic Disease Caused by Equine Herpesvirus-1 at a University Equestrian Center. Henninger RW, Reed SM, Saville WJ, Allen GP, Hass GF, Kohn CW, Sofaly C. *J Vet Intern Med* 21, 157–165, 2007.

These authors describe an outbreak of EHV-1 infection causing neurologic disease among a group of horses at a university equestrian center beginning in January 2003. Out of the 135 horses at this facility, 117 displayed signs of EHV-1 infection ($117/134=87.3\%$). Forty-six horses developed neurologic disease ($46/135=34\%$) and 12 ($12/135=8.9\%$) became recumbent and did not survive (12%). There were two waves of fevers among horses on this facility with 42 horses affected with neurologic signs in the first wave of EHV-1 infection. The authors indicated that the time interval from the end of the febrile period to the onset of neurologic signs ranged from 1-4 days and that all horses were afebrile at the onset of neurologic signs. Factors associated with development of neurologic disease at this facility included age of the horse (>5 years), location in south or arena stall area, and highest rectal temperature on day 3 or later in the febrile period. Resident horses at this facility were vaccinated every 3 months with an inactivated EHV-1/EHV-4 vaccine product (FluVac® Innovator, Fort Dodge Animal Health), with the last vaccine being administered 2 months prior to the outbreak. The one pregnant mare had received two vaccinations with an inactivated vaccine product containing EHV-1 abortigenic strains (EHV-1p and EHV-1b, Pneumabort-K® +1b, Fort Dodge Animal Health). Newly arriving horses were required to be vaccinated against influenza and herpesvirus 10-45 days prior to arrival at this facility. The type of vaccine product to be administered to newly arriving horses was not mandated. Only four of the horses at the facility at the time of the outbreak had received the modified live EHV-1 vaccine (Rhinomune®, Pfizer Animal Health). The authors indicated there was no apparent difference in effect of vaccine type or manufacturer on the incidence of EHV-1 infection or development of neurologic signs, but pointed out that only four horses had received the modified-live vaccine prior to the outbreak. There did appear to be an association between horses that were vaccinated three to four times per year preceding the outbreak and the development of neurologic manifestations of EHV-1. The authors suggested that this apparent association between more frequent vaccination and development of neurologic disease needs to be interpreted with caution as the majority of horses that were vaccinated three to four times annually were those that were older resident horses to the facility, whereas many young horses had been vaccinated for the first time before entering the facility. They also pointed out that since age was also associated with the development of neurologic disease, it is difficult to assess the impact of vaccination alone.

6) Transmission of EHV-1 by Horses with EHV-1 Myeloencephalopathy: Implications for Biosecurity and Review. Kohn CW, Reed SM, Sofaly CD, Henniger RW, Saville WJ, Allen GP, Premandan C. *Clinical Techniques in Equine Practice* 5, 60–66, 2006.

This article described the occurrence of nosocomial EHV-1 myeloencephalopathy in hospitalized horses associated with admission of EHV-1 myeloencephalopathy cases into the hospital from a 2003 outbreak at the University of Findlay. The authors pointed out that the transmission of EHV-1 from neurologic cases to other hospitalized horses not associated with the original outbreak indicates that the previous assumption that horses with EHV-1 myeloencephalopathy are no longer shedding virus is erroneous. Although the precise means by which EHV-1 was spread in this university veterinary hospital is unknown, the authors suggested several potential means by which the virus may have spread. These include: (1) the close proximity of the index cases and subsequent EHV-1 myeloencephalopathy cases; (2) people and horse traffic through the area with the index cases and their movement into other areas of the hospital; and (3) movement of hospitalized cases around the hospital. The EHV-1 transmission occurred despite personnel wearing barrier precautions when working with EHV-1 myeloencephalopathy cases.

These authors recommended that vigorous biosecurity precautions be instituted when EHV-1 myeloencephalopathy cases are admitted for veterinary care including strict isolation of cases, preferably in a dedicated facility well away from the main hospital. Attendants should wear occlusive barrier clothing (coveralls, rubber or plastic boots, and gloves) and access to EHV-1 myeloencephalopathy cases should be restricted as much as possible. In addition, they suggested strict quarantine of all horses having had recent contact with EHV-1 myeloencephalopathy case(s), with implementation of monitoring to detect signs of EHV-1 infection for a minimum of 21 days following the last clinical evidence of active EHV-1 disease. These authors reported that some outbreaks can be characterized by new waves of disease, as reported at the University of Findlay, and that this necessitates an even longer period of quarantine of the premises.

7) Comparison of the Diagnostic Sensitivity of Nasopharyngeal and Nasal Swabs and Use of Viral Loads for the Molecular Diagnosis of Equine Herpesvirus-1 Infection. Pusterla N, Mapes S, Wilson DW. AAEP Proceedings 53, 220–224, 2007.

1. This study indicated there was a similar recovery and quality of viral DNA between nasopharyngeal swab samples and nasal swab samples, when collected from the same horse at the same sampling time in the course of EHV-1 infection, during a naturally occurring outbreak of disease. There were 19 study horses in which EHV-1 was detected on both nasopharyngeal and nasal swabs. There were an additional 14 horses that were real-time PCR test-positive on either the nasal swab or the nasopharyngeal swab. A larger number of horses were test-positive for EHV on the nasal swabs than on the nasopharyngeal swabs.
2. Viral load in nasal swab samples from neurologic EHV cases was high, and the authors concluded this confirmed the importance of these horses as a source of contagion to other horses.
3. Of 15 neurologic horses tested, viral loads were significantly higher in blood than in nasal secretions, but only 9 of the 15 neurologic horses tested PCR-positive on blood samples, whereas EHV-1 was detected in all of the nasal secretions. For the nine horses in which EHV-1 was detected in both blood and nasal secretions, viral loads were higher in nasal secretions.
4. Of 41 subclinical horses tested, only 5 had positive PCR test on blood while 40 tested positive on PCR test of nasal secretions.
5. When viral loads in blood were compared between subclinical, febrile, and neurologic horses, febrile horses had significantly higher viral loads than did subclinical or neurologic horses. In contrast, viral loads in nasal secretions of neurological horses were significantly higher than those of febrile or subclinically infected horses.
6. The authors suggested that neurologic EHV-1 infected horses pose a contagious risk to other horses based on high viral load in nasal secretions.
7. They also concluded that the random testing of healthy horses for EHV-1 by PCR should be avoided, because practicing veterinarians and regulatory veterinarians who submit such samples may be unaware of the complexities involved in test interpretation. The situation is likely different when healthy horses determined to be at high risk of exposure are tested for surveillance purposes during active outbreaks of EHV-1 infection. Under such circumstances, horses that test positive by PCR on nasal secretions should be isolated and closely monitored for development of clinical disease, because the viral load pattern of infected horses during the early incubation period is similar to that of subclinical carriers. Followup

assessment of viral loads in blood and nasal swabs can be used to help guide modification of infectious disease-control measures, including lifting quarantine, for individual horses that test negative on subsequent sample.

8) Characterization of viral loads, strain and state of equine herpesvirus-1 using real-time PCR in horses following natural exposure at a racetrack in California. Pusterla, N, Wilson WD, Mapes S, Inno C, Isbell D, Arthur R, Farraro G. *The Veterinary Journal*, in press. Available online via Science Direct, DOI number: doi:10.1016/j.tvjl.2007.09.018. Accessed online April 15, 2008.

Viral loads, strain type (neuropathogenic versus non-neuropathogenic) and state (lytic, non-replicating, or latent) of EHV-1 were determined by real-time PCR on whole blood and nasopharyngeal secretions of adult horses after natural exposure. The index case of EHM and potentially exposed horses were sampled as part of this study. The authors suggested that the PCR tests typically performed at veterinary diagnostic laboratories do not differentiate the state of the virus (lytic, non-replicating, or latent) or report viral load (quantification of amount of virus detected).

Several key findings from this study included:

1. The index case that exhibited signs of EHM at the time it was initially tested had high viral shedding, based on testing of nasal swab samples, with concurrent low level viremia. This horse was afebrile at this time but had a history of fever in the 3 previous days. The authors concluded that horses with EHM pose a substantial risk to other horses and should be isolated away from other horses in order to decrease the risk to other horses.
2. PCR assay targeting the gB gene of EHV-1 was associated with a higher detection rate when compared to the assay that targets the ORF 30 gene (used to distinguish the neuropathogenic from the non-neuropathogenic variant). Typically those cases with low viral loads tested negative when the ORF30 gene was targeted.
3. Only the index horse and the horse in the neighboring stall tested positive solely for the neuropathogenic strain of the virus.
4. Other horses that were exposed to the index case were most commonly found to be positive, based on PCR testing, for either the non-neuropathogenic strain or both the neuropathogenic and non-neuropathogenic strain. Some of these horses remained clinically normal despite testing positive on the same sample for both the neuropathogenic and non-neuropathogenic strain of EHV-1.
5. Horses with evidence of the lytic infection characterized by presence of the transcriptional activity of the gB gene were associated with high viral loads at the gDNA level, while non-replicating virus was routinely seen with low

viral loads. To assist in defining the non-lytic state, samples were tested for markers of functional latency, EHV-1 LAT; latency was detected in some of the samples tested as part of this field investigation.

6. The authors concluded that there is a need for consensus on the use and interpretation of molecular diagnostic techniques in the diagnostic evaluation of field cases of suspected EHV-1 infection, since this information may influence the risk of exposure to other horses and may help practitioners and regulatory officials make appropriate decisions regarding the management of horses that test positive on PCR.

9) Detection of Nasal Shedding of EHV-1 and 4 at Equine Show Events and Sales by Multiplex Real-Time PCR. Yactor J, Lunn KF, Traub-Dargatz JL, Morley PS, Barnett CD, Kohler AK, Kasper KS, Kivi AJ, Lunn DP. AAEP Proceedings 52, 223–227, 2006.

1. This study was based on samples collected from horses attending four equine events (shows and sales) and from horses at a farm with an epidemiologic link to horses at one of the sales. Sampling was directed toward juvenile horses attending these events. A total of 451 horses were sampled on arrival at the event with 122 of these same horses having a repeat sample several days later.
2. The testing performed on the nasal swab samples was a multiplex real-time PCR test conducted in a research laboratory at Colorado State University.
3. Overall 3.8 percent of the samples were positive for EHV-1 on arrival and 1.8 percent of the repeat samples were positive for EHV-1.
4. These samples were not tested further to determine if the virus detected was the neuropathogenic variant of EHV-1.
5. This study illustrated that horses at events can shed EHV-1 that is detectable by real-time PCR, yet none of these horses showed signs of neurologic disease while at the event. The authors indicated further analysis of data will be conducted to determine if animal risk factors for shedding of virus can be ascertained.

Part IV: EHM Reporting in the National Animal Health Reporting System

The National Animal Health Reporting System (NAHRS) is a joint effort of USAHA, AAVLD, and APHIS. NAHRS was designed to provide data from State animal health officials on the presence of confirmed OIE-reportable diseases in specific commercial livestock, poultry, and aquaculture species in the United States. It is intended to be one part of a comprehensive and integrated animal-health surveillance system.

NAHRS is based on the reporting of recognized presence or absence of each of the OIE-reportable diseases, but does not require the reporting of the prevalence of these diseases. Confirmed disease is reported as present if the State animal health official determines there was at least one case that met NAHRS reporting criteria for that specific disease. If a case does not specifically meet all of the NAHRS reporting criteria, the State animal health official may also use additional information or epidemiological information to decide if the case should be reported as a confirmed case. Within a State, data about animal disease occurrences are gathered from as many verifiable sources as possible and consolidated into a monthly report that is submitted to the APHIS-VS National Surveillance Unit, where the information is verified, summarized, and compiled into a national report.

Historically, the NAHRS category for reports of equine herpesvirus was “EHV-1 or EHV-4” (see B208 below). The States reported “Yes” or “No” to indicate the detection (or lack of detection) of “EHV-1 or EHV-4,” with no further differentiation. In August 2007 the NAHRS Steering Committee approved the addition of reporting capabilities for neurological EHV-1 EHM for the NAHRS monthly reports submitted by the States. In October 2007 this proposal was approved by the USAHA/AAVLD Committee on Animal Health Information Systems. This reporting was implemented in January 2008.

Method of Reporting EHV and EHM in NAHRS

B208 Equine Rhinopneumonitis (Equine Herpes Virus, EHV 1 and 4):

Proposed Reporting Criteria: Presumptive diagnosis based on clinical signs, histological lesions (inclusion bodies) and/or a positive fluorescent antibody. Definitive diagnosis requires either virus isolation and/or PCR detection of the virus, or a 4X rise in titre in paired serum samples on the serum neutralization test.

If the response is “Yes” to B208, then States report “Yes” or “No” to B208a.

B208a EHV-1 Myeloencephalopathy (EHM):

NAHRS reporting criteria for EHM:

A case of EHM is defined as a horse exhibiting signs of CNS dysfunction, including most commonly posterior incoordination, weakness, and bladder atony. Additionally, the horse tests positive for EHV-1 by virus isolation and/or PCR assay on nasal swab or blood (buffy coat). In cases of sudden death or where the horse dies as a result of neurological complications, the postmortem lesions are consistent with those of myeloencephalopathy and EHV-1 has been isolated, detected by PCR, or demonstrated by immunohistochemical examination of the CNS.



Photo by Chad Mendell

Appendix A: Interview Form for Mitigators of Recent Outbreaks of EHM

The goal is to gather information, through a telephone interview, about your experience with managing or involvement in mitigation of recent outbreak(s) of equine herpesvirus myeloencephalopathy (EHM). The purpose of the interview is to gather background information about the outbreak, then ask some questions that will allow me to understand how you investigated the outbreak, how the outbreak was managed/controlled, and any lessons learned from dealing with the outbreak. Lastly, I would like to get your opinion on research and education as well as communication needs related to EHM.

First, I will ask you to describe the location, type of facility where outbreak took place, and dates of the outbreak (from the date the initial case was identified until the date the outbreak was declared resolved or the quarantine was lifted). Then I will lead into the following outline of talking points listed below.

1. Describe how you recognized you had an EHM case(s)

a. Who recognized first occurrence of EHM?

- i. Clinical signs and testing criteria for index case(s)
- ii. Was EHV-1 actually isolated, using virus isolation technique, from any of the samples?
- iii. Was testing done to determine if the EHV-1 had mutation associated with the neurologic form of EHV?

b. Did you have a specific case definition for EHM and if so what was it?

c. What made you consider this an outbreak (disease occurrence above the norm or expected)?

2. Once you recognized the first EHM case(s) what measures were taken for as yet unaffected horses? List and explain all that apply.

a. If you instituted some form of active surveillance can you describe what that entailed?

i. If they monitored body temperature, probe regarding what criteria were used to describe a horse as febrile.

1. Temperature cut-off used to describe a fever
2. Did horses have to have a fever more than one occasion to be called a “febrile horse?”
3. How often did they take temperatures and on which horses?

4. Did they have a log or written record of actual temps or just a fever? [yes/no]; outcome to be reported to someone involved with control of the outbreak
 - b. If you instituted sampling and test protocols for as-yet nonclinical horses, please describe how you decided which horses to sample, what samples were collected, and what tests were performed.
 - i. Describe, during your outbreak of EHM, how you interpreted various examinations and test results, including how the horses' clinical signs were integrated into interpretation of laboratory test results.
- 3. How did you classify or categorize horses relative to their EHV status?**
- a. For example, if I asked how many "cases" you had in your outbreak, how would you report horses that only had a fever, or had no clinical signs of disease but from which virus was isolated?
 - b. What action did you take based on the clinical and/or laboratory findings?
 - c. Can you describe what you did to define "exposed" or "at-risk" horses once you identified the first case of EHM?
 - d. Did you have any laboratory tests reported as "inconclusive" and, if so, how did you interpret these test results?
- 4. What was done to mitigate the outbreak?**
- a. List all that apply and describe how it was implemented.
 - i. Potential responses might include:
 1. Isolate confirmed cases of EHM away from other horses.
 - a. If so, describe how you isolated these cases. Did you move them to another location? Was each case kept so it did not have physical contact with any other equids? Describe ventilation of isolation site, barrier precautions taken, how you staffed the area used for isolation.
 2. Instituted biosecurity precautions for handling of febrile horses.
 - a. If so, describe what these were and how you did this.
 3. Instituted biosecurity precautions for handling of all at risk horses.
 - a. If so, describe what your procedures were.

4. Did you trace horses that might have been exposed to the EHM case(s)? [For example, those that might have shared a housing area in the recent past, shared a trailer or had the same exercise rider or farrier with the EHM case?]
 - a. What criteria did you use to determine exposure? [For example, how much contact was considered exposure? (e.g., shared a pony horse or shared a water bucket)]
 - b. If so, can you describe how you did this?
 5. What were the challenges with doing this tracing?
 6. Instituted surveillance to detect febrile horses.
 - a. If so, what temperature did you use to describe a fever and how were you alerted to occurrence of a febrile horse?
 - b. If a febrile horse was detected, what did you do?
 7. Performed surveillance testing to determine horses shedding status of EHV-1.
 - a. Was this done on all horses, or just those with fever, or just those with neurologic signs?
 8. Instituted some form of formal identification system during quarantine and testing and, if so, how was this done?
 9. Did you vaccinate at-risk horses to attempt to control the outbreak?
5. **How many cases of EHM did you have as part of the outbreak?**
 - a. Were EHM cases recognized throughout outbreak, with equal severity of signs, or only at beginning of the outbreak?
 6. **Did you have horses that had a fever and confirmed infection but that did not develop neurologic signs?** If so, how many?
 7. **How many horses were determined to be infected with EHV-1 during this outbreak?**
 - a. How many were tested?
 - b. How many were test-positive for EHV?
 - c. How many of these had any clinical signs of disease?
 8. **How many horses were at the premises when the outbreak occurred?**
 - a. How many of these were at risk of exposure to EHV-1 as part of this outbreak?

9. Did you collect any information about the cases such as signalment, EHV-1 vaccination history, travel history, response to treatment or diet?

a. If so, did you collect this same information on horses that were exposed during the outbreak but that did not become cases (e.g., controls)?

10. Was a quarantine imposed?

a. If so, what were the specific criteria for quarantine e.g. which horses and for how long?

i. Describe if additional housing was required, or if horses were quarantined on-site where the outbreak began and in original housing

b. Who imposed the quarantine? How was the quarantine enforced and by whom?

c. How long was the quarantine in place?

d. What criteria were used to remove the quarantine?

11. Who did you communicate with during the outbreak regarding the status of the situation?

a. List all with whom you had to communicate--for example, owners of horses that were cases, owners of horses that were exposed or potentially exposed, private veterinarians, the general public, health regulatory officials, equine-oriented media, general media.

b. If so, how did you conduct this communication?

i. Was there a designated spokesperson? If so, what was that person's position?

ii. Did you have selected talking points?

iii. Did you have written press releases?

iv. Did you post press releases on a Web site?

v. Did you conduct or participate in conference calls?

vi. Did you have meetings with equine owners/trainers to give updates on the outbreak?

vii. Other?

12. Estimate of cost and please describe who paid for:

a. Testing, cost per test, number of tests, cost of shipping samples, cost of collection of samples for testing;

b. Number of days of stopped horse movement and per day estimate of loss number and type of personnel involved in mitigation of outbreak and number of days each contributed to this outbreak situation;

- c. Cost of treatment of cases and number of cases treated—if there is a range of treatment cost, then what was the number with upper cost of treatment and the number of cases; the number with average cost of treatment and number of cases; and lastly, the cost of treating a mild case, the number with mild disease and number of cases;
- d. Cost of deceased horses due to this disease outbreak; this would be based on the number of horses that died and average or range of value of these horses;
- e. Cost of biosecurity procedures, PPE supplies, disinfectant, hand hygiene products, barriers, and signage;
- f. Other costs, specify what this cost was and the amount.

13. *What would have been helpful to you in mitigation of this outbreak that was unavailable at the time of this outbreak?*

14. *Are there needed educational materials about EHM? If so specify what info is needed and format that would be helpful to have.*

Examples: biosecurity guidelines specific to EHM, survey instruments/forms for outbreaks, standard epi questionnaire

15. *Was EHM a reportable disease prior to this outbreak? Did your reporting criteria for EHM change based on this outbreak?*

- a. Do you feel reporting has changed or just reporting criteria have changed? What are the criteria for reporting now?

16. *What would you describe as lessons you learned from your involvement in this outbreak?*

- a. Have you altered your methods of detection of first cases of EHM based on the outbreak you were involved with? If so, describe.
- b. What would you do differently based on the outcome of your outbreak investigation and mitigation? This could include how you handled first cases, surveillance, communication, treatment, etc.
- c. What advice would you give others based on your experience?

17. *Are there needed research areas for EHM? If so, what are they?*

Appendix B: USDA:APHIS:VS Center for Emerging Issues Emerging Animal Disease Notice

APHIS**Info Sheet**Veterinary Services
Centers for Epidemiology and Animal Health

January 2007

Equine Herpesvirus Myeloencephalopathy: A Potentially Emerging Disease

Introduction

Concern has been voiced within the U.S. horse industry that the neurologic (also known as myeloencephalopathic or paralytic) form of equine herpesvirus type 1 (EHV-1) may be increasing in prevalence and/or morbidity and mortality. This concern is based on an increased number of neurologic cases reported in recent years, as well as the occurrence of several high profile outbreaks of neurologic EHV-1 affecting several sectors of the U.S. equine industry. These outbreaks are the first reported EHV-1 outbreaks at large facilities or events involving neurologic cases that resulted in euthanasia. At least part of the increased interest and concern are related to these highly publicized events. It is possible that reporting has increased, as opposed to an actual increase in number and severity of cases; more data is needed to determine the actual situation.

Profile of Disease Emergence

The question of whether neurologic EHV-1 is emerging can be evaluated using standard definitions of disease emergence. A disease is considered to be "emerging" when it meets at least one of three general criteria. The first is when a disease is identified for the first time. Recent examples of this would be SARS or Ebola. Another criterion is when a disease evolves and changes in virulence, host capable of being infected or other pathogen behavior. The monkeypox outbreak in prairie dogs in 2003 in the United States would be an example of this type of disease emergence, as a new species was infected. The third criterion is a change in disease geographic range or incidence within a range. The appearance of West Nile virus in the United States in 1999 is a good example of emergence in a new geographic location, as is the previously mentioned monkeypox example. The current EHV-1 outbreaks are of concern because they likely fit the criteria of a disease that is evolving and changing in virulence and behavior. It is possible that the disease has not changed in incidence or character, and that testing and/or reporting has been increasing awareness, or that the animals affected are higher profile, causing more interest. However, it is not possible at this time to make this distinction.

All types of disease emergence are driven by a variety of emergence factors. The factors can be environmental, agent- or host-specific, related to use of the animal, industry standards or any other factor that can affect the health of an animal or place selective pressure on an infectious agent. Typically, multiple factors come together to create a situation where a disease can evolve, newly emerge or spread to new environments. In the case of neurologic EHV-1 in the United States, the disease appears to be increasing in incidence, mortality and morbidity. While there has not been much field research on neurologic EHV-1, mainly due to the sporadic nature of outbreaks, the available data support the theory of disease emergence and are cause for concern. Some research has been done that suggests that a mutation in the virus is playing a role in these changes in the disease behavior, which could indicate evolution of the viral agent.

Source: USDA:APHIS:Veterinary Services: Centers for Epidemiology and Animal Health, Center for Emerging Issues

Background of EHV-1

Equine herpesvirus type 1 (EHV-1) is primarily a respiratory pathogen associated with a variety of clinical manifestations in horses. In addition to being a significant cause of respiratory illness and abortion in horses, EHV-1 is responsible for paralytic neurological disease. EHV-1 is enzootic throughout the world and almost all horses older than 2 years of age have been exposed. Following initial exposure, EHV-1 has the ability to develop into an inapparent, latent infection. It is this ability to reside as a silent and persistent infection in horses which provides a reservoir of virus for continual transmission. The incubation period of EHV-1 is 1–10 days; typically signs are seen within 1–3 days. Viral shedding occurs for 7–10 days, but can occur up to 28 days from the onset of signs. The neurologic signs include ataxia, urinary bladder atony and reduced tail tone. In severe cases, horses will be unable to stand; these cases have a very poor prognosis. Foals are rarely affected with the neurologic form of EHV-1, and no sex predilection is seen. Treatment is supportive and tailored to the specific case. Antivirals such as acyclovir, valcyclovir, famciclovir and penciclovir have been used, but efficacy of these drugs has yet to be determined in equids.

Sources: USDA-APHIS 2005 United States Animal Health Report, pp. 78-79, http://www.aphis.usda.gov/publications/animal_health/2005animal_health.shtml; Equine Infectious Diseases, Sellon & Long; Chapter 13; Josh Slater, pp. 150-152; Equine Herpesvirus Type 1 Virulence and Vaccine Efficacy, Osterrieder, Zweig Memorial Fund for Equine Research, Cornell; EHV-1 Outbreaks, Lenz, TR, www.xcodesign/aaep/displayArticles.cfm?ID=222;

History of Recent Neurologic EHV-1 Outbreaks in the United States

Prior to 2003, the U.S. reports of neurologic EHV-1 outbreaks in the United States were sporadic, with typically none to few outbreaks identified annually. Table 1 shows outbreaks of equine herpesvirus; many of these cases may not have been typed for the neuropathogenic mutation, and there was not a standard method of defining a case across the time period. In 2005, seven outbreaks of neurologic EHV-1 were reported in 5 different States. In 2006, the number of reported outbreaks grew to 11, and involved 8 States. The outbreaks have been primarily concentrated in the eastern United States, with a few midwestern and western States experiencing outbreaks. The last outbreak of 2006 involved a group of 15 horses shipped from Germany that were subsequently shipped to 8 States. Five of the horses went to Florida; this resulted in 13 horses identified as infected, with neurologic signs of in seven cases and 6 associated deaths. Ten Florida premises were quarantined. One horse was shipped to California from the original group from Germany and died shortly after arrival due to the neurologic form of EHV-1. The exposed horses were identified, and the horses that were shipped to the remaining 6 States were quarantined and monitored for EHV-1 signs; none were found.

Outbreaks of neurologic EHV-1 continue to be identified in early 2007.

Table 1. Reported Neurologic EHV-1 Outbreaks in the United States Annually from 2001-2006

State	2001	2002	2003	2004	2005	2006
CO						1
FL						1
GA						1
KY			1		3	
MD				1	1	4
MI				1		1
NH			1			
NJ						1
NY					1	
OH			1			
OR			1			
PA			1		1	1
VA		1				
WI						1
WY	1					
Totals	1	1	4	2	6	11

Sources: 2006 NIAA Proceedings, *Emerging Diseases, "Neurological Equine Herpes Update"*, Promed, *The Horse*, *Pittsburgh Post Gazette*, Kentucky Dept. Of Agriculture, 2005 U.S. Animal Health Report, WJZ-TV Baltimore, U.S. States News, *Newark Star Ledger*

The clustering of outbreaks in certain regions of the country could be related to where high-level performance horses are located or where they tend to travel, but other ecological factors could also play a role in outbreaks; this aspect of the disease is not well

understood at this time. The number of reported outbreaks in the United States has increased, and the numbers infected in an outbreak appear to be much higher than what was seen previous to 2001. Data from 6 U.S. neurologic EHV-1 outbreaks (2001–2005) involving 403 at-risk horses were combined and analyzed; a mean attack rate of 33%, and a mean case fatality rate of 40% were found (2006 NIAA Proceedings).

Nationally, reports of neurologic EHV-1 have increased in recent years; this may be attributable to a strain of EHV-1 with a mutation that encodes for a particularly robust replicase enzyme. The result of this mutation is that the virus can reproduce rapidly with a predilection for nervous tissue, therefore the viremia occurs earlier, it reaches a higher peak, and it lasts longer. Beginning with the Ohio outbreak during January 2003, the progression of the disease in a population as well as in individual cases has been seen to be much more rapid than in the past. Response to currently available vaccines for EHV-1 does not appear to be strong enough to protect all immunized animals against the disease induced by the mutated strain of EHV-1. In some outbreaks, such as the Ohio outbreak of 2003, well-vaccinated populations of horses have experienced severe disease outbreaks and some animals have died. However, serious outbreaks have occurred in equine populations where no EHV-1 vaccines are used, such as in the Netherlands. It is still unknown what factors are involved in the emergence and/or maintenance of the viral mutants. It is also unclear at this time what role the poor immunogenic response to the mutated strain is playing in the outbreaks that have occurred in recent years.

Variations in EHV-1 reporting requirements and case definitions make it difficult to accurately identify the true number of cases. Creating a standard case definition for both the first case on a premise, as well as for subsequent cases, would alleviate some of the discrepancies seen in reporting and facilitate better understanding of the epidemiology of the disease.

Sources: Florida Department of Agriculture and Consumer Services, http://www.doacs.state.fl.us/ailehv1/daily_status_table_and_definitions.shtml, *Equine herpesvirus-associated myeloencephalopathy; Aspects of epidemiology and pathogenesis*, Goehring, L.S., *Univeritiet Utrecht*, 2005; *Gluck Equine Research Center, University of Kentucky*, <http://www.ca.uky.edu/gluckj/>; 2006 NIAA Proceedings, *Emerging Diseases, "Neurological Equine Herpes Update,"* Harrison, LR; Promed; *The Horse*; *Pittsburgh Post Gazette*, Kentucky Dept. Of Agriculture; 2005 U.S. Animal Health Report, http://www.aphis.usda.gov/publications/animal_health/2005animal_health.shtml; WJZ-TV Baltimore; U.S. States News, *Newark Star Ledger*

International EHV-1 Situation

The United States is not the only region or country that has recognized the issue regarding neurologic EHV-1 cases; other countries have also seen an increase in the number and virulence of reported neurologic EHV-1 outbreaks. In 2005, significant outbreaks occurred in Canada, Ireland, South Africa and Switzerland as well as the United Kingdom and the United States. Studies

conducted by the Gluck Equine Research Center in Kentucky indicate that in both the United States and the United Kingdom, the number of paralytic outbreaks of EHV-1 has increased dramatically since 2001. Greater than 85% of the outbreaks identified over a 30-year period have been caused by the mutated strain of EHV-1 as compared to the wild-type or "original" strain of EHV-1.

Horse Industry in the United States

Estimates on the value and numbers of equids of the U.S. horse industry vary widely. The Census of Agriculture estimates that there were 3.6 million horses and ponies in the United States in 2002 residing on operations fitting the definition of a "farm." Although this source of equine population data only estimates a segment of the industry, one can compare across States for relative size of their equine population. Texas, California, Oklahoma, Kentucky, Missouri and Ohio were the 5 States with the largest equine populations based on the Census of Agriculture. The overall value of the horse industry in the United States is in the billions of dollars. The most valuable subgroups of the horse industry are racing, competition and recreation.

In the United States, the recent outbreaks of the neurologic form of EHV-1 appear to be affecting race horses and other types of competition horses. The response to these outbreaks has been to identify potentially exposed animals and quarantine them. Since these sectors of the horse industry require horse movement in order to function, the EHV-1 outbreaks have had a major impact on these segments of the industry.

Sources: American Horse Council Foundation, USDA-NASS Census of Agriculture

Table 2. EHV-1 Paralytic Outbreaks: United States and United Kingdom caused by wild-type and mutant virus strains

5-year interval	No. outbreaks	No. outbreaks caused by wild-type	No. outbreaks caused by mutant
1970–1975	1	0	1
1976–1980	3	0	3
1981–1985	4	2	2
1986–1990	6	1	5
1991–1995	5	1	4
1996–2000	6	2	4
2001–2005	32	2	30

Source: 2006 NIAA Proceedings, Emerging Diseases, "Neurological Equine Herpes Update," Harrison, LR

International Horse Trade in the United States

The United States imported 25,000 to 30,000 live horses per year from 2003 through 2006 (statistics for 2006 are not yet complete). The vast majority (60–70%) of these live horse imports originated from Canada. Import requirements for horses from Canada are a health certificate and negative Coggins or ELISA test for equine infectious anemia (EIA) within 180 days preceding exportation to the United States.

The Netherlands, Mexico and Germany are the next top exporters to the United States. Horses from these countries are required to be detained at the United States port of entry while tests for dourine, glanders, equine piroplasmiasis, and EIA are conducted. Test results from NVSL are generally available three days after the date of arrival of the horses.

The index case for the recent outbreak affecting Florida originated from a shipment of 15 horses from Germany.

Sources: World Trade Atlas, APHIS Veterinary Services National Center for Import-Export

Discussion

Equine herpesvirus 1 neuropathogenic form is not a "new" disease, but the evidence currently supports the observation that paralytic EHV-1 is emerging as a more virulent strain that has a higher incidence, morbidity and mortality. In the past, outbreaks of neurologic EHV-1 were sporadic and typically involved one or a few cases within a herd or on a premises. The recent outbreaks in the U.S. and Europe have involved large numbers of infected animals with many of these showing neurologic signs. In the EHV-1 outbreak in Ohio during 2003, more than 30% of the 138 horses on the premises developed neurologic disease (<http://www.thehorse.com>, articles #4104 and #4272). This disease behavior is different than what was seen prior to 2001 in U.S. outbreaks.

The factors involved in this emergence are not clearly identified, but several factors have been suggested. Animal movement appears to be associated with several of the recent outbreaks. Movement could result in introduction of the virus to a new population; it is also possible that transport stress plays a role in allowing the disease to express itself or re-emerge from the latent stage. The role of vaccination is controversial; based on available information from recent outbreaks, the disease has occurred in well-vaccinated animals. What the attack rate would have been had the population been unvaccinated is unknown. The disease has occurred in equine populations where no vaccination occurred. There is much yet to learn about the ecology of the disease. It is likely that other factors may be playing a role. Potential temporal associations also exist; most outbreaks have been seen in the fall and early spring, yet there is likely more horse movement nationally in the summer.

The interest level in this disease remains high. The economic impact is substantial; not only are the horses

that die from the disease lost, but there are many costs associated with treatment, quarantines, cancelled events, and the inability of horses to compete in events.

Horse practitioners and horse owners should continue to quarantine suspect and diagnosed cases. Using strict biosecurity measures in day-to-day procedures, even when disease is not suspected, is a key strategy in preventing the introduction and spread of infectious diseases. APHIS Veterinary Services has developed a brochure titled *Biosecurity – The Key to Keeping Your Horses Healthy*, which can be found at http://www.aphis.usda.gov/lpa/pubs/HorseBioSecurity_final.pdf. Another resource available to equine veterinarians who are members of the American Association of Equine Practitioners (AAEP) is *Equine Infectious Disease Outbreak: AAEP Control Guidelines*. The AAEP guidelines provide guidance for veterinarians who encounter contagious infectious disease in horses, and covers topics such as pre-outbreak considerations, considerations when equine infectious disease is suspected, and sign-based flowcharts and guidelines for response-plan recommendations.

Conclusions

It appears that neurologic EHV-1 is emerging as a more virulent strain of the disease than seen previously in the United States. Many data gaps exist, and more investigations need to be done to better understand the situation and to identify factors playing a role in possible emergence. Identifying such factors will also assist with control of future outbreaks. The general ecology of this disease is not fully understood; additional research is needed. A standard case definition and standardized reporting requirements for the neurologic form of EHV-1 would be good starting points for further study, with subsequent studies comparing cases to controls to determine risk factors for the disease.

For more information, contact:

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Or visit CEI on the Web at
<http://www.aphis.usda.gov/vs/ceah/cei/>

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Appendix C: Example of a Study Design for Collection of Epidemiologic and Cost Estimate Data from Future EHM Outbreaks

Data needed to make cost estimation for EHM disease event

To fully quantify the impact of EHM disease events, costs of various aspects of management of the disease event would need to be collected and compiled. The components which need to be collected in the field in order to estimate the regional economic impact of an EHM disease event are listed below.

a. Testing costs:

1. number of tests
2. kit cost
3. sample shipment costs
4. sample collection costs
5. cost of running test

b. Lost use: average number of days horses unavailable for normal use and number of horses unavailable for use

c. Treatment costs, including number of cases treated. If there is a range of treatment costs, cases may be broken into categories (such as severe, moderate, and mild) and treatment costs calculated and applied according to severity.

d. Deaths:

1. number of horse deaths
2. value of each horse that died or was euthanized

e. Biosecurity costs (must be additional to normal biosecurity expenses):

1. PPE supplies
2. disinfectant
3. hand hygiene products
4. barriers and signage
5. additional labor

f. Facility (loss of income and expenses incurred):

1. betting revenue
2. ship-in lessons revenue
3. spectator revenue
4. hospital income lost due to closure
5. expense of keeping horses at the facility for a longer period due to quarantine

Example of study design and survey instruments related to EHM disease events

Introduction

This example study design is included as an illustration of how critical data related to description of the disease event and for eventual risk factor analysis for EHM could be gathered. Utilization of a standardized method for data collection on EHM disease events could meet two major goals:

1. To provide a better description of EHM disease events by describing basic information on index EHM case as well as the likely exposed population, and
2. To gather data necessary to determine risk factors for EHM at the horse level.

To achieve these goals, two types of horse/equine-level questionnaires (available upon request) were created--one captures basic descriptive information related to the index case as well as all equids likely exposed to the EHM index case, and the second focuses on collecting more detailed information about the index case, the subsequent EHM cases (if they occur), any febrile horses, and selected controls. To assure uniformity in data collection, a suggested definition to use for likely EHM-exposed equines would include "equids that have shared airspace and/or had direct physical contact with the index case."

General information about the premises at which the outbreak occurred will also need to be collected in order to describe the outbreak and help determine risk factors. Form A: Premises Level Questionnaire provides background information about the general practices of the premises, and a separate diagram (Premises Diagram) describes spatial design of the premises.

The accurate classification of cases and controls is vital to assess the risk factors for EHM. An EHM case is defined as an equid with neurological manifestations and a positive biological test for EHV-1. Since fever may be an indicator for a future neurological disease, daily temperature logs need to be kept on all exposed equids, with neurological exams to be conducted on all febrile (>101.5°F) equids. Controls would not be classified until the end of the outbreak or disease event period (at least 28 days after the last identified EHV-1 clinical case [fever or EHM]).

Historically, in many outbreaks, only one to a few EHM cases are identified; thus, the data should be collected across multiple outbreaks in order to attain the goal of determining risk factors for EHM. Due to the time involved in the data collection, it is recommended that someone other than those involved in outbreak mitigation collect the data.

Explanation of documents for EHM data collection once index case is identified

- 1. Premises Diagrams:** Aerial view and interior barn/housing schematic should be created first in order to assign the “location on premises” numbers to the horses. The interior barn/housing schematic diagram is used to determine if the location of the horses on the premises plays a role in equine herpesvirus transmission.
- 2. Form A=Premises Level Questionnaire.** Detailed questionnaire about the equine premises.
- 3. Form B=Initial Equine Index EHM Case and Likely Exposed to EHM Index Case Chart.** General chart to be filled out for each horse on the premises.
- 4. Form C=Index Case Questionnaire.** This form is to be completed for the horse determined to be the index case on the premises.
- 5. Form D=Questionnaire for Horses with Fever, Neurologic Signs, and Exposed to Index EHM Case at Initial Data Collection.** To be filled out at the initial visit by data collection personnel for horses with fever or neurologic signs in the last 30 days. For each horse with a fever or neurologic signs, three randomly selected controls need to be assigned and those controls need to have Form F: Case/Control Questionnaire filled out for each of them.
- 6. Form E=Followup Chart for the Equine Index EHM Case, Subsequent Cases, and Controls.** General chart to be filled out for each horse for which a Form D was completed.
- 7. Form F=Followup Questionnaire for the Equine Index EHM Case, Subsequent Cases, and Controls.** This questionnaire is to be completed for the index case, subsequent EHM cases, and controls at the followup visit.

Followup, after outbreak is considered over:

1. Premises Diagram to be updated
2. Chart Code document to be updated
3. Case/Control Questionnaire to be updated for all equids that were subjected to an initial Case/Control Questionnaire

At time of initial data collection:

Step 1: Complete the premises diagrams (see example aerial view and interior design diagrams).

Step 2: Complete Form A=Premises questionnaire

Step 3: Complete Form B=Chart for index EHM case and horses exposed to index case

Step 4: Complete Form C=Index case questionnaire

Step 5: Complete Form D=Questionnaire for horses that have history of fever or neurologic signs other than the index case.

At time of followup data collection (e.g., when outbreak has resolved):

Step 1: Update the premises diagram, as the horses' locations may have changed since the premises diagram was completed during the initial data collection.

Step 2: Complete Form E (chart for index case and any exposed horses). Refer to the chart that was completed during initial data collection in order to determine which horses should be included in this followup data collection.

Step 3: Complete Form F for:

- a) the index EHM case,
- b) any horse that had a fever or neurologic signs during initial data collection or based on data collected in Form E
- c) three randomly selected controls for each horse that was an EHM case or febrile horse based on data from Forms B or E.

Forms A through F are available upon request from:

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Premises Diagram

The Premises Diagram provides a visual overview of the equine premises layout and identifies the housing specifics for the index case and the locations of all likely exposed equids at this premises. The Premises Diagram has two sections:

1. Aerial Overview
2. Interior Barn or Housing Schematic

In the Aerial Overview, the general layout of the premises can be obtained through photography. Google Earth™, www.earth.google.com, provides an aerial picture of the premises after entering the address into the Web site. This image should include neighboring farms and roads to better understand the location of this premises in relation to other premises that may have equids. Once produced, the image should be geographically oriented by labeling north, property boundaries, and building names/identification. An example is provided (page 72).

In the second section, an interior schematic of the buildings and/or other housing types which contain equids, including the index case and likely exposed horses and other equids,¹ should be created. This schematic should include all interior structures of each building, including stalls and common use areas, such as wash racks or stocks, tack areas, feed storage, and indoor exercise arenas. This schematic should also include the doors throughout the building with an indication of the direction that the doors open. Each equid needs to be assigned a location on the property, which can be accomplished by numbering stalls or pens (for stalls, an example would be S1, S2, S3, etc.; for pens, an example would be P1, P2, P3, etc.; for pastures, PA1, PA2, etc.). This number can be included as a label on the schematic to identify the locations of all equids in the barn, pens, and pastures. An Interior Building/Barn Schematic example is provided to illustrate the optimal detail such a diagram would include (page 73). This diagram can be drawn freehand or in a computer program.

The location designations that are assigned will be used as identifiers for the equids in Form B. This, along with the two diagrams, will allow you to better describe the outbreak or disease event and to track the location of horses as the disease event is monitored. Specifically, you will have knowledge about the location of the index case on the premises and the location of subsequent cases; this documentation could be used in the determination of risk factors for subsequent EHM cases in this disease event situation.

1. Exposed equids would include equines which have shared airspace and/or had direct physical contact with the index case.

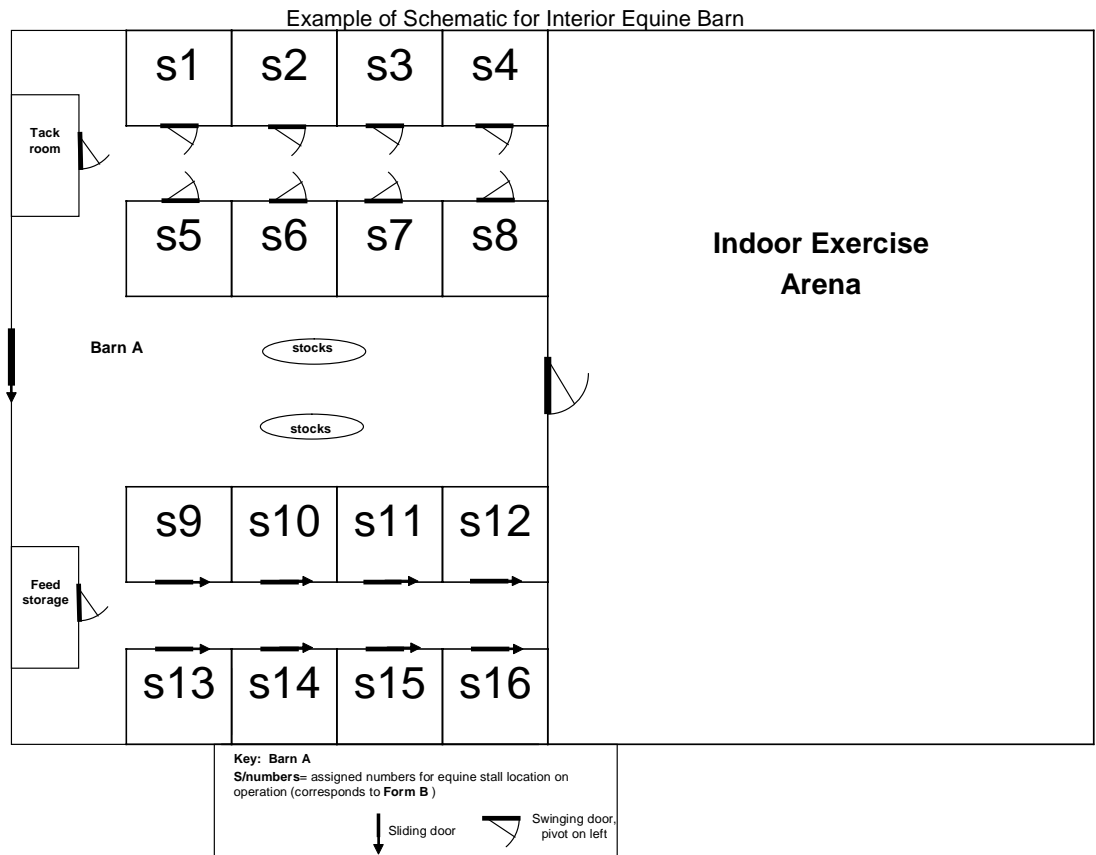
Example of an Aerial View of an Equine Operation with Google Earth



<p>The following equine numbers correspond to the "Schematic of an Interior Equine Barn" and Form B :</p> <p>Barn A houses equines 1-16 Barn B houses equines 17-30 Barn C houses equines 30-50 Isolation barn houses equine 31, the index case</p>	<p>Index case was moved from Barn C to the Isolation Barn on 1/1/08. No other equines are using the isolation building.</p>	<p>All equines use Outdoor and Indoor Riding Arenas.</p>	<p>Neighbor's farm contains only beef cattle, no equines.</p>
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Interior Barn or Housing Schematic

Indicate where nose-to-nose contact can occur (e.g., bars between stalls).
Use dotted lines for nose-to-nose contact areas.



Appendix D: List of Selected Sources of Information on EHM

The following Web sites have information related to EHV, EHM, and biosecurity.

<http://www.vetmed.ucdavis.edu/ceh/topics.htm>

http://www.aaep.org/control_guidelines_nonmember.htm

http://www.aaep.org/vaccination_guidelines.htm

http://www.aphis.usda.gov/lpa/pubs/HorseBioSecurity_final.pdf

<http://www.cfsph.iastate.edu/BRM/equineresources.htm>