EHV-1 and EHV-4: Their Roles in Equine Viral Respiratory Disease, Abortions, and Equine Herpes Myeloencephalopathy (EHM)

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Equine herpesvirus-1 (EHV-1) and equine herpesvirus-4 (EHV-4) are large double-stranded DNA viruses that are ubiquitous pathogens of horses. Estimates of prevalence show most adult horses are infected with EHV-1, EHV-4, or both throughout their lifespan and establishment of lifelong latency is detected in up to 70% of infected horses. Infection with EHV-1/4 is one of the most common causes of viral respiratory disease in horses worldwide.

Clinical Signs

Clinically, the respiratory disease caused by EHV-1 and EHV-4 is indistinguishable and can be mild or asymptomatic in older or previously exposed horses. In contrast, the respiratory disease observed in young immunologically naïve horses is often severe, lasts for two to three weeks, and is characterized by a biphasic fever, depression, anorexia, coughing, and oculonasal discharge that is initially serous and then becomes mucopurulent. Further, EHV-1 causes equine herpesvirus myeloencephalopathy (EHM), late-term abortions in the last trimester of pregnancy, death of neonatal foals, and chorioretinopathy. In contrast to respiratory disease, the risk for abortions in the third trimester of pregnancy and outbreaks of neurological disease is of greater significance in middle aged or older horses. EHV-4 has been implicated occasionally in causing late term abortions and EHM, but its etiological role is considered to be very minor and this occurs far less commonly than is observed with EHV-1.

Differences in Pathogenesis

The distinct difference between EHV-1 and EHV-4 is based on the viruses' differing ability to successfully infect a variety of cell types. While EHV-4 has a limited cell tropism towards epithelial and neuronal cells with limited potential for infection of lymphoid cells, EHV-1 has a broader tropism which includes vascular endothelium. These differences in tropism between EHV-1 and EHV-4 lead to important differences in their pathogenesis (see figure).

Infection with both viruses occurs via the respiratory tract by inhalation of infectious virus, nose-to-nose contact, or contact with fomites. Following infection, the virus replicates in the respiratory airway epithelium and causes erosion of the respiratory mucosa and viral shedding via nasal secretions. Nasal viral shedding can be detected as early as one day post-infection and continues for one to three weeks post-infection, although the duration of shedding depends on pre-existing immunity and viral properties. Because prolonged shedding has been detected, particularly in cases of EHM outbreaks, current recommendations by the American Association of Equine Practitioners are to wait 28 days before lifting quarantine measures. For EHV-1, the virus then spreads quickly to the cells of the underlying tissues before a cell-associated viremia is established between days four and 10 after infection. In contrast, EHV-4 is mostly limited to the respiratory tract and a cell-associated viremia is typically not reported.

Outbreaks of EHM

In recent years, outbreaks of EHM have increased in North America. Because of this, the Center for Emerging Issues released an emerging disease notice report regarding the neurologic form of EHV-1 in January 2007. Despite this knowledge and strong efforts to control this disease, EHM outbreaks continue to be a problem. In May of 2011 the largest outbreak ever was reported.
and in the first quarter of 2018 (January - March), the Equine Disease Communication Center (www.equinediseasecc.org/) lists more than 20 outbreak alerts for confirmed or suspected cases of EHM nationwide.

The reason for this increase in the prevalence of EHM is not clear, and there are a number of identified viral, host, and environmental components that factor into the incidence of EHM. These include age, breed, gender, season, past exposure, a secondary fever several days after primary exposure, stress, magnitude and duration of viremia, and infection with the D752 genotype.

To date, the most important identified factor is the essential role of viremia in transmitting the virus to the vasculature of the CNS. Allen et al. found that EHV-1 strains with high neuropathogenic potential are characterized by a longer duration and greater magnitude of viremia when compared to EHV-1 strains with a low neuropathogenic potential. This evidence supports the argument that prolonged exposure of the CNS vascular endothelium to high viral loads increases the risk of EHM. Further, the identification of a single nucleotide polymorphism in the viral polymerase gene that results in a coding change (N752 to D752) has been associated with increased neuropathogenicity and high levels of viremia.

Diagnostic Options

Diagnosis of equine herpesvirus infections in the laboratory include methods to detect viral DNA, infectious virus, viral proteins, and antibodies.

- Deep nasal or nasopharyngeal swabs are sufficient to diagnose respiratory disease induced by EHV-1 or EHV-4.
- When it is important to assess the risk of virus transmission, abortion or EHM associated with EHV-1, a combination of deep nasal or nasopharyngeal swabs and whole blood collected in EDTA is required. Since fever is closely correlated to virus shedding of EHV-1, it is important to take temperatures of horses on infected farms twice daily and to submit samples from febrile horses. Testing of asymptomatic horses is done to verify absence of shedding at the end of the quarantine period.
- PCR is the most commonly used method to detect viral DNA in diagnostic samples and differentiate between EHV-1 and EHV-4. A positive PCR signal obtained from a nasal swab may indicate virus shedding, but is not absolute proof since non-infectious virus can be present. Positive PCR results from whole blood extracts indicate that a horse is viremic, which can lead to EHM or transplacental infection. It is recommended, therefore, that both a nasal swab and whole blood are submitted and tested separately.
- A follow-up test to a positive PCR result is to type the strain detected. This is done by a PCR assay that targets a single nucleotide polymorphism in the DNA polymerase gene. The result of this typing typically demonstrates whether a “neurotropic” or “non-neurotropic” strain has been detected and has to be interpreted in the context of the information currently available. Approximately 75% of the samples from horses with EHM are infected with the D752 genotype, which labels them as neurotropic. However, the so-called non-neurotropic (N752) strain is detected in the other 25% of EHM cases. It is clear that EHM is not exclusively associated with a single genetic marker within the viral genome.
- Virus isolation (VI) is regarded as the gold standard method, since it detects infectious virus. A positive VI result is directly correlated to active virus shedding and potential for transmission. Limitations of VI are potential loss of infectious virus during storage or mailing and the three to four day minimum turnaround time of a VI attempt.
- Immunohistochemistry is a very useful method to examine formalin fixed tissues for the presence of viral antigens. An advantage of this morphological method is that a positive test directly correlates the detection of viral proteins within specific histologic lesions.
- Virus neutralization testing is available for the retrospective diagnosis of equine herpesvirus infections. It is essential that paired sera, collected within a three to four week interval, are submitted for this testing. A titer increase that is at least four-fold between the acute and convalescent samples is needed to make the diagnosis. Standard virus neutralization tests do not distinguish between antibodies induced by EHV-1 or EHV-4.

Our laboratory has the capability to test for the presence of equine herpesviruses by all the approaches described above. In addition, type-specific neutralization tests, which differentiate between antibodies induced by EHV-1 or EHV-4, will be introduced later this year. For more information on specific collection protocol, sample and shipping requirements, and other relevant details, please see our list of available tests at animalhealth.msu.edu or contact the laboratory at 517.353.1683.
Preventing Six Common Mistakes in Small Poultry Flocks

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Increasingly, veterinarians at small animal practices in urban and suburban areas are finding that their clients are looking to them for information about poultry. Many mistakes that small flock poultry growers make are due to lack of knowledge and/or false assumptions. Following the simple guidelines below can prevent a lot of problems for small flock growers.

1. Temperature

Baby poultry are not able to regulate their body temperature and must have a warm environment. Their environment must be kept at 95 degrees F for the first week of life and then decreased five degrees per week until an environmental temperature of 70 degrees is reached.

Watching how baby poultry relate to their heat source will indicate their comfort level. If they are huddled under the heat source, they are cold. If they are as far away as possible from the heat source, they are too hot. Being scattered throughout their environment demonstrates they are comfortable. Feed and water should be placed far enough away from the heat source that hot birds will find it and near enough to the heat source that cold birds can find it. It is usually a good idea not to place feed and water directly under the heat source.

If young poultry become chilled, they often develop diarrhea. If close attention is not paid, manure will cling to the feathers around the birds’ vent (anus) and form a plug which causes the bird to die from cloacal impaction. The plug can be removed easily with warm water.

2. Feed

Always start baby chickens and turkeys with medicated feed for the first six weeks of life. This feed includes amprolium. Amprolium is not an antibiotic. Amprolium blocks the uptake of thiamine in coccidia which prevents the disease coccidiosis. After 6 weeks, feed should be gradually changed from 100% medicated to 100% non-medicated over a period of 10 days. The gradual changeover allows the birds to develop immunity to coccidia and thus also prevents the disease.

Coccidiosis in chickens and turkeys will typically cause diarrhea, often bloody, and in some instances cause a death loss in the flock. Finding coccidial oocysts on fecal floatation of a normal healthy flock does not indicate the presence of disease and therefore does not warrant treatment. While ducks, geese, and guinea hens don’t require coccidiosis prevention, game birds such as pheasants, quail, and chukkar partridges do.

Begin feeding layer mash, the feed given to chickens that are laying eggs, when the first egg is found. Layer mash should not be given to birds that are not laying eggs. Calcium level in layer mash is about 4% while in other rations it is slightly less than 1%. Supplemental sources of calcium, such as oyster shells, should be provided, free choice, to older laying hens since it helps maintain the egg shell quality in the later stages of production.

Broiler (meat type) chicks should not be fed turkey starter. Broiler chickens grow so rapidly that if they have a more concentrated diet (turkey starter versus chicken starter), they will develop growth problems which often result in heart failure and ascites (water belly). To keep growth of broilers to a moderate pace, they should go without food for a period of at least eight hours per day. The easiest way to do that is to make sure they have eight hours of darkness at night so they sleep and do not eat 24 hours a day.

3. Light

The typical lighting program for all poultry is to start them at 24 hours of light for the first week of life. This allows baby poultry to find the feed and water. For broiler chickens, one hour or more of darkness should be added each subsequent week until 8 hours of darkness is reached. For egg laying chickens, two hours of darkness should be added per week and then 12 hours of darkness should be maintained until they are 10 weeks of age. After 10 weeks of age, 15 minutes of light should be added each week thereafter until reaching 16 hours of light. Decreasing the length of light will cause the birds to go out of egg production. To have eggs in the winter, light will need to be added at the beginning or end of the day to maintain 16 hours of light. A 40 watt bulb is all that is needed for a 10 foot by 10 foot area.

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4. Vaccinations

The only vaccination necessary for chickens is Marek’s disease. Marek’s vaccine is typically given when birds are hatched. The best vaccine is provided at hatcheries since it is stored in liquid nitrogen. Chickens are not automatically vaccinated at hatcheries and buyers must request that their chicks be vaccinated. For people that hatch their own chicks, a freeze-dried vaccine, MD-Vac CFL, is available from Zoetis. Unfortunately, it is only available in 1,000 dose vials. Once mixed, the virus only lives for two hours so the remaining doses cannot be stored for later use.

The only other vaccine for chickens and turkeys is pox vaccine which is given at six to eight weeks of age. Pox vaccine should be given if pox is in the local area. The pox vaccine is given in the wing web (skin between the humerus and radius) in chickens and in the legs of turkeys.

Do NOT vaccinate chickens for infectious laryngotracheitis (ILT). Unfortunately, the vaccine for ILT that is readily available on the internet is a modified live virus that can spread to non-vaccinated chickens and cause disease. This vaccine has caused many issues at fairs and exhibitions. The only ILT vaccine that should be used is a genetically modified pox vaccine, Vectormune® FP LT manufactured by Ceva Animal Health. That vaccine protects the chickens from both pox and ILT. There is no chance of the vaccine causing disease in other chickens because it only contains the protective portion of the ILT virus and not the complete virus.

5. Parasites

Small flocks should be treated for worms twice a year: once in the fall before they are brought inside for the winter and again just before they are allowed outside in the spring. The only approved drug for parasites in egg laying chickens is SAFE-GUARD® Aquasol For Chickens (fenbendazole) by Merck Animal Health which is given in the drinking water at one mg/kg for five days.

6. Safe Separation

Baby poultry should not be raised in the living quarters of humans, especially not in bedrooms, bathrooms, and kitchens. Do not kiss or cuddle baby poultry. Children and adults should wash their hands with soap and water after handling poultry. Too many people get sick with salmonella each year because they don’t follow these suggestions.

As a word of caution, chickens and turkeys should not be raised together since chickens harbor disease agents that are asymptomatic in chickens but cause overt disease in turkeys. In addition, new poultry should not be added to existing flocks without observing them for hidden diseases. Chickens often harbor disease agents that cause overt disease when they are mixed with non-infected chickens.