Equine Viral Arteritis

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ABSTRACT: Equine viral arteritis (EVA) is a reportable, highly contagious disease associated with sporadic outbreaks of acute respiratory disease and abortion in horses. EVA is a disease syndrome characterized by a wide variety of clinical signs. Although EVA is transmitted primarily by the respiratory route, the disease’s greatest economic impact is on the horse-breeding industry. Infection with the etiologic agent of the disease, equine arteritis virus, most commonly results in subclinical infection. Horses with clinical signs usually recover fully from the disease and gain immunity against reinfection. Proper vaccination of susceptible breeding stock can prevent spread of the disease. EVA is manageable through public and professional education that emphasizes prevention and control measures.

E quine viral arteritis (EVA) made headlines during the 2006 multistate outbreak, which resulted in vaccine shortages.1 EVA has generated fear and controversy in the horse industry since a 1984 outbreak in the Kentucky Thoroughbred industry. Because outbreaks of this disease are uncommon and clinical signs are nonspecific, many veterinarians do not include EVA in the differential diagnosis (Box 1) in appropriate situations and are unfamiliar with effective prevention and control strategies. Many horse owners are also uninformed about the disease. The 1998 National Animal Health Monitoring Survey (NAHMS) conducted by USDA-APHIS found that about 60% of surveyed horse operations were unaware of EVA, and only 2.9% of operations vaccinated one or more horses against the virus.2 In 2005, the number of operations vaccinating horses against EVA rose to 11.7%, indicating a modest increase in public awareness of the disease. It is especially important for veterinarians to understand EVA because of the impact of outbreaks on horse owners. A solid understanding of the basics of EVA epidemiology, testing, prevention, and control strategies can help prepare practicing veterinarians to address owners’ questions and concerns. Equine veterinarians should strive to actively educate horse owners to help prevent the mass confusion that outbreaks can engender.

EQUINE ARTERITIS VIRUS
It is crucial to recognize the difference between EVA and equine arteritis virus (EAV) and to use these terms properly. EVA is the disease syndrome characterized by a variety of clinical signs (Box 2), while EAV refers to the viral disease agent itself (Figure 1). EAV can cause sporadic outbreaks of respiratory disease and abortion in horses worldwide. It is not a newly discovered organism; it was first isolated in 1953 from lung tissue of aborted fetuses during an outbreak of respiratory disease and abortion on a Standardbred breeding farm in Bucyrus, Ohio.3 The virus infects equids only: ponies, horses, donkeys, and mules are susceptible to natural infection.4 Historically, the breeds of horse most affected in the
United States are the Standardbred, Thoroughbred, and Warmblood. The 1998 NAHMS study of US horses found that 23.9% of unvaccinated Standardbreds, 4.5% of Thoroughbreds, 3.6% of Warmbloods, and 0.6% of Quarter Horses were seropositive for antibodies against EAV. In 2006, there was a significant outbreak of EVA in the immunologically naive Quarter Horse population.

Although the venereal transmission route is better known, most EAV infections are transmitted via the respiratory route. These dual routes of transmission make the virus an economic threat to shows, sales and performance events, and the breeding industry. Mares infected by the venereal route develop viremia and can disseminate the virus to other susceptible horses through respiratory secretions. There is no evidence to suggest that mares exposed to semen from a carrier stallion will abort later in gestation. Pregnant mares abort 1 to 4 weeks after respiratory infection, not as a result of being bred to a carrier stallion. Abortion can take place any time between 3 and 10 months of gestation. EAV infection does not seem to affect the subsequent fertility of mares, although stallions can have a transient decrease in the number of morphologically normal sperm cells due to fever when they are first infected. Many times, susceptible pregnant mares abort without exhibiting signs of disease. The aborted fetus and its associated tissues and fluids are infective to susceptible horses and, along with respiratory secretions from infected horses, may help propagate an abortion storm in a herd of pregnant mares. Fetal tissues are often partially autolyzed, and there are no pathognomonic lesions for EVA.

Most EAV infections are subclinical or result in mild clinical disease. Those that result in signs of disease generally resolve in 1 to 2 weeks with simple supportive care. Mortality is rare, except in very young, old, immuno-compromised, or debilitated horses. Mares infected late in pregnancy may give birth to infected foals that can die from interstitial pneumonia and/or enteritis. Administration of colostrum from immune mares has been found to attenuate or prevent infection in newborn foals. While EAV seroprevalence is fairly high in many horse populations worldwide, most equine abortions are caused by other agents.

Horses that are immunologically naive to EAV become either subclinically or acutely clinically infected after

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**Box 1. Primary Differential Diagnosis of Equine Viral Arteritis**

- Equine herpesvirus 1 or 4 infection
- Equine influenza
- Purpura hemorrhagica
- Allergic reaction causing inflammation and urticaria
- Toxicosis due to a plant (e.g., hoary alyssum)
- Equine infectious anemia
- African horse sickness
- Dourine
- Getah virus infection

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**Box 2. Clinical Signs of Equine Viral Arteritis**

- Abortion
- Anorexia
- Ataxia
- Conjunctivitis
- Depression
- Edema (of the limbs, mammary glands, prepuce, scrotum, and ventral body wall as well as above or around the eyes)
- Excessive lacrimation
- Fever
- Leukopenia
- Petechial hemorrhage of mucous membranes
- Rhinitis and nasal discharge
- Stiff gait
- Urticaria (on the head and/or neck; sometimes generalized)
- Diarrhea
- Icterus

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"Any or all of these signs may be present. No individual sign or set of signs is specific to the disease. However, if both respiratory disease and edema are present, EVA should be a top differential. The most consistent clinical signs are fever, leukopenia, and dependent limb edema."
Diagnostic testing must be conducted to definitively diagnose EVA in sick horses because the clinical signs are indistinguishable from those of other, more common infectious and noninfectious equine diseases.

**DIAGNOSTIC TESTING**

The most commonly used serologic test to detect EAV antibodies is virus neutralization. Box 3 lists the veterinary laboratories that are approved by the USDA to conduct diagnostic testing for EAV.

**Box 3. Laboratories That Conduct Virus Neutralization Testing for EAV**

- California Animal Health and Food Safety Laboratory System (University of California, Davis)
- Clemson Veterinary Diagnostic Laboratory (Columbia, South Carolina)
- Colorado State University (Fort Collins)
- CS Roberts Veterinary Diagnostic Laboratory (Auburn, Alabama)
- Kansas State University (Manhattan)
- Kissimmee Diagnostic Laboratory (Kissimmee, Florida)
- Murray State University (Breathitt, Kentucky)
- National Veterinary Services Laboratory (Ames, Iowa)
- New Jersey Department of Agriculture (Trenton)
- New York State Animal Health Diagnostic Laboratory (Ithaca)
- Ohio Department of Agriculture (Reynoldsburg)
- Oklahoma Animal Diagnostic Laboratory (Stillwater)
- Oregon State University (Corvallis)
- Texas Veterinary Medical Diagnostic Laboratories (Amarillo and College Station)
- The University of Georgia Diagnostic Laboratory (Athens)
- University of Illinois (Urbana)
- University of Kentucky Livestock Disease Diagnostic Center (Lexington)
- Veterinary Diagnostic and Investigational Laboratory (Tifton, Georgia)
- Washington Animal Disease Laboratory (Pullman)

exposure to the virus. Mares, foals, and geldings stop shedding the virus after recovering from infection and do not become permanent carriers. Stallions, however, can become chronically infected without showing overt clinical signs of infection and can continuously shed virus in their semen for years while remaining apparently healthy. Chronically infected stallions can spontaneously and permanently stop shedding the virus for unknown reasons. Castration of chronically infected stallions terminates viral shedding, as testosterone is necessary to maintain the carrier state. Temporarily decreasing the testosterone level has shown limited success as a therapy for reducing or eliminating viral shedding in the semen of carrier stallions, although further studies of this method are needed.

Cooled and frozen semen from infected stallions is a well-known route of viral transmission because the virus can remain infective in frozen semen for years. A recent study found that the use of a two-stage processing technique involving density-gradient centrifugation followed by a “swim-up” step shows promise for removing the virus from infected semen.

EAV primarily infects macrophages and vessel endothelium throughout a horse’s body. The initial infection is followed by viral dissemination via the bloodstream, resulting in viremia. Clinical signs first appear 2 to 13 (average: 7) days after infection, and a fever may continue for 2 to 9 days (Box 2). Acutely infected horses shed the virus in nasal secretions for up to 16 days. Diag-

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**Figure 1. Rabbit Kidney-13 cells were infected with EAV**

the virus neutralization test. Acute and convalescent blood samples should be collected for serology 3 to 4 weeks apart in red-top or serum-separator tubes. A fourfold or greater rise in antibody titers between paired serum samples indicates recent infection. A titer of 1:4 or greater on a single sample is considered positive and indicates previous EAV exposure, exposure to natural infection, or vaccination. It is important to note that neutralized antibody titers can persist for several years after natural EAV infection.

During the 2006 EVA outbreak, horses participating in sales events and shows in certain areas were required to test negative for EAV antibodies. Clients who are unfamiliar with this disease may be confused or concerned about such regulations, so it is very important for veterinarians to be familiar with the implications of different diagnostic tests. Horses that are clinically normal and serologically positive for EAV antibodies were either naturally exposed to the virus or vaccinated against it. These horses should be differentiated from acutely infected horses. Infection can be confirmed by viral isolation testing of nasopharyngeal or conjunctival swabs, unclotted blood, or semen. Reverse-transcription polymerase chain reaction (RT-PCR) testing is very useful as a rapid, sensitive method for detecting EAV. However, the World Organization for Animal Health (OIE) recommends using the RT-PCR assay in conjunction with viral isolation and not as an alternative to it, as existing RT-PCR testing must undergo further standardization and validation. Viral isolation and RT-PCR testing can be conducted on blood, semen, or tissue samples. Importantly, no currently available serologic test can distinguish past natural infection from past vaccination.

During an outbreak, nasopharyngeal swabs, conjunctival swabs, or unclotted blood should be submitted for virus isolation to identify acutely infected horses. Blood samples for PCR or virus isolation testing should be collected in EDTA or citrate tubes because heparin interferes with these tests. Samples for virus isolation should be collected as early as possible in the course of infection. Blood samples should be refrigerated; other specimens should be chilled or, preferably, frozen. All samples should be sent via overnight shipping to a USDA-approved laboratory. An aborted fetus can be evaluated for EAV infection by submission of samples for virus isolation, PCR testing, and immunohistochemistry. Appropriate tissues and fluid to submit for testing include placenta; fluid from body cavities; tissue from the spleen, lung, or liver; and lymph nodes associated with the respiratory and gastrointestinal systems.
Up to 30% to 50% of stallions that test seropositive for antibodies against EAV may be chronically infected with the virus. Therefore, viral isolation should be conducted on the sperm-rich fraction of at least two semen samples to determine whether a seropositive stallion is shedding the virus. Antiseptic or disinfectant should not be used to clean the stallion’s external genitalia before collecting semen samples. It is important to disclose confirmed cases of EAV-shedding stallions to state authorities, as EVA is a reportable disease. The names and locations of state veterinary services are listed in Box 3.

**TREATMENT**

No specific antiviral treatment is available for EVA. Supportive care, including stall rest, NSAID therapy, and a diuretic to control edema, can help mitigate clinical signs in most patients. Most affected animals recover completely. In some patients, antimicrobial therapy may be warranted to prevent secondary bacterial infections or to treat pneumonia or cellulitis. Treatment of young foals with EAV-induced pneumonia and/or enteritis has been largely unsuccessful. A modified-live vaccine called Arvae (Fort Dodge Animal Health) is the only commercial vaccine for protection against EAV infection in the United States. It has been shown to be safe and effective for administration to nonpregnant horses. The vaccine is not recommended for use in pregnant mares, especially during the last trimester, or foals younger than 6 weeks of age. Vaccination of pregnant mares in the last 2 months of gestation has led to a few instances of fetal invasion by the vaccine virus. However, it may be beneficial to vaccinate pregnant mares in high-risk situations (when the risk of exposure to EAV is high and the mare tests seronegative). Many hundreds of pregnant mares have been vaccinated without adverse effects. The antibody response generated by inoculation with this vaccine cannot be serologically differentiated from natural infection. Therefore, it is extremely important to ensure that clients have written, official certification of their horses’ negative serologic status based on virus neutralization testing at an approved laboratory before initial vaccina-

**PREVENTION AND CONTROL**

EVA can be controlled and is considered a manageable disease. Educating horse owners about prevention and control strategies before an outbreak occurs is the best method of avoiding confusion during an outbreak. Prevention involves vaccination of susceptible horses and avoidance of breeding susceptible mares to carrier stallions. A recent study shows promise for future development of a live or modified-live virus vaccine that could enable serologic differentiation between vaccinated and naturally infected horses. Castillo-Olivares et al. created an avirulent viral strain without the major antigenic epitope of the naturally occurring virus. Inoculation with this mutant EAV protected ponies from experimental infection with a virulent EAV strain.

A comprehensive EAV management program involves vaccinating all colts 6 to 12 months of age that could be prospective breeding stallions to prevent the development of the carrier state. In addition, all stallions should be vaccinated annually at least 4 weeks before the start of the breeding season. (The AAEP guidelines call for annual vaccination of seronegative mares before breeding to carrier stallions.) Seronegative mares should be
vaccinated at least 3 weeks before being bred with a seropositive stallion and should be isolated from other seronegative horses during this time. On high-risk farms, clinicians should consider vaccinating all horses 6 months of age or older. A single intramuscular dose of vaccine is sufficient for protective antibody titers to develop. Vaccinated horses should receive an annual booster. New arrivals to breeding farms, including horses returning from other farms, shows, and race tracks, should be isolated for 3 to 4 weeks to prevent the spread of EVA and other infectious diseases. Pregnant mares should be segregated from other horses. All unvaccinated breeding stallions should be serologically tested before the season starts.

Virus isolation testing should be conducted on all semen that will be used to artificially inseminate susceptible mares. Regardless of whether breeding is by natural cover or artificial insemination, carrier stallions should be bred only to mares that test seropositive for EAV, including those that have been properly vaccinated. When carrier stallions are bred, precautions must be taken to prevent spread of the virus. The stallion and mare should be isolated for 24 hours after breeding to prevent the spread of EAV from voided semen, and all potential fomites should be carefully disinfected. Horses that are vaccinated for the first time and subsequently exposed to EAV may experience a restricted reinfection cycle with short-term respiratory virus shedding. For example, when a mare is bred with a carrier stallion after the mare’s first vaccination, she should be isolated from other horses for 3 weeks.

Many countries do not allow importation of seropositive horses without proof of vaccination and seronegative prevaccination status. Some countries do not allow seropositive stallions to be imported regardless of their vaccination history. Therefore, it is very important to inform clients of the implications of vaccination for international export before vaccinating their horses for the first time. Before having their horses vaccinated, clients planning to export horses should check the importation regulations of the country to which they plan to export. Carrier stallions (only those actively shedding EAV) and their semen cannot be imported into any country other than the United States and Canada.

The 2006 EVA outbreak was characterized by clinical signs of the disease along with abortions from 3 to 7
months of gestation. Several Quarter Horse stallions on a large breeding farm in New Mexico were infected, and several hundred mares were exposed by artificial insemination with shipped semen or by visiting the index premises during the outbreak. Nineteen states received semen from the infected stallions and/or had mares visit the index premises during this outbreak.17

Ten states had confirmed cases of EVA or strong circumstantial evidence of infection.17 This outbreak demonstrates how quickly EAV can spread in an immunologically naive equine population, especially when popular stallions are infected and untested or test results are not made public.

During an outbreak, the primary control strategy should be isolation of clinically affected horses from susceptible animals and thorough disinfection of possible fomites. Vaccination of susceptible horses is also a good means of controlling an outbreak. Any facility experiencing an EVA outbreak should be quarantined for at least 3 weeks after all active infections have resolved. To control spread of the disease, contact of susceptible animals with the secretions and excretions of infected animals should be minimized or eliminated and at-risk horses should be vaccinated. EAV is easily inactivated with exposure to heat, sunlight, desiccation, or common disinfectants. Disinfection of breeding phantoms (periodically or between uses) is particularly important. The 2006 multistate EVA outbreak was not confined to Quarter Horses because horses of other breeds were exposed to the virus through contact with infected Quarter Horses. The practice of keeping large numbers of animals in close physical contact greatly facilitates disease spread by the respiratory route. During this outbreak, every mare, stallion, and foal on the intensively managed index farm was infected.17

Semen from imported stallions is another important potential route of infection, as Hullinger et al18 showed in a 2001 study of horses in California (1.9% of resident horses and 18.6% of imported horses surveyed were seropositive for EAV). This included 16.1% of imported stallions. Even if no other methods of prevention are used, veterinarians should stress to clients who own breeding farms and mares the importance of testing stallions or semen that they plan on using before the start of the breeding season.

REFERENCES


**ARTICLE #1 CE TEST**

The Auburn University College of Veterinary Medicine approves this article for 3 contact hours of continuing education credit. **Subscribers may take individual CE tests or sign up for our annual CE program.** Those who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program. **CE subscribers can take CE tests online and get real-time scores at CompendiumEquine.com.**

1. **The primary diagnostic differentials for EVA do not include**
   a. purpura hemorrhagica.
   b. equine herpesvirus 1.
   c. equine infectious anemia.
   d. equine protozoal myeloencephalitis.

2. **A(n) __________________________ is most likely to be seropositive for EAV.**
   a. Thoroughbred
   b. Standardbred
   c. Arabian
   d. Akhal-Teke

3. **Before vaccinating a horse against EAV for the first time, a clinician should**
   a. conduct serologic testing and record the horse’s pre-vaccination titer.
   b. inform the owner that vaccination will result in a positive blood serum titer that may prevent the horse or its semen from being exported to certain countries.
   c. conduct virus isolation testing and record the horse’s prevaccination status.
   d. a and b

4. **Which treatment is indicated for EVA?**
   a. stall rest
   b. administration of mannitol
   c. administration of amantidine
   d. administration of EAV antiserum

5. **Samples that could be submitted for diagnosis of EVA do not include**
   a. semen.
   b. nasal secretions.
   c. cerebrospinal fluid.
   d. blood.

6. **EAV infection primarily targets**
   a. T cells.
   b. vessel endothelium.
   c. endometrium.
   d. erythrocytes.

7. **After diagnosing EVA in a patient, a clinician should not**
   a. report the diagnosis to state authorities.
   b. isolate the affected animal.
   c. begin aggressive treatment.
   d. disinfect possible fomites.

8. **Which of the following cannot be used to definitively diagnose EVA in a sick horse?**
   a. clinical signs
   b. virus isolation testing
   c. RT-PCR testing
   d. paired serum samples

9. **Which test can differentiate between a mare that was vaccinated against EAV and one that had past natural exposure to EAV?**
   a. serologic testing
   b. virus isolation testing
   c. RT-PCR testing
   d. none of the above

10. **If an extremely valuable breeding stallion has tested positive for EAV by serology, what should the clinician recommend to the owner?**
    a. castration of the horse
    b. virus isolation testing on the semen to confirm EAV carrier status
    c. public disclosure of the horse’s status and breeding the horse with only seropositive or properly vaccinated mares using appropriate precautions to prevent infection of susceptible horses
    d. b and c