Equine Infectious Anemia

Swamp Fever,
Mountain Fever,
Slow Fever,
Equine Malarial Fever,
Coggins Disease

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Importance

Equine infectious anemia is an economically important viral disease of equids, caused by a retrovirus that is carried by infected animals for life. The virus is generally transmitted mechanically on the mouthparts of certain blood-sucking insects, which usually occurs only when animals are relatively close to each other, or via iatrogenic blood transfer. Some infected horses become acutely ill or develop chronic, recurring clinical signs; however, many have mild signs or inapparent infections even on first exposure, and others become asymptomatic after experiencing one or more bouts of illness. The owners of subclinically infected animals are unlikely to realize they are infected unless tested, and many countries have testing and control programs that require infected animals to be destroyed or permanently isolated from other equids to prevent virus transmission.

Etiology

Equine infectious anemia is caused by equine infectious anemia virus (EIAV), a member of the genus *Lentivirus* in the family Retroviridae, subfamily Orthoretrovirinae. Isolates in different regions can differ, which can affect the accuracy of diagnosis by tests such as PCR.

Species Affected

Equine infectious anemia virus is reported to infect all members of the Equidae, though there do not appear to be any published investigations of EIAV in zebras. Clinical cases are seen most often in horses and ponies, and have also been reported in mules. Some horse-adapted viral isolates replicate to low levels without clinical signs in donkeys; however, unpublished evidence suggests that serially-passaged, donkey-adapted isolates may be pathogenic for this species.

Zoonotic potential

EIAV is not zoonotic. While vectors based on this virus have been investigated for use in people, e.g., as gene therapy, these vectors are highly modified to remove restrictions on EIAV replication in human cells.

Geographic Distribution

EIAV is widespread in equids, and infections have been documented in most countries were testing has been done. The incidence is higher in wet, warm regions where the insects responsible for mechanical transmission are more prevalent, and the virus appears to be absent from a few countries, including Iceland and possibly parts of the Middle East.

Transmission

EIAV is transmitted primarily via blood, usually by biting insects, which act as mechanical vectors, or iatrogenic means. This virus persists in an equid's mononuclear phagocytes for life, and also occurs in plasma during febrile episodes, which can be brief and are not always clinically apparent. Virus replication fluctuates in horses and mules. It also varies between animals, and some animals appear to control EIAV at very low levels that are unlikely to result in transmission. Less is known about donkeys, though animals inoculated with certain horse-adapted strains had significantly lower viral titers than horses.

Biting flies in the family Tabanidae, especially horse flies *(Tabanus* spp. and *Hybomitra* spp.) and deer flies (*Chrysops* spp.), are thought to be the most effective insect vectors for EIAV; however, other large biting insects such as stable flies (*Stomoxys calcitrans*) may also play a role. The bites of tabanids are painful, the animal's reaction interrupts feeding, and the fly usually attempts to resume feeding immediately, which can transfer blood on its mouthparts if it lands on a different host. Because EIAV survives for a limited time on insect mouthparts, it is mainly transmitted to nearby equids. Iatrogenic transmission can occur in blood transfusions or on contaminated needles, surgical instruments and teeth floats, with one study reporting that EIAV persisted for up to 96

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hours on hypodermic needles. This virus can be passed can be passed from a mare to her foal *in utero*, though many foals born to infected mares are uninfected.

Other rare mechanisms have also been reported, some of which might result from the contamination of secretions and excretions by blood. EIAV has been detected in milk, and possible transmission by this route has been reported uncommonly in nursing foals. It also occurs in semen and, while venereal transmission does not seem to be a major route of spread, one stallion appears to have transmitted the virus to a mare with a vaginal tear. The possibility of airborne transmission during close contact was raised during an outbreak in Ireland, where the pattern of infections from an infected horse suggested some animals at this clinic became infected in aerosols. This horse was hemorrhaging through the nostrils, and power washing was used for cleaning; however, viral antigens have also been detected in epithelial and endothelial cells of the lungs, raising the possibility of other mechanisms. While EIAV does not appear to be shed in urine, antigens were detected in kidney tubules in one study.

Disinfection

Enveloped viruses such as EIAV are readily destroyed by most common disinfectants. In one study, this virus was rapidly inactivated by substituted phenolics, iodophors, sodium hypochlorite, chlorhexidine and 70% ethanol, and more slowly (< 5 minutes) by 5% sodium hydroxide, 2% formalin or 2% glutaraldehyde.

Incubation Period

The incubation period ranges from a week to 45 days or more. Some horses remain asymptomatic until they are stressed.

Clinical Signs

Horses may develop acute clinical signs when first infected by EIAV, though some infections are subclinical. Milder cases may be limited to fever, which sometimes lasts less than 24 hours and can be accompanied by transient inappetence and other nonspecific signs. More severely affected horses can be febrile, weak, depressed and inappetent, and may also have develop jaundice, ventral pitting edema, thrombocytopenia, petechiae on the mucus membranes, epistaxis or blood–stained feces, and perhaps anemia. Horses occasionally become gravely ill during the acute stage, and, while this is uncommon, these animals may die.

Many horses become asymptomatic carriers after the initial illness; however, some have recurrent signs that range from transient bouts of fever, or mild illness and failure to thrive, to overt chronic signs with fever, depression, petechiae on the mucus membranes, weight loss, anemia and dependent edema. Bouts of illness are often triggered by factors such as concurrent illnesses, severe stress or hard work, or the administration of immunosuppressive drugs, and are occasionally fatal. Some infected horses also have ongoing ophthalmic lesions, characterized by depigmentation with prominent choroidal vessels. In many cases, horses with recurring signs become asymptomatic carriers after a year or two.

Donkeys and mules appear less likely to develop clinical signs or to be severely affected. In one study that followed a group of naturally infected mules, most animals had relatively mild signs, even after immunosuppression with corticosteroids, with febrile episodes lasting 1-5 days, sometimes accompanied by transient mild to moderate depression, mild anemia and/or thrombocytopenia, and edema. These signs were usually mild enough that they could have been missed if the animals were not observed closely; however, one mule was profoundly depressed throughout the study, with mild anemia, jaundice and thrombocytopenia, and was culled due to worsening of its condition. Donkeys inoculated with two horse-adapted strains became infected but remained asymptomatic in one experiment, but donkeys inoculated with a serially-passaged, donkey-adapted strain in China are reported to have developed typical signs of equine infectious anemia.

Post Mortem Lesions

Affected animals often have edema of the legs and ventral abdominal wall, anemia can result in in pale mucous membranes, and emaciation may be noted in some chronic cases. Common gross lesions of internal organs include enlargement of the spleen, liver and abdominal lymph nodes, as well as petechiae on some organs. Mucosal and visceral hemorrhages and blood vessel thrombosis have also been reported. Chronically infected horses that die between clinical episodes usually have no gross lesions, though some can have ocular lesions or signs of proliferative glomerulonephritis on histology.

Diagnostic Tests

EIAV infections are usually confirmed by serology, as infected animals carry the virus lifelong; however, reverse-transcriptase polymerase chain reaction (RT-PCR) assays can also be useful, and other methods, such as virus isolation, are possible though rarely used. While serology is generally considered the method of choice in identifying asymptomatically infected animals, titers can fluctuate, and there are reports of infected horses, detected by RT-PCR on leukocytes, that remain persistently seronegative for years.

Commonly used serological tests include agar gel immunodiffusion (AGID or Coggins test), ELISAs and, in some countries, immunoblotting. ELISAs can detect antibodies earlier than AGID and are more sensitive, but false positives are more likely. For this reason, positive results on ELISA are confirmed with AGID. However, some infected equids, particularly mules, have been found to be ELISA positive but AGID negative or low reacting, and some countries now confirm an animal's status by immunoblotting if the results from AGID and ELISA disagree. The accuracy of serological tests in donkeys is poorly understood, though false negative results or equivocal precipitin lines on AGID appear to be relatively common,

and certain ELISAs used in horses were found to have high false positive rates in this species.

RT-PCR on blood samples can be used to supplement or confirm serological tests, particularly when there are conflicting results or when an infection is suspected but serology is negative or equivocal. It can also be valuable in determining the infection status of foals with maternal antibodies, and to ensure that blood donors are uninfected. EIAV is genetically diverse, and RT-PCR assays may not detect some variants. The level of viral RNA can also fluctuate, and some infected animals with very low copy numbers may be undetectable at some time points.

EIAV can be isolated, if necessary, in horse leukocyte cultures; however, these cells are difficult to grow and virus isolation is not usually available in ordinary diagnostic laboratories. This virus may be found in both plasma and blood leukocytes during febrile episodes; between these periods, it is usually cell-associated, and may be latent. The identity of isolated virus can be confirmed with antigen-specific ELISAs, immunofluorescence or RT-PCR. If the status of an equid cannot be determined by other methods, blood may be inoculated into a susceptible horse. Antibody status and clinical signs in the test animal are monitored for at least 45 days.

Treatment

Treatment of clinical cases is supportive.

Control

Disease reporting

Veterinarians who encounter or suspect equine infectious anemia should follow their national and/or local guidelines for reporting. State regulations should be consulted in the U.S., where it is often a reportable disease.

Prevention

Many countries have testing and control programs for equine infectious anemia, often focused on certain organized activities, sales and/or other horse movements. While the risk of transmission from individual carriers varies, it is currently impossible to quantify; thus, regulations generally treat all infected animals alike. Many countries require that these animals be euthanized or, in some nations, permanently isolated from other equids. They must sometimes be marked, e.g., with a tattoo or brand. Foals born to infected mares are not necessarily restricted for life; however, they should be isolated from other equids until testing determines they are not carriers. The existence of EIAV in feral equids may complicate some control programs.

Regular testing on a farm, as well as testing of new animals before introduction, is helpful in maintaining an EIAV-free herd. Many horses are infected subclinically; thus, the presence of this virus often goes unnoticed until some horses develop the chronic form of the disease or routine testing is done. Iatrogenic blood transfer, including in small quantities, was thought to be important in some outbreaks, and should be considered in biosecurity programs. No vaccine is currently available.

During an outbreak, spraying to control insect vectors, as well as the use of insect repellents and insect-proof stabling, may aid in interrupting transmission. Placing animals in small groups separated by at least 200 yards/ 200 meters, the distance over which transmission is considered unlikely, might be beneficial when the virus is being transmitted within a farm. In countries where equine infectious anemia is not present, outbreaks are contained with quarantines and movement controls, tracing of cases and surveillance.

Morbidity and Mortality

Virus transmission is influenced by the number and species of flies, the density of equids, level of viremia in the host and quantity of blood transferred, and is generally higher from symptomatic animals. The prevalence of infections ranges from less than 5% in some areas to greater than 30% in others. Infections are particularly prevalent in humid, swampy regions where the insect vectors are common. Up to 70% of the animals may be infected on some farms where the disease has been endemic for many years.

Morbidity is influenced by the strain and dose of the virus, and the health of the animal. Horses appear to be more likely to develop clinical signs than donkeys or mules; nevertheless, some mules can have virus titers as high as horses. Immunosuppression and various stressors such as hard work can result in subclinical carriers developing clinical signs. Bouts of illness often become less common and eventually stop, as an apparent broadening of the immune response leads to better control of the virus. While epizootics with high morbidity and mortality rates have been reported, ordinarily deaths are uncommon in naturally infected horses. Experimental inoculation with a high viral dose can result in up to 80% mortality, but this is not generally seen in the field where animals usually receive a much smaller dose of virus.

Internet Resources

Food and Agriculture Organization of the United Nations (FAO). Manual for the Recognition of Exotic Diseases of Livestock

The Merck Veterinary Manual

USDA APHIS. Equine Infectious Anemia Disease Information

World Organization for Animal Health (WOAH)

WOAH Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

WOAH Terrestrial Animal Health Code

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