Equine Infectious Anemia

This course is designed to provide updated information on the major domestic diseases for which Veterinary Services (VS) has program responsibility. It will provide information on surveillance, disease control and eradication for these diseases. It will also give an overview of the duties of a field Veterinary Medical Officer (VMO) as a support worker of VS animal disease programs and how they interact with other units in APHIS.

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1. DISEASE INFORMATION

a. Agent
Equine infectious anemia (EIA), also known as swamp fever, is an infectious disease of horses and other Equidae caused by the equine infectious anemia virus (EIAV). The virus is a member of the genus Lentivirus of the viral family Retroviridae. These viruses are characterized by containing the unique enzyme reverse transcriptase. This enzyme allows the viral RNA to be converted into a complementary DNA strand that is then inserted into the host's DNA where it eludes the host's immune system. EIAV is closely related to other retroviruses, such as caprine arthritis-encephalitis virus, and human and feline immunodeficiency viruses.

EIAV is an enveloped, single-stranded RNA virus. The virus utilizes the host cell plasma membrane to derive the exterior envelope which surrounds the viral core. The surface of this envelope is covered with viral glycoproteins gp90 and gp45 that cause significant immune stimulation. However, as the virus replicates within the host, new antigenic variants of the surface glycoproteins develop which are no longer recognized by the immune system. This shift in viral glycoproteins is responsible for the recurrent viremia and subsequent bouts of fever seen in the clinical presentation of EIA.

The core of the virus contains the viral RNA, four structural proteins and the reverse transcriptase enzyme. The most common core protein, p26, also induces a strong immune response and is used as the target for most serologic diagnostic tests for EIAV.

b. Transmission
EIAV is transmitted from infected to uninfected equine through transfer of blood or blood products. The most common route is through the bite of a blood feeding insect, mainly deerflies and horseflies from the family Tabanidae. These insects are very efficient carriers due to their large mouthparts and a painful bite. When bitten, the animal will often interrupt the insect's blood meal by shaking, twitching or other body movements. The insect will then immediately attempt to finish the blood meal by either attaching to the same animal or one standing nearby. The combination of interruption and immediate continuation of the blood meal allows the virus to be efficiently transferred from one animal to another.

Other modes of transmission do occur. Iatrogenic transmission occurs through the use of contaminated needles or surgical instruments, such as teeth floats. Transplacental and colostral transmission between mares and foals and venereal transmission are possible in horses with a high viral load.

Upon inoculation of the virus into the skin, EIAV multiplies locally in histiocytes and then travels to the bloodstream. After an initial viremia, the virus localizes in macrophages, histiocytes, and monocytes where they continue to multiply and elude the immune system. The main site of in vivo replication is in tissue macrophages.

c. Clinical Signs
Horses suffering from EIA may present with a variety of clinical signs. Those suffering from an acute bout of EIAV often present with a high fever, thrombocytopenia, and anemia. Severely infected horses may develop epistaxis and pitting edema which is often fatal. Following recovery from the initial viremia, most horses will recover and appear clinically normal for a
varying period of time but subsequently suffer from intermittent episodes of fever, anemia, and thrombocytopenia.1,4,9 The episodes correspond with the rise of new antigenic variants of EIAV.4,9 The occurrence and severity of these episodes decreases over time, with the vast majority of horses becoming chronic carriers within 12 months post infection.9 However, a minority of horses will develop the chronic form of the disease which is characterized by weight loss, anemia, edema, and eventual death.9

The vast majority of seropositive horses never develop clinical signs and most likely suffer from inapparent fever and thrombocytopenic episodes.1,4,9 Nonetheless, these horses can still carry the virus and serve as a lifelong reservoir of infection and a risk for uninfected horses.

d. Epidemiology
Horses and other equine are the only animals found capable of being infected with the EIAV. Chronic carriers are the most likely reservoir of infection.1,3,4,9,11 The incubation period for the disease is variable ranging from a couple of days to over a month; however, it averages 1 to 3 weeks.1 Antibodies to the virus will develop within three weeks and last for the life of the horse.9

The true prevalence of EIA in the national equine herd is unknown; however, in two free roaming populations of horses located in Shackleford Banks, North Carolina and the Uintah Basin, Utah, both herds were found to have a seroprevalence of 40%.3,6

e. Diagnosis
Equine infectious anemia is a difficult disease to diagnose based on its inconsistent clinical and pathologic presentations along with the presence of inapparent carriers. Acutely infected horses will most commonly suffer from thrombocytopenia, a low pack cell volume, and moncytosis which will reoccur with subsequent viremic episodes.1,9 Platelet counts can become low enough for epistaxis or petechial hemorrhaging of the mucous membranes to occur.4,9 Anemia and thrombocytopenia are present due to intravascular and extravascular hemolysis of complement coated erythrocytes and platelets.9 Anemia is also enhanced by the EIAV's ability to inhibit bone marrow erythropoiesis.9 Most commonly, horses with severe anemia have suffered from multiple concurrent febrile episodes.9 In chronically infected horses, circulating sideroleukocytes (phagocytic cells containing hemosiderin aggregates from ingesting complement coated erythrocytes), and a nonspecific hypergammaglobulinemia are commonly found.9 The presence of sideroleukocytes was often used as a diagnostic test for EIA until the now commonly used Coggins test was developed.9

Post-mortem lesions of a horse suffering from an acute episode of EIA will often consist of generalized enlargement of the lymph nodes, liver and spleen, mucosal and serosal hemorrhages, and ventral subcutaneous edema.1,9 Histopathology often reveals lymphoproliferative lesions in the lymph nodes, adrenal gland, spleen, meninges, and lungs.9 The liver is often characterized by fatty degeneration and hepatic cell necrosis.9 Kupffer cells may contain hemosiderin aggregates.1

Necropsies of EIAV-infected horses that have no apparent clinical signs are often unremarkable.9 Some horses may show evidence of perivascular cuffing around the vessels in many organs especially the liver.1,9 A proliferative glomerulonephritis may also be found in the kidneys with deposits of immunoglobulins and complement in the glomeruli.1 Retinal
depigmentation and enlarged choroidal vessels have also been found in infected horses that appear clinically normal.9

Since most EIAV-infected horses do not show clinical signs, diagnosis is by one of two types of laboratory tests. The most common test used for laboratory diagnosis of EIAV is the agar gel immunodiffusion (AGID) or Coggins test.3,4,9 Developed in the early 1970s, this test is specific for EIAV.4,9 The test is performed on agar gel in a Petri dish.8,9 Soluble EIAV antigen of the p26 core protein is deposited in a central well with wells containing control and test sera surrounding the central well.6,9 The antigen and sera diffuse easily through the gel forming a circular concentration gradient for each well.8,9 When an optimal proportion of antigen and anti-EIAV antibody is found, a line of precipitation will form.8,9 No line is found between the wells of negative serum and the EIAV antigen.8,9 Most horses can be detected by the Coggins test within 45 days of infection and test results are available in a minimum of 24 hours.4,8,9

Currently, there are three enzyme-linked immunosorbant assays (ELISA) approved by the USDA for detection of EIAV.1,9,10 The competitive ELISA (cELISA) and the Vira-CHECK™ ELISA detect the p26 core protein and favorably compare with the Coggins test.9,10 The synthetic antigen ELISA (SA-ELISA II) detects the gp45 viral transmembrane protein.10 All three ELISA tests give results within minutes; however a higher number of false positives occur.4,9 To combat this problem, any positive ELISA must be confirmed with a positive Coggins test before test results are reported.4,8,10

Horses with conflicting test results may be tested for virus-specific antibodies using a Western immunoblot assay.8,9 Virus isolation may also be used by inoculating horse leukocyte cultures and detecting the virus using polymerase chain reaction (PCR), immunofluorescence assays, reverse transcriptase assays, or inoculation of culture fluids into susceptible horses.8 Virus isolation is rarely attempted due to large amounts of time, expense, and difficulty involved in the process.8

Foals born to EIAV-positive mares may have the presence of EIA antibodies that are absorbed through passive transfer from the mares’ colostrum. The antibodies may persist for a period of six months.9,10

f. Prevention and control

Infected horses and other Equidae are often discovered by routine surveillance testing of animals being shipped to different regions of the country.1,3,4,9 A Coggins test or equivalent test is required by all states on any animal being moved interstate, changing ownership, entered into exhibitions or competitive events, or being sold at auctions of sales markets.10 If an equine is found positive, it is placed under quarantine. The equine must be separated from uninfected animals by a minimum of 200 yards and cannot be moved unless traveling to a slaughter facility, diagnostic or research facility, or to the herd of origin.3,4,9,10

EIAV is easily inactivated by commonly used disinfectants, such as sodium hypochlorite (bleach).1,11 Hypodermic needles and surgical instruments should be sterilized before each use to prevent iatrogenic inoculation.1,4,9 Insect control and destruction of insect habitats in stables and pastures can also help to reduce vector transmission.1,4,9 Horse owners should also test and isolate all new equine brought onto premises until their EIA status is known.4,9


\textbf{g. Public health consequences}

EIA has never been demonstrated to cause disease in humans. However, the virus has been the subject of much recent research, due to its close relationship to the human immunodeficiency virus.\textsuperscript{3,4,9}

\textbf{h. Economic impact}

In 1997, the equine industry spent $34 million on EIA testing, with an average cost per test of $24.65.\textsuperscript{5}

\section*{2. HISTORY OF EQUINE INFECTIOUS ANEMIA AND ITS CONTROL PROGRAMS}

EIA was first described in the U.S. by Watson in 1896 in northern Wisconsin when he described a syndrome of horses know as “equine relapsing fever”.\textsuperscript{7} The disease was later observed during an extensive outbreak in Wyoming in 1901 and in Minnesota in 1903.\textsuperscript{7} By 1909, the disease, then known as “swamp fever”, was found in Nevada, Minnesota, Wyoming, Montana, North Dakota, Kansas, Nebraska, Colorado, and Texas.\textsuperscript{7} Veterinarians reported fewer incidences of disease between the periods of 1916 through 1928 lessening concern.\textsuperscript{7} However, in 1941, EIAV was found to be more prevalent than previously thought. Twenty-nine states reported cases of the disease, and in 15 of the states, EIA was confirmed through horse-inoculation tests.\textsuperscript{7} By 1947, EIA had been reported in 34 of 48 states, with most occurrences being small localized outbreaks with little spread.\textsuperscript{7} Nevertheless, the disease was then enzootic in the Mississippi Delta where it was maintained in the mule population in the chronic form.\textsuperscript{7}

In 1919, a researcher named Scott advocated immediately destroying all horses that were affected, providing the diagnosis was correct.\textsuperscript{7} He had also provided evidence showing the virus was being transmitted from horse to horse via biting flies. He suggested that if infected animals were not destroyed, they should then be placed in a dry pasture far from other equine to prevent the passage of biting flies.\textsuperscript{7}

Vaccine companies also suffered from the effects of EIAV. Three thousand horses had to be destroyed following the contamination of a vaccine against Borna disease with brain tissue from an EIAV infected horse.\textsuperscript{7} The incident lead to recommendations from the U.S. Bureau of Animal Industry to heat all equine antiserums at 58 to 59 °C (136 to 138 °F) for one hour before use.\textsuperscript{7}

In the fall of 1964 and the summer of 1965, several epizootics of EIA in horses at racetracks in Illinois, New York, Maryland, Florida, and Washington lead the Thoroughbred Racing Association to take action.\textsuperscript{7} In January 1966, the equine industry asked for help from the veterinary community to help evaluate and contain the EIA problem.\textsuperscript{7} On Feb 8, 1966, the American Veterinary Medical Association (AVMA) along with the American Association of Equine Practitioners (AAEP) held a combined meeting to discuss the current EIA problems and possible solutions.\textsuperscript{7} Later on Feb 13, 1966, the U.S. Livestock Sanitary Association sponsored a meeting with representatives from the equine and veterinary arenas along with governmental officials.\textsuperscript{7} The representatives attending this meeting developed a document entitled “A Prospectus on Equine Infectious Anemia with Guidelines” which outlined a standard method for handling EIA-infected horses at racetracks, along with reporting and animal inoculation procedures.\textsuperscript{7} The prospectus was revised by the U.S. Livestock Sanitary Association and adopted in 1967.\textsuperscript{7} However, only a few states followed the prospectus and reports of EIA were minimal.\textsuperscript{7}
In 1972, Dr. Leroy Coggins developed the Coggins test, which could accurately diagnose both clinically infected and carriers of the EIAV. In August 1973, the USDA amended the Code of Federal Regulations (CFR) to prohibit the interstate transport of equine found positive to the Coggins test and those animals displaying clinical signs of infectious disease, including EIA. However, states still had power over the major regulatory actions to control EIA and soon control programs varied greatly by individual states.

In 1997, the Infectious Diseases of Horses Committee (IDOHC) of the U.S. Animal Health Association (USAHA) drew up a set of guidelines for the control of EIA to be used by the states as a basis for regulation legislation. The guidelines were adopted by the USDA as the Equine Infectious Anemia, Uniform Methods and Rules (UM&R) (Effective January 1, 1998) to assist in the standardization of control recommendations in different states. The guidelines have been subsequently revised with the latest edition effective March 1, 2002.

3. CURRENT CONTROL PROGRAM STATUS

The U.S. control program for EIA is aimed at eliminating carriers of the virus; however, current estimates report that nearly 80% of the nation’s horses are not being tested. The regulations concerning EIA have remained relatively unchanged since their inception. Currently, Title 9 of the CFR, Part 75 (2003) contains provisions for the interstate movement of EIA reactors and for the approval of laboratories, diagnostic and research facilities, and stockyards to house reactors. Under these provisions, no EIA reactor can be moved interstate unless the reactor is officially identified. Exceptions are made for reactors moving directly to slaughter while traveling under a permit and in a sealed transport. The reactor can also only move interstate if it is traveling to a federally inspected slaughtering facility, a federally approved diagnostic or research facility, or to the home farm of the reactor.

The UM&R contains the minimum standards for detecting, controlling, and preventing EIA along with the minimum requirements for intra- and interstate transport of equines. Any equine that is being entered into exhibitions or competitive events, moved interstate, changing ownership, or entering horse auctions or sales markets must be tested for EIAV. The sample must be drawn from the horse by an accredited veterinarian and all laboratory submissions must be accompanied by a completed VS Form 10-11, “Equine Infectious Anemia Laboratory Test”.

The official laboratory tests to be used include the AGID or Coggins test, cELISA, Vira-CHEK™ ELISA, or the SA-ELISA II. Any positive ELISA test must be confirmed by a secondary agar-gel immunodiffusion (AGID) test. Horses that test positive are labeled as reactors and are required to be placed in quarantine within 24 hours and remain there until a final classification can be made.

An epidemiologic investigation is performed to find the potential source of infection and the reactor’s travel history to assess the risks of disease transmission and possible locations of new cases. Once the equine has been confirmed as EIA positive, it is removed from the herd by euthanasia, removal for slaughter, or by being quarantined on the premises. A reactor may not leave the premises unless a permit is granted to move the horse to a federally inspected slaughter facility, a federally approved diagnostic or research facility, or to the herd or farm of
All horses within 200 yards of the reactor are also placed in quarantine and cannot be removed from quarantine until subsequent testing finds all equine on the premise to have negative test results for a minimum of 60 days.

In fiscal year 2003, almost two million (1,951,582) equine were tested for EIAV with 285 confirmed positive horses. The following map shows the number of positive horses in each state along with the total number of tests in each state.

4. THE ROLE OF THE VMO IN THE CONTROL OF EQUINE INFECTIOUS ANEMIA

No positive equine may be moved unless it is officially identified by a National Uniform Tag code number followed by the letter “A” which is assigned to the state the reactor was tested in by the USDA. The number must be permanently applied to the equine using either a hot or chemical brand, freeze marking, or a lip tattoo. Brands or freeze marking must be applied to the left shoulder or left side of the neck and shall not be less than two inches high. The lip tattoo must be applied to the upper lip and not be less than one and one-half inches high. If the reactor is traveling directly to slaughter upon notification of EIA status, no permanent identification is required as long as the equine is transferred in a transport that has an official seal placed over the latch of the door.
Any officially identified reactor being transported to a federally inspected slaughter facility, a federally approved diagnostic or research facility, or the herd or farm of origin must obtain a certificate at the point of origin that contains a description of the reactor, the purpose for movement, the consignee and consignor, and the points of origin and destination.\textsuperscript{2} If the reactor is going directly to slaughter a permit (VS Form 1-27) is issued rather than a certificate which contains the same information plus, an individual identification mark such as a registered breed association tattoo or registration number.\textsuperscript{2}

5. ROLE OF THE FEDERAL GOVERNMENT, STATES, AND INDUSTRY

State governments are primarily responsible for legislation indicating the requirements in testing and eliminating potential carriers of EIAV.\textsuperscript{3,4,9} The industry encourages equine owners to participate in annual EIA testing and provides owners with current research information and regulations.\textsuperscript{3,4} The individual owner is responsible for the costs of testing and is ultimately responsible for the control and prevention of the disease by following recommended guidelines and practices.\textsuperscript{3,4}

6. REFERENCES


