Equine Influenza

Etiology

Equine influenza viruses belong to the species *influenza A virus* (genus *Alphainfluenzavirus*, family Orthomyxoviridae), a large group of highly variable viruses that are adapted to circulate in particular hosts, but can occasionally infect other species. Most influenza A viruses are maintained in birds (avian influenza viruses), but a few circulate in mammals. In addition to horses, mammalian reservoir hosts include people (human influenza A viruses), pigs (swine influenza viruses) and dogs (canine influenza viruses). Additional viruses circulate in bats, but do not seem to be transmitted to other species. On rare occasions, influenza viruses can adapt to a new host species, either “whole” or after reassorting with another influenza virus.

Influenza A viruses are classified into subtypes based on two variable surface proteins, the hemagglutinin and neuraminidase. There are currently 18 recognized hemagglutinins (H1 to H18) and 11 neuraminidases (N1 to N11). These two proteins are major targets for the immune response, and there is ordinarily little or no cross-protection between different HA or NA types. Mutations cause gradual changes in a virus’s HA and NA genes, a process called ‘antigenic drift.’ If the hemagglutinin and neuraminidase proteins change enough, a host’s existing immune responses against that virus may no longer be protective. Genetic reassortment, which results from “re-shuffling” the 8 viral gene segments when two different viruses infect a single cell, can result in more rapid changes. The high variability in influenza viruses also means that two viruses with the same subtype (e.g., an H3N8 equine influenza virus and the many different H3N8 avian influenza viruses in birds) may be only distantly related.

Equine influenza viruses seem to change more slowly than the viruses circulating in some other species; however, they do evolve. Two subtypes of influenza viruses circulated widely in equine populations during the last century, H7N7 (equine virus 1) and H3N8 (equine virus 2). H7N7 equine influenza viruses were last isolated in 1979, and most authors think they are likely to be extinct, although a few anecdotal reports or serological studies suggest they might persist in limited areas where there is little surveillance. In the 1980s, equine H3N8 viruses diverged into distinct Eurasian and American evolutionary lineages. The American lineage divided further into 3 sublineages: the classical American (or Kentucky) lineage, the Florida sublineage and the South American sublineage. The Florida sublineage became widespread and has diverged into 2 clades, which continue to evolve. The Eurasian lineage, which has not been isolated in at least 5 years, is now uncommon or absent, and the classical American lineage is now found only occasionally and in limited areas.

Influenza viruses of other mammals and birds can also infect horses occasionally. A novel H3N8 virus from birds (A/eq/Jilin/89) virus caused an extensive outbreak among horses in China in 1989. It circulated for a few years before disappearing, but it is not known to have spread outside China. An H9N2 avian influenza virus was found in a horse, and horses were experimentally infected with an H3N2 human influenza virus. There are also sporadic reports of antibodies to various avian influenza viruses (e.g., H1, H3, H5, H7, H9, H10) and, rarely, human influenza viruses in domestic or wild equids. The H3N8 canine influenza virus, which originated from a Florida lineage equine influenza virus, no longer seems to infect horses efficiently: although they can be infected experimentally, its ability to replicate in this species appears to be greatly reduced, and horses did not become infected when kept in close contact with experimentally infected dogs. A study from Asia found antibodies to the (avian origin)
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H3N2 canine influenza virus in a small number of horses, and these antibodies correlated with dog contact; however, cross-reactivity with avian influenza viruses could not be ruled out.

Species Affected

Equine influenza viruses mainly affect horses (Equus caballus) and other Equidae such as donkeys (E. asinus), mules, zebras (E. zebra, E. quagga or E. grevyi), Asian wild horses (E. przewalskii) and Asiatic wild asses/onagers (E. hemionus). They can also affect dogs, and one H3N8 equine virus became established in dogs as a canine influenza virus. An H3N8 equine influenza virus was found during surveillance of healthy Bactrian camels (Camelus bactrianus), another H3N8 virus was isolated from sick pigs in China, and a reassortant between swine and equine influenza viruses (H1N7) was detected in pigs in Europe. Experimental infections have also been established in cats, ferrets and mink. Cattle were susceptible in an older experiment, but in a recent study, there was no evidence of infection when they were exposed to an aerosolized H3N8 virus.

Zoonotic potential

Serological evidence and experiments in volunteers suggest that humans might occasionally be susceptible to equine influenza viruses, though infections seem to be rare.

Geographic Distribution

Equine influenza viruses tend to occur wherever equids are found. However, the circulating lineages or variants of H3N8 viruses may depend on the region. Only a few island countries, such as New Zealand, Iceland and Australia, are known to be entirely free from these viruses.

Transmission

Equine influenza viruses are transmitted in droplets and aerosols created by coughing and sneezing, and by contact with nasal discharges, either directly or on fomites. Close contact and closed environments favor transmission. Influenza viruses enter the body via the respiratory tract, but the eye can also be a portal of entry. While aerosol transmission is usually thought to occur only during close contact, the possibility of local airborne spread was suggested during an epidemic among naive horses in Australia.

Environmental survival of influenza A viruses is influenced by the type of surface, ambient conditions and presence of organic matter (e.g., feces). Low temperatures and protection from sunlight enhance survival. Influenza viruses are also reported to persist longer suspended in liquid, which protects these enveloped viruses from desiccation. Human influenza A viruses remain viable for less than 24-48 hours on most surfaces, and seem to be infectious for just a few minutes to hours in many environments. An H3N8 equine influenza virus was inactivated by UV light within 30 minutes, even when at high concentrations. Mixed with sterilized soil in a test tube, it remained viable for 8 hours at 15°C (59°F) in sunlight, and 24 hours at 18°C (64°F) in the dark. However, it survived for 14 days in 4°C (39°F) tap water, up to 2 days in 24-37°C (75-99°F) tap water, and 14-18 days in 22-37°C (72-99°F) canal water. This virus was inactivated in less than a day in horse blood at 37°C, though it persisted for 5-6 days in horse urine at 4-37°C. Avian influenza viruses, which have been studied more extensively, can survive several weeks to several months or more when suspended in distilled water or sterilized environmental water in the laboratory; however, they may remain viable for only a few days (or less) to a few weeks in natural water sources at some temperatures.

Disinfection

Influenza A viruses are susceptible to a wide variety of disinfectants including sodium hypochlorite, 60-95% ethanol, quaternary ammonium compounds, aldehydes (glutaraldehyde, formaldehyde), phenols, acids and iodides. Common household agents including 1% bleach, 10% malt vinegar or 0.01-0.1% dishwashing liquid in water (“washing up liquid”) were found to destroy the viability of human influenza A viruses, although hot water alone (55°C/131°F) did not eliminate these viruses rapidly. Influenza A viruses can also be inactivated by heat of 56-60°C (133-140°F) for a minimum of 60 minutes (or higher temperatures for shorter periods), as well as by ionizing radiation or extremes of pH (pH 1-3 or pH 10-14).

Incubation Period

The clinical signs of equine influenza usually appear within a few days of exposure. In laboratory studies, the incubation period ranges from 1 to 5 days.

Clinical Signs

Equine influenza is an acute respiratory disease that usually begins with a high fever and other nonspecific signs of illness, followed by a deep, dry, often paroxysmal cough. Affected animals usually have a serous to mucopurulent nasal discharge and may also wheeze and/or have an elevated respiratory rate. Submandibular and retropharyngeal lymphadenopathy is sometimes, though not always, present. Animals with partial immunity can have milder, atypical or subclinical infections, and reduced performance may be the only sign in some vaccinated horses. Increased fetal losses (stillbirths, dystocia, ‘red bag’ deliveries) may be seen in some mares that become ill late in pregnancy during outbreaks in naive populations. Severe and fulminant viral pneumonia, with a high case fatality rate, has been described in a few cases in young foals without maternal antibodies, and rarely in adults.

Healthy adult horses usually recover within 1-3 weeks, although the cough may persist longer. However, some cases may be complicated by secondary bacterial infections, sequelae such as chronic bronchitis, or rare complications such as neurological signs, myocarditis, myositis or limb edema. Convalescence may take months in severely affected animals.
Other influenza viruses in horses

An avian H3N8 virus epidemic among horses in China in the late 1980s/early 1990s, resembled equine influenza. Mortality was initially high (20-30%), but subsequently became minimal. An Asian lineage H5N1 HPAI virus was isolated from donkeys during a respiratory disease outbreak in Egypt, and a subsequent investigation detected antibodies to these viruses in some healthy donkeys and horses. The role of the H5N1 virus in this outbreak was unclear, as the affected donkeys responded well to antibiotics. The consequences of exposure to other avian influenza viruses, if any are unknown; however, the detection of antibodies in healthy equids suggests these infections might be subclinical or similar to common respiratory diseases of equids. Horses experimentally infected with one human influenza virus (H3N2 ‘Hong Kong’) developed a mild febrile illness.

Equine influenza viruses in other animals

Mild to severe respiratory signs have been reported in dogs naturally infected with H3N8 equine influenza viruses. One virus caused bronchointerstitial pneumonia in a group of foxhounds in the U.K. in 2002. The clinical signs included coughing, lethargy and weakness, which sometimes progressed to loss of consciousness. One dog died and several were euthanized. However, an H3N8 equine influenza virus in Australia caused milder signs, with anorexia, depression, slight nasal discharge, and in some cases, a cough that persisted for several weeks, and all of the dogs recovered. Dogs experimentally infected with H3N8 equine influenza viruses remained asymptomatic or had very mild clinical signs (e.g., periodic anorexia and sneezing). Cats experimentally infected with an H3N8 isolate from 2013 developed respiratory signs. Another isolate from 1963 did not cause any clinical signs, though two cats seroconverted.

Depression and respiratory signs, including coughing, were reported in pigs infected with an H3N8 equine influenza virus in China. Streptococcus suis was also recovered from these herds, and hemorrhagic pleuritis was noted in some animals at necropsy. However, no clinical signs have been seen in pigs experimentally infected with equine H3N8 viruses. One H3N8 virus was recovered from a healthy camel. Mink experimentally infected with an H3N8 equine influenza virus remained asymptomatic despite shedding virus.

Post Mortem Lesions

Upper respiratory tract involvement alone is common in milder cases; however, concurrent bacterial infections can result in bronchopneumonia. Foals with severe viral bronchointerstitial pneumonia had gross lesions of diffuse consolidation or extensive areas of coalescing consolidation interspersed with normal or slightly hyperinflated parenchyma. The lymph nodes associated with the respiratory tract were slightly enlarged in these foals, but there no gross lesions in other tissues.

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Diagnostic Tests

Equine influenza viruses, their antigens and nucleic acids can be detected in respiratory samples from live animals and/or lung tissue samples collected at necropsy. Nasopharyngeal swabs were found to detect a higher percentage of infected horses than nasal swabs, but nasal swabs are also considered adequate for routine diagnosis. Other samples, such as tracheal washes and nasal scrapings, may also be employed. Virus shedding is usually brief, and samples should be collected as soon as possible after the onset of clinical signs.

Most clinical cases are diagnosed by RT-PCR and/or antigen detection. Viral antigens in upper respiratory samples are usually identified with ELISAs or other rapid tests, but immunohistochemistry or immunofluorescence can be used on tissue samples, nasal scrapings and tracheal washes. The rapid antigen tests employed should be validated for horses; most of these assays were originally developed to detect influenza A viruses in humans, and can have lower sensitivity for equine influenza viruses.

Virus isolation is generally not necessary or practical for routine equine influenza diagnosis, but it can be helpful in the characterization of new influenza viruses. Equine influenza viruses are more likely to be recovered in embryonated chicken eggs than mammalian cell lines (e.g., MDCK cells); however, the use of both eggs and cell cultures may maximize the recovery of some viruses. Virus isolation is most likely to be successful when samples are taken during the first 1-2 days of overt clinical signs. Recovered viruses can be identified as influenza A viruses with agar gel immunodiffusion (AGID), antigen-detection ELISAs or other immunoassays, or by a molecular test such as RT-PCR. They can be subtyped with specific antisera in hemagglutination and neuraminidase inhibition tests, by RT-PCR, or by sequence analysis of the viral HA and NA genes.

Serological tests for horses include hemagglutination inhibition (HI), ELISAs, immunodiffusion/ single radial hemolysis and virus neutralization. Serology is most often used for surveillance and vaccine testing. HI and ELISAs may also be employed in the retrospective diagnosis of a clinical case. Diagnosis generally requires paired serum samples and a rising antibody titer; however, a single antibody test may be suggestive in equine influenza virus-free countries. Cross-reactivity between equine influenza viruses and other influenza A viruses may be an issue in serological tests. Most serological tests cannot distinguish infected from vaccinated animals; however, an ELISA for this purpose was developed and used with a canarypox-vectored vaccine during the 2007-2008 equine influenza virus eradication campaign in Australia.

Treatment

Equine influenza is usually treated with supportive and symptomatic care, rest, and antibiotics as needed to control secondary bacterial infections. Antiviral drugs used for
Influenza in humans are not generally given to animals; however, the neuraminidase inhibitors peramivir and oseltamivir appeared to shorten the duration of the illness in experimentally infected horses, and some authors have speculated that they might be of use in valuable horses. One issue with these antiviral drugs is that the brief period when influenza viruses are most susceptible (48 hours) has often passed by the time the animal is seen. The potential for influenza viruses to develop resistance to the drugs is also a concern.

**Control**

**Disease reporting**

Veterinarians who encounter or suspect equine influenza should follow their national and/or local guidelines for disease reporting. However, this disease is widespread and common in many countries, and generally not reportable. State reportable disease lists should be consulted in the U.S.

**Prevention**

Preventing the entry of equine influenza virus into a facility can be difficult, but the risk of outbreaks can be reduced by quarantines and vaccination. The World Organization for Animal Health (OIE) recommends a 4-week quarantine for equids entering countries free of equine influenza, but a 2-week quarantine with vaccination is considered an adequate compromise for most facilities in an endemic area. Vaccination needs and frequency may differ depending on the individual animal (e.g., age, past vaccination/exposure history) and its environment. Vaccines are particularly important for animals that are transported frequently and mixed with others, such as racehorses. They can also be used during an outbreak and appear to reduce the severity of the disease in animals that are not yet affected. For the best protection, equine influenza vaccines should be closely matched to the circulating virus(es). A multi-country surveillance program for these viruses recommends changes in vaccine strains. Practitioners should, however, remain aware that vaccinated animals can become subclinically infected and shed the virus.

During an outbreak, early isolation of infected animals seems to reduce virus spread within a facility. Other routine infection control measures include cleaning and disinfection of fomites, and good hygiene including hand washing. Clothing can be cleaned by washing it with detergent at normal laundry temperatures.

Elimination of established equine influenza viruses from an entire country would generally not be cost-effective even if it were feasible; however, Australia successfully eradicated a recently introduced virus with quarantines, movement controls and other biosecurity measures; vaccination; and surveillance with both serological and virological tests, including an ELISA that could distinguish vaccinated from infected horses.

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**Morbidity and Mortality**

In areas where vaccination is uncommon, there may periodically be large epidemics of equine influenza. They typically occur at long intervals, with little obvious disease between these times. Epidemics and large outbreaks are also possible in a vaccinated population if a new virus that has a poor match with the vaccine is introduced. Smaller outbreaks occur occasionally in these areas, probably due to factors such as changes in the circulating viruses, a limited duration of immunity from the vaccines, and variations in the strength of immune responses in individual animals and groups.

Equine influenza outbreaks can occur any time of the year. They are most common where groups of animals are in close contact, such as at racetracks, horse shows and sale barns, and are often associated with the introduction of a new animal. Viruses can spread rapidly in a fully susceptible group, affecting all animals within hours to days. However, outbreaks can last up to 3-4 weeks in partially immune groups, where transmission rates can be lower and subclinically infected, partially protected (e.g., vaccinated) horses may shed viruses for a longer time. Dispersal of horses from a facility while they are still shedding the virus has sometimes propagated outbreaks.

Equine influenza morbidity can be 60-90% or higher in some epidemics among naive horse populations, but it is usually around 20-40% in most outbreaks in endemic areas. The severity of the illness can vary with the dose and strain of virus; host factors such as age, pregnancy (more severe clinical signs have been reported in pregnant mares close to parturition) and pre-existing immunity; stressors such as transport or the inability to rest the horse; concurrent illnesses; secondary bacterial infections; and the availability of good veterinary care.

The overall mortality rate in horses is usually < 1%, but it may be higher in naïve populations. Approximately 2% of the horse population was estimated to have died during a massive historical outbreak in the U.S. in 1872, which may have been caused by the emergence of the H7N7 equine influenza virus. In 1989, the introduction of a completely novel H3N8 avian influenza virus in China initially resulted in a 20-30% mortality rate; however, few deaths were seen in subsequent years. Conversely, mortality was very low when an H3N8 equine influenza virus was introduced to the naïve horse population in Australia. Possible reasons for the low mortality included monitoring of viral spread and the provision of good veterinary care to horses that became ill. Elevated mortality may be seen in neonates in non-immune populations. In endemic areas, however, maternal antibodies reduce the risk of illness during this critical period.

**Public Health**

Human infections with equine influenza viruses appear to be possible but uncommon. One putative clinical case was reported during an outbreak in South America; however, the virus was not subtyped and the association of
the illness with the outbreak could have been coincidental. The symptoms in experimentally infected human volunteers varied: while some people remained asymptomatic, others developed an upper respiratory illness, which was sometimes accompanied by fever and/or systemic signs of illness. In 3 studies, the proportion of people with symptomatic disease ranged from 12% to 87%, and some shed the virus. Antibodies to equine influenza viruses have been found in about 3-12% of people with horse exposures tested in the U.S., Mongolia and Australia; however, the titers were sometimes low, and some could have been caused by cross-reactivity with other H3 viruses, including human H3N2 viruses.

Internet Resources

The Merck Veterinary Manual
United States Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS)
World Organization for Animal Health (WOAH)
WOAH Manual of Diagnostic Tests and Vaccines for
OIE Terrestrial Animal Health Code

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References


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