Foot and Mouth Disease

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Importance

Foot-and-mouth disease (FMD) is a highly contagious viral disease that primarily affects cloven-hooved livestock and wildlife. Although adult animals generally recover, the morbidity rate is very high in naïve populations, and significant pain and distress occur in some species. Sequelae may include decreased milk yield, permanent hoof damage and chronic mastitis. High mortality rates can be seen in young animals. Although foot-and-mouth disease was once found worldwide, it has been eradicated from some regions including North America and most of Europe. Where it is endemic, this disease is a major constraint to the international livestock trade. Unless strict precautions are followed, FMD can be readily re-introduced into disease-free livestock. Once this occurs, the disease can spread rapidly through a region, particularly if detection is delayed. Outbreaks can severely disrupt livestock production, result in embargoes by trade partners, and require significant resources to control. Direct and indirect economic losses equivalent to several billion US dollars are not uncommon. Since 1997, a PanAsia lineage virus has caused a series of outbreaks in Asia, Africa, the Middle East and Europe. Some outbreaks, particularly those in Taiwan and the United Kingdom, have been devastating.

Etiology

The foot-and-mouth disease virus (FMDV) is a member of the genus *Aphthovirus* in the family Picornaviridae. There are seven immunologically distinct serotypes - O, A, C, SAT 1, SAT 2, SAT 3 and Asia 1 - and over 60 strains within these serotypes. New strains occasionally develop spontaneously.

FMDV serotypes and strains vary within each geographic region. Serotype O is the most common serotype worldwide. This serotype is responsible for a pan-Asian epidemic that began in 1990 and has affected many countries throughout the world. Other serotypes also cause serious outbreaks. Immunity to one serotype does not provide any cross-protection to other serotypes. Cross-protection against other strains varies with their antigenic similarity.

Species Affected

FMDV can infect most or all members of the order Artiodactyla (cloven-hooved mammals), as well as a few species in other orders. Each species varies in its susceptibility to infection and clinical disease, as well as its ability to transmit the virus to other animals. Livestock susceptible to FMD include cattle, pigs, sheep, goats, water buffalo and reindeer. Lllamas, alpacas and camels can be infected experimentally, but do not appear to be very susceptible. FMDV can also infect at least 70 species of wild animals including African buffalo (*Syncerus caffer*), bison (*Bison* spp.), elk, moose, chamois, giraffes, wildebeest, blackbuck, warthogs, kudu, impala, and several species of deer, antelopes and gazelles. Susceptible non cloven-hooved species include hedgehogs, armadillos, kangaroos, nutrias, capybaras, guinea pigs, rats and mice. Infections have been reported in African and Asian elephants in zoos; however, African elephants are not considered susceptible to FMD under natural conditions in southern Africa.

On most continents, cattle are usually the most important maintenance hosts for FMDV, but some virus strains are primarily found in pigs, sheep or goats. Cattle and African buffalo are the usual maintenance hosts for FMDV in Africa; African buffalo are currently thought to carry only the SAT serotype. With this exception, wildlife hosts do not seem to be able to maintain FMD viruses, and are usually infected by contact with domesticated livestock. Early reports suggested that transmission also occurred between cattle and European hedgehogs, but there is no evidence that this species has helped to propagate FMDV in the last 40 years.

Geographic Distribution

Foot-and-mouth disease is endemic in parts of Asia, Africa, the Middle East and South America. In parts of Africa, virus persistence in wild African buffalo makes eradication unfeasible. North America, New Zealand, Australia, Greenland, Iceland

and most of Europe are free of this disease. Sporadic outbreaks have occurred in disease-free countries, with the exception of New Zealand, Greenland, Iceland and the smaller islands of Oceania. The last U.S. outbreak occurred in 1929.

Transmission

FMDV can be found in all secretions and excretions from acutely infected animals, including expired air, saliva, milk, urine, feces and semen. Pigs, in particular, produce large quantities of aerosolized virus. Animals can shed FMDV for up to four days before the onset of symptoms. This virus is also found in large quantities in vesicle fluid, and peak transmission usually occurs when vesicles rupture. Transmission can occur by direct or indirect contact with infected animals and contaminated fomites; routes of spread include inhalation of aerosolized virus, ingestion of contaminated feed, and entry of the virus through skin abrasions or mucous membranes. The importance of each of these routes varies with the species. For example, pigs are less susceptible to aerosolized virus than cattle or sheep. Sheep may have less obvious symptoms than other species, and have been important in disseminating the virus in some outbreaks. Sexual transmission could be a significant route of spread for the SAT type viruses in African buffalo populations.

Some animals carry FMDV for prolonged periods after recovering from acute disease. Animals with natural or vaccine-induced immunity can also become carriers if they are later exposed to virus; these animals can remain asymptomatic. FMDV can persist for up to nine months in sheep and up to four months in goats. Most cattle carry this virus for six months or less, but some animals remain persistently infected for up to 3.5 years. Individual African buffalo have been shown to be carriers for at least five years, and the virus can persist in a herd of African buffalo for at least 24 years. Llamas do not become carriers. A single study suggested that pigs may become carriers, but many other studies have found that this species cleared the infection within 3 to 4 weeks. In carriers, FMDV is found only in the esophageal-pharyngeal fluid. The amount of virus is small, and it may be found only intermittently. Carriers might be able to transmit FMDV to other animals if they come in close contact; the importance of this route of transmission is controversial. Unequivocal evidence for transmission from carriers has been reported only from Africa, where African buffalo can spread the disease to cattle. With the exception of African buffalo, wildlife seems to be infected by contact with domesticated animals; FMDV disappears from the wildlife populations when outbreaks in livestock are controlled. Persistent infections have been reported in some experimentally infected wildlife including fallow (*Dama dama*) and sika deer (*Cervus nippon*) and kudu (*Tragelaphus strepsiceros*), and occasionally in red deer (*Cervus elaphus*). Deer could carry FMDV for up to 11 weeks.

FMDV can be transmitted on fomites including vehicles, as well as mechanically by animals and other living vectors. Airborne transmission can occur under favorable climatic conditions. FMDV is thought to have been transmitted via aerosols from Brittany to Jersey (approximately 30 miles or 48 km) and for approximately 70 miles (113 km) from Jersey to the Isle of Wight. There is limited information on the survival of FMDV in the environment, but most studies suggest that it remains viable, on average, for three months or less. In very cold climates, survival up to six months may be possible. Virus stability increases at lower temperatures; in cell culture medium at 4°C (39°F), this virus can remain viable for up to a year. It was reported to survive on bran and hay for more than three months in a laboratory. It can also remain viable for approximately two months on wool at 4°C, with significantly decreased survival when the temperature increases to 18°C (64°F), and for 2 to 3 months in bovine feces. Organic material protects the virus from drying, and enhances its survival on fomites. Virus survival is also enhanced when FMDV is protected from sunlight. FMDV is inactivated at pH below 6.5 or above 11. This virus can persist in meat and other animal products when the pH remains above 6.0, but it is inactivated by acidification of muscles during rigor mortis. It can survive for long periods in chilled or frozen lymph nodes or bone marrow.

In humans, FMDV may be carried in the nasal passages for a period of time. In one study, this virus was detected in the nasal passages of one of eight people 28 hours after exposure to infected animals, and from none of the eight at 48 hours. More recent studies have found that FMDV is not transmitted by people when personal hygiene and biosecurity protocols are followed, and suggest that nasal carriage of the virus may be unimportant. The discrepancy between these studies remains to be resolved.

Incubation Period

In cattle, the incubation period varies from two to 14 days, depending on the dose of the virus and route of infection. In pigs, the incubation period is usually two days or more, but can be as short as 18-24 hours. The incubation period in sheep is usually 3 to 8 days. Incubation periods as short as 24 hours and as long as 12 days have been reported in this species after experimental infection.

Clinical Signs

Foot-and-mouth disease is characterized by fever and vesicles (blisters) on the feet, in and around the mouth, and on the mammary gland. Occasionally, vesicles may occur at other locations including the vulva, prepuce or pressure points on the legs. Vesicles often rupture rapidly, becoming erosions. Pain and discomfort from the lesions leads to a variety of symptoms including depression, anorexia, excessive salivation, lameness and reluctance to move or rise. Lesions on the coronary band may cause

growth arrest lines on the hoof. In severe cases, the hooves may be sloughed. Although FMDV does not cross the placenta, abortion may occur in pregnant animals. Most adults recover in two to three weeks, although secondary infections may lead to a longer recovery time. Possible complications include temporary or permanent decreases in milk production, chronic lameness or mastitis, weight loss and loss of condition. Deaths usually occur only in young animals, as the result of multifocal myocarditis; vesicles are not always found. In some outbreaks, the mortality rate in young animals can be high. Severe disease may also cause sudden deaths among older animals, particularly some species of wildlife, but this is rare.

The symptoms and severity of FMD vary with the species of animal, and the serotype and strain of the virus. Cattle usually become febrile and develop lesions on the tongue, dental pad, gums, soft palate, nostrils or muzzle. The vesicles on the tongue often coalesce, rupture quickly, and are highly painful, and the animal becomes reluctant to eat. Profuse salivation and nasal discharge are common; the nasal discharge is mucoid at first, but becomes mucopurulent. Affected animals become lethargic, may lose condition rapidly, and have gradual or sudden, severe decreases in milk production. Hoof lesions occur in the area of the coronary band and interdigital space. Foot lesions cause reluctance to rise, or stamping or shaking of the feet. Pregnant animals may abort. Young calves can die of heart failure without developing vesicles. In areas where cattle are intensively vaccinated, the entry of FMD into the herd can sometimes cause swelling of tongue and severe symptoms that resemble an allergic disease.

In pigs, the most severe lesions usually occur on the feet. The first symptoms may be lameness and blanching of the skin around the coronary bands. Vesicles develop on the coronary band and heel, and in the interdigital space. The lesions may become so painful that pigs crawl rather than walk. The horns of the digits are sometimes sloughed. Lesions at other sites are less common and less severe. Vesicles are sometimes found on the snout or udder, as well as on the hock or elbows if the pigs are housed on rough concrete floors. Mouth lesions are usually small and less apparent than in cattle, and drooling is rare. Affected pigs may also have a decreased appetite, become lethargic and huddle together. Fever may be seen, but the temperature elevation can be short or inconsistent. In some cases, the temperature may be near normal or even below normal. Young pigs up to 14 weeks may die suddenly due to heart failure; piglets less than eight weeks of age are particularly susceptible.

Foot-and-mouth disease tends to be mild in sheep and goats. Common symptoms include fever and mild to severe lameness of one or more legs. Vesicles may develop in the interdigital cleft and on the heel bulbs and coronary band, but they may rupture and be hidden by foot lesions from other causes. Mouth lesions are often not noticeable or severe, and generally appear as shallow erosions. Vesicles may also be noted on the teats, and rarely on the vulva or prepuce. Milk production may drop, and rams can be reluctant to mate. Ewes may abort. Up to 25% of infected sheep remain asymptomatic, and 20% have lesions only at one site. Young lambs and kids may die due to heart failure, without vesicles. In some epidemics, large numbers of lambs may fall down dead when stressed.

Minimal lesions and fever have been reported in llamas, which rarely become anorexic or demonstrate pain and discomfort.

The symptoms in wildlife resemble those seen in domesticated livestock. Vesicles and erosions may be found at various sites, particularly on the feet and in the mouth. More severe lesions occur where there is frequent mechanical trauma, e.g. on the feet and snout of suids or the carpal joints of warthogs. Loss of horns has also been seen. Some wildlife species typically experience subclinical infections or mild disease, while others develop severe, acute disease. Infections with SAT-type viruses in African buffalo are often subclinical, although small mouth and/or foot lesions have been reported. Severe disease has been documented in mountain gazelles, impala, blackbuck, white tailed-deer, warthogs and a kangaroo. In one outbreak in mountain gazelles, at least half the animals died due to heart failure or pancreatic atrophy and emaciation. Young animals of any species can die suddenly of myocarditis.

Post Mortem Lesions

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The characteristic lesions of foot-and-mouth disease are single or multiple, fluid-filled vesicles or bullae from 2 mm to 10 cm in diameter. The earliest lesions can appear as small pale areas or vesicles. Some vesicles may coalesce to form bullae. Vesicles are generally present for only a short period. Once they rupture, red, eroded areas or ulcers will be seen. These erosions may be covered with a gray fibrinous coating, and a demarcation line of newly developing epithelium may be noted. Loss of vesicular fluid through the epidermis can lead to the development of “dry” lesions, which appear necrotic rather than vesicular. Dry lesions are particularly common in the oral cavity of pigs.

The location and prominence of FMD lesions varies with the species. In cattle, numerous erosions, ulcers or vesicles may be found in the oral cavity. In pigs, sheep and goats, these lesions may be more common on the heel, coronary band and interdigital cleft of the feet. Some lesions may extend to the skin. Coronitis may be seen on the hooves, and animals with severe disease may slough their hooves or claws. In addition, vesicles may be found in other locations including the teats or udder; pressure points of the legs, ruminal pillars, prepuce or vulva. In young animals, cardiac degeneration and necrosis can cause gray or yellow streaking in the myocardium; these lesions are sometimes called “tiger heart” lesions.

Morbidity and Mortality

The morbidity rate varies with the species, immunity and other factors. Recovery from infection leads to immunity against the infecting virus, but little or no immunity develops to other serotypes. If several serotypes are endemic in a region, periodic episodes of disease may be seen. If only a single, persistent serotype circulates in a population, clinical disease may be mild and mainly occurs in young animals as they lose their protection from maternal antibodies. Carriers occur in endemic areas. In wild African buffalo populations, 50-70% of the animals may become carriers. Carrier rates from 15% to 50% have been reported in cattle and sheep.

In regions where FMD is not endemic, the morbidity rate can be as high as 100%. All susceptible species may not be affected during an outbreak. During one Asian epidemic, only pigs were infected. The mortality rate is generally less than 1% in adult livestock, but it can be much higher in young animals. Mortality rates of 40-94% have been reported in lambs. During one epidemic in Taiwan, the overall mortality rate in piglets was 40%. Up to 100% of suckling pigs may die.

Among wildlife, impala seem to be particularly susceptible to disease; regular epidemics of FMD occur in this species in southern Africa. Most outbreaks in wildlife are similar to those in domesticated species, with animals usually recovering in a week or two; however, higher mortality rates have occasionally been reported. A case fatality rate of at least 50% was reported in mountain gazelles in Israel. The same virus caused the usual symptoms and few deaths in cattle.

Diagnosis

Clinical

The symptoms of FMD vary with the species, but vesicles and erosions in the oral cavity or on the feet, teats or other areas are suggestive. In cattle, suspicion should be raised by simultaneous salivation and lameness, particularly when a vesicular lesion has been seen or is suspected to exist. Profuse salivation is uncommon in pigs or sheep, where lameness is more typical. Suspect or febrile animals should be examined closely for lesions. When sudden death is observed in young cloven-hooved livestock, older animals should also be examined; young animals that die of heart disease may not have vesicular lesions. Tranquilization may be necessary for a thorough examination as vesicles are painful and may be difficult to see. Laboratory confirmation is necessary, as all vesicular diseases have almost identical clinical signs.

Differential diagnosis

FMD cannot be distinguished clinically from other vesicular diseases including vesicular stomatitis, swine vesicular disease and vesicular exanthema. In domesticated animals, the symptoms may also resemble foot rot, traumatic stomatitis, and chemical and thermal burns. In cattle, oral lesions can resemble rinderpest, infectious bovine rhinotracheitis, bovine viral diarrhea, malignant catarrhal fever and epizootic hemorrhagic disease. In sheep, the lesions can be confused with bluetongue, contagious ecthyma, and lip and leg ulceration.

Laboratory tests

Foot-and-mouth disease can be diagnosed by virus isolation, detection of viral antigens or nucleic acids, and serology. FMDV can be isolated in primary bovine thyroid cells or primary pig, calf or lamb kidney cells. BHK-21 or IB-RS-2 cells can also be used, but cell lines are less sensitive than primary cells. If necessary, unweaned mice may be inoculated with the virus. In cell cultures, FMDV is identified using enzyme-linked immunosorbent assay (ELISA), complement fixation or reverse transcription polymerase chain reaction (RT-PCR) tests. ELISAs can also identify viral antigens directly in tissues; complement fixation is less specific and sensitive. RT-PCR techniques are also available. The virus serotype can be determined with either ELISA or RT-PCR. Electron microscopy is sometimes used to distinguish FMDV from other viruses in lesions.

Serological tests can be used for diagnosis as well as to certify animals for export. Antibodies to FMDV structural proteins are used to diagnose previous or current infections in unvaccinated animals. These tests include ELISAs and virus neutralization tests, and are serotype specific. Serological tests that detect antibodies to nonstructural proteins (NSP) can diagnose previous or current infections in vaccinated animals. Anti-NSP tests include ELISAs, and are not serotype specific. Some vaccinated animals that become persistently infected may not be detected by anti-NSP tests.

Carrier animals can be identified by isolating FMDV from the esophageal-pharyngeal fluids, but the virus may be present in low amounts and shed only intermittently. Repeated sampling may be necessary. RT-PCR can also be used to identify these animals.

Samples to collect

Before collecting or sending any samples from vesicular disease suspects, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent spread of the disease. Since vesicular diseases cannot be distinguished clinically, and some are zoonotic, samples should be collected and handled with all appropriate precautions.

In acute disease, the preferred sample for virus detection is epithelium from unruptured or freshly ruptured vesicles, or vesicular fluid. Sedation is generally advisable before these samples are collected. FMDV is extremely sensitive to low pH, and virus isolation is dependent on good buffering; epithelial samples should be shipped in a transport medium, and kept refrigerated or on ice. If vesicles are not available, blood (serum) and esophageal-pharyngeal fluid samples can be collected for

virus isolation or RT-PCR. Esophageal–pharyngeal fluids are taken by probang cup from ruminants, or as throat swabs from pigs, and are shipped in transport medium. These samples should be refrigerated or frozen immediately after collection. Vesicles are the preferred sample from animals that died of heart failure, but myocardial tissue or blood can be collected if vesicles are not present. FMDV may also be found in milk, other secretions and excretions, and other organs. Serum should be collected for serology.

In animals suspected to be carriers, esophageal-pharyngeal fluids should be collected.

Recommended actions if foot and mouth disease is suspected

Notification of authorities

A quick response is vitally important in containing an outbreak of FMD. State and federal veterinarians should be immediately informed of any suspected vesicular disease.

Federal: Area Veterinarians in Charge (AVIC):
http://www.aphis.usda.gov/animal_health/area_offices/

State Veterinarians:
http://www.aphis.usda.gov/vs/sregs/official.html

Control

FMDV is usually introduced into a country in contaminated feed or infected animals. Waste food (swill) fed to swine is a particular concern. In countries where foot-and-mouth disease is not endemic, the importation of animals and animal products from FMD-endemic areas is strictly controlled. Heat-treatment of all swill fed to pigs reduces the risk of an outbreak. Some countries have banned swill feeding altogether, due to difficulties in ensuring that adequate heat-treatment protocols are followed. Low-temperature pasteurization [72°C (162°F)] for 15 seconds) does not inactivate FMDV. High temperature short time (HTST) pasteurization greatly reduces the amount of viable FMDV in milk, but some studies suggest that residual virus may sometimes persist.

FMD outbreaks are usually controlled by quarantines and movement restrictions, euthanasia of affected and in-contact animals, and cleansing and disinfection of affected premises, equipment and vehicles. Effective disinfectants include sodium hydroxide (2%), sodium carbonate (4%), citric acid (0.2%) and Virkon-S®. Iodophores, quaternary ammonium compounds, hypochlorite and phenols are less effective, especially in the presence of organic matter. Infected carcasses must be disposed of safely by incineration, rendering, burial or other techniques. Milk from infected cows can be inactivated by heating to 100°C (212°F) for more than 20 minutes. Slurry can be heated to 67°C (153°F) for three minutes. Rodents and other vectors may be killed to prevent them from mechanically disseminating the virus. Good biosecurity measures should be practiced on uninfected farms to prevent entry of the virus.

Vaccination may be used to reduce the spread of FMDV or protect specific animals (e.g. those in zoological collections) during some outbreaks. The decision to use vaccination is complex, and varies with the scientific, economic, political and societal factors specific to the outbreak. Vaccines are also used in endemic regions to protect animals from clinical disease. FMDV vaccines must closely match the serotype and strain of the infecting strain. Vaccination with one serotype does not protect the animal against other serotypes, and may not protect the animal completely or at all from other strains of the same serotype. Currently, there is no universal FMD vaccine. Vaccine banks contain a wide variety of strains, particularly those judged to be the greatest threat of introduction, for use in an outbreak. Some countries maintain individual vaccine banks. There are also three international vaccine banks: the North American FMD Vaccine Bank (for Canada, the U.S. and Mexico), the E.U. Vaccine Bank (for all EU countries) and the International Vaccine Bank (for a variety of countries including Australia, New Zealand and some European nations).

Humans are thought to carry FMDV mechanically for a short period of time, based on a study that found this virus in the nasal passages of one of eight people 28 hours after they had been exposed to infected animals and none of the eight people at 48 hours. People who have been exposed to infected animals should avoid susceptible livestock for a designated period, usually a few days to a week. Some recent studies suggest that extended avoidance periods may not be necessary if good biosecurity practices, including effective personal hygiene protocols (showering or washing hands, and changing clothing), are followed. The discrepancy between these studies remains to be resolved, and government authorities should be consulted for the most recent waiting period recommendations.

Transmission of FMDV from wildlife in southern Africa is controlled by separating wildlife from domesticated livestock with fences, and by vaccination of livestock.

Public Health

Foot-and-mouth disease is not considered to be a public health problem. FMDV infections in humans are very rare, with approximately 40 cases diagnosed since 1921. Vesicular lesions and influenza-like symptoms can be seen; the disease is generally mild, short-lived and self-limiting.

[Note: Foot=and-mouth disease is not related to hand, foot and mouth disease, a condition seen only in humans.]

Internet Resources

U.K. Department for Environment, Food and Rural Affairs. Foot and mouth disease. http://www.defra.gov.uk/animalh/diseases/fmd/default.htm

U.S. Department of Agriculture. Foot and Mouth Disease http://www.aphis.usda.gov/newsroom/hot_issues/fmd/fmd.shtml

United States Animal Health Association. Foreign Animal Diseases http://www.vet.uga.edu/vpp/gray_book02/fad/index.php

World Organization for Animal Health (OIE) http://www.oie.int

OIE Disease Outbreak Maps. http://www.oie.int/wahid-prod/public.php?page=disease_outbreak_map

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals http://www.oie.int/eng/normes/mmanual/a_summry.htm

OIE Terrestrial Animal Health Code http://www.oie.int/eng/normes/mcode/A_summry.htm

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