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 sometimes occur in young animals or in some wildlife populations. Foot and mouth disease was once found worldwide; however, it has been eradicated from some regions including all of North America and western 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 regions via animals or animal products. Once introduced, the virus can spread rapidly, particularly if livestock densities are high or 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 the 1990s, a number of outbreaks have occurred in FMD-free countries. Some, such as the 2001 outbreak in the U.K., were devastating.

Etiology
The foot and mouth disease virus (FMDV) is a member of the genus Aphthovirus in the family Picornaviridae. There are seven major viral serotypes: O, A, C, SAT 1, SAT 2, SAT 3 and Asia 1. Serotype O is the most common serotype worldwide. It 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. Serotype C is uncommon and has not been isolated since 2004; however, there is serological evidence that it (or reintroduced serotype C vaccine strains) might still be found in parts of Africa.

Some FMDV serotypes are more variable than others, but collectively, they contain more than 60 strains. New strains occasionally arise. While most strains affect all susceptible host species, some have a more restricted host range (e.g., the O Cathay strain, which only affects pigs). Immunity to one FMDV serotype does not protect an animal from other serotypes. Protection from other strains within a serotype varies with their antigenic similarity.

Species Affected
FMDV mainly affects members of the order Artiodactyla (cloven-hooved mammals). Most species in this order are thought to be susceptible to some degree. Important livestock hosts include cattle, pigs, sheep, goats, water buffalo and yaks. Cattle are important maintenance hosts in most areas, but a few viruses are adapted to pigs, and some isolates might circulate in water buffalo. It is uncertain whether small ruminants can maintain FMDV for long periods if cattle are absent. Other susceptible species include camels and farmed cervids such as reindeer (Rangifer tarandus), deer and elk (Cervus elaphus nelsoni). Llamas and alpacas can be infected experimentally, and infections in alpacas were suspected during one recent outbreak.

FMDV has also been reported in at least 70 species of wild (or captive wild) artiodactyls including African buffalo (Syncerus caffer), bison (Bison spp.), moose (Alces alces), chamois (Rupicapra rupicapra), giraffes (Giraffa camelopardalis), wildebeest (Connochaetes gnou), blackbuck (Antilopa cervicapra), warthogs (Phacochoerus aethiopicus), kudu (Tragelaphus strepsiceros), impala (Aepyceros melampus), wild suids (e.g., warthogs, bush pigs) and several species of deer, antelopes and gazelles. African buffalo are important maintenance hosts for FMDV in Africa. They are mainly thought to maintain the SAT serotypes, although antibodies to other serotypes have been found in buffalo populations. Other species of wildlife do not seem to be able to maintain FMD viruses, and are usually infected when viruses spread from livestock or buffalo.

FMDV can also infect a few animals that are not members of the Artiodactyla, such as dogs, hedgehogs (both Erinaceus europaeus and Atelerix prurei), bears, armadillos, kangaroos, nutrias (Myocastor coypus), capybaras (Hydrochaeris hydrochaeris)
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Transmission

FMDV can be found in all secretions and excretions from acutely infected animals including expired air, saliva, milk, urine, feces and semen, as well as in the fluid from FMD-associated vesicles, and in amniotic fluid and aborted fetuses. The amount of virus shed by each route can be influenced by the host species and viral strain. Pigs produce large amounts of aerosolized virus, and the presence of large herds of infected swine may increase the risk of airborne spread. Peak virus production usually occurs around the time vesicles rupture and most clinical signs appear. However, some animals can shed FMDV for up to four days before the onset of clinical signs.

The virus can enter the body by inhalation or ingestion, and through skin abrasions and mucous membranes. Susceptibility to each route of entry can differ between species. Cattle are particularly susceptible to aerosolized virus, while pigs require much higher doses to be infected by this route. Sexual transmission could be a significant route of spread for the SAT type viruses in African buffalo populations.

Mechanical transmission by fomites and living (e.g., animal) vectors is important for this virus. Airborne transmission can occur under favorable climatic conditions, with some viruses potentially spreading long distances, particularly over water. In 1981, one viral strain apparently traveled more than 250 km (155 miles) from Brittany, France to the Isle of Wight, U.K. However, aerosolized FMD viruses are rarely thought to travel more than 10 km (approx. 6 miles) over land. 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. The presence of organic material, as well as protection from sunlight, also promote longer survival. Reported survival times in the laboratory were more than 3 months on bran and hay, approximately 2 months on wool at 4°C (with significantly decreased survival at 18°C [64°F]), and 2 to 3 months in bovine feces. FMDV is sensitive to pH, and it is inactivated at pH below 6.0 or above 9.0. 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. Because acidification does not occur to this extent in the bones and glands, FMDV may persist in these tissues.

Humans as vectors for FMDV

People can act as mechanical vectors for FMDV, by carrying the virus on clothing or skin. The virus might also be carried for a time in the nasal passages, although several studies suggest prolonged carriage is unlikely. In one early study, nasal carriage was reported for up to 28 hours but less than 48 hours after contact with animals. In two recent studies, people did not transmit serotype O viruses to pigs or sheep when personal hygiene and biosecurity protocols were followed, and no virus could be detected in nasal secretions 12 hours after contact with the animals. In another recent study, FMDV nucleic acids (serotypes O or Asia 1) were found in only one person tested 16-22 hours after exposure to infected animals, and live virus could not be isolated from this sample. Because factors such as sub-optimal facility sanitation or poor compliance with personal hygiene and biosecurity protocols could also influence transmission to animals, these studies might not apply directly to the situation in the field.

Carriers

FMDV carriers are defined as animals in which either viral nucleic acids or live virus can be found for more than 28 days after infection. Animals can become carriers whether or not they had clinical signs. In most species, FMDV can be found only in esophageal-pharyngeal fluid, and not in other secretions or excretions (e.g., oral or nasal swabs); however, virus isolation was recently reported from the nasal fluid of experimentally infected water buffalo for as long as 70 days. Nonreplicating virus has also been found in the lymph nodes of ruminants for up to 38 days. The epidemiological significance of livestock FMDV carriers is uncertain and controversial. Although there are anecdotal reports of apparent transmission from these animals in the field, and esophageal-pharyngeal fluid is infectious if it is injected directly into an animal, all attempts to demonstrate transmission between domesticated livestock in close contact

and some other rodents including rats. Early reports suggested that transmission occurred between cattle and European hedgehogs (Erinaceus europaeus), but there is no evidence that this species has helped to propagate FMDV in the last 50 years. Rodents are likewise not thought to be epidemiologically important hosts, except as mechanical vectors.

Several clinical cases have been reported in captive Asian elephants (Elephas maximus), but there are few reports of FMDV in African elephants (Loxodonta africana), and the latter species is not considered susceptible under natural conditions in southern Africa. Experimental infections have been reported in cats and wild rabbits.

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during controlled experiments have failed. The only successful experiments were those that involved African buffalo carrying SAT viruses, which transmitted the virus to other buffalo and sporadically to cattle. Some authors have speculated that sexual transmission might have been involved in this case, as FMDV can be found in semen and all successful experiments included both bulls and cows.

How long an animal can remain a carrier varies with the species. Most cattle carry FMDV for six months or less, but some animals can remain persistently infected for up to 3.5 years. The virus or its nucleic acids have been found for up to 12 months in sheep (although most seem to be carriers for only 1 to 5 months), up to 4 months in goats, for a year in water buffalo, and up to 8 months in yaks (*Bos grunniens*). Individual African buffalo can be carriers for at least five years, and the virus persisted in one herd of African buffalo for at least 24 years. Camelids do not seem to become carriers. Pigs are not thought to become carriers, although there have been a few reports documenting the presence of viral nucleic acids after 28 days. One study suggested this might have been an artifact caused by slow degradation of this RNA. Persistent infections have been reported in some experimentally infected wildlife including fallow (*Dama dama*) and sika deer (*Cervus nippon*), kudu and red deer (*Cervus elaphus*). Some deer could carry FMDV for up to 2.5 months. In one early study, experimentally infected brown rats (*Rattus norvegicus*) were carriers for 4 months.

**Disinfection**

Various disinfectants including sodium hydroxide, sodium carbonate, citric acid and Virkon-S® are effective against FMDV. Iodophores, quaternary ammonium compounds, hypochlorite and phenols are reported to be less effective, especially in the presence of organic matter. The disinfectant concentration and time needed can differ with the surface type (e.g., porous vs nonporous surfaces) and other factors.

**Incubation Period**

The incubation period for FMD can vary with the species of animal, the dose of virus, the viral strain and the route of inoculation. It is reported to be one to 12 days in sheep, with most infections appearing in 2-8 days; 2 to 14 days in cattle; and usually 2 days or more in pigs (with some experiments reporting clinical signs in as little as 18-24 hours). Other reported incubation periods are 4 days in wild boar, 2 days in feral pigs, 2-3 days in elk, 2-14 days in Bactrian camels (*Camelus bactrianus*), and possibly up to 21 days in water buffalo infected by direct contact.

**Clinical Signs**

While there is some variability in the clinical signs between species, FMD is typically an acute febrile illness with vesicles (blisters) localized on the feet, in and around the mouth, and on the mammary gland. Vesicles occur occasionally at other locations including the vulva, prepuce, or pressure points on the legs and other sites. The vesicles usually rupture rapidly, becoming erosions. Pain and discomfort from the lesions leads to clinical signs such as 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 or footpads may be sloughed. Reproductive losses are possible, particularly in sheep and goats. Deaths are uncommon except in young animals, which may die from multifocal myocarditis or starvation. Most adults recover in 2 to 3 weeks, although secondary infections may slow recovery. Possible complications include temporary or permanent decreases in milk production, hoof malformations, chronic lameness or mastitis, weight loss and loss of condition.

**Cattle**

Cattle with FMD, especially the highly productive breeds found in developed countries, often have severe clinical signs. They usually become febrile and develop lesions on the tongue, dental pad, gums, soft palate, nostrils and/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 in this species; the nasal discharge is mucoid at first, but becomes mucopurulent. Affected animals become lethargic, may lose condition rapidly, and may have gradual or sudden, severe decreases in milk production. In some cases, milk may not be produced again until the next lactation, or milk yield may be lower indefinitely. Hoof lesions, with accompanying signs of pain, occur in the area of the coronary band and interdigital space. Young calves may 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 clinical signs that resemble an allergic disease.

In addition to other complications such as mastitis or hoof malformations, some cattle that recover from FMD are reported to develop heat-intolerance syndrome (HIS; also called ‘hairy panters’). This poorly understood syndrome is characterized by abnormal hair growth (with failure of normal seasonal shedding), pronounced panting with elevated body temperature and pulse rate during hot weather, and failure to thrive. Some affected animals are reported to have low body weight, severely reduced milk production and reproductive disturbances. Animals with HIS do not appear to recover. The pathogenesis of this syndrome is not known, and a definitive link with FMD has not been established, but endocrine disturbances were suspected by some early investigators.

**Water buffalo**

Both mouth and foot lesions can occur in water buffalo, but the clinical signs are reported to be milder than in cattle, and lesions may heal more rapidly. Some studies reported that mouth lesions were smaller than in cattle, with scant fluid. In one study, foot lesions were more likely to occur on the bulb of the heel than in the interdigital space.
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Pigs

Pigs usually develop the most severe lesions on their feet. In this species, the first signs of FMD may be lameness and blanching of the skin around the coronary bands. Vesicles then 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. Mouth lesions are usually small and less apparent than in cattle, and drooling is rare. However, 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. 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 is near normal or even below normal. Young pigs up to 14 weeks of age may die suddenly from heart failure; piglets less than 8 weeks of age are particularly susceptible.

Lesions may be less apparent in feral pigs than domestic pigs, in part due to their thicker skin and long, coarse hair.

Sheep and goats

Although severe cases can occur, FMD tends to be mild in sheep and goats. A significant number of infected animals may be asymptomatic or have lesions only at one site. Common signs in small ruminants are fever and mild to severe lameness of one or more legs. Vesicles occur on the feet, as in other species, 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. Significant numbers of ewes abort in some outbreaks. Young lambs and kids may die due to heart failure (vesicles may be absent) or from emaciation. The clinical signs in young animals can include fever, tachycardia and marked abdominal respiration, as well as collapse. In some cases, large numbers of lambs may fall down dead when stressed.

Camelids

Experimentally infected llamas and alpacas are generally reported to have only mild clinical signs, or to remain asymptomatic, although some reviews indicate that severe infections can also occur. Mild signs were reported in alpacas during one FMD outbreak in Peru, but the virus could not be isolated and these cases are unconfirmed. There are no reports of naturally-occurring cases in llamas.

Two experimentally infected Bactrian camels developed moderate to severe clinical signs, with hindleg lesions including swelling and exudation of the footpad, but no oral lesions. However, mouth lesions and salivation, as well as severe footpad lesions and skin sloughing at the carpal and tarso-metatarsal joints, the chest and knee pads were reported from Bactrian camels during outbreaks in the former Soviet Union. Detachment of the soles of the feet has been noted in several reports.

Other species

The clinical signs in wildlife resemble those in domesticated livestock, with vesicles and erosions 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. Bears developed vesicles on the footpads, as well as nasal and oral lesions. The severity of the illness varies; subclinical infections or mild disease are common in some species, while others are more likely to become severely ill. Infections with SAT-type viruses in African buffalo are often subclinical, although small mouth and/or foot lesions have been reported. However, severe outbreaks have been documented in wild populations of some species such as mountain gazelles (Gazella gazelle), and high mortality or severe clinical signs has been reported in some captive wildlife species (see Weaver et al., 2013 for a detailed review). Young animals can die suddenly of myocarditis.

Weakness and lethargy were reported in fatal illnesses in 5 puppies infected during serotype O outbreaks in Iran, and at least some of the puppies had cardiac lesions thought to have caused or contributed to the deaths. Historical cases of possible FMD in dogs, as well as old reports of experimental inoculation, likewise included reports of cardiac abnormalities and/ or vesicles, including small vesicles at the inoculation site in some experimentally infected dogs. Some experimentally infected dogs died.

Post Mortem Lesions

The characteristic lesions of foot and mouth disease are single or multiple, fluid-filled vesicles or bullae; however, these lesions are transient and may not be observed. The earliest lesions can appear as small pale areas or vesicles, while ruptured vesicles become red, eroded areas or ulcers. 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. Among domestic animals, dry lesions are particularly common in the oral cavity of pigs.

The location and prominence of FMD lesions can differ with the species (see ‘Clinical Signs’); however, common sites for lesions include the oral cavity and snout/ muzzle; the heel, coronary band and feet; the teats or udder; pressure points of the legs; the ruminal pillars (in ruminants); and the prepuce or vulva. Coronitis may be seen on the hooves, and the hooves or claws may be sloughed in severe cases. Involvement of the pancreas, as well as heart failure and emaciation, were reported in mountain gazelles. The pancreas was also severely affected in experimentally infected pronghorn (Antilocapra americana). In young animals, cardiac degeneration and necrosis can result in irregular gray or yellow lesions, including streaking, in the myocardium; these lesions are sometimes called “tiger heart”
lesions. Piglets can have histological evidence of myocarditis without gross lesions in the heart. Signs of septicemia, abomasitis and enteritis, as well as myocarditis, have been reported in lambs.

Only nonspecific gross lesions were described in infected fetuses from experimentally infected sheep. They included petechial hemorrhages in the skin, subcutaneous edema, ascites with blood-tinged peritoneal fluids and epicardial petechiae. Vesicles were not found, and the placenta did not appear to be affected. Some infected fetuses had no gross lesions. In another study, infected fetuses were generally autolyzed.

**Diagnostic Tests**

Testing for foot and mouth disease varies with the stage of the disease and purpose of the test. In acutely infected animals, FMDV, its antigens or nucleic acids can be found in a variety of samples including vesicular fluid, epithelial tissue, nasal and oral secretions, esophageal-pharyngeal fluid, blood and milk, and in tissue samples such as myocardium collected at necropsy. (The OIE-recommended samples at this stage are epithelium from unruptured or freshly ruptured vesicles, or vesicular fluid. In cases with no vesicles, the OIE recommends blood [serum] and esophageal–pharyngeal fluid samples, taken by probang cup from ruminants, or as throat swabs from pigs.) Carrier animals can only be identified by collecting esophageal-pharyngeal fluids for virus isolation and/or the detection of nucleic acids. Repeated sampling may be necessary to identify a carrier, as the amount of virus is often low and fluctuates.

Viral antigens are usually identified with enzyme-linked immunosorbent assays (ELISAs), and nucleic acids by reverse transcription polymerase chain reaction (RT-PCR). Other commercial tests to detect antigens, such as lateral flow devices, may be available in some countries. Virus isolation can be performed in primary bovine thyroid cells, primary pig, calf or lamb kidney cells, or BHK-21 or IB-RS-2 cell lines. The virus is generally identified with ELISAs or RT-PCR; however, complement fixation is still in use in some countries or for some purposes. If necessary, unwheaned mice can be used to isolate FMDV. Nucleotide sequence analysis can identify viral strains.

Serological tests can be used in surveillance, to certify animals for export, to confirm suspected cases during an outbreak, to monitor immunity from vaccination, and in matching vaccines to field strains. Test cutoff values can differ with the purpose of the test. Some serological tests detect antibodies to the viral structural (e.g., capsid) proteins. They include ELISAs and virus neutralization tests, and are serotype specific. Because FMDV vaccines also induce antibodies to structural proteins, these tests can only be used in unvaccinated animals. Other serological tests (e.g., some ELISAs and the enzyme-linked immuno-electrotransfer blot) detect antibodies to FMDV nonstructural proteins (NSPs), which are expressed only during virus replication. NSP tests are not serotype specific, and can be used in both vaccinated and unvaccinated animals. However, they are less sensitive and may not detect cases with limited virus replication, including some vaccinated animals that become infected. Due to such limitations, serological tests that detect antibodies to NSPs are generally used as herd tests.

**Treatment**

There is no specific treatment for FMD, other than supportive care. Treatment is likely to be allowed only in countries or regions where FMD is endemic.

**Control**

**Disease reporting**

A quick response is vital for containing outbreaks in FMD-free regions. Veterinarians who encounter or suspect this disease should follow their national and/or local guidelines for disease reporting. In the U.S., state or federal veterinary authorities should be informed immediately of any suspected vesicular disease.

**Prevention**

Import regulations help prevent FMDV from being introduced from endemic regions in infected animals or contaminated foodstuffs fed to animals. Waste food (swill) fed to swine is a particular concern. Heat-treatment can kill FMDV in swill and reduces the risk of an outbreak; however, some countries have completely banned swill feeding, due to difficulty in ensuring that adequate heat-treatment protocols are followed. Protocols for the inactivation of FMDV in various animal products such as milk products, meat, hides and wool have been published by the OIE. Global FMD control programs have recently been established to reduce virus circulation and the incidence of this disease.

Measures taken to control an FMD outbreak include quarantines and movement restrictions, euthanasia of affected and exposed animals, and cleaning and disinfection of affected premises, equipment and vehicles. Additional actions may include euthanasia of animals at risk of being infected and/or vaccination. Infected carcasses must be disposed of safely by incineration, rendering, burial or other techniques. They should not be fed to carnivores, including dogs and cats, which may be infected by the viruses in raw tissues. Rodents and other vectors may be killed to prevent them from mechanically disseminating the virus. People who have been exposed to FMDV may be asked to avoid contact with susceptible animals for a period of time, in addition to decontaminating clothing and other fomites. 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 illness. FMDV vaccines only protect
that sustained wildlife outbreaks might be theoretically possible, depending on animal density and other factors.

Reports of FMD in carnivores are apparently limited to a few putative cases in dogs described from the late 1800s to early 1900s; experimental infections in dogs and/or cats published between 1920 and 1950; and a recent description of 5 fatal illnesses in puppies, which had been fed infected tissues from lamb carcasses in two separate incidents in Iran. Viral antigens and nucleic acids were demonstrated in the puppies in the latter report. A review from the 1970s described no recent infections in dogs or cats, and noted that, with the exception of mechanical transmission, transmission from these species to livestock appeared to be very rare.

### Public Health

Foot and mouth disease is not considered to be a public health problem, as infections seem to be rare and their consequences mild. In the past, many people who worked with FMDV in vaccine laboratories or other locations developed antibodies to this virus, but there were few clinical cases. One laboratory reported only 2 cases in more than 50 years, and a large FMD vaccine manufacturer documented 3 cases among its workers. It may be that exposure to extremely large amounts of virus or a predisposing condition is necessary for infection.

Between 1921 and 1969, reports of more than 40 laboratory-confirmed cases of FMD in humans were published. The symptoms included vesicular lesions and influenza-like symptoms, and the disease was usually mild, short-lived and self-limiting. Broken skin was a recognized route of entry for some human cases, with the initial lesions developing at the inoculation site. There is also a report that three veterinarians deliberately infected themselves in 1934, by drinking virus-contaminated, unpasteurized milk for three days. One review from 1970 suggested that infections may have been more common in children than adults. Person-to-person transmission has never been reported; however, vesicles from affected people do contain virus.

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

### Internet Resources

Emergency Prevention System for Animal Health (EMPRES). Foot and mouth disease

The European Commission for the Control of Foot-and-Mouth Disease

U.K. Department for Environment, Food and Rural Affairs. Foot and Mouth.
http://www.defra.gov.uk/animal-diseases/a-z/foot-and-mouth/

USDA Animal Disease Information (including links to District Offices, Import Information) https://www.aphis.usda.gov/aphis/ourfocus/animalhealth


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


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