FOOT AND MOUTH DISEASE

AETIOLOGY

Classification of the causative agent

Foot and mouth disease (FMD) is caused by a virus of the family Picornaviridae, genus *Aphthovirus*. The virus has seven immunologically distinct serotypes: A, O, C, SAT1, SAT2, SAT3, and Asia1, which do not confer cross immunity. There have been no reports of FMD cases due to serotype C since 2004 and this serotype is now considered to be extinct. New FMD virus (FMDV) variants arise due to constant mutation during error-prone viral RNA replication, recombination, and host selection.

Resistance to physical and chemical action

Temperature: Preserved by refrigeration and °freezing. Progressively inactivated by temperatures above 50°C. Heating meat to a minimum core temperature of 70°C for at least 30 minutes inactivates the virus.

pH: Quickly inactivated by pH <6.0 or >9.0.

Disinfectants: Inactivated by sodium hydroxide (2%), sodium carbonate (4%), citric acid (0.2%), acetic acid (2%), sodium hypochlorite (3%), potassium peroxymonosulphate/sodium chloride (1%), and chlorine dioxide. Resistant to iodophores, quaternary ammonium compounds, and phenol, especially in the presence of organic matter.

Survival: Destroyed in muscle tissue at pH <6.0 i.e. after *rigor mortis* but survives in other tissues that remain at neutral pH, including lymph nodes and bone marrow and after freezing. Residual virus may survive in milk and milk products after a single cycle of pasteurisation (72°C), but is inactivated by ultra high-temperature pasteurisation. Survives drying and may persist for days to weeks in organic matter under moist and cool temperatures. Can persist in contaminated fodder and the environment for up to 1 month, depending on the temperature and pH conditions.

EPIDEMIOLOGY

- One of the most contagious animal diseases, with important economic losses
- Low mortality rate in adult animals, but often high mortality in young due to myocarditis

Hosts

- Of the domesticated species, cattle, pigs, sheep, goats and water buffalo (*Bubalus bubalis*) are susceptible to FMD. Cattle are usually the main host, although some strains appear to be specifically adapted to domestic pigs. Within the family Artiodactyla, all domestic cloven-hoofed animals of the suborder ruminantia including yaks and of the family suidae are susceptible.
- African buffalo are important maintenance hosts for the SAT serotypes of FMDV in Africa.
- Wild cloven-hoofed animals are also susceptible to natural or experimental infection, including deer, antelope, wild pigs and giraffe
- Bactrian camels (*Camelus bactrianus*) are susceptible to FMD. Old World camels may be resistant to natural infection with some strains and South American camelids such as alpacas and llamas are mildly susceptible, but are probably of no epidemiologic significance
- On occasion FMDV has also infected animals that are not members of the Artiodactyla, such as dogs, hedgehogs, bears, elephants, armadillos, kangaroos, nutrias, and capybaras.
- Rats, mice, guinea-pigs and armadillos can be infected experimentally

Transmission

- Direct contact between infected and susceptible animals, especially by inhalation of infectious aerosols
- Direct contact of susceptible animals with fomites (hands, footwear, clothing, vehicles, etc.)
- Consumption (primarily by pigs) of untreated contaminated meat products (swill feeding).
- Ingestion of contaminated milk (by calves)
- Artificial insemination with contaminated semen
- Long distance airborne spread, especially in temperate zones (up to 60 km overland and 300 km over water)

Humans can harbour FMDV in their respiratory tract for 24–48 hours, leading to the common practice of 3–5 days of personal quarantine for personnel exposed in research facilities. During an active outbreak, this may be reduced to an overnight period of time after thorough shower and shampoo, change of clothing, and expectoration.

Sources of virus

- Incubating and clinically affected animals
- 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 in sheep (up to 4 days before clinical signs). Peak virus production usually occurs around the time vesicles rupture and most clinical signs appear.
- Meat and by-products in which pH has remained above 6.0
- Carriers: recovered or vaccinated and exposed animals in which FMDV persists in the oropharynx for more than 28 days. The rates of carriers in cattle vary from 15–50% but the carrier state in cattle usually does not persist for more than 6 months, although in a small proportion it may last up to 3 years. Circumstantial field evidence indicates that on rare occasions carriers may transmit infection to susceptible animals of close contact, but the mechanism involved is unknown and direct evidence of transmission from carrier domestic species is lacking.

Occurrence

FMD 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.

Different serotypes and strains occur in different parts of the world and give rise to periodic outbreaks, associated with lack of protection between serotypes and the limited cross-protection between some strains, waxing and waning of population immunity, new incursions and variably effective control measures.

FMD is the first disease for which the OIE established an official list of free countries and zones.

FMD is one of the diseases for which the OIE has a procedure for the recognition of disease-free areas within a country or at national level. For more information, visit the status portal on the OIE website [http://www.oie.int/en/animal-health-in-the-world/official-disease-status/]

For more recent, detailed information on the occurrence of this disease worldwide, see the OIE World Animal Health Information Database (WAHID) Interface [http://www.oie.int/wahis/public.php?page=home]

DIAGNOSIS

For the purposes of the OIE *Terrestrial Animal Health Code*, the incubation period for FMD is 14 days.

It is reported to be 1–12 days in sheep, with most infections appearing in 2–8 days; 2–14 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.

Clinical diagnosis

Signs can range from mild or inapparent to severe, where the severity of clinical signs varies with the strain of virus, exposure dose, age and breed of animal, host species, and degree of host immunity. Deaths are uncommon except in young animals, which may die from multifocal myocarditis or starvation. Most adults recover in 2–3 weeks, although secondary infections may slow recovery.

Morbidity may approach 100%. Mortality in general is low in adult animals (1–5%) but higher in young calves, lambs and piglets (20% or higher). Recovery in uncomplicated cases usually takes about 2 weeks.

Cattle

- The highly productive dairy breeds found in developed countries have the most severe clinical signs. Pyrexia, anorexia, shivering, reduction in milk production for 2–3 days, then
    - smacking of the lips, grinding of the teeth, drooling, lameness, stamping or kicking of the feet: caused by vesicles (aphthae) on buccal and nasal mucous membranes and/or between the claws and coronary band
    - after 24 hours: rupture of vesicles leaving erosions
    - vesicles can also occur on the mammary glands
- Recovery generally occurs within 8–15 days
- Complications: tongue erosions, superinfection of lesions, hoof deformation, mastitis and permanent impairment of milk production, myocarditis, infertility, abortion, permanent loss of weight, and loss of heat control (‘panters’).
- Death of young animals from myocarditis

Sheep and goats

- A significant number of infected animals may be asymptomatic or have lesions only at one site. Common signs are fever and mild to severe lameness of one or more legs
- Vesicles occur on the feet, in the coronary band and interdigital spaces, 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
- Pyrexia
- Agalactia in milking sheep and goats is a feature. Significant numbers of ewes abort in some outbreaks
- Death of young stock may occur without clinical signs

Pigs

- Pyrexia
- May develop severe foot lesions and lameness with detachment of the claw horn, particularly when housed on concrete
- Vesicles often occur at pressure points on the limbs, especially along the carpus (‘knuckling’)
- Vesicular lesions on the snout and dry lesions on the tongue may occur
- 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

- Vesicles or blisters on the tongue, dental pad, gums, cheek, hard and soft palate, lips, nostrils, muzzle, coronary bands, teats, udder, snout of pigs, corium of dewclaws and interdigital spaces
- Erosions on rumen pillars at post mortem. Gray or yellow streaking in the heart from degeneration and necrosis of the myocardium in young animals of all species (‘tiger heart’)

Differential diagnosis

Clinically indistinguishable:

- Vesicular stomatitis
- Swine vesicular disease
- Vesicular exanthema of swine
- Infection due to Senecavirus A (Seneca Valley virus)

Other differential diagnosis:

- Rinderpest (globally eradicated)
- Bovine viral diarrhoea and Mucosal disease
- Infectious bovine rhinotracheitis
- Bluetongue
- Epizootic haemorrhagic disease
- Bovine mammillitis
- Bovine papular stomatitis; Contagious ecthyma
- Malignant catarrhal fever
- Non-infectious causes, such as trauma or chemical burns

Laboratory diagnosis

Samples

- Epithelium from an unruptured or recently ruptured vesicle or vesicular fluid
- Epithelial samples should be placed in a transport medium which maintains a pH of 7.2–7.6 and kept cool (see OIE *Terrestrial Manual*)
- Where collecting epithelial samples is not possible, blood and/or oesophageal–pharyngeal fluid samples taken by probang cup (https://www.wrlfmd.org/laboratory-protocols/probang-manufacturing) in ruminants or throat swabs from pigs provide an alternative source of virus.
- Probang samples should be refrigerated or frozen immediately after collection
- Myocardial tissue or blood can be submitted from fatal cases, but vesicles are again preferable if present

NB!!	Special precautions are required when sending perishable suspect FMD material within and between countries. See OIE *Terrestrial Manual* Chapter 1.1.3 *Transport of biological materials*

Procedures

Identification of the agent:

Detection of live FMD virus, FMD viral antigen or FMDV nucleic acid is sufficient for a positive diagnosis.

All laboratory manipulations with live FMD viral cultures or potentially infected/contaminated material such as tissue and blood samples must be performed at an appropriate containment level determined by biorisk analysis (see Chapter 1.1.4 *Biosafety and biosecurity: Standard for managing biological risk in the veterinary laboratory and animal facilities*)

- Reverse-transcription polymerase chain reaction (RT-PCR) – widely used as front-line tests to recognise FMDV-specific nucleic acids in a range of sample types including epithelium, milk, serum, OP. Formats include:
  - Agarose gel-based RT-PCR
  - Real-time RT-PCR
  - Lineage-specific RT-PCR methods
  - RT-PCR amplification for nucleotide sequencing

- Virus isolation:
  - Inoculation of primary bovine (calf) thyroid cells or primary pig, calf and lamb kidney cells. Susceptible cell lines such as BHK-21, LFBK-αVβ6 or IB-RS-2 can also be used
  - Once cytopathic effect is complete, culture fluids can be used in CF, antigen ELISA or RT-PCR tests
- Antigen detection ELISA – using monoclonal antibody or polyclonal antisera-based assays are can be used to detect and type FMD viral antigen
- Complement fixation test – less specific and sensitive than ELISA; affected by pro- and anti-complement factors

Serological tests

Serological tests for FMD are performed in support of four main purposes namely:

1. to certify individual animals prior to import or export (i.e. for trade)
2. to confirm suspected cases of FMD
3. to estimate the prevalence of infection or to substantiate its absence
4. to demonstrate the efficacy of vaccination

- Virus neutralisation test
  - The quantitative VN microtest for FMD antibody is performed with IB-RS-2, BHK-21, lamb or pig kidney cells in flat-bottomed tissue-culture grade microtitre plates
- Solid-phase competition ELISA
  - Can be used for the detection of antibodies against each of the seven serotypes of FMDV. As an alternative to guinea-pig or rabbit antisera, suitable MAbs can be used peroxidase-conjugated to detect antigens coated to ELISA plates either directly or after capture by MAbs.
- Liquid-phase blocking ELISA
  - Antigens are prepared from selected strains of FMDV grown on monolayers of BHK-21 cells
- Non-structural protein antibody tests
  - Indirect or competitive ELISA formats
  - Enzyme-linked immunoelectrotransfer blot assay (EITB)

For more detailed information regarding laboratory diagnostic methodologies, please refer to Chapter 3.1.8 Foot and mouth disease in the latest edition of the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* under the heading "Diagnostic Techniques".

PREVENTION AND CONTROL

Sanitary prophylaxis

- Protection of free zones by border control of the movements of animals and their products and by surveillance.
- Application of OIE recommended procedures for inactivation of FMDV in animal-derived products.
- Quarantine measures
- Slaughter of infected, recovered, and FMD-susceptible contact animals
- Cleaning and disinfection of premises and all infected material, such as implements, cars, and clothes
- Disposal of carcasses, bedding, and contaminated animal products in the infected area

Medical prophylaxis

Inactivated vaccines

Traditional FMD vaccines contain defined amounts of one or more chemically inactivated cell-culture-derived preparations of a seed virus strain blended with a suitable adjuvant/s and excipients. FMD vaccines may be classified as either 'standard' or 'higher' potency vaccines.

- Standard Potency Vaccines (commercial vaccines): formulated with sufficient antigen and appropriate adjuvant to have a minimum potency level of 3 PD_{50} [50% protective dose]
    - Provide 6 months of immunity after two initial vaccinations given 1-month apart.
    - Vaccine strains are selected based on antigenic relationship with circulating strains
    - Many are multivalent to ensure broad antigenic coverage against prevailing circulating strains
- Higher potency vaccines (emergency vaccines): formulated with sufficient antigen and appropriate adjuvant to have a minimum potency level of 6 PD_{50} [50% protective dose]
    - Higher potency vaccines are recommended for vaccination in naïve populations for their wider spectrum of immunity as well as their rapid onset of protection

Live attenuated vaccines

Live FMD vaccines are not acceptable due to the danger of reversion to virulence and as their use would prevent the detection of infection in vaccinated animals.

For more detailed information regarding vaccines, please refer to Chapter 3.1.8 Foot and mouth disease in the latest edition of the *OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animal*s under the heading "Requirements for Vaccines".

For more detailed information regarding safe international trade in terrestrial animals and their products, please refer to the latest edition of the *Terrestrial Animal Health Code*.

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The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Science Department (scientific.dept@oie.int). Last updated January 2021.