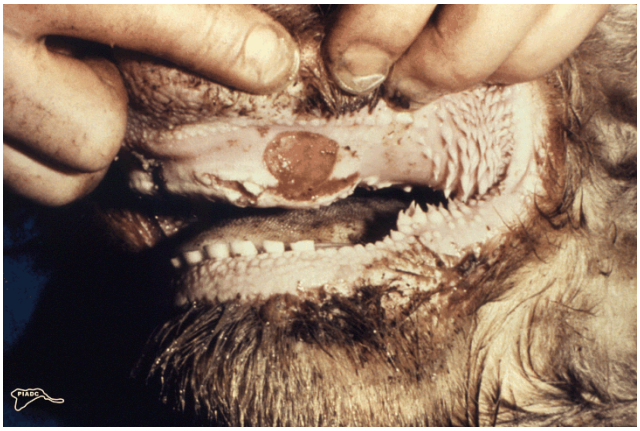
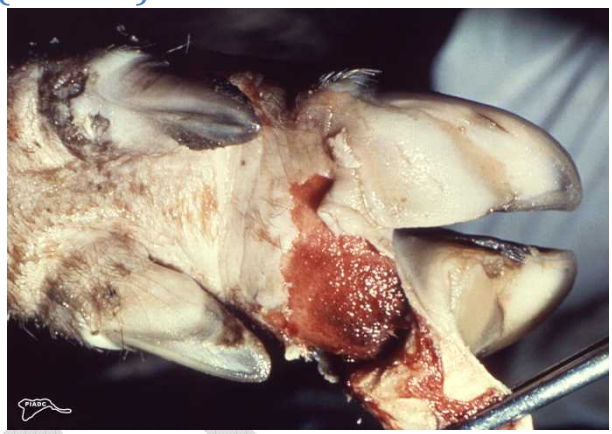
Foot-and-mouth disease virus (FMDV) Fact Sheet





Source: US CDC Public Health Image Library

Agent

Aphthae epizooticae

Morphology and genome characteristics

- Picornavirus
- RNA virus
- Non-enveloped icosahedral nucelocapsid
- 27-30 nm
- 8.2kb genome
- Linear non-segmented
- 7 serotypes (A, O, C, South African Territories (SAT) 1, SAT 2, SAT 3, Asia 1
    - More than 60 subtypes

Host range

Cloven hoofed **domestic** animals:

- Cattle
- Buffalo
- Sheep
- Goats
- Swine

Cloven hoofed **wild** animals

- Camels
- Deer
- Bison
- Feral hogs
- Antelope
- Giraffes
- Elephants

- Armadillos
- Hedgehogs
- Nutria
- Elk

Most domestic and wild cloven-hoofed animals can be hosts, including cattle, sheep, goats, swine, water buffalo, bison, deer, elk, antelope, camels, giraffes, and elephants. Infected ruminants typically stop shedding virus after two weeks, but some may shed for six to 24 months. Water buffalo can be carriers for five years. Llamas and alpacas are susceptible but do not play an epidemiological significant role in transmission. Rats and hedgehogs are also susceptible. Camels are resistant to natural infection.

Humans can be vectors, FMDV can replicate in human respiratory tract for 24-48 hours, do not become symptomatic; rare cases associated with laboratory exposure have been reported.

The highest incidence of disease and deaths is seen among young animals. Most adult animals recover from disease over time but suffer long-term sequelae.

Incubation period

2-14 days

Transmission

Infected animals can shed FMDV up to 14 days prior to developing clinical disease. Infected animals can shed up to 400,000 viral particles.

- Direct contact between infected and susceptible animals
- Indirect contact between susceptible animals and contaminated fomites (hands, footwear, clothing, vehicles, etc.)
- Ingestion of contaminated meat products (primarily porcine related to swill feeding), or contaminated milk (calves)
- Parenteral (artificial insemination with contaminated semen)
- Inhalation of infectious aerosols
- Airborne in temperate zones (transmitted via wind up to 60km overland and 300km over sea)

Infectious Dose

Respiratory (based off tissue culture infective dose (TCID50)

	Respiratory Route	**Oral Route**
Cattle	12	1×10^6
Pigs	20	8×10^3
Sheep	10	n/a
Impalas	1	n/a

Immunity

Duration of immunity following vaccination depends on the efficacy (formulation and antigen payload)

Vaccination only confers immunity to the viral strains included in the vaccine

Animals that survive natural infection experience immunity

Clinical Presentation

Foot and mouth disease affects cloven-hoofed livestock but does not infect horses. The symptoms are indistinguishable from vesicular stomatitis. General clinical signs include vesicular lesions, erosions and ulcers in the mouth, interdigital areas, on the muzzle, teats, and coronary band. In cattle the symptoms include slobbering, lameness, abortion, lethargy, nasal discharge, shivering, fever, lip smacking, and sores and blisters on the feet and mouth. Vesicles also form on the epithelium of lips, tongue, gums, nostrils, coronary bands, and interdigital space. Dairy cows exhibit reduced milk yields; young calves may die even before forming lesions. Sheep and goats show similar but much milder symptoms such as sudden acute lameness, unwillingness to move, a tendency to lie down, and vesicles on the hoof and the mouth. Infected swine display signs of acute lameness, fever, fatigue, constant squealing, and vesicles on the upper edges of the hoof, snout, nostrils, feet, coronary bands, interdigital spaces, udder, and tongue. In the rare case of human infection, symptoms may include fever, headache, malaise, excessive saliva, painful blisters in the oral cavity, and between fingers.

Differential diagnosis (DDx)

- Vesicular Stomatitis
- Bovine Mamilitis
- Bovine Viral Diarrhea
- Bovine Papular Stomatitis
- Mucosal disease (foot lesions)
- Infectious Bovine Rhinotracheitis
- Rinderpest
- Bluetongue (foot lesions)
- Peste des Petits Ruminants
- Foot Rot
- Chemical Irritants
- Swine Vesicular Disease
- Vesicular Exanthema (swine)

Laboratory Confirmation

Specimen types

Preferred

Tissue (epithelium from unruptured or freshly ruptured vesicles) or vesicular fluid

Acceptable, but not ideal

Blood

Oesophageal-pharyngeal fluid samples taken in probing cup (ruminants)

Throat swabs (pigs)

Myocardial tissue from fatal cases

Shipping/transport and storage

The International Air Transport Association (IATA) Dangerous Goods Regulations for requirements should be followed for packaging and shipment of diagnostic specimens by commercial means of transport as should any local or national regulations regarding shipment of clinical specimens or potentially hazardous materials.

Epithelial samples

Transport media consisting of phosphate buffer, tissue culture media, or phosphate-buffered saline (pH 7.2-7.6) with added antibiotics to inhibit bacterial growth. Keep refrigerated or on ice until received by the laboratory

Oseophageal-pharngeal (OP) fluid samples

Collect by probang cup or swab in transport media containing 0.08M phosphate buffer with 0.01% bovine albumin, 0.0002% phenol red, and antibiotics (1,000IU) and pH 7.2-7.6. Freeze immediately to -40C and transport on dry ice (solid carbon dioxide) or liquid nitrogen until received by the laboratory.

Testing

Virus	***Antibodies***
Virus Isolation	Virus neutralization
ELISA	Agar gel immunodiffusion
PCR	

Acceptable confirmation

Demonstration of FMD viral antigen or nucleic acid

Detection of virus-specific antibody

Detection of antibodies to viral nonstructural proteins (NSPs)

Not recommended due to biosafety and biosecurity considerations

Viral isolation

Methodology	***Turn Around Time (approximate under ideal conditions)***	***Acceptable Specimen Types***			
		Tissue	Vesicular Fluid	Probang Cup	Swab
Enzyme-linked immunosorbent assays (ELISA) Antigen	5hrs	X	X		
Complement fixation Antigen	3hrs	X	X		
Reverse Transcriptase Polymerase Chain Reaction (RT-PCR)	6hrs	X	X	X	X
Realtime PCR	2hrs	X	X	X	X
Virus isolation*	>7days	X	X	X	X

*requires a virus identification step following isolation to identify strain

Control Measures

- Vaccination
- Movement restrictions between FMD endemic and FMD free zones
- Stamping-out: slaughter of infected, recovered, and FMD susceptible contact animals
- Disinfection of premises and all infected material (implements, cars, clothing)
- Quarantine measures

Endemic regions

Quarantine

Vaccination

FMD-free regions

Rapid detection and stamping out of all animals within three kilometers of outbreak, burn carcasses

Distribution

Foot and mouth disease (FMD) is endemic in Asia, Africa, the Middle East, most of South America, and parts of Europe. There is a high prevalence throughout Africa (except in the African nations of Zimbabwe, Namibia, Botswana, and South Africa). Significant outbreaks have also occurred in the United Kingdom, Japan, Korea, Taiwan, and Egypt. FMDV is endemic in many South American nations, except for Chile, Uruguay, Argentina, Paraguay, and the southern states of Brazil. The World Organization for Animal Health (OIE) reports 61

countries are free of the virus. The United States is FMDV-free; all research occurs at the Plum Island Animal Disease Center.

Strain Information:

There are at least seven immunologically distinct types of FMDV: O, A, C, Asia 1, SAT1 (Southern African Territories), SAT2, and the SAT3. Within these, at least 60 various subtypes have been identified. There is little virulence information on most strains. The O type appears to be the most ubiquitous, causing most African outbreaks. In Asia, the O, A, and Asia-1 strains are endemic to India, China, Bangladesh, Myanmar, Thailand, Laos, and Cambodia. Outbreaks of types A and O occur sporadically in the Middle East, Turkey, Iran, Israel, Saudi Arabia, and Kuwait. In Spring 2012, an outbreak of a SAT strain was seen in the Middle East which does not typically vaccinate against SAT strains.

Agent Sources:

Infected bovines release high titers of virus in their saliva, nasal fluid, lachrymal fluid, vesicular fluid, milk, and even their breath. FMDVis also present in urine and feces, although at lower titers. Viral loads drop four to five days after the onset of clinical disease. Fomites can also be viable sources of virus.

Stability

FMDV is extremely stable in normal environmental conditions. The virus is most stable at 4°C at a neutral pH (it is very sensitive to basic or acidic pH), and under moist conditions. FMDV can remain active for 26 to 200 days in soil, on wood, hay, and straw for approximately 15 weeks, footwear and clothing up to 14 weeks, cow's hair for four to six weeks, and wool for about two weeks. Viable virus is capable of spreading at least 250 km over water and 60 km over land.

Laboratory Factors

US Select Agent; OIE Risk Group 4;

Relatively high volume of laboratory work/research (PubMed)

Many laboratories in Asia, the Middle East, Latin America, and Eastern Europe contain FMD isolates or clinical specimens containing.

Little is known about how many commercial culture collections may have the virus worldwide. There are many FMDV vaccine production facilities worldwide and many produce large volumes of inactivated virus vaccine.

General Growth Conditions

Conventional virus culturing protocols are typically used to isolate, purify, and propagate FMDV. Fluid specimens are diluted in buffered cell culture media. Epithelial specimens should be ground with a mortar and pestle then immersed in buffered media. The solution is next clarified by centrifugation and inoculated into monolayer cell cultures of swine kidney cells, calf kidney cells or BHK-21 cells. After inoculation, Eagle's Maintenance Medium is added. If FMDV is present, cytopathic effects can be seen with a microscope. When the cytopathic effect is most pronounced, the supernatant nutrient fluid can then be harvested, centrifuged, and stored. Numerous diagnostic tests (immunofluorescence, ELISA, PCR) have been developed to detect virus in clinical specimens and culture.

Risk of Disease Contraction

Disease transmission is extremely efficient between animals, and occurs by direct contact between animals or with contaminated fomites (shoes, clothing, tires, and equipment). Aerosols also often spread the disease rapidly.

FMD is technically considered a zoonotic disease. However, human infection is extremely rare: only 40 cases have been documented between 1921 and 1969. Even upon contraction, clinical symptoms are rarely seen. Laboratory acquired infections are also extremely rare.

Countermeasures (PPE and Medical):

In the United States and other places where the virus is not endemic, FMDV work is restricted to just a few highly secure locations. Infected animals should be kept in ABSL3 laboratories. Strict decontamination procedures should be adhered to. Basic PPE (gloves, laboratory coats) should be worn by staff.

Vaccines are available widely for animals, however vaccination against one subtype often does not necessarily protect against others, and immunity is short-term requiring additional vaccinations two to three times a year. Despite utilizing a multivalent vaccine tailored to the major circulating strains, effective vaccination can be quite difficult.

No vaccine or specific treatment is available in the event of human infection.

References

Aceto D, Astuto-Gribble L, and Gaudioso J. The Acquisition of Dangerous Biological Materials: Technical Fact Sheets to Assist Risk Assessments of 46 Potential BW agents. Sandia National Laboratories. Albuquerque, New Mexico 87185 and Livermore, California 94550. SAND2007-7496. Unlimited Release.

"Foot-and-mouth Disease: Introduction." *The Merck Veterinary Manual*. 2011. Merck Sharp & Dohme Corp., Whitehouse Station, NJ. Accessed online http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/51000.htm on 12 November 2012.

"Foot and mouth disease." *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2012.* Accessed online http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.05_FMD.pdf on 12 November 2012.

Foot-and-Mouth Disease. *Center for Infectious Disease Research and Policy (CIDRAP).* Accessed online http://www.cidrap.umn.edu/cidrap/content/biosecurity/ag-biosec/anim-disease/foot-mouth.html#_References on 14 November 2012.

Foot and Mouth Disease. *The Center for Food Security and Public Health, Iowa State University.* Accessed online http://www.cfsph.iastate.edu/Factsheets/pdfs/foot_and_mouth_disease.pdf on 13 November 2012.

Fact sheet- foot and mouth disease. Candaian Food Inspection Agency. Accessed online http://www.inspection.gc.ca/animals/terrestrial-animals/diseases/reportable/foot-and-mouth-disease/eng/1323993172781/1323993252010 on 14 November 2012.