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Foot-and-mouth disease: An overview

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Abstract
The highly contagious and debilitating Foot and Mouth disease in cloven-footed animals results in significant economic losses due to reduced animal productivity. The international market for animal products from countries with FMD infection is closed. The disease cannot be controlled only through vaccination. But implementing strict biosecurity measures, prophylactic measures and early treatment, along with continued surveillance, monitoring to curtail this disease, efforts are ways to bring the disease under control.

Keywords: Infection, prophylactic, monitoring

Introduction
FMD is one of the most important economic diseases of cloven-footed animals. It affects cattle, buffaloes, sheep, goats, pigs and many wildlife species. FMD does not have public health risk, but it has significant economic and international trade impacts.
The globalization of trade of animal products has made it obligatory to design integrated FMD control strategies to either eliminate or more effectively control FMD worldwide. The World Organization for Animal Health (OIE) classifies countries in 3 categories with regard to FMD i.e. FMD present with or without vaccination, FMD-free with vaccination, and FMD-free without vaccination (OIE, 2014) [9]. More than 100 countries are still affected by FMD worldwide. The disease is endemic in Asia, Africa and Middle East countries. Some developed countries have eradicated the disease e.g. Canada, The United States, and UK.

Etiology
The genus Aphthovirus, which belongs to the Picornaviridae family, is responsible for causing foot and mouth disease through the use of single-stranded positive sense RNA virus. With a diameter of approximately 25-30 nanometers, the virus forms an oval structure (Brooksby, 1958) [3]. A protein capsule that contains 60 copies of the capsomers surrounds the RNA genome in the virus. 4 structural polypeptides, specifically VP1, VC2, VF3, and V4, make up the 4 components of each capsomer. The genetic characterization of FMD virus strains, deducing evolutionary dynamics, and establishing epidemiological relationships among genetic lineages have relied on the use of VP1 coding region nucleotide sequences for tracking outbreak strain origins (Jamal *et al*., 2012) [7].
Seven serotypes of FMD virus are identified *viz*., A, C, O, Asia 1, SAT1, SAT2 and SAT3. Only four serotypes i.e. O, A, C and Asia 1 are recorded in India. According to the reports, about 85% of the outbreaks of FMD are caused by serotype O, about 8-10% by serotype A, and the rest due to Asia 1 in India. Serotype A has been found more active in North Eastern Hilly Regions of the country. Multiple subtypes occur within each serotype and at least 7 genotypes of serotype Asia 1 are known until now (Jamal *et al*., 2011) [6].

Transmission
The FMD virus can be spread through different means, such as close contact, animal-animal transmission, long-distance aerosol transmission (through fungi), or inanimate objects. The virus may infect feed, standing water, clothing and skin of animal handlers (such as coccyx or foxgloves), motor vehicles, and food supplements that contain infected animal products. Viruses are present in milk, semen and urine, and feces.

By smelling milk droplets, calves can contract an infection. How. Infection can also be transmitted through the sperm of infected bulls.

Some infected ruminants may remain unaffected and carry the virus for up to 3 years, even after showing no symptoms (Grubman and Baxt, 2004) [4]. Carrying can occur in both vaccinated and unvacuously treated animals (Stenfeldt, *et al*., 2016) [11]. Pigs cannot be carriers without exhibiting any symptoms (Stenfeldt *et al*., 2014) [14].

Humans are very rarely infected by foot-and-mouth disease virus (FMDV). Humans, specifically young children, can be affected by hand-foot-and-mouth disease (HFMDV), which is often confounded with FMDV. HFMDV is a viral infection caused by Coxsackie A virus belonging to the Enteroviruses within the Picornaviridae family, but it is distinct from FMDV (CDC, 2019).

Pathogenesis

The virus replicates in steps of Adsorption, Penetration, Uncoating, Viral transcription, Genome replication, Encapsidation and Maturation. Research has found that the lung or pharyngeal areas are the sites of initial virus replication with rapid dissemination of the virus to oral and pedal epithelial areas, possibly mediated by cells of monocyte/macrophage origin (Grubman and Baxt, 2004) [4].

Clinical Signs

The incubation period of foot and mouth disease is between 1 and 12 days. Common symptoms in cattle are fever that drops rapidly after two to three days, excessive salivation or frothy saliva, thirst, lip smacking, and blisters or blisters on the tongue, lips, diapers, teats, and feet. Sheep and pigs show similar symptoms, but they often do not speak. Blisters and blisters can be painful and cause loss of appetite and limping. Burst cysts can lead to further infection and sepsis.

FMD can cause myocarditis and death, especially in newborn animals (Artz *et al*., 2010) [1]. The mortality rate of older animals with FMD is low (2-5% mortality). However, this disease has negative effects such as weight loss, decreased milk production, lack of competition and causes the animal's ability to decrease.

Subclinical disease can be classified as new disease or persistent disease. Nowadays, subclinical disease (asymptomatic state) is a serious illness lasting 1 to 8 days. The infection is characterized by high levels of infection in the pharynx. In today's subclinical disease, the infection remains in the pharynx and does not cause sepsis; however, large amounts of bacteria are released through nasal secretions and saliva. Recently, subclinical disease occurs mostly in vaccinated animals, but can also occur in unvaccinated animals (Stenfeldt and Arzt, 2020) [12]. A persistent subclinical infection (carriage state) occurs when the animal recovers from a serious infection but only a small portion of the virus replicates in the pharynx.

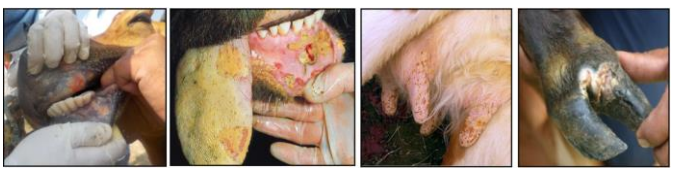

Fig 1: Blisters and vesicles on the gums, tongue, lips, dental pad, teats and feet of FMD affected cattle

Diagnosis

The disease is diagnosed based on its characteristic clinical signs. Differential diagnosis diseases in which similar signs can be seen are Vesicular Stomatitis, Swine Vesicular Disease, Vesicular Exanthema of Swine (Bachrach, 1968) [2].

Considering the rapidity of spread of FMD outbreak and its serious economic consequences, prompt, sensitive and precise laboratory diagnosis and identification of the serotype of the viruses involved in disease outbreaks is crucial. Determination of the serotype involved in field outbreaks gives clear interpretation for determining proper control and vaccination programs to be followed.

Various recent techniques have been used to diagnose the disease and to ascertain the serotype of the virus which includes Virus Neutralization Test (VNT), Enzyme linked immunosorbent assay (ELISA), Complement Fixation Test (CFT), Virus Isolation, Reverse transcription-polymerase chain reaction (RT-PCR), Reverse transcription loop-mediated isothermal amplification (RT-LAMP), Chromatographic strip test (Jamal and Belsham, 2013) [8].

Treatment

Even though the disease is self-limiting, the nature of the symptoms makes the animal prone to pain and sufferings. Inability to masticate makes the animal cachexic and generalized loss of appetite is observed. Treatments of these symptoms help in early recovery and in reduction of the associated losses and mortality.

1. Isolation of sick and affected animals.
2. Symptomatic treatment of affected animals as follows:
3. Broad spectrum antibiotics to check secondary bacterial infection e.g. Amoxicillin-Sulbactum, Ceftriaxone-Taxobactum, Ceftiofur, Enrofloxacin, etc.
4. Anti-inflammatory and anti-pyretic drugs e.g. Meloxicam, Flunixin, Tolfenamic acid, etc.
5. Rinsing mouth lesions 2 to 3 times per day with mild lotions e.g. 2% sodium bicarbonate solution, 2% alum lotion, 1-2% potassium permanganate solution.
6. Application of Boroglycerine over mouth lesions.
7. Foot bath at least twice a day with 4% potassium permanganate solution, 2% copper sulphate, Chlorhexidine solutions, etc. Dressing of foot lesions with boric acid, zinc oxide ointments.
8. Administration of parenteral or oral multivitamins.
9. Administration of intravenous fluid therapy in anorectic patients.
10. Provision of soft fodder and semi-solid to liquid diet.

Vaccination

1. Healthy animals above 3 weeks of age should be vaccinated.
2. Deworming 21 days prior of vaccination should be done.
3. Vaccination should be carried out during early morning or evening hours.
4. Maintenance of proper cold chain of vaccine should be strictly followed.
5. Separate needles and syringes should be used to avoid any cross infection.
6. Sick and affected animals should not be vaccinated.
7. In outbreak, ring vaccination with 5 to 10 kilometers of radius should be carried out.

Table 1: Vaccination Schedule

Species	Age of Primary Vaccination	Booster	Vaccination Interval	Dose and Route
Cattle, Buffalo	3 weeks and above	3 months after primary	Twice a year	3 ml S/C or I/M at mid- neck region or as per manufacturer's instructions
Sheep, Goat	4 months and above	-	Twice a year	1 ml S/C or I/M or as per manufacturer's instructions
Pig	4-8 weeks and above	3 weeks after primary	Twice a year	2 ml S/C or I/M or as per manufacturer's instructions

Table 2: Vaccines available in India

Trade Name	Manufacturer	Vaccine type	Contents
Raksha Ovac	Indian Immunologicals	Inactivated tissue culture FMD virus	Strains O, A, Asia 1 and subtype A22
Raksha FMD vaccine	BAIF/Hoechst	Polyvalent inactivated vaccine	Strains O, A, Asia 1 and subtype A22
Clovac FMD vaccine	Intervet India	Polyvalent inactivated vaccine	Strains O, A, Asia 1
FUTVAC	Brilliant Bio Pharma	Killed virus	Strains O, A, Asia 1

Prevention and Control

1. Strict isolation and quarantine of sick and affected animals.
2. Avoid direct introduction of newly purchased animal in flock. Follow quarantine.
3. Prohibition of common open pasture grazing, drinking water from common ponds.
4. Strict control over animal movement in affected and surrounding areas.
5. Prohibition of fair, exhibition and animal markets from 10 kilometer radius of affected area.
6. Through cleaning and disinfection of premises, equipments, animal holdings with disinfectants e.g. 1% formalin, 2% sodium hypochloride, 4% sodium carbonate, etc.
7. Usage of Personal Protective Equipments for treatment and sample collection of affected animals in an outbreak, and its proper disposal after use.
8. Following precautionary hygienic practices to avoid any further spread.
9. Restrict collection of bovine semen samples affected with FMD.
10. Tissue samples of suspected animals should be collected for laboratory examination before treatment and should be sent in 50% Glycerine Phosphate Buffer solution (Vesicular fluid, Foot lesions, mouth lesions) to Regional Diagnostic Laboratory.

National Animal Disease Control Program for FMD

Objectives of this Program are to control FMD by 2025 with vaccination and its eventual eradication by 2030. It is a Central Sector Scheme where 100% of funds shall be provided by the Central Government to the States and Union Territories for vaccinating the entire susceptible population of bovines, small ruminants and pigs at every six-monthly intervals.

Discussion and Conclusion

Although much information is available about FMD, its classes and vaccines, it still poses a threat to the global livestock industry.

Reasons for noncompliance with disease control include sending samples to the laboratory and defects in the samples. Like other RNA viruses, new strains of FMD continue to evolve and mutate, sometimes creating new strains that hinder vaccination and lead to massive spread.

In addition, vaccination only provides temporary protection that lasts from a few months to several years. One problem with FMD vaccination is the large variation between serotypes and even within serotypes. The foot-and-mouth disease vaccine should be specific to the disease in question. There is no cross-protection between serotypes, meaning that antibodies against one serotype do not protect against other serotypes. Additionally, the nucleotide sequence of genes derived from two different strains within a serotype can differ by up to 30%. Therefore, if the vaccine is to be used to prevent the disease, it is important to know the disease and change the vaccine accordingly (Jamal and Belsham, 2013) [8]. Injections alone cannot control the disease. Information obtained in the laboratory should be interpreted together with information regarding the infection. Early diagnosis and early intervention are needed to effectively control the spread of the disease. Publish information on foot and mouth disease in a timely manner, especially in border areas, share information in a timely manner, and implement simultaneous management to appropriately control foot and mouth disease. The availability of high-quality FMD vaccines with similar serotypes should be improved to ensure mass vaccination and protection of animals.

In summary, continuous monitoring, strict biosecurity, prophylactic measures, isolation and early treatment of affected animals may be helpful. Prevent this illness.

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