Foot and Mouth Disease (FMD): A Zoonotic Threat to Animal and Humans

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ABSTRACT

Foot and Mouth Disease (FMD) is a highly contagious ailment caused by a single-stranded RNA virus, belonging to the picornaviridae family. The virus exhibits seven distinct serotypes with multiple subtypes, affecting a wide range of animals, including cattle, buffalo, sheep, goats, pigs, and various wild ruminants. While FMD is endemic in several countries, it remains a concern for global livestock due to its economic impact and rapid transmission. This comprehensive review explores the historical context, etiology, epidemiology, geographical distribution, and transmission modes of FMD. The disease's impact extends beyond animals, affecting humans through zoonotic transmission. The primary site of infection is the pharynx mucosa, with subsequent spread through the lymphatic system, causing vesicles in the mouth, feet, muzzle, and teat. Various factors contribute to the swift global dissemination of FMD, including its contagious nature, genetic adaptability, diverse transmission pathways, and host range. The study delves into the specific characteristics of different FMDV serotypes, highlighting the prevalence of serotype O and its significant role in outbreaks. It also discusses the pathogenesis of FMD, emphasizing the viral replication process and host interactions. The zoonotic potential of FMD is acknowledged, with historical instances of human cases linked to close contact with infected animals. Geographically, FMD plagues numerous nations in Africa, southern Asia, and the Middle East, impacting the livestock environment. The disease's economic repercussions are staggering, with global losses estimated between 10-20 billion US dollars in endemic regions. The review provides a detailed analysis of the economic impact in various regions, emphasizing both direct and indirect losses. Diagnostic methods for FMD, including clinical diagnosis, laboratory procedures, and serological testing, are elucidated. The paper concludes with insights into the challenges of controlling FMD and the ongoing efforts to manage and prevent its outbreaks. Understanding the complexities of FMD is crucial for implementing effective control measures and safeguarding animal and human health on a global scale.

Keywords: animal, human. FMD, zoonosis, Epidemiology

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1. INTRODUCTION

Foot and mouth disease (FMD) is a swiftly spreading ailment with substantial economic consequences. The causative agent is a single-stranded RNA virus with a positive sense, classified within the picornaviridae family. This virus comprises seven distinct serotypes, each composed of multiple subtypes that exhibit unique antigenic and epidemiological characteristics. The spectrum of affected animals encompasses cattle, buffalo, sheep, goats, pigs, and wild ruminants (Alexandersen et al. 2005).

FMD is endemic in various countries; however, few countries remain FMD-free (Kohler et al. 2000). Tremendous economic damage to commercial cattle and buffalo farms suppresses the growth of livestock and its yielding (USDA et al. 2007). It is considered endemic in South Asian countries, inculcating serotypes O, A, and Asia 1 (Zahur et al. 2006; Tosh et al. 2002), and these serotypes are a consistent threat to these areas (Kesy et al. 2007).

Hand, foot, and mouth are other names for diseases that affect humans, and hoof-and-mouth disease is another name for the disease that affects animals with cloven hooves (Coetzer et al. 1994). FMD is a disease-causing concern for production losses worldwide because of its extensive host range and rapid aerosol transmission. The infection spreads through direct animal-to-animal contact, grub, lifeless things, and transport vehicles (Prempeh et al. 2001).

The primary site of infection is the pharynx mucosa, but the virus can also enter the body through wounds and the GIT. The virus then spreads through the lymphatic system, forming vesicles that burst within 48 hours in the mouth, feet, muzzle, and teat. Because it sheds in milk, FMDV can spread from one cow to another via raw milk. The Foot-and-Mouth Disease Virus (FMDV) can cause infection in sheep lasting around nine months, in goats lasting about four months, in cattle lasting approximately six months, and in individual African buffalo, the infection can endure for at least five years. This infection can persist within a herd for at least 24 years (Calkins et al. 2020). Morbidity may touch 100% in non-endemic regions. After recovery, animals grow immunity to the infectious strain. Young animals can die much more quickly than adults; adult mortality is typically less than one percent (Gibbens et al. 2001).

2. HISTORY OF FMD

Hieronymus Fracastorius was the first person to describe FMD in cattle in 1514. He had observed vesicles on the animals' feet and mouths and that the infected animals would not eat. In any case, Loeffler and Frosch's historical show that FMD was brought about by a filterable agent (virus) was the most vital move toward understanding the illness' pathogenesis. In 1898, FMD became the first disease that animals were infected with (Arzt Jonathan et al. 2011). However, the majority of advanced nations have eradicated this disease. Beginning in 1870 and culminating in 1914, the United States experienced nine significant outbreaks, the most devastating of which harmed 170,000 animals and cost approximately 4.5 million dollars in mitigation efforts. 442,000 animals were slaughtered in the UK in 1967 as a result of an outbreak of FMD. In 1997, FMD infected 100% of the pig population in Taiwan, killing 3.8 million pigs and causing 6.9 million dollars of damage. In 2001, the skillet Asia strain of FMD brought about approximately 2,000 cases to the UK (Paton et al. 2005).

In 2005, China and the Assembled Realm were infected with Asia-1, bringing about critical financial misfortunes. In 2011, Japan and Korea were tainted with serotype A in January and serotype O in April, with 3 million animals deceased, including cows and pigs. In Pakistan, FMD is a pervasive sickness with regular flare-ups. Type O is the most widely recognized serotype in Pakistan, with roughly 70% of cases; Asia-1 is about 25%, and type A is about 4% (Abubakar et al. 2012).

3. ETIOLOGY

The FMDV is categorized as a member of the Aphthovirus genus and is part of the Picornaviridae family. This viral species comprises seven well-defined serotypes: Asia 1, Asia O, Asia A, Asia C, SAT 1, SAT 2, and SAT 3. Notably, Serotype O is the most widely acknowledged on a global scale. It's worth noting that since 2004, there has been limited documentation of Serotype C isolation, rendering it uncommon. Although some FMDV serotypes are more diverse than others, there are 70 subtypes. The level of antigenic likeness between strains in a serotype impacts its protection from different strains (Abubakar et al. 2012).

4. EPIDEMIOLOGY AND TRANSMISSION OF FMD

According to the World Organization for Animal Health (WOAH), FMD is rapidly and extensively advancing across countries and can create significant societal and economic repercussions (Sansamuret et al. 2020). In FMD outbreaks, the most common control measures, including animal culling or vaccination and shipment restrictions, are implemented following the control policy and the infected area's landscape and population (Tsao et al. 2020).

Immunizations don’t safeguard among serotypes. FMD-free Countries either illegalize importing unvaccinated animal products against FMD or only allow it if additional risk-mitigating measures are taken. As a result, there are fewer opportunities for international trade (Kijazi Ahmed et al. 2021). Zoosanitary measures, often accompanied by vaccination campaigns, have successfully eliminated the disease from North America, Australia, Europe, and a significant part of South America (Paton et al. 2021).

5. GEOGRAPHICAL DISTRIBUTION OF FMD

FMD plagues numerous nations in Africa, southern Asia, and the Middle East. Infected animals make spreading the virus easy (Belsham et al. 2020). The disease has affected virtually every aspect of the environment where domesticated animals are kept. More than 100 countries are currently affected by FMD, and the spread of the disease typically reflects economic conditions (Dabasa et al. 2021).

Due primarily to the seven recognized serotypes, FMD weighs seven immunologically distinct diseases from an epidemiological and disease control perspective. Consequently, the immunity developed by animals against a specific FMDV serotype does not confer protection against other serotypes. Additionally, the level of immunity animals have against distinct strains within a serotype is contingent upon the similarity of their antigens. The rapid global dissemination of FMD can be attributed to its exceptional contagiousness, swift genetic adaptability, diverse transmission pathways (including direct contact, airborne transmission, and fomite transmission), and a broad spectrum of host affinities (Wubshet and Ashenafi, 2019).

The disease is anticipated to cause annual losses of between 10-20 billion US dollars in nations where it is prevalent (Belsham et al. 2020). As the new examination reports indicate, six FMD infection serotypes (O, A, Asia-1, SAT-1, -2, and 3) flow universally.

Serotype O is the most pervasive and answerable for roughly 70% of worldwide flare-ups (Samuel et al. 2001). Even though SAT 2 FMDV persisted long enough in Egypt, the SAT (Southern African Territories) serotypes are typically only found in sub-Saharan Africa. Most of the time, the scope of some of the serotypes is limited (Brito et al. 2017).

5.1. FMDV Type O

The most widely studied and prevalent FMD serotype worldwide. It contains eight topotypes.

5.2. FMDV Type A

The serological FMD virus subtype A is often acknowledged as the most varied antigens among the Eurasian serotypes. Recently, it has given rise to new antigenic variants, particularly in the western Asian region, where no cross-protection is observed between these variants.

5.3. FMDV Type SATs

The genetic diversity of FMDV Types SAT1 and SAT-2 differs markedly. SAT1 is characterized by eight distinct topotypes tightly confined to specific geographic regions. On the other hand, SAT-2 showcases a more extensive genetic diversity, encompassing 14 topotypes. Notably, South African variants exhibit significantly higher sequence diversity than those of serotype O. In contrast, SAT-3 displays a comparatively lower epidemiological presence on the continent and is infrequently identified in African bison populations (Wubshet et al. 2019).

5.4. TRANSMISSION

Infected animals can quickly and directly transmit FMDV to susceptible animals. Another critical method is indirect transmission through contaminated objects, animal products, or vapor (Gao et al. 2021). FMD can spread directly between animals or indirectly through fomites, and both can occur frequently over shorter distances (Tsao et al. 2020). However, aberrant strategies for transmission, for example, employing the airborne course, have been displayed to assume a significant part in the spread of the sickness. Because a particular set of factors needs to pave the way for airborne proliferation, airborne dissemination of FMD is considered a low-probability event with high consequences (Brown et al. 2022). Although most FMD outbreak transmission events occur locally, larger-scale transmission, such as animal shipments, has been crucial in spreading the infection to new locations and launching new local transmission chains. Catching different transmission sizes is a significant part of FMD reenactments (Tsao et al. 2020).
A prolonged, asymptomatic infection in ruminants and the virus's presence may occur in all infected animals' body secretions. The shedding of the virus is an essential factor in the transmission of FMD (Nawaz et al. 2019). Due to airborne spread, the virus poses a particular challenge for transmission from infected pigs, which exhale large quantities of the virus in their breath, to cattle, which are highly susceptible to infection by airborne virus but highly resistant to this route (Belshamet al. 2020).

6. MODES OF TRANSMISSION TO HUMANS AND ANIMALS

It is inevitable for living things to interact with one another. Even though it is necessary to give a typical advantage in interspecies connection for the progression of life, when the equilibrium is weakened, life is risked correspondingly (Bhabhor et al. 2020). Air, spit, milk, pee, dung, and the sperm of intensely contaminated creatures all contain FMDV (Calkins et al. 2020). Cows, bison, camels, goats, sheep, pigs, and deer all contain it. Abraded skin becomes infected when it comes into close contact with infected animals or their droppings. Animal hides may have been a source of viruses for some time. Blisters on the finger, the palm, the underside of the foot, or oral depression are symptoms of this mild illness in humans(Pal et al. 2013).

7. ANIMAL RESERVOIR AND HOST

Over 70 cloven-hoofed creatures, such as pigs, cattle, sheep, goats, and African buffaloes, can fall victim to the Foot-and-Mouth Disease Virus (FMDV), as it exhibits a wide range of hosts. The symptomatic

effects of FMD encompass fever, lameness, and vesicular lesions on the hooves, tongue, and teats. The livestock sector bears a significant brunt from FMD, as it restricts the international trade of animals and their byproducts. FMD virus can endure in sheep herds for up to nine months, goat herds for four months, cattle herds for six months, and individual African buffaloes for a minimum of five years, given that the infection persists within the group for at least 24 years (Calkins et al. 2020).

8. FMD PATHOGENESIS

Each virion particle is made up of a single strand of RNA that is about 8.5 kilobytes long. This is transformed into a solitary polypeptide and then separated into the underlying and non-primary infection proteins (Grubman et al. 2004). The infectious proteins are formed from the open reading frame (ORF), surrounded by the 5' and 3' untranslated regions. The ORF undergoes post-translational cleavage to yield ten non-structural proteins (Lpro, 2A, 2B, 2C, 3A, 3B1–3, and 3Dpol) and four structural proteins (VP1, VP2, VP3, and VP4). These proteins are produced as a single polyprotein and then divided. Interestingly, FMDV's 5'UTR is notably more extended than other Picornaviridae members. It contains various optional RNA sequences of different lengths and is covalently linked to the 5' end of the short peptide VPg (a structure found among the three VPg forms). At the 5'end, the S piece, running someplace in the scope of 350 and 380 nucleotides, occurs as an extended stem circle construction that contains essentially 4.5% of the whole FMDV genome and is fundamental for multiplication of the viral RNA is proposed (Kloc et al. 2017).
A series of interactions between the virus and the host constitutes the pathogenic mechanism of the virus. Depending on the virus and the host, different actions may be required. Notwithstanding, a general model that applies to most cases can be utilized to make sense of how the infection causes disease:

1. Access to a vulnerable host
2. Multiplication to increase the viral load
3. Spreading from the passage site to the tissues and target organs, promoting contamination and causing damage to cells and organs
4. Dumping, polluting, and spreading to the environment
5. The persistence of the environment
6. Starting a new cycle and spreading to new hosts (Finlay et al. 2006)

9. ENTRANCE AND REPLICATION OF VIRUS IN HOST CELL

The respiratory system is the main pathway through which the FMDV generally disseminates among animals. The virus gains access to the body through airborne particles discharged when animals cough or sneeze. This transmission is frequently observed in infected pigs, cattle, and sheep. Additionally, the virus has been detected in high concentrations in milk and fecal matter sprays, indicating their potential role in spreading the infection. In many species, the disease typically starts with few viral particles, except for pigs, which are more impervious to respiratory contamination than cows or sheep. Still, it is much more likely to get an infection in the mouth. Therefore, five to ten viral particles can infect cattle, sheep by fifteen to twenty, and swine by respiratory route require significantly more (Rodríguez-Habibe et al. 2020).
By binding to specific cell surface receptors, viruses enter host cells. The FMDV receptors that have been reported are the integrin receptor, the heparan sulfate (HS) receptor (Xin et al. 2015; Xin 2018), and the unidentified third receptor (Bai et al. 2019; Bao 2019). The chemical stripping and release of the virus's genome, which translocates through the endosome membrane to the cytosol, is initiated by the low pH of an endosome—6.0 to 5.5 pH for the late endosome and 6.5 to 6.0 pH for the early endosome. This translocation is cap-independent (Gutiérrez M et al. 2010; Torres et al. 2009). Infectious is the positive polarity of genomic RNA (gRNA), the messenger RNA (mRNA). The cytidine-rich poly(C) 5′ UTR region,

which is approximately 834 nucleotides long and contains the internal ribosome entry site (IRES), which binds directly to the ribosomes, follows the genome-associated viral protein (gVP) at the 5′ extreme. The ORF comes next (Rodríguez-Habibe et al. 2020).

While handling viral polyproteins, protein precursors are delivered through proteolytic cleavage: L proteinase (Lpro), the polypeptides P1, P2, and P3 (Gullberg M et al. 2017). While P1 is in charge of assembling the structural proteins VP1, VP2, VP3, and VP4 into the viral capsid, P2 is in charge of the three non-structural proteins 2A, 2B, and 2C, and P3 is in charge of the four non-structural proteins: 3A, 3B, 3C, and 3D (Xie et al. 2016).

After characteristic contamination, the infection begins to reproduce, generally in oropharyngeal cells. Primary ulcer sores, some of the vesicles that result from this, usually go unobserved (Alexandersen S et al. 2003). Following the initial replication, the virus infiltrates the bloodstream. Elevated body temperature and the animal's discomfort indicate the resultant viremia phase. Throughout this period, the Foot-and-Mouth Disease Virus (FMDV) undergoes further replication within reticuloendothelial cells and the parenchyma of specific target organs, such as the liver, spleen, bone marrow, and striated muscle. Subsequently, the viral presence returns to the epithelial cells within the nose, hooves, and mammary organs, culminating in the characteristic vesicles that define the disease's symptoms. The mechanism for transporting viral particles from the bloodstream to less vascularized epithelial regions remains undisclosed. It is plausible that this process is linked to the quantity of infectious particles introduced into the host or facilitated by the migration to infected macrophage tissue (Arzt et al. 2014).

10. ZOONOTIC POTENTIAL OF FMD IN THE WORLD

The World Organization for Animal Health (WOAH) has designated Foot-and-Mouth Disease (FMD) as a "notifiable condition." This disease is estimated to impact approximately 77% of the global livestock population, leading to substantial economic repercussions within the livestock sector. Recently, novel strains of the Foot-and-Mouth Disease Virus (FMDV) have consistently surfaced, giving rise to a persistent epidemic. The dynamic emergence of these new strains presents a formidable challenge in managing the causative pathogen, as it spreads rapidly and poses significant risks to global health, particularly in regions that have remained free from the disease (Santos et al. 2018; Mahapatra et al. 2018).

FMD rarely affects humans when it crosses species boundaries owing to the disease's high prevalence in animals, both in the past and in more recent global outbreaks, limiting human exposure. The last human case of foot and mouth disease reported in Britain was in 1966, during the final outbreak. However, all of the cases that have been reported involved close contact with infected animals; it is unclear when humans contract the disease (Prempeh et al. 2001).

10.1. ASIA

Among seven serotypes, only the O serotype poses a threat worldwide; perhaps, more than 80% of outbursts about the O serotype seem to occur in Southeast and East Asia. Chronologically, three strains of FMDV serotype O**:** O/CATHAY, O/SEA/Mya-98, and O/ME-SA/PanAsia remain. Southeast and East Asia have seen a rise in these lineages in recent years. An additional variant, O/MESA/Ind-2001, was initially detected and contained within the Indian subcontinent, leading to extensive outbreaks of foot-and-mouth disease (FMD). Epidemiology has been more difficult (Hemadri et al. 2002).

Since its discovery in 2013, this lineage has spread throughout the Middle East and North Africa. In 2015, O/ME-SA/Ind-2001 emerged in Myanmar, Vietnam, and the Lao People's Democratic Republic (Qiu et al. 2018). 2019 Cambodia, Pakistan, and Malaysia reported O/ME-SA/Ind-2001e (Jamal et al. 2021).

China possesses the most livestock of any Asian nation. However, the prevalence of FMD impedes economic growth significantly in several regions owing to the enormous animal population and frequent animal transport. China's national FMD reference laboratory was the first to identify the appearance of O/ME-SA/Ind-2001 in 2017. In China, cases of FMD have been reported since 1958. The advent of new subtypes makes FMDV epidemiology and control parameters more challenging. Between 2005 and 2021, China reported 175 FMD epidemics to the WOAH (Zhang et al. 2023).

10.2. AFRICA

Among seven known FMDV serotypes, five (O, A, SAT 1, SAT 2, and SAT 3) are available in Africa. Nonetheless, serotype C has only been reported a handful of times in the past 15 years, with the most recent confirmed outbursts appearing in Kenya and Brazil in 2004 (Rweyemamu et al. 2008). FMDV's genome is highly adaptable and rapidly evolves due to replication-related errors. By sequencing these viruses, we can precisely describe novel FMDV isolates and follow their origins and movements across international borders. Variants and serotypes vary widely worldwide (Samuel and Knowles 2001).
The intrusion of FMDV strains into other regions rather than their endemic pool is cause for grave concern due to the possibility of disease unfolding in previously unaffected areas (Vosloo et al. 2010). For instance, livestock mortality rates of up to 20% were reported following a recent incursion of SAT 2 into Egypt, which demonstrated the host's vulnerability to new strains (Ahmed et al. 2012).

11. FMD ACROSS THE BORDERS

FMD is known to be the most contagious virus, twenty times more virulent than Variola. Consequently, a single vaccine does not progress in controlling disease. Approximately 15 different FMD vaccines are produced worldwide, and the production and utility of whole live viruses are required. A brand-new molecular FMD vaccine that can be administered to cattle was recently granted a conditional license by the USDA.
The last outbreak of FMD in the United States occurred in 1929; Russia, the European Union, Australia, North and Central America, and New Zealand represent FMD-free countries. However, the rest of the world experiences it regularly. Despite being FMD-free countries, importing live animals and animal products that might contain the virus remains illegal. A world-leading, highly productive agribusiness built on these animal herds generates a significant portion of our GDP and exports abroad (Morse et al. 2017).

12. ECONOMIC IMPACTS

The global dairy industry produced more than 655 million tons of milk in 2014. This number is expected to rise by 23% between 2014 and 2025. However, numerous potentially perilous diseases, particularly FMD, prevent adequate milk yield (FAO 2017; Rushton 2009).
The FMD impact on the economy results in both direct and indirect losses. A loss due to death, vigor loss, milk production, and the value of livestock products are all examples of direct losses. The increased costs for vaccination, movement control, diagnostic and surveillance, and treatment of secondary bacterial infections in diseased herds are the causes of the indirect losses. Smallholder farmer's earnings deescalate with FMD's influence on productivity and food security, making its economic impact particularly significant (Alhaji et al. 2020). Table 1 shows the economic impact of FMD throughout the world.

13. DIAGNOSIS

The World Organization for Animal Health (OIE) Terrestrial Animal Health Code states that FMD requires a 14-day incubation period. It is said to take anywhere from one to twelve days for sheep to get sick, with

Table 1: FMD Economic Impact Worldwide.

Region	Economic impact per year (US$)	Reference
Endemic regions	11 B (90% range of6.5-21 B)	(Alhaji et al. 2020)
USA	1.5B	(Alhaji et al. 2020)
Africa	830M (17% global annual cost)	(Kerfua et al. 2023)
Bangladesh	1.5 M	(Giasuddin et al. 2020)
Pakistan	629 M	(Abubakar et al. 2022)
Indonesia	6.6 B	(FAO 2023)

the majority of infections showing up within two to eight days; two to fourteen days for cattle; also, typically for at least two days in pigs (with some trials reporting clinical signs within 18-24 hours). There have been reports of incubation times of four days for wild boars, two days for feral pigs, two to three days for elk, and two to fourteen days for Bactrian camels.

13.1. CLINICAL DIAGNOSIS

The extent of clinical symptoms is influenced by various factors, including the type of virus strain, the degree of exposure, the age and genetic makeup of the animal, the species of the host, and the host's immune response. Although fatalities are infrequent, they can occur among young animals due to causes like starvation or multifocal myocarditis. Secondary infections can slow recovery, but most adults recover in two to three weeks. Morbidity can reach 100%. Young calves, lambs, and piglets have higher mortality rates than adult animals, with a 1 to 5% mortality rate. Recovery typically takes about two weeks in straightforward cases.

13.2. CATTLE

- The severe clinical manifestations are commonly observed in highly productive dairy breeds in developed countries. These symptoms include shivering, anorexia, pyrexia, and a notable decline in milk production lasting for two to three days. Additional signs of the ailment include lip smacking, teeth clenching, drooling, impaired movement, or even kicking or stamping of the foot. These behaviors result from the development of vesicles (aphthae) on the mucous membranes within the oral and nasal regions, as well as between the claws of the animals. Furthermore, vesicles can also manifest on the mammary organs. As the condition progresses, approximately 24 hours later, the vesicles rupture, leading to the formation of erosions. Recovery from these symptoms typically takes place within 8 to 15 days.
- Complications associated with this ailment include erosions on the tongue, secondary infections of the lesions, deformities in the hooves, mastitis, and lasting impairment in milk production. These tongue erosions can also result in infertility, abortion, persistent weight loss, and a loss of thermoregulation, often referred to as "panters."Another consequence of this ailment is myocarditis, which can lead to the fatalities of young animals.

13.3. GOAT AND SHEEP

- Many infected animals can be asymptomatic or only have lesions at one location. Fever and mild to severe leg numbness are common symptoms.
- Vesicles are found in the coronary band and interdigital spaces on the feet, but they can rupture and be obscured by other foot lesions.
- Mouth lesions typically appear as shallow erosions and are rarely severe or noticeable.
- Pyrexia

- A characteristic of milking sheep and goats is agalactia. In some outbreaks, a significant number of ewes give birth.
- Young stock can die without showing any clinical signs.

13.4. PIG

- It may foster extreme foot injuries and weakness with the separation of the hook horn, mainly when housed on concrete.
- Vesicles frequently form along the carpus, the "knuckle," and other pressure points on the limbs.
- Dry tongue lesions and snout vesicular lesions are possible.
- Heart failure can cause sudden death in young pigs as young as 14 weeks; Piglets younger than eight weeks are especially vulnerable.

13.5. LESION

- Blisters or vesicles can manifest on various oral and facial areas, including the tongue, dental pad, gums, cheeks, hard and soft palate, lips, nostrils, muzzle, coronary bands, pig snout, udder, dewclaw corium, and interdigital regions.
- After death, erosions may appear on rumen pillars with gray or yellow streaks in the heart, stemming from myocardial degeneration and necrosis in young animals of all species; this condition is commonly referred to as "tiger heart."

14. DIFFERENTIAL DIAGNOSIS

- Vesicular stomatitis
- Swine vesicular disease
- Vesicular exanthema of swine
- The infection was caused by Seneca virus A, also known as Seneca Valley virus.

14.1. LABORATORY DIAGNOSIS

14.1.1. SAMPLES

- Fluid extracted from vesicles or epithelial tissue of unruptured or recently ruptured cysts.
- Epithelial specimens should be placed in a transport solution with a pH ranging from 7.2 to 7.6 and kept stable.
- In cases where epithelial samples are not attainable, ruminant blood and esophageal-pharyngeal fluid collected using a probang cup or swabs from the pig's throat can be utilized as an alternative viral source.
- Following collection, probang samples should be promptly refrigerated or frozen.
- For fatal cases, myocardial tissue or blood can be submitted; nevertheless, vesicle samples are once again the preferred choice if available.

15. METHODS

15.1. AGENT IDENTIFICATION

To establish a diagnosis, it is imperative to detect the presence of the live Foot-and-Mouth Disease (FMD) virus, FMD viral antigen, or FMDV nucleic acid.

A comprehensive bio-risk assessment should determine the appropriate containment level for laboratory procedures involving live FMD viral cultures or potentially contaminated materials, such as blood and tissue samples.

The reverse-transcription polymerase chain reaction (RT-PCR) is the initial diagnostic test to identify FMDV-specific nucleic acids in various sample types like epithelium, milk, and serum. Different RT-PCR formats include:

- Agarose gel-based RT-PCR
- Real-time RT-PCR
- Lineage-specific RT-PCR methods
- RT-PCR amplification for nucleotide sequencing

15.2. VIRUS INOCULATION

- Inoculation can be performed using primary pig, calf, lamb kidney cells, or primary bovine (calf) thyroid cells. Alternatively, susceptible cell lines such as BHK-21, LFBK-V6, and IB-RS 2 can be utilized.
- After reducing cytopathic effects, culture fluids can be subjected to complement fixation (CF), antigen ELISA, or RT-PCR tests.

Antigen Detection via ELISA:

- ELISA assays that rely on monoclonal antibodies or polyclonal antisera can effectively detect and classify FMD viral antigens.
- The complement fixation test, which is less sensitive and specific compared to ELISA, is influenced by multiple factors.

15.3. SEROLOGICAL TESTING

Serological tests for FMD serve several vital purposes:

1. Verification of individual animals before import/export (for trade)
2. Confirmation of suspected FMD cases
3. Estimation of infection prevalence or verification of absence
4. Demonstration of vaccine efficacy

- Virus Neutralization Test:

A quantitative VN micro-test for FMD antibodies uses IB-RS-2, BHK-21, lamb, or pig kidney cells in flat-bottomed tissue-culture grade microtitre plates.

- Solid-Phase Competition ELISA:

This method can identify antibodies against each of the seven FMDV serotypes. Peroxidase-conjugated monoclonal antibodies can be substituted for rabbit or guinea pig antisera to directly or indirectly detect antigens coated onto ELISA plates.

- Liquid-Phase Blocking ELISA:

Antigens are produced from specific FMDV strains cultured on BHK-21 cell monolayers.

- Non-Structural Protein Antibody Tests:

Enzyme-linked immunoelectrotransfer blot assay (EITB) formats, both indirect and competitive, are utilized for this purpose.

16. PREVENTION AND CONTROL

16.1. SANITARY PROPHYLAXIS

- Border surveillance and animal and product movement control for the protection of free zones

- Implementing the OIE-recommended methods for FMDV inactivation in animal-derived products
- Quarantine measures
- The killing of infected recovered and contact animals that are susceptible to FMD.
- Disinfection and cleaning of the premises as well as all infected objects like tools, automobiles, and clothing
- Removal of tainted creature items, bedding, and cadavers in the contaminated region

17. MEDICAL PROPHYLAXIS

17.1. INACTIVATED VACCINES

One or more chemically inactivated cell-culture-derived preparations of a seed virus strain are mixed with the appropriate adjuvants and excipients in traditional FMD vaccines. The potency of FMD vaccines can be categorized as either "standard" or "higher."

- Commercial vaccines of standard potency: formulated with enough antigen and the suitable adjuvant to have a minimum PD50 [50 percent protective dose] of 3

1. Provide immunity for six months following two one-month-apart initial vaccinations.
2. The antigenic relationship between vaccine and circulating strains is the basis for selection.
3. Many are multivalent to protect against prevalent circulating strains and provide extensive antigenic coverage.

- Vaccines with greater potency (emergency vaccines): formulated with enough antigen and the suitable adjuvant to have a minimum PD50 [50 percent protective dose] of 6

❖ Higher-potency vaccines are recommended in adolescent populations due to their rapid onset of protection and a more comprehensive range of immunity (Brown et al. 2008; WOAH 2018; WOAH 2019).

18. CONCLUSION

This article discusses the zoonotic effects of foot and mouth disease (FMD) on animals and humans and its economic and production repercussions. The illness predominantly targets cloven-hoofed creatures like cattle, pigs, sheep, goats, and wildlife. The livestock sector experiences substantial setbacks in production and finances due to FMD. Although the disease rarely leads to severe illness or fatalities in humans, there exists a potential for transmission to occur via direct interaction with infected animals or materials carrying the virus.

Preventing and controlling FMD requires stringent biosecurity measures, including vaccination, quarantine, and movement restrictions. Rapid detection and response are crucial to containing outbreaks and minimizing the risk of transmission to humans. Surveillance systems and international cooperation are vital in monitoring and managing the disease, as FMD can easily spread across borders through trade and animal movement. By implementing comprehensive control strategies, the risk of FMD transmission to animals and humans can be significantly reduced, safeguarding animal health, livelihoods, and public health.

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