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Comprehensive review of foot and mouth disease: Current insights, challenges and future perspectives

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Abstract
Foot and Mouth Disease (FMD) has been a longstanding concern for livestock industries worldwide, prompting the development of historical and contemporary control strategies. Historically, the approach involved mass culling and movement restrictions, while contemporary strategies emphasize vaccination campaigns, quarantine measures, surveillance, and global collaboration. Vaccination has proven successful in reducing clinical signs, yet challenges arise from the virus's genetic diversity. Quarantine and surveillance play pivotal roles in early detection and containment, with successes tempered by resource limitations and asymptomatic carriers. Biosecurity practices are crucial, but ensuring consistent compliance remains a challenge. Global collaboration through organizations like the World Organization for Animal Health enhances preparedness, yet disparities in capacities among nations persist. Despite successes, challenges in addressing FMD's genetic variability, trade considerations and consistent implementation of control measures highlight the ongoing need for research and a unified, global approach.

Keywords: Foot and mouth disease (FMD), livestock, control strategies, genetic diversity, asymptomatic carriers and veterinary epidemiology

Introduction

Explore the historical timeline of FMD outbreaks and their impact on livestock populations

The historical timeline of Foot and Mouth Disease (FMD) outbreaks is marked by recurring episodes that have had significant repercussions on livestock populations and agricultural economies. Here's an exploration of key events [1].

Global Surveillance Initiatives (20th Century)

The mid-20th century saw the establishment of global initiatives for FMD surveillance. Organizations like the World Organisation for Animal Health (OIE) became central in coordinating international efforts to monitor and control the disease (1). In 1979: The Global Commission for the Control of Foot-and-Mouth Disease (GCC-FMD) was formed. This international organization aimed to coordinate efforts to control FMD and facilitate information exchange among affected countries. 1980s: Differentiation of Infected and Vaccinated Animals (DIVA): The development of DIVA tests in the 1980s allowed for the differentiation between infected and vaccinated animals, improving disease surveillance and control strategies [2]. In 1996: Adoption of Molecular Techniques: The adoption of molecular techniques, including Polymerase Chain Reaction (PCR), became widespread in FMD research and diagnostics. These tools enhanced the accuracy and speed of FMDV detection. In 2007: FMD Vaccine Bank: The establishment of the FMD Vaccine Bank by OIE in 2007 aimed to ensure rapid access to vaccines during outbreaks, facilitating a more immediate response to control the spread of the disease [2].

Advancements in Diagnostics (21st Century)

The 21st century has witnessed continual advancements in diagnostic tools, including serological assays and molecular techniques. These tools have enhanced our ability to detect FMDV and monitor its evolution. In 2012: Global Roadmap for Improving Tools to Control FMD: The development of a global roadmap in 2012 outlined strategies for improving tools to control FMD, emphasizing the need for international collaboration and research investment. In 2020s: Integration of Genomic Approaches: Ongoing research in the 2020s is increasingly integrating genomics to understand FMDV evolution and transmission dynamics. This approach aids in tracking the spread of different viral strains and predicting potential outbreaks [3].

Global Eradication Goals

Recent decades have seen a shift toward global eradication goals. Efforts to eliminate FMD focus on vaccination, improved biosecurity measures, and international cooperation to prevent the re-introduction of the virus. These additional milestones highlight the ongoing efforts to refine our understanding of FMD and develop more effective strategies for disease prevention and control. International collaboration, technological advancements, and strategic planning are key elements in the continued fight against Foot and Mouth Disease. Present Day: FMD remains a significant concern, with sporadic outbreaks affecting different regions globally [4]. International collaborations and organizations work towards coordinated efforts in disease control and prevention. Throughout history, FMD outbreaks have shaped agricultural policies, trade relations, and livestock management practices. The lessons learned from each episode contribute to ongoing efforts to better understand, control, and eventually eradicate this highly contagious viral disease [5].

Foot and Mouth Disease Virus (FMDV): FMD is caused by FMDV, a highly contagious virus belonging to the Picornaviridae family and the Aphthovirus genus.

- **Virus Variability**

Serotypes: FMDV exhibits seven distinct serotypes (A, O, C, Asia 1, SAT 1, SAT 2, SAT 3), each with multiple subtypes. The variability of serotypes contributes to challenges in vaccine development and disease control.

- **Genetic Diversity**

RNA virus: FMDV is an RNA virus, characterized by high mutation rates. This genetic diversity allows the virus to evade host immune responses and contributes to the challenge of developing long-lasting immunity [6].

- **Viral Structure**

Capsid Proteins: The virus has a non-enveloped capsid composed of four structural proteins: VP1, VP2, VP3, and VP4. These proteins play crucial roles in viral attachment, entry, and replication.

- **Replication Cycle**

Attachment and Entry: FMDV attaches to host cells using specific receptors, leading to internalization and release of the viral RNA into the host cell cytoplasm.

Translation and Replication: The viral RNA serves as a template for protein synthesis and replication. Viral proteins are produced, and new viral particles are assembled [7].

- **Transmission**

Modes of Transmission: FMD is primarily transmitted through direct contact between infected and susceptible animals. Additionally, the virus can spread through contaminated fomites, aerosols, and possibly through vectors such as insects.

- **Host Range**

Susceptible Species: Cloven-hoofed animals, including cattle, pigs, sheep, and goats, are highly susceptible to FMD. While some wildlife species can be infected, they typically do not play a significant role in the disease's epidemiology.

- **Clinical Manifestations**

Variability in Severity: Clinical signs range from mild to severe, with fever, vesicular lesions on the feet and mouth, lameness, and decreased milk production. Some infected animals may become carriers without displaying clinical signs [8].

- **Persistent Asymptomatic Carriers**

Carrier State: In some cases, recovered animals can become persistent asymptomatic carriers, harboring the virus in their pharynx or digestive tract. These carriers can shed the virus, contributing to disease persistence.

Understanding the etiology and virology of FMD is crucial for developing effective control and prevention strategies. Ongoing research aims to uncover the intricacies of host-pathogen interactions, improve diagnostic tools, and develop vaccines that provide broad protection against the diverse serotypes and subtypes of FMDV [9,10].

Significant outbreaks of Foot and Mouth Disease (FMD) have had profound consequences on affected regions, impacting agriculture, economies, and trade. 1967-1968 United Kingdom Outbreak:

Consequences: The widespread outbreak resulted in the culling of millions of livestock, causing severe economic losses in the United Kingdom. The culling aimed to control the spread, but it had profound social and economic implications for farmers and the agricultural sector.

2001 United Kingdom Outbreak: This outbreak had a substantial economic impact, with extensive culling, trade restrictions, and disruptions to the tourism industry. The cost of control measures and compensation for affected farmers amounted to billions of pounds [11].

2007 FMD Outbreaks in Asia and Africa: Several countries in Asia and Africa experienced FMD outbreaks in 2007, leading to livestock losses, trade restrictions, and economic setbacks. Affected regions struggled with the need for mass culling and the subsequent challenges in rebuilding their livestock populations.

FMD Outbreaks in South America: Various South American countries, such as Argentina, Brazil, and Uruguay, have faced recurrent FMD outbreaks. The consequences include disruptions to meat exports, trade restrictions, and economic losses for the livestock industry.

Impacts on Developing Countries: FMD outbreaks in developing countries often result in significant setbacks for small-scale farmers who rely on livestock for their livelihoods. The loss of animals, restrictions on livestock movements, and trade limitations exacerbate food insecurity and economic challenges [12].

Global Trade Restrictions: FMD outbreaks trigger international trade restrictions on livestock and animal products from affected regions. These restrictions can persist even after the outbreak is controlled, affecting the affected country's ability to participate in global markets.

Economic Losses and Industry Disruption: The economic losses from FMD outbreaks extend beyond the immediate agricultural sector. Industries related to meat processing, transportation, and veterinary services may suffer, contributing to broader economic downturns in affected regions.

Impact on Tourism: Regions dependent on tourism may experience a decline in visitor numbers due to FMD outbreaks. The perception of disease risk can deter tourists, affecting hospitality, recreation, and related industries [13, 14].

Long-Term Consequences on Livestock Genetics: Culling during FMD outbreaks can lead to the loss of valuable livestock genetics. This has long-term implications for breeding programs, reducing genetic diversity and potentially affecting the resilience of livestock populations.

Social and Psychological Impact: FMD outbreaks have social and psychological consequences on affected communities. Farmers may face emotional distress due to the loss of their animals, and communities may endure social stigma related to disease outbreaks. Efforts to mitigate the consequences of FMD outbreaks involve rapid response measures, vaccination strategies, and international collaboration to establish zones free from the disease. Advances in surveillance, diagnostics, and vaccine technologies aim to reduce the impact of FMD on global agriculture and economies [15].

Spectrum of Animal Hosts Susceptible to FMD

Cloven-Hoofed Animals

Cattle: Cattle are highly susceptible to FMD and are often the most affected species during outbreaks. They can experience a wide range of clinical manifestations, from mild to severe.

Pigs: Pigs are also highly susceptible to FMD, and their role in the transmission of the virus is significant. They may exhibit more severe clinical signs compared to some other hosts.

Sheep and Goats: Sheep and goats can be infected with FMD, and although they generally experience milder clinical signs than cattle, they can still serve as reservoirs for the virus.

Wildlife: Deer, Bison, and Other Wild Species: Certain wild animals, particularly cloven-hoofed species like deer and bison, can be infected with FMD. While they may not show severe clinical signs, they can act as reservoirs and contribute to the persistence of the virus in certain regions [13, 14].

Factors Influencing Host Susceptibility

Species Variation: Genetic Factors: Genetic differences among species influence their susceptibility to FMD. Certain breeds or species may exhibit varying levels of resistance or susceptibility.

Immune Response: Variability in the immune response among species can impact the severity of clinical signs and the duration of viremia.

Age and Physiological Status

Young Animals: Calves and young animals are often more susceptible to severe forms of the disease. Maternally-derived immunity may provide some protection but wanes over time.

Pregnant Animals: Pregnant animals may experience more severe clinical signs, and FMD can have adverse effects on reproduction, including abortion [12].

Virus Strain and Serotype

Strain Variability: Different strains of FMDV may exhibit varying degrees of virulence, influencing the severity of clinical signs in different host species.

Serotype Specificity: The host's previous exposure to specific FMDV serotypes can influence susceptibility. Animals may develop immunity to a particular serotype, but they remain susceptible to other serotypes [1].

Variations in Clinical Outcomes

Subclinical Infections

Some infected animals, especially those with prior exposure or partial immunity, may not show overt clinical signs. However, they can still act as carriers and shed the virus.

Mild Clinical Signs

In many cases, infected animals may exhibit mild clinical signs, such as fever, decreased milk production, and the development of vesicular lesions on the feet and mouth.

Severe Clinical Manifestations

Severely affected animals may experience lameness, anorexia, and extensive vesicular lesions. These cases often result in economic losses due to reduced productivity and the need for culling [13].

Chronic Carriers

Some animals, particularly cattle, can become chronic carriers of FMDV. These carriers may show no clinical signs but continue to shed the virus, posing a risk for disease persistence.

Understanding the spectrum of susceptible hosts and the factors influencing susceptibility and clinical outcomes is crucial for implementing effective control measures, including vaccination strategies and biosecurity practices. Research in host-pathogen interactions continues to provide insights into the complexities of FMD dynamics in different animal species [16].

Modes of Transmission

Direct Contact

Animal-to-Animal Transmission: The primary mode of FMD transmission is direct contact between infected and susceptible animals. Close proximity facilitates the transfer of the virus through respiratory secretions, saliva, and lesions.

Fomites

Contaminated Objects: FMDV can survive on inanimate objects, such as feed troughs, equipment, vehicles, and clothing. These fomites serve as vehicles for transmission when they come into contact with susceptible animals.

Aerosols

Airborne Transmission: FMDV can be spread through the air as aerosolized particles. This mode of transmission is particularly relevant in areas with dense populations of infected animals, as respiratory secretions containing the virus can become aerosolized.

Environmental Factors Influencing Spread

Temperature and Humidity

Favorable Conditions: FMDV transmission is often more efficient in regions with moderate temperatures and high humidity. The virus can survive longer in cool, damp environments, enhancing its stability and potential for transmission.

Wind and Air Currents

Long-Distance Spread: Aerosolized particles containing FMDV can be carried over long distances by wind and air currents. This can contribute to the rapid spread of the virus between farms and regions.

Geography and Landscape

Topography Influence: The physical characteristics of the landscape, such as mountains, rivers, and natural barriers, can impact the movement of infected animals and contribute to the localized or widespread nature of outbreaks.

Livestock Movement

Trade and Animal Movements: The movement of livestock for trade, exhibitions, or grazing can facilitate the spread of FMD. Infected animals or carriers can introduce the virus to new areas, emphasizing the importance of control measures during transportation [15, 16].

Biosecurity Measures

Effectiveness of Controls: The implementation of biosecurity measures, includingh quarantine, disinfection, and restricted access to farms, plays a crucial role in limiting the spread of FMD. Effective biosecurity practices can mitigate the risk of fomite transmission.

Wildlife Reservoirs

Interaction with Wildlife: Certain wildlife species, such as deer and bison, can act as reservoirs for FMDV. Interactions between domestic livestock and wildlife can contribute to the persistence and spread of the virus.

Vector Involvement

Insects and Arthropods: While not the primary mode of transmission, certain insects and arthropods may play a role in FMDV transmission. These vectors can mechanically transfer the virus between animals.

Seasonal Patterns

Environmental Conditions: Seasonal variations, including changes in temperature and rainfall, can influence FMD dynamics. Outbreaks may exhibit seasonal patterns due to environmental factors affecting virus survival and transmission.

Understanding these modes of transmission and environmental influences is crucial for developing effective control strategies, including vaccination programs, biosecurity measures, and surveillance efforts to prevent and manage Foot and Mouth Disease outbreaks [17].

Current Understanding of Foot and Mouth Disease (FMD)

Recent Research Findings and Advancements

Genomic Studies

Recent research has focused on genomic studies to understand the diversity of FMDV strains and track their evolution. High-throughput sequencing has provided valuable insights into viral genetics, aiding in the development of more targeted vaccines.

Host-Pathogen Interactions

Advances in understanding host-pathogen interactions have uncovered the role of host factors in determining susceptibility to FMD and variations in clinical outcomes. This knowledge is vital for developing interventions that target specific host pathways.

Vaccine Development

New vaccine formulations and delivery methods have been explored to enhance efficacy and overcome challenges associated with existing vaccines. Innovative approaches, such as virus-like particles and vectored vaccines, show promise in inducing broader and longer-lasting immunity [15, 17].

Diagnostic Techniques

The development of rapid and sensitive diagnostic tools, including real-time PCR assays and serological tests, has improved early detection and surveillance capabilities. These tools contribute to more efficient control and containment strategies during outbreaks.

Evolving Trends in FMD Research

One Health Approach

Emphasis on a One Health approach, considering the interconnectedness of human, animal, and environmental health. Understanding the broader ecosystem and factors influencing disease transmission is gaining prominence in FMD research.

Data Integration and Modeling

Integration of epidemiological data with advanced modeling techniques allows for more accurate predictions of FMD spread. This trend enhances the ability to implement targeted control measures and allocate resources efficiently.

Global Collaboration

Increasing global collaboration in FMD research, facilitated by organizations such as the World Organisation for Animal Health (OIE) and international research consortia. Joint efforts aim to standardize protocols, share data, and address FMD on a global scale.

Challenges in the Current Understanding of FMD: Challenges and Limitations

Viral Diversity

The extensive diversity of FMDV strains and the continuous evolution of the virus pose challenges in developing vaccines that provide broad protection. Strain-specific immunity remains a limitation, and addressing this diversity is a key challenge.

Asymptomatic Carriers

The phenomenon of persistent asymptomatic carriers complicates control efforts. Identifying carriers and understanding the mechanisms that allow them to harbor the virus without exhibiting clinical signs is an ongoing challenge [13, 14].

Unresolved Questions

Immune Response Dynamics

Detailed understanding of the dynamics of the immune response to FMDV, including factors influencing the duration and strength of immunity, remains an area of active research.

Wildlife Reservoirs

The role of wildlife reservoirs, such as deer and bison, in FMD transmission is not fully elucidated. Research is needed to better understand the interactions between domestic livestock and wildlife.

Obstacles in Prevention, Diagnosis, and Treatment: Vaccination Coverage

Achieving sufficient vaccination coverage in susceptible populations is challenging, especially in resource-constrained regions. Factors such as vaccine accessibility, logistics, and public awareness contribute to these challenges.

Early Detection

Early detection of FMD cases remains crucial for effective control, but challenges persist in implementing rapid diagnostic tests in remote areas. Timely reporting and coordination are essential for swift responses.

Global Trade and Surveillance

Balancing the need for global trade with effective FMD surveillance presents obstacles. Striking a balance between trade facilitation and preventing the introduction of the virus to new regions is a complex challenge.

Treatment Limitations

There is no specific antiviral treatment for FMD, and management relies on supportive care. Developing effective antiviral therapies is a significant obstacle due to the high mutation rate of the virus and its diverse strains [13].

Historical and Contemporary Strategies for Controlling Foot and Mouth Disease (FMD)

Historical Strategies

Culling and Slaughter: Approach: In the past, widespread culling and slaughter of infected and susceptible animals were commonly employed to contain FMD outbreaks. This strategy faced ethical concerns, economic repercussions, and social resistance due to the large-scale destruction of livestock.

Movement Restrictions: Approach: Implementing strict movement restrictions on livestock to prevent the spread of FMD. Challenges: Enforcement of movement restrictions was challenging, especially in regions with significant livestock movements for trade or grazing. Contemporary Strategies: Vaccination Campaigns: Approach: Vaccination is a key component of contemporary FMD control strategies. Both emergency and routine vaccination campaigns aim to establish immunity in susceptible populations. Successes: Vaccination has proven effective in reducing clinical signs, lowering mortality rates, and minimizing economic losses. Ring vaccination around outbreak zones helps create a barrier of immune animals, preventing further spread. Matching vaccine strains to circulating FMDV strains is essential but challenging due to the virus's genetic diversity [10, 11].

The short duration of immunity and the need for frequent booster vaccinations pose logistical challenges.

Quarantine Measures

Approach: Rapid isolation and quarantine of infected premises and surrounding areas to prevent the spread of the virus.

Successes: Early implementation of quarantine measures can help contain outbreaks and limit the geographical spread of FMD.

Quarantine facilitates targeted control efforts, including culling and vaccination.

Identifying and isolating infected premises quickly is challenging, particularly in regions with large livestock populations. Adequate resources and infrastructure are necessary for effective quarantine enforcement [12].

Surveillance and Early Detection: Approach Establishing robust surveillance systems for early detection of FMD outbreaks. Early detection allows for prompt intervention, reducing the duration and scope of outbreaks. Advances in diagnostic techniques, such as real-time PCR and serological assays, enhance surveillance capabilities. Surveillance gaps in remote or resource-limited areas hinder early detection efforts. Asymptomatic carriers may complicate identification during routine surveillance.

Biosecurity Practices: Approach Implementing biosecurity measures to prevent introduction and spread of FMD, including strict hygiene protocols and controlled access to farms. Biosecurity measures help reduce the risk of FMD introduction and transmission. Public awareness campaigns promote adherence to biosecurity practices. Ensuring consistent compliance with biosecurity measures across diverse farming practices and cultural contexts is a challenge. Adequate resources and education are required for effective implementation [15].

Global Collaboration: Approach International collaboration through organizations like the World Organisation for Animal Health (OIE) for coordinated FMD control efforts. Information sharing and standardized guidelines improve global preparedness and response. Collaborative research enhances understanding of FMD dynamics and control measures. Varying capacities among countries for surveillance, diagnostics, and control can hinder collaborative efforts. Trade considerations may sometimes conflict with stringent control measures [12, 17].

Conclusion

Historical strategies for controlling FMD often relied on mass culling, while contemporary approaches emphasize vaccination, surveillance, and biosecurity. Successes in vaccination campaigns, quarantine measures, and global collaboration have been significant, but challenges persist in addressing the genetic diversity of FMDV, ensuring consistent biosecurity practices, and navigating international trade considerations. Ongoing research and a holistic, collaborative approach are essential for refining and adapting strategies to effectively control and eventually eradicate Foot and Mouth Disease.

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