



Foot-and-Mouth Disease: A Brief Review of the Etiologic Agent and the Disease Which It Causes

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Abstract

Foot-and-Mouth Disease Virus (FMDV) is the etiologic agent of Foot-and-Mouth Disease (FMD), which is a disease of cattle, swine, and other cloven-footed animals. FMD is characterized by the formation of vesicles on the tongue, nose, muzzle, and coronary bands of infected animals. The virus has several unique characteristics that enable it to cause one of the most economically devastating diseases in today's world. The ease by which it may be transmitted by contact and aerosol, combined with its enhanced ability to initiate infections, virtually ensures that most, if not all, animals in a herd will contract FMD. The long-term survival of FMDV in infected animals' tissues and organs, especially when refrigerated, offers an opportunity for its national and international transmission through the food chain. Multiple serotypes and numerous subtypes reduce the effectiveness and reliability of vaccines. The possible development of carriers in vaccinated animals and those that have recovered from FMD provide additional potential sources of new outbreaks. These features create a disease which can have a major economic impact on farmers and entire nations.

Introduction

As the recent outbreak in the United Kingdom and several countries in Western Europe have demonstrated, FMDV is probably the most feared livestock pathogen in the world because of its devastating effect

on cattle, swine, and other domesticated livestock animals which serve as economic pillars of many nations. The unique nature of the virus provides inherent difficulties in its control and eradication. FMDV can be easily and rapidly transmitted by aerosol and direct contact from animal to animal, as well as through mechanical transfer from contaminated environmental materials such as soil and feed. In addition, indirect contact with meat, milk, and hides from infected animals can further spread FMD. Furthermore, FMDV's wide host range, multiple serotypes which contribute to less than effective vaccination and physiologic effects on infected animals can cause economic devastation for farmers. The purpose of this communication is to briefly review the salient characteristics which create FMDV's feared reputation.

Viral Characteristics

Foot-and-Mouth Disease is caused by a small icosahedral RNA virus (picornavirus) with a diameter of 23 nm. The virus is classified in the genus Aphthovirus (from the Greek word *aptha*, meaning vesicles of the mouth) within the family Picornaviridae. Closely related viruses include the rhinoviruses, polio virus, and the coxsackie viruses. The viral capsid, consisting of approximately 69% of the virion mass, is composed of 60 copies each of 4 polypeptides (i.e., Viral Protein (VP)-1, VP-2, VP-3, VP-4). Subtype specific neutralization epitopes have been identified, among the four capsid proteins, primarily within VP-1.

Host Range

The virus can infect most cloven-footed animals including cattle, swine, sheep and goats, wild pigs, wild ruminants, hedgehogs, armadillos, rats, nutria, and grizzly bears. Human beings are not normally susceptible.

Geographical Distribution

At present, FMD does not exist in North America, Central America, Australia, New Zealand, and until recently, in most countries in Western Europe. The disease is enzootic in Africa, Asia, and most of South America.

Clinical Signs

Cattle and swine show clinical symptoms as early as 24 to 48 hours after infection by FMDV. High viral titers can be demonstrated at this time in the sera of infected animals. FMD is characterized by fever, shivering, drooling of saliva, and the formation of blisters or vesicles on the epithelium of the tongue, nose, coronary bands, and teats as a result of the replication of FMDV. The vesicles are packed with virus particles, as many as 10^8 per ml. Loss of epithelium is most pronounced on the upper dorsal surface of the tongue, and its desquamation leaves a raw red surface that bleeds easily. Most affected animals will recover within 2 weeks of the onset of symptoms. Secondary bacterial infections of desquamated tissues may delay recovery. The mortality rate for mature animals seldom exceeds 5%, but young animals may have mortality rates as high as 50%. The disease varies somewhat with the species of animals but in general is similar to that of cattle and swine.

Serotypes

FMDV is readily neutralized by antibodies in suckling mouse and cell culture assays. These antibodies are considered the major component of the immunologic defense against the virus. Based on cross serum neutralization tests, FMDV may be classified into seven major serotypes (Types A, O, C, Asia 1, SAT 1-3) and 60 or more subtypes.

Vaccines

Inactivated vaccines for each of FMDV's major serotypes, as well as multivalent vaccines (e.g., to types A, O, and C) are available. However, vaccines to one major serotype do not cross-protect animals against infections caused by any of the other serotypes. In addition, vaccines produced with one subtype of a major serotype of FMDV may not provide complete protection against infections caused by one or more of the other subtypes of the same serotype. Furthermore, currently available vaccines stimulate the production of antibodies indistinguishable from those produced by infected animals in response to live virus. Thus, vaccination makes it impossible to tell which animals are infected and which are protected. Finally, vaccinated animals may also serve as carriers for several months after being exposed to infected animals. Some countries (e.g., United States, Western Europe) have chosen not to vaccinate because of the cost, logistics of the vaccination process, the carrier state, problems of differentiating vaccinated from infected animals, and reliability problems associated with the vaccines.

Transmissibility

One of the outstanding characteristics of FMDV is its transmissibility. The virus has the unique characteristic of replicating in the nasopharynx and epithelium of the tongue, nose, muzzle, and coronary bands of livestock animals. The coronary bands are located at the junction of the hoofs and skin of livestock animals. It is the replication of FMDV at these sites that leads to the name of the disease, Foot-and-Mouth Disease.

Replication of the virus in the epithelium at these sites causes the formation of blisters or vesicles which are packed with FMDV particles. As the blisters erode, vesicular fluid containing high concentrations of viral particles contaminates the local environment including soil, and grass. Humans may serve as passive vectors of transmission by carrying the virus on their clothes, shoes, tools, etc., to distant locations.

Infected animals can also transmit FMDV by exhaling virus particles from their lungs and nasopharynx into the atmosphere. Swine are particularly potent amplifiers of the virus and can release huge amounts of

virus into the atmosphere through exhaled air. Under appropriate conditions, FMDV can be carried considerable distances by the winds to infect additional animals. The 1981 FMD outbreak in the United Kingdom, which occurred on the Isle of Wight in the English Channel, is believed to have resulted from the airborne spread of the virus from Brittany in Northern France. Because of the high transmissibility of FMD by both the aerosol and contact routes, it is likely that if one bovine or swine in a herd is infected, most, if not all, other animals will be infected within a relatively short period of time.

FMDV may persist in tissues of dead animals for considerable periods of time (e.g., upwards of several months in the refrigerated internal organs, green unsalted hides, bone marrow, lymph nodes, and residual blood). Any product or by-product of infected animals can contain viable viral particles capable of infecting livestock in the country of origin or in countries which have imported these products. In 1967, the spread of FMDV in England resulted from the consumption of infected meat scraps by pigs. It is likely that the current outbreak of FMD in the United Kingdom originated in a similar fashion.

The Carrier State

Cattle, and perhaps other susceptible animals, that have recovered from FMD may carry the viable viral particles in their esophageal-pharyngeal fluid for 4 to 24 months post infection. Vaccinated animals exposed to FMDV have also been shown to be able to serve as carriers. Although vaccination does not prevent the carrier state, it does appear to reduce the spread of the virus among cattle. Laboratory studies have not documented the transmission of FMDV from carrier to susceptible animals, but carriers nevertheless remain a potential vehicle for transmission under field conditions.

Economic Consequences

As the vesicles on the tongue erode, it becomes painful for the infected animal to eat or drink and the animal begins to salivate excessively. Similarly, erosion of the vesicles on the feet makes it difficult for animals to walk as they begin to demonstrate lameness. Thus,

infected cattle may lose up to 30% of their body weight in a week or two because of difficulty eating, drinking, and walking to food. In dairy cattle, vesicular lesions can also occur on the teats and udder, sometimes leading to secondary bacterial mastitis.

While the vesicles heal in a week or two, the severe loss in body weight of meat cattle can become an economic disaster as the farmer's profit margins are dependent upon the weight of the animals when presented at market. In addition, dairy farmers may also suffer a significant economic impact through decreased milk production of infected animals.

Laboratory Containment

Laboratory work with FMDV in the United States is restricted by law to an island separate from the mainland. Since 1954, work with FMDV, as well as a number of other exotic animal disease agents, has been confined to the United States Department of Agriculture's Plum Island Animal Disease Center (PIADC), located off the eastern tip of Long Island, New York. At PIADC all work is carried out in enhanced BSL-3 laboratory and animal facilities. Enhancements include passage of exhaust air through HEPA filters, heat inactivation of all liquid wastes, incineration of animal tissues and carcasses, and decontamination of all other materials leaving the containment facilities by steam under pressure, ethylene oxide, formaldehyde gas, and other suitable disinfectants. Further enhancements include mandatory change clothes in/shower out requirements for all personnel and mandatory quarantine of all personnel and visitors from contact with cloven-footed animals for seven days after leaving the island.

Conclusion

Because of the high transmissibility of FMDV from both animals and animal products, disease-free countries will not import animals or their products from countries undergoing an outbreak for at least 6 months after the termination of the outbreak. The economic consequences of these actions could well be the loss of hundreds of millions, perhaps billions, of dollars in revenues for the exporting nation. The national programs which must be instituted to control the transmis-

sion of FMDV (e.g., destruction of herds in which there is even one infected animal, disinfection and quarantine of farm premises, and implementation of import restrictions by other nations for animals and animal products from the affected nation) will further impact the outbreak nation's economy. Finally, there is the compensation that must be paid to affected farmers. The recent outbreak in the United Kingdom serves to remind us of the fearsome nature of the virus and the disease which it causes.

Reference

Committee on Foreign Animal Diseases of the United States Animal Health Association. *Foreign animal diseases: Their prevention, diagnosis and control*. United States Animal Health Association: Richmond, VA.

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