Dissemination of Foot-and-Mouth Disease Virus Through Animal Products

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Before commercial aircraft, and especially in the pre-jet age, movements of livestock and animal products from one country to another were not only less frequent and less voluminous, but also much slower. The days or weeks required for the animals to be shipped or driven to their destination served as an effective quarantine period during which those animals showing signs of disease could be disposed of or their entry into a country prevented. Today, because of the demand for animal protein and breeding stock, coupled with modern methods of international transportation, the volume of trade in livestock and animal products has dramatically increased. At the same time, more rapid movement of such products has severely limited or even eliminated some of the natural barriers that formerly helped to keep down the importation of diseases. Increasing population of people and animals, along with the greater mobility of both, have enhanced the chances for rapid spread of animal diseases among continents and countries.[1]

Traditionally, meat and livestock products have been produced principally for domestic markets. It has been estimated that only about 5 percent of the world's supply of carcass meat enters the international trade. There are, however, wide varieties of meat products and by-products such as hides, glands, casein, etc., on the international market. Any and all of them, when they originate in a country having an animal disease that does not exist in the importing country, could serve as a means of introducing the disease into the latter.[2] The disease agent may be carried in a product from an infected animal (primary contamination) or, in the case of processed items, contamination could even occur after processing (secondary contamination).

The South American countries currently contribute about 40 percent of the world's supply of meat for export purposes. The chief difficulties in the meat are caused by restrictions imposed by the importing countries to guard consumers against the public health risk and to protect their livestock industry from both animal diseases and the economical effects of such diseases. Countries that are beef exporters are finding that cattle diseases are difficult and expensive to eradicate, although the need to do so is clearly recognized. Many countries have considerable exporting potential, a negative national trade balance, large areas of grazing land, and ranchers who traditionally would raise cattle; however, the development of beef exports in some countries is drastically impeded by endemic animal diseases.[2] The result is that a major national resource cannot be utilized on a national economic scale.

In many respects, those of us in the Americas are fortunate. We have a large percentage of the protein-producing farm animals of the world and a ratio of food animals to human population which is among the highest in the world. In the Americas there is a lower incidence of some of the infectious animal diseases that are a major problem in certain other areas of the world. Moreover, and of major importance, there are many animal diseases that we do not have in the Americas, and these are the diseases that we must all guard against importing. Protective procedures at the borders of a given country are no longer enough. The problem must be faced on a continent or even on a hemispheric basis. We must be concerned with what our neighbors are doing to control the diseases that they have. These diseases can no longer be regarded as exotic curiosities. Many of these infectious diseases can literally cross the border within hours,[1] and in the case of arthropod-borne diseases, there are no borders other than seas around a continent or natural temperature zones.

The principal topic with which this paper deals is the problem of FMD in the Americas with particular reference to its transportation via animals and animal products. An examination of the pathogenesis of FMD is in order before an evaluation of the risk caused by products from infected animals can be made. In brief, the animal inhales or ingests the virus; the cells of the oropharynx are infected; the virus replicates in the epithelium; and spreads throughout the upper respiratory tract and pharynx. From this region, the virus spreads to the lymph and blood systems. This is then followed by infection of tissue cells at the sites of predilection where gross lesion development occurs for the first time. The virus at this stage, for practical purposes, is present in all body fluids. The animal has a fever and anorexia and has observable oral, nasal, and foot vesicles. The animal salivates; there is a nasal discharge; and usually lameness. This stage of the infection is followed by rupture of the vesicles, increased clinical signs of the disease, termination of fever and viremia, and the appearance of detectable serum antibody. Then there is a decline of virus in certain tissues and fluids, healing of lesions, and resumption of eating. Healing is complete in 2 to 4 weeks, with clinical recovery,[3]

but there may be continued presence of virus in the pharynx with slow viral replication which results in the carrier state. The percentage of animals that become carriers varies with the species and virus strain.

Studies of carrier animals have shown that the oesophageal-pharynegeal (OP) fluids and respiratory aerosols from FMD-infected animals may contain virus before, during, and after appearance of clinical signs of the disease. Thus, normal appearing animals in the prodromal stage, that have recovered from clinical infection or were vaccinated for FMD and then came into contact with the virus, may harbor the virus in their pharynx for variable periods of time. This may vary from 6 to as long as 24 months in cattle, and about 4 to 6 months in sheep and goats, but only for days or during the clinical stage of the disease in swine. Thus far, the full role of the carrier animal in the spread of FMDV has not been fully explored or explained. There is circumstantial evidence that such animals may, in fact, be responsible for spread of the infection. However, this has never been experimentally demonstrated.[3] Fortunately, there are tests available to determine when animals have been infected, and there are also tests available to detect carriers. The value of the test result is, however, only as good as the validity of the test and the technical competence of the laboratory.

The presence of FMD in some countries is a serious, if not complete, obstacle to its exportation of animals and animal by-products to many importing countries. Certain of these products, because of the industrial processing that they receive, are rendered free of infective virus. Other products that in the past may have been accepted by countries free of the disease, may subsequently be banned because of the acquisition of new knowledge which indicates risks in their importation.

The conditions under which the virus of FMD survives in animal tissues have long been matters of fundamental interest to all officials concerned with the prevention and control of the disease. These conditions have been studied extensively in many countries--those which import as well as those which export animal products, especially meat. As a result of such studies, a mass of information has been accumulated.

The virus, as detailed above, becomes distributed throughout the body of the infected animal and can be found in different concentrations for varying periods in the tissues, secretions, and excretions. After death of the animal, the persistence of virus is dependent on the stage of the disease at time of slaughter, on the characteristics of the strain of virus, and on environmental factors such as temperature and hydrogen ion concentration. The available evidence shows that the virus of FMD in skeletal muscle is inactivated within 3 days after slaughter due to reduced pH. In contrast, the virus may survive for weeks or months in refrigerated internal organs, bone marrow, lymph and hemal nodes, glands, and residual blood.[4]

It has been conclusively shown that the period of cure and storage reduces the likelihood of virus recovery from lymph nodes of cattle. Virus may be recovered from fresh lymph nodes of even vaccinated animals. The presence of antibody in the tissues of vaccinated cattle seems to be an important factor in the elimination of infectious virus. In meat from infected animals, we can rely heavily upon nature to inactivate the virus, for nature has provided an effective mechanism for inactivation of the virus in muscle. Unfortunately, the problem does not end at this point. Boned meat, as customarily prepared, also contains lymph nodes and large blood vessels. Muscles taken from the vertebrae may be particularly contaminated with bone because they are near the point where the carcass is split. Lymph nodes, large blood clots, and bone marrow are well buffered. They seem to provide physical and chemical barriers that prevent lactic acid and other substances from penetrating and inactivating the virus. It has been conclusively shown that meat derived from animals infected with FMD is not rendered free of the virus by usual commercial procedures of ripening, boning, salting, and storage even if the muscle itself is free due to the other tissues present.[5]

Milk

As indicated above, cattle infected with FMD shed the virus through various pathways. This includes mammillary secretions. As a result, milk and milk products from infected animals are of special concern to animal health authorities. During the 1967-68 outbreak of FMD in Great Britain, observations were made on the involvement of the milk in the spread of the virus. Samples of milk taken from milk collection trucks were shown to contain virus, even milk taken from premises where the disease had not been diagnosed, and from milk on store shelves. This observation led to a study which demonstrated the presence of high concentrations of virus in milk from infected cows, before clinical disease was observed. In addition, the virus may persist in mammary tissue of convalescent cows.[6]

The inactivation of FMDV in milk has been studied by various workers. This includes milk to which virus is added and milk from infected animals. FMDV in milk from infected animals may be extracellular by Pastuerization, 72°C for 15 seconds; however, there is a small fraction which persists. This resistant fraction is also not inactivated by evaporation, the production of casein or caseinate, or the production of some cheeses. In some instances, as in the case of cheeses, they have been shown to contain virus immediately after production, but virus can no longer be domonstrated after 30 days storage of the cheese. In studies in the Soviet Union, workers found that FMDV can be inactivated at a temperature of 90°C for 3 minutes. Other workers have reported inactivation of virus in milk heated at 72°C for 20 minutes. These differing results may relate to whether the virus is intracellular or extracellular, the virus strain, and perhaps more importantly, the sensitivity of the

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medium which is used to test for surviving virus. Some workers have found that the milk is the bovine itself. With the bovine as the test or detection host, the heat treated milk or milk product is inoculated intradermally into the tongue and/or large test quantities may be inoculated intramuscularly.[7]

In further studies, it has been shown that milk from FMD-infected cattle containing up to 10^6 infectious doses of FMDV per ml can be sterilized and the virus rendered noninfectious for cattle by ultra high temperature (UHT) processing. Temperatures of 148°C for not less than 2 ½ seconds are required to assure sterility. UHT processed milk can be used for all diary by-products except culture or fermentation derived producst such as cheeses. The reason for this is that the coagulability of UHT-treated milk is poor. Dairy processing investigators feel that it is only a matter of adjusting the starting culture and fermentation conditions, and these products may then also be made from UHT-treated milk. However, such products have not yet been produced, and additional production research is needed in this area. Milk sterilized by UHT processing can then be put through regular commercial channels. Treatment of milk containing FMDV by these processes has at least three advantages in that it renders the milk noninfectious, provides a means of disposing of it, and salvages the milk as human food.[8]

Semen

As early as 1914, it was reported that cattle might carry FMDV in their reproductive organs. French workers showed that cattle urine may be infectious before clinical signs of FMD appear.

Grunnert, cited by Callis,[9] found FMDV in the semen of infected bulls 2, but not 3, days after infection and not in the semen of 10 bulls which had been vaccinated against FMD. In a study in Brazil, DeNetto examined semen from 22 bulls taken randomly from semen destined for artificial insemination and found FMDV in 7 of the 22 samples. He concluded that semen could be one of the means whereby FMDV was spreading in Brazil.[10]

Semen from bulls experimentally infected with FMD and subsequent transmission of the disease by artificial insemination has been studied at PIADC. In this study, FMDV was shown to occur in the semen of 2 bulls as early as 12 hours after inoculation and in all cases before the appearance of clinical disease. The virus was found in 58 of 71 semen samples from 16 bulls for as long as 10 days. The highest titer in semen was $10^{5.8}$ mouse LD_{50} per ml. Five of the 16 heifers artificially inseminated with FMDV added to various diluents also developed FMD. It was concluded from these studies that semen of bulls contains FMDV prior to signs of illness and that the disease could be transmitted by artificial insemination.[11]

It is known that FMD-vaccinated cattle may be carriers of FMD after contact exposure to FMD-infected cattle. It was not known if vaccinated and exposed bulls also would have infectious virus in their semen. To determine this point, Cottral *et al.* exposed groups of vaccinated and non-vaccinated bulls to the FMD-infected cattle for a week. Severe signs of FMD developed in all 7 of the nonvaccinacted bulls. They had FMDV in their throat fluids 4 to 10 days after contact exposure, and 4 of 7 were carriers for 56 days. FMDV was found in the semen of one of the 7 nonvaccinated bulls 14 days after exposure and intermittently in another for 42 days. Two of the 9 vaccinated bulls failed to become carriers of FMD while 5 of the 9 remained carriers for 56 days. Virus was found in the semen 7 days after exposure in one of the 9 vaccinated bulls. Thus, vaccination does not solve the problem.

Using the information available on the FMD carrier animal, tests for antibody in serum from donor bulls and tests of a portion of each ejaculate, it has been possible to design procedures whereby bovine semen has been imported into the United States from countries where FMD is endemic. Such a regulation was issued in 1964, and in the intervening years more than 1,700,000 doses of semen were imported into the USA from FMD-infected countries. The test procedures, which include examination of (1) history of the donor animal on the farm of origin; (2) the animal for evidence of the disease; (3) serum from the animal for antibody; (4) OP sample for virus; and (5) semen collected over a 60-day period for virus, have been proven to be safe steps to allow for the importation of bovine semen. **The procedures are laborious; however, the end result more than justifies the expense. It is vital to point out that a final determination for release of the imported semen is not based on any single factor such as animal history, observation, or test result, but that all conditions or steps prescribed in the regulation and detailed above must be satisfactorily met before an importation is made.[9]**

In summary, any and all products from animals infected with FMD may be possible sources of the virus and a means whereby the disease can be transported from one country to another. Some animal products may be imported; however, the procedures which are followed must be exacting, based on sound knowledge about the product and closely controlled. One means of handling these materials is to permit their entry only under special conditions which provide for transport, quarantine, and processing, all of which must be under official supervision and which must be done in such a way to assure that the processing inactivates the virus and that the virus does not escape by way of a by-product of the manufacturing process.

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Role Of Wildlife In Exotic Diseases

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According to a relatively recent U.S. Department of Agriculture (USDA) Report, on January 1, 1977, there were 122,896,090 head of cattle in the United States. On that day, the cash farm value of all cattle and calves in this country was approximately $35.5 billion. At present, the total cash farm value of major forms of domestic livestock and poultry in the United States is between $45-50 billion.

For comparative purposes, according to data compiled by the Wildlife Management Institute in Washington, D.C., in 1977 the combined hunting expenditure, table meat, and aesthetic value of white-tailed deer in the United States was appraised at approximately $8.2 billion per annum.

In considering these three factors, the monetary value placed on white-tailed deer alone in this country is in excess of $20 billion. This is more than half the cash farm value of all cattle and calves in the United States, or almost two times the cash farm value of all the hogs and pigs or chickens and turkeys in this country.

Of an ultra-conservatively estimated population of 12.7 million white-tailed deer in the United States, a price tag of $1,657 thereby is placed on each animal. The estimated population of one million white-tailed deer in the State of Alabama, for example, has a monetary value equivalent to three items of all the sheep and lambs in the United States.

The few examples that have been cited relate to white-tailed deer only. This merely reflects a "tip of the proverbial iceberg" that comprises the wildlife resources of this nation.

According to the "1975 National Survey of Hunting, Fishing and Wildlife-Associated Recreation," released in 1977 by the U.S. Fish and Wildlife Service, in 1975 there were 20.6 million recreational hunters; 53.6 million recreational fishermen; 15 million wildlife photographers; and 49.3 million wildlife observers.

According to this report, 20.6 million hunters participated in 478.6 million days of hunting. They spend $5.8 billion for hunting activities, but valued those activities at $84.9 billion per year.

In considering the major form of outdoor recreation, 53.9 million fishermen participated in more that 1.3 billion days of fishing. They spent $15.2 billion fishing, but valued those activities at $154.5 billion per year.

The 1975 Survey, compared to the 1970 Survey, shows that hunting and fishing have grown considerably as recreational activities. The number of reported hunters increased about 44 percent during the five-year period, and the number of recreation days spent hunting more than doubled. The number of fishermen increased 62 percent during the five-year period, and the number of recreation days spent fishing almost doubled.

Another interesting aspect of the 1975 Survey was that approximately 50 percent of the ranks of wildlife observers and photographers was comprised of hunters and fishermen. These figures show that sportsmen value wildlife in a much broader context than for just hunting and fishing.

It has been conservatively stated that, "Sportsmen spend enough money each year to purchase all the baseball and football stadiums in this country, including the players; plus all the automobile speedways and horse racing tracks, including the automobiles and horses; with enough left over to buy post offices in wholesale quantities." Aesthetic values are not included, only monies spent!

But few people realize that hunters and fishermen pay their own way. General taxes are not a significant source of funds for developing and maintaining this nation's wildlife resources, as is the case with many other government-provided goods and services. Sportsmen share the cost through self-imposed excise taxes on sporting arms, ammunition, fishing tackle, etc.; they also pay use and license fees to Federal and State agencies; and they contribute directly to numerous programs sponsored by