

REVIEW ARTICLE

Foot-and-Mouth Disease in Pigs: Current Epidemiological Situation and Control Methods

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Summary

Foot-and-mouth disease (FMD) is the paradigm of a transboundary animal disease. Beyond any doubt, it is the most serious challenge for livestock's health. Official Veterinary Services from free countries invest considerable amount of money to prevent its introduction, whereas those from endemic countries invest most of their resources in the control of the disease. A very important volume of scientific production is developed every year in different aspects of FMD, and for that reason, the current knowledge makes the diagnosis of the disease easier to a great extent. However, FMD is still endemic in about two-thirds of the countries, and periodically re-emergent in several countries. This paper is a review of recent publications, focusing mainly on control measures and current world epidemiological situation, emphasizing primarily pigs.

Introduction

Foot-and-mouth disease (FMD) is a highly contagious viral disease affecting cattle, pigs, sheep, goats, buffalo and artiodactylous wildlife species, caused by the FMD virus (FMDV). It is characterized by fever and vesicles in mouth, teats and feet. In a susceptible population, morbidity may approach 100%. Growth and productivity are severely affected due to fever, pain and distress. Although adult animals generally recover, it frequently causes high mortality in young animals.

Foot-and-mouth disease has two of the basic criteria for the inclusion in the List of Diseases of the World Organization for Animal Health (OIE): international spread and significant spread within a naïve population. According to EMPRES Programme of Food and Agricultural Organization of the United Nations (FAO), FMD is a typical Transboundary Animal Disease, as it complies with the three required characteristics: (i) it is of significant economic, trade and/or food security importance for a considerable number of countries; (ii) it can easily spread to other countries and reach epidemic proportions; (iii) it requires cooperation between several countries for

its control/management or exclusion (FAO-EMPRES, 2011). For these reasons, it is a major impediment to international trade in livestock and livestock products.

Currently, 66 of 178 OIE member countries are recognized as free countries, 65 of 66 do not practise vaccination except 1, where vaccination is practised. Furthermore, 11 countries have free zones, either with or without practice of vaccination. Of the 101 remaining countries, 96 are endemic or have never proved the absence of FMDV circulation and 5 were free countries that are at the present suffering re-emergence of FMD. Therefore, infected countries represent more than 56% of the total of OIE member countries.

The role of pigs in these FMD episodes was crucial. Among the 38 immediate notifications made to OIE from January 2010 to April 2011, there were seven cases in which pigs were involved. They occurred mainly in Eastern Asia, affecting China, Chinese Taipei, North Korea, South Korea and Hong Kong. The objective of this article is to review the most recent innovations in topics concerning FMD in pigs, particularly focusing on the current worldwide epidemiological situation and the strategies for the prevention and control of the disease.

Aetiology

Foot-and-mouth disease is caused by FMDV, which belongs to the genus *Aphthovirus*, family *Picornaviridae*. There are seven serotypes of FMDV namely, O, A, C, SAT 1, SAT 2, SAT 3 and Asia 1 (Brown, 2003; Suttmoller et al., 2003; Grubman and Baxt, 2004; Lubroth et al., 2006). All serotypes produce indistinguishable clinical signs, but the immunological response is distinct. Antibodies can be differentiated by various serological tests. Infection with one serotype does not confer immunity against another (Alexandersen et al., 2003).

There is a large and indeterminate spectrum of subtypes and variants that have been recognized. This extensive genetic heterogeneity is considered one of the major obstacles for the control of FMD by vaccination (Araújo et al., 2002; Grubman and Baxt, 2004). A substantial part of the genetic variability observed in the field is expressed particularly in the capsid proteins VP1, VP2 and VP3 (Haydon et al., 2001). L, 3A and 3B protein coding regions have also been identified as RNA regions accumulating levels of genetic variation among different FMDV isolates similar to those of the structural proteins (Carrillo et al., 2005).

Determination of antigenic and genetic profiles of FMDV strains is important for epidemiological studies and for the selection of the most appropriate vaccine strains for a region where vaccination is practised. For the purpose of epidemiological studies, molecular information of isolates at regional level, including all neighbouring countries, should make disease tracing more effective (Samuel and Knowles, 2001; Domingo et al., 2003; König et al., 2007). Continued monitoring of newly emergent strains is necessary to perform vaccine-matching studies to support the efficacy of actual vaccine formulations (Knowles and Samuel, 2003; Paton et al., 2009).

Some FMDV strains have a pronounced predilection for one livestock species or another. For instance, the Hong Kong topotype of type O is well adapted to pigs, to the extent that it has only once been isolated from a species other than pig, and it was in a bovine (Kitching, 2002b); the Cathay topotype of serotype O, including the Taiwan 1997 outbreak strain, is adapted to and highly virulent in pigs, but attenuated in cattle (Samuel and Knowles, 2001).

Susceptible Species

All members of the order Artiodactyla (cloven-hooved mammals) can be infected by FMDV. Each species varies in its susceptibility to infection and clinical disease, as well as in its ability to transmit the virus to other animals (Lubroth et al., 2006; Rovid Spickler et al., 2010). Other

susceptible species to infection are hedgehogs (Insectivora), tapirs (*Perissodactyla*), elephants (*Proboscidea*), bears (*Carnivora*), although they have not been proved to be of importance in the epidemiology of the disease.

Cattle are usually the most frequently involved in epidemics, and play an important role in the maintenance of the FMDV as the status of persistent infected animal occurs in high proportion of individuals from this species (Kitching, 2002a; Suttmoller and Casas Olascoaga, 2002). Small ruminants may be naturally infected; however, they show very few or no clinical signs, and persistent infection is less frequent and of shorter duration than in cattle (Kitching and Hughes, 2002). Although pigs are highly susceptible to FMDV, there is no evidence that they may become carriers (Kitching and Alexandersen, 2002; Suttmoller and Casas Olascoaga, 2002; Kitching et al., 2005; Lubroth et al., 2006). Other species, such as llamas, alpacas and camels, can be infected experimentally, but do not appear to be very susceptible. Deer, buffalos and at least 70 species of wild animals may be infected by FMDV (Rovid Spickler et al., 2010).

Transmission

An FMD outbreak starts when one or more animals become infected as a consequence of the exposition of a susceptible population to the FMDV. Once infection is established in a limited population, such as a pig farm or other type of herd, the within-farm spreading of the FMDV begins, through animal-to-animal transmission.

Excretion of the virus can begin up to 4 days before the onset of clinical signs. This is of great epidemiological significance. The agent is excreted in large quantities in expired air, in all secretions and excretions and from ruptured vesicles. Pigs may liberate vast quantities of airborne virus in their expired breath, about 3000 times as much as cattle (Geering and Lubroth, 2002). Active viraemia and virus excretion start during incubation period (Quan et al., 2004); however, the maximum excretion of virus coincides with the development of clinical disease and lesions on the snout, tongue and feet, and declines over the following 3–5 days as the antibody response develops.

Transmission by direct contact between infected and susceptible animals can be very rapid, and many routes of viral entry may be involved, such as aerosol, oral, mucosal and even through damaged epithelium. The respiratory route is likely to be the most usual portal of entry for pigs, even if they may require as much as 600 times more than the exposure to aerosol virus required by a bovine or an ovine, to cause infection. On the other hand, pigs are much more susceptible to infection by the oral route than ruminants (Kitching and Alexandersen, 2002; Grubman and Baxt, 2004; Paton et al., 2010). Unlike ruminants that

have recovered from FMD infection, pigs do not become carriers, and there is no evidence of viral ribonucleic acid persisting in infected pigs after 3 or 4 weeks of becoming infected (Kitching and Alexandersen, 2002; Lubroth et al., 2006).

The next step in the development of an FMD epidemic, after the establishment of the infection in a farm, is the between-farms spreading. The virus may spread from an infected premise to susceptible premises through different ways, among which the most relevant are: by movement of infected animals, by direct contact with animals from neighbouring premises, by movement of infected animal products, such as meat and offal used as unprocessed waste food for pigs or milk for calves, by mechanical transmission, e.g. milking machines, vehicles, tools and people, and aerogenous transmission by wind (Donaldson et al., 2001; Oleksiewicz et al., 2001; Donaldson and Alexandersen, 2002; Alexandersen et al., 2003; Grubman and Baxt, 2004). Probably, the most often spread of FMDV is associated with the movement of infected animals which excrete virus, and then, other animals, especially ruminants, which are usually infected via inhalation of infectious droplets (Alexandersen et al., 2003).

An additional method is spread by the wind, most often from pigs to cattle or other ruminants (Alexandersen et al., 2003). This is because pigs excrete high concentrations of virus in their breath, but are relatively resistant to airborne infection, while cattle and other ruminants excrete fewer viruses in their breath, but are highly sensitive to infection by the airborne route (Donaldson et al., 2001; Oleksiewicz et al., 2001; Grubman and Baxt, 2004). Airborne virus excretion reaches maximum values with the appearance of vesicular lesions and occurs within the phase of viraemia (Donaldson and Alexandersen, 2003; Kitching et al., 2005). However, virus excretion starts during the incubation period, before the first clinical signs are evident, increasing significantly the risk of virus spreading. This situation is particularly important in pigs (Orsel et al., 2009). In pigs experimentally infected with two different types of FMDV (O and C) at two challenging doses per virus, it was shown that for both virus strains and initial doses of inoculum, airborne virus was detected over a 3-day period and commenced either currently with or 1 day before the detection of clinical signs (Gloster et al., 2008). Coincident results were found in another study in which pigs were inoculated with type O FMDV only (Amaral Doel et al., 2009).

If the FMD epidemic develops in a country or a zone, the following step would be the between-countries transmission. Illegal activities, such as the import of infected meat and feeding to pigs of non-heat treated swill, or the illegal transboundary movement of animals, have often been attributed to introductions of FMD into

non-infected countries. Recent examples are: (i) the Pan-Asia type O outbreak in South Africa in 2000 on a pig farm where swill coming from ships was given as food (Sutmoller et al., 2003; Kitching et al., 2005); (ii) the involvement of a swill-fed pig unit in the spread of FMD during the Pan-Asia type O outbreak in the UK in 2001 (Sutmoller et al., 2003; Kitching et al., 2005; Paton et al., 2009); (iii) the type O outbreak in Uruguay, near the border with Brazil, caused by the feeding of contraband slaughterhouse offal to pigs living in close contact to cattle (Sutmoller et al., 2003); (iv) the Pan-Asia type O FMD epidemic in South Korea in 2002, where 15 of 16 outbreaks were detected in piggeries (Yoon et al., 2006). Imported straw was also assumed to be the source of FMD in Korea in 2000 (Shin et al., 2003) and might also have been the source of the FMD outbreak in Japan in the spring of 2000 (Sugiura et al., 2001).

Clinical Signs and Lesions

Incubation period in natural conditions varies according to virus strain, the exposure dose and the route of entry. It may range from 24 h to a maximum of 11 days (Kitching and Alexandersen, 2002; Quan et al., 2004).

Early signs of FMD in pigs are characterized by fever, inappetence and reluctance to move. Usually, the more severe lesions occur in the feet, starting by lameness and blanching of the skin around the coronary bands. Vesicles develop on the coronary band, heel and interdigital space. Lesions at other sites are less frequent and less severe. Sometimes, vesicles may be found on the snout or the udder, being relatively uncommon on the tongue. Adult pig recovery depends on the severity of lesions, some of them may suffer chronic lameness. Fattening pigs will require a longer time to reach their slaughter weight. Young pigs up to 14 weeks may die suddenly due to heart failure; piglets are particularly susceptible. In some herds, piglet mortality is the first sign of the disease (Geering and Lubroth, 2002; Kitching and Alexandersen, 2002; Lubroth et al., 2006; Rovid Spickler et al., 2010).

The incidence of the disease in non-immunized populations can be as high as 100%. Mortality rate in adult animals is usually negligible, but, as previously mentioned, it can be extremely high in suckling piglets (Lubroth et al., 2006; Rovid Spickler et al., 2010).

Diagnosis

In farms presenting high mortality of piglets and a significant proportion of pigs showing lameness, fever and vesicular lesions, FMD should be strongly suspected. Actions should be taken immediately to secure a definitive diagnosis and prevent further spread on the agent. It

must also be stressed that, when a vesicular disease in pigs (or other species) is detected, the practitioner should immediately contact the official veterinary authorities to conduct a thorough epidemiological evaluation of the incident and collect the appropriate samples for proper laboratory submission (Lubroth et al., 2006).

In the laboratory, FMD can be diagnosed by identification of the agent or by serological tests. The main methods and procedures for these studies are well described in the Chapter 2.1.5. of the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2010 (version adopted by the World Assembly of Delegates of the OIE in May 2009) (OIE, 2011a).

For identification of FMDV, different type of samples can be used, according to the laboratory method to be applied: virus isolation or RT-PCR: epithelium, oesophageal-pharyngeal (OP) samples and serum; ELISA CF and the lateral flow device: epithelial suspensions, vesicular fluids or cell-culture supernatants.

Serological tests for FMD are performed in support of four main purposes namely:

- 1 To certify individual animals prior to import or export (i.e. for trade);
- 2 To confirm suspected cases of FMD;
- 3 To substantiate absence of infection;
- 4 To prove the efficacy of vaccination.

Pigs may be affected by other vesicular diseases, which are clinically indistinguishable from FMD. Thus, laboratory diagnosis of any suspected FMD case in pigs is therefore a matter of urgency. Other pig vesicular diseases are:

Vesicular stomatitis (VS): it is a viral disease that primarily affects cattle, horses and swine, and occasionally sheep, goats, llamas, and alpacas. Two distinct immunological classes of VS virus have been recognized: New Jersey and Indiana. It is endemic in northern parts of South America and all Central America, being less frequent in USA. It is not present in other continents (Lubroth et al., 2006; OIE, 2011b).

Swine vesicular disease (SVD): it does not affect other species. It can be a subclinical, mild or severe vesicular condition depending on the strain of virus involved, the route and dose of infection, and the husbandry conditions under which the pigs are kept (Lubroth et al., 2006). Recent outbreaks of SVD have been characterized by less severe or no clinical signs; infection has been detected when samples are tested for a serosurveillance programme or for export certification. The last immediate notification reported to OIE from a European country was from Portugal in 2007: one farm was affected, with a population of 1800 pigs. All of them were eliminated by stamping out. The origin of the outbreak remains unknown (OIE-WAHID, 2011). The disease was present in the Southern parts of Italy until 2005 (Bellini et al., 2007).

Vesicular exanthema (VES): it does not affect other species than pig. It originated in California, and became widespread in the USA during the 1950s, but the vigorous campaign to eradicate the disease was successful. In 1959, the USA was declared free of VES, and the disease was designated a foreign animal disease. It has never been reported as a natural infection of pigs in any other part of the world (Merck & Co. Inc, 2008).

Measures of Control

In scenarios with recent introduction of FMDV into a fully susceptible population, the number of expected secondary cases due to contact with the primary case/s will depend on the basic reproductive ratio (R_0). This is the expected number of new infectious individuals produced by one infectious individual during its period of infectiousness in a population that is completely susceptible (Halloran, 1998). R_0 depends on (i) the infectiousness of the agent for the specific host; (ii) the contact rate, or number of effective contacts between infectious and susceptible animals per time period; and (iii) the duration of the infectious period for the specific host. The contact rate is the most variable factor affecting R_0 , and is expected to vary among herd types with the same species of animals, depending on management differences such as stocking density, within-herd movements and nature of physical facilities (Thurmond, 2003).

What is said for R_0 is valid only in fully susceptible populations. In endemic situations, where a given proportion of individuals are immunized, the expected number of new cases produced by an infected animal is less than R_0 and it is called the effective reproductive number (R). It depends on R_0 and on the proportion of susceptible individuals in the population (Halloran, 1998). Both R_0 and R can be referred to transmission either among animals within a herd or among herds in a region or country. The latter estimates the number of new herds that will become infected as a result of transmission from an infected herd (Estrada et al., 2008).

Both R_0 and R are estimated by calculations made from data obtained from different sources, such as real epidemics, experimental studies or simulation models. For instance, in an experimental study, R_0 was estimated for the pre-clinical period (incubation period) in two groups of piglets challenged with FMDV type O, non-vaccinated and vaccinated. The observed values were 13.2 and 1.26 respectively. This means that the introduction of FMDV in a pig farm may result in spreading to a larger number of animals during the incubation period, which could imply that, during this time, the herd is already infectious to other herds (Orsel et al., 2009). From the 2001 FMD epidemic in the UK, R_0 was estimated to be 2.99 at the

beginning of the epidemic, before the movement ban was implemented, but when infectious cases linked to markets were removed from the calculation, the estimate fell to 1.95, revealing the substantial effect of the markets in disseminating infection. After implementation of the ban, transmission of FMD was predominantly local, with estimates of R falling, shortly after, to about 1.5 (Matthews and Woolhouse, 2005). In a different scenario, R for between-herd transmission was estimated in an FMD outbreak that took place in Peru in 2004, where a value of 5.3 was observed at the beginning of the epidemic, and progressively declined to values below 1 after 3 weeks of intervention (Estrada et al., 2008). A more recent example is the 2010 FMD epidemic in Japan, where R for between-herd transmission was highly variable along the 50 first days of the epidemic, ranging from 2 to 10. A significant decline of R values was observed from day 50 after the beginning of the infection (Nishiura and Omori, 2010).

In both endemic areas and areas that suffered recent reintroduction of FMDV, the control measures have the objective of reducing R to values below 1. For FMD, as well as for any other transmissible disease, those measures include three possible and independent strategies:

1. *Eliminating sources of infection:* to accomplish this objective, the sources of infection should be first identified. The main sources of infection are infected animals. Other sources are contaminated premises, tools, vehicles, wild animals, etc. For the identification of these sources, epidemiological surveillance programmes have to be implemented by the official veterinary services. Epidemiological surveillance is an active, ongoing, formal and systematic process aimed at early detection of a specific disease or agent in a population or early prediction of elevated risk of a population acquiring an infectious disease, with a pre-specified action that would follow the detection of disease (Thurmond, 2003). This definition is in agreement with that from other authors (Toma et al., 1999; Salman, 2003; OIE, 2011c). Passive and active surveillance, as defined in the OIE Terrestrial Animal Health Code, differ in methodology, but have both the same aim, demonstrating the absence of disease or infection, determining the occurrence or distribution of disease or infection, as well as detecting, as early as possible, exotic or emerging diseases (OIE, 2011c).

Surveillance on FMD requires at least the fulfilling of the following items:

- 1 Participation of all actors involved in the animal production chain. They must be aware of FMD clinical signs and the procedures for its notification. This implies a great deal of communication and continuous education;
- 2 Training of members of the official veterinary services as regards the notifications of vesicular diseases. A

programme of continuous education of staff, not only on aspects regarding the disease but also on legal and regulatory frame, is crucial. Simulation exercises should be regularly performed;

- 3 Having a specialist FMD diagnosis team; adequate knowledge of the susceptible population: number of farms and animals per species and production system, size of herds, geographical distribution of farms, distance between them, patterns of animal movements;
- 4 Knowledge of the location of places of animal concentration, such as live markets, slaughterhouses and others;
- 5 Access to laboratory diagnostic capabilities for rapid and certain diagnosis;
- 6 Access to a network of international reference laboratories.

Passive surveillance is the strategy of choice for early detection; however, implementation of a highly sensible system requires a great effort on the part of the veterinary authorities. Obviously, non-official veterinary service is able to regularly and frequently check for vesicular syndromes in all susceptible animals in a population. However, on the other hand, producers, private veterinarians, markets and slaughterhouse workers have access to the totality of the herd and may detect from the beginning any vesicular syndrome. The system may work if all these actors are involved in a network, are well informed about the clinical signs of FMD and are aware of the importance of prompt notification to official authorities (Salman, 2003; Dufour and Hendriks, 2009). The procedures for notifications must be clearly communicated to all of them, as well as the consequences. The role of official veterinary services in passive surveillance concerns communication for the motivation of actors, and of course, their capacity to rapidly respond to notifications such as visit to the affected premises, clinical checks, collection of epidemiological data, sampling and access to laboratory for confirmation or rejection of the suspicion. Active surveillance may not be as useful as passive surveillance in endemic or re-emerging scenarios if an early detection of FMD is the main aim of surveillance (Kitching et al., 2005).

Given that FMD is a typical Transboundary Animal Disease, the surveillance strategy should take into account the area in which it will be implemented, either at the national level or at the regional level, the latter option being clearly the preferred (Rweyemamu et al., 2008). However, the implementation of this type of regional actions, where many countries are involved, normally presents serious difficulties of many orders, particularly in developing countries, where FMD is unfortunately more frequent.

The time to detect, report and confirm FMD is one of the most important measures of the effectiveness of a

surveillance system (Thurmond, 2003). In this sense, it was estimated that if the national movement ban in the 2001 FMD epidemic in the UK had been imposed 2 days earlier, the final size of the epidemic would have been reduced to 48% of its observed size (Matthews and Woolhouse, 2005). By modelling the 2002 FMD epidemic in South Korea, it was determined that initiating actions 5 days earlier would produce less than half of the actual observed infected premises (Yoon et al., 2006).

Once the source of infection has been identified, it has to be eliminated. This is the second stage, and can be performed by application of different means, such as stamping out, slaughtering, disinfection, bio-containment measures and even vaccination. The objective of stamping out is to stop the production of virus in livestock, so that any aerosol or local spread of infection is kept to a minimum. This means that animals in infected premises should be slaughtered as soon as possible after the disease is confirmed (Mouat, 2003). The effect of stamping out is a reduction of R for between-herd transmission (Nishiura and Omori, 2010).

Stamping out was the main strategy used by UK authorities to control the 2001 FMD epidemic. Following confirmation of the disease, all the infected animals and the dangerous contacts had to be slaughtered within 24 h, and in some areas, all animals within a 3 km radius. By the end of the epidemic about 1.3 million animals were slaughtered from infected/confirmed premises and more than 2.7 million animals from dangerous contact premises. Other measures of bio-containment were imposed, such as disinfection of facilities, vehicles, clothing and footwear (Mouat, 2003; Kitching et al., 2005). At the same time, a similar modality was implemented by the French authorities. When the UK informed them about the discovery of FMD outbreaks, a preventive culling policy (slaughter, destruction and disinfestations) was immediately implemented on 25 000 imported animals as well as on 30 000 animals from susceptible species that had been in contact with the imported ones (Chmitelin, 2003).

2. Interrupting contact between infected and susceptible individuals: movement interdictions, sanitary barriers, zoning, bio-exclusion measures. As stated above, R depends on the infectiousness of the agent, the duration of the infectious period and the contact rate. The first one depends on the nature of the agent, and usually it cannot be modified. The duration of the infectious period could be reduced at an individual level by certain treatments (e.g. vaccination increases resistance to infection, but if infected, animals excrete less virus for shorter periods of time), and at the farm level through the elimination of the infectious source. The contact rate is directly affected by population density and movement of animals, both highly related to the productive system.

At the farm level, the direct contact between animals is usually difficult to avoid. At the beginning of an outbreak, when animals still do not show clinical signs of the disease, during the incubation period, there is no reason to interrupt contact. Once the first case is diagnosed, measures to reduce contact can be put in place, depending on the producing system and facilities. Intensive systems with isolated compartments may help in this sense, as well as all classical measures of bio-containment and biosecurity.

The results of two experimental studies may be the best example of the magnitude of the effect of reducing contact between infective and susceptible animals. In one study, five infected pigs with FMDV type O were placed in a central pen, surrounded by four pens with one susceptible pig each, at a distance of 40–70 cm. The experiment was replicated twice, and none of the susceptible pigs became infected, confirming that pigs are relatively resistant to aerosol exposure. A similar experiment was performed, but this time the four pens with the susceptible pigs were in direct contact with the central pen. Pen walls were made of solid wood, leaving narrow openings up to 1 cm at the corners and near the floor. In this instance, four of eight pigs became infected, and R was estimated at 1.1. As the within-pen R_0 had been previously estimated as 23 new infections per infected pig, so one pen wall between adjacent pens reduced transmission by 20-fold (van Roermund et al., 2010). In other experimental study, comparing dynamics of infection with FMDV type O in pigs kept separate from each other and in pigs housed in groups, it was shown that the increase in the number of infected pigs housed together had the effect of increasing the interaction between animals and the activity of individual pigs, which had the effect of shortening the time to onset of clinical signs (Quan et al., 2004).

Movement of animals or materials susceptible to be contaminated out of infected premises is probably the most important way for spreading of FMDV (Geering and Lubroth, 2002; Kitching, 2002a). When an infected animal is moved, the direct and indirect contact that arises from mixing increases the risk of introducing the disease into populations previously free of it (León et al., 2006). For this reason, the first step in any control programme must be an absolute standstill of all livestock movement in the infected area (Sutmoller et al., 2003; Kitching et al., 2005). The effect of movement restriction is a reduction in the value of R .

Figure 1 shows the evolution of the number of new cases of FMD that are expected to occur as a consequence of introducing an infected animal in a 1000 fully susceptible pig herd, as a function of five different levels of effective contact rate: 10, 8, 6, 4 and 2. The calculations were performed using the Reed and Frost formula. When the

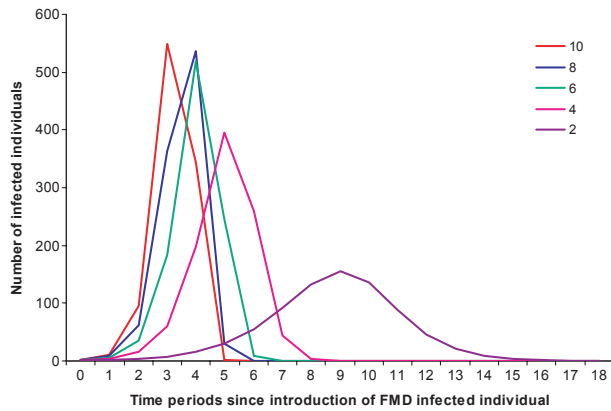


Fig. 1. Evolution of the number of FMD cases in a 1000 fully susceptible pigs herd, after introduction of an infected animal. Each curve represents the expected number of cases as a function of the effective contact rate. Calculations were performed according to Reed-Frost model.

number of cases is increasing, the value of R is >1 , meaning that one case generates, on average, more than one new case. On the other hand, when the number of cases decreases, R is below 1, meaning that each case produces on average <1 new case. The results are very simplistic, as the method assumes that: (i) the probability of receiving an effective contact is the same for all individuals in the population; (ii) no action is taken to stop contacts. However, it is a clear way of illustrating the effect of contact. The introduction on time period 0 of an infected animal in a population with a contact rate of 10 will produce a rapid spreading of the infection, with the peak of cases on time period 3 and the totality of individuals infected by the end of time period 5. In a scenario with a more moderate contact rate, for instance six, the peak of the curve will take place later on, on time period 4, and all animals will become infected at time period 6. With a contact rate of two the peak will occur at time period 9 and transmission of disease will stop at time period 18, resulting in 20% of animals that did not suffer infection.

A similar response to contact rate could be expected for spreading between farms: the lower the contact between farms (direct or indirect), the smaller the probability of FMDV spreading will be. The effect of applying movement restrictions on the expected number of outbreaks as well as the duration of an FMD epidemic in Dutch conditions was estimated through a simulation modelling. The results indicated that a significant reduction of both parameters occurred in low animal density areas, whereas the effect was less significant in high density areas, where local spread can still transport the virus outside the affected premises (Velthuis and Mourits, 2007). The implementation of sanitary barriers between

countries or zones within countries is another way of interrupting undesirable contact.

3. *Decreasing proportion of susceptible animals:* vaccination programmes. Vaccination against FMDV is another of the strategies that can be implemented to control the disease. Certainly, it is the most controversial one, as the time required to regain the free status strongly depends on it. Most current FMD vaccines are formulated using inactivated viral antigen produced in baby hamster kidney cells. The FMDV is fully virulent and inactivated with binary ethylenimine. The antigen must be then purified before vaccine formulation. Adjuvants commonly used include oil-in-water emulsions or aluminium hydroxide/saponin emulsions (McVey and Shi, 2010).

A distinction between conventional and emergency vaccines has to be made: emergency vaccines are of higher potency, usually six or more protective dose 50, having the effect of inducing rapid protective immunity and wider antigenic coverage within FMDV serotypes. These vaccines are usually elaborated with a higher antigen load per dose than conventional ones (Barnett and Carabin, 2002; Barnett et al., 2002). The onset of immunity is 3–4 days in cattle and sheep, but only 10 days after inoculation, clinical protection is broadly insured, provided there is optimal quality of the vaccine. These periods are longer in pigs; 3 weeks appear to be a minimum delay for some authors (Toma et al., 2002), while others have obtained effective within-pen protection between 7 and 14 days after vaccination (Eblé et al., 2004).

The efficacy of vaccination is affected by the lack of cross-protection between serotypes, as well as incomplete protection between some subtypes (Mattion et al., 2004). Additionally, new variant viruses are emerging periodically. For these reasons, in case of outbreak, the immediate requirement is to detect the circulating virus serotype, which is generally achieved by antigenic-typing ELISA or by genetic typing (sequencing of the VP1 gene). Once the serotype of the virus is established, vaccine-matching assays have to be carried out in order to select a suitable vaccine strain (Parida, 2009).

The probability of stopping FMDV spreading by vaccination depends on many factors, among which the most relevant are the efficacy of the vaccine (proportion of vaccinated animals that are protected), the time interval between the beginning of the outbreak and the beginning of vaccination, and the proportion of vaccinated animals (Keelling et al., 2003).

Countries or areas free from the disease may implement emergency vaccination as a complement for the previous two strategies. The broadest sense of emergency vaccination is the use of vaccines to control an outbreak of FMD in a country, or area, normally free from the

disease, in which routine prophylactic vaccination is not practised (Cox and Barnett, 2009).

Emergency vaccination may be implemented in different manners. For instance, ring vaccination around identified infected premises, with elimination of vaccinated animals once the outbreak is controlled, and the absence of virus circulation is demonstrated by serological surveillance. Ring vaccination may also be applied, without elimination of vaccinated animals (Parida, 2009).

Ring vaccination does not significantly reduce the risk of FMDV between premises, compared with the strategy of elimination of infected and contact animals by stamping out. But in those scenarios where stamping out cannot be applied, ring vaccination is the best method for reducing virus circulation (Toma et al., 2002). When the number or distribution of outbreaks exceeds the expectations, the strategy of blanket vaccination could be another option.

It is important to remark that current vaccines have the ability to protect animals (provided matching between vaccine and field strains and time to induce immunity) against clinical signs of FMD, but they cannot fully protect against infection (even if virus transmission is significantly reduced, it is not completely interrupted). This means that the control of an epidemic by vaccination only is unlikely, and the other strategies have to be simultaneously implemented (Barnett and Carabin, 2002).

Choosing the Most Convenient Strategy

None of the three strategies described is perfect. For that reason, the simultaneous implementation of more than one is convenient. The choice of the applicable strategies depends on many aspects, among which the epidemiological situation, access to economic resources and need to recover status are probably the most relevant.

In free countries or zones where vaccination is not practised, the elimination of the infection sources and the interruption of the contact between infected and susceptible individuals are the two basic strategies normally implemented to control a re-emergence of FMD. Such conditions allow the recovering of the free status in the least possible time, which is 3 months after the elimination of the last case, provided that serological surveillance is applied and results demonstrate the absence of virus circulation. Recovering the status in the shortest time is of great importance for exporting countries; therefore, it is the main reason why vaccination is not applied. In certain cases, the two strategies are complemented with emergency vaccination of animals at risk, for instance, when a great number of premises are infected and/or the affected area becomes too extended. The application of the three strategies simultaneously may reduce the num-

ber of eliminated animals, reducing the global costs of eradication. If vaccination is followed by the slaughtering of all vaccinated animals, the free status may be recovered 3 months after elimination of all vaccinated animals, provided that serological surveillance is applied and results demonstrate the absence of virus circulation. If vaccination is not followed by the slaughtering of all vaccinated animals, the recovering of the free status takes longer, 6 months after the last case or the last vaccination, provided that a serological survey based on the detection of antibodies to non-structural proteins of FMDV demonstrates the absence of infection in the remaining vaccinated population. Free countries that cannot afford compensation to producers associated to sanitary sacrifice of animals might reject the strategy of stamping out, and implement the interruption of the contact between infected and susceptible individuals and the emergency vaccination. In such case, the recovery of the free status would require 1 year, with demonstration of non-circulation of FMDV.

In countries or zones where vaccination is practised, recovery of free status takes 6 months after the elimination of the last case, if a stamping-out policy, emergency vaccination and serological surveillance are applied. In the case where a stamping-out policy is not applied, the required period is 18 months, provided that emergency vaccination and serological surveillance are properly performed.

Due to the high transmissibility of FMDV, the control measures taken in endemic areas will have little probability of success if they are taken individually by a country or area. The control policies have to be undertaken at a regional basis. For that, strong collaboration and transparency between parts are needed.

Measures of Prevention

In FMD-free areas or countries, import control including quarantine, is the first line of defence. Because of the infectious nature of FMD, often a country's strategy is best served by working in and for a regional programme (Geering and Lubroth, 2002; Rweyemamu et al., 2008). The OIE Terrestrial Animal Health Code, Chapter 8.5 on FMD, provides guidelines for the safe importation of live animals, meat and other animal products, from FMD-free and infected countries and zones (OIE, 2011d).

An important issue to be taken into consideration is the quality of the Official Veterinary Services of the exporting country, mainly in those topics affecting transparency (authority and capability to notify the OIE their status and other relevant matters pursuant to the established procedures), international certification (authority and capability to certify animals, animal products, services and processes under their mandate, in accordance with

national legislation and regulations, and international standards) and even more important, epidemiological surveillance (authority and capability to determine, verify and report on the sanitary status of the animal population under their mandate) (OIE-PVS, 2010).

A distinction between the risk of FMDV entry via importation of an animal product and the risk of an FMD outbreak resulting from such event must be made. It is quite likely that very small quantities of FMDV are occasionally imported into FMD-free countries, but outbreaks as a result of this are rare. For an outbreak to occur, a sufficient quantity of infectious virus must contact a susceptible animal and initiate infection. In that sense, pigs are at greater risk from contaminated products than sheep or cattle, as they may consume waste food and the infectious oral dose is lower for pigs than ruminants (Ryan et al., 2008). Concerning importation of live animals, the quarantine policy should include pre-export testing and quarantine, animal health certification and any necessary post-arrival inspection testing and quarantine. These policies should be based on the results of risk analyses.

Importation of animal products may be of greater risk than live animals, as diagnostic test or quarantine measures are of more restricted use. Regarding bovine meat, the acidification of the skeletal muscle that take place during carcass maturation is normally sufficient to inactivate all FMDV in this tissue, even when animals are killed at the height of viraemia. The problem is the existence of bone marrow or lymph node tissues in the meat, which is regarded as a significant risk factor (Ryan et al., 2008; Thomson et al., 2009; Paton et al., 2010). Other tissues and organs that may harbour FMDV do not undergo acidification and here, the virus can survive the maturation process and subsequent low-temperature storage. These include blood, heads and viscera.

There may be considerable variation between pigs in the time taken for the pH of the *latissimus dorsi* muscle to fall from 6.5 to a final pH of 5.5 at 37°C (150–400 min). In commercial production, the pH of pork seldom falls below 5.7. Thus, a reduction of pH below 6 is not a reliable feature for commercial pork meat. Concerning pig products, FMDV survival is even more variable, depending on the temperature of processing and storage, pH, time of storage, water activity, moisture protein ratio, salinity and any additives that may be included. The interaction of these factors with the enzymatic proteolysis, which occurs in many products determines the extent of FMDV inactivation (Ryan et al., 2008).

In free countries or zones where the risk of FMDV reintroduction is not negligible, for instance many South American countries, mass and compulsory vaccination programmes may be applied to complement the other preventive measures.

World Epidemiological Situation

At present, OIE has 178 member countries. According to their FMD status, they are recognized as:

- 1 Free country where vaccination is not practised (n : 65; 36.5%);
- 2 Free country where vaccination is practised (n : 1; 0.6%);
- 3 Country with an FMD-free zone where vaccination is not practised (n : 10; 5.6%);
- 4 Country with an FMD-free zone where vaccination is practised (n : 6; 3.4%).

Some countries have both types of zones. Countries not classified in any of these categories are either endemic or are suffering from the recent re-emerging of the disease (n : 100; 56.2%). These figures reflect the extensive

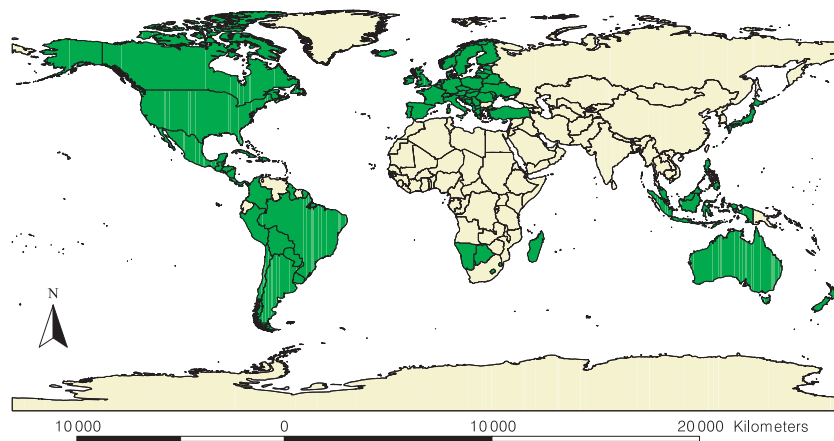


Fig. 2. Countries with OIE status of FMD free, where vaccination is practised and not practised, and countries having FMD-free zones where vaccination is practised and not practised (Source: OIE).

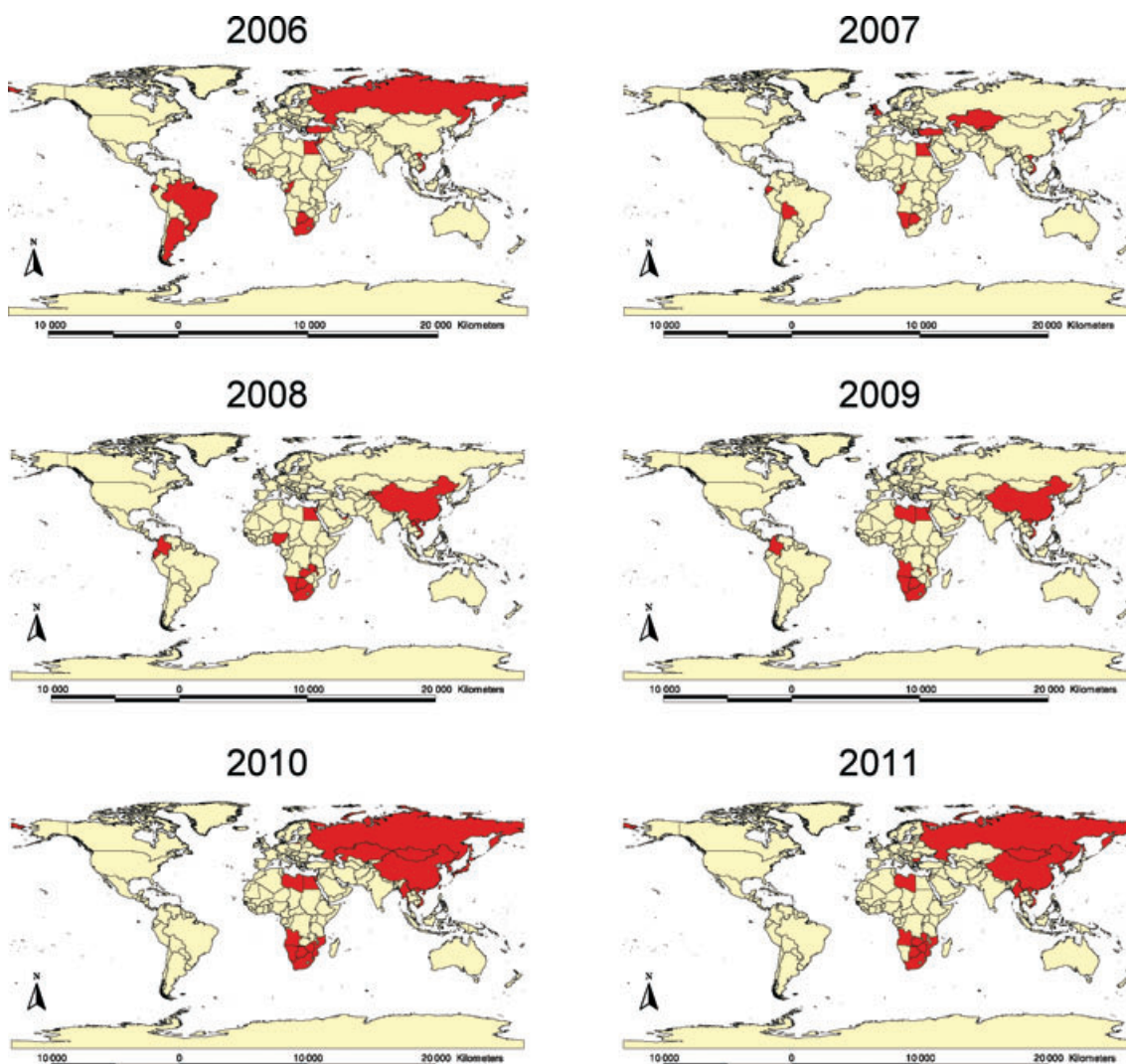
Table 1. Data of 1795 FMD outbreaks notified to OIE from January 2006 to May 2011, recorded in WAHID

Parameter	Cattle	Small ruminants	Pigs	Buffaloes	Wild species
Animals exposed to virus	1 634 922	119 222	708 731	1303	3290
Diseased animals	48 334	28 525	25 973	311	1840
Deaths	753	2702	17 189	32	772
Destroyed	90 609	25 420	629 533	123	1248
Slaughtered	6741	662	261	359	0

distribution that the disease has in the world. Actually, there are only three regions free of it: North & Central America plus Caribbean, Europe and Oceania (Fig. 2).

From January 2006 to May 2011, a total 1,795 outbreaks of FMD were notified to OIE, affecting 42 countries from four continents. A description of infected animals according to different parameters is presented in Table 1 (OIE-WAHID, 2011). These records are the result of immediate notifications, meaning that cases occurring in endemic countries or zones are not included. Annual distribution of countries that notified FMD to OIE from 2006 to 2010, including all species, can be observed in Fig. 3. In the last years, reported cases have shown a strong concentration in four zones namely, Southern and North-western Africa, Middle East and Eastern Asia.

The outbreaks were due to six FMDV serotypes: A, O, Asia1, SAT1, SAT2 and SAT3. Nearly 1100 outbreaks involved pigs, in which more than 25 000 pigs were directly affected by the disease, producing more than

**Fig. 3.** Countries that notified FMD to OIE from 2006 to 2010, all species included (Source: OIE-WAHID).

17 000 deaths, representing about 66% of lethality. The FMDV serotype that affected pigs more frequently was O, identified in more than 88% of outbreaks, followed by Asia1, which was isolated in 9% of outbreaks.

The role of pigs in the recent FMD epidemics has been significant, mainly in countries from Eastern Asia. Pigs were involved in 7 of 38 immediate notifications made to OIE from January 2010 to May 2011, affecting China, Chinese Taipei, North Korea, South Korea and Hong Kong. In the epidemic that took place in Miyazaki, Japan, between April and July 2010, 292 farms were affected by FMD, 84 of them were pig herds, representing a cumulative herd incidence of 36.4%, when the same value for cattle was 8.5% (Nishiura and Omori, 2010). In the 2001 FMD epidemic in the UK, pigs also played a significant role, as three of the first five reported outbreaks contained pigs (Donaldson and Alexandersen, 2003).

As a consequence of these outbreaks, near 630 000 pigs were killed. These are the direct costs of the disease. Economic losses in terms of international trade interruption, costs of control measures and many other indirect costs should be added to the direct costs to have a rough estimation of general losses (James and Rushton, 2002; Thompson et al., 2002; Perry and Randolph, 2003; Forman et al., 2009).

The knowledge of the current epidemiological situation of FMD in exporting countries is probably the main input for risk analysis regarding importation of animals or animal products. OIE records of notifications are an extremely valuable source of information for that. However, even if member countries have accepted their obligation of notifying every FMD event, it is known that a number of countries with endemic FMD status and substantial animal populations provide no information on FMD outbreaks or provide data that are considered a significant under-reporting of the true situation. On this basis, an assessment of world FMD distribution has been recently carried out, combining official disease information with expert opinion and livestock populations. This study generated maps of prevalence, where the areas of highest prevalence were China for pigs, India for cattle, the Near East for small ruminants and the Sahara region of Africa for small ruminants and cattle (Sumption et al., 2008).

Conclusion

Probably, the most relevant conclusion from this literature revision is that FMD is still endemic in more than half of the countries of the world, and very little progress has been made in this sense in the last years. Another dramatic conclusion is that the disease re-emerges in free countries with certain frequency.

At the same time, a very prolific generation of knowledge is being developed that has been strongly stimulated as a consequence of some episodes that took place recently, such as the 2001 and 2007 UK epidemics, and the re-emergence of the disease in South Korea and Japan. Enormous progress has been made in the understanding of FMDV transmission, as well as in the molecular epidemiology of the disease. However, gaps in knowledge still exist. It could be mentioned, among others, the transmission of FMDV from one country to another, the predilection of some FMDV strains for specific species, the high variability of the virus and the rapid response of vaccines.

But certainly, the very little progress observed in FMD eradication cannot be attributed to lack of knowledge. The disease is mainly concentrated in developing countries having little or no possibility of exporting animals or animal products. Many of those countries have extreme reduced budget for Official Veterinary Services, and have no interest in investing for improving animal health. This reality leaves geographical clusters where the virus is endemically maintained, at the time that makes impossible to undertake the control of the disease at regional basis.

International efforts should be strengthened to promote the regional control of the disease. The actions should be financially supported in high proportion by the countries that most will benefit with global eradication.

Conflict of Interest

The author declares no conflict of interest.

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