# Foot-and-Mouth Disease (FMD)

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INTRODUCTION

Foot and mouth disease (FMD) is caused by viruses that belong to seven immunologically distinct serotypes of the genus *Aphthovirus* which is classified within the *Picornaviridae* family. The disease naturally affects cloven-hoofed animals although the severity of the resulting disease varies between different species. FMD viruses may rarely induce disease in other artiodactyls such as Bactrian camels (*Camelus bactrianus*) but apparently not dromedaries (*C. dromedarius*) and Indian- but not African elephants. The susceptibility of alpacas and llamas is disputed but, at worst, they only become infected under exceptional circumstances and have played no significant part in the maintenance and spread of FMD in South America. Some other mammalian species can be infected artificially, e.g. African elephants, mice and guinea pigs.

The disease is characterized by the development of vesicles in the mucosa of the mouth (with the exception of the ventral surface of the tongue) and the skin of the coronets and interdigital spaces of the feet. Lesions may also occur on the muzzle/snout. In dairy cattle it may cause teat lesions and severe mastitis. FMD rarely causes fatal illness — myocarditis in neo-natal animals being an exception — but the disease may be severely debilitating in intensively farmed livestock, pigs and cattle particularly, rendering intensive livestock farming unprofitable. In extensive farming systems the disease is often mild and most affected animals make an uneventful recovery within three weeks.

Although FMD viruses may spread quickly and efficiently, including over long distances via air currents when the epidemiological circumstances are suitable, in warm, dry climates where stocking rates are low its spread may be slow. Thus the frequently repeated claim that this is the most contagious disease of vertebrates is not altogether correct; rate of spread is variable and dependent on epidemiological circumstance.
EPIDEMIOLOGY

Spatial and temporal distribution of the causative agents

The 7 serotypes of FMD virus are derived from two evolutionary pathways: A, O, C and Asia 1 were originally confined to Eurasia where they were closely associated with domestic livestock, cattle and pigs particularly. In the 18th Century serotypes A, O and C spread to the Americas and became established in South America; in North America FMD was eradicated in the early 20th Century. Even earlier, these serotypes spread to Africa and became endemic in northern, western & eastern parts of the continent. Serotype C seems in recent years to have spontaneously disappeared from all its historical habitats but confirmation of this is required.

The three SAT serotypes (1, 2 & 3), by contrast, evolved in Africa in association with African buffalo (*Syncerus caffer*) which maintain these infections efficiently but with little untoward effect to themselves. Because buffalo were historically widely distributed in Africa, SAT viruses too are likely to have been historically widespread south of the Sahara. These viruses may periodically spread from buffalo to other species, cattle particularly, which are then able, at least in some circumstances, to maintain them independently of buffalo. Transmission of SAT serotypes from buffalo to cattle occurs more readily for SAT2 than SAT1 and SAT1 more frequently than for SAT3. The available evidence indicates that only buffalo and cattle are able to maintain SAT viruses independently for protracted periods of time.

Maintenance of FMD viruses by wildlife is unique to sub-Saharan Africa; elsewhere, while wildlife may become infected through contact with infected livestock, wildlife have so far proven epidemiologically insignificant in the maintenance of A, O, C & Asia 1 serotypes.
Some FMD viral variants may develop a predilection for particular host species, e.g. become more-or-less restricted to pigs (Arzt et al., 2011b).

**Immunological relationships between FMD viruses**

Immunity to any one of the 7 serotypes does not confer cross protection against any of the other 6 serotypes. The inter-relationship between serotypes, based on genome sequence, is shown in Fig. 1. Considerable variation in genome nucleotide sequence and consequently biological characteristics may occur between isolates within a serotype. This intratypic variation is most marked within the SAT serotypes and serotype A.
Because FMD viruses like most RNA viruses evolve rapidly, viruses prevalent within different ecosystems evolve independently and consequently the geographic distribution of genotypes within a serotype is often well known. Genotypes that have a particular geographic distribution are known as ‘topotypes’. Through sequencing of the genomes, or parts of the genomes, and comparing the sequences with those of viruses contained in data-bases, the origin of viruses that cause outbreaks in new locations can frequently be inferred. This field of molecular epidemiology has added a new dimension to our ability to
trace or track the spread on FMD viruses, both world-wide and more locally in southern Africa (Bastos et al., 2003).

**What’s a topotype?**

A genotype with a distinct geographical distribution

Geographic distribution of SAT3 buffalo virus topotypes in southern Africa

**Epidemiological patterns**

FMD has a complex epidemiology; not only because of the viral diversity summarised above but also because of differences in the interaction between various host species and particular viral variants (sometimes incorrectly referred to as ‘strains’) as well as environmental factors. As a result, the way the disease presents in different parts of the world may differ widely. A further factor relates to the reaction of people – official veterinary services, farmer groups, conservationists, politicians and the general public – to the disease. In some parts of the world this has resulted in irrational reaction to the occurrence of the disease. FMD has even been referred to as ‘a manufactured plague’ (Woods, 2004). Thus what distinguishes FMD from most other animal diseases is the reaction, hysteria even, which its occurrence engenders. That can be more harmful than the disease itself.

Much of southern Africa differs from the rest of sub-Saharan Africa in relation to FMD because only the SAT serotypes occur endemically – maintained by African buffalo. The latter are increasingly restricted to...
conservation areas. Periodically, and increasingly since the turn of the 21st Century, SAT infections – SAT2 especially – has spread from buffalo populations to cattle in and around conservation areas. This problem is likely to be compounded in future by the establishment of new and/or enlargement of transfrontier conservation areas (TFCAs) in southern Africa as part of bio-diversity conservation initiatives (SADC, 2008).

Transmission

FMD is a directly transmitted disease with the predominant means of spread being direct or close contact between infected and susceptible animals. However, less frequently, transmission may occur indirectly through infection enabled by transporting healthy animals in vehicles which have previously transported infected livestock or through people handling healthy animals soon after being in contact with infected ones. Other mechanisms of local spread – such as short-distance air-borne transmission during outbreaks – are suspected but unequivocal evidence is yet to be provided in this respect.

Much confusion has resulted from the finding in northern Europe that long-distance transmission has very rarely occurred through virus-containing aerosols being transported for many kilometers by air currents (i.e. air-borne spread). For this form of transmission to occur, a number of climatic and epidemiological circumstances need to prevail including a potent source of infection – usually large piggeries suffering an explosive outbreak (because pigs excrete FMD virus more efficiently than other animals) – high density of susceptible animals, cool temperature, often involving temperature inversion that prevents convection, gentle wind blowing in a constant direction and cattle as recipients of the aerosols, because cattle are more susceptible to aerosol infection than other species owing to their large inspiratory volume (Thomson & Bastos, 2004a). In tropical/sub-tropical climates these requirements are seldom, if ever, met. A recent publication has postulated that aerosols may be derived from the skin of infected animals but that remains to be proven (Dillon, 2011).

Among ruminants, cattle certainly, infection usually occurs via the respiratory tract and cattle may be infected by small numbers of infectious virions (Thomson & Bastos, 2004a). Conversely, large amounts of infectivity are required to cause infection by the oral route in cattle. In pigs by contrast, the oral route of infection is most common with infection resulting from the feeding of pigs with untreated swill being a common source of FMD outbreaks in Europe and Asia. There has only been one recorded case of this type of outbreak in southern Africa.

It has been shown experimentally that animals infected with a FMD virus may excrete significant amounts of ‘infectivity’ for up to 3 days before obvious clinical signs develop and this has been considered epidemiologically important. Recently, however, it was shown in a series of experiments in cattle that the amounts of virus excreted before the development of clinical signs were insufficient to result in transmission; only about half a day after clinical signs developed did transmission occur (Charleston et al., 2011). It remains to be proven that this finding reflects the norm but if so it would simplify the management of FMD outbreaks.
Livestock Health, Management and Production › High Impact Diseases › Contagious Diseases › Foot-and-Mouth Disease (FMD) ›

For reasons not fully understood but probably to some extent related to the species predilection of SAT viruses, sheep and goats are only infrequently infected during FMD outbreaks in eastern and southern Africa but this is not invariably the case (Thomson & Bastos, 2004a; Arzt et al., 2011a).

For SAT-serotype infections in southern Africa the usual start of FMD outbreaks in livestock results from close contact between infected buffalo and susceptible cattle (Thomson & Bastos, 2004a). However, because buffalo rarely show evidence of disease the mechanism whereby this occurs is open to conjecture. There is good evidence that within breeding herds of buffalo, young animals become infected more-or-less simultaneously when a significant cohort of susceptible calves builds up within breeding herds and that at such times these animals contaminate the environment with FMD virus. This has been inferred from the fact that most young buffalo have actively acquired antibody to all 3 SAT serotypes by the time they reach one year of age and, secondly, that buffalo cows in southern Africa calve predominantly in mid-summer (December-February). The calves therefore lose their maternally-derived immunity more-or-less synchronously over the next 3-6 months. Thus by approximately May-July, when water is scarce and buffalo and other ungulates, including cattle, tend to congregate around water points, buffalo herds likely present a source of infection for other susceptible animals which come in close proximity to them.

Probably less frequently buffalo-cattle transmission occurs between susceptible cattle and so-called ‘carrier buffalo’. These are buffalo which have recovered from the acute phase of infection (i.e. at least 4 weeks after initial infection) but, while the virus disappears from all other tissues, (with the possible exception of lymph nodes – Juleff et al., 2011), secretions and excretions, it persists in the oesophageopharyngeal (O/P) mucosa of 50% or more of individual buffalo, i.e. carriers, for a variable period. Some individuals may remain carriers for periods of 5 years or more. However, it has been shown experimentally that carriers rarely transmit SAT viruses to cattle with which they have been in close contact for periods of several months (Thomson & Bastos, 2004a). Transmission of SAT viruses to cattle by carrier buffalo is therefore inefficient at best.

The issue of carrier transmission between cattle is a contentious issue but it is clear that cattle are less effective carriers of FMD viruses than African buffalo. Nevertheless, up to 50% of cattle retain the infecting virus in the O/P mucosa for periods as long as 6 months and even longer in some circumstances. However, proof of carrier transmission between cattle, despite careful investigation, is lacking. For other ruminants where virus may persist in the O/P mucosa for shorter periods than in buffalo and cattle such as sheep and goats, the probability of ‘carrier’ transmission occurring is probably remote. However, the issue of carrier animals remains – probably unjustifiably – an important consideration in the international control of FMD (Arzt et al., 2011a).

The role of free-living wildlife other than buffalo in the maintenance and spread of FMD in southern Africa has important implications for management of the disease. A longitudinal study conducted in the Kruger National Park (KNP) in South Africa over a 10 year period has shown that impala (*Aepyceros melampus*) in some parts of the KNP regularly become infected by buffalo herds in the vicinity and that most of these
infections do not result in disease (Bastos et al., 2000; Vosloo et al., 2009). Furthermore, historical data suggest that on occasion in the past impala have been instrumental in transmitting the infection to cattle. This is an important factor in the management of FMD in southern Africa, especially in relation to design of fencing systems for separation of animal populations.

**PATHOGENESIS**

The pathogenesis of FMD has recently been reviewed in detail; these reviews not only reveal the complexity of FMD’s pathogenesis but identify many gaps in the level of present understanding – altogether 33 knowledge gaps are listed in the two papers – so a simple account of the pathogenesis of FMD is currently impossible (Arzt et al., 2011a; Arzt et al., 2011b).

The route of infection of cloven-hoofed animals, other than in pigs where it is generally oral (Terpstra, 19720), is thought to be respiratory. In cattle the tissues most consistently infected during the pre-viraemic phase of the disease are the epithelia of the naso-pharynx and larynx (Arzt et al., 2011a). It is therefore likely this is the primary replication site in ruminants.

The tissues of the naso-pharynx and FMD viruses have a complex relationship because not only does initial infection of ruminants take place there but the naso-pharynx is also the site of viral persistence in chronically infected animals (so-called carriers). Vesicle formation, cell lysis and significant inflammation occur at secondary replication sites (oral mucosa, skin of the horn hoof junction & skin of the teats) but not in the epithelium of the primary replication site. The cells which support viral replication are located in the basal layer of naso-pharyngeal epithelium. However, the mechanism by which viral replication occurs in the naso-pharyngeal epithelium without causing cell lysis is unknown; nor is there an explanation as to why virus can be readily cultured from pharyngeal scrapings (obtained using probing cups) that, in recently infected animals, may contain high levels of antibody (mainly IgA) directed against the infecting virus. In pigs, delayed clearance of viral RNA from pharyngeal and lymphoid tissues has been observed but that has not been shown for infectious virus (Arzt et al., 2011b). It is currently concluded that persistent infection of pigs does not occur or at least is not epidemiologically important.

One or two days before the onset of clinical signs, cattle and pigs develop viraemia which may endure for up to 3 days. The source of virus in the circulation remains a matter of conjecture (i.e. another knowledge gap) but viraemia ensures distribution of virus to all parts of the animal’s body. In infected animals the vesicles which develop at the sites of secondary replication contain by far the highest levels of infectivity; however, high concentrations of virus can also be found in lymph nodes, myocardium, lungs and skin even in the absence of obvious lesions (Burrows et al., 1981; Zhang & Alexandersen, 2004; Arzt et al., 2010). Virus may also accumulate in the spleen, liver, adrenals, myocardium, pancreas, thyroid and mammary glands. In mammary tissue and myocardium, however, viral replication occurs in secretory epithelial cells of the alveoli and myocytes respectively, resulting in clear microscopic lesions.
There is an association between FMDV and dendritic cells in lymph nodes that results in localization of virus in germinal centres but the details of this association remain to be elucidated (Arzt et al., 2011a).

Epithelial lesions at secondary replication sites are initiated by infection of single cells in the stratum spinosum (Woodbury, 1995). Following infection of these cells, bullae develop either by lysis of cells swollen as a result of ballooning degeneration and the release of intracellular fluid, or by the formation of areas of focal intercellular oedema. The bullae then coalesce, rupture or, more rarely, the fluid seeps away resulting in desiccation of the lesion.

Development of characteristic vesicular lesions in FMD is dependent on persistent local irritation or friction. In transplantation studies in guinea pigs it was shown that epithelium from predilection sites grafted to other body areas lost that predilection and vice versa (Platt, 1960). This explains why the mouth, feet and teats are predilection sites for the development of lesions and why pigs often develop lesions on the dorsum of the snout, i.e. as a result of “snuffling”. Similarly, warthog which often “kneel” on their carpal joints while feeding tend to develop lesions on their “knees”.

In various parts of the world including South America, East Africa and India/Pakistan, a heat-intolerance syndrome (sometimes referred to as ‘hairy panters’) has been associated with previous infection or ‘chronic FMD’, with a putative endocrine-related pathogenesis. The limited information available on this syndrome has been reviewed recently indicating that the extent of the syndrome’s association with FMD remains speculative (Arzt et al., 2011b).

**Immunity**

The immune response of domestic animals to FMD is characteristically ephemeral and this, together with the wide immunological diversity of FMD viruses (SAT serotypes particularly) often results in ineffective herd immunity following vaccination and even following disease outbreaks.

Although the responses of very young piglets and calves differ from those of more mature animals, they are immunologically competent to FMD viruses from an early age. The poor antibody responses of calves and piglets to immunization are probably due more to immunological interference by colostral antibody than to immunological immaturity.

Cattle are immune to re infection with homologous virus for one to three years, and occasionally for up to 4.5 years (Bachrach, 1968). Circumstantial evidence suggests that the duration of immunity after infection with SAT serotypes may be shorter. The duration of immunity in other domestic species is largely unknown, but it is probably shorter than in cattle.
Tongue lesions commence as blanched foci which develop into vesicles containing serous fluid.

Ruptured vesicles lead to the appearance of irregular erosions with serrated edges.

Since recovery from infection with FMD is the rule, little attention has been paid to the immunological mechanisms involved in recovery from infection. Conversely, since it is clear that the level of neutralizing antibody in the circulation correlates with resistance to infection or re-infection in immunized and recovered animals respectively, the humoral immune response and the antigens which are able to induce it have been better studied. The relationship between neutralizing antibody activity and the degree of resistance to infection is, however, not simple and depends on the virus serotype as well as in immunized animals the period between immunization and exposure to infection. It is important to appreciate that vaccinal immunity may not prevent infection but it rather prevents subsequent spread within the body of infected animals. Thus FMD vaccines do not induce so-called sterile immunity (Thomson & Bastos, 2004a).

The antibody response to FMDV is T cell dependent (Francis et al., 1987). However, since different species recognize different determinants as T cell recognition sites, not all FMDV antigens are equally immunogenic in different species.

**DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS**

**Clinical signs & pathology**

In cattle and pigs the clinical diagnosis of FMD is usually not difficult because the signs and lesions are characteristic and consistent. However, in some situations where livestock are raised in extensive
Foot-and-Mouth Disease (FMD) systems the clinical signs may be mild and therefore detection of diseased animals may be difficult. Indigenous cattle breeds in southern Africa are also thought to have some innate resistance to development of disease but this is unproven. In other species such as sheep, goats and African wildlife, clinical diagnosis may also be difficult because the signs are often less pronounced or even unapparent (Arzt et al., 2011b).

FMD is characterized by development of vesicles, which soon rupture leaving erosions, in the mouth, including the tongue (but not the ventral surface of the tongue), and at the skin-hoof junction of the feet. However, before that occurs, affected animals develop fever, lose their appetite and the milk production of dairy cows declines sharply. Abortion may result from infection with FMD viruses and is thought to occur more frequently in sheep than other species (Arzt et al., 2011b). Affected animals may lie down continuously, evidence pain when walking or show lameness in one or more legs. The lesions in the mouth frequently result in salivation, which in southern African conditions, is often not copious (as often depicted in popular photographs), and grinding of the teeth or ‘lip smacking’. In the extensive farming systems of sub-Saharan Africa cattle herds afflicted by FMD may show remarkably few signs. In such situations it requires an experienced eye, detailed physical inspection and sometimes even serology to detect the presence of FMD. This was apparently the situation associated with the FMD outbreak that was identified in northern KwaZulu-Natal in March-April 2011.

Epithelial separation can leave lesions on the tongue up to 60mm in diameter

Older tongue lesions with debris that accumulated in the centre where epithelialisation is not yet complete
A healed FMDV-induced tongue lesion showing the absence of regeneration of tongue papillae

Cows may develop vesicles and erosive / ulcerative lesions on the teats and udder

In all species foot (claw) lesions develop in the skin of the interdigital space and at the bulbs of the heel and coronet. As in the mouth these are vesicles which soon rupture to form erosions

Ring lesions on the claw of a bovine that recovered from FMD showing the separation between the new outgrowing tissue and the horn of the hoof that were present distal to the coronet prior to lesion development
In cattle a mucoid nasal discharge develops that later becomes mucopurulent.

Mouth lesions are generally less common and less pronounced in sheep.

Clinical signs in antelope species are similar to lesions observed in cattle.

FMDV-induced lesions on the dental pad and lips of an impala.
As the new horn grows down inside the old it may appear as if the animal is wearing ‘slippers’

Severe lesions at the skin-hoof junctions of an impala in the Kruger National Park, South Africa

An early sign of the presence of FMD may be the sudden death (due to myocarditis – ‘tiger-heart’ disease) of neo-natal animals. However, neonatal myocarditis appears to be an infrequent occurrence with SAT infections. Sudden death of young calves, lambs or piglets is sometimes what farmers notice first in an outbreak. The hearts of such animals may have visible grey streaks in the myocardium.

Video link: http://www.youtube.com/watch?v=P3N0KBtiZN0&feature=youtu.be
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In pigs especially, severe cases of FMD may result in the sloughing of the hooves of one or more feet causing obvious severe pain. Furthermore, secondary bacterial infection of foot lesions leading to severe and debilitating lameness, especially when animals are kept in unhygienic conditions, may occur. Foot lesions, in any case, heal more slowly than mouth lesions.

Early vesicular lesions on the snout of a pig

In pigs lesions may occur on the snout whereas in other species lesions on the muzzle are rare

Pigs often develop lesions at the base of the supernumary digits

Feet lesions in pigs are often severe and are likely aggravated by the nature of the floor surfaces on which pigs are kept

Most animals recover uneventfully from FMD within 10-21 days of disease onset.

**Laboratory diagnosis**

Because of the potentially serious implications that a diagnosis of FMD may have and the importance of an accurate understanding of the virus/viruses involved in FMD outbreaks, it is essential that clinical
diagnoses are confirmed by follow-up laboratory testing. Furthermore, recognition of the FMD disease-free status of countries and/or zones can only be achieved through surveillance dependent on laboratory testing.

The recommended tests for FMD diagnosis and surveillance are described in detail in the chapter on FMD in the OIE (World Organisation for Animal Health) ‘Manual for Diagnostic Tests and Vaccines for Terrestrial Animals’ (www.oie.int).

The best source of material for diagnosis of FMD and characterization of the viruses involved is fragments of epithelium from freshly-ruptured vesicles in the mouths or on the feet of affected animals. These are only available for a day or two following rupture of the vesicle and for that reason acute cases are the best source of diagnostic material. The epithelial fragments need to be kept cool in a buffered solution (pH 7.2-7.4) and transported to a recognized and suitable equipped laboratory as soon as possible. Such fragments usually contain high levels of infectivity and for that reason the outer surfaces of containers and packaging need to be properly decontaminated prior to dispatch (Thomson & Bastos, 2004a).

A number of techniques can be applied for the laboratory analysis of epithelial fragments including:

- direct sero-typing of the virus(es) using ELISA systems (kits are available) on suspensions prepared from vesicle fragments;
- isolation of the virus(es) involved using appropriate cell cultures followed by genomic and antigenic analysis of the cultured viruses;
- direct rt-PCR on the epithelial material and sequencing of the PCR product; from that the serotype and genotype can be determined and phylogenetic relationships with other viruses within the serotype inferred.

It is important to understand that sero-typing alone rarely provides information adequate for rational management of FMD; for that reason further analysis to identify the relationship of outbreak viruses and comparison with other viruses of the same serotype is essential.

Detection of antibodies to FMD (in reality to different functional parts of the FMD virion [virus particle]) is also vital for diagnosis and surveillance of FMD. This is a complex field and the type of test most appropriate for a particular field situation varies. Essentially the following types of test are commonly used:

- ELISAs for the detection of antibodies to structural viral proteins (SP tests);
- ELISAs for the detection of antibodies to one or more of the non-structural viral proteins (NSP tests);
- virus neutralization (VN) tests;
immuno-blot (western blot or ‘EITB’ tests) are sometimes used instead of NSP ELISAs.

As long as vaccines used in particular localities are ‘purified’ (i.e. NSPs are removed from the vaccine), serological systems can be designed to differentiate antibody responses of vaccinated cattle from those that follow infection (so-called DIVA systems). However, for SAT viruses the systems presently available commercially may have low sensitivity and, for that reason, should be applied with circumspection.

For identification of persistently infected (carrier) animals a ‘probang’ may be inserted into the oropharynx of the animal concerned to recover epithelial cells and secretions from that region. From such samples viruses may be recovered or, alternatively, rt-PCR can be performed on the recovered material and the product so derived further analysed to establish the presence of FMD virus. For more detail on this see Thomson & Bastos (2004a). It is important to understand that the presence of virus in the oropharynx of carrier animals may only be detectable intermittently and that in any case the quantities are invariably low. Hence such testing, even in the hands of experienced veterinarians, has low sensitivity.

Differential diagnosis

Especially in pigs, there are other viral infections that cause vesicular disease that cannot be differentiated clinically from that caused by FMD, viz. swine vesicular disease (SVD), vesicular
exanthema (VE) and vesicular stomatitis (VS) (Thomson & Bastos, 2004a). Of these SVD could potentially occur almost anywhere because it is a specific pathogen of pigs. The natural host of VE virus, on the other hand, is sea-lions. In the 1960s it caused serious outbreaks in the USA resulting from pigs being fed discarded material from fisheries. Vesicular stomatitis is an arthropod-transmitted virus which affects cattle and horses predominantly and is native to tropical and sub-tropical Americas and, so far, nowhere else.

There are also toxins which may produce vesicular lesions that can be confused with FMD — see Thomson & Bastos, 2004a.

**CONTROL**

How FMD is best managed depends on (1) the epidemiological situation and (2) rural development policies (livestock development and wildlife conservation in particular) in the locality (region or country) concerned. Generic international standards and recommendations are available on the OIE website ([www.oie.int](http://www.oie.int) – Animal Health Code for Terrestrial Animals; FMD chapter) but these cannot cover all situations throughout the world. For that reason, management of FMD – which is usually the responsibility of the official veterinary service of the country – needs to be carefully considered in the light of the above two factors. As an example, while many countries of the world aim at establishing and maintaining freedom of the country (or one or more zones within it) from infection with FMD viruses, that is exceptionally difficult for many parts of southern and eastern Africa because wildlife populations maintain SAT serotypes, rendering eradication impossible unless buffalo were to be removed. Thus, in parts of sub-Saharan Africa, eradication or even creation of effective FMD-free zones, is not presently feasible and alternative approaches to manage the disease impacts are necessary.

In sub-Saharan Africa FMD may be endemic as a result of two situations, i.e. where SAT serotype infection is maintained by wildlife populations (African buffalo being crucial in this respect) or where infection with SATs or other serotypes (A or O) is maintained by cattle populations. Of course, both may occur in the same locality.

There are presently only 3 interventions practiced in sub-Saharan Africa against FMD:

- Vaccination of domestic animal populations (usually only cattle) in which infection with one or more (usually several) serotypes is endemic or where the cattle population is at risk of infection from sympatric or nearby wildlife populations;

- Separation of infected or high-risk populations of wildlife and/or domestic livestock from uninfected populations; enabled through fencing systems;
Careful management of the movement of animals and animal products between localities of different FMD-status or FMD-risk; usually effected through permit systems operated by the official veterinary service of the country concerned.

The OIE recognizes two types of FMD-freedom for both countries and zones, viz. freedom where vaccination is practiced or is not practiced. However, so far, although some southern African countries (i.e. Botswana, Namibia, South Africa) have zones recognized as FMD-free where vaccination is not practiced, no country of the Region has attempted to gain recognition of freedom from FMD where vaccination is applied (see Animal Health Code for Terrestrial Animals, FMD Chapter - www.oie.int). In other parts of the world this has been done.

Because pigs excrete large quantities of FMD virus, especially in the case in large piggeries which may contain many thousands of pigs, prevention of pigs becoming infected is vital in the control of FMD. For that reason the feeding of swill or at least untreated swill is illegal in most countries.

Vaccines and vaccination

Presently all vaccines used around the world (with the possible exception of China) are inactivated, i.e. they contain viruses grown in cell cultures, concentrated and chemically ‘killed’ using an aziradine compound. Increasingly, ‘purified’ vaccine is being manufactured, i.e. the NSPs are removed which enables application of DIVA systems (see above). The other important component of FMD vaccines is the
adjuvant. Traditionally, the adjuvant of choice is a composite of aluminium hydroxide (alum) and saponin (an extract of tree-bark with surface-active properties). However, various oil emulsions are increasingly replacing the traditional adjuvant because they may stimulate longer-lasting antibody responses.

As is the case for many inactivated vaccines, establishment of effective primary immunity using alum/saponin-adjuvanted vaccine requires two inoculations of vaccine initially 2-8 weeks apart. Ideally, vaccine should only be administered to calves that have lost maternally-acquired antibodies to FMD virus. These antibodies may persist in calves for up to 6 months of age. Thereafter, booster doses need to be applied at least bi-annually and more frequently in high risk situations. However, once cattle are 4-5 years old, annual revaccination is normally adequate. Thus young animals may need to be vaccinated 4-5 times a year which is logistically taxing and expensive. Alum/saponin-adjuvanted vaccines are ineffective in pigs.

It is frequently overlooked that the aim of prophylactic vaccination is to generate a level of herd immunity (HI) that will reduce the reproductive number of an infection to less than 1. If this is achieved any infection introduced into the vaccinated population will not be able to sustain itself even though one or more animals may become infected. However, the level of HI required for FMD under southern African conditions is yet to be determined. It is, nevertheless, generally agreed that HI levels of 70-80% are likely to be adequate (Thomson & Bastos, 2004a). Generating such HI levels is extremely difficult for two reasons: (1) the immunological relationship (degree of matching) between field viruses and viruses incorporated into the vaccine may be poor and (2) very often the way vaccine is stored, handled and administered in the field is less than optimal. This means that expensive vaccination programmes frequently do not achieve the required HI level. For that reason monitoring of vaccination programmes is vital but, unfortunately, rarely conducted effectively. Without auditing of vaccination programmes and addressing the deficiencies identified, it is impossible to be sure that expensive and logistically complicated vaccination programmes are worthwhile.

Recent investigation has shown that the current common practice in southern Africa of immunizing high-risk cattle populations at 6-monthly intervals is inadequate to generate levels of HI with currently available vaccine. Trials to establish more cost/effective schedules are being planned. In the meantime, advice should be sought from vaccine manufacturers when it comes to devising immunization schedules.

MARKETING AND TRADE / SOCIO-ECONOMICS

More than any other animal disease, FMD has its major impact on trade; FMD status determines to a remarkable degree whether animals and animal products derived from specific locations can gain access to regional and international markets. Bearing in mind that FMD is generally not a lethal disease, vaccines and other control measures are available and, currently, the disease is not globally eradicable (despite what some international organizations propagate in this respect), the present approach is not rational. It
also needs to be acknowledged that import bans on products due to the ostensible risk of importing FMD have often been used as a (unjustifiable) non-tariff trade barrier.

FMD’s reputation as a devastating disease is derived largely from experiences of the developed world in the late 19th and early 20th Centuries when it was found that developing intensive production systems were uneconomic in the face of repeated outbreaks of FMD. Countries in North America, western Europe and the Pacific Rim began to develop eradication strategies that were bye-and-large successful, albeit expensive and logistically difficult. At the same time, care was taken to ensure that FMD viruses were not reintroduced from outside the country and from there it was a short step to insisting that animals and animal products were only imported from countries and regions free from FMD. This meant that any locality where FMD was endemic was excluded from exporting animals and their products to high-value markets. This stance was to some extent ameliorated by permitting countries to establish FMD-free zones (regions) from which exports were permitted and some southern African countries continue to exploit this opportunity. However, the presence of wildlife populations in or near livestock farming areas precludes this approach for many localities in eastern and southern Africa. The situation is, furthermore, likely to deteriorate because of biodiversity conservation initiatives based on TFCAs which seek to re-establish the connectedness and migration patterns of wildlife populations (SADC, 2008). Therefore, the historic clash between livestock development and conservation in southern Africa will likely exacerbate in future unless new approaches are developed.

In an attempt to address this problem in sub-Saharan Africa it has been proposed that risk management can be made more effective through a commodity-based approach (Thomson et al., 2004b). This is founded on the concept that the risk of spreading FMD and other transboundary animal diseases can be achieved through ensuring that traded products of animal origin are produced in ways that minimize the risk of their spreading FMD or other infectious agents. This need not necessarily be dependent on the FMD status of the source location (although, of course, only products derived from healthy animals may enter the human food chain). Basically there are more ways of managing risk of food products posing a minimal FMD risk than sourcing them from FMD-free localities. The case for de-boned beef being a ‘very safe’ commodity in respect of FMD and other transboundary animal diseases has been addressed in a scientific publication (Thomson et al., 2009) and a report conducted on behalf of the OIE (Paton, 2010). This has been accepted by the OIE which provides an international standard through which export of deboned beef from cattle and domestic buffaloes (Bubalis sp.) can be traded safely (Article 8.5.25 of Terrestrial Animal Health Code – www.oie.int). The same principle can be applied to many dairy and other processed meat products (Thomson et al., 2004b).

The commodity-based trade approach has two important potential effects; increasing access to regulated markets for products derived from livestock and wildlife and rendering livestock production and biodiversity conservation more compatible.
IMPORTANT OUTBREAKS

For reasons that are probably complex, FMD outbreaks in cattle in southern Africa have increased in frequency since the turn of the 21st Century. In the period 1981-2000 a significant decrease in the occurrence of FMD outbreaks in Botswana and South Africa was evident but in the period 2001-2010 the situation deteriorated significantly (Fig. 7). The reasons for this pattern of events are probably multifactoral.

Most recent SAT outbreaks have occurred in or near to the Kavango-Zambesi Transfrontier Conservation Area (KAZA TFCA – by far the largest in southern Africa) and the Greater Limpopo TFCA. About 1.5 million people and their livestock live in KAZA TFCA which is about 440 000 km² in extent and incorporates parts of 5 countries. This area also has a large (about 250 000) and growing elephant population which places increasing pressure on existing and planned fences designed to assist in controlling FMD. Some of the recent outbreaks have also proven difficult to manage, e.g. the so-called Habu outbreak in Ngamiland (northern Botswana) in 2008 persisted for about two years despite repeated rounds of vaccination. Spread of this outbreak south of the Kuki fence, i.e. into the Ghansi District – part of Botswana’s recognized FMD-free zone – resulted in temporary suspension of all Botswana’s beef exports to the European Union in 2009.

In 2011 an outbreak of FMD occurred in northern KwaZulu-Natal which apparently produced little clinical disease although SAT1 viruses were isolated from cattle with clinical disease (Fig. 8). At roughly the same time infection with SAT3 virus was detected in buffalo in the Ndumu Game Reserve which lies within the area of the cattle outbreak. This buffalo population was previously free from FMD.
Unfortunately, little official information on these events has so far been provided by South Africa’s Directorate of Veterinary Services but laboratory data indicate that the viruses were related to SAT1 viruses endemic to the Kruger National Park (KNP) area and, more distantly, to viruses in southern Zimbabwe. Similarly, the SAT3 viruses obtained from the Ndumu game reserve buffalo are related to SAT3 viruses from the KNP and southern Zimbabwe. There is no direct connection between the KNP or southern Zimbabwe and northern KwaZulu-Natal. Therefore, how these SAT1 and SAT3 viruses spread to northern KwaZulu-Natal is not obvious (Fig. 8).

![Map of South Africa showing the area where serological evidence of SAT1 infection in cattle was detected in 2011 & the consequent infection and protection zones](image)

**Fig 8:** Map of South Africa showing the area where serological evidence of SAT1 infection in cattle was detected in 2011 & the consequent infection and protection zones.

Also in 2011, Botswana suffered 3 SAT2 outbreaks in cattle – one in Ngamiland and the other two at locations close to one another on the border with Matabeleland South (Zimbabwe), i.e. in Botswana’s Zones 6 and 7. Viruses involved in the two Botswana outbreaks on the Zimbabwean border could not so far be matched with SAT2 viruses isolated in Matabeleland South in 2010 (Quarterly reports of the FAO World Reference Laboratory for FMD; Pirbright Laboratory - [www.wrfmd.org](http://www.wrfmd.org)). Strangely, however, the Botswana SAT2 outbreak viruses from Zones 6 and 7 were closely related to viruses that caused
outbreaks in Gaza and Maputo Provinces of Mozambique in 2010; possibly spread from Chicualacuala which is on Zimbabwe’s south-eastern border.

Collectively, the FMD incidents summarized above are indicative of a rapidly worsening FMD situation in southern Africa in the last 10-11 years. This is clearly a serious regional problem.

There have been assertions that inability to prevent and manage SAT2 outbreaks in the recent past in southern Africa was due to poor vaccine performance – possibly as a result of poor matching between vaccine strains and field viruses. However, it is clear from investigations conducted on behalf of the Food, Agriculture & Natural Resources (FANR) Directorate of the SADC Secretariat and the Food & Agriculture Organisation (FAO) that poor vaccine administration and inadequate application of other zoosanitary control measures (including management of animal movement) were also important factors in the occurrence and persistence of these outbreaks (SADC, 2010). Nevertheless, recent evidence for greater antigenic variation occurring within the SAT2 serotype as compared with SAT1 has been provided despite the fact that the range of amino acid variation within the genomes of the two serotypes were similar (Maree et al., 2011). This may provide the technical basis for better understanding why SAT2 outbreaks have generally occurred more frequently and proven more difficult to control than outbreaks caused by SAT1 and SAT3 viruses.

FAQs

1. **Why is FMD such an important disease if it does not affect humans and is not generally a lethal infection of animals?**

   The answer to this question is subjective because it is often held that because the disease is capable of rapid spread over long distances (highly contagious) and, because of the diversity of FMD viruses with little or not cross protection, the disease is very difficult to manage under intensive farming conditions that prevail in the developed world. Therefore, North America, most of Europe and some Pacific Rim countries spent huge amounts of money, time and effort in eradicating FMD and go to great lengths to prevent its re-introduction.

   On the other hand, in extensive farming regions, such as in most of sub-Saharan Africa, FMD often spreads slowly and has limited impact on either wild or domestic animals. These regions are usually arid and so the people there are very dependent on livestock production and export of live animals and meat. However, international trade regulations and conventions prohibit the export of livestock and meat from FMD endemic areas to high value markets in North America, Europe and Japan. Thus FMD has huge impact on the ability of developing countries to access markets where good prices can be obtained.
So the importance of FMD is largely determined by the reaction of governments and trading organisations to it rather than the direct effects of the disease. In other words, it’s not so much the disease that determines FMD’s importance but man-made rules that do not always make technical or economic sense.

2. **What is the role of wildlife in the maintenance and spread of FMD?**

In most of the world FMD viruses infrequently spill over from domestic animals into wildlife populations but, so far, wildlife such as gazelles and deer have not proven capable of maintaining FMD viruses independently of livestock. In sub-Saharan Africa the situation is different because there is good evidence that the three SAT serotypes of FMD virus co-evolved with African buffalo over a wide area of the subcontinent. These SAT viruses can also infect livestock, cattle particularly, as well as other cloven-hoofed wildlife. The evidence is that only buffalo and cattle are able to maintain SAT serotypes independently of other species.

African buffalo therefore play a central role in the maintenance and spread of FMD. Most free-living buffalo populations are infected with the SAT viruses although a few were historically free from infection such as those of the Addo Elephant Park (Eastern Cape) and northern Zululand (South Africa). Breeding programmes of captive buffalo can be used to raise FMD-free buffalo and this was widely done in Zimbabwe initially and later in South Africa.

3. **Can FMD affect people?**

People are essentially not susceptible to infection with FMD viruses. However, there are reports in the scientific literature of people being infected with FMD viruses and so it is impossible to be dogmatic on the issue. If people do become infected it is exceedingly rare and the lesions it causes are not life-threatening. Therefore FMD in people has little if any practical importance. Most reports of FMD in people are related to hand, foot and mouth disease virus, a common infection of children especially in institutions such as nurseries and schools (see below).

4. **What is the relationship between foot and mouth disease (FMD) and hand, foot and mouth disease (HFMD)?**

Although both these diseases are caused by viruses within the same family (Picornaviridae) they belong to different genera. There is therefore no real connection between the two diseases at all; HFMD affects humans only while FMD is a disease of animals that does not affect people or, if it does, only in the most exceptional circumstances.

5. **Are there treatments or vaccines available for used against FMD?**

There are currently no drugs commercially available that can be used to treat animals suffering from FMD. However, it is likely that in future they will become available.
Vaccines to prevent the disease in animals are available but even the best FMD vaccines are not very effective because: (1) there are so many different variants of FMD viruses (7 serotypes with many variants within each serotype) that provide little or no cross protection and (2) the vaccines induce immunity which is of short duration unless animals have been vaccinated repeatedly.

Because FMD is considered a very serious problem the use of drugs or vaccines against FMD are usually strictly controlled by most governments, i.e. these are not generally available for farmers to administer.

REFERENCES


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