Foot-and-Mouth Disease (FMD)

Author: Prof Gavin R Thomson

Licensed under a Creative Commons Attribution license.

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 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](http://www.youtube.com/watch?v=P3N0KBtiZN0&feature=youtu.be)

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](http://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-blots (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.
A probang cup is used to collect tissue scrapings from the oropharynx for laboratory identification of animals persistently infected with FMD virus.

**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.