Chapter 3.1.8.

Foot and mouth disease (infection with Foot and Mouth disease virus)

SUMMARY

Foot and mouth disease (FMD) is a ~~the most~~ contagious disease of mammals and has a great potential for causing severe economic loss in susceptible cloven-hoofed animals. There are seven serotypes of FMD virus (FMDV), namely, O, A, C, SAT 1, SAT 2, SAT 3 and Asia 1. Infection with one serotype does not confer immunity against another. FMD cannot be differentiated clinically from other vesicular diseases, such as swine vesicular disease, vesicular stomatitis and vesicular exanthema. Laboratory diagnosis of any suspected FMD case is therefore a matter of urgency.

Typical cases of FMD are characterised by a vesicular condition of the feet, buccal mucosa and, in females, the mammary glands. Clinical signs can vary from mild to severe, and fatalities may occur, especially in young animals. In some species the infection may be subclinical, e.g. African buffalo (Syncerus caffer). The preferred tissue for diagnosis is epithelium from unruptured or freshly ruptured vesicles or vesicular fluid. Where collecting this is not possible, blood and/or oesophageal–pharyngeal fluid samples taken by probang cup in ruminants or throat swabs from pigs provide an alternative source of virus. Myocardial tissue or blood can be submitted from fatal cases, but vesicles are again preferable if present.

It is vital that samples from suspected cases be transported under secure conditions and according to international regulations. They should only be dispatched to authorised laboratories.

Laboratory diagnosis of FMD is by virus isolation or by the demonstration of FMD viral antigen or nucleic acid in samples of tissue or fluid. Detection of virus-specific antibody can also be used for diagnosis, and antibodies to viral nonstructural proteins (NSPs) can be used as indicators of infection, irrespective of vaccination status. Confirmation of a case of FMD should take account of all relevant clinical, epidemiological and laboratory findings.

**Identification of the agent:** The presence of FMD virus is confirmed by demonstration of ~~FMD viral~~ specific antigen or nucleic acid, ~~is sufficient for a positive diagnosis~~ with or without prior amplification of the virus in cell culture (virus isolation). Due to the highly contagious nature and economic importance of FMD, the laboratory diagnosis and serotype identification of the virus should be done in a laboratory with an appropriate level of bio-containment, determined by risk analysis in accordance with Chapter 1.1.4 Biosafety and biosecurity: Standard for managing biological risk in the veterinary laboratory and animal facilities.

Enzyme-linked immunosorbent assays (ELISA) can be used to detect FMD viral antigens and for serotyping. Lateral flow devices (LFD) are also becoming more readily available and can also be used to detect FMD viral antigens. The ELISA has replaced complement fixation (CF) in most laboratories as it is more specific and sensitive and it is not affected by pro- or anti-complement factors. If the sample is inadequate or the diagnosis remains uncertain, sample materials can be tested by reverse transcription polymerase chain reaction (RT-PCR) ~~and/~~or virus isolation using susceptible cell to amplify any nucleic acid or live virus that may be present. The cultures should preferably be of primary bovine (calf) thyroid, but pig, lamb or calf kidney cells, or cell lines of comparable sensitivity may be used. Once a cytopathic effect (CPE) is complete in the cultures, harvested fluids can be tested for FMDV using ELISA, CF or RT-PCR.

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b. DIAGNOSTIC TECHNIQUES

Table 1. Test methods available for the diagnosis of FMD and their purpose

| Method | **Purpose** | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| Population freedom from infection | Individual animal freedom from infection prior to movement | Contribute to eradication policies | Confirmation of clinical cases | Prevalence of infection – surveillance | Immune status in individual animals or populations post-vaccination |
| **Detection of the identification[[1]](#footnote-1)** | | | | | | |
| **Virus isolation** | – | + | +++ | +++(b) | – | – |
| **Antigen detection ELISA** | – | – | +++ | +++ | – | – |
| **CFT** | – | – | + | + | – | – |
| **LFD** | – | – | +++ | +++ | – | – |
| **Real-time  RT-PCR** | + | + | +++ | +++ | + | – |
| **RT-PCR** | + | + | +++ | +++ | + | – |
| **Detection of immune response** | | | | | | |
| **NSP Ab ELISA** | +++ | ++ | +++ | +++ | +++ | – |
| **SP Ab ELISA(a)** | ++ | ++ | +++ | +++ | ++ | +++ |
| **VNT(a)** | ++ | ++ | +++ | +++ | ++ | +++ |
| **AGID** | + | + | + | + | + | – |

Key: +++ = recommended method, validated for the purpose shown; ++ = suitable method but may need further validation;   
+ = may be used in some situations, but cost, reliability, or other factors severely limits its application;   
– = not appropriate for this purpose; n/a = purpose not applicable.

ELISA = enzyme linked immunosorbent assay; CFT = complement fixation test; LFD: lateral flow device;   
RT-PCR = reverse-transcriptase polymerase chain reaction; AGID = Agar gel immunodiffusion;  
NSP Ab ELISA= ELISA for antibodies against nonstructural proteins; SP Ab ELISA = ELISA for antibodies against structural proteins; VNT = Virus neutralisation test

(a)The test does not distinguish infected from vaccinated animals.  
(b)It is essential to confirm the presence of FMDV following virus isolation by an antigen or nucleic acid detection test.

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1. Detection of the agent

A range of sample types, including epithelium, OP samples, milk and serum, may be examined by virus isolation or RT-PCR. By contrast, ELISA CF and the lateral flow device are suited to the examination of epithelial suspensions, vesicular fluids or cell culture supernatants, but are insufficiently sensitive for the direct examination of OP samples or serum. It is essential to confirm the presence of FMDV following virus isolation by an FMDV-specific antigen or nucleic acid detection test. A virus isolate or an RT-PCR product can be further characterised by sequencing, but a viral isolate is needed for some *in-vitro* serological tests and for *in-vivo* studies of transmission, virulence and vaccine induced protection.

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1. A combination of agent identification methods applied on the same clinical sample is recommended. [↑](#footnote-ref-1)