Clinical variation in foot and mouth disease: cattle

R.P. Kitching

National Centre for Foreign Animal Disease, 1015 Arlington Street, Winnipeg, Manitoba R3E 3M4, Canada

Summary
Foot and mouth disease (FMD) in cattle is usually clinically obvious in the unvaccinated herds of countries in which the disease occurs only occasionally. However, in vaccinated herds and in some breeds indigenous to areas in which FMD is endemic, the disease may circulate undetected.

Keywords
Cattle – Control – Diagnosis – Foot and mouth disease.

Introduction

Foot and mouth disease (FMD) in the highly productive beef and dairy breeds of Europe, North America and Australasia is characterised by severe clinical signs. Index cases on farms exposed to low level aerosol virus may develop only mild or even subclinical infection, but as the virus replicates in the first infected animal and is produced in large quantities, so the remaining animals in the herd appear with multiple vesicles in the mouth and on the feet and udder. The disease is considerably less obvious in the breeds of cattle indigenous to Africa and Asia, where FMD is mostly endemic. However, FMD is also economically important in these regions, further reducing an already low milk yield, causing the death of young calves, and interfering with the function of adult cattle to pull a plough or cart.

Foot and mouth disease is caused by strains of seven immunologically distinct serotypes of virus and consequently, recovery from infection with a strain of one serotype does not provide protection against strains of the other six serotypes. In many of the FMD endemic regions, more than one serotype may circulate, creating waves of infection as different serotypes enter, infect the susceptible animals and then move on to reappear a few years later as a new susceptible population becomes established. Alternatively, one serotype may persist in a region and rarely appear clinically, producing only mild infection in the young stock as they lose their maternal antibody. Clinical disease may then only be seen when a new serotype is introduced.

Transmission

Foot and mouth disease is usually spread by the movement of infected animals. Susceptible cattle coming into contact with an infected animal, whether sheep, goat, pig or wildlife species may be infected by the respiratory route or through an abrasion on the skin or mucous membranes. Cattle are very susceptible by the respiratory route, requiring as little as 20 $TCID_{50}$ (tissue culture infective dose) of virus to establish infection, but may require 10,000 times more to become infected by the oral route (5). Calves drinking infected milk can be infected by insufflation of milk droplets as they drink. Of the domesticated susceptible species, cattle are the most likely to be infected by aerosol virus generated by other infected animals, particularly pigs, because of their larger respiratory volume when compared with small ruminants and their higher susceptibility by this route of infection compared with pigs (5). In 1981, cattle on the Isle of Wight in the United Kingdom (UK) were infected by windborne aerosol virus produced by infected pigs in Brittany, France and the virus was carried over 250 km across the English Channel. Infected cattle also produce up to $\log_{10}$ 5.1 $TCID_{50}$ of aerosol virus per day, and a large dairy herd could infect neighbouring herds with their combined output of virus (16). The transmission of FMD virus within an unvaccinated herd is usually rapid, as was seen during the recent outbreak in the UK in which over 90% of a group could be showing clinical signs by the time disease was first identified (1). Even within a vaccinated herd, the aerosol production of virus from a single infected animal can overcome the immunity of others in the herd resulting in a further increase in the level of challenge and the appearance of clinical disease. Milk and semen from

infected cattle may contain virus up to four days before the onset of visible signs. By the time clinical signs appear, the virus titre peaks at $\log_{10}$ 6.7 $TCID_{50}$ per ml of milk and $\log_{10}$ 6.2 $TCID_{50}$ per ml of semen (5). Urine may contain $\log_{10}$ 4.9 $TCID_{50}$ per ml and faeces $\log_{10}$ 5.0 $TCID_{50}$ per gram (10).

More than 50% of cattle that have recovered from infection with FMD virus and vaccinated cattle that have had contact with live virus become carriers (15). The FMD virus persists particularly in the basal epithelial cells of the pharynx and dorsal soft palate (17), and can be recovered from some animals for over three years, although the carrier state does not usually extend beyond a year (15). The significance of the carrier animal in the epidemiology of FMD is not clear and is discussed in another paper in the present book (11).

Clinical signs

The incubation period for FMD in cattle is between two and fourteen days, depending on the infecting dose, the strain of virus and the susceptibility of the individual host. Typically, between-farm transmission has a longer incubation period, but once the quantity of virus in the environment increases on an infected farm, the incubation period reduces. Following an initial pyrexia in the region of 40°C, lasting one or two days, a variable number of vesicles develop on the tongue, hard palate, dental pad, lips, gums, muzzle, coronary band and interdigital space. Vesicles may also be seen on the teats, particularly of lactating cows. Young calves may die before the appearance of vesicles because of the predilection of the virus to invade and destroy cells of the developing heart muscle.

Acutely infected cattle salivate profusely (Fig. 1) and develop a nasal discharge, at first mucoid and then mucopurulent, which covers the muzzle. They stamp their feet as they try to relieve
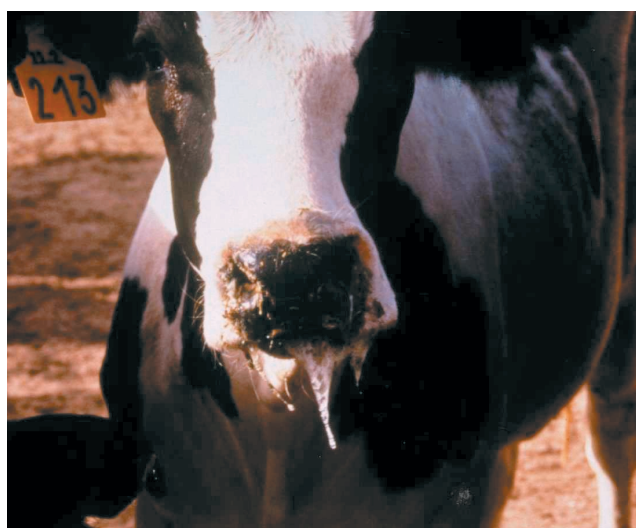

Fig. 1
Young bovine with foot and mouth disease
Courtesy of J. Fishwick

the pressure on first one foot and then another. They may prefer to lie down and resist attempts to raise them. Lactating cattle with teat lesions are difficult to milk and the ruptured vesicles frequently become infected, predisposing to secondary mastitis. The vesicles in the mouth rupture rapidly, usually within 24 hours, leaving a shallow erosion surrounded by shreds of epithelium. The vesicles on the tongue frequently coalesce and a large proportion of the dorsal epithelium may be displaced (Fig. 2). The vesicles on the feet may remain intact for two or three days before rupturing, depending on the terrain or floor

Fig. 2
Cow with ruptured tongue vesicle, two days after start of clinical signs of foot and mouth disease

surface of the cattle accommodation. Healing of the mouth lesions is usually rapid: the erosions fill with fibrin and by day 11 after vesicle formation, they appear as areas of pink fibrous tissue, without normal tongue papillae (Fig. 3). Healing of the ruptured vesicles on the feet is more protracted and the lesions are susceptible to secondary bacterial infection, sometimes resulting in under-run sole and chronic lameness (Fig. 4).

Affected cattle quickly lose condition and the drop in milk yield can be dramatic and will not recover during the remaining lactation. Secondary bacterial mastitis is common. Yearling cattle may fail to fully recover their production potential, due to damage of glandular tissue such as thyroid and some have been referred to as 'hairy panters' because of changes to their coat and what appears to be impaired respiratory function, although the pathological changes are not well documented (10).

Intensive vaccination does not always prevent the appearance of clinical FMD. Some very high yielding dairy herds in the Middle East are vaccinated every ten weeks with vaccine produced under European standards containing eight strains of FMD virus (8). However, because of the severe challenge originating predominantly from the nomadic herds of sheep, goats and cattle which graze freely in the area, introduction of virus into the dairies is inevitable. When these dairy cattle become infected, they frequently exhibit a very severe form of

Rev. sci. tech. Off. int. Epiz., **21** (3)

501

a) Appearance of lesion eleven days after the start of clinical signs

b) Healing tongue lesion four days after the start of clinical signs

Fig. 4
Ruptured vesicle on foot, five days after the appearance of clinical signs

Fig. 3
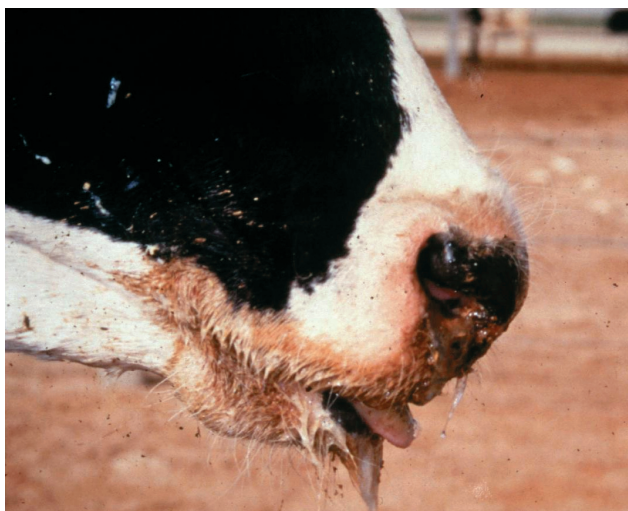**Tongue lesions on a cow after the start of clinical signs of foot and mouth disease**

Fig. 5
Protruding tongue of a vaccinated cow affected with foot and mouth disease
Courtesy of J. Fishwick

disease, in which the tongue swells and protrudes from the mouth (Figs 5 and 6), and the majority of the tongue epithelium is shed. The clinical impression is of a hypersensitivity reaction to the viral antigen, but there have been no pathological studies to confirm this hypothesis.

The recognition of FMD following the introduction of virus into a vaccinated herd has been examined in detail using data from the large dairy herds in the Middle East (8). The data show that in herds that had only recently been vaccinated, disease was usually first apparent in a large number of infected animals, because the high level of immunity within the herd kept the clinical disease suppressed and the virus circulated subclinically until the level of viral challenge had reached a sufficiently high level. This level of virus within the herd environment overcame the vaccinal immunity of a large group of animals throughout the herd. In herds with lower levels of immunity, the first appearance of disease was frequently only in a single animal and if surveillance within the herd was good, a rapid response by re-vaccinating the herd would bring the outbreak under control.

Fig. 6
Lesions on the tongue of a vaccinated cow affected with foot and mouth disease
Courtesy of J. Fishwick

Pathology

The FMD virus replicates at the site of entry, either in mucosa and lymphoid tissue of the upper respiratory tract or in the dermal and subdermal tissue of a skin abrasion (10). The virus enters the blood circulation as free virus or associated with mononuclear cells and is distributed around the body to glandular tissue and predilection sites in the stratum spinosum, where secondary replication occurs. The cells of the stratum spinosum undergo ballooning degeneration and as the cells rupture and oedema fluid accumulates, vesicles develop which coalesce to form the aphthae and bullae that characterise FMD (10). The squamous epithelium of the rumen, reticulum and omasum may also develop gross lesions. In young animals, the virus invades the cells of the myocardium and macroscopic grey areas may be observed, particularly in the wall of the left ventricle, which appears striped (tiger heart). Cells of the skeletal muscle may also undergo hyaline degeneration (10).

Diagnosis

Initial diagnosis is usually made on the basis of clinical signs, with or without a history of contact between the herd and an infected animal, or report of FMD in the vicinity. In a fully susceptible herd, the clinical signs are frequently severe and pathognomonic. However, in endemic regions in cattle that have partial natural or vaccinal immunity, clinical signs may be mild and may be missed. In 1999, infection of Chinese yellow cattle in Taipei China with the pan-Asian type O virus failed to cause clinical disease and was only detected by routine probang sampling, after the virus had already been introduced onto the island (6). These cattle were still able to transmit the virus to other susceptible in-contact animals, in spite of the subclinical nature of their infection. Similarly, Brahman cattle in Zimbabwe were responsible for introducing FMD, serotype South African Territories (SAT 2) into a pedigree cattle show in Bulawayo in 1989, having been noticed as only slightly lame during the pre-show inspection.

The success of the laboratory confirmation of a presumptive diagnosis of FMD depends on the submission of adequate material, sent under suitable conditions. A minimum of 2 cm^2, of epithelium from a ruptured vesicle in a 50/50 mixture of glycerine and 0.04 molar buffered phosphate (pH 7.4-7.6) should be sent to a laboratory designated for handling live FMD virus and equipped with the necessary reagents for typing a positive sample. Whole and clotted blood samples and probang samples may also be sent.

The diagnostic procedures employed have been described in another chapter in this book (13).

Antibodies to FMD virus can be detected in the milk of cattle that have recovered from FMD, using either the liquid phase blocking enzyme-linked immunosorbent assay (ELISA) (LPBE)

or a specific isotype assay (SIA) for bovine immunoglobulin G1 (IgG1) (2). However, whereas the LPBE would not detect antibodies derived as a consequence of vaccination, the SIA was able to identify 95% of cattle vaccinated up to twelve months previously, in the study reported. There was also a strong correlation between serum antibody titres and milk antibody titres (3), to the extent that individual and herd immunity levels against FMD could be assessed using the SIA on individual or bulk tank milk samples, respectively (4).

The use of tests for antibodies to the non-structural proteins (NSPs), to show evidence of infection has been discussed (11). The development of antibodies to NSPs and the duration of their detection are probably correlated with the severity of clinical disease and level of virus replication. Animals which fail to show clinical disease, for example the Chinese yellow cattle infected with the pan-Asian serotype O, only show transient levels of NSP antibody, which could reduce the value of these tests (7).

Control

Procedures for the control and eradication of FMD are well documented and will depend on the existing disease status of the affected country or zone prior to the outbreak. In countries free of the disease, a policy of slaughter of all infected and in-contact susceptible animals is usually employed, whereas vaccination would be used to control an outbreak in an endemic area. Vaccination may also be used to surround a focal outbreak of disease to prevent the virus spreading and the vaccinated animals may be subsequently slaughtered to reduce the delay in re-establishing trading status (14). A buffer zone containing vaccinated animals may be used to separate an area within a country in which FMD is endemic from an FMD-free area, from which exports of cattle and cattle products are sourced.

A difficulty encountered in herds that are regularly vaccinated against FMD has been the interference in response to vaccination by young animals with high levels of maternally derived antibody (12). Calves obtain anti-FMD virus antibody in the colostrum, but the level will depend on the immunity of the dam, and the absorption of the antibody by the calf. This passive antibody declines with a half-life of approximately 22 days and only when it is below a LPBE titre of 1:45 will the calf respond to vaccination. However, the calf can be susceptible to infection at titres below 1:100. This is further complicated by the different levels of antibody each calf obtains from its dam, and consequently, timing the FMD vaccinations of calves from immune dams in order to ensure their maximum immunity becomes a compromise. This has been addressed by pooling colostrum and keeping it frozen until required, and therefore ensuring that each calf in the herd receives approximately the same quantity of antibody and by vaccinating the calves at four, five and six months of age, even

Rev. sci. tech. Off. int. Epiz., **21** (3)

503

though it is only advised that a single booster dose is required to start a vaccination course. Those calves that fail to respond at four months of age, will respond at five months and receive their booster at six months; those that responded at four months will have received an additional, possibly unnecessary, dose at six months. The problem of the approximately one month time gap between susceptibility to infection and vaccination can only be managed by keeping the calves isolated from any source of FMD virus during that period. By being aware of the relative susceptibility to FMD of the different production groups within a vaccinated herd, the animals may be spatially organised to reduce the potential for spread of infection within the farm, should the virus be introduced (9).

■

Variation des signes cliniques de la fièvre aphteuse chez les bovins

R.P. Kitching

Résumé
En général, les signes cliniques de la fièvre aphteuse s'observent dans les troupeaux de bovins non vaccinés, dans les pays où la maladie survient uniquement de façon sporadique. En revanche, la maladie peut diffuser sans être dépistée dans les troupeaux d'animaux vaccinés et chez quelques races indigènes des régions enzootiques.

Mots-clés
Bovins – Diagnostic – Fièvre aphteuse – Prophylaxie.
■

Variación de las manifestaciones clínicas de la fiebre aftosa en los bovinos

R.P. Kitching

Resumen
En los bovinos, la fiebre aftosa suele resultar clínicamente ostensible en rebaños no vacunados de países donde la enfermedad se presenta sólo ocasionalmente. Sin embargo, en el caso de rebaños vacunados y de algunas razas autóctonas de zonas donde la enfermedad es endémica, es posible que ésta circule sin ser detectada.

Palabras clave
Bovinos – Control – Diagnóstico – Fiebre aftosa.
■

References

1. Alexandersen S., Kitching R.P., Sørensen J.H., Mikkelsen T., Gloster J. & Donaldson A.I. (2002). – Epidemiological and laboratory investigations of five outbreaks during the early stages of the 2001 foot-and-mouth disease epidemic in the United Kingdom. *Vet. Rec.* (submitted for publication).

2. Armstrong R.M. (1997). – Development of tests for antibodies against foot-and-mouth disease virus in cattle milk. *J. virol. Meth.*, **63**, 175-180.

3. Armstrong R.M., Mathew E.S. & Mackay D.K. (2000). – Validation of the specific isotype assay to detect antibodies against foot-and-mouth disease virus in bovine milk. *J. virol. Meth.*, **85**, 193-201.

4. Armstrong R.M. & Mathew E.S. (2001). – Predicting herd protection against foot-and-mouth disease by testing individual and bulk tank milk samples. *J. virol. Meth.*, **97**, 87-99.

5. Donaldson A.I. (1987). – Foot-and-mouth disease: the principal features. *Irish vet. J.*, **41**, 325-327.

6. Huang C.-C., Jong M.-H. & Lin S.-Y. (2000). – Characteristics of foot and mouth disease virus in Taiwan. *J. vet. med. Sci.*, **62**, 677-679.

7. Huang C.-C., Lee F., Tu W.-J., Lee S.-H., Huang T.-S., Lin Y.-L., Jong M.-H. & Lin S.-Y. (2001). – Anti-3AB antibodies in the Chinese yellow cattle infected by the O/Taiwan/99 foot-and-mouth disease virus. *Vet. Microbiol.*, **84**, 317-326.

8. Hutber A.M., Kitching R.P. & Conway D.A. (1999). – Predicting the level of herd infection for outbreaks of foot-and-mouth disease in vaccinated herds. *Epidemiol. Infect.*, **122**, 539-544.

9. Hutber A.M. & Kitching R.P. (2000). – The role of management segregations in controlling intra-herd foot-and-mouth disease. *Trop. anim. Hlth Prod.*, **32**, 285-294.

10. Kitching R.P. (1992). – Foot-and-mouth disease. *In* Bovine medicine: diseases and husbandry of cattle (A.H. Andrews, R.W. Blowey, H. Boyd & R.G. Eddy, eds). Oxford, Blackwell Science Inc., Malden & Oxford, 537-543.

11. Kitching R.P. (2002). – Identification of foot and mouth disease virus carrier and subclinically infected animals and differentiation from vaccinated animals. *In* Foot and mouth disease: facing the new dilemmas (G.R. Thomson, ed.). *Rev. sci. tech. Off. int. Epiz.*, **21** (3), 531-538.

12. Kitching R.P. & Salt J.S. (1995). – The interference by maternally derived antibody with active immunization of farm animals against foot-and-mouth disease. *Br. vet. J.*, **151**, 379-389.

13. Kitching R.P. & Hughes G.J. (2002). – Clinical variation in foot and mouth disease: sheep and goats. *In* Foot and mouth disease: facing the new dilemmas (G.R. Thomson, ed.). *Rev. sci. tech. Off. int. Epiz.*, **21** (3), 505-512.

14. Office International des Epizooties (OIE) (2001). – Foot and mouth disease, Chapter 2.1.1. *In* International animal health code: mammals, birds and bees, 10th Ed. OIE, Paris, 63-75.

15. Salt J.S., Samuel A.R. & Kitching R.P. (1996). – Antigenic analysis of type O foot-and-mouth disease virus in the persistently infected bovine. *Arch. Virol.*, **141**, 1407-1421.

16. Sørensen J.H., Mackay D.K., Jensen C.O. & Donaldson A.I. (2000). – An integrated model to predict the atmospheric spread of foot-and-mouth disease virus. *Epidemiol. Infect.*, **124**, 577-590.

17. Zhang Z.D. & Kitching R.P. (2001). – The localization of persistent foot-and-mouth disease virus in the epithelial cells of the soft palate and pharynx. *J. comp. Pathol.*, **124**, 89-94.