Foot and mouth disease

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SUMMARY

Foot and mouth disease (FMD) affects cloven-footed animals. It is caused by seven species ("types") of Foot and Mouth virus (FMDV) in the genus aphthovirus, family Picornaviridae (ICTV 2000). FMDV is a single-stranded RNA virus, with a protein coat consisting of four capsid proteins enumerated as VP1, VP2, VP3, and VP4 (Garland and Donaldson 1990). C11

HOST SPECIES

CATTLE, sheep, goats, and pigs are the main domesticated species infected. The Water Buffalo (Bubalus bubalis) can become infected and may also transmit infection to other species. Camelids, experimentally infected, contract the disease (Lubroth et al 1990) but there is no evidence of transmission to other domestic livestock and there seems to be some doubt as to whether they play any role in the epidemiology of the disease in domestic livestock (Fondevila et al 1995).

A wide range of wild cloven-footed animals contract FMD including deer and pigs. During the 2001 epidemic in the United Kingdom there was great concern that the various species of deer now abundant in the country might contract the disease and act as a persistent reservoir of infection. In the event, investigation of a number of cases of apparent disease failed to reveal the presence of FMD virus. The African Buffalo (Syncerus caffer) appears to be particularly susceptible to infection and may act as a reservoir host (see later).

Although FMD is known as a disease of cloven-footed animals it can occur naturally in other animals, e.g., the hedgehog (Erinaceus spp.) (McCauley 1963), and infection has been established experimentally in a number of other species. However, it is doubtful whether these animals play any part in the epidemiology of the disease (Snowdon 1968).

FMD is not considered zoonotic. Although clinical cases have been proven in human, these are extremely rare in relation to human exposure during outbreaks (Sellers et al 1970).

PATHOGENESIS

The replication of the infectious particles is extremely rapid after entry through the upper respiratory tract or lung, with viraemia seeding infection into the epithelium where secondary virus multiplication results in vesicles and shedding from the udder in milk (Hyslop 1965, Sellars 1971). The incubation period, from infection to clinical signs, may be as short as 2/3 days or as long as 14 days (Garland and Donaldson 1990) and infected animals may become infectious before showing clinical signs (Burrows 1968a). The virus is excreted during viraemia for some days; thereafter as serum antibody develops viraemia decreases, and the animal ceases to be infectious as the lesions heal.

DISTRIBUTION

The seven types of FMD virus are: A, O, C, South African Territories (SAT) 1, 2, and 3 and Asia 1. Types O, A, and C are the strains that have been identified in Europe and South America whilst O, A, and Asia 1 are common throughout Asia. SAT strains 1 and 2 are found throughout Africa whilst SAT 3 is confined to Southern Africa. The strains found in the Middle East include A, O, Asia 1, and SAT 1. These serotypes are so defined because they do not cross-protect.

FMD is endemic in much of Africa and Asia and parts of South America. Meat exporting countries such as Argentina and Uruguay have made great efforts to eliminate infection and were successful until 2001. North America, Australia, and New Zealand have either never encountered the disease or have been free for many years. Europe is also free apart from periodic incursions, mainly from the Middle East. The world situation has been reviewed by Kitching (1998) but the position is fluid and up-to-date accounts of the incidence of FMD can be found in Food and Agriculture Organisation (EMPRES) and Office International des Epizooties (OIE) bulletins.

The development of molecular techniques has enabled the characterisation of individual strains of virus (Kitching 1992). The genetic relationship between strains can be calculated from the percentage nucleotide differences and it is now possible to trace the movement of individual strains across countries and continents. Thus the Pan-Asia O strain was first identified in Northern India before spreading westward to Bulgaria and Greece in 1996 and now to the United Kingdom (Knowles et al 2001).
The disease is characterised by vesicular lesions on the coronary band of the hooves and in the mucosa of the mouth including the tongue and palate. The vesicles typically contain clear or straw-coloured fluid before they burst and heal. There is a rise in body temperature of some 3–4 °C. The lesions in sheep are often difficult to find and may be confused with other conditions (Ayers et al 2001).

The disease varies considerably in its severity. It may result in death or severe morbidity particularly in neonates but in areas where the infection is endemic the disease may be mild and the few vesicles that appear may heal without further damage.

**EPIDEMIOLOGY**

Few descriptions of FMD epidemics have been published with the exception of the 2001 UK epidemic (Gibbens et al 2001) and the 1993 Italian epidemic (Marangon et al 1994).

Several factors determine the epidemiology of the disease and therefore the control measures. The factors are:

- the incubation period,
- the infectious period and the quantity of virus particles expelled,
- the spread of virus by aerosol,
- the survival of virus in fomites,
- the persistence of the virus in carcases,
- the existence of carriers,
- the density of the host populations.

**THE SPREAD OF THE VIRUS**

Infected animals are only infectious for a matter of days (Burrows 1968a,b) but during that period the amount of virus expelled may vary enormously with the species affected, the stage of the disease and the virus strain. Pigs excrete considerably greater quantities of virus than either cattle or sheep (Sellars and Parker 1969).

During the 1967 FMD epidemic in the UK, it was discovered that airborne virus spread could infect animals some distance away. Survival of the virus in aerosols depends on the relative humidity (Donaldson 1972, Donaldson et al 2001) and airborne spread is a feature of the disease in moist temperate as opposed to dry tropical climates. Computer models have been developed to predict the extent of airborne spread (Gloster et al 1982, Sorensen et al 2000).

**VIRUS SURVIVAL**

FMD virus can survive for long periods at neutral pH, particularly at low temperatures. Faeces and other organic matter may protect it and the virus can survive in straw for up to 15 weeks (Cottral et al 1969). However, the virus is acid and alkali labile and acidic preparations at a pH 6.5 or below are effective disinfectants (Sellars 1968). Cleansing and disinfection, whilst laborious, is effective in eradicating the agent from infected premises.

Virus survival in carcases is a crucial factor in regulating the international trade in meat. Following slaughter the virus is inactivated within 48 hours provided the pH drops to below 6.0. as normally occurs in the skeletal muscles during the period of rigor mortis. However, the virus may survive in lymph nodes and bone marrow (Cottral et al 1969) and when tissues containing FMDV are frozen the virus can survive for years.

**THE CARRIER STATE**

The carrier state in FMD is the subject of much debate and it is no exaggeration to say that it has achieved iconic status in the international regulations governing trade because of the concern that some animals recovering from the disease may become carriers and spread the disease to others. The extensive literature relating to the carrier state in FMD has been reviewed by Salt (1993), Thomson (1996), and Moonen and Schrijver (2000).

A carrier animal is defined as one from which the virus can be recovered 28 days or more after infection. The carrier state in FMD is an apparently infected in which the intermittent isolation of the virus from the oropharynx is currently the sole means of detection. Carriers have been recorded in cattle (Van Bekkum et al 1959), African buffalo (Hedger and Condy 1985), sheep (Burrows 1968a,b), and goats but not in pigs. It occurs with all serotypes and has been identified in both experimentally and naturally infected animals (Van Bekkum et al 1959, Hedger 1968). It is well established that a proportion of animals infected by FMD virus eventually become “carriers” with equal facility irrespective of whether they have been vaccinated, passively immunised or are immunologically naive cattle (Sutmoller 1971).

The prevalence of carriers is high immediately after infection but declines, as do the virus titres, with time and most cattle clear the infection after 4–5 months (Thomson 1996). The carrier period appears to vary between species, being in excess of 12 months in cattle, up to 9 months in sheep and goats and at least 5 years in African Buffalo (Condy et al 1985).

Although the carrier state in FMD is well documented, the evidence for carrier animals transmitting infection to others is uncertain. When oro-pharyngeal fluid containing residual virus is injected into cattle or pigs infection results (Van Bekkum 1973). However, a large number of experiments have failed to demonstrate transmission from carrier animals (usually cattle) to susceptible in-contact animals.

The field evidence for transmission from carriers is equivocal and relates, in the main, to the carrier state in African buffalo infected with SAT strains of virus. Thomson (1996) states that “to date there are no unequivocal reports of transmission of FMD from persistently infected domestic livestock to susceptible animals other than the circumstantial data available from historical accounts and the events associated with.
SAT 2 outbreaks in cattle in Zimbabwe between 1983 and 1991”.

In summary there is no reliable contemporary field data on which to base a quantitative assessment of the risk posed by carrier animal. The experimental data indicates that, if transmission of infection from carriers occurs, it does so at very low frequencies or under a particular set of, as yet unidentified, circumstances.

CONTROL

There are two approaches to controlling or eradicating FMD: slaughter and vaccination. Slaughter may be used on its own, as in the UK, or in some combination with vaccination as in the Continental countries during the post war period. Most countries, and particularly those where incursions of FMD are a constant threat, vaccinate without resorting to slaughter. All control programmes must include strict controls on the movement of animals.

DIAGNOSIS

Control programmes that include an element of slaughter depend on prompt diagnosis.

The symptoms of FMD in cattle and pigs are usually discernable during clinical examination and, for the greater part, the identification of FMD infected herds relies on clinical judgements. These may be confirmed by laboratory tests and confirmatory tests are essential when the disease makes its first appearance in a country or zone. Clinical diagnosis in sheep can be less certain (Ayers et al 2001) and for this species laboratory confirmation is desirable if not essential.

Erosive lesions in the buccal cavity are characteristic of other diseases such as mucosal disease and rinderpest, whilst foot lesions in sheep may be caused by foot rot. However salivation, lameness in all four feet, and a sharp rise in temperature are characteristics of FMD and should always be a cause for suspicion.

During the recent epidemic in the UK, where the initial spread was amongst the sheep population, laboratory tests were widely used either to confirm clinical diagnoses or to establish disease freedom. Laboratory facilities were established to handle a volume of 100,000 tests for antibody a week.

Tests were used either to detect virus antigen or serum antibody as described in the OIE Manual of Standards. Virus in tissue samples was identified using an antigen detection ELISA. Negative samples were further examined in tissue culture. Serum samples were tested for antibody using a liquid phase blocking ELISA (Ferris and Dawson 1988) or, in the later stages by a solid phase blocking ELISA, positive samples being further tested by the virus neutralisation test.

VACCINATION

Vaccines are widely employed to control FMD. The nature of the immune response and the prospects for improve vaccines have been reviewed by Doel (1996). The vaccines currently available are inactivated and contain whole virus in a semi-purified state. The immunological component of the virus appears to be the VP1 polypeptide and protection can be conferred with this peptide alone (Bittle et al 1982). Vaccines may include one or several of the serotypes but the strain used should match the field strains that are causing the disease. Most vaccines contain aluminium hydroxide as an adjuvant but oil based vaccines are also used in pigs. A high level of immunity can be induced by potent vaccines within a few days in both cattle and pigs (Salt et al 1998, Doel et al 1994) but the interval between vaccination and protection may be some 14 days with the usual commercial vaccines.

The current generation of FMD vaccines protect animals for periods up to 12 months (Cox and Barnett 2000) but the immunity conferred is not absolute and FMD wild virus may multiply to a greater or lesser extent in a vaccinated animal. Vaccine programme failures may be attributable to overwhelming challenge as in large intensive units (Donaldson and Kitching 1989) or to inadequate population cover that leaves sufficient unvaccinated and therefore susceptible animals for the virus to maintain itself and continue circulating.

Vaccines can be employed prophylactically to protect a population against future challenge, or in emergency, to deal with a current epidemic.

Prophylactic vaccination on a national scale is usually confined to cattle and such programmes successfully eliminated FMD from Continental post-war Europe. It is widely assumed that for vaccine to be used on a national scale, 80% cover of the population is sufficient, which is a broad generalisation derived from experience in human populations. The structure of domesticated animal populations in herds and flocks, and their variable density in intensive units or range conditions, are important factors. Preliminary investigations by Keeling and others suggest that livestock populations can be protected against major epidemics of FMD if 50% or more of the susceptible animals are vaccinated.

Vaccination in the face of an epidemic is a contentious issue. A recent epidemic in Uruguay was eliminated by vaccination without recourse to slaughter (Sutmoller 2002) but it is more usual for vaccination to supplement the slaughter of infected and in-contact herds. The disadvantage of vaccination is said to be the inevitable delay before the animals are protected but with high potency vaccines the delay is only of the order of 4–5 days (Salt et al 1998).

The advantage of vaccination is that it does not require large numbers of operatives and little in the way of equipment whereas slaughter requires large teams to diagnose, slaughter, disinfect premises, and bury or burn carcases. Immediate destruction of animals on farms where clinical cases have occurred is vital (Howard and Donnelly 2000).

The general reluctance to vaccinate in the face of an epidemic is due to international adherence to OIE and other standards governing trade in animals and animal products. As matters stand at the moment a country
can be granted FMD free status and resume exports 3 months after the last outbreak if control is by slaughter. If animals are vaccinated the interval is 12 months (OIE Animal Health Code).

The rationale for this difference appears to be that clinical signs of infection would be masked in vaccinated populations and that traditional serological tests would not distinguish vaccines from animals that have encountered live infection. There is also the risk that vaccines, which have encountered infection and become carriers, may later become infectious and spread disease. As discussed above this latter claim rests on flimsy foundations but the problem of distinguishing vaccines from infected stock by serological testing is one that is the subject of extensive research.

Responses to vaccination may be differentiated from natural infection either by employing “marker” vaccines that give rise to a distinctive serological response because of gene deletions, or by devising tests that distinguish responses to vaccine from those to field virus. There are as yet no FMD marker vaccines but a great deal of progress has been made in devising tests to distinguish vaccines from infected animals and these rely on the fact that modern FMD vaccines contain few non-structural proteins (NSPs). This area of research has been reviewed by Mackay (1998) and the conclusions are that whilst the tests are adequate for distinguishing naturally infected herds from vaccinated herds, the sensitivity for detecting individual animal is not high enough to allow the tests to be used to identify and remove individual animals in a post-vaccination surveillance programme.

**FOOT AND MOUTH DISEASE IN INTERNATIONAL TRADE**

Foot and mouth disease is an OIE list A disease (OIE Animal Health Code). This list is reserved for transmissible diseases that are considered to be of socio-economic importance within countries and that are of significance in international trade. There is little hard evidence to support the claim that FMD is of considerable economic importance as the few published cost-benefit studies do not set down actual morbidity and mortality rates in infected stock. This is understandable as in developed countries the disease is eradicated before it can cause damage. The losses are the cost of the slaughter and other control measures (Davies 1993, Perry et al 1999). Nevertheless the disease and its control are of the greatest importance in the formulation of international animal health strategies and the authorities have, over the years, adopted a zero risk approach in drafting regulations for international trade. The United Kingdom epidemic has highlighted the deficiencies of such an approach in the face of the epidemiological risks posed by increasing volumes of global travel and the integration of widely diverse societies and economies. It is to be hoped that the epidemic will stimulate a fresh approach to the problem of FMD: one that recognises that perfect risk free solutions are not always possible and that progress can only be made by devising risk reduction measures that are consonant with the reality of world trade.

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