

THE CHALLENGE OF FMD CONTROL IN THE 2001 UK FMD EPIDEMIC

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Introduction

The 2001 UK foot-and-mouth disease (FMD) epidemic resulted in 2030 cases of disease (2026 on mainland GB) being confirmed over a seven month period between March and September 2001. A review of the course of the epidemic, the successes and failures and the results of post-epidemic analysis, are presented in an effort to better aid the understanding of the problems encountered, so as to guide and inform future control programmes.

The virus

Foot-and-mouth disease is a highly contagious disease of cloven-hoofed animals, in particular cattle, sheep, pigs, goats and domestic buffalo, as well as wild ruminants such as deer. It is characterized by fever and vesicles on the mouth, feet and udder of lactating animals. Pregnant animals may abort and young stock may die suddenly due to myocardial infarction. FMD is caused by strains of aphthovirus, in the family Picornaviridae, of which there are seven immunologically distinct serotypes, namely O, A, C, SAT1, SAT2, SAT3 and ASIA1. Animals that have recovered from infection with a strain of one serotype remain fully susceptible to infection with strains of the other six. Within each serotype there are a substantial number of strains showing a variable degree of antigenic diversity. The genome of the virus contains a single strand of positive-sense RNA, of approximately 8.2 Kb, and in common with other RNA viruses has a high mutation rate, which together with the apparent 'plasticity' of the major neutralising sites on its surface, explains a high antigenic variability.

The clinical severity of FMD varies with the strain of virus, as well as the infecting dose, the route of infection, the species and individual susceptibility of the host. It is clinically most apparent in high-yielding dairy cattle and intensively-reared pigs, in which the lesions can be severe and debilitating. In adult sheep and goats, FMD is frequently only a mild disease, with transitory clinical signs which can easily be missed by the stockman or veterinarian, or confused with other diseases presenting similar lesions (De la Rua *et al*, 2001; Watson, 2002; Ayers *et al*, 2001) but can cause a severe clinical picture in lambing flocks including high levels of neonatal mortality (Hancock and Prado, 1993). The virus replicates to a high titre in epithelial cells, particularly those undergoing repair, and consequently lesions may also be seen on the hocks or elbows of pigs being housed on concrete flooring where damage to legs is common.

The most common method of spread of FMD virus is by contact between an infected and a susceptible animal. An infected animal produces a large amount of virus in exhaled breath. Cattle and sheep are particularly susceptible to infection by the aerosol route, requiring as little as 10 Tissue Culture Infective Doses 50 (TCID₅₀) (Donaldson *et al*, 1987). Pigs are considerably less susceptible to aerosol infection, possibly requiring as much as 6000 TCID₅₀ (Alexandersen *et al*, 2002a). During the clinical phase all excretions and secretions contain huge quantities of virus, and infection can occur

either across damaged epithelium or orally. Pigs produce up to 3000 times more aerosol virus per day during the acute stage of infection. Under appropriate weather conditions, infectious levels of aerosol virus can potentially spread a considerable distance, particularly if the source is a large infected pig herd (Donaldson *et al*, 1982). Prediction models have been developed which can predict the likely dispersion of infectious levels of aerosol virus if the number and species of animals infected and the weather conditions at the time of virus excretion are known. The animals most at risk are usually cattle since they are especially susceptible to infection by the aerosol route, and because they have a higher respiratory volume than sheep.

When an animal infected with FMD virus is slaughtered, all meat and organs contain FMD virus. The build-up of lactic acid post-mortem kills any virus in the meat by reducing the pH to below 6, however no reduction in pH occurs in the glands or bone marrow in which virus may survive for 120 days at 4°C (Cottral, 1969). Milk from infected animals contains large quantities of live virus and semen from infected bulls and ova from infected cows may also be contaminated with live virus.

It is possible for virus to survive days or weeks in the environment if kept moist and at neutral pH. The hands, clothes or nasal passages of personnel handling infected animals may become contaminated with live FMD virus, and mechanically carry virus and infect susceptible animals by close contact. Vehicles can carry infected material between farms, although, for transmission of infection to occur, there is the necessity that the material makes direct contact with a susceptible animal. Milk tankers venting during filling operations can create an aerosol of virus contaminated milk droplets and spread disease.

Convalescent ruminants and those that have been vaccinated against FMD and subsequently exposed to live virus, may become carriers remaining infected for a variable period of time. Cattle may carry the virus for over three years, sheep for up to nine months and goats for up to four months in the epithelial cells of the pharynx (Zhang and Kitching, 2001; Kitching, 2002a), despite there being high levels of circulating neutralizing antibody. The mechanism by which the virus is protected from the host immune response is not understood (Salt, 1998). Nor is it known what risk these carrier animals represent in terms of causing new outbreaks of FMD. It has not been possible experimentally to show transmission from a bovine carrier animal to an in-contact susceptible animal. However there is circumstantial field evidence that carriers may initiate a new outbreak (Kitching, 2002a, Thomson, 1996).

The PanAsia O strain responsible for the 2001 GB epidemic was first identified in India during 1990. It spread northwards into Nepal in 1993 and westward into Saudi Arabia during 1994 and then throughout the Middle East, becoming essentially endemic and progressively replacing the other Type O strains in circulation. In 1996 it reached Bangladesh and Turkey

from where it spread into Greece and Bulgaria. The virus reached mainland China by 1999, as well as Taiwan, and in 2000 it was identified in South Korea, Mongolia, eastern Russia and Japan. In September 2000 it caused the first outbreak of FMD type O in the Republic of South Africa where the origin was attributed to the feeding to pigs of untreated shipping waste. Phylogenetic analyses showed an extremely close relationship between the UK and South African virus isolates, and between them and virus from the Far East, with the Japanese isolate being the closest.

National Control Policies

The control policy operated by a country depends very much on its individual disease status and geographical location. Countries free of the disease with well defined boundaries, such as the UK, have traditionally relied on stamping-out policies. These require a well developed State Veterinary Service for the early recognition of the disease complemented by swift slaughter and carcass disposal, efficient cleansing and disinfection procedures and effective movement controls. Such policies are backed up by strict import controls on animals and their products in an attempt to prevent the importation of virus, backed up by veterinary checks of imports and waste feed controls should virus be inadvertently imported. Members of the OIE adopt veterinary certification and disease notification procedures so as to underpin international trade. Many countries have no national geographic barriers protecting their borders allowing free movement of nomadic herdsmen, wild animals and disease, thus countries in Africa, the Middle and Far East have no choice but to control FMD by mass vaccination. Between the two approaches of stamping out and mass annual vaccination many variations are practised, notably strategic vaccination in the face of an outbreak where barrier or ring vaccination is applied.

Overview of the 2001 FMD epidemic in GB

A total of 2,026 cases of FMD, caused by the PanAsia O strain of virus, were confirmed in Great Britain between 20 February and 30 September 2001. This marked the end of the country's longest period of freedom from FMD in recent history, the last epidemic on the mainland occurring in 1967-'68.

Although the first case to be confirmed in GB in 2001 was in pigs at an abattoir in Essex, in south east England, this was not the index case in the epidemic. The oldest disease found in any animals during the epidemic (and therefore the index case) was in pigs, on a waste-food feeding premises 400 km to the north, near Newcastle-upon-Tyne in Northumberland. There was unprocessed waste food on the premises to which the pigs had access, moreover cutlery was found in the troughs and pens with the pigs. Investigations in April 2001 discovered commercial quantities of illegally imported, air-dried, bone-in, pork legs from Asia, (DEFRA, 2002) on the premises of a wholesaler supplying local restaurants in the Newcastle area, from which the index farm collected waste.

It was estimated that clinical disease had been present on this farm since at least 12 February 2001 (Alexandersen *et al* 2002b, Alexandersen *et al* 2003, Gibbens *et al*

2001). Sufficient virus could have been released to form a viral plume from about this time and analysis of the meteorological conditions during early February showed they favoured spread of virus to farms up to 10km away, particularly in the period 12 to 13 February (Gloster *et al* 2003). Airborne dispersal of virus from the pig farm is considered to have been the most likely method of introduction of virus into sheep and cattle on a Ponteland farm 5 km distant. Exhaustive investigations into the source of infection for this farm found no evidence of disease on any farm with which there had been any contact from 1 January 2001 nor on any farms within a 3 km radius (DEFRA, 2002).

It seems likely that the sheep and cattle on the Ponteland farm were exposed to infection shortly before 19 sheep from the farm were sold for slaughter at Hexham livestock market, on 13 February. Nine of the 19 sheep went for slaughter (introducing disease to two premises) whilst the remaining 10 were bought (unfortunately) by a livestock dealer who mixed them with 174 other sheep. The 184 sheep remained in close contact for almost 48 hours at Hexham then nearby Longtown markets, before entering the national sheep marketing system (Mansley *et al* 2003). This is a sophisticated, interlinking network of livestock markets, dealers and hauliers capable of collecting, processing and rapidly transporting tens of thousands of animals daily. February is traditionally a busy sheep marketing time in Britain as ewe replacements are being bought, there is a demand for over-wintered hogs for further fattening and there is a market for barren ewes and cast tups underpinned by the export trade. Longtown market is one of Europe's biggest sheep markets, selling animals originating predominantly from the north of England and southern Scotland, and attracting livestock dealers from throughout the British Isles who supply the UK and Europe. By definition, dealers buy and sell commodities, often on the same day, and livestock trading is little different. Groups of animals, particularly sheep, are bought, split up, resold (either privately or through markets, sometimes on the same day), transported long distances, mixed with more animals, resold, and so the cycle continues. Each dealer often has several premises between which stock and personnel regularly move. Some premises are used by more than one dealer and trading between dealers is frequent. The conditions of close contact between animals found in market pens and livestock transport vehicles are particularly favourable for virus transmission, both directly between susceptible animals and indirectly between animals and virus contaminated surfaces, as the potential for FMD virus to survive outside the host is well documented (Cottral, 1969). It is therefore a most efficient means of spreading infectious agents, especially one as contagious as foot and mouth disease virus, which in sheep may produce little clinical evidence of its presence whilst replicating and being released in large quantities into the environment.

Epidemiological investigations at the two markets concluded that the subsequent movement of the 184 sheep was responsible for the introduction of infection, before 20 February, to as many as 79 premises in GB, 20 of which were operated by large-scale dealers, in 10 of the 12 separate geographic epidemiological groups of IPs

that were identified during the epidemic (Mansley *et al*, 2003, Gibbens *et al*, 2001). Virus was further disseminated from these premises by the subsequent movement of animals, particularly sheep, and fomites, both locally and over longer distances. Once it became apparent that the disease was not confined to Essex, national animal movement controls were imposed on 23 February. It has been estimated that at this point in time animals on as many as 150 farms could have been exposed to infection. In reality Britain was faced with what amounted to multiple-seeded cases of FMD, scattered widely across the country, from which virus had already begun to spread, seven days before the first case was confirmed. The national animal movement controls were a draconian measure, the implementation of which so early in an outbreak was without precedent in the history of FMD control in Great Britain. It is without doubt that this single control measure played a pivotal role in minimising the potential for further distribution of disease and greatly reduced the scale of the epidemic.

The scale and temporal pattern of FMD cases in the first months of the 2001 epidemic was similar to that in 1967/68 (Gibbens, *et al*). Both reflected the practical problems of controlling epidemics characterised by initial multiple seeding followed by local spread. However the evidence suggests that in the 2001 epidemic, the index case was the source of infection for all other cases, whereas the 1967/68 epidemic had a multi-centric origin in which a number of pig farms were infected concurrently from the same source. The two epidemic curves differ only slightly in that the peak of the 1967/68 epidemic was greater and occurred slightly sooner after the first case than in 2001.

The national epidemic curve of confirmed FMD cases shows a steep rise over time until 27 March; this high level of 40 to 50 cases per day was maintained for about a week. Case numbers then fell, more steeply than they had risen, to reach a steady 5 to 10 cases per day for a month from 26 April. Of the approximately 1600 IPs that were confirmed in this time period almost half were in the county of Cumbria in the north-west of England. Epidemiological investigations concluded that over 100 farms, spread widely throughout the county, could have been infected before the first case had been confirmed in the area on 1 March. The national peak on 27 March was largely due to the effect of the Cumbrian cluster of cases, the peak being earlier in other areas; 22 March in Dumfries and Galloway (D&G) in Scotland and in Devon in south-west England. Using a conservative 5-day incubation period (Kitching, 2002b) it could be said that the spread of disease had been brought under control in Cumbria (and nationally) by 22 March and somewhat earlier elsewhere e.g. 17 March in D&G and Devon. The early intense part of the epidemic was virtually over by the end of April.

The 2001 epidemic however, was characterised by a prolonged 'tail' comprising almost 400 cases, confirmed over a 20 week period from May to September, appearing as a series of sporadic outbreaks in previously unaffected, widely separated, geographic areas of the country. The source of many of these defied identification although long distance fomite spread and inapparent infections of sheep were implicated. Local fomite spread was believed

to have perpetuated the disease during the epidemic 'tail' as most of the outbreaks occurred in areas of farm fragmentation. At this time of year most farm animals had been turned out to grass and essential seasonal activities, such as silaging and sheep shearing, were in full swing, resulting in an increased frequency of movements by people and vehicles.

The disease was eventually controlled in the 'tail' following the introduction, in late July, of legislation to enhance biosecurity measures in cartographically delineated Restricted Infected Areas (RIAs). The special measures applied in the RIAs included:

- Proper cleansing and disinfection of all vehicles entering or leaving all farms
- Licensing of feed lorries and milk tankers, the latter to be accompanied by DEFRA staff
- Cleansing and disinfection of agricultural vehicles entering or leaving the RIA
- Continuous biosecurity patrols by the Police and DEFRA
- Slurry and forage movement only by license
- Licensing of sheep shearing and agricultural contractors' activities
- Structured sero-surveillance of all sheep flocks

The last case in the epidemic was confirmed on clinical grounds in sheep on 30 September 2001 in Cumbria; laboratory samples were negative for this and the three preceding cases.

Post-epidemic analysis revealed that in 86% of confirmed cases sheep were present on the premises and that 25% of IPs were laboratory negative. The high incidence of sheep on IPs may well reflect the underlying population, although the distribution of sheep on farms in Great Britain is not clear. It is not possible to give a clear picture of the relative risk of infection in sheep and cattle, as the speed of imposition of control measures often prevented complete examination of all stock on a premises. During the bulk of the epidemic, if disease was detected in cattle on a holding, it wasn't always possible to closely examine all the sheep in detail, or test them serologically, due to lack of resource and the overwhelming requirement for rapid slaughter. The evidence suggests that they have a similar risk of infection. During the early weeks infection was confirmed more frequently in sheep, reflecting its early dissemination, then the disease moved into the cattle herds which became the predominant species affected although disease continued to be identified in sheep. Once cattle became involved the amount of virus being released would have increased drastically; this seemed to be particularly the case once dairy herds were involved. Widespread serological testing of sheep during the 'tail' of the epidemic, and afterwards in the national sero-surveillance programme to demonstrate country freedom from disease, found little evidence to support the belief that cryptic infection in sheep was responsible for perpetuating the epidemic.

Animal movements, rather than fomite or airborne transmission, infected most of the major geographic clusters of cases before restrictions came into force. Thereafter the fomite-mediation appears to have been the predominant method of secondary transmission between

IPs during the epidemic. Infected Premises often had several potential sources of infection and there remains no doubt that proximity to an infected place is an important risk factor for becoming infected with FMD. However, spatio-temporal analyses of the epidemic in Cumbria (Taylor *et al* 2004) concluded that spread of infection beyond 1.5 km occurred in over 50% of cases, indicating that limiting disease control measures to contiguous premises (i.e. within 1.5 km) was unlikely to stop the epidemic. Similar conclusions were reached by Thrusfield *et al* (2004) in Dumfries and Galloway. This emphasises the need to limit contact between farms and to ensure that adequate cleansing and disinfection procedures are implemented and maintained to achieve disease control, hence the apparent success of the RIAs.

The size and scale of the 2001 epidemic can be attributed to a variety of factors

- There was an initial delay in reporting suspicion of FMD on the index case
- 90% of the 540 pigs on the index farm were affected
- There had been windborne spread from the index farm to sheep on a nearby farm
- Inapparently infected sheep from this farm entered the livestock marketing system
- The movement coincided with a seasonal peak in sheep marketing
- The GB sheep dealing and marketing system is sophisticated and complex
- Sheep bear no individual identification and movements may be poorly recorded
- FMD is often difficult to detect clinically in sheep
- Sheep are susceptible to the PanAsia O strain
- Farm size and fragmentation have increased in recent years
- Stock numbers on each holding have increased
- There is a greater reliance on shared or contract labour and equipment
- The prevailing cold, damp climatic conditions favoured virus survival
- The State Veterinary Service had been progressively reduced in size
- The widespread dissemination of virus rapidly stretched resources beyond their limit

Control procedures adopted in GB in 2001

Stamping out:

- Rapid slaughter and disposal of all susceptible animals on IPs and on premises considered by veterinarians to be at risk of being exposed to infection ('Dangerous Contacts': DCs)
- National animal movement restrictions
- 3km Protection Zone and 10km Surveillance Zone farm restrictions
- Enhanced biosecurity
- Veterinary inspections of 'at-risk' livestock e.g. on contiguous farms
- Veterinary epidemiological investigations to identify potential sources and spread of infection.

Novel policies:

- Pre-emptive contiguous culling was practised around IPs from 26 March

- Culling of all small ruminants and pigs on premises within a 3km radius of IPs in Cumbria and D&G began on 23 March, the 3km cull
- Confirmation of disease on clinical signs, only, without recourse to laboratory confirmation, became a policy on 26 March, along with the new category, 'Slaughter on Suspicion' (SOS)
- Restricted Infected Areas were implemented from 27 July
- Post-epidemic sero-surveillance of small ruminants was carried out

An assessment of the control policies used in GB in 2001

Import Controls – failed, breached by smugglers

Waste Food Controls – failed, breached by indifference, greed, idleness

Early Notification – failed, breached by indifference, ignorance, idleness

National Animal Movement Ban – successful, instituted sooner than ever before

Stamping-out Policy – successful in controlling disease spread

– nationally 22 Feb to 22 March (30 days)

– locally, Cumbria, 1 March to 22 March (21 days),
Dumfries and Galloway, 1 March to 17 March (16 days)

– failed to prevent the 'tail' occurring

– successful in helping to control the 'tail'

Novel Policies

3km cull

– untargeted, 6 weeks to complete, began after epidemic peaked (5 days after in D&G, 1 day after in Cumbria)

– sero-surveillance of 3km culled sheep, 2 of 115 flocks positive (1/32 low positive, 9/56 positive)

Contiguous cull – began after epidemic peak, (9 days after in D&G, 4 days after in Cumbria)

– not implemented in north Cumbria (700 IPs), 50% of premises survived with stock, epidemic curve identical to rest of GB

Compulsory clinical confirmation/SOS – to what benefit?, led loss of support of Farmers and vets (in

extensive sheep populations FMD is usually self-limiting, virus output is low, could restrict and bleed)

Restricted Infected Areas – successful, helped control the 'tail'

Other Difficulties Faced During the 2001 Epidemic

In the first eight weeks of the epidemic there was a serious lack of resources. Most of the staff of the State Veterinary Service had had no experience of foot-and-mouth disease and had just completed long spells working away from their homes during the outbreak of classical swine fever. There was a general impatience with the apparent lack of success of the control measures in place, usually driven by Press elements more interested in sensational headlines, fuelling public disenchantment and misunderstanding. Some of the novel control procedures met serious opposition from farmers, veterinarians and the public. Vaccination was continually presented as the only solution. There was an inability to measure the progress of the Control Policies in 'real time'. As in most crises a wide range of instant "experts"

appeared (comprising veterinary scientists, biological scientists, mathematical scientists and non-scientists). The Canadian CVO observed in 1952, "I find it truly amazing, the number of foot-and-mouth disease experts (self proclaimed) who appeared almost overnight." (Childs 1952). Theoretical disease simulation models, prepared by bio-mathematicians, containing improbable assumptions (especially veterinary), were widely publicised and used for the first time in a major disease epidemic.

Real Time Data Analysis During An Epidemic

The key distributed epidemiological analyses should be calculated routinely, on a local basis, as daily counts, 3 or 5 day retrospective rolling averages and automated to allow the rapid review and assessment, as near to real time as possible, the pattern of disease spread, the effectiveness of control measures and the formulation of new strategies.

Data to be collected

- Species and number present on each IP
- Species and number clinically affected on each IP
- Species with oldest lesion on each IP
- Location of species on IP (housed, fields)
- Location of affected species on IP (housed, fields) and location of animal with oldest lesion
- Type of farm in PZ/SZ/IA (sheep, cattle, beef, dairy) provides data for calculation of attack rates
- Type of farm affected (sheep, cattle, beef, dairy) as a count and as a proportion of all farms of that type within the PZ/SZ/IA
- Laboratory results for each IP, positive or negative
- Numbers of other culls (DC) and numbers found to be infected

Routine analyses

- Epidemic curve
- EDR / Case ratio
- Average age of oldest lesion
- First lesion to slaughter
- First lesion to report
- Report to confirmation
- Report to slaughter
- DC:IP ratio
- Case finding (Report, patrol, tracing, DC cull)
- PZ area added by each new IP
- Rate of increase of area within protection zones
- Source of infection
- Cluster and sub-cluster analysis
- Nearest possible source (based on shedding and incubation windows)

Swift and accurate data gathering from IPs, its recording and collation allows real time analysis to be completed. The parameters selected are best calculated as retrospective 3 and 5 day rolling averages and should be completed for each spatio-temporal cluster of cases as this allows the distinct differences of the epidemiology and application of control measures between heterogeneous clusters to be assessed.

The Estimated Dissemination Rate (EDR), or a similar ratio of current cases compared to cases in a previous time period, are good indicators of the progress being made. Thus when this falls below 1 it can be said that the spread of infection has been controlled. Honhold and others 2004 (in press) concluded that the time from the estimated date of the first lesion to the date of slaughter (FLtoS) was a valid predictor of EDR. This is a simple calculation from data routinely collected on each IP by the veterinarians investigating the disease. FLtoS can itself be split into two periods, which provide information on the performance of the control programme. The time between first lesion and report of suspect disease to the authorities measures the speed with which disease is being detected. Time from report to end of slaughter measures the speed with which infected farms are being depopulated.

The area added by each new 3km Protection Zone is a useful indicator of the spatial spread of disease. The initial control procedures can have little effect against the first and second waves of infection, as these have already taken place and their whereabouts are unknown, and are instead intended to minimise subsequent spread from them. Once the increase in area added by new PZs indicates that the maximum spatial extent of infection has been discovered, and that newly reported cases are tending to occur within that area ('in-fill'), other control measures such as targeted veterinary surveillance visits or vaccination areas can be formulated.

Conclusion

The initial dissemination of FMD starkly illustrates the ability of the virus to be spread through the movement of infected animals showing little or no clinical signs. The virus entered the country at a time when the prevailing cold, damp climatic conditions favoured its survival away from the host, when the meteorological conditions favoured airborne dispersal from the index case and when sheep sales and movements were entering one of their seasonal peaks. However, the early imposition of movement restrictions, coupled with the rapid slaughter of infected animals and their contacts, and the implementation of strict biosecurity measures effectively contained and eventually halted the epidemic. The rapid collection, collation and analysis of field data is of paramount importance when trying to follow the course of the epidemic and judge the effects of the control measures being used.

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