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Predicting the spread of foot and mouth disease by airborne virus

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Summary

Foot and mouth disease (FMD) can spread by a variety of mechanisms which, under certain climatic and epidemiological conditions, includes the windborne spread of disease. Recent advances in knowledge of the aerobiological features of FMD are described. The strain of virus and species of infected animal are major determinants of airborne virus emission. Pigs emit most virus, cattle and sheep lesser but similar amounts to each other. Peak excretion of airborne virus by sheep occurs before the clinical phase of disease, whereas with cattle and pigs, it coincides with the development of early clinical disease. The probability of aerogenous infection differs greatly between livestock species. Cattle are the most susceptible, followed by sheep, whereas pigs are very resistant. Computer-based simulation models have been developed to analyse and predict the risk of airborne spread of FMD and have been used successfully during outbreaks to support decision-making. Further research is required to refine and extend the models for operational use.

Keywords

Airborne prediction – Foot and mouth disease – Models – Simulation – Spread – Transmission.

Introduction

The highly contagious nature of foot and mouth disease (FMD) is a reflection of a series of factors, including the following:

– the wide range of cloven-hoofed animals which are susceptible

– the enormous quantities of virus liberated by infected animals

– the range of excretions and secretions which can be infectious

– the multiplicity of the routes of infection

– the small doses of virus that can initiate infection

– the moderate stability of the virus in the environment.

The most common mechanism by which FMD is spread among ruminants and from pigs to ruminants, is by the movement of infected animals and aerogenous transmission to susceptible animals of infectious droplets and droplet nuclei. These particles originate mainly from the respiratory tract and are emitted in the exhaled breath of infected animals. The next most common mechanism of spread is by the movement of contaminated animal products, including meat, offal, milk, etc. Pigs consuming infected meat or offal as waste food and calves, drinking infected milk, are the species most likely to be infected by these routes. Foot and mouth disease virus (FMDV) can also be transmitted mechanically, e.g. by contaminated milking machines, by vehicles, especially those used for transporting animals and by people (4, 22). In addition, FMDV can be spread by the wind (13, 14, 15, 16, 24, 25, 30). The spread of FMDV by the wind is an uncommon event that requires the simultaneous occurrence of particular epidemiological and climatic conditions. However, when these conditions are united, spread of the disease can be both rapid and extensive and involve areas well beyond disease-control areas. For example, during the first three weeks of the 1967-1968 epidemic in the United Kingdom (UK), approximately 300 outbreaks were reported downwind of the primary outbreak (3). Spread of FMDV by the wind is uncontrollable, but simulation models have been developed which can be used to predict the risk of virus dissemination and the probable direction and distance of spread. Models are available which can simulate spread over short or long distances (8, 18, 19, 20, 21). This information can assist control procedures during emergencies enabling the manpower for surveillance activities to be directed in the most efficient manner. Recently, more sophisticated, faster prediction models have been developed. They can be linked to geographical information systems so that the predicted plumes can be displayed in a format that is easily analysed and interpreted (25, 26).

This paper discusses the significance of data from recent investigations of the aerobiology of FMD and their relevance to the simulated modelling of airborne spread of the disease.

Results

Minimum dose of airborne virus to infect pigs

The data for the minimum infectious doses of airborne FMDV for different species during a 24-hour exposure period have been summarised previously (25). The data have been re-evaluated for pigs because the published results were based on the use of artificially generated aerosols and a relatively insensitive virus assay system (29). Earlier studies on the quantities of airborne virus excreted by infected animals were also extended by including additional strains of FMDV. Initially, findings showed that an airborne dose of more than 800 50% tissue culture infectious dose ($TCID_{50}$) of the O_1 Lausanne strain was required to establish infection and disease, i.e. 50% minimum infectious dose (MID_{50}), in a pig. Further studies indicated that this initial estimate of 'above' 800 $TCID_{50}$ had probably been under-estimated and that the actual dose might be as high as 6,000 $TCID_{50}$. A dose of approximately 650 $TCID_{50}$ of the O South Korea (SKR) 2000 strain failed to infect any pigs. When a series of pigs were exposed for 24 h-48 h periods to natural aerosol doses of approximately 50 $TCID_{50}$ per minute of the type O UK 2001 virus or to 130 $TCID_{50}$ per minute of a C Noville virus, only one pig exposed to the C Noville virus developed a transient antibody reaction (subclinical infection). These results confirmed previous findings that pigs are very resistant to infection by airborne FMDV when compared to cattle and sheep.

The collection of air samples near pigs experimentally infected with the strains mentioned above showed that the peak amount of virus (in $TCID_{50}$) emitted per pig per 24 h was $10^{5.8}$ for O South Korea 2000, $10^{6.1}$ for O UK 2001, $10^{6.4}$ for O Lausanne and $10^{7.6}$ for C Noville (1, 2; Alexandersen *et al.*, unpublished results). By contrast, an earlier paper records that a strain of C Noville virus was excreted at levels of up to $10^{8.6}$ (7).

Characteristics of airborne virus excretion

Cattle and pigs affected by FMD emit airborne virus for a period of four to five days while sheep can excrete the virus for up to seven days. Cattle and pigs excrete maximally during the early acute stages of the disease, i.e. around the time when vesicles first appear, however, sheep behave differently with maximum airborne virus emission occurring for one to two days before the onset of clinical disease. Pigs are by far the most potent emitters of airborne virus (5, 7, 23). Cattle and sheep excrete similar amounts of airborne virus but in significantly less quantities than pigs. As mentioned previously, the strain of virus influences the amount of airborne virus excreted by the various species and also the difference between pigs and sheep/cattle. With some strains, the quantitative difference between pigs and cattle/sheep can be several thousand-fold while with others this difference is not more than 1/60th of the amount excreted by a pig (1, 2, 5, 23). Examples of these variations are given in Table I.

Table I
Peak amount of airborne foot and mouth disease virus emitted in 24 hours by an infected pig (90 kg-100 kg), sheep (30 kg-40 kg) or heifer (approximately 200 kg)

Species	Strain of virus	Amount (log $TCID_{50}$ [a]/24 h)
Pig	C Noville	8.6 [b]
Pig	O UK 2001	6.1 [c]
Heifer	O UK 2001	4.3 [c]
Sheep	O UK 2001	4.3 [c]

a) $TCID_{50}$ = 50% bovine thyroid tissue culture infectious dose
b) The values for this virus are used as a 'worst case scenario' in the virus production model (7, 25; Alexandersen *et al.*, unpublished results)
c) (2, 10; Alexandersen *et al.*, unpublished results)

Airborne virus is excreted mainly in the exhaled breath of infected animals as droplets and droplet nuclei originating from the upper and later from the lower respiratory tract (6). The precise details of the mechanism of release have not been determined.

Risk of infection to different species

The MID_{50} data were used to estimate the concentration of airborne virus within a plume required to infect different species during a 24-h exposure period (Table II). However, the data for cattle and sheep were derived from short-term

Table II
Minimum doses of airborne foot and mouth disease virus required to infect different species during a 24-hour exposure period [a]

Species	Minimal dose [a] $TCID_{50}$ [b]	Inhalation rate m^3/24 h [c]	Threshold concentration to infect ($TCID_{50}/m^3$)
Heifer	10	150	0.07
Pig	>800	50	>16 [d]
Sheep	10	15	0.7

a) The dose to infect a heifer and a sheep is given as the 'minimal' dose to cause clinical disease (9, 12) while the dose for a pig is given as the 50% minimal infectious dose to cause clinical disease. These are not absolute quantities but represent low probabilities of infection. Doses below a 'minimal' dose could possibly be infectious if a large number of cattle or sheep were exposed (27). Pigs are relatively resistant to airborne infection (1, 2) so fractions of a 'minimal' dose are unlikely to infect that species
b) $TCID_{50}$ = 50% bovine thyroid tissue culture infectious dose
c) Average inhalation rate of a 90 kg-100 kg pig, 40 kg-80 kg sheep and 500 kg-700 kg heifer (28, 1)
d) Experimental data suggest that a concentration of at least 1,000 50% tissue culture infectious dose ($TCID_{50}$)/m^3 is required to infect a pig

exposure periods and it cannot be assumed that these can be extrapolated to 24-h averages. Data generated from the long-term exposure of pigs, however, indicate that the minimum concentration required to infect this species is even higher than that predicted from short-term experiments, i.e. concentration of virus above 1,000 $TCID_{50}/m^3$ (10).

Operational use of simulation models

The input data for the models which generate the simulated plumes of airborne virus from infected premises are derived from a virus production model (VPM). The VPM uses as input data the number of animals with vesicular lesions on the holding, the species affected and the age of their lesions (25). In the absence of information about the aerobiological characteristics of the causal virus, a 'worst case scenario' can be assumed until specific data is obtained. Such a 'worst case scenario' will show all the areas at risk downwind and will, if the causal virus is excreted at very high levels, be of immediate operational value. When specific data on the causal virus becomes available, the predictions can be adjusted to give a 'most likely scenario'.

All of the airborne spread prediction models require meteorological data, either recorded from meteorological stations or derived from numerical weather prediction models, such as the High Resolution Limited Area Model in Denmark (25). Many countries record meteorological data hourly. Ideally, actual observed meteorological data from sites within 5 km-20 km (or less) of the source premises should be used. The number of animals at the source, the virus strain and species affected have a significant effect on the distance that a plume of virus can travel and still be infectious. Hypothetical examples of the predicted distances of spread when animals were infected with either the C Noville strain (25) or the UK 2001 strain (11) have previously been provided. The distances were estimated using the local scale model Rimpuff produced in Denmark (19, 20). The much shorter distances given in the second example (11) were due to the lesser amounts of airborne virus emitted by animals infected with the UK 2001 virus (Table I). In both examples, the meteorological and topographical conditions assumed were those which were most favourable for the airborne dispersion of FMDV (13, 14, 26). The simulations did not include the effect of topographical features, such as hills and mountains, which would cause a plume to deviate, nor structures, such as urban areas and forests, which would cause turbulence and a dilution of the particle concentration. These effects would reduce the distance of transmission (24). By contrast, the distances of spread could have been underestimated if fractions of a minimal infectious dose infected animals downwind (11). Therefore, the distances of spread predicted by the model are estimates and a variability of up to ten-fold should be included for measurement of virus concentrations, resulting in an approximate three-fold variability of the distances predicted. Consequently, in a 'worst case scenario', the plume generated by 1,000 infected pigs could infect cattle as far away as 20 km-300 km and sheep up to 10 km-100 km. However, pigs would only be at risk if they were less than 1 km from the source. If 100 pigs were infected, they could transmit sufficient virus to infect cattle, the species most susceptible to airborne infection (9), up to 6 km-90 km away. One hundred affected cattle or sheep could generate a plume capable of infecting cattle located less than 1 km away. The lower value in each distance prediction was estimated using the airborne excretion values for the UK type O 2001 virus while the higher value was estimated using the data obtained with the C Noville virus.

Discussion

Foot and mouth disease is one of the most contagious diseases known to human and veterinary microbiology and is the single most important constraint to international trade in livestock and animal products. In the event of an outbreak, the prevention of the development of an epidemic requires rapid reporting, accurate diagnosis and speedy implementation of control and eradication measures. The difficulty of ensuring that these actions are completed rapidly and the devastating consequences which can result if they are not, makes FMD greatly feared by farmers, the livestock industry and state Veterinary Services.

Foot and mouth disease is a difficult disease to eradicate because of its contagious nature and the variety of mechanisms by which the virus can be transmitted. When an outbreak occurs in a country or zone normally free from the disease, the traditional response is to apply the so-called 'stamping-out' policy. This entails the slaughter of all the affected and in-contact cloven-hoofed animals on the infected holding and the disposal of the carcasses by burning, burial or rendering. Simultaneously, quarantine measures are imposed on the livestock in the surrounding area and vehicles and people are disinfected before they leave the control area. The effective application of these measures should prevent further spread by the movement of infected livestock, animal products, vehicles or people. However, these strategies leave open the possibility of spread by uncontrollable mechanisms which include the airborne transport of virus particles (droplets and droplet nuclei) by the wind and possibly, transmission by wildlife, either mechanically or following infection. Airborne spread is the most important mechanism of uncontrollable spread and although this is not a common event, when it occurs the speed and extent of spread can be spectacular (3, 8, 13, 14, 15, 16, 24, 30). Most commonly, the pattern of airborne spread is from pigs at source to cattle downwind. This reflects the vast quantities of airborne virus emitted by infected pigs and the extreme susceptibility of cattle to aerogenous infection (2, 5, 7, 9, 12, 23).

The topographical and climatic factors which favour airborne spread are a flat terrain, high humidity, low precipitation and low to moderate wind speed (25, 26). Long distance transport of virus in plumes is especially likely across seaways as the surface turbulence is low and the concentration of airborne particles can be maintained for greater distances than over land. The longest distance of airborne spread is believed to be 300 km when outbreaks in pig farms in Brittany (northern France), in March 1981, spread infection to cattle on the Isle of Wight (8). By contrast, the longest recorded distance for spread over land occurred at the commencement of the FMD epidemic which took place in the UK in 1967-1968 when disease was spread over 60 km. In the latter epidemic, the same pattern of spread prevailed, i.e. pigs at source to cattle downwind (3).

Models for simulating the airborne spread of FMD have been developed in England, Denmark, France and Spain. They fall into two categories, those designed for predicting spread over short distances (<10 km) and those predicting spread over distances of up to several hundred km (8, 18, 19, 20, 21, 25, 26). Models can be improved as a result of advances in knowledge of the behaviour of particles in the atmosphere, computer technology and the aerobiology of FMDV.

The results summarised in this paper have confirmed that pigs emit larger amounts of airborne FMDV than cattle and sheep and that the amounts of virus emitted by cattle and sheep are comparable. These results also confirmed that the strain of virus markedly influences the amount of airborne virus emitted. Therefore, the major determinants of the quantity of airborne virus emitted from an infected holding and the distance downwind that animals will potentially be at risk are the species affected on the holding, the number of animals affected, the strain of virus, the weather and the topography. The relative risks of spread have been simulated using data obtained from experiments with strains at either end of the spectrum of airborne excretion, i.e. the UK type O 2001 strain, excreted in low amounts and the C Noville strain, excreted in high amounts. The simulations suggested that 100 affected pigs could transmit sufficient virus to infect cattle up to 6 km-90 km away depending on the strain of virus, but in the case of pigs downwind, the predicted distance of spread was less than a few hundred meters. In this context, the relatively large differences in the maximum amounts of airborne virus excreted by pigs infected with different strains of virus will have a significant influence on the distance of spread to cattle and sheep. A fraction of a 'minimal' dose could potentially be infectious, especially if a large number of cattle were exposed (27). Theoretically, the exposure of pigs to a fraction of a MID_{50} could result in a few animals becoming infected (17, 27). These animals could then amplify the amount of virus and transmit the disease to others, either directly or indirectly. In the experiments conducted by the authors, pigs were only infected when exposed to a very large dose of airborne virus. Doses below the MID_{50} resulted in a weak, transient antibody reaction in a few animals. These pigs did not transmit infection to others in contact with them. This suggests that, at least in pigs, there is a threshold level below which infection does not occur, or more likely, where respiratory clearance can prevent the establishment of infection. The distances over which plumes of virus originating from cattle or sheep would present a risk are much shorter. The simulations predict that 100 infected cattle or sheep would be required at source for an infectious dose to travel a distance of less than 1 km and be sufficient to infect cattle. Pigs are unlikely to be infected by this route unless they were located very close to infected cattle or sheep. These predictions are based on the virus emissions by animals at rest. Data is not available for the excretion rates of active animals but a higher respiratory rate would probably lead to an increase in the amount of virus emitted.

The remarkable resistance of pigs to infection by airborne virus compared to cattle and sheep has been confirmed. Indeed pigs were so resistant that the minimal infectious doses for the different strains were difficult or impossible to establish. Therefore, during outbreaks, the risk of infection of pigs under plumes of airborne virus would probably be extremely low. A zero risk could not be predicted since some strains of virus might be more infectious and furthermore, if a large concentration of pigs was exposed, the probability would be greater that a few animals might initially succumb to infection. Infection could then develop within the herd and form a potential source for dissemination further afield.

Conclusions

Among the various mechanisms by which FMD can be spread is the transport of virus on the wind. This is an uncommon means of spread over long distances, requiring the coincidence of particular epidemiological and climatic factors. However, when airborne spread occurs, the consequences can be spectacular. This mechanism of spread is important because infection can be carried beyond control areas and across borders and seaways. Computer-based simulation models have been developed which can analyse the risk of airborne spread during outbreaks. The generation and depiction of airborne plumes by these models can assist decision-making and help to optimise the efficiency with which personnel are deployed for surveillance purposes. Further research is required to refine the input data for the models and to improve their accuracy.

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Prévision de la diffusion du virus de la fièvre aphteuse par voie aérienne

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Résumé

La fièvre aphteuse peut se propager par plusieurs mécanismes y compris, dans certaines conditions climatiques et épidémiologiques, par voie aérienne. Les auteurs décrivent les récents progrès enregistrés dans la connaissance des caractéristiques aérobiologiques de la fièvre aphteuse. La souche virale et les espèces animales contaminées jouent un rôle déterminant dans la diffusion du virus par voie aérienne. La plus forte excrétion de virus est observée chez les porcins. Elle est plus faible chez les bovins et les ovins, qui en produisent des quantités équivalentes. L'excrétion maximale intervient en phase préclinique de la maladie chez les ovins, alors qu'elle coïncide avec l'apparition des premiers signes cliniques chez les bovins et les porcins. La probabilité d'infection aérogène varie considérablement selon l'espèce animale. Les bovins y sont les plus sensibles, suivis des ovins ; les porcs sont très résistants. Des simulations sur ordinateur ont été effectuées pour analyser et prévoir le risque de diffusion du virus de la fièvre aphteuse par voie aérienne ; elles ont été utilisées avec succès lors des épizooties, pour appuyer la prise de décision. Des études complémentaires sont nécessaires pour affiner et développer ces simulations en vue d'un usage opérationnel.

Mots-clés

Diffusion – Fièvre aphteuse – Modélisation – Prévision de la diffusion aérienne – Simulation – Transmission.

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Predicción de la propagación de la fiebre aftosa por transmisión aérea del virus

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Resumen

La fiebre aftosa puede propagarse por diversos mecanismos, entre ellos, en determinadas condiciones climáticas y epidemiológicas, la transmisión del virus por vía aérea. Los autores describen los hallazgos más recientes sobre las características aerobiológicas de la fiebre aftosa. La cepa vírica y la especie del animal infectado son factores decisivos en la emisión aérea del virus. Los porcinos emiten la mayor cantidad de virus, y los bovinos y ovinos una cantidad menor, aunque parecida en ambos casos. En la oveja, el máximo nivel de excreción aérea del virus es anterior a la fase clínica de la enfermedad, mientras que en los bovinos y porcinos el pico de excreción coincide con la aparición de los primeros signos clínicos. La probabilidad de infección aerógena es muy distinta según la especie de que se trate. Los bovinos son los más susceptibles, seguidos por los ovinos. Los porcinos, en cambio, son muy resistentes a esa vía de contagio. Con objeto de analizar y predecir el riesgo de propagación de la fiebre aftosa por vía aérea se han elaborado modelos de simulación por ordenador, utilizados con éxito, en el curso de brotes infecciosos, como instrumento de apoyo a la adopción de decisiones. No obstante, es necesario seguir investigando para perfeccionar y ampliar los modelos y mejorar así sus prestaciones en la práctica.

Palabras clave
Fiebre aftosa – Modelos – Predicción de la transmisión por vía aérea – Propagación – Simulación – Transmisión.

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