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Quantitative Data on Airborne Foot-and-Mouth Disease Virus: Its Production, Carriage and Deposition [and Discussion]

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Quantitative data on airborne foot-and-mouth disease virus: its production, carriage and deposition

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The evidence for the airborne spread of foot-and-mouth disease during outbreaks in Europe between the turn of the century and the late 1960s is reviewed. The early experimental evidence is also outlined. More recent experimental investigation is then described in detail, including the procedures used to quantify airborne foot-and-mouth disease virus levels excreted by different susceptible species, the probably origin of this virus, the times of maximum virus release, the influence of virus strain and the nature of virus–aerosol particle association. Further experiments are described in which the influence of environmental factors such as ultraviolet light, relative humidity and pollutants on the survival of foot-and-mouth virus in aerosols has been examined. Finally, the extent of knowledge about the amounts of foot-and-mouth disease virus required to infect susceptible livestock by the airborne route is discussed.

Introduction

Foot-and-mouth disease (FMD) is an acute condition of cloven-hoofed livestock caused by an aphthovirus and characterized by the appearance of vesicular lesions on the feet, in and around the mouth and on the mammary gland. The mortality rate in adult animals is generally low but can be high in young stock, which may die peracutely without developing external lesions. Some species of wildlife, notably deer, are also susceptible.

FMD was the first animal disease shown to have a viral aetiology, and its highly contagious nature and marked ability to spread was recognized from a very early stage (Loeffler & Frosch 1898). Characteristic is the occasional spread to animals remote from known foci of infection without any history of contact. Spread can be over considerable distances, crossing land borders and seaways between countries. Examples are: the Netherlands to eastern England: northern Germany to Denmark and Denmark to Sweden. Whereas Scandinavian authorities (Bang 1912; Forssman 1931) proposed that long-distance spread could be explained by wind transportation of virus, either as free virus or in association with particulate matter, most British authorities believed that the carriage of virus by birds was more likely (*Report of Departmental Committee on Foot-and-Mouth Disease* 1952–4). However, a series of laboratory-associated outbreaks and field epidemics during the 1960s provided a mass of circumstantial evidence to support the windborne theory. The important climatic conditions (Donaldson 1979) were wind direction (Hugh-Jones & Wright 1970; Sellers & Forman 1973), wind speed (Tinline 1969; Sellers & Forman 1973), wind veer (Tinline 1969) and high humidity (Sellers & Forman 1973; Sasov & Taranova 1973).

The extent and rapidity of spread at the start of the 1967–8 epidemic in the U.K. created enormous logistic problems for the Animal Health Division of the Ministry of Agriculture, Fisheries and Food when more than 300 premises were affected during the first three weeks.

Because the primary mechanism of spread during this period was later attributed to wind transport of virus (Henderson 1969; Wright 1969; Smith & Hugh-Jones 1969; Tinline 1969; Hugh-Jones & Wright 1970), there was a need to establish data on the quantitative aspects of this type of spread and to determine if this information could be useful in devising future control procedures by predicting airborne spread. For descriptive and historical reasons it is convenient to review the development of knowledge of this topic before and after the 1967–8 epidemic in the U.K. under the headings of dispersal of airborne virus, survival of airborne virus, and infection by airborne virus.

Dispersal of airborne virus

The hedgehog played an important part in early attempts to demonstrate excretion of airborne FMD virus when Gibbs (1931) and Edwards (1934) showed that hedgehogs infected with FMD excreted virus in their breath and that infection could be transmitted between caged hedgehogs held separately within the same room. The first investigators to report the recovery of airborne FMD virus from domesticated species were Hyslop (1965) and Kiryukhin & Pasechnikov (1966) working with adult cattle and calves, respectively. More detailed investigations were subsequently carried out by Sellers & Parker (1969) and Donaldson *et al.* (1970). These workers established that the quantity of virus excreted is a function of the strain involved, the species of animal and the stage of clinical disease. The strains found to yield the highest quantities of airborne virus were several O strains and C Noville; lower yields were obtained from animals infected with C Lebanon, A_5 and A_{22} strains. Pigs excreted considerably more airborne virus than sheep or cattle. On a 24 h basis, the maximum recoveries from sheep and cattle were $\log_{10}5.4$ i.d.$_{50}$, whereas pigs excreted $\log_{10}8.0$ i.d.$_{50}$ (Sellers 1971). After very recent studies, the figure for pigs has been revised to $\log_{10}8.6$ i.d.$_{50}$ (Donaldson *et al.* 1982). The duration of excretion for all species was around 4–5 days. The highest levels were obtained from sheep on day 1 after inoculation, when only primary lesions were evident. Cattle and pigs, however, excreted maximally when vesicular lesions were at an early acute stage of generalization. The pattern of excretion and the quantities of airborne virus obtained from other ruminants such as deer and goats have been found to be similar to those with sheep and cattle (Forman *et al.* 1974; Donaldson *et al.* 1981).

Animals exposed by contact excreted airborne virus in two periods: an early period between 30 min and 22 h after exposure and a second period at the time of appearance of lesions (Gibbs *et al.* 1975; Sellers *et al.* 1977; Donaldson & Ferris 1980). The first period probably represented virus trapped on the bristles, hair or wool of the animal, and perhaps also along the lumen of the upper respiratory tract, with virus being dislodged from these sites by mechanical movement and airflow. The second phase of excretion followed the replication of virus in the respiratory tract. In pigs the excretion of airborne virus from the upper respiratory tract preceded that from the lower regions (Donaldson & Ferris 1980). High levels of immunity are required to prevent the replication of virus in the respiratory tract of cattle, sheep and pigs and its subsequent liberation in aerosols (Sellers *et al.* 1977).

The virus excreted into the air by infected animals is associated with a range of particle sizes, 65–71 % of the total infectivity being in particles greater than 6 μm in diameter, 19–24 % in particles 3–6 μm in diameter and 10–11 % in particles less than 3 μm in diameter (Sellers & Parker 1969; Donaldson *et al.* 1981). The nature of the relation between virus and host material

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in infective aerosol particles has not been determined, though preliminary investigations suggest that the amount of infectivity in larger particles can be highly variable, ranging from 1 plaque-forming unit (p.f.u.) to more than 200 p.f.u. (Donaldson 1979).

The mechanism by which virus is liberated from sites of replication into the air is also unknown, though the nature of FMD virus replication in cell cultures, and histological observations, suggest that cell lysis and microvesicle formation followed by rupture, are probably involved (Edwards 1934; Korn 1957).

Survival of airborne virus

Russian workers were the first to report stability studies on FMD virus in aerosols. Voinov & Khor'kov (1968) sprayed a suspension of rabbit-adapted A_{22} virus into an airtight dark room and took air samples at various conditions of relative humidity (r.h.) and temperature at intervals over 48 h. Infectivity was recovered in samples taken up to 24 h but the environmental conditions that favoured survival were not recorded. In collaboration with workers from the Microbiological Research Establishment, Porton Down, preliminary studies at Pirbright showed that at 20 °C aerosols of strain O_1 BSF 1860 survived well at high r.h. but lost infectivity in dry air conditions (G. J. Harper, J. N. Wilson & R. F. Sellers, personal communication). More detailed investigations demonstrated that when aerosol clouds were sampled at 1 s of age there was a critical r.h. range separating good from poor airborne survival. This was between 55 and 60% r.h. (Barlow 1972; Donaldson 1972). A similar profile of r.h.-dependent survival was found with other FMD virus strains representing serotypes O, A and C. No SAT or Asia 1 serotypes were examined. Further tests showed that strains originating from regions of relatively dry climate (A_{22}, Iraq; C, Lebanon; O_1 Pacheco, Argentina) survived better than those from more temperate regions (O_1 Lombardy and O_2 Brescia, Italy; O_1 BFS 1860, England). More recent studies with an O_1 strain from Malta showed that it behaved as a strain from a 'dry' region (Donaldson *et al.* 1981). When these stability results were compared with excretion yields of airborne virus obtained from animals infected with the different strains, an inverse relation was found between the quantity of virus excreted and its stability in aerosols (Donaldson *et al.* 1970; Donaldson 1972).

An important factor that was shown to influence the survival of airborne FMD virus under experimental conditions was the nature of the suspending fluid from which aerosols were generated (Donaldson 1973; Barlow & Donaldson 1973). Aerosols of O_1 BFS 1860 virus produced from milk, nasal fluid, cell culture fluid or a suspension of faeces showed little or no loss of infectivity at 70% r.h. over 1 h. However, aerosols from bovine saliva lost more than $\log_{10} 3.0$ $i.d._{50}$ of infectivity under the same conditions. Further studies revealed that bovine saliva contains an organic anti-viral molecule that is dialysable and sensitive to heating at 70 °C for 3 h but not at 60 °C for the same time. By spraying virus from immune fluids it was shown that the complexing of virus with antibody protected it against inactivation at low r.h. When these complexes were recovered from aerosol clouds they could be dissociated by treatment with trichlorotrifluoroethane to liberate infectious virus. It was concluded that the protection of virus against r.h. inactivation was due to surface coating by antibody and that a similar mechanism may be involved in the apparent prevention of spread of infection from carrier animals to susceptible in-contacts (Kaaden *et al.* 1975; Donaldson & Ferris 1979).

The influence of outdoor factors on airborne FMD virus survival has also been examined

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by using the microthread technique of Druett & May (1969). Provided that the r.h. was higher than 60%, neither daylight nor the 'open air factor' greatly influenced virus survival (Donaldson & Ferris 1975). Although the influence of temperature on airborne FMD virus survival was not examined in detail, high recoveries of infectivity were obtained from microthreads after 30–60 min exposure periods at 27 °C, and experience with other viruses in aerosols suggests that the effect of temperature is of minor influence compared with r.h. (Akers 1969).

The size of aerosol particle used in all these airborne stability studies was in the range 0.5–3.0 μm diameter. As most of the infectivity produced by FMD-infected animals is associated with considerably larger particles, it is very probable that under natural conditions the influence of environmental factors on the survival of infectivity is less than that seen experimentally (Sellers & Parker 1969; Benbough & Hood 1971).

Infection by airborne virus

Early attempts to transmit FMD between livestock by the airborne route under experimental conditions were unsuccessful (Lebailly 1925; Traub & Wittman 1957), which led Schang (1960) to suggest that the separation of animals by fences 10 m wide might be a useful control procedure to use in the event of outbreaks in the field. However, in the same year, from Denmark, Fogedby *et al.* (1960) reported the transmission of disease between housed cattle separated by a distance of greater than 10 m. Two serotypes of virus were used and transmission was achieved more readily with an O than an A serotype. With the latter strain it was necessary to abrade the muzzles and tongues of the recipient animals to achieve transmission.

Hyslop (1965) and Eskildsen (1969) showed that cattle could also be infected with artificially generated aerosols of FMD virus. Eskildsen's results demonstrated that small particle aerosols containing $\log_{10} 2.7 \times$ mouse l.d.$_{50}$ of infectivity were sufficient to initiate infection and that the probable route of virus invasion was the lungs. Sutmöller & McVicar (1973) proposed that large airborne particles might play a role in initiating infection via the eye. They demonstrated that cattle could be infected with droplets containing $\log_{10} 2.0$ p.f.u. applied to the conjunctiva. The dose required to infect cattle with virus sprayed into the nostrils was in the same range as that via the eye but varied with virus strain (Henderson 1952; Sutmöller *et al.* 1968).

The infection of pigs with aerosols of FMD virus has been reported by Terpstra (1972). With small particle aerosols, infection took place via the lungs and a dose of $\log_{10} 2.6 \times$ mouse l.d.$_{50}$ was required. When larger particles were used and instilled within the mouth or sprayed into the nostrils a higher dose was needed. In the latter case early replication of virus began in the tonsils and lymph nodes of the head and throat region, and the incubation period was shorter.

The dose required to infect sheep with intranasally administered virus was $\log_{10} 4.0$ i.d.$_{50}$ (McVicar & Sutmöller 1969), but dose levels with aerosols have not been reported.

Although there has been some controversy over the importance of precipitation in the airborne spread of FMD, analyses of outbreaks suggest that infection of animals downwind is more likely by inhalation than by ingestion (Sellers 1971; Sellers & Forman 1973; Gloster *et al.* 1982). Also, in view of their susceptibility to infection by the respiratory route and the higher volume of tidal air that they sample, it has been proposed that in instances where cattle, sheep and pigs are at risk it will be in the cattle that evidence of the downwind spread of FMD

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will be seen first (Sellers 1971). Analyses of a series of outbreaks in which airborne spread of FMD is believed to have taken place supports this proposal (Hugh-Jones 1972; Sellers & Forman 1973; Gloster *et al.* 1982; Donaldson *et al.* 1982).

In collaboration with the Meteorological Office the information outlined in this paper on the main factors influencing the airborne excretion, survival and transmission of FMD virus has been integrated with the biophysical, meteorological and mathematical factors influencing airborne particulate dispersion to develop numerical models for forecasting and analysing the airborne spread of FMD. Two models are now available, one for forecasting secondary spread over short distances (up to 10 km), the other for greater distances (Gloster, this symposium). There is, however, a requirement for much more information on the fate of different-sized particles within the respiratory tracts of livestock and the minimal doses of airborne FMD virus required to initiate infection. Such information would be valuable for refining the numerical models previously mentioned and also for developing standardized procedures for challenging animals with aerosols of virus and evaluating vaccination regimens for protecting them against airborne infection.

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Discussion

R. F. Sellers (*Animal Virus Research Institute, Pirbright, U.K.*). To answer the question of whether airborne foot-and-mouth disease virus is excreted by infected animals in saliva or on oral bacteria or skin scales, the spread of foot-and-mouth disease over long distances is more likely to be as nasal secretion rather than as saliva. As Dr Donaldson has shown, survival of virus is much worse in saliva. Whether it spreads on rafts of oral bacteria or on skin scales is not known, but experiments done at Pirbright tend to show that the largest amounts of virus come from nasal exhalations.

J. Lacey (*Rothamsted Experimental Station, Harpenden, U.K.*). Early in his paper Dr Donaldson mentioned that all excretions and secretions were rich sources of foot-and-mouth disease virus. However, he subsequently made little reference to these, although urination could perhaps be a rich source of aerosolized virus (Lacey, J. & Gregory, P. H. (1980) In *Contemporary microbial ecology* (ed. D. C. Ellwood *et al.*), pp. 75–91. London: Academic Press). Initially, a target film or pool would be formed on the ground. Incident liquid then hitting this would throw up vast numbers of droplets with a wide spectrum of sizes. Those larger than 5 μm are likely to be projected above the surface boundary layer, aided by convection above the pool, which is initially at body temperature. Assuming 4% dissolved solids, the large number of splash droplets in the range 20 ± 200 μm in diameter will evaporate in seconds to droplet nuclei of only 5–35 μm diameter. These will be carried out of buildings in ventilation and diffuse downwind. They could become relatively innocuous until concentrated by rain falling through the diffusing cloud and 'scrubbing out' the suspended particles. Prolonged rain would wash the virus to the ground, but the impact of rain drops on wet herbage could propel into the air 1000–5000 virus-laden droplets of a size capable of being inhaled by animals in the field or drawn into animal houses with ventilation air.

A. I. Donaldson. I agree that it would seem quite feasible that airborne foot-and-mouth disease virus could be dispersed in the way that Dr Lacey has proposed and perhaps also by other procedures such as the splashing of infected milk or spraying of slurry (Donaldson, A. I. (1979) *Vet. Bull.* **49**, 653–659). However, compared with the breath of pigs, these fluids do not contain such high levels of infectivity (Sellers, R. F. (1971) *Vet. Bull.* **41**, 431–439) and so these mechanisms of airborne virus dispersal are probably of secondary importance.

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