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Quantitative Risk Assessment of FMD Virus Transmission via Water

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Foot-and-mouth disease (FMD) is a viral disease of domesticated and wild cloven-hoofed animals. FMD virus is known to spread by direct contact between infected and susceptible animals, by animal products such as meat and milk, by the airborne route, and mechanical transfer on people, wild animals, birds, and by vehicles. During the outbreak of 2001 in the Netherlands, milk from dairy cattle was illegally discharged into the sewerage as a consequence of transport prohibition. This may lead to contaminated discharges of biologically treated and raw sewage in surface water that is given to cattle to drink. The objective of the present study was to assess the probability of infecting dairy cows that were drinking FMD virus contaminated surface water due to illegal discharges of contaminated milk. So, the following data were collected from literature: FMD virus inactivation in aqueous environments, FMD virus concentrations in milk, dilution in sewage water, virus removal by sewage treatment, dilution in surface water, water consumption of cows, size of a herd in a meadow, and dose-response data for ingested FMD virus by cattle. In the case of 1.6×10^2 FMD virus per milliliter in milk and discharge of treated sewage in surface water, the probability of infecting a herd of cows was estimated to be 3.3×10^{-7} to 8.5×10^{-5}, dependent on dilution in the receiving surface water. In the case of discharge of raw sewage, all probabilities of infection were 100 times higher. In the case of little dilution in small rivers, the high level of 8.5×10^{-3} is reached. For 10^4 times higher FMD virus concentrations in milk, the probabilities of infecting a herd of cows are high in the case of discharge of treated sewage (3.3×10^{-3} to 5.7×10^{-1}) and very high in the case of discharge of raw sewage (0.28–1.0). It can be concluded that illegal and uncontrolled discharges of contaminated milk into the sewerage system may lead to high risks to other cattle farms at 6–50 km distance of the location of discharge within one day. This clearly underlines current measures that prohibit such discharges, and also asks for strict control. This risk assessment clearly demonstrated the potential significance of FMD virus transmission via water, and the results will be useful on an international scale, and could also serve as a basis for other FMD risk-assessment models.

KEY WORDS: Cattle; foot-and-mouth disease virus; probability of infection; waterborne transmission

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1. INTRODUCTION

Foot-and-mouth disease (FMD) is a viral disease of domesticated and wild cloven-hoofed animals. It is characterized by the development of vesicles in and around the mouth and on the feet. FMD virus is highly contagious in nature, which is reflected by its wide host

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range, the high virus concentrations that are excreted, the low dose required for infection, and the multiplicity of transmission routes (Alexandersen *et al.*, 2002). FMD virus is excreted in saliva, blood, semen, breath, feces, urine, milk, and other bodily fluids and tissues of infected animals. FMD virus is known to spread in a number of ways: by direct contact between infected and susceptible animals, by animal products such as meat and milk, by the airborne route and mechanical transfer on people, wild animals, and birds, and by vehicles (Sellers, 1971).

Airborne transmission of FMD virus contained in aerosols occurs directly between animals in a stable, but also over large distances by the wind (Alexandersen *et al.*, 2002; Daggupatty & Sellers, 1990; Sellers, 1971). In addition, it has been reported that FMD virus is 10^4–10^5 times more infective when inhaled than when ingested (Sellers, 1971). For these reasons, airborne transmission of FMD has received much attention as being the most important route of transmission. Although airborne transmission of FMD virus by wind occurs infrequently, its effects are dramatic. In addition to being rapid and extensive, it can result in transmission of infection beyond established disease control areas and has been recorded to spread over a distance of 60 km over land and more than 250 km over sea (Alexandersen *et al.*, 2002).

Waterborne transmission is considered to be a transmission route of minor importance because of the apparently higher infectious dose that is required to cause an infection by ingestion of FMD virus in water. To our knowledge, no publications exist on transmission of FMD virus via water. In fact, the actual contribution of water to the spreading of FMD virus is unknown. However, because of the high concentrations that are excreted in liquids, and the longer survival of FMD virus in liquids compared to aerosols, transmission by water may be underestimated. Besides that, water pathways are highly branched and the flow of water may be very rapid.

Until 2001, no outbreak of FMD virus had occurred in England for a period of 20 years. On February 20, 2001 a sample was found positive for FMD virus serotype O (Samuel & Knowles, 2001). After this first reporting, the FMD virus was found to spread quickly to France and the Netherlands. Between March 21 and April 22, 26 Dutch farms were found to have FMD virus infected animals, mostly dairy cattle. The outbreak had a large impact on daily life because of transport prohibitions, preventive killing of nearly 300,000 farm animals, closing of nature parks, and threats to husbandry animal species.

During the outbreak in the Netherlands, milk from dairy cattle was illegally discharged into the sewerage. Such discharges of milk were a consequence of transport prohibition and occurred on farms that were not yet identified as being contaminated, but were located near contaminated areas. This situation existed especially at the end of the winter period in 2001 when it became impossible to discharge milk into cellars that were already completely filled with liquid manure. Illegal discharge of milk directly into surface water (ditches) is not likely because it will be noticed. Nevertheless, during the 2001 outbreak some of such discharges did occur and colored surface waters white. In addition, this caused oxygen deficiency and massive fish mortality. A similar effect can be expected (and occurred) from milk discharges into the sewerage. The high oxygen demand of the milk paralyzes the sewage treatment plants, resulting in discharge of not totally biologically treated or raw municipal wastewater into surface water.

Cattle that are grazing are given the surface water to drink that abuts the meadow. In the case of illegal discharges of contaminated milk they may be exposed to contaminated surface water, which is diluted to some extent.

The objective of the present study was to assess the risk of infecting dairy cattle with FMD virus spread by water. To that aim the probability of infecting dairy cows drinking from FMD virus contaminated surface water due to illegal discharges of contaminated milk was estimated. This allows evaluation of measures that are taken to prevent or reduce spreading of FMD virus in water. This risk assessment is conditional on the discharged milk being contaminated.

2. METHODS

2.1. Outline of Quantitative Risk Assessment

The following pathway of spreading FMD virus was evaluated:

1. Illegal discharge of contaminated milk into sewerage.
2. Transport to a sewage treatment plant (STP).
3. Discharge of biologically treated and raw sewage into surface water.
4. Dilution of discharged sewage in surface water depending on size of STP and receiving surface water.
5. Exposure of cows to FMD virus by consumption of contaminated surface water.

Table I. Inactivation of FMD Virus in Liquid Manure

	°C	Time Period (Days)	Inactivation Rate Coefficient ($\log_{10}$/day)	Reference
20% cattle manure in water	4	0–66	0.048	Parker (1971)
Cattle liquid manure	Winter	0–63	0.05	
Pig liquid manure	5		<0.042	Haas *et al.* (1995)
Cattle liquid manure	4		0.041	
	17		0.049	
	20		0.12	

6. Calculation of the probability of infection using dose-response relationship data.

The following data were collected from literature:

1. Inactivation rate coefficient of FMD virus in aqueous environments.
2. Concentrations of FMD virus in milk.
3. Dilution in sewage water.
4. Virus removal by sewage treatment.
5. Dilution of FMD virus in surface water.
6. Average consumed volume of water per cow and per day.
7. Average size of a herd in a meadow.
8. Dose-response data for ingested FMD virus by cattle.

The following quantities were calculated:

1. FMD virus concentrations in sewage and surface water.
2. Total dose D ingested via water.
3. Probability of infection, r_o, of ingested FMD virus by cattle.
4. Probability of infection, r_a, of inhaled FMD virus by cattle.
5. Probability of infecting an individual cow within exposure period T, P_i.
6. Probability of infecting at least one cow out of herd of N cows within exposure period T, P_N.

2.2. Inactivation of FMD Virus in Aqueous Environments

Generally, FMD virus particles are more stable in aqueous suspensions than in aerosols. The most important factor determining inactivation of FMD virus in aerosols is relative air humidity (Donaldson, 1988). At a relative air humidity of over 55–60%, inactivation is at its lowest, but at a lower humidity inactivation can be very rapid. The inactivation rate of FMD virus strain O_1 is 0.6 $\log_{10}$ $TCID_{50}$ (dose that infects half of the tissue cultures) per hour at 60% relative air humidity and 4.2 $\log_{10}$ $TCID_{50}$ per hour at 40% relative air humidity.

Inactivation of FMD virus in aqueous suspensions was found to proceed at two different rates (Donaldson, 1997; Sellers, 1971). Initially, inactivation is rapid, followed by a phase of much slower inactivation. However, when conditions for survival are more favorable, first-order rate inactivation can reasonably be assumed. More favorable conditions are at relatively low temperature and near neutral pH. Such conditions existed in surface water during the outbreak of 2001 in the Netherlands. Table I summarizes first-order inactivation rate coefficients of FMD virus in liquid manure from pigs and cattle. From these data, it was concluded that inactivation of FMD virus in liquid manure at 4–17°C proceeds slowly at a rate of 0.04–0.05 $\log_{10}$ per day.

On inactivation in milk only qualitative data are available. FMD virus could still be detected in milk at 18°C after seven days and at 4°C after 15 days (Hedger, 1970). FMD virus is rapidly inactivated at pH values lower than 7. The pH of milk from infected cows varies between 6.7 and 7.7 (Sellers, 1969). During the 1982 Denmark outbreak, FMD virus contaminated milk was heated for 15 seconds to 72°C and for 3 seconds to 80°C and then pH was adjusted to 4.5. Milk that was treated this way was fed to farm animals on the isle of Funen without causing an outbreak (Donaldson, 1997). For calculations in the present study, it was assumed that pH of the milk and the water into which it was discharged remained near neutral.

No data on inactivation of FMD virus in wastewater or in surface water are available. Because the Netherlands outbreak took place in early spring, water and air temperatures were approximately 10°C. Inactivation under those conditions was assumed to be 0.05 $\log_{10}$ per day in milk, wastewater, and liquid manure. In the calculations, the inactivation rate coefficient $\mu = \ln(10) \times 0.05 = 0.12$ per day was applied.

2.3. Concentrations of FMD Virus in Milk

During the FMD outbreak of 1967–1968 in England, virus concentrations in the milk in milk tanks were found to be 10^4 mouse ID_{50} (dose that infects half of the mice) per milliliter and those in milk churns 3×10^5 mouse ID_{50} per milliliter (Sellers, 1969). Cow milk contains FMD virus particles up to 4 days before the animal develops blisters (Donaldson, 1997). In milk from an infected cow showing no clinical symptoms a maximum of 4×10^6 $TCID_{50}$ per milliliter was found. However, concentrations of FMD virus in contaminated milk that leaves a farm may be lower due to dilution with milk from uninfected cows. Furthermore, the production of milk by an infected cow is reduced from the beginning of the infection (hypogalactia), as was observed during the Isle of Wight outbreak in 1981 (Sellers, 1969). Although in the milk of some cows concentrations of 4×10^6 $TCID_{50}$ per milliliter were found, those found in the milk tank were only 1.6×10^2 $TCID_{50}$ per milliliter. This difference by a factor of 10^4 cannot be explained just by dilution with milk from uninfected cows. Probably, inactivation of virus plays a role too. A large variation in FMD virus concentration is probably the case. On one hand, dilution with milk from uninfected cows and inactivation result in lower concentrations. On the other hand, direct contact between cows will lead to rapid infection of a large part of the herd and consequent excretion of FMD virus in milk by most of them. In addition, excretion of FMD virus in milk by an infected cow may fluctuate substantially.

For our purposes, a concentration of FMD virus in milk, C_m, of 1.6×10^2 $TCID_{50}$ per milliliter is chosen by default. However, because of the large uncertainties about the extent of dilution and inactivation, calculations will also be conducted applying a 10^4 times higher concentration in milk to demonstrate the effect concentrations in milk may have on the estimated probability of infection.

2.4. Dilution of Discharged Milk with Sewage and Removal of FMD Virus by Biological Treatment in a STP

In the present study, calculations were based on a discharge of a volume, V_m, of 5 m^3 of FMD virus contaminated milk (LEI, 2002). The discharged milk will be diluted strongly by the sewage before it reaches the STP. The average flow rate of all STPs in the Netherlands, F_s, amounts to 11,000 m^3/day, but varies strongly from 620 to 80,000 m^3/day dependent on STP capacity, but also between STPs of similar capacity (CBS, 1999).

Of importance for inactivation are residence times in sewage and surface water. Commonly, sewage resides 15 hours in the aeration tank, 1.5 hours in the first, and 2.5 hours in the second sedimentation tank, amounting to a total residence time of 19 hours. Assuming an average travel time of 5 hours from point of discharge to STP, a total residence time in sewage, T_s (day), of 1 day from milk discharge into the sewerage till sewage discharge into surface water was applied.

Data on removal of FMD virus by biological treatment of sewage do not exist. FMD virus belongs to the family of *Picornaviridae* (small RNA viruses), like enteroviruses. Because of their similarity in shape and size, one may assume that their removal by sewage treatment is as efficient as that of enteroviruses. Biological treatment of sewage in two large sewage treatments plants in the Netherlands was found to reduce enterovirus concentrations by a factor of 100 (Hoogenboezem *et al.*, 2001). Therefore, the same removal efficiency was assumed to be the case for FMD virus in our calculations.

In the case of storm water overflow or if treatment efficiency of the STP is completely reduced due to the high oxygen demand of the milk, raw sewage will be discharged in surface water. Therefore, two scenarios were followed: discharge of raw and biologically treated sewage. Concentrations are, therefore, reduced by a factor R_s equal to 1 or 100. Thus, concentration of FMD virus in discharged sewage (effluent), C_e (m^{-3}), was calculated as follows:

$$C_e = \frac{C_m V_m}{F_s T_s} e^{-\mu T_s} \frac{1}{R_s}. \tag{1}$$

2.5. Dilution of Discharged Sewage in Surface Water

Generally, small STPs discharge into small surface waters and large STPs into large surface waters, but a large range in dilution of discharged sewage with surface water is obvious. For calculating FMD virus concentrations in surface water, C_r (m^{-3}), complete mixing of sewage effluent with surface water during the 1-day discharge of FMD virus contaminated effluent was assumed.

$$C_r = \frac{F_s}{F_r} C_e, \tag{2}$$

where F_r (m^3/day) is the flow rate of the water in a river.

Table II. Dimensions of STPs and Receiving Rivers (CBS, 1999; CIW, 2000)

STP		Receiving River					
Size[a] (pe × 1,000)	F_s (m^3/day)	Size	F_r (m^3/day)	F_r/F_s	Width (m)	Depth (m)	L_r (m)
≤25	2.0×10^3	Small	8.6×10^4	44	10	1.5	5.8×10^3
25 to 100	9.6×10^3	Medium	2.2×10^6	226	50	2.6	1.7×10^4
>100	4.3×10^4	Large	2.3×10^7	529	125	3.8	4.8×10^4

[a]pe = population equivalent; F_s is discharge rate of STP; F_r is flow rate of river; L_r is characteristic length (1-day flow) of river.

Table II summarizes characteristic discharge rates of STPs and flow rates of receiving rivers in the Netherlands (CBS, 1999; CIW, 2000). Thus, the calculations were conducted for three different dilution factors: 44, 226, and 529. After 1 day of discharge, river water will be contaminated over a stretch or characteristic length L_r of 5.8, 17, and 48 km, respectively.

2.6. Cow Data

On average, a dairy farm in the Netherlands has 53 cows and 27 ha of grassland (LEI, 2002). Pastures are commonly divided into 2-ha parcels. During summertime a herd of cows stay on such a parcel for a few days and is then transferred to the next parcel. Ditches that are used for watering the cattle separate the parcels. On average, 53 cows are present on a parcel of 2 ha in the Netherlands. Each day, a cow drinks on average 50 L of water (Keuning & Groenwold, 1993), so we have a drinking rate F_c of 0.05 m^3/day.

2.7. Exposure

Exposure to FMD virus decreases in time, t (day), due to inactivation of FMD virus. The total dose of FMD virus particles over a period of T days is

$$D = \int_0^T F_c C_r e^{-\mu t}\, dt = \frac{F_c C_r}{\mu}(1 - e^{-\mu T}). \qquad (3)$$

The probability of infection was calculated for an exposure period T of 1 day, which is the day of discharging contaminated sewage into the river water. The next day, FMD virus concentrations at a specific location in the river will be reduced by a combination of dispersion and advection with the flowing water.

2.8. Dose-Response Data

The exponential dose-response relation according to a "single hit" model (one virus is able to cause one infection) is as follows (Haas, 1983):

$$P_i = 1 - e^{-rD}, \qquad (4)$$

where r is the probability of infection by one virus and D is the dose. P_i is the probability of infection of an individual that was exposed to the average dose D. This model was applied to calculate the probability of infection by FMD virus.

Dose-response data from calves that were exposed to FMD virus strain O_1 in artificially formed aerosols and FMD virus strain SAT2 in naturally formed aerosols (Donaldson *et al.*, 1987), from pigs exposed to naturally formed aerosols contaminated with FMD virus strain O_1 Lausanne (Alexandersen *et al.*, 2002), and from pigs orally exposed to different O strains (Sellers, 1971) were applied to estimate values of r. To that aim the software Mathematica 4.2 (Wolfram Research, Oxfordshire, UK) was used to estimate maximum likelihood values.

2.9. Probability of Infection

The probability of an individual cow becoming infected within 1 day of exposure, P_i, was calculated by applying Equation (4). Because all cows in a herd may drink the same water it is very likely that all or most cows of the herd become infected this way (primary transmission). An infected cow with or without clinical signs will excrete FMD virus particles and may infect other cows in the herd (secondary transmission). Regardless of the occurrence of secondary transmission, if at least one cow in a herd is infected, the whole herd is considered to be infected and will be destroyed. Therefore, it is important to calculate the probability that at least one cow out of N cows becomes infected, P_N (Sutmoller & Vose, 1997). The probability that a cow does not become infected is described by:

$$P_i\,[0] = 1 - P_i = e^{-rD}. \qquad (5)$$

Table III. Dose-Response Data from Exposure with FMD Virus of Calves by Inhalation and of Pigs by Ingestion and Estimated r Values from Fitting to the Exponential Dose-Response Model

Calf, Inhalation (Donaldson *et al.*, 1987)			Pig, Inhalation (Alexandersen *et al.*, 2002)			Pig, Ingestion (Sellers, 1971)		
Dose $\log_{10}$ $TCID_{50}$	N_{inf}	N_{tot}	Dose $\log_{10}$ $TCID_{50}$	N_{inf}	N_{tot}	Dose $\log_{10}$ $TCID_{50}$	N_{inf}	N_{tot}
1.1	1	1	1.7	0	3	5.0	2	30
1.2	0	1	1.9	0	7	5.2	1	5
1.4	3	4	2.4	0	5	5.4	5	7
1.6	4	5	2.5	2	9	6.5	1	6
1.7	1	4	2.5	1	5			
1.8	1	1						
1.9	5	5						
2.1	1	1						
2.4	3	3						
2.5	1	1						
2.6	1	1						
4.0	1	1						
4.1	1	1						
4.2	1	1						
4.4	1	1						
5.2	2	2						
r	3.0×10^{-2}		1.6×10^{-3}			4.1×10^{-7}		
95% CI	1.7×10^{-2} to 5.1×10^{-2}		7.4×10^{-4} to 3.0×10^{-3}			2.0×10^{-7} to 7.5×10^{-7}		

N_{inf} is the number of infected animals, N_{tot} is the number of exposed animals.

The probability that none of the cows in a herd of N cows becomes infected is described by

$$P_N[0] = (P_i[0])^N = e^{-rDN}. \quad (6)$$

Thus, the probability that at least one cow out of N cows becomes infected is described by

$$P_N = 1 - e^{-rDN}. \quad (7)$$

3. RESULTS

The exposure data as well as the estimated values of r obtained from fitting the dose-response model (Equation (4)) are presented in Table III. Similar estimates were obtained by French *et al.* (2002) for cattle (0.03, using the same data) and for sheep (0.04). Fig. 1 shows the combined dose-response data of calves that were exposed to FMD virus in aerosols (Donaldson *et al.*, 1987), of pigs exposed to FMD virus in aerosols (Alexandersen *et al.*, 2002), of pigs orally exposed to different FMD virus O strains (Sellers, 1971), and the fitted exponential dose-response curves. Pigs seem to be less sensitive to FMD infection through aerosols than calves.

Dose-response data of oral dosage to cattle are even more scarce (Sellers, 1971). An oral dose of 3.2×10^6 did not lead to an infection among cattle and less than half of a group of cattle became infected by a dose of 6.3×10^5 to 6.3×10^6. Based on this information, the dose-response of cattle to FMD virus via oral administration is clearly not very different from that observed for oral infections of pigs. Therefore, it was assumed that the dose-response relation of ingested FMD virus is the same for cows and pigs.

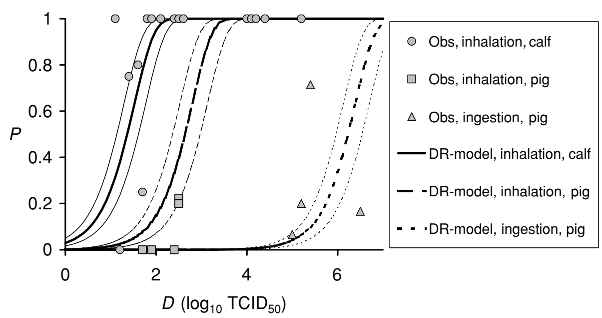

Fig. 1. Dose-response curve of calves exposed to artificial aerosols with FMD virus type O_1 BFS 1860 and to natural aerosols with FMD virus type SAT2 SAR 3/79 (Donaldson *et al.*, 1987); dose-response curve of pigs exposed to natural aerosols with O_1 Lausanne (Alexandersen *et al.*, 2002) and dose-response curve of pigs orally exposed various O-strains FMD virus (Sellers, 1971). Thick lines represent dose-response curves for average r and thin lines for 95% confidence limits of r. See Table III for dose-response data.

Table IV. Probability of Infection of an Individual Cow (P_i) and of at Least 1 Out of 53 Cows (P_N)

	Discharge of Treated Sewage		Discharge of Raw Sewage	
F_r/F_s	P_i	P_N	P_i	P_N
		$C_m = 1.6 \times 10^2$/mL		
529	6.1×10^{-9}	3.3×10^{-7}	6.1×10^{-7}	3.3×10^{-5}
226	6.4×10^{-8}	3.4×10^{-6}	6.4×10^{-6}	3.4×10^{-4}
44	1.6×10^{-6}	8.5×10^{-5}	1.6×10^{-4}	8.5×10^{-3}
		$C_m = 1.6 \times 10^6$/mL		
529	6.1×10^{-5}	3.3×10^{-3}	6.1×10^{-3}	2.8×10^{-1}
226	6.4×10^{-4}	3.4×10^{-2}	6.2×10^{-2}	9.7×10^{-1}
44	1.6×10^{-2}	5.7×10^{-1}	8.0×10^{-1}	1.0

F_r/F_s: dilution factor of sewage in surface water.

The probability of infection by a single virus from inhaling contaminated aerosols (r_a) is much larger than from drinking contaminated water (oral exposure) (r_o):

$$\frac{r_a}{r_o} = 7.1 \times 10^3. \tag{8}$$

Table IV summarizes the probabilities of infection according to the different scenarios. Starting with C_m equal to 1.6×10^2/mL and treated discharge, P_i is only 6.1×10^{-9} for the exposure to contaminated water from a large river (dilution factor of 529), the probability of infection is 10 times higher in the case of a dilution factor of 226 but still only 1.6×10^{-6} in the case of a dilution factor of 44. However, of more importance is P_N, which is approximately 100 times higher for all dilution factors. In the case of dilution factors 226 and 529, these probabilities may be considered to be low. The probability of infection of a herd of 53 cows in the case of a dilution factor of 44 is 8.5×10^{-5}.

Obviously, in the case of discharge of raw sewage, all probabilities are 100 times higher. In the case of a dilution factor of 44 times, the probability of infecting a herd of cows is estimated to be 8.5×10^{-3}, which is high. The results in Table IV also show that for 10^4 times higher FMD virus concentrations in milk the probabilities of infection increase 10^4 times. This increase is lower for the higher probabilities. In the case of discharge of raw sewage, the probabilities of infection of a herd of cows are very high.

4. DISCUSSION

In the present article, probabilities of infecting cows with waterborne FMD virus were estimated. Due to the lack of data there is considerable uncertainty in concentrations of FMD virus in milk and in the probability of infection by one virus, r. Estimates on the level of uncertainty associated with many model parameters would rely for a large part on expert opinion. Therefore, in our approach we chose to make use of ranges, like for the virus concentration in milk, the difference between treated and raw discharges of wastewater, and the dilution into surface water. These ranges reflect our uncertainty about the values of these parameters. Given this range of parameter values a strong indication could be given on the significance of spreading FMD virus via this pathway.

It was found that illegal and uncontrolled discharges of contaminated milk into the sewerage system may lead to high to very high risks to other cattle farms at 6–50 km distance of the location of discharge within 1 day. The following day that same water has been transported over a larger distance, but by then probabilities of infection may have dropped, primarily due to further dispersion of FMD virus in the water. Nevertheless, probabilities of infecting cows may still be high.

The probabilities of infections due to drinking from FMD virus contaminated large river waters are much lower than from small river waters due to more dilution. However, in the larger rivers, contamination will stretch over larger distances. How many herds of dairy cattle are at risk of infection obviously will depend very much on the spatial distribution of those herds.

The difference in infectivity between inhaled and ingested FMD virus is likely due to the sensitivity of FMD virus to low pH. FMD virus and poliovirus, both being Picornaviruses, consist of a single RNA molecule and 60 copies of four coat proteins VP1–VP4 and a small but variable number of copies of protein VP0 (Newman & Brown, 1997). Although strong similarities exist in RNA sequence, structure, and physical properties between different Picornaviruses, they have evolved different ways of entering a host and its susceptible cells and they recognize different receptors (Oliveira *et al.*, 1999). Poliovirus persists under a large range of pH (3–9) and is able to pass the digestive tract and withstand the low pH in the stomach, whereas FMD virus is unstable at pH values lower than 7.

In this study, the exponential dose-response model (Haas, 1983) was applied. In addition, the beta-Poisson model (Teunis & Havelaar, 2000) was also fitted to the dose-response data and likelihoods were compared in a likelihood ratio test. For the calf inhalation data (Donaldson *et al.*, 1987), neither a significant difference between both models was found nor between these two models and a binomial likelihood supremum (Teunis *et al.*, 1996). Therefore, in this case the simplest (most parsimonious) model was chosen: the exponential dose-response model. However, likelihood estimates for the pig ingestion data (Sellers, 1971) were significantly lower than for the supremum model, indicating that both dose-response models cannot describe these data adequately. Probably, unidentified confounding factors exist, such as heterogeneity in virus infectivity across isolates, differences in animal susceptibility, and/or extra-Poisson uncertainties in the actual dose that was given to the pigs. Note that these ingestion data originated from three different studies using two different virus isolates (Sellers, 1971).

During sewage treatment aerosols may be formed. Because a 7.1×10^3 times lower dose (Equation (5)) would be needed to cause infection by inhalation of contaminated aerosols compared to drinking of contaminated water, it is possible that the aerosols formed in a STP are also a potentially important source of contamination. Concentrations of fecal indicator microorganisms in the air leeward to the STP are approximately 10^7–10^9 times lower than in the sewage water of the STP (STOWA, 2002). A cow inhales on average 120 m^3 of air per day. If a cow was to inhale such aerosols directly in the vicinity of a STP, the daily dose would be 2 to 4 orders of magnitude lower than the ingested dose from surface water following discharge of raw sewage. However, due to the much higher infectivity of FMD virus via inhalation, probabilities of infection would be 2 to 3 orders of magnitude higher. Commonly, there will be considerable dispersion of the aerosols with distance, but concentrations in air need to drop by a factor of 100–1,000 in order not to be a potentially more important source of infection than the contaminated surface water. This roughly gives an idea on the relative importance of airborne versus waterborne transmission of FMD virus. Obviously, it depends very much on distance, wind velocity, and direction whether the probability of infection by this pathway is higher or lower than that by drinking contaminated surface water.

The conclusion that spreading of FMD virus in water due to discharges of contaminated milk can lead to high to very high probabilities of infecting cattle clearly underlines current measures that prohibit such discharges, and also asks for strict control. The importance of milk as a source of FMD virus can be reduced drastically by inactivating FMD viruses. For example,

Table V. Maximum FMD Virus Concentrations in Milk, Urine, and Feces of Infected Farm Animals (Sellers, 1971; Parker, 1971; Donaldson, 1987)

		Cattle	Pig	Sheep
Milk	ID_{50}/mL	4.0×10^6		
Urine	ID_{50}/mL	7.9×10^4		
Feces	ID_{50}/g	3.2×10^5	7.9×10^2	5.0×10^2

by means of adding citric acid (2%) to the milk at least 24 hours before it leaves the farm (preferably to a destruction plant). This treatment is prescribed in a strategy scheme of the Dutch Ministry of Agriculture (LNV, 2001). Also, stables and the premises of a farm need to be decontaminated by means of applying citric acid.

If infected animals were out in a meadow, the soil needs to be decontaminated with acid and then be ploughed. However, the strategy scheme does not describe disposal of manure. Table V summarizes maximum concentrations of FMD virus that were found in milk, urine, and feces. Although those in milk are the highest, FMD virus concentrations in urine and feces may be more stable because of a higher pH. In addition, more urine and feces are produced than milk. Manure (feces plus urine) and rinse water are collected as slurry in cellars and periodically applied to agricultural land. After land application, manure may run off by rainfall and contaminate surface water. The contribution of FMD virus in surface water from runoff is difficult to evaluate because this is highly dependent on the presence of cattle defecating near a ditch, as well as on rainfall intensity. The probability of FMD virus reaching surface water from leakage out of manure to groundwater and subsequent transport to surface water can be assumed to be negligible because of more dilution, longer travel times, and adsorption to soil (Schijven & Hassanizadeh, 2000).

In addition, wastewater is produced from cleaning the milking installations in the parlor and the milk tank. This cleaning is conducted twice a day in three steps. The first step is rinsing with warmish water that is collected in the slurry cellar. The second step is rinsing with water and detergents, the third step with water. The water from the second and third steps is discharged into the sewerage. The milk tank is rinsed 5 times per fortnight applying the same three steps (CUWVO, 1995). Most of this wastewater reaches a sewage treatment plant, where it is treated and then discharged into surface water. In the outer regions, wastewater of dairy farms is either treated in small wastewater treatment systems, like constructed wetlands, before discharging into surface water. FMD virus concentrations in this rinse water are obviously lower than those in milk.

Spreading of FMD virus by means of water seems to be of more concern for dairy farms than for pig and sheep farms. In pig farms the animals usually stay indoors and get drinking water. Surface water is also used as a source for producing drinking water. However, drinking water treatment in the Netherlands achieves reduction of virus concentrations by 5–8 $\log_{10}$.

This risk assessment clearly demonstrated the potential significance of FMD virus transmission via water and underlines the importance of prohibiting discharges of contaminated milk. The results will be useful on an international scale and could also serve as a basis for other FMD risk-assessment models.

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