Risks of spreading foot and mouth disease through milk and dairy products

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Summary
A review of epidemics of foot and mouth disease (FMD) has highlighted the important role which raw (untreated) milk can play in the spread of the disease in a country which is normally free of FMD and whose cattle are not routinely vaccinated. The greatest hazard is likely to be in the early stages of an outbreak, before disease control measures have been implemented. The spread of FMD through milk can be prevented by the effective application of control measures combined with 'codes of practice' for the treatment of potentially infected milk. The author considers the probable mechanisms of transmission of FMD by milk and dairy products. These mechanisms are based on the quantities of virus excreted in milk, the survival of the virus under various management and manufacturing conditions and the minimum doses required to initiate infection in susceptible animals by different routes. The key points for consideration when making a risk assessment of the importation of milk and dairy products are also discussed.

Keywords

Introduction
Milk and dairy products are very important commodities in international trade. The World Trade figures for 1993 were (in thousands of tonnes): whole milk (1,085); skimmed milk (923); powdered milk (31); condensed milk (462); cheese (977) and butter (779) (27).

The possibility of the transmission of foot and mouth disease (FMD) by milk has been known from the beginning of this century (26). Examples of outbreaks attributed to the movement of infected milk are as follows:
- the 'Crewe episode' during the 1951-1952 epidemic in the United Kingdom (UK), when the feeding of infective milk to calves in transit led directly or indirectly to 101 new outbreaks (5)
- 22 outbreaks resulting from the collection of milk from 25 infected premises during the 1967-1968 UK epidemic (12, 20)
- 5 outbreaks of a total of 22 during the Denmark epidemic in 1982 on the islands of Funen and Zealand (11).

Terbruggen (31) demonstrated the important epidemiological feature that FMD virus may be excreted in the milk of animals before clinical signs of the disease are apparent. He also showed that the survival of virus in milk is dependent on temperature, the bacterial content and pH. His attempts to provide precise quantitation were constrained, however, by a lack of sensitive techniques. The 1967-1968 UK epidemic stimulated a fresh impetus for both epidemiological and experimental studies on the role of milk in FMD (6, 7, 12, 20, 30).

The role of milk and dairy products in the epidemiology of foot and mouth disease

Movement of milk
Dawson (12) divided the movement patterns of milk transportation in the UK into two categories: the primary movement of milk, i.e. the collection and subsequent
movement of milk from the premises of origin (the farm) to a second premises (the dairy); and the secondary movement of milk, i.e. the movement of milk or dairy products from the primary collection centre to other dairies, distribution centres or to the consumer. This category also included the activities of the producer-retailer.

Dawson detailed possible ways in which the movement of milk might be involved in the spread of the disease and investigated the evidence by conducting case studies on outbreaks during the UK 1967-1968 epidemic. He obtained evidence that the primary movement of raw (untreated) milk was a major hazard and that, when infective milk was collected and moved from high probability 'source premises', there was a high frequency of subsequent outbreaks of disease on other premises. In the case of the secondary movement of raw milk, no evidence could be found that this was associated with the spread of disease, despite the enormous quantities transported from the infected area. He concluded that this was probably because all of that milk was transported to large conurbations for human consumption or was used in manufacturing processes.

During the epidemic an association was found, however, between the secondary movement of skimmed milk and some outbreaks. Three outbreaks, all in pig farms, were attributed to the feeding of infected skimmed milk delivered by a single bulk milk tanker (21). This is one of the few examples in the literature of the involvement of a dairy product in the spread of FMD.

The majority of the milk-associated cases identified by Dawson occurred during the early stages of the epidemic. Later, evidence for the involvement of milk was found less frequently. This was attributed to a greater awareness of the problem and the implementation of control measures, which reduced the hazards, by the authorities, milk hauliers and dairies.

Transmission associated with bulk milk tankers

The hazards associated with bulk milk tanker collections during the 1967-1968 UK epidemic were analysed by Dawson (12), who identified the following special epidemiological features:

a) the short length of the pipe on the tanker for connection to the farm tank, which is usually close to the site of milking, presents a high risk of transfer of virus in contaminated milk from the tanker to the ground, the driver and onwards to the milking herd

b) the high probability that, unless the pipe is washed out, some milk remaining in it from a previous collection will be spilt during coupling/uncoupling

c) the dip-stick measurement of the amount of milk in the farm tank by the driver which may contaminate his hands and clothing if the milk is infective

d) the filling of the tanker with milk will result in the displacement of air from the tanker. Agitation within the tanker during filling and transportation could then result in the release of infective aerosols.

Epidemiological links were found between the routes taken by bulk milk tankers and the spread of FMD during both the 1967-1968 UK and 1982 Denmark epidemics (11, 20). It was not established, however, which of the mechanisms proposed by Dawson (12) was involved in the transmission of virus.

Experimental investigations at that time at the Microbiological Research Establishment, Wiltshire, UK, in which Bacillus globigii spores were added to the milk in a tanker, showed that the number of spores recovered when the vented air was sampled was a very small proportion of those present in the milk (19). It was concluded that ground contamination was a more likely route of dissemination of FMD virus than air-borne spread. Although the probability of spread by infective aerosols from milk tankers may be low, some veterinary authorities have included steps in their contingency plans to eliminate it. These include the following:

- fitting filters on the vent pipes
- piping vent air through the tanker engine
- filling tankers by positive displacement from the bottom of the tank to reduce splashing and aerosol generation within the tanker (11; M. Sabirovic, personal communication).

Mechanisms of transmission of foot and mouth disease by milk

Sellers (30) has suggested that there are three possible mechanisms by which animals could be infected by contaminated milk. They may drink the milk, inhale infective droplets or aerosols of milk or the milk may contaminate people who subsequently handle animals.

The milk from cattle incubating FMD may contain virus for up to four days before vesicular signs of the disease become evident (6). A sample of milk collected from a clinically normal animal during an outbreak has been shown to contain up to $10^{5.5}$ TCID$_{50}$ per ml (15). Theoretically, less than 0.1 ml of that milk would contain in excess of an infective dose (ID) for a pig by ingestion. (The infective dose is the smallest quantity of virus which, in theory, is capable of initiating infection leading to clinical disease.) This dose has been shown to be approximately $10^{3.0}$ ID$_{50}$ by a series of investigators (22, 32).

However, during an outbreak in milking cattle, it is likely that the quantities of virus in the milk leaving a farm will be much less. First, given the high degree of surveillance of milking animals, it is improbable that all the cows would be infected and excreting virus in their milk before the disease was recognised, and so there would be dilution of infected milk with that from uninfected animals. Furthermore, since
hypogalactia is a feature of FMD in milking animals, generally commencing from the early onset of clinical signs, the volume of milk from affected animals would be reduced. Evidence supporting these proposals was found during the Isle of Wight outbreak in the UK in 1981, when, although the quantities of virus in milk samples from some individual cows were as high as 10^6.6 TCID_{50}/ml, the amount of virus in the bulk milk tank on the farm was 10^5.2 TCID_{50}/ml (15). A daily intake of 0.7 litres of such bulk milk would be sufficient to infect a pig. In the case of calves requiring a dose of 10^6.3 ID_{50} by ingestion to initiate infection, the concentration would have to be between 10^2.5 and 10^2.0 ID_{50}/ml for sufficient virus to be consumed in the daily requirements of 0.5 to 9 litres (30).

The spillage of infected milk has also been proposed as a mechanism for the spread of FMD (12). There are three ways in which an animal could be infected subsequently: by inhaling the aerosols arising from the splashes; by drinking the milk (see above); or the milk could contaminate people who then handle animals (30). Cattle may be infected by inhaling very small amounts of FMD virus. Fifty percent of cattle exposed experimentally to the air-borne strain O1 BFS virus in the infectivity range 10^{1.1} to 10^{2.9} TCID_{50} and 46% of cattle exposed to air-borne Southern African Territories (SAT) 2 virus developed clinical disease (16). Available data indicate that pigs are approximately 1,000-fold less susceptible by this route. Terpstra (32) calculated that an air-borne dose of at least 10^2.6 mouse ID_{50} is required to infect a pig. The amount of air-borne virus which would result from the splashing of milk is not known but it seems possible that droplets containing 10^4.0 ID_{50} could be produced from milk with titres as high as 10^6.6 TCID_{50}/ml.

Transmission by people would require direct contact with the muzzle, mouth or udder of the animal. Damage to the epithelium is essential and this could occur during milking by hand when there are teat abrasions; when a stockman restrains an animal by inserting fingers in its nostrils, especially if this is done roughly; or during physical inspection of the mouth (30). Sellers also proposed other ways of transmission by people: they could inhale air-borne virus and later disperse it by exhalation, coughing or sneezing, allowing it to be inhaled by an animal, or virus on the clothing might be inhaled by an animal, but the probability of transmission by these routes is much lower than those involving handling of the (susceptible) epithelium.

**Influence of vaccination**

The epidemiological and experimental findings discussed above primarily relate to the UK and Denmark, countries where prophylactic vaccination is not used. By comparison, the quantities of virus excreted in the milk of cattle in a country where vaccination is routine could be expected to be reduced or even nil, depending on the degree of immunity of the cattle to the challenge strain of virus. Additionally, the milk from vaccinated cows would contain sufficient antibody to have a neutralising effect when mixed with that from non-vaccinated animals. Dutch workers found that milk samples obtained from individual cows which had been vaccinated under field conditions, and from milk samples taken from a bulk tanker and a retail shop, inactivated 90% to 99% of the FMD virus which had been mixed with it, either as primarily infected milk or as a virus filtrate (13).

Vaccinated cattle may fail to develop clinical disease when exposed to FMD virus but they can act as a source of infection for other animals (17). The inapparent dissemination of virus and the contamination of milk and dairy products is a possibility under such circumstances. In an assessment of the risk associated with milk or a dairy product from a country or zone where vaccination is practised, the standards of practice in dairies and manufacturing plants are important considerations in the context of the possibility of cross-contamination of a dairy product by raw (untreated) milk.

**Codes of practice for the treatment of potentially infected milk**

The realisation that the movement of infected milk may be a major hazard in the control of FMD has prompted veterinary authorities to include 'codes of practice' for treating milk in their national contingency plans for dealing with the disease. For example, the code of practice for milk destined for feeding to animals during the 1982 Denmark epidemic consisted of two heat treatment steps (72°C for 15 sec and 80°C for 3 sec), followed by acidification to below pH 4.5. Subsequently, it was estimated that about 18 million kg of milk treated in this manner were fed to domestic animals on the island of Funen during the epidemic without causing any outbreaks (11).

**Foot and mouth disease virus survival in milk and dairy products**

The biphasic characteristics of the slopes for FMD virus inactivation in fluid suspensions subjected to temperature and pH treatment have long been recognised (1, 18). The slopes indicate that there is an initial phase of rapid inactivation of virus followed by a more protracted period of inactivation. In many cases, a temperature- or pH-resistant fraction of infectious virus will remain, the demonstration of which requires the use of a very sensitive method. Sellers (29) demonstrated that the inactivation curves of FMD virus suspended in whole milk and in fluid dairy products subjected to heat or pH treatment are biphasic.

Many investigators have demonstrated the presence of a resistant fraction of FMD virus after the treatment of infected
milk and dairy products by exposure to high temperature or pH. However, in order to detect this virus, it has generally been necessary to inject the treated material into cattle (3, 4, 9, 10, 14, 24). These findings have some relevance to an assessment of the risk associated with products originating from milk, e.g. lactalbumin and lactoglobulin, which are incorporated into pharmaceutical preparations destined for inoculation into susceptible animals or for use in laboratories in media for tissue culture systems where there is a very small possibility of the amplification of virus. However, they have little relevance to an assessment of milk and dairy products involved in international trade, where the primary consideration is the probability of animals becoming infected by natural routes of exposure, in particular by the oral route. As outlined previously (see section above), relatively high doses of FMD virus are required to initiate infection in pigs and cattle by the oral route – the infective doses being about 10^5.0 ID_{50} and 10^5.0 ID_{50}, respectively (22, 30, 32). Henderson and Brooksby (22) remarked on the difficulty of infecting cattle by feeding virus in glass tubes which were masticated by the animals. In the case of pigs, groups of three and six animals fed with beef and pork, respectively, from freshly killed infected animals failed to develop the disease. However, when the size of the group was increased to thirty animals for a repeat experiment, two were infected. In a separate investigation, Terpstra (32) found that the oral dose for a pig was over 10^4.4 mouse ID_{50}. He cited earlier work by Nathans in which irregular results were obtained with small amounts of virus – two of five pigs instilled with 10^2.4 to 10^3.6 mouse ID_{50} became infected. By contrast, seven animals which received 10^5.4 mouse ID_{50} all developed disease. These results emphasise the importance of considering the probable number of animals which may be exposed in making a risk analysis.

The following example is provided to illustrate the degree of risk which may be associated with milk or a dairy product which has passed through a stage of pasteurisation:

a) suppose that 10% of a herd of fully susceptible lactating cows becomes infected and that their milk contains the maximum concentration recorded under natural conditions, i.e. 10^6.6 ID_{50}/ml (15)

b) this infective milk will be mixed with non-infected milk, first in the tank on the farm and then in the bulk milk tanker, which will reduce the virus concentration. Dilution factors of 10-fold and then 5-fold for these two steps are not improbable. The virus concentration in the milk will be lowered first to 10^5.6 ID_{50}/ml and then to 10^4.9 ID_{50}/ml

c) at the dairy, further mixing with uninfected milk and the normal practice of filtration to remove coarse particles, which would also remove large-sized infectious cell clumps, would further reduce the virus concentration by, say, 10-fold. The concentration of virus will then be 10^3.9 ID_{50}/ml (or 10^6.9 ID_{50}/litre)

d) high-temperature-short-time (HTST = 72°C for 15 sec) pasteurisation of the milk will produce a 10^4.9 to 10^5.0 ID_{50} reduction in infectivity (28, 29). The concentration of virus will then be at 10^1.9 to 10^1.9 ID_{50}/litre

e) for a high probability of infection, a single pig would have to ingest 125 to 1,250 litres of this milk to obtain an infective dose of virus (10^5.0 ID_{50}) and a calf would have to consume 1,250 to 12,500 litres. These are physical impossibilities. Viewed alternatively, the daily milk intakes for a pig and a calf are 0.5 to 4.5 litres and 0.5 to 9.0 litres, respectively (30). Therefore, a pig with maximum intake could ingest 10^2.4 to 10^3.7 ID_{50} of virus. This is 20- to 200-fold below the infective dose for a pig. While there is no evidence that pigs can be infected by virus at these concentrations, there is a low theoretical possibility that if a large number of pigs were exposed infection might occur.

It can be concluded, therefore, that the risk of pigs or calves becoming infected by the ingestion of pasteurised milk, or a dairy product derived from it, is low.

The insufflation, i.e. inhalation, of infected milk or a dairy product is another possible route by which pigs or calves might be exposed to virus. The infective doses by the respiratory route for a pig and a calf are approximately 10^6.6 ID_{50} and 10^5.0 ID_{50}, respectively (16, 32). Taking the example given previously for HTST-pasteurised milk, a pig would have to inhale between 500 and 5,000 ml of milk and a calf between 12.5 and 125 ml of milk to become infected. Therefore, the risk by insufflation for a pig is extremely low and that for a calf very low.

The risk of a dairy product being a vehicle for the transmission of FMD virus after a process which involves a higher temperature than conventional HTST treatment, or HTST followed by a further heat treatment, or pasteurisation followed by acid treatment, is remote. Ultra-high temperature (UHT) treatment, for example, produces a 10-fold greater reduction of infectivity than HTST treatment (10).

In European countries, milk and skimmed milk used for the production of milk powder is heated to 80°C to 90°C for 30 s (33). This time-temperature treatment has been shown to produce a 10^6.4 to 10^5.0 ID_{50} decrease in infectivity (24). The subsequent roller or spray-drying procedures involved in the production of milk powder could be expected to further inactivate any residual virus.

The survival of FMD virus in Cheddar and Camembert cheese has been investigated by Schjerning-Thiesen (28), who found that infectious FMD virus could not be detected in Cheddar cheese two weeks after processing and that a trace amount of virus was present in Camembert cheese, one day after processing, but not on the second day or thereafter. The milk samples, which contained serotypes O, A or C virus, and infectivity in the range from 10^5.2 to 10^6.5 mouse ID_{50}/ml at the beginning, had been heated at 63°C for 15 min before being processed into the cheeses. Callis et al. (8) cited the work of Blackwell, in which FMD virus survived curing in
Cheddar cheese for 60 days but not 120 days (pH 5.0); however, in this case the cheese had been manufactured from milk which had not been preheated. The infectivity titre of virus in the milk at the beginning of the experiment was not stated. Kihm et al. (25) found that Emmentaler cheese produced from infective milk contained infectious virus during the manufacturing process up to the end of piling. The milk was a pooled mixture from cows, six to ten days after they had been infected by contact with an ox excreting type C virus, and had an initial infectivity of $10^{1.1}$ to $10^{2.5}$ TCID$_{50}$. Samples of cheese taken on days 1, 2 and 5 after manufacture were negative for FMD virus by cattle inoculation. Kihm et al. stressed that the results for one type of cheese should not be extrapolated to another as the manufacturing conditions, particularly temperature, pH and time, differ considerably.

Sweet whey obtained as a by-product of either Cheddar or Camembert cheese manufacture has been found to contain infectious FMD virus (2) but the amounts were extremely low, and the reservations expressed previously about the relevance of such findings to the possibility of infection by natural routes apply. Blackwell (3) reported that acid whey (pH 4.7) obtained as a by-product of casein did not contain detectable FMD virus by cattle inoculation.

The report of Walker et al. (34), which provides a thermal 'death' time curve for the time required at different temperatures to inactivate fully FMD virus in whole milk and skimmed milk, is of relevance for risk assessment of milk components used by the pharmaceutical industry, e.g. lactalbumin and lactoglobulin, which ultimately may be injected into FMD-susceptible animals or incorporated into laboratory tissue culture systems where infectious virus could replicate.

**Risk of foot and mouth disease for countries importing milk and dairy products**

The factors to be considered in making a risk assessment of importing milk and dairy products can be subdivided into exporting country factors and importing country factors.

The principles are the same as for other animal products. Detailed descriptions of the way in which the Australian Quarantine and Inspection Service uses risk assessment and risk management have been provided by Wilson and Banks (35). Heng and Wilson (23) report a risk assessment on the importation of milk and milk products (excluding cheese) from countries which are not free from FMD. However, the latter authors exaggerated the risks by concluding that any residual infectious virus in milk and dairy products after manufacturing processes would pose a risk to livestock. In doing so, they overlooked the crucially important consideration of the infective doses of virus which are required to initiate infection in susceptible animals.

**Discussion**

There is abundant evidence that the movement of infective raw milk can play an important part in the spread of FMD during outbreaks. Of considerable epidemiological importance is the fact that cattle, and probably other milking animals, such as goats and sheep, can excrete the virus in their milk for several days before the clinical signs of disease become apparent. Once the presence of the disease has been recognised, however, the implementation of control measures and 'codes of practice' for treating potentially infected milk should prevent further spread by that means. Available evidence suggests that the risk of spread by pasteurised milk or dairy products derived from pasteurised milk is very low. Support for this conclusion is provided by van Bekkum and de Leeuw (33), who stated, '... in the period that FMD was widespread on the European continent, no outbreak has ever been attributed to imported milk products, that had been submitted to any kind of heat treatment, although no restrictive measures on importation were taken as nobody was aware of an existing risk'. Exceptions might be pharmaceutical products originating from contaminated milk which are injected into animals.

In this paper the author has endeavoured to identify the risks associated with infective milk and dairy products during outbreaks of FMD and treatment by various manufacturing processes. It is absolutely essential to consider the risks in terms of both the probable amount of infectious virus present in a product and the route by which an animal might be exposed to it. It is the opinion of the author that, too often, these considerations have been either ignored or overstated in the past, resulting in the imposition of unnecessary restrictions on trade.

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Risques de propagation de la fièvre aphteuse par le lait et les produits laitiers

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Résumé
Une étude portant sur les épidémies de fièvre aphteuse a montré le rôle important que pouvait jouer le lait cru (non traité) dans la propagation de la maladie dans un pays normalement indemne de fièvre aphteuse et où le cheptel bovin n’est pas soumis à une vaccination régulière. Le risque maximum semble se situer aux premiers stades de la maladie, avant que des mesures de prophylaxie n'aient été mises en œuvre. L’application concrète de mesures préventives et de « codes de bonnes pratiques » pour le traitement du lait potentiellement contaminé peut éviter la transmission de la fièvre aphteuse par le lait.

L’auteur étudie les mécanismes probables de transmission de la fièvre aphteuse par le lait et les produits laitiers. Ces mécanismes sont fonction de la quantité de virus excrétée dans le lait, de la survie du virus selon les conditions de traitement et de production du lait et des doses minimales requises pour déclencher, par différentes voies, une infection chez des animaux sensibles.

L’auteur examine les principaux points à prendre en considération lors d’une analyse des risques liés à l’importation de lait et de produits laitiers.

Mots-clés

Riesgos de propagación de la fiebre aftosa a través de la leche y productos lácteos

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Resumen
Un estudio retrospectivo de las epidemias de fiebre aftosa ha puesto de relieve el importante papel que la leche cruda (no tratada) puede desempeñar en la propagación de esta enfermedad en un país habitualmente libre de fiebre aftosa y donde no se practica la vacunación sistemática del ganado. El mayor peligro reside probablemente en las primeras fases de un brote epidémico, antes de la puesta en aplicación de medidas para el control de la enfermedad. Es posible prevenir la propagación de la fiebre aftosa a través de la leche mediante la aplicación efectiva de medidas de control combinadas con «códigos de buenas prácticas» relativos al tratamiento de leche potencialmente contaminada.

El autor examina los posibles mecanismos de transmisión de la fiebre aftosa a través de la leche y los productos lácteos. Estos mecanismos residen en la cantidad de virus excretado con la leche, la supervivencia del virus en diversas condiciones de manejo y tratamiento de la leche y las dosis mínimas requeridas para iniciar, por vías distintas, el proceso infeccioso en animales sensibles. También se abordan los puntos esenciales que deben considerarse cuando se evalúan los riesgos asociados a la importación de leche y productos lácteos.

Palabras clave
Epidemiología - Evaluación de riesgos - Factores de riesgo - Leche - Productos lácteos - Transmisión - Virus de la fiebre aftosa.
References


