

# Rate of inter-herd transmission of classical swine fever virus by different types of contact during the 1997–8 epidemic in The Netherlands

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(Accepted 18 February 2001)

## SUMMARY

In this study we quantified the rate at which classical swine fever had been transmitted by several different types of inter-herd contact during the 1997–8 epidemic in The Netherlands. During that epidemic 428 CSFV-infected pig herds were detected, 403 of which were included in this study. The estimated rates of transmission were 0·065 per shipment of live pigs, 0·011 per contact by a pig transportation lorry, 0·0068 per person contact, 0·0007 per dose of semen, 0·0065 per contact with a potentially contaminated pig assembly point, 0·027 per week per infected herd within a radius of 500 metres and 0·0078 per week per infected herd at a distance between 500 and 1000 metres. These transmission rates can be used to optimize the strategy to stop future epidemics of CSF in The Netherlands. In addition, the analysis demonstrated in this paper, can be used to quantify CSFV transmission rates from other epidemics.

## INTRODUCTION

Classical swine fever (CSF, hog cholera) is a disease of pigs that is caused by CSF virus (CSFV), which belongs to the genus *Pestivirus*. The symptoms of the disease include fever, lethargy, anorexia and conjunctivitis [1]. In addition nervous symptoms, respiratory disorders, diarrhoea or fertility disorders may occur. The severity of the clinical signs and the mortality depend on, for example, the virulence of the CSF strain and the age of the infected pigs. Regions containing CSFV-infected pig populations are subjected to trade restrictions worldwide.

Whenever CSF is detected on a pig farm in one of the member states of the European Union (EU) an eradication programme is implemented immediately [2]. Because in the 1980's it was decided not to use

vaccination [3], the programme consists of pig movement restrictions and rapid diagnosis and destruction of infected herds. However, despite this strategy CSF epidemics have occurred frequently within the EU [4]. A recent disastrous example was the epidemic caused by CSFV strain Paderborn during 1997–8 that affected the pig populations of Germany, The Netherlands, Belgium, Spain and Italy. In The Netherlands alone, this epidemic resulted in the destruction of almost 11 million pigs. Meuwissen et al. [5] estimated the total costs of the epidemic in The Netherlands at 2·3 billion Euro. Because epidemics of CSF can lead to such a mass destruction of pigs and high financial losses to the society, the strategy to free the European pig population from CSFV needs improvement. For that purpose, better understanding of the virus transmission between herds is useful.

The transmission of CSFV between pig herds is determined by the rate at which the agent is transmitted in case of contact between an infected herd and

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a susceptible herd. In addition, the number of contacts per unit of time and the number of herds that are in contact with each other are important [6]. As a consequence, if the probability of CSFV transmission by the different types of inter-herd contacts and the contact structure between pig herds is known, the quantitative contribution of each different type of contact to the overall inter-herd transmission can be established. Such knowledge would be very helpful to design sets of measures that efficiently eliminate the virus.

Many papers have been written on the possible role of different types of contacts in inter-herd CSFV transmission. Often, the distribution of the most likely routes of viral transmission has been reported (see [4] and [7] for reviews). However, the transmission rates of contacts by these routes cannot be estimated from those papers, because the total number of contacts between infected and uninfected herds were not reported and in case a herd was exposed to CSFV by more than one route it is unclear by which route virus had been introduced. Also from the studies by Koenen et al. [8] and Bernard et al. [9], it is impossible to estimate CSFV transmission rates for different types of contact. This is because the risk factors in those studies either are not really to transmission routes (for example the density of pigs in an area), or the contacts included in the study were not restricted to those contacts originating from infected herds (for example number of contacts by a transport lorry as a risk factor instead of only the number of contacts by a transport lorry that previously visited an infected herds). Finally, Staubach et al. [10] and Laevens [7] reported the odds ratio's (OR) of the relation between the probability of a herd getting infected and the distance to an infected herd. However, the interpretation of these OR's in the above context assumes that there is a certain base-line rate at which infected herds arise 'spontaneously'. This is not biologically plausible for infectious diseases. Additionally, the authors assumed that susceptible herds in a neighbourhood were only exposed to virus by a primary outbreak. However, secondary outbreaks also emitted virus into the neighbourhood and thus the OR's have probably been overestimated (see [11] for an explanation).

Thus, although many papers have been written on the possible role of different types of contacts in inter-herd virus transmission, the actual rates at which the virus was transmitted by these types of contacts have never been quantified. The purpose of this study was to estimate the rate at which CSFV had been transmitted by several different types of inter-herd

contacts during the 1997–8 CSF epidemic in The Netherlands.

## METHODS

### Data

This study was based on data collected during the CSF epidemic in The Netherlands that took place between February 1997 and May 1998. A general overview of that epidemic has been written by Stegeman et al. [12]. A total of 429 pig herds were diagnosed as CSFV-infected during the epidemic. Shortly before depopulation, samples for virus isolation and antibody detection had been collected in all compartments of these herds according to a standard protocol [13]. On the basis of the results of these samples, for each herd a probability distribution of the day of virus introduction had been constructed in an earlier study [14]. Thus, in that study the time of virus introduction of infected herds had been estimated independent of the contacts of that herd, which is essential for the analysis presented here. From the herd specific probability distributions we obtained the day of virus introduction for each individual herd by use of Monte Carlo simulation. Nineteen herds were excluded from the study, because we were unable to estimate the date of infection as described above and we also assume that they did not play a role in the transmission of CSFV between herds (see [14] for explanation). In addition, seven other herds were excluded from the analysis, because the method to construct the probability distribution of the day of virus introduction into populations of breeding pigs was based on the serological observations and registered contact pattern of these herds [15]. As a consequence, the results of these seven herds could not be used to estimate the rate of CSFV transmission per contact independently from the contact structure. We assumed that the infectious period of infected herds started one week after the introduction of the virus. The reason for this delay is that, introduction of infected animals excepted, the virus first has to infect one or more animals and it subsequently takes 4–6 days before these animals start to excrete virus. The infectious period ended on the day the herd was depopulated.

Shortly after the diagnosis CSF had been confirmed by the reference laboratory, official veterinarians traced the forward contacts of each infected herd [13]. This resulted in a list for each infected herd that included all contacts specified by date, type and identification number of the 'recipient' herd. The

Table 1. *The rate at which classical swine fever virus was transmitted from an infected to a susceptible herd by various types of contact during the 1997–8 epidemic in The Netherlands*

Type of contact	Definition	No. of contacts	Rate of transmission (95% CI)
Live pigs	Shipment of pigs	172	0.0647 per contact (0.0043–0.1251)
Lorry	Lorry that has been used to transport pigs of an infected herd subsequently visits an uninfected herd on the same day	3123	0.0110 per contact (0.0014–0.0206)
Person	Person, in contact with pigs, that has visited an infected herd subsequently visits an uninfected herd on the same day, mutual use of equipment is also included in this type of contact in the same manner	2468	0.0068 per contact (0.0007–0.0129)
Artificial Insemination (AI)	Single dose of semen from an infected boar centre that is transferred to a pig breeding herd	25505	0.0007 per dose (0.0002–0.0012)
Assembly point	Lorry that goes to an uninfected herd after leaving an assembly point where pigs of an infected herd have been brought to be killed (buying out)	1876	0.0065 per contact (0.0000–0.0133)
Rendering	Pick up service of the rendering plant has picked up a dead pig from an infected herd and subsequently picks up dead pigs from uninfected farms	10102	0.00002 per contact (0.00001–0.00003)
D0-500	During one week an infected herd located within a radius of 500 metres of an uninfected herd	4014	0.0270 per infectious herd per week (0.0176–0.0364)
D500-1000	During one week an infected herd located within the zone between 500 and 1000 metres of an uninfected herd	7649	0.0078 per infectious herd per week (0.0037–0.0119)
D1000-2000	During one week an infected herd located within the zone between 1000 and 2000 metres of an uninfected herd	18375	0.00006 per infectious herd per week (0.00004–0.00008)
Manure	Manure of an infected herd has been spread over the land that borders on the farm, or mutual use of equipment to transport manure	173	*
Feed	Lorry from the feed company has brought pig feed to an infected farm and subsequently brings feed to an uninfected farm	146	*

\* Not in final multivariate statistical model, because  $P > 0.10$ .

different types of contact that were recorded and the definitions of these types of contact are listed in Table 1. The reasons why the types of contact listed in Table 1 were chosen in this study are as follows. Live pigs, lorries, persons (also including materials) and manure have all been reported as possible modes for CSFV transmission [1]. Recently, artificial insemination (AI) has been added to this list [16] and because two boar

centres had become infected during the epidemic, AI was included as a contact in this study. In addition, Elbers et al. [4] suggested that CSFV could be transmitted by the pick-up service of the rendering plant, whereas the same could be true for lorries of the feed company. Furthermore, Plumiers et al. [13] and Bernard et al. [9] suggested that virus had been transmitted by lorries used to partly depopulate

overstocked farms for welfare reasons. The three distance related variables in Table 1, D0-500, D500-1000 and D1000-2000, actually are not contact types. However, because in recent epidemics quite often no contact between an infected herd and a previously infected herd has been traced [4, 17–19] and earlier studies [7, 10] indicated a relationship between the risk of a herd getting infected with CSFV and the distance to an infected herd, these variables were included in the study.

From the lists of contacts of the infected herds during their infectious period, we constructed a table of contacts for each pig herd (infected and uninfected) that had been in contact with an infected herd at least once. In this table the rows are the weeks of 1997 and 1998 and the columns are the numbers of contacts specified by type. Each cell of the table was filled with the number of contacts of a certain type that took place in that specific week. Finally, a column was added to the table that included the probability that CSFV had been introduced into the herd in that specific week (1 if the day of virus introduction was in that week, otherwise 0).

### Data analysis

If  $\lambda$  is the rate of virus transmission per contact, then the probability of virus transmission equals  $1 - e^{-\lambda}$  (see e.g. [20]). For each contact type  $\lambda$  was estimated by means of a multivariate generalized linear model, using a binomial error distribution (GLM) [21]. After an idea by Becker [22] the probability that a herd escaped from infection in a week ( $e^{-\lambda}$ ) was the dependent variable in the model and the above mentioned numbers of the different types of contacts in a week were the independent variables. In the analysis, the random and systematic components of the model were linked by a log function and as a consequence the outcomes of the model are the values of  $-\lambda$  of the different types of contact ( $\ln(e^{-\lambda})$ ). Furthermore, we did not fit a constant in the model, because in that way the outcome is an actual rate instead of an OR against a base-line transmission rate. Starting with a model that included all dependent variables, the variables with a type I error ( $\alpha$ ) larger than 0.1 were excluded from the model one at a time, starting with the highest  $\alpha$  (stepwise backward elimination). The effect of a variable was considered significant if  $\alpha$  was smaller than 0.05. The fit of the model was investigated by plotting standardised residuals against predicted values.

## RESULTS

The numbers of contacts between infected and susceptible herds that were traced are shown in Table 1. The variables feed ( $P = 0.48$ ) and manure ( $P = 0.51$ ) were eliminated from the model in the stepwise backward elimination. The rates of transmission of the contact types included in the final model and their accompanying 95% confidence intervals are shown in Table 1. The rate of transmission by animal contacts was highest, followed by the rate of transmission associated with an infectious herd within a 500 meters radius of a susceptible herd for a period of 1 week. However, the total number of contacts of the latter contact type was much higher. Consequently, the overall contribution of these so-called neighbourhood infections to the epidemic was higher than the contribution of animal contacts. The rate of CSFV transmission at D500-1000 is significantly lower than the rate of CSFV transmission at D0-500. Although the contact type assembly point remained in the final model, its rate of transmission did not differ significantly from zero at the desired  $\alpha$  level of 0.05 ( $P = 0.060$ ). In addition, even though the estimated rates of transmission of the contact types rendering and D1000-2000 were significantly larger than zero, the magnitude of these estimates in relation to the number of contacts makes the contribution of these types of contact to the CSFV transmission negligible.

## DISCUSSION

In this study we quantified the rate at which CSFV had been transmitted by several different types of inter-herd contacts during the 1997–8 epidemic in The Netherlands. Although the estimated transmission rates were generally low, most of the contact types studied had a transmission rate significantly larger than zero. As a consequence, the results of this study indicate that shipments of live pigs, lorries, persons, AI and neighbourhood infections contributed to the 1997–8 CSF epidemic in The Netherlands and they also indicate the magnitude of these contributions.

The study described here is unique, because, to our knowledge, it is the first time that the actual rates at which CSFV had been transmitted during an epidemic by different types of inter-herd contact have been quantified. The multivariate GLM enabled us to estimate these transmission rates from the data collected during the epidemic, while taking into account that a herd may have been exposed to CSFV

by several ‘competing’ contacts. Usually, from CSF epidemics the distribution of the most likely routes of virus introduction (types of contact) is reported [4, 18, 23–25]. However, when several possible routes of transmission for an outbreak had been traced, an arbitrary choice of the most likely one was made in those studies. Thus, the observed distributions depend heavily on the a-priori ranking of the importance of the different routes of transmission. Furthermore, those studies only reported the number of contacts between infected and uninfected herds that resulted in transmission of CSFV, not the number of contacts that failed to transmit the virus. As a consequence, the rate of transmission could not be estimated from the results of those studies.

The rates of transmission as observed in this study are generally low. However, one should realize that most of the contacts registered took place when it was known that CSFV was present in the country. This awareness probably urged farmers to take actions that reduced the probability of virus introduction by most of the types of contact under study. As a consequence, the transmission rates presented in this study most likely are an underestimation of the transmission rates of those same types of contact during periods before an epidemic is detected. However, in this study the amount of data available of that period in the epidemic was too small to make separate estimates. In addition, the rates may have been underestimated because not all of the information that was recorded may have been correct because of recall bias. Despite the low transmission rates, a huge epidemic of CSF occurred. The reason is that the total number of inter-herd contacts that had been traced was very high. This is even more striking, because the number of contacts may have been underreported because of recall bias. In addition, CSFV may have been transmitted by, yet unresolved, contact types not included in this study.

Although it has been shown that CSFV can be transmitted by AI under experimental conditions [16], until now there was no proof whether this had actually happened in the field. This is because most herds that received potentially contaminated semen had also been exposed to CSFV by other types of contact. However, the results of this study showed that AI contributed to the number of outbreaks of the epidemic, because the transmission rate is significantly greater than zero. It can be ruled out that the variable AI is entwined with the person who inseminates the sows, because the vast majority of the farmers (> 90%) inseminates the sows themselves. In ad-

dition, in case a person of the boar centre inseminated the sows instead of the farmer, this person was included in the analysis as a person contact.

The transmission rate associated with lorry contact indicates that removing pigs from herds in regions under movement restrictions for welfare reasons contributes to the inter-herd transmission of CSFV. Although not significantly different from zero at the level of  $\alpha = 0.05$ , the transmission rate associated with the contact type assembly point further stresses the risks to spread CSFV by welfare slaughter. These findings support other reports that have suggested the risk of transmitting CSFV in the process of welfare slaughter [9, 13].

Table 1 shows that the distance related variables D0-500 and D500-1000 contributed most to the transmission of CSFV between herds and that the probability of CSF infection decreases as the distance from an infected herd increases. Staubach et al. [10] and Laevens [7] showed previously that the risk of CSFV infection increases when a herd is located closer to an infected herd. However, the results of Staubach et al. indicate that such neighbourhood infections only play a role within 350 metres of an infected herd, whereas the results of Laevens suggest that in large herds (> 1000 pigs, as was common in our region) neighbourhood infections may easily exceed a distance of 1000 metres. Our results indicate a role of neighbourhood infections within a 1000-meter radius of an infected herd. However, because the mechanisms behind neighbourhood infections are still poorly understood, it is not clear whether the results of these three studies are in conflict with each other. In addition, the number of infected pigs in a herd and the time between introduction of the virus and detection of the infection may also influence the relation between the distance to an infected herd and probability that a susceptible herd becomes infected.

The transmission rates estimated in this study can be used to optimize the CSF control in the pig dense parts of The Netherlands. Stegeman et al. [14] showed that a policy that consisted of diagnosing and depopulating infected herds as soon as possible after detection resulted in an inter-herd reproduction ratio ( $R_h$ , average number of secondary infections caused by one infected herd) of 1.3. To stop an epidemic this value needs to be smaller than 1. In the 1997–8 epidemic this was eventually achieved by extending the eradication programme with the policy to depopulate herds that had been in contact with infected herds preventively (pre-emptive slaughter). In that



way  $R_h$  was reduced to 0.5. However, given the transmission rates estimated in this analysis, the effect of different strategies to reduce the number of inter-herd contacts and implement pre-emptive slaughter on  $R_h$  could be estimated by a modelling study. Subsequently, a cost benefit analysis could indicate the optimal control strategy.

It is unclear to what extent the results of this study can be extrapolated to epidemics in other regions. Due to differences in procedures, the amount of virus transferred during contact, and thus the rate of CSFV transmission, may vary from one region to another. In addition, we cannot exclude that other factors, for example the virus strain that causes the epidemic, influence these rates. However, the analysis demonstrated in this paper can also be used to study inter-herd transmission of other epidemics of CSF. In that way more knowledge would be gathered concerning the variation associated with the rates of inter-herd transmission of CSFV by different types of contact. Such knowledge could help to improve the CSF control strategy within the EU. Another interesting part of future work is research into the factors that influence the rate at which the different types of contact transmit CSFV. Finally, more efforts should be directed to elucidate the mechanisms behind the distance related spread of CSFV. This could further help to develop effective control strategies that are less dependent on the massive killing of healthy pigs in the framework of pre-emptive slaughter.

This study demonstrates that the rate at which CSFV is transmitted by different types of contact can be estimated from data collected during an epidemic, while taking into account that herds are at risk for CSFV introduction by several contacts. The estimated rates of transmission during the 1997–8 epidemic of CSF in The Netherlands were 0.065 per shipment of live pigs, 0.011 per contact by a pig transportation lorry, 0.0068 per person contact, 0.0007 per dose of semen, 0.0065 per contact with a potentially contaminated pig assembly point, 0.027 per week per infected herd within a radius of 500 metres and 0.0078 per week per infected herd at a distance between 500 and 1000 metres.

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