Introduction, persistence and fade-out of porcine reproductive and respiratory syndrome virus in a Dutch breeding herd: a mathematical analysis

G. NODELIJK[1]*, M. C. M. DE JONG[2], A. VAN NES[1], J. C. M. VERNOOY[1], L. A. M. G. VAN LEENGOED[1], J. M. A. POL[3] AND J. H. M. VERHEIJDEN[1]

[1] *Department of Farm Animal Health, Faculty of Veterinary Medicine, University of Utrecht, P.O. Box 80151, 3508 TD Utrecht*
[2] *Department of Immunology, Pathobiology & Epidemiology, Institute for Animal Science & Health (ID-Lelystad), P.O. Box 65, 8200 AB Lelystad*
[3] *Department of Avian Virology, Institute for Animal Science & Health (ID-Lelystad), P.O. Box 65, 8200 AB Lelystad, The Netherlands*

SUMMARY

The objective of this study was to investigate the dynamics of PRRSV infection and to quantify transmission within a breeding herd, and its impact on herd performance. For this purpose a longitudinal study was performed in a closed breeding herd of 115 sows. Statistical methods and Monte Carlo simulations based on stochastic SIR models were used to analyse the observational data. Moreover, a case-control study was performed to determine whether seroconversion of sows during gestation was associated with aberrant litters. The transmission parameter R was estimated to be 3·0 (95% confidence interval 1·5–6·0) for the model version based on the most plausible assumptions that the infectious period lasts 56 days and no lifelong immunity exists after infection. Based on simulations using a breeding herd of equal size the average time-to-extinction was estimated to be 6 years; using a herd of twice the size, it was 80 years. Furthermore, in contrast to the epidemic phase of the disease, the endemic phase was not detrimental to herd performance.

INTRODUCTION

The first outbreaks of porcine reproductive and respiratory syndrome (PRRS) in The Netherlands were observed early in 1991, after which the disease spread rapidly through the pig-producing areas of the country. In its epidemic form, PRRS is characterized by massive reproductive disorders of pregnant sows, perinatal losses and respiratory distress of piglets [1]. The causative agent, porcine reproductive and respiratory syndrome virus (PRRSV), was isolated by Wensvoort and colleagues [2]. The virus is a small enveloped RNA virus that is classified as member of the family Arteriviridae, order Nidovirales [3, 4]. PRRSV has been confirmed to be endemic in The

Netherlands since 1991 [5, 6], but in its endemic form little is known about the effect of PRRSV infection on the reproductive performance of sows. Nevertheless, some veterinarians suggest that it causes recurrent reproductive failure.

For the development of effective PRRSV prevention and control strategies quantitative studies regarding the transmission of PRRSV in pig populations are essential. By knowing where the virus circulates one can target interventions and only by understanding the dynamics one can attempt to calculate the expected consequences of interventions. The latter is also essential for the design of field trials to test theoretically promising intervention measures [7, 8]. Mathematical models can be used to study the dynamics of an infectious agent and to interpret

* Author for correspondence.

Table 1. *Description of possible events occurring in the stochastic SIR model*

Event	Symbolic representation*	Rate†
Infection	$(S, I) \rightarrow (S-1, I+1)$	$\beta SI/N$
Recovery of an infectious pig	$(S, I) \rightarrow (S, I-1)$	αI
Resusceptibility of an immune pig	$(S, I) \rightarrow (S+1, I)$	$\gamma(N-S-I)$
Replacement of a susceptible pig	$(S, I) \rightarrow (S, I)$	ρS
Replacement of an infectious pig	$(S, I) \rightarrow (S+1, I-1)$	ρI
Replacement of an immune pig	$(S, I) \rightarrow (S+1, I)$	$\rho(N-S-I)$

* S, number of susceptible pigs; I, number of infectious pigs; † N, total number of pigs; β, transmission rate parameter; α, recovery rate parameter; γ, resusceptibility rate parameter; ρ, replacement rate parameter.

observed patterns by estimating parameters and testing hypotheses on different dynamical behaviour of the infectious agent. As measure for the transmission of an infection the reproduction ratio R is used, which is defined as the average number of cases infected by one infectious case [9]. An infection cannot spread extensively and persist unless R is larger than one. When $R > 1$ the introduction of virus in a closed population can not only result in a major outbreak, but also in a minor outbreak, since in an early stage, the infection can fade-out by chance. Persistence can occur when $R > 1$ and new susceptible animals are added to the population at a sufficiently high rate. Although several studies have demonstrated that PRRSV persists in individual pigs [10–14], little is known about PRRSV transmission among pigs [5, 15, 16] and about its persistence within herds.

The objective of this longitudinal study was to investigate the population dynamics of PRRSV infection and to quantify transmission within a breeding herd. Statistical methods and Monte Carlo simulations based on stochastic SIR models were used to analyse the observational data. Also, to study the impact of PRRSV infection on herd performance, a case-control study was performed to determine whether seroconversion of sows during gestation was associated with aberrant litters.

MATERIALS AND METHODS

Data collection

All samples and data were collected from the Tolakker farm, which comprises a closed breeding-to-finish herd (± 115 sows) belonging to the University of Utrecht. After weaning, sows are housed with boars and gilts in a breeding unit, and after insemination, pregnant sows are moved to a gestation unit. Piglets

are born, weaned (at 28 days), and housed in farrowing units until 9–10 weeks of age. They are then selected as rearing or finishing pigs and moved to rearing or finishing units. Female rearing pigs are designated as sows after first insemination, and male rearing pigs are designated as boars after first service. Sows are replaced at an annual rate of 60% ($\rho = 0.012$ per week, see Table 1).

Blood samples were collected from sows and rearing pigs in March 1991, just before the outbreak occurred, and again in April and May 1991, during the outbreak. Samples were collected thereafter 2–3 times a year for a period of 6 years. A total of 3222 sera were tested for antibodies directed against PRRSV.

Samples of abdominal fluid were collected from piglets born dead between January 1993 and November 1994 and were stored at $-70\,^\circ$C until being used for virus isolation.

Herd and litter performance data were collected through the 'Veterinary Automated Management and Production Control Program' (VAMPP) system [17].

Laboratory procedures

Sera were tested for antibodies directed against PRRSV in the immunoperoxidase monolayer assay (IPMA). The IPMA was performed according to standard methods previously described [2]. Briefly, porcine alveolar macrophages were seeded in microtitre plates. After attachment, the macrophages were infected with 1000–2000 $TCID_{50}$ of PRRSV isolate NL1. After a 24 h incubation period at 37 $^\circ$C and in an atmosphere of 5% CO_2, the macrophages were fixed and used as a cell substrate for serological examination. Sera were diluted in fourfold steps with a starting dilution of 1:10 and incubated for 1 h at 37 $^\circ$C on the infected macrophages. Plates were than

washed and incubated with rabbit anti-swine immuno-globulin conjugated to horseradish peroxidase (Dakopat). Finally, the plates were washed and stained with 3-amino-9-ethyl-carbazol. An intense red staining of the cytoplasm of infected macrophages indicated binding of the sera to the PRRSV antigen. Results were interpreted as either negative (titre $= 0$) or positive (titre $\geqslant 10$). Seroconversion was defined as a change from negative to positive.

Samples of abdominal fluids were tested for the presence of PRRSV as previously described [2]. Briefly, porcine alveolar macrophages were seeded at a concentration of 10^5 cells in each well of microtitre plates, and were inoculated with tenfold dilutions (starting at 1:10) of abdominal fluids shortly there-after. First and second passage cultures were incubated for 2–5 days and were observed daily for cytopathic effects. If these effects were observed for both passages or for the second passage only, the presence of PRRSV was confirmed by immuno-staining with a PRRSV-positive antiserum.

Analysis of performance data

Herd performance data were analysed according to the method described by Schukken and colleagues [18]. Over a period of 6 years the following three reproductive parameters of the Tolakker herd were monitored monthly: the average number of piglets born alive per litter (PBA), the average number of piglets born dead per litter (PBD), and the average number of piglets that died before weaning per litter (PDW). In order to compare these parameters with parameters measured before the outbreak, we used the average herd reproductive parameters of 1990 as refer-ences ($\mathrm{PBA_{ref}} = 10.3$, $\mathrm{PBD_{ref}} = 1.0$ and $\mathrm{PDW_{ref}} = 1.3$, respectively). Assuming a normal distribution of these parameters, we used a one-sided test with a 95% confidence interval to determine whether the para-meters were significantly changed. The reproductive status of the herd was identified as being aberrant when at least two of the following conditions were met:

$$\mathrm{PBA} < [\mathrm{PBA_{ref}} - 1.64 \times \mathrm{s.d.}/\sqrt{n}]$$
$$\mathrm{PBD} > [\mathrm{PBD_{ref}} + 1.64 \times \mathrm{s.d.}/\sqrt{n}]$$
$$\mathrm{PDW} > [\mathrm{PDW_{ref}} + 1.64 \times \mathrm{s.d.}/\sqrt{n}]$$

where s.d. is standard deviation and n is number of litters. The estimates for s.d. were 2·90, 1·22 and 1·62 for PBA, PBD and PDW, respectively [18].

Periods with aberrant reproductive status of the herd were analysed in a case-control study. For each litter born within these periods, it was determined whether the litter was aberrant (case) or not (control), and whether the risk factor seroconversion to PRRSV of the sow during preceding gestation was present or not. These data were tested for association by use of a 2×2 contingency table [19] for all periods together and for separate periods.

To determine whether an individual litter was significantly aberrant, the parameters of a litter were compared with the average herd reproductive para-meters of 1990. In a modified version of the statistical approach, a litter was identified as aberrant when one of the following conditions were met: PBA < 6, PBD > 3 and PDW > 3.

Modelling of the dynamics of infection

The model

To study the dynamics of PRRSV infection, we used a modification of the stochastic susceptible-infectious-recovered (SIR) model [20, 21]. The Tolakker herd is conceptually modelled as two linked randomly mixed groups of sows and rearing pigs. Pigs enter the group of sows as gilts just before first insemination and leave the group when they are culled. Some of the piglets born to these sows are housed in a rearing unit until they are used as replacement gilts. The rearing unit is the second group considered in the model.

Pigs in each group are classified as susceptible, infectious or recovered (immune). Table 1 describes the possible events that can occur. Virus can be transmitted within each group by contact between pigs and also between groups, when infectious pigs are moved from the rearing group to the sow group. There is a continuous influx of susceptible newborn pigs into the rearing group. The infection status of pigs entering the sow group depends on their status in the rearing group. In addition, depending on how immunity develops, pigs can become susceptible again after their infectious period.

Data processing

Raw serological data (test result per animal per date) were used to compose six sets of interval data for further analysis. The composition of the data sets was based on two assumptions: (1) that the infectious

Table 2. *Prevalence of PRRSV in sows and rearing pigs based on serological findings over a period of 6 years*

	Sows		Rearing pigs	
Date	Prevalence*	ND†	Prevalence	ND†
16/03/91	0·00 (0/102)	13	0·00 (0/26)	46
15/04/91	0·86 (89/103)	13	0·16 (5/32)	36
10/05/91	0·95 (91/96)	15	1·00 (38/38)	33
11/10/91	0·87 (110/126)	2	0·84 (31/37)	3
20/12/91	0·88 (111/126)	1	0·77 (23/30)	1
06/03/92	0·98 (113/115)	0	0·21 (11/52)	1
04/06/92	0·70 (89/127)	3	0·04 (2/45)	1
14/08/92	0·55 (67/121)	6	0·00 (0/53)	9
12/03/93	0·52 (60/115)	0	0·13 (7/55)	14
29/09/93	0·33 (40/123)	0	0·30 (21/71)	7
15/12/93	0·48 (58/122)	0	0·42 (36/86)	0
18/05/94	0·37 (46/125)	3	0·67 (37/55)	1
02/11/94	0·50 (64/128)	0	0·33 (27/81)	3
22/03/95	0·04 (6/138)	1	0·09 (5/57)	0
16/06/95	0·12 (17/137)	0	0·09 (7/77)	0
17/01/96	0·00 (0/138)	1	0·00 (0/63)	0
12/06/96	0·00 (0/141)	0	0·00 (0/61)	0
06/11/96	0·00 (0/139)	1	0·00 (0/81)	0

* Prevalence = (number of positive samples/number of pigs tested).
† ND, serology not done.

period (T) lasts 10, 56 or 157 days after seroconversion to PRRSV, and (2) that a pig is immune for its entire life after seroconversion or until it becomes sero-negative again. Although it was not shown to be transmissible, virus was isolated from oropharyngeal samples of individual pigs for up to 157 days after experimental infection [13]. Nevertheless, virus transmission to susceptible contacts was already shown for up to 56 days after experimental infection [5]. To complete the data sets, we chose a relative short infectious period of 10 days, which is common for infectious diseases. For all sampling intervals the following four variables were calculated separately and on a daily base for sows and rearing pigs: the average number of susceptible pigs (S), the average number of infectious pigs (I), the average total number of pigs (N), and the average infection rate (number of seroconversions per day). Given the assumed length of the infectious period (T) and the length of the sampling interval (D), the calculation of the average number of infectious pigs in each interval had to account for the following possibilities: (1) pigs infected in one interval can still be infectious in the

subsequent interval(s), and (2) pigs infected in the rearing unit can still be infectious when they enter the sow group. Assuming that a pig was infected randomly between two sampling dates, the number of infectious days (y) spent in the subsequent sampling interval(s) was computed as follows:

$$y = \int_0^D \frac{1}{D}(T-x)\,dx = T - \tfrac{1}{2}D$$

if $T \geqslant D$,

$$\text{or } y = \int_0^T \frac{1}{D}(T-x)\,dx = \tfrac{1}{2}(T^2/D)$$

if $T \leqslant D$.

Consequently, for the sampling interval with sero-conversion ($T-y$) infectious days were computed. When lifelong immunity after seroconversion was assumed, the serological results after seroconversion of individual pigs were interpreted as positive. When transient immunity after seroconversion was assumed, more cases of seroconversion could be registered for individual pigs.

Estimation of transmission parameter

To estimate the transmission parameter β (Table 1) we used a Generalized Linear Model (GLM) with a log link function, a Poisson error term, and log (SI/N) as offset [20]. Analysis of the six data sets was based on the incidence rate (the number of new infections per unit of time) as dependent variable. Because log (SI/N) was used as offset, we obtained one estimate for β for each data set without any explanatory variables. Further analysis was done by choosing explanatory variables such as group (either sow or rearing group), and phase of infection (either epidemic or endemic phase; from March 1991 until March 1992 and from March 1992 until November 1996 respectively). The calculations were performed in Genstat 5 release 3 [22]. The estimates of β were used to calculate the reproduction ratio R as βT, in which T is the duration of the infectious period (used for constructing the data sets).

Monte Carlo simulations

To determine how long PRRSV infections can persist on farms, we used Monte Carlo simulations to estimate the time-to-extinction after introducing PRRSV within a fictive closed breeding herd. The
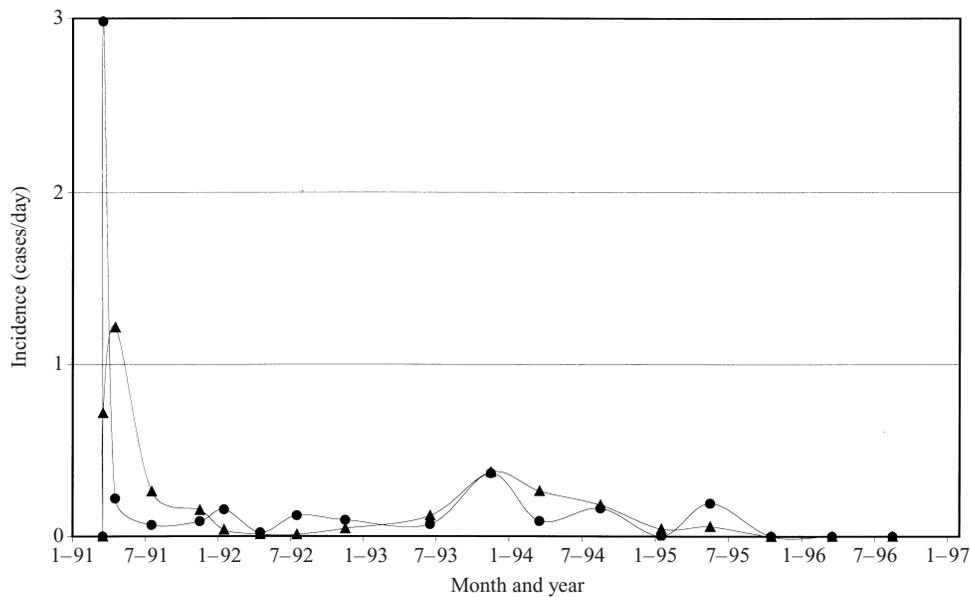
Fig. 1. Incidence of PRRSV among sows (●) and rearing pigs (▲) during a 6-year observation period at the Tolakker herd.

results of the simulations were also compared to the observational data of the Tolakker herd to evaluate which model versions were most realistic.

The simulations were undertaken with the stochastic SIR model (Table 1) under additional assumptions. The breeding herd that was modelled resembled the Tolakker herd, namely 115 sows and 72 rearing pigs and 8 compartments: 1 rearing, 1 breeding, 1 gestation, and 5 farrowing. Assuming random contact, the transmission of virus between pigs within a compartment and between compartments was weighed as $9:1$. Transmission between compartments was also possible by moving infectious pigs from one compartment to another. Six versions of the model were run using the appropriate transmission parameters estimated by GLM, $\alpha = 1/T$, $\wp = 0.012$ per week, and $\gamma = 0.005$ per week. The replacement rate parameter γ was based on an annual replacement rate of 60%. The resusceptibility rate parameter γ was based on a 25% increase of cases in the observational study when transient immunity was assumed in stead of lifelong immunity. To avoid numerous minor outbreaks, the infection was started by making three sows infectious. A Pascal program was used for the simulations, in which stochastic chance events were mimicked by drawing a random number to decide whether or not a particular event will happen; time steps were changed so that the chance of concurrent events was less than 1 in 10^4. The 1000 runs of the six model versions resulted in a probability distribution of the time-to-extinction of PRRSV infection.

To examine the effect of herd size on the time-to-extinction, we repeated the simulations with one of the model versions ($T = 56$ days, no lifelong immunity) for a herd with twice the number of animals (230 sows and 144 rearing pigs).

To estimate the average time-to-extinction for two model versions, we used a method previously described by De Jong and colleagues [23]. When the rate of extinction is constant, the natural logarithm of the cumulative frequency (p_t) of the simulated time-to-extinction is a linear function of the time-to-extinction (t). The estimated rate of extinction is the estimated b value in the expression $\ln(1-p_t) = a + bt$, and the estimated average time-to-extinction is $1/b$.

RESULTS

Serology and virus isolation

Table 2 shows the prevalence of PRRSV as the ratio between number of positive samples and number of pigs tested; Figure 1 shows the incidence of PRRSV as the number of cases per day.

In 1991, during the first sampling interval March–April, the virus was introduced among sows at a rate of 2·98 cases per day; 80% of them seroconverted during this period. Although some rearing pigs seroconverted in the first sampling interval, during the second interval April–March rearing pigs were infected at a rate of 1·22 cases per day; 49% of them seroconverted during this period. In 1992, during the
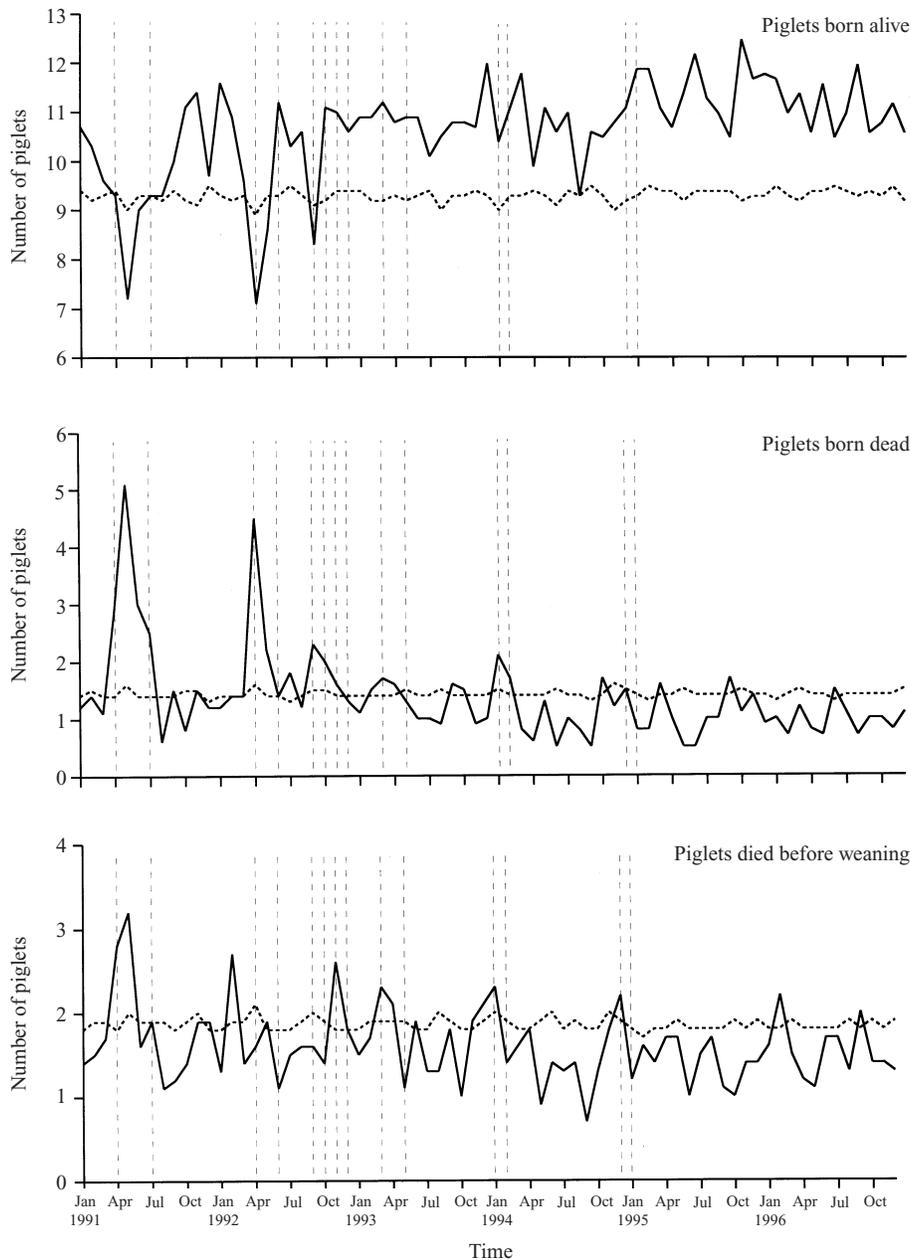
Fig. 2. The time course of three reproductive parameters (——) with one-sided 95% confidence interval (---) on the Tolakker herd: piglets born alive, piglets born dead, and piglets that died before weaning. The periods of an aberrant reproductive status are marked by vertical dotted lines.

sampling interval March–June, the incidences among sows and rearing pigs were low, with 0·02 and 0·01 cases per day respectively. In 1993, during the sampling interval September–December, the incidence among both sows and rearing pigs reached 0·37 cases per day. From June 1995 until the end of the study none of the pigs seroconverted, and by 1996 all sera were negative for PRRSV, indicating total fade-out of the virus.

Between January 1993 and November 1994, no

PRRSV was isolated from 212 abdominal fluid samples collected from piglets born dead.

Herd performance data

The reproductive status of the herd was aberrant in 1991 from April to July; in 1992 in April, May, September and November; in 1993 in March and April; in 1994 in January and December (Fig. 2). The overall analysis for these periods showed a positive

Table 3. *The estimated transmission parameters β and R (with 95% confidence interval) for six versions of the SIR model*

Assumptions underlying model version	β (95% CI)	R (95% CI)
Lifelong immune: no		
$T = 10$ days	0·199 (0·100; 0·396)	2·0 (1·0; 4·0)
$T = 56$ days	0·054 (0·027; 0·108)	3·0 (1·5; 6·0)
$T = 157$ days	0·028 (0·014; 0·055)	4·4 (2·2; 8·6)
Lifelong immune: yes		
$T = 10$ days	0·206 (0·099; 0·426)	2·1 (1·0; 4·3)
$T = 56$ days	0·061 (0·030; 0·127)	3·4 (1·7; 7·1)
$T = 157$ days	0·036 (0·018; 0·075)	5·7 (2·8; 11·8)

Table 4. *Results of 1000 simulations with a stochastic SIR model: probability of fade-out of PRRSV per year after introduction in a closed breeding herd in relation to three parameters (herd size, infectious period, and lifelong immunity)*

Parameters	Probability (%) of fade-out of PRRSV in year									
	1	2	3	4	5	6	7	8	9	> 9
	Herd size = 115 sows									
Time* = 10 days										
Lifelong immunity: yes	99·8	0·2	0	0	0	0	0	0	0	0
Lifelong immunity: no	99·9	0·1	0	0	0	0	0	0	0	0
Time = 56 days										
Lifelong immunity: yes	6·8	10·7	13·7	12·1	9·0	9·3	5·3	5·9	3·8	23·4
Lifelong immunity: no	9·3	14·4	14·5	10·2	7·2	8·0	5·1	5·3	3·8	22·2
Time = 157 days										
Lifelong immunity: yes	1·4	0	0·1	0·2	0	0·2	0·2	0	0·1	97·8
Lifelong immunity: no	3·4	0	0	0	0	0·1	0	0·1	0	96·4
	Herd size = 230 sows									
Time = 56 days										
Lifelong immunity: no	7·5	0·7	0·9	0·9	0·4	1·3	0·8	1·0	0·9	85·6

* Time = infectious period.

association between seroconversion of pregnant sows to PRRSV and aberrant litters (Pearson's χ^2: 19·82, $P < 0·01$; odds ratio = 4·24; $n = 192$).

In 1991, after PRRSV was introduced among the sows in March–April, the following percentage of litters born were aberrant: 63% in April, 69% in May, 45% in June and 38% in July. During this period there was a high positive association between seroconversion of pregnant sows and aberrant litters (Yates' corrected χ^2: 7·88, $P < 0·01$; odds ratio = 16·41; $n = 58$).

In September and November of 1992, March of 1993, and December of 1994, no seroconversion to PRRSV was recorded. No association between seroconversion of pregnant sows and aberrant litters could be found for the other periods of aberrant reproductive status.

Quantification of transmission

The SIR model fitted well for all six sets of interval data, since the maximum likelihood χ^2 goodness of fit showed no significant difference between the observed and predicted values, and the χ^2 values ranged from 0·79 to 12·5 (D.F. = 28). The estimated transmission parameters β and R are shown in Table 3. No significant difference was found with the Generalized Linear Model between β among sows and rearing pigs, nor between β in the epidemic and endemic phase of PRRSV infection.

Monte Carlo simulations

The observational data of the Tolakker herd showed that the PRRSV infection faded out 5 years after the

major outbreak of 1991. The simulations of the two model versions for an infectious period of 10 days resulted in 100% fade-out of PRRSV within 2 years (Table 4), indicating that these model versions did not mimic the observational data. These results were expected, since the interval data showed that the average daily number of infectious pigs was less than one for several sampling intervals, and PRRSV infection would have faded out 1 year after it was introduced at the Tolakker herd. The simulations of the two model versions for an infectious period of 157 days resulted in 1·4 and 3·4% fade-out within 1 year (Table 4); these outbreaks were all minor outbreaks. Furthermore, only 0·8 and 0·2% fade-out within the following 8 years was recorded. Therefore, the observational data of the Tolakker herd would be a most unlikely outcome for these model versions. The simulations of the two model versions for an infectious period of 56 days showed a broad range of possible outcomes of fade-out of PRRSV and included the actual outcome of the Tolakker herd. Therefore, we concluded that the intermediate model versions of 56 days were better than the more extreme ones. Furthermore, most simulations for a breeding herd that was twice the size of the Tolakker herd showed that PRRSV persisted for more than 9 years (Table 4).

In the simulations all minor outbreaks occurred within 1 year after virus was introduced. In following years, because the infection quasi-persisted and random extinction occurred at a constant rate, the rate of extinction was estimated in this period of time. Assuming an infectious period of 56 days and no lifelong immunity, the estimated rate of extinction was 0·0034 per week and the average time-to-extinction was about 6 years in a herd of 115 sows. However, the estimated rate of extinction was 0·00024 per week and the average time-to-extinction was as long as 80 years in a herd of 230 sows.

DISCUSSION

The observational study of the Tolakker herd of 115 sows showed that a PRRSV infection became endemic after a major outbreak and finally faded-out 5 years after it was introduced. The transmission parameter R was estimated 3·0 (95% CI 1·5–6·0) for the model version based on the most plausible assumptions that the infectious period lasts 56 days and no lifelong immunity exists after infection. In addition, from simulations for a breeding herd of equal size the average time-to-extinction was estimated to be

6 years, but for a herd of twice the size as long as 80 years. These findings indicate that when PRRSV is not reintroduced from outside, the infection can 'rapidly' become extinct in small sow herds, but it can persist for a very long time in large sow herds. The case-control study showed that while PRRSV infection adversely affects herd performance during the epidemic phase of the disease, it apparently does not so during the endemic phase.

Acute reproductive failure in sows was observed when PRRSV was introduced in the Tolakker herd, which agreed with numerous other reports [1, 2, 24–26]. Four months later, the performance parameters returned to the level before the outbreak. Schukken and colleagues [18] concluded that the average number of piglets born dead, the average number of piglets born alive, and the average number of piglets that died before weaning were reasonable criteria to use in case of PRRS and described a statistical approach to define periods of aberrant reproductive status of a herd. Although we also used these periods in our case-control study, we found no evidence that PRRSV adversely affects herd performance during the endemic phase of the disease. Finding no association between aberrant litter and seroconversion to PRRSV of the sow during gestation could be explained by subclinical course of PRRSV infection, as it is accepted that clinical effects can vary greatly among herds [18, 27] and subclinical infections are common. Furthermore, the fraction of sows in a certain stage of gestation at the moment of PRRSV infection can play a role. Although fetuses are susceptible throughout gestation [28, 29], transplacental infection and measurable effects of PRRSV infection are more likely in late gestation [30]. However, in our study we could not define the stage of gestation because the sampling intervals were relatively long. Therefore, it is possible that the effect on litter performance was underestimated. No additional information was obtained from the abdominal fluid samples of stillborn piglets about transplacental infection, as no virus was isolated. Unfortunately, not all stillborn piglets were sampled. Furthermore, the power of our study was limited by a relative small number of cases and controls.

In accordance with our previous study [31] we used a low critical value for the IPMA (titre ⩾ 10: positive), which can result in overestimation of the number of PRRSV cases. However, the IPMA results of the first sampling of 1991 and the last three samplings of 1996, when PRRSV was presumably not present, supported

a high specificity for this critical value, because all samples ($n = 520$) had a titre of zero. On the other hand, because seroconversion was defined as a change of negative to positive sample in stead of a rise in titre, the number of cases can be underestimated. Also, cases may have been missed due to the relative long sampling intervals (up to 215 days).

Although some form of protective immunity after PRRSV infection is likely, the humoral and cellular immune response in protection after challenge is not yet quantified. We investigated how the estimation of transmission parameters was influenced by the assumption of lifelong immunity. For the model versions based on an assumed infectious period, the estimated β and R were higher when lifelong immunity was assumed than when transient immunity was assumed, because the number of susceptible pigs present at any moment is lower. For the model versions based on an infectious period of 56 days, R was estimated as 3·4 (95 % CI, 1·7–7·1) and 3·0 (95 % CI, 1·5–6·0), and there was a great overlap in confidence intervals. Consequently, the simulations differed little in possible outcomes.

In The Netherlands the first outbreaks of PRRSV were observed in 1991 and the disease spread rapidly throughout the country. Spread between farms was explained by pigs being transported between farms and by airborne transmission [32]. Within farms, PRRSV spreads rapidly by moving infectious pigs from one compartment to another and by close contact between infectious and susceptible pigs. Additionally, although probably of minor importance, transmission between compartments is possible by indirect contact. Moreover, studies have shown that it is difficult to transmit PRRSV by air under experimental conditions [33]. Therefore, for the simulations of this study with the stochastic SIR model we allowed some transmission between pigs of different compartments by indirect contact. Airborne transmission between farms is probably not of importance during the endemic phase of the infection because less aerosolised virus is present.

The simulations in this study showed that the probability of persistence increases with herd size, which is in accordance with others studies [34]. Although we assumed that after an initial introduction of PRRSV in the breeding herd, the virus was not reintroduced, in reality we cannot exclude this possibility. For example, risk factors as purchase of gilts or presence of fattening pigs can increase the probability of transmission within and between farms.

The persistence of virus in larger sow herds and the transmission of virus between herds might explain why PRRSV could become endemic in The Netherlands.

In conclusion, the present paper demonstrates that a stochastic model and mathematical analysis are useful tools providing quantitative information concerning the transmission of PRRSV on breeding farms. However, observational data are essential to refine and validate models and the underlying assumptions of the model. Modelling can also be used to study the efficacy of control measures such as vaccination and to indicate the conditions to which vaccines and other control measures have to fulfil to reduce PRRSV transmission.

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