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Stochastic simulation modeling to determine time to detect Bovine Viral Diarrhea antibodies in bulk tank milk

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ABSTRACT

A stochastic simulation model was developed to estimate the time from introduction of Bovine Viral Diarrhea Virus (BVDV) in a herd to detection of antibodies in bulk tank milk (BTM) samples using three ELISAs. We assumed that antibodies could be detected, after a fixed threshold prevalence of seroconverted milking cows was reached in the herd. Different thresholds were set for each ELISA, according to previous studies. For each test, antibody detection was simulated in small (70 cows), medium (150 cows) and large (320 cows) herds. The assays included were: (1) the Danish blocking ELISA, (2) the SVANOVIR® BVDV-Ab ELISA, and (3) the ELISA BVD/MD p80 Institute Pourquier. The validation of the model was mainly carried out by comparing the predicted incidence of persistently infected (PI) calves and the predicted detection time, with records from a BVD infected herd. Results showed that the SVANOVIR, which was the most efficient ELISA, could detect antibodies in the BTM of a large herd 280 days (95% prediction interval: 218; 568) after a transiently infected (TI) milking cow has been introduced into the herd. The estimated time to detection after introduction of one PI calf was 111 days (44; 605). With SVANOVIR ELISA the incidence of PIs and dead born calves could be limited and the impact of the disease on the animal welfare and income of farmers (before detection) could be minimized. The results from the simulation modeling can be used to improve the current Danish BVD surveillance program in detecting early infected herds.

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1. Introduction

Bovine Viral Diarrhea (BVD) is caused by a pestivirus (BVDV) and can result in substantial economic losses in dairy herds (Sørensen et al., 1995; Houe, 1999). The principal sources of infection are the persistently infected animals (PIs) (Houe et al., 1995), which become infected in utero during the first 120 days of pregnancy (Brownlie et al., 1987; Fray et al., 2000). PIs shed BVDV throughout their entire lifetime. Cattle that have been exposed to BVDV subsequently become transiently infected (TI) (Brownlie et al., 1987). After an incubation period of four to seven days, TI cattle become viremic and shed the virus in small amounts, compared to PIs, for approximately two weeks (Baker, 1990; Mars et al., 1999). These animals seroconvert

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two to three weeks after infection and develop a lifelong immunity (Brownlie et al., 1987; Baker, 1990). Some studies indicate that BVDV can circulate within a herd for long periods due to TI animals (Moerman et al., 1993; Moen et al., 2005). However, Niskanen et al. (2000) considered this kind of BVDV spread to be negligible. Moreover, the herd structure can affect the BVDV spread between animal groups within infected herds (Viet et al., 2004; Ezanno et al., 2007; Ezanno et al., 2008).

Surveillance of BVD in dairy herds is usually based on testing for antibodies in BTM samples with follow-up testing of individual blood samples in BTM positive herds. Antibody enzyme linked immunosorbent assays (ELISAs) are preferred because they are considered to be sensitive and cheap (Niskanen, 1993; Kramps et al., 1999; Beaudeau et al., 2001). A general assumption is that the test performance is constant over time and for herds of different sizes, while in reality newly infected herds can be detected only when a certain prevalence of antibody positive milking cows is reached in the herd, as Graat et al. (2001) showed for Infectious Bovine Rhinotracheitis (IBR). The prevalence at which the BTM can be classified as positive represents the threshold parameter (Graat et al., 2001). The time needed to reach the threshold in herds of different size should be estimated.

In Denmark, BVD is considered to have been eradicated since 2005 (Uttenthal et al., 2005). Currently (2014), it is suspected that long time could elapse between new BVDV introduction into a dairy herd and detection of antibodies in bulk milk, because during the past decade the dilution of individual antibodies in the BTM has increased (due to increased herd sizes). For this reason, a higher number of antibody positive milking cows in a herd may be needed in order to be able to detect the disease using an ELISA.

The aims of our study were (i) to determine whether the herd size and ELISA test used for BTM testing would significantly affect the detection time since BVDV introduction (by a PI or a TI animal) into Danish dairy herds, and (ii) to compare the detection times of three antibody ELISAs.

2. Materials and methods

2.1. Simulation model

A stochastic, individual based and dynamic simulation model running with “day” as a discrete time event was developed using the freeware R (R Development Core Team, 2012). The modeling process consisted of: (1) modeling the herd structure, (2) modeling infection spread, and (3) modeling antibody detection using ELISAs on BTM samples. The model was then validated internally using methods from literature (Halasa et al., 2009) and externally using available field data from an infected herd (A). A sensitivity analysis on input parameters was subsequently carried out.

2.1.1. Modeling herd structure

Herd parameters were set based on herd structure data from 2010 obtained from the Danish Cattle Federation. The data, including distributions that were used to represent stochasticity, are synthesized in Table 1. The model was designed to fit the structure of a typical closed Danish dairy herd (where e.g. BVDV introduction could occur due to imported embryos, semen and contaminated trucks/materials). Animal movements and disease transmission patterns in the herd were dependent on the presence of several groups (Ezanno et al., 2008) that were defined by age and lactation length. Three herd sizes were considered in the study: small (70 cows), medium (150 cows) and large (320 cows). These herd sizes were close to the first quartile, the mean and the 95th percentile of Danish herd size.

Table 1
Herd input parameters and distribution used to estimate the detection time, the number of PIs and dead born calves occurring in small, medium and large dairy herds before detection.

Parameter	Value
Herd size (cows, heifers, calves):	
Small	(70, 58, 4)[a]
Medium	(150, 115, 8)[a]
Large	(320, 250, 18)[a]
Culling rate per year for cows	Pert distribution (min = 32%, mode = 38%, max = 43%)[a]
Culling rate per year for heifers	Pert (4, 7, 12%)[a]
Culling rate per year for calves	Pert (5, 12, 17%)[a]
Parity distribution (1st, 2nd, 3rd and 4th)	(31, 27, 22, and 20%)[b]
Percentage of dry cows	Pert (12, 17, 20%)[b]
Age in the heifers group (in days)	(700; 768; 870)[c]
Days of inter-calving per cow between parity 1 and 2	(365, 399, 451)[c]
Lactation length per cow between parity 1 and 2	(305, 339, 391)[c]
Days of inter-calving per cow after parity 2	(370, 391, 456)[c]
Lactation length per cow after parity 2	(310, 331, 396)[c]

[a] Source: Danish data (2010).
[b] As in herd A (which was used to validate the model) and according to our experience.
[c] As the 1st quartile, median, and 3rd quartile of herd A and according to our experience.

The simulated herds included animals in several age groups: calves (aged between 1 and 60 days), heifers (aged between 61 and 900 days) and cows (dry or milking). According to the Council Directive 97/2/EC, no calf should be confined in an individual pen after the age of two months. The average age at first calving was set at 798 days, because usually, Danish Holsteins calve when they are 26.6 months old (Kristensen and Kristensen, 1998, Kaspar Krogh personal communication).

The dry period between two consecutive lactations was set to 60 days. The maximum age that a cow could reach was seven years, according to the age of first calving and lactation length (Table 1). The distributions used for the lactation length, intercalving period, parity and for the percentage of dry cows, are presented in Table 1. Such distributions were found in the infected herd (A) that we used to validate the model (see Section 2.1.4), and according to our knowledge of the Danish cattle industry, they can be generalized to other Danish dairy herds.

It was also assumed that heifers joined the group of dry cows one month before calving. The average culling rates

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