

Influence of herd structure and type of virus introduction on the spread of bovine viral diarrhoea virus (BVDV) within a dairy herd

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Abstract – A herd is a population structured into groups not all equally in contact, which may influence within-herd spread of pathogens. Herd structure varies among cattle herds. However, published models of the spread of bovine viral diarrhoea virus (BVDV) assume no herd structure or a unique structure chosen as a representative. Our objective was to identify – for different index cases introduced into an initially BVDV – free dairy herd – risky (favourable) herd structures, which increased (decreased) BVDV spread and persistence compared to a reference structure. Classically, dairy herds are divided into calves, young heifers, bred heifers, lactating cows and dry cows. In the reference scenario, groups are all equally in contact. We evaluated the effect of isolating or merging groups. Three index cases were tested: an open persistently-infected (PI) heifer, an open transiently-infected heifer, an immune heifer carrying a PI foetus. Merging all groups and merging calves and lactating cows were risky scenarios. Isolating each group, isolating lactating cows from other groups, and merging calves and young heifers were favourable scenarios. In most structures, the most risky index cases were the following: first, the entry of a PI heifer; second, the birth of a PI calf; last, the entry of a transiently-infected heifer. Recommendations for dairy herds are to raise young animals together before breeding and to isolate lactating cows from others as much as possible. These recommendations will be less efficient if a PI adult enters into the herd.

contact structure / epidemiological model / pestivirus / cattle

1. INTRODUCTION

Dairy herds are often structured into groups [2]. The population structure is known to influence disease spread [8, 19]. In a population, different groups of individuals may show very different risks that a given pathogen spreads within or between groups. First, infectiousness of individuals may vary among groups. For example, the population can be structured into age groups (juveniles vs. adults), whereas infectiousness may also depend on age (e.g. in bovine paratuberculosis: infectiousness of cows is higher

than that of calves [4]). Second, variations in the within-group contact rate influence the within-group prevalence of the disease (e.g. [5]). As a consequence, this influences the number of individuals in a given group who may spread the disease to other groups. Third, the between-group contact rate may be group-specific. For example, groups may be super-spreaders and have a high rate of contact with a large number of other groups (e.g. core groups in sexually-transmitted diseases in humans [18]). On the contrary, groups can be isolated in the population with very little (if any) contact with other groups (e.g. individuals in quarantine after having been exposed to infectious individuals [6]).

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Furthermore, dairy herds are generally open populations where the purchase and sale of animals occur [9]. Several types of animals (e.g. of different ages or physiological statuses) may enter into open herds, potentially giving rise to pathogen introduction in the herd [31]. The type of primary introduction of the pathogen within a population may influence disease spread. The infectiousness and survival of the primary infected individual influence the initial spread of the disease, i.e. the number of secondary cases, as calculated using the basic reproductive number (R_0 [7]). Moreover, in structured populations, the group in which this primary infected individual enters impacts disease spread in relation with the group's characteristics [29].

Control strategies are implemented in the field to limit the spread of bovine viral diarrhoea virus (BVDV) in cattle herds [13, 21], this virus being source of potential considerable economic losses for farmers [11, 17]. These strategies aim at controlling infection consequences by preventing virus introduction, limiting the within-herd virus spread and eliminating infected animals. To limit control costs, tests available to detect herd infection are implemented with a 3–12 months interval, depending on the countries. The delay between virus introduction and its detection is then usually long. Moreover, in Europe, BVDV eradication is the target in several countries or regions [13]. In such a context, the decrease in prevalence and the subsequent increase in the number of BVDV-free herds may lead to specific issues. In particular, the consequences of potential BVDV re-introductions in BVDV-free herds should be limited. Therefore, it would be of value to identify the herd structures with the highest risk in terms of BVDV persistence vs. the most favourable ones in terms of BVDV clearance, according to the type of virus introduction in the herd.

The within-herd BVDV spread has been modelled and its persistence in herds has been largely studied, especially in dairy herds. Herd structure has rarely been modelled [32]. When it is accounted for, it influences the within-herd BVDV spread, as highlighted by the high sensitivity of the model representing

this within-herd spread to the between-group BVDV transmission rate [10]. However, herd structures have, to our knowledge, never been compared in terms of within-herd BVDV spread, whereas various herd structures may be encountered in the field, even within a herd type (dairy or beef). These herd structures are related to the number of groups within a herd, the definition of the groups (i.e. which animals are in which group) and the between-group contact rates (which may be group specific).

The objective was to study the influence of the herd structure on the within-herd BVDV spread and persistence, under several types of virus introduction (i.e. different infectious states of the index case) in an initially BVDV-free dairy herd consisting of 90 animals, corresponding to a medium sized French dairy herd. The most risky vs. protective herd structures were to be identified.

2. MATERIALS AND METHODS

2.1. The model

A stochastic compartmental model in discrete time was developed to represent the BVDV spread in an initially BVDV-free dairy herd over a seven-year period. The time step (14 days) was chosen to be the longest possible that allowed transiently-infected animals to be represented in the infection process. This model has been previously described [10]. It is briefly described hereafter.

2.1.1. Herd dynamics

A typical structure for a dairy herd of about 90 animals was modelled. For such a herd size, possible herd structures are well known (which groups may be considered, which between-group contact structure, etc.). Based on experts' opinions, we assumed that the herd consisted of at most five groups: calves (c), young heifers (h), bred heifers (H), lactating cows (LC) and dry cows (DC). Each group was divided into several physiological intervals to account for age, stages of pregnancy, etc. (for more details, see [10]). Males were either sold or culled at two weeks of age. Hence, in the model, only females belonged to the herd after this age, corresponding to strict dairy herds in which male calves are not fattened. Females changed groups according to their age or reproductive status.

Table I. Definition and value of the parameters in the infection process when modelling BVDV spread in a structured dairy herd.

θ	Value	Definition	References
$m_{g,P,i}$	0.026	Mortality of P animals ^a in group g and physiological status i	[1, 16]
$m_{c,P,0}$	0.01	Mortality at birth of P animals	
β_w^P	0.50	Within-group transmission rate for P animals	[26, 32 ^b]
$\beta_{b,g_1-g_2}^P$	0.10	Transmission rate for P animals between groups g_1 and g_2	[24, 27, 32 ^b]
β_w^T	0.03	Within-group transmission rate for T animals ^a	[1, 32 ^b]
a_{Ra}	0.80	Abortion rate due to infection in early pregnancy	[14]
a_{Rb}	0.25	Abortion rate due to infection in mid-pregnancy	[14]
n_X		Probability of giving birth to a calf in state X if infection in mid-pregnancy and no abortion	[12, 14]
n_P	0.934		
n_M	0.033	($X = P, M$ or R)	
n_R	0.033		

^a P animals correspond here to persistently-infected (PI) animals, whereas T animals correspond to transiently-infected animals.

^b The review [32] has been provided to give an overview to readers of what has been done in previous modelling studies of BVDV spread in a dairy herd for the transmission parameters.

Females were randomly culled (parameters for the population dynamics can be found in [10]).

$$I_{g,i}(t) = \text{Bin}(S_{g,i}(t); \text{prob}_{\text{inf}}(g,t)) \quad (3)$$

$$T_{g,i}(t+1) = \text{Bin}(I_{g,i-1}(t); 1 - e_{g,T,i}) \quad (4)$$

2.1.2. Within-herd infection dynamics

Animals were classified into mutually exclusive BVDV health states: susceptible (S), transiently-infected (T), recovered, i.e. immune (R), protected by maternal antibodies (M) or persistently-infected (PI; P). The duration of the maternal protection is generally of 4–6 months [20]. The M to S transition was chosen here to occur at 20 weeks of age, occurring only in the group of young heifers. The S to T transition represented horizontal transmission that depended on the proportions of shedding animals (T, P) in the different groups. The transmission rate (1), the probability of infection (2), and the number of susceptible animals of status i in group g at time t which were infected (3), and which were in state T at time $t+1$ (4) were:

$$p_{\text{inf}}(g,t) = \beta_w^P \frac{P_g(t)}{N_g(t)} + \beta_w^T \frac{T_g(t)}{N_g(t)} + \sum_{a \neq g} \beta_{b,g-a}^P \frac{P_a(t)}{N_a(t) N_g(t)} \quad (1)$$

$$\text{prob}_{\text{inf}}(g,t) = 1 - \exp(-\Delta p_{\text{inf}}(g,t)) \quad (2)$$

with a denoting groups other than group g ; β_w^X the within-group transmission rates for animals in infectious status X (P or T); $\beta_{b,g-a}^P$ the transmission rate between groups g and a , per day for P animals (Tab. I); $P_g(t)$, $T_g(t)$ and $N_g(t)$ the number of P animals, of T animals and the total number of animals in group g at time t , respectively; $X_{g,i}(t)$ the number of animals in state X , physiological status i and group g at time t ; Δ the length of the time step in days; $e_{g,T,i}$ the probability of exit from the herd for T animals in group g and physiological status i . The infectious period of T animals was consistently 14 days, representing a worst-case scenario [1, 3].

In the model, several consequences may occur after infection during pregnancy. Embryonic or foetal deaths were assumed to be highly probable after infection in early (weeks 1 to 6) or mid (weeks 7 to 22) pregnancy (Tab. I). On the contrary, infection occurring in late pregnancy led to the birth of calves of state R , the foetus having produced antibodies. In addition, vertical transmission was assumed to potentially lead to persistent infection of the foetus when females were infected in mid-pregnancy or for PI females, giving birth to PI

Table II. Definition of the model outputs, point estimates and corresponding 95% probability intervals for the reference scenario (entry of an immune heifer carrying a PI foetus in a dairy herd composed of five groups all equally in contact).

Output	Definition	Point estimate (95% CI)
<i>timeto80</i>	Time needed (as a number of two-week periods) to reach a probability of 80% of virus extinction in the herd	58 (40–69)
<i>per_1yr</i>	Probability of BVDV persistence one year after virus introduction	0.30 (0.23–0.36)
<i>EpSizT</i>	Epidemic size in transiently-infected animals	30.1 (0–101)
<i>EpSizP</i>	Epidemic size in persistently-infected (PI) animals	2.9 (0–8)
<i>NbT</i>	Mean number of transiently-infected animals in an infected herd	1.3 (0–3.6)
<i>NbP</i>	Mean number of PI animals in an infected herd	1.0 (0–2.1)
<i>NbPF</i>	Mean number of immune dams carrying a PI foetus in an infected herd	0.7 (0–1.6)

calves [12, 25]. Due to higher lethality, PI animals were assumed to have a half-life of one year [1, 16]. Moreover, PI animals shed the virus their entire life.

2.1.3. Initial conditions

A medium sized French dairy herd was modelled with 45 cows, 20 heifers and the other associated young stock, corresponding in total to 90 animals. Initially, all animals were susceptible. BVDV was introduced once initially in the herd. It was assumed not to be further reintroduced, e.g. via relationships with neighbouring infected herds or via movement of infected animals.

2.1.4. Outputs

To characterise herd infection and to compare scenarios, two kinds of outputs were analysed (Tab. II): (1) global outputs using information from all repetitions, (2) outputs specific to herds still infected which characterised the so-called “herd infectiousness”, using information only from repetitions in which the virus was still present in the herd. Global outputs included the probability of virus persistence in the herd (i.e. infected herds having ≥ 1 *P* or *T* animal, or ≥ 1 immune dam carrying a PI foetus) one year after virus introduction, the time needed to reach a probability of 80% of virus extinction in the herd, and the epidemic size (cumulative number of animals that have been in states *P* or *T* over the simulation

time, i.e. seven years). Outputs specific to infected herds included the mean numbers of animals in state *P*, of animals in state *T* and of immune dams carrying a PI foetus. To make sure the virus was explicitly present in all scenarios and thus to enable comparisons between means, a five-month delay was used before calculating the means, which was long enough for the PI calf to be born when an immune heifer carrying a PI foetus initially entered into the herd. Moreover, means were calculated on the first two years after herd infection. Within such a period, it is plausible that BVDV is not re-introduced as long as there are no or very few contacts at pasture with a neighbouring herd and no purchase of infected animals.

2.2. Scenarios

A scenario was defined here as a given herd structure subject to a given type of initial virus introduction. Twelve different herd structures were compared to a reference herd structure (a dairy herd composed of five groups all equally in contact) in combination with three types of virus introduction, resulting in a total of 39 scenarios (including the reference).

2.2.1. Within-herd contact structure

Two approaches were used to modify the within-herd contact structure: (1) a given herd structure was considered in which some of the

between-group transmission parameters ($\beta_{b,g-a}^p$) varied; (2) several herd structures (in terms of group definitions considered) were compared. The reference scenario was the same for both approaches and corresponded to a contact structure with the same value for all between-group transmission parameters (0.1; Tab. I) in a five-group herd. First, to evaluate the efficacy of theoretical perfect hygiene measures to prevent between-group transmission, isolating groups were modelled (six scenarios: isolating all groups, isolating separately groups *c*, *h*, *H*, *LC* or *DC*): all the between-group transmission rates for a given group were nil. Between-group animal movements were still allowed (demographic process). Second, several herd structures were modelled in terms of the number of groups and group definitions. These structures were chosen based on experts' opinions. Generally, in field observations, pairs of groups, which are the most often in contact with each other than with other groups, are the following: '*c-h*', '*h-H*', '*H-DC*', '*LC-DC*'. Moreover, merging the '*c-LC*' pair and merging all groups together were considered as theoretical worst-case scenarios. The between-group transmission rates remained at their initial value (Tab. I) for all groups. For a given scenario (six possible scenarios), the function of transmission was modified to account for the merging. In the example of merging two groups (g_1 and g_2), the new function was the following:

$$p_{\text{inf}}(g_1, g_2, t) = \beta_w^p \frac{P_{g_1}(t) + P_{g_2}(t)}{N_{g_1}(t) + N_{g_2}(t)} + \beta_w^T \frac{T_{g_1}(t) + T_{g_2}(t)}{N_{g_1}(t) + N_{g_2}(t)} + \sum_{a \neq g_1, g_2} \beta_{b-g_1,a}^p \frac{P_a(t)}{N_a(t)(N_{g_1}(t) + N_{g_2}(t))}$$

with $\beta_{b-g_1,a}^p = \beta_{b-g_2,a}^p$.

2.2.2. Virus introduction in the herd

In dairy herds without any fattening facility, only heifers and lactating cows enter into the herd [9]. Since little difference in within-herd BVDV spread was observed after introducing a heifer or a lactating cow of the same infectious status (not shown), only heifer introductions are presented here. For each of the tested within-herd contact structures (see above), three types of initial BVDV introduction in the herd were considered: the introduction

of an immune heifer carrying a PI foetus (which can be randomly a male or a female) which was used as the reference type of virus introduction, the introduction of an open transiently-infected heifer, and the introduction of an open PI heifer. The first two types of BVDV introduction in the herd correspond to real animal introduction (e.g. after purchase) or to infection through contact with an external source of infection (e.g. in a pasture through contact with infected animals from neighbouring herds). The third type of introduction is only possible by buying an animal. Only one initial introduction was allowed to clearly evaluate the influence of the herd structure in within-herd BVDV spread and persistence, without confusion with potential re-introduction of the virus.

2.2.3. Comparison of scenarios

Model outputs were compared among scenarios using the Cochran test, which allows comparing the means of two distributions with different variances.

3. RESULTS

3.1. Effect of the within-herd contact structure

3.1.1. Isolating groups

When initially introducing an immune heifer carrying a PI foetus, isolating any group generally decreased the infection persistence (the time needed to reach a probability of 80% of virus extinction: *timeto80*); and infection persistence after one year: *per_1yr*), the epidemic size in transiently-infected animals (*EpSizT*) and the mean number of immune dams carrying a PI foetus in infected herds (*NbPF*). The deviation from the reference for *per_1yr* was similar to the one for *timeto80*, but smaller. It was significant only when isolating calves, lactating cows or all groups. It is not described thereafter. Isolating all groups simultaneously had the highest effect (Fig. 1). Then, isolating lactating cows (group *LC*) was the most efficient way of reducing persistence and herd infectiousness, but had no effect on epidemic size. Isolating calves (group *c*), young heifers (group *h*) or bred heifers (group *H*) led to almost comparable results. Isolating dry cows (group *DC*) only significantly decreased *timeto80*.

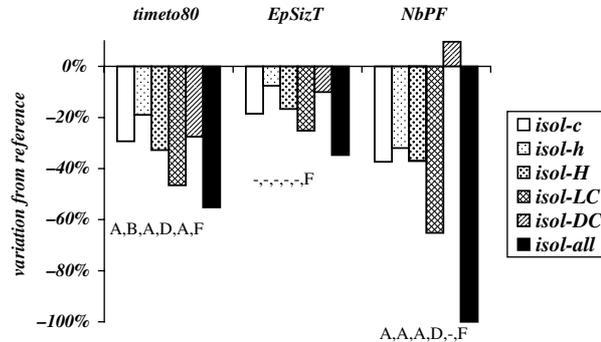


Figure 1. Effect of isolating groups on model outputs (see Tab. II for definitions). The reference was the entry of an immune heifer carrying a PI foetus in a herd composed of five groups (calves, young heifers, older heifers, lactating cows, dry cows) in contact; $\beta_{b, g_1 - g_2}^P = 0.1$ for all pairs of groups. Other scenarios were isolating a given group from other groups (*isol-c*, *isol-h*, *isol-H*, *isol-LC*, *isol-DC*) and isolating all groups from each other (*isol-all*). Variations among scenarios were tested by the Cochran test (capital letter: $p < 0.01$; -: not significant; different letters indicate significantly different scenarios).

When initially introducing a transiently-infected open heifer or a persistently-infected open heifer, isolating groups had hardly any effect. The differences among scenarios within a given type of virus introduction were very low and rarely significant. Isolating all groups significantly decreased the epidemic size in transiently-infected animals when initially introducing a PI heifer. Isolating either calves (*c*), bred heifers (*H*) or lactating cows (*LC*) significantly decreased the mean number of immune dams carrying a PI foetus in infected herds when introducing a transiently-infected heifer. The trend was the same but not significant when introducing a PI heifer.

3.1.2. Merging groups

When initially introducing an immune heifer carrying a PI foetus, merging groups significantly influenced persistence (*per_1yr* and *timeto80*), the epidemic size in persistently (*EpSizP*) and transiently-infected animals (*EpSizT*) and herd infectiousness, except in terms of the number of transiently-infected animals (Fig. 2). As before, variations from the reference for *per_1yr* (not shown) were closely related to the ones for *timeto80* but were lower. In addition, variations from the reference for *EpSizT* were close to the ones

for *EpSizP*, but lower and the increase in epidemic size when merging all heifers (*h + H*) was not significant (not shown). Merging all groups into a single group, merging calves and lactating cows (*c + LC*) and merging all heifers (*h + H*) significantly increased outputs (Fig. 2). Merging calves and lactating cows had the same effect on persistence, epidemic size and herd infectiousness than merging all groups into a single group. Merging groups *h* and *H* had a lower effect. Merging calves and young heifers (*c + h*) significantly decreased the infection persistence and the mean number of immune dams carrying a PI foetus in infected herds, but did not influence other outputs (Fig. 2). Merging bred heifers and dry cows (*H + DC*) significantly decreased the persistence only. Merging all cows (*LC + DC*) had no effect.

When initially introducing a transiently-infected open heifer, the trends in risky vs. favourable herd structures in terms of BVDV spread were very similar to when introducing an immune heifer carrying a PI foetus. However, the disease spread was far lower, the time needed to reach a probability of 80% of virus extinction being very short in all scenarios. As a result, differences among herd structures were not significant for most outputs. The persistence after one year still

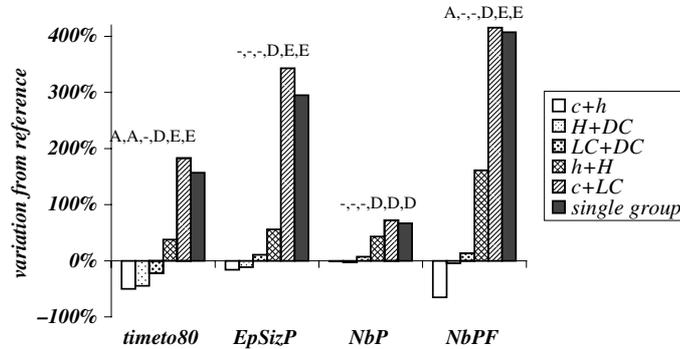


Figure 2. Effect of merging groups on model outputs (see Tab. II for definitions). The reference was the entry of an immune heifer carrying a PI foetus in a herd composed of five groups (calves, young heifers, older heifers, lactating cows, dry cows) in contact; $\beta_{b,g_1-g_2}^P = 0.1$ for all pairs of groups. Other scenarios were merging calves and young heifers ($c + h$), merging bred heifers and dry cows ($H + DC$), merging all cows ($LC + DC$), merging all heifers ($h + H$), merging calves and lactating cows ($c + LC$), and merging all groups (*single group*). Variations among scenarios were tested by the Cochran test (capital letter: $p < 0.01$; -: not significant; different letters indicate significantly different scenarios).

significantly increased when merging calves and lactating cows or when merging all groups.

On the contrary, the introduction of a PI open heifer resulted in a large spread of BVDV. It also resulted in non significant differences among herd structures for most outputs. The epidemic size in PI animals significantly increased when merging calves and lactating cows, as well as the mean number of immune dams carrying a PI foetus. The latter also significantly increased when merging all groups.

3.2. Effect of the type of virus introduction in the herd

For all types of within-herd contact structure, the type of BVDV introduction in the herd significantly influenced persistence, epidemic size and herd infectiousness. Whatever the herd structure, the introduction of an open PI heifer resulted in significantly larger persistence and epidemic size than the two other types of BVDV introduction (Fig. 3). Herd infectiousness was also higher for this type of virus introduction, but the difference from other types of introduction was not significant for all tested herd structures for the

mean number of PI animals in infected herds. As an exception, the mean number of immune dams carrying a PI foetus was identical for the three types of introduction when merging all groups into a single group. The difference was low when merging calves and lactating cows, whereas this number was much higher for all other herd structures when introducing a PI heifer than when introducing the two other types. Whatever the herd structure, introducing an open transiently-infected heifer resulted in significantly lower infection persistence and epidemic size than introducing an immune heifer carrying a PI foetus (the latter being the reference in Fig. 3). In most herd structures, herd infectiousness (in terms of the mean numbers of PI, transiently-infected animals, or immune dams carrying a PI foetus) did not significantly differ between these two types of BVDV introduction. As an exception, the number of immune dams carrying a PI foetus in infected herds was significantly higher after the introduction of an open transiently-infected heifer than after the introduction of an immune heifer carrying a PI foetus in some of the herd structures tested (in the reference structure (herd composed of five groups equally in contact), when isolating heifers or lactating cows, or when merging all heifers).

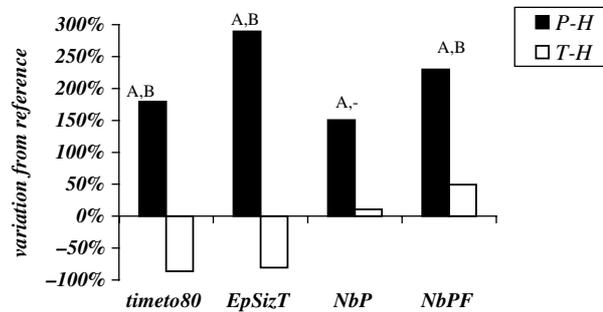


Figure 3. Effect of the type of virus introduction on model outputs (see Tab. II for definitions). The reference was the entry of an immune heifer carrying a PI foetus in a herd composed of five groups (calves, young heifers, older heifers, lactating cows, dry cows) in contact; $\beta_{b,g_1-g_2}^P = 0.1$ for all pairs of groups. Other scenarios were the entry of an open PI heifer (*P-H*) and the entry of an open transiently-infected heifer (*T-H*). Variations between *P-H*, *T-H* and the reference were tested two-by-two with the Cochran test (capital letter: $p < 0.01$; -: not significant; different letters indicate that both also differed significantly).

4. DISCUSSION

Accounting for the population structure in epidemiological models is known to be important [8]. However, to our knowledge, this is the first study on the influence of herd structure on the spread of a pathogen. We propose original recommendations about dairy herd structure to better control BVDV spread and persistence. The most risky herd structures in terms of BVDV spread and persistence within a dairy herd were the following: merging the whole herd into a single group and merging calves and lactating cows. The most favourable scenarios were first to isolate all groups, second to isolate lactating cows.

4.1. Model assumptions on virus introduction and herd size

Risky herd structures were found for a unique virus introduction in an initially BVDV-free dairy herd of 90 animals. BVDV-free herds become frequent in countries or regions where control strategies of BVDV spread have been implemented, especially if eradication of the disease is the target [13]. The effect of herd structure on within-herd BVDV spread was expected to be the largest in such BVDV-free herds in case BVDV is introduced, because all animals are initially susceptible. However, other cases may be

encountered in the field in terms of pathogen introduction frequency, as well as in terms of herd size.

On the one hand, the virus may be re-introduced, through purchases [9] or contacts with neighbouring infected herds at pasture. For recurrent virus introductions, the influence of herd structure may decrease because a large number of resistant animals belong to herds that have already been exposed to the virus resulting in a lower BVDV spread than in fully susceptible herds. Moreover, BVDV introduction in different groups of the herd may also decrease the effect of herd structure, leading to a homogenisation of the presence of the virus whatever the herd structure. That is to say that the dynamics of virus introduction overpass the within-herd infection dynamics by constraining the BVDV persistence in specific groups as well as in the herd as a whole.

On the other hand, dairy herds are actually of various size, ranging from small to very large herds. Very small herds are generally not structured or all animals are raised individually. Large herds can be composed of more groups, e.g. heifers and cows may be divided into two or more groups [2, 28]. However, it will be mainly a decomposition of the groups considered in this study into more groups instead of completely new groups. Hence, as long as groups are of the same

type and order of size, the conclusions in terms of risky herd structures are expected to remain the same. However, BVDV spread and persistence is expected to be different in larger herds, depending on how the groups of adults are in contact with each other (e.g. management by cohort vs. regularly rebuilt groups). Moreover, if groups were to be very large, the within-group transmission may change. For example, the transmission which was assumed to be related to the proportion of infected animals (frequency-dependent transmission) in quite small groups may potentially change to a density-dependent transmission in very large groups if animals cannot be in contact with all animals of their group during one time interval. In such a case, the model should be modified by changing the function of transmission. Further work is needed to quantify the herd size effect on BVDV spread and persistence.

4.2. Infection characteristics

The identified herd structures influencing BVDV spread and persistence are clearly related to infection characteristics, especially to the existence of PI animals. The between-group transmission rate for PI animals and the PI mortality rate have been identified as key parameters in BVDV spread within a dairy herd [10]. The entry of PI animals in a herd is mainly due to the birth of PI calves (except when, accidentally, PI animals are purchased). Hence, most PI animals pass through the calf group. In addition, PI animals have a lower life expectancy than other animals [16]. Hence, the risk of having a PI animal in the calf group is higher than in other groups. As a result, merging the whole herd and merging calves and cows were the two scenarios that increased the most the exposure of gestating females to the virus and so the spread and persistence of BVDV. However, if the group of lactating cows is isolated from other groups and BVDV is introduced into another group, no transmission can occur among lactating cows and fewer PI animals will be born. Isolating lactating cows was more favourable than isolating heifers if a PI calf was to be

born. This may be explained by the lower probability that a PI animal becomes a cow than a heifer because of its reduced life expectancy, and also because cows are the most numerous among pregnant females. For other pathogens, especially pathogens without vertical transmission, risky and favourable herd structures could be different from the ones found here for BVDV.

In previously published models, the duration of transient infection varied between 5 days and 14 days [32]. Here, this duration has been chosen to be exactly of one time interval. It was a balance between the length of the time interval and the possibility of representing transiently-infected animals in the infection process. This duration cannot be decreased explicitly in the model, but can be mimicked by decreasing the transmission rate per time interval for transiently-infected animals. It has been shown that the model used here was sensitive to variation in this parameter [10]. However, no interaction with the between-group transmission rates significantly contributed to variation in model outputs. Hence, modifying it (or the transient infection duration) will not modify our conclusions in terms of risky herd structures.

4.3. Herd management

In our model, cows calved year long as it is mainly the case in dairy herds. Seasonal management of reproduction may give rise to different risky herd structures. Furthermore, since calves and cows are raised together in beef herds, it is expected that BVDV spread and persistence will largely vary from dairy to beef herds. The results obtained in dairy herds cannot be generalised to the beef case.

The scenarios of the herd as a single group or of merging calves and cows are clearly theoretical scenarios for dairy herds, since these herds are structured into groups with calves generally being separated from cows very early after birth (e.g. in the USA [15]). However, in some dairy herds, calves may remain with cows for a few days to a few weeks (e.g. with the use of a nursing cow in Denmark in organic herds [30]). Hence, it

would be interesting to further evaluate the impact of merging calves and cows for a short period of time and to identify if there is a threshold in contact duration between these groups related to the risk of BVDV spread and persistence.

Isolating all groups from each other was also a theoretical scenario. It assumed perfect hygiene measures such as not using material contaminated by another group, not allowing contact between groups in the same building, etc. Perfect separation is not possible in the field. However, as shown in a previous study [10], decreasing the between-group contact rate, and therefore the between-group transmission of BVDV, also largely influences BVDV spread and persistence. Hence, even if isolation is not perfect, limiting contacts between groups is a way to control BVDV spread within dairy herds. Isolating dairy cows appears to be pivotal whereas contact of dry cows with other groups has little effect.

Merging calves and young heifers was a favourable scenario. When an immune heifer carrying a PI foetus entered into the herd, the virus was transmissible between animals only after calving. It would have been exactly the same if an immune cow carrying a PI foetus had entered: the most exposed group here was the group of calves. When merging calves and young heifers, the number of exposed animals increased, resulting in more animals becoming immune before breeding. We showed here that, to limit BVDV spread in a herd, it is more favourable to group young animals all together from birth to the first insemination and to favour contacts between them than to split them into several more or less isolated groups.

4.4. Type of initial virus introduction

The recommendations proposed above assumed an intermediate risk of BVDV spread, obtained when introducing an immune dam carrying a PI foetus. There are other types of virus introduction: transiently-infected animals or adult PI animals may also enter into a herd. Introducing an adult PI animal has different consequences than the birth of a PI

calf. First, half the PI calves born in the herd are males and thus are sold after two weeks, having almost no influence on BVDV spread. Second, because of the low life expectancy of PI animals, only a quarter of the PI females born in the herd survive until breeding age. On the contrary, a PI heifer is generally apparently healthy with quite a high probability of survival and breeding, giving birth to a PI calf. Third, dairy herds are often structured into groups. In such a case, a PI calf mainly infects calves and only indirectly adults, whereas a PI heifer mainly infects bred heifers and cows after calving. As a result, the type of BVDV introduction has been shown to largely influence its spread and persistence. The influence of herd structure was not equivalent for all types of virus introduction. When the risk of BVDV spread was low (introduction of a transiently-infected animal), the effect of herd structure was also low. When it was high (introduction of an adult PI animal), the effect of herd structure was low again, BVDV spread being large (within-group, to calf group by subsequent birth of PI calves and to other groups by between-group transmission) whatever the herd structure.

Recommendations in terms of herd structure to limit BVDV spread in a herd will be less efficient when the virus introduction leads to a large spread of the virus (and has a limited impact for low spread). However, the entry of a resistant dam carrying a PI foetus in the herd, leading to an intermediate spread of the virus in the herd, is a frequent case of virus introduction because these animals are not easily identified [22, 23] and at the moment not detected in routine at purchase in the field, on the contrary to PI animals. In that case, the herd structure influences BVDV spread.

The spread of BVDV was modelled within a BVDV-free dairy herd of 90 animals, taking into account the herd structure into groups. We identified risky herd structures that enhanced BVDV spread and persistence vs. favourable herd structures. The principal recommendations that can be made to limit BVDV spread and persistence are first to separate lactating cows from other groups, especially from calves, as much as possible

and second to raise young animals from birth to first insemination (calves and young heifers) together. The entry of a PI animal in the herd, especially if it is an adult, and the initial herd infectious status reduce the effect of these recommendations. As a result, BVDV control measures in BVDV-free dairy herds should also aim at preventing the entry of PI animals.

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