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Transmission dynamics of intramammary infections caused by *Corynebacterium* species

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ABSTRACT

The development of reliable models for transmission of intramammary infections (IMI) is the subject of extensive research. Such models are useful to enhance the identification and understanding of factors that affect pathogen-specific IMI dynamics. Longitudinal transmission models are valuable for predicting infection outbreak risks, quantifying the effectiveness of response tactics, and performing response planning. In this work, we focused on modeling *Corynebacterium* spp. by using a compartmental model. Previous investigations have considered modeling the transmission dynamics of several bacterial pathogens, but not *Corynebacterium* spp. We established a *Corynebacterium* spp. Susceptible–Infectious–Susceptible (SIS) model. We simulated the model numerically by using parameters that we estimated by a generalized linear model approach, using month of study as the time variable. The data, from which the parameters of the model were estimated, were obtained in a field trial conducted in 2 US dairy herds. Altogether, 786 cows were sampled at least once during the 13-mo study period. The total number of quarter milk cultures and cases of IMI caused by *Corynebacterium* spp. were 11,744 and 556, respectively, in farm A; the corresponding figures for farm B were 11,804 and 179. Our modeling study included only transmission from persistent IMI caused by *Corynebacterium* spp. within the lactation pens. The rate of new infections was significantly related to preexisting IMI in both farms, underscoring the importance of preexisting *Corynebacterium* spp. IMI for the transmission of *Corynebacterium* spp. within lactation pens. The estimated basic reproduction numbers (R_0) in the 2 farms were 1.18 and 0.98, respectively. The nonsignificant disparity in R_0 was associated with significant differences in cure rates between farms.

Key words: intramammary infection, *Corynebacterium* spp., transmission model

INTRODUCTION

Mastitis is one of the economically most important diseases in dairy production (Halasa et al., 2007; Hogeveen et al., 2011). Much of the economic loss is due to reduced milk production following subclinical mastitis (Hogan et al., 2016). Intramammary infections with *Corynebacterium* spp. are generally mild with limited milk production loss. However, significant elevations in SCC have been observed (Brooks et al., 1983; Brooks and Barnum, 1984a). Although *Corynebacterium* spp. are classified as minor pathogens (Brooks and Barnum, 1984b; Harmon, 1994; Blagitz et al., 2013), the increased prevalence of *Corynebacterium* spp. IMI in some modern dairy farms (Pitkälä et al., 2004) warrants further investigation into the specific properties and roles of the bacteria.

Some authors have reported a protective effect of *Corynebacterium* spp. IMI against IMI caused by other pathogens (Rainard and Poutrel, 1988; Lam et al., 1997a), whereas others report an increased risk of mastitis (Pankey et al., 1985; Berry and Hillerton, 2002; Parker et al., 2007). When investigating the relationship between secondary infections and a preexisting IMI by *Corynebacterium* spp., Parker et al. (2007) suggested that the diverging effects reported for *Corynebacterium* spp. IMI were due to the increased disposition for clinical mastitis of glands with a preexisting IMI. There is also evidence that *Corynebacterium bovis* can colonize the teat canal without affecting the udder past Furstenberg's rosette (Black et al., 1972).

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Mathematical models are powerful tools for understanding infection dynamics by providing predictions about the potential transmission of infections and the effectiveness of control measures (Magal and Ruan, 2008; Otto and Day, 2011). Pathogen-specific transmission patterns have been described for other major and minor mastitis pathogens (Lam, 1996; Zadoks et al., 2002; White et al., 2006; Reksen et al., 2012; Barlow et al., 2013), but not for *Corynebacterium* spp. The basic reproduction number, $\boldsymbol{R_0}$, is used in compartmental transmission models to determine transmission of a disease at the population level. It is defined as the number of secondary cases that one infectious case can produce if introduced into a susceptible population (Grossman, 1980; Diekmann et al., 1990; Hethcote, 2000). Modeling the progression of a disease depends on appropriate parameter values that are often unknown and must be estimated from field data. In this study, we have used a generalized linear model for parameter estimation. The parameters estimated were used in a deterministic state-transition model to describe the transmission dynamics of *Corynebacterium* spp. from preexisting IMI within lactation pens.

The main aim of this study was to develop a novel mathematical description of the transmission dynamics of *Corynebacterium* spp. IMI. Specifically, we first wanted to assess the importance of preexisting IMI by *Corynebacterium* spp. on new IMI caused by this group of bacteria. Second, we wanted to compare transmission parameters and cure rates for *Corynebacterium* spp. IMI between 2 US dairy farms with differing prevalences of *Corynebacterium* spp. IMI.

MATERIALS AND METHODS

Field Study

Data were obtained from a 13-mo longitudinal observational study in 2 commercial Holstein dairy herds (one in New York and one in Vermont). Cows were housed in pens of approximately 100 cows and milked 3 times per day. In farm A, the monthly mean number of lactating cows was 319, the mean milk production per cow per day was 32.7 kg, and the average cow composite SCC was 404,000 cells/mL. In farm B, the monthly mean number of lactating cows was 346, the mean milk production per cow per day was 35.0 kg, and the average cow composite SCC was 292,000 cells/mL. The herds participated in a DHIA program with monthly milk quality testing. Both farms had reliable identification of animals and used standardized mastitis control practices, including pre- and postmilking teat disinfection and blanket dry-cow therapy. Further details on the herds, microbial analyses, and sampling framework have been published previously (Reksen et al., 2012; Barlow et al., 2013).

Quarter milk samples were collected monthly from approximately 200 lactating cows on each farm. Additional samples were collected within 3 d after parturition and when animals were moved to or from the lactation compartment.

Trained field technicians collected the scheduled monthly samples. Selected farm personnel, who had received training for this, obtained the additional samples. All samples were collected according to recommended guidelines (Hogan et al., 1999). Samples collected monthly were kept on ice after collection and during transport to the laboratory, where they were frozen before microbiological analyses. Additional samples collected by farm personnel were frozen immediately after collection. Samples were thawed in the laboratory and bacteriological culture was performed according to standard procedures (Hogan et al., 1999). Samples with culture results presenting more than 3 morphologically different colony types were treated as contaminated and excluded from further analyses.

A quarter was considered to have an IMI with *Corynebacterium* spp. when meeting at least one of the following criteria: (1) $\geq$1,000 cfu/mL of the pathogen were cultured from a single sample, (2) $\geq$500 cfu/mL of the pathogen were cultured from 2 out of 3 consecutive milk samples, (3) $\geq$100 cfu/mL of the pathogen were cultured from 3 consecutive milk samples, or (4) $\geq$100 cfu/mL of the pathogen were cultured from a clinical sample (Zadoks et al., 2002). A case was considered clinical when there was abnormal milk, with or without pain or swelling in the udder, or systemic signs such as anorexia, lethargy, or elevated rectal temperature (Harmon, 1994). Positive bacterial cultures that did not meet any of the above criteria were classified as representing a transient colonization with *Corynebacterium* spp.

Statistical Analysis

Statistical analysis was conducted using SAS software (version 9.1; SAS Institute, Inc., Cary, NC). Transmission parameters (β) and cure rates (α) were calculated using the generalized linear model approach (PROC GENMOD). Evidence of overdispersion was evaluated and models were subsequently adjusted using an overdispersion parameter estimated from the ratio of the Pearson Chi-squared estimate divided by the remaining degrees of freedom (Pscale option).

The transmission parameter (β) was estimated in a linear model with number of new *Corynebacterium* spp. IMI events in each monthly interval (I_M) as the outcome; S = quarter-days in a susceptible udder, I =