Theoretical Population Biology 116 (2017) 27–32

Contents lists available at ScienceDirect

Theoretical Population Biology

journal homepage: www.elsevier.com/locate/tpb

Modeling the effects of variable feeding patterns of larval ticks on the transmission of *Borrelia lusitaniae* and *Borrelia afzelii*

Luca Ferreri [a,*], Silvia Perazzo [b], Ezio Venturino [b], Mario Giacobini [a,c], Luigi Bertolotti [a], Alessandro Mannelli [a]

[a] Department of Veterinary Sciences, University of Torino, largo Paolo Braccini 2, IT-10095 Grugliasco (TO), Italy
[b] Department of Mathematics "Giuseppe Peano", University of Torino, via Carlo Alberto 10, IT-10123 Torino (TO), Italy
[c] Molecular Biotechnology Center, University of Torino, via Nizza 52, IT-10126 Torino (TO), Italy

ARTICLE INFO

Article history:
Received 23 September 2014
Available online 6 July 2017

Keywords:
Lyme disease
Borrelia lusitaniae
Borrelia afzelii
Lizard
Rodent
Mathematical model

ABSTRACT

Spirochetes belonging to the *Borrelia burgdoferi* sensu lato (sl) group cause Lyme Borreliosis (LB), which is the most commonly reported vector-borne zoonosis in Europe. *B. burgdorferi* sl is maintained in nature in a complex cycle involving *Ixodes ricinus* ticks and several species of vertebrate hosts. The transmission dynamics of *B. burgdorferi* sl is complicated by the varying competence of animals for different genospecies of spirochetes that, in turn, vary in their capability of causing disease. In this study, a set of difference equations simplifying the complex interaction between vectors and their hosts (competent and not for *Borrelia*) is built to gain insights into conditions underlying the dominance of *B. lusitaniae* (transmitted by lizards to susceptible ticks) and the maintenance of *B. afzelii* (transmitted by wild rodents) observed in a study area in Tuscany, Italy. Findings, in agreement with field observations, highlight the existence of a threshold for the fraction of larvae feeding on rodents below which the persistence of *B. afzelii* is not possible. Furthermore, thresholds change as nonlinear functions of the expected number of nymph bites on mice, and the transmission and recovery probabilities. In conclusion, our model provided an insight into mechanisms underlying the relative frequency of different *Borrelia* genospecies, as observed in field studies.

1. Introduction

Lyme borreliosis (LB), caused by spirochetes belonging to the *Borrelia burgdorferi sensu lato* (sl) group, is the most commonly reported vector-borne zoonosis in temperate climates. In Europe, *B. burgdorferi* sl is maintained in transmission cycles involving the tick *Ixodes ricinus* (in combination with *I. persulcatus* in areas in North Eastern Europe), and several species of vertebrate reservoir hosts that can be infected by ticks and that, in turn, are able to transmit the infection to other susceptible ticks (Gern et al., 1998; Gern and Humair, 1998). A distinct feature of the transmission cycle in Europe is a certain degree of reservoir host-specificity of different genospecies of *B. burgdorferi* sl. In fact, among pathogenic genospecies, rodents and other small mammals transmit *B. burgdorferi* sensu stricto and *B. afzelii*, birds are reservoirs for *B. garinii*, whereas lizards transmit *B. lusitaniae* (detected in human patients especially in Portugal (Collares-Pereira et al., 2004)).

Although *B. burgdorferi* sl is widespread through the geographic range of *I. ricinus*, the prevalence of infection in host-seeking ticks, and the relative frequency of different genospecies may vary within short distances. The composition of populations of vertebrate hosts, which are characterized by varying reservoir competence for *B. burgdorferi* sl genospecies, might play a major role in the ecological processes underlying such a variability. More specifically, geographic variations of the intensity of transmission of *B. burgdorferi* sl genospecies might be the result of the relative contribution, by each vertebrate host species, to the overall infection of susceptible larvae; this depends upon the host's population density, the average number of larvae per individual of that species, and the host's infectivity to larvae (the fraction of larvae that acquire the infection after feeding on vertebrates of a certain species) (Mather et al., 1989).

Large mammals, such as deer and other wild and domestic ungulates, are considered unable to serve as reservoirs for *B. burgdorferi* sl. On the other hand, they play a major role as hosts for adult ticks. Consequently, the effects of population densities of non competent hosts on *B. burgdorferi* sl transmission dynamics cannot be easily predicted, due to their potential, contrasting effects of dilution and amplification of transmission (Keesing et al., 2006).

* Corresponding author.
E-mail address: luca.ferreri@unito.it (L. Ferreri).

http://dx.doi.org/10.1016/j.tpb.2017.06.004
0040-5809/

More specifically, non-competent hosts may reduce nymphs infection prevalence by feeding relatively large proportions of larvae that moult to non-infected nymphs, and by diverting ticks from competent reservoirs, resulting in a dilution effect. Nevertheless, non-competent hosts may feed large numbers of ticks and, therefore, augment the vector population. This may result in a larger probability that ticks feed on an infected host with the consequent amplification of *B. burgdorferi* sl transmission.

In the European situation, an animal species may serve as a reservoir host and, therefore, amplify the transmission of certain *B. burgdorferi* sl genospecies. It may simultaneously affect transmission of other genospecies through dilution and/or vector augmentation (see (Mannelli et al., 2012) for a summary of transmission in multi-host systems). These complex mechanisms might, at least in part, explain why several genospecies may thrive in certain areas, whereas, at other locations, one genospecies might be dominant while the others are rare.

In a study area on Le Cerbaie Hills, in Tuscany (Central Italy), previous studies hypothesized that lizards were responsible for the maintenance of *B. lusitaniae* as the dominant genospecies and, at the same time, reduced the transmission of other genospecies through dilution. A simple mathematical model indicated that, on Le Cerbaie, persistence of *B. afzelii* ($R_0 > 1$) was only possible under conditions of relatively large density of mice reservoir hosts (*Apodemus* spp) and large attachment rate of *I. ricinus* nymphs to mice (Ragagli et al., 2011). Indeed, mouse population fluctuations, and the frequency of bites by immature *I. ricinus* were recognized as key factors affecting these hosts' specificity and, consequently, the intensity of transmission of *B. afzelii* (Mannelli et al., 2012). Our work fits within this context adding some details (the dynamical model and the explicit definition of densities of vertebrate hosts) in order to increase the accuracy of the model and to further confirm the previous finding.

In this study, we build a simple dynamical model to study the transmission of *B. burgdorferi* sl genospecies under variable scenarios regarding the relative contribution of different hosts to the feeding of larval ticks, and the frequency of bites by infectious nymphs on the same vertebrates. After the model's general formulation, we use it to gain an insight into mechanisms underlying the observed variations in the prevalence of *B. burgdorferi* sl genospecies in ticks and hosts on Le Cerbaie. Specifically, we explore conditions leading to persistence or extinction of *B. lusitaniae* and *B. afzelii* in the study area.

2. Methods

We used a set of recurrence relations to describe the complex interactions underlying the transmission of different genospecies of *B. burgdoferi* sl among *I. ricinus* immature stages (larvae and nymphs) and vertebrate hosts. Adult ticks were not included in our model. As a consequence, the vector augmentation effect of animals serving as hosts for this stage was not considered. Therefore, the focus of our study was limited to the contribution of each host species to larval feeding, and to the frequency of bites by infectious nymphs on different hosts and their effects on the persistence of *B. burgdoferi* sl genospecies. Furthermore, we only considered the infection of larvae through feeding on systemically infected hosts — the most common transmission route of *B. burgdorferi* sl in nature (Mannelli et al., 2012; Gern et al., 1994). Accordingly, we disregarded transovarial infection of larvae from female ticks of the previous generation, and transmission of spirochetes among ticks feeding in close proximity on the host's skin (transmission via co-feeding), (Matuschka et al., 1998; Patrican, 1997; Ogden et al., 1997; Randolph and Rogers, 2006).

Feeding larvae may acquire a certain genospecies of *B. burgdorferi* sl depending on the specific reservoir competence of the parasitized host (*B. lusitaniae* can be acquired by feeding on lizards, *B. afzelii* by feeding on mice). On the other hand, larvae feeding on non-competent hosts (such as deer), do not acquire these agents. Infected, fed larvae molt into infected nymphs, which are subsequently able to transmit the infection to susceptible hosts.

Across most of the geographic range of *I. ricinus*, including Le Cerbaie, nymphs are active before larvae during the same year (Bisanzio et al., 2008). Such a seasonal pattern is particularly favorable to the maintenance of *B. burgdorferi* sl. In fact, in Spring, spirochetes are transmitted by nymphs to susceptible hosts that, in turn, develop a systemic infection and are able to transmit it to susceptible larvae in the following Summer (Mannelli et al., 2012). Therefore, in our model, we consider a time-step, Δt, of six months, and we assume that, for each year, larvae feed on hosts only during the second semester (July–December), whereas nymphs feed during the first semester only (January–June). Under such conditions, competent hosts ensure transmission of the infection between nymphs and larvae belonging to different tick generations, allowing the maintenance of *B. burgdorferi*.

2.1. Recurrence relations

In order to understand the role of varying host populations on the endemic condition of the genospecies we introduce a parameter h_S, the specificity of host-species S on feeding larvae, denoting the fraction of larvae feeding on a particular host species, S. In fact, we have h_L, for those feeding on lizards, h_R, for those feeding on rodents, and h_H, for those feeding on other, non-competent hosts (thus $h_L + h_R + h_H = 1$). Furthermore, we assume that the vector and host populations are constant in time.

Now, since we do not assume any correlation between the probability for a nymph to feed on a rodent and the probability that the nymph was already infectious before the moult, the prevalence of *B. afzelii*, π_a, among nymphs feeding on rodents at the beginning of time $t + \Delta t$ is equal to the prevalence among larvae that have completed a blood meal at the end of time t. In particular, assuming frequency-dependent transmission (Begon et al., 2002), the latter is a function of the prevalence of *B. afzelii*, $p_a(t)$, among rodents on which larvae fed and is given by the probability that a feeding larvae gets infected at the end of its blood meal. That is

$$\pi_a(t + \Delta t) = \beta_{RT} \cdot \delta_T(t) \cdot h_R \cdot p_a(t) \tag{1}$$

where δ_T is the Kronecker delta, which is one if t is the semester of activity of larvae (i.e. second half of the year) and zero otherwise (i.e. January–June), and β_{RT} is the probability that a larva biting an infectious rodent becomes infectious. In a similar way we depict the prevalence of *B. lusitaniae* among feeding nymphs, π_l:

$$\pi_l(t + \Delta t) = \beta_{LT} \cdot \delta_T(t) \cdot h_L \cdot p_l(t) \tag{2}$$

where β_{LT} is the probability that a larva biting an infectious lizard gets the infection and $p_l(t)$ is the prevalence of *B. lusitaniae* among lizards. On the other hand, the prevalence of *B.afzelii*, $p_a(t + \Delta t)$, among rodents is nothing but a function of those mice still infected from previous time-step, i.e. $(1 - \mu_R) \cdot p_a(t)$, where μ_R is the probability for a mouse to die and to be replaced (in order to keep the population stable in time), and those rodents that get infected as consequences of infecting bites at the previous time-step. We do not consider the possibility of hosts recovery due to the low probability of this event, (Gern et al., 1994; Kurtenbach et al., 2002, 1994; Zhong et al., 1997). Moreover, defining β_{NR} as the probability that an infected nymph bite is infective and K_R as the expected number of nymph bites for a mouse in a time step Δt, we could expect a number of $\beta_{NR} \cdot K_R \cdot \pi_a(t)$ potentially infectious bites for mouse. Therefore, since one potentially infectious bite comes independently from the others, we could assume the random variable "*number of infectious nymph bites for mouse at time step* $[t, t + \Delta t)$"