Modeling Lyme disease transmission

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ABSTRACT

Lyme disease, a typical tick-borne disease, imposes increasing global public health challenges. A growing body of theoretical models have been proposed to better understand various factors determining the disease risk, which not only enrich our understanding on the ecological cycle of disease transmission but also promote new theoretical developments on model formulation, analysis and simulation. In this paper, we provide a review about the models and results we have obtained recently on modeling and analyzing Lyme disease transmission, with the purpose to highlight various aspects in the ecological cycle of disease transmission to be incorporated, including the growth of ticks with different stages in the life cycle, the seasonality, host diversity, spatial disease pattern due to host short distance movement and bird migration, co-infection with other tick-borne pathogens, and climate change impact.

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1. Introduction

Lyme disease (LD) is a common tick-borne infection in the temperate northern hemisphere (Dennis et al., 1998; Ogden et al., 2009). In the United States of America, it is the fifth most commonly reported nationally notifiable disease and more than 36,000 confirmed and probable disease cases were reported in 2013 with the true number of cases estimated to be approximately 300,000 per year (Mead, 2015). There may be over 200,000 European cases annually, with high incidences in parts of southern Scandinavia, central and eastern Europe. About 1200 cases are serologically confirmed annually in the UK (O'Connell, 2014). Although the annual Lyme disease cases have been fairly low in Canada, northward invasive spread of the tick vectors from United States endemic foci to non-endemic Canadian habitats has been a major public health protection and promotion issue (Dennis et al., 1998; Ogden et al., 2009). Recent studies have suggested that the number of known endemic areas of Lyme disease in Canada is increasing because of the expanding range of *Ixodes scapularis*, a process that is predicted to accelerate with climate change (Ogden et al., 2009). The reported cases in Canada rose significantly from 144 in 2009 to 338 in 2012 (Ogden et al., 2015). Erythema migrans (EM), an early skin lesion, is the most common clinical presentation. However, the infecting pathogen can spread to other tissues and organs, causing more severe manifestations, including facial palsy, viral-like meningitis, radiculitis and arthritis, usually affecting the knee (Ogden et al., 2008a; O'Connell, 2014; Stanek, Wormser, Gray, & Strle, 2012). Although it is virtually never fatal, it can be clinically very serious (Randolph et al., 2007).

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Lyme disease is caused by spirochaetes of the *Borrelia burgdorferi* sensu lato species complex, which are transmitted by *Ixodes* ticks (Stanek et al., 2012). Various pathogenic species are responsible for the Lyme disease at different regions in the world (Bergström, Noppa, Gylfe, & Östberg, 2002). For example, in North America, the species of Lyme borrelia known to cause human disease is *B. burgdorferi* sensu stricto while in Europe, at least five species of Lyme borrelia (*B. afzelii*, *B. garinii*, *B. burgdorferi*, *B. spielmanii* and *B. bavariensis*) can cause the disease, leading to a wider variety of possible clinical manifestations in Europe than in North America (Bergström et al., 2002; Stanek et al., 2012). Various *Ixodes* tick species can serve as vectors for the Lyme disease transmission: the main vector of Lyme borrelia in Europe is *I. ricinus*, whereas *I. persulcatus* is the main vector in Asia. *I. scapularis* is the main vector in northeastern and upper midwestern USA and *I. pacificus* serves as the vector in western USA (Stanek et al., 2012).

The pathogen transmission involves three ecological and epidemiological processes (Ogden et al., 2008b; Ostfeld, 1997; Thompson, Spielman, & Krause, 2001) between two post-egg but immature stages larvae and nymphs: nymphal ticks infected in the previous year appear first; these ticks then transmit the pathogen to their susceptible vertebrate hosts during a feeding period; the next generation larvae acquire infection by sucking recently infected hosts' blood and these larvae develop into nymphs in the next year. The transmission cycle is depicted in Fig. 1. Lyme disease results when a human is inadvertently bitten by an infectious tick.

Prevention and control of tick-borne diseases, in general and Lyme disease in particular, are important to human health, animal welfare and economics. Understanding the factors that regulate the abundance and distribution of the Lyme-pathogen is crucial for the effective control and prevention of the disease. Mathematical modeling has become an important tool in analyzing the epidemiological characteristics of infectious diseases and providing cost-efficient control measures (Anderson and May, 1992). There have been a range of tick-borne disease modeling efforts dedicating to different aspects of Lyme disease transmission: the basic tick population ecology (Caraco et al., 1998; Porco, 1999), effect of different hosts and their densities on the persistence of tick-borne diseases (Pugliese & Rosà, 2008; Rosà & Pugliese, 2007; Rosà, Pugliese, Norman, & Hudson, 2003), threshold dynamics for disease infection (Foppa, 2005; Hartemink, Randolph, Davis, & Heesterbeek, 2008), seasonal tick population dynamics and disease transmission (Dobson, Finnie, & Randolph, 2011; Ghosh & Pugliese, 2004), climatic effects (Ogden et al., 2005; Wu, Duvvuri, & Wu, 2010), spatial invasion of ticks and spreading of the disease (Caraco et al., 2002; Gaff & Gross, 2007; Zhang & Zhao, 2013), among others. These modeling efforts can be classified into two broad types: models that aim to explore theoretically the behaviours of the systems, which may or may not use the basic reproduction number $\mathscr{R}_0$ as an index of the relative contributions or effects of different model parameters (e.g. (Caraco et al., 2002; Foppa, 2005; Ghosh & Pugliese, 2004; Hartemink et al., 2008; Norman, Bowers, Begon, & Hudson, 1999; Randolph et al., 1999; Rosà & Pugliese, 2007; Rosà et al., 2003; Schmidt & Ostfeld, 2001)); and simulation models that aim to explicitly simulate certain aspects of the biology of vectors and vector-borne disease systems as accurately as possible (e.g. (Dobson et al., 2011; Mount & Haile, 1989; Mount, Haile, & Daniels, 1997; Ogden et al., 2005; Porco, 1999)). The outcomes of these studies, and
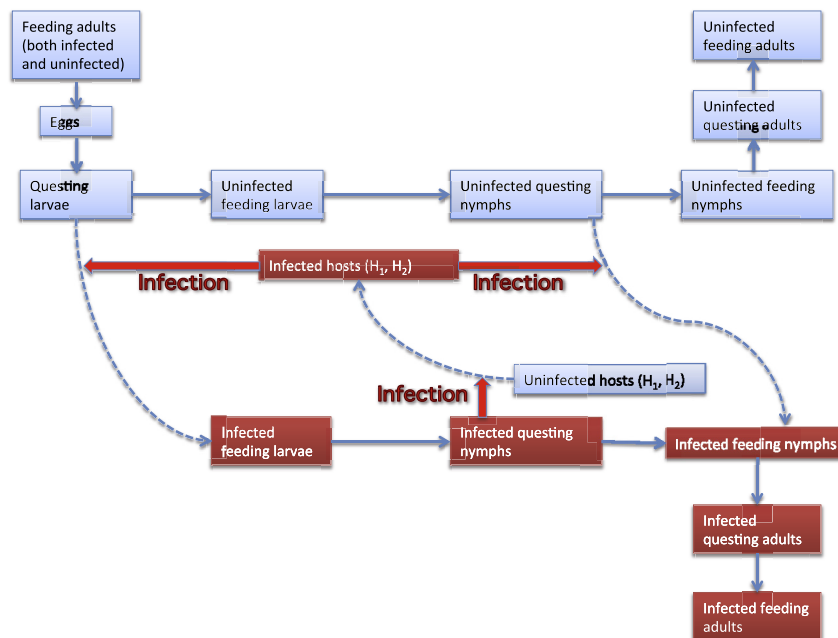

Fig. 1. A schematic diagram for the Lyme disease transmission (reproduced from (Lou, Wu, & Wu, 2014)). To describe the tick development and biting activities, the tick population is divided into 7 stages, stratified further as the uninfected or infected epidemiological classes for postegg stages. Immature ticks can feed on two host species, the mouse (H_1) and an alternative host (H_2), while adult ticks are assumed to feed only on deer in the study.