Theoretical Population Biology xx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Theoretical Population Biology

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

Modelling leptospirosis in livestock

A.M. Babylon *, M.G. Roberts, G.C. Wake

Institute of Natural and Mathematical Sciences, Massey University, Private Bag 102 904, North Shore Mail Centre 1311, Auckland 0745, New Zealand

ARTICLE INFO

Article history:
Received 29 September 2016
Available online xxxx

Keywords:
Leptospirosis
Mathematical model
Compartmental model
Livestock
Periodic
Cyclical

ABSTRACT

New Zealand has one of the highest (per capita) incidences of human leptospirosis in the world. It is the highest occurring occupational disease in New Zealand, often transmitted from livestock such as deer, sheep and cattle to humans. A cyclical model, showing the dynamics of infection of leptospirosis in farmed livestock in New Zealand, is presented. The limit cycle, bifurcation diagram and quasi-R_0 value of the system are determined. Leptospire death rate is used as a control parameter. Previously published parameter values are used in a case study to produce figures demonstrating analytical results. The model is used to predict conditions under which the infection will persist in the population.

1. Introduction

Leptospirosis is a disease resulting from a bacterial infection. It occurs when contaminated material, such as water polluted with the urine of an infectious animal, comes into contact with broken skin, or mucus membranes, or is ingested internally (Victoriano et al., 2009). It causes abortions and decreased weight gain in livestock (Heuer et al., 2012a). In humans, symptoms are usually flu-like and result in an average of six weeks absence from work (Leptospirosis in New Zealand, 2014; Leptospirosis, 2007). It is the highest occurring occupational disease in New Zealand with between 80 and 180 cases per year, 60% of which result in hospitalisation (Leptospirosis in New Zealand, 2014; Leptospirosis, 2007; Thornley et al., 2002; Institute of Environmental Science and Research Limited, Porirua, 2012). Leptospirosis costs the country an estimate of at least 24 million New Zealand Dollars each year due to human disease, production losses, and vaccination costs (Frigolett, 2016; Leptospirosis, 2014).

It has been shown that regularly moving deer to different fields (the word "field" here is used to refer to the area in which livestock are confined) decreases the incidence of paratuberculosis (caused by *Mycobacterium avium* subspecies *paratuberculosis*) in red deer by 50%, when compared to permanent grazing (Heuer et al., 2012b). A similar control strategy could be used for leptospirosis. This study focuses on one field with a new flock of sheep being introduced at the beginning of each year. After some time in the field, the sheep are removed and the field remains empty for the remainder of the year. This strategy is similar to farming practices already in place in New Zealand, where lambs are kept in a single field for 11 months, before being moved (C. Heuer, personal communication, 2014).

We are not aware of any previous model of leptospirosis in New Zealand. Many models for leptospirosis overseas exist, however, most compartmental SIR type models do not include periodic, time varying parameter values. Infectious disease models that do, do so in relation to pulse vaccination or culling of the host population (Shulgin et al., 1998). The structure of the model here is similar to a compartmental model of paratuberculosis specific to New Zealand conditions studied by Verdugo, however that analysis was purely numerical (Verdugo, 2013). We present an analytical model for leptospirosis that is unique not only in that it incorporates New Zealand conditions, but also in that it focuses on how the resetting of the population impacts on the free living infectious agent, which in turn impacts on each new generation of the host population.

2. Model

A simple *SI* model is used to describe the spreading of leptospirosis in lambs. A number of lambs are introduced into a field containing free living leptospires, L. We assume a constant lamb population, at stocking density N. The lambs become infected, I, through grazing, at rate γ and consequently start shedding back into the environment at rate α, subsequently infecting other lambs. The lambs remain in the field for a set period of time, t_r, before being removed for the remainder of the year. This allows the field to recover from infection, as the free living leptospires die off at rate ρ while the field is unoccupied. At the beginning of the next period, a new flock is introduced to the field, at the same density, N, and the process is repeated. All lambs are assumed to be susceptible when they are introduced, that is, at the beginning of

* Corresponding author.
E-mail addresses: A.Babylon@massey.ac.nz (A.M. Babylon), M.G.Roberts@massey.ac.nz (M.G. Roberts), G.C.Wake@massey.ac.nz (G.C. Wake).

https://doi.org/10.1016/j.tpb.2018.03.005
0040-5809/© 2018 Published by Elsevier Inc.

the grazing period $S(0) = N$. Note that $N = S + I$. A non-linear term, $L/(L + H)$, is included in the model as a saturation term. This term was used in a numerical model on leptospirosis in rats in Tanzania by Holt et al. (Holt et al., 2006). It limits the effect of transmission to lambs as free living leptospire values become large, while still allowing infection transmission to increase as free living leptospires increase. The equation describing free living leptospire growth is also from (Holt et al., 2006). This model differs from that of Holt et al. in that it includes removal of the population. A more analytical approach is taken here, and only one age class is considered. The whole system can be described using the following set of differential equations.

The system before removal ($0 < t < t_r$),

$$\frac{dI}{dt} = \frac{\gamma(N - I)L}{L + H}, \tag{1}$$

$$\frac{dL}{dt} = \alpha I - \rho L. \tag{2}$$

The system after removal ($t_r < t < t_y$), reduces to

$$\frac{dL}{dt} = -\rho L. \tag{3}$$

In Eq. (1) the per capita rate of infection is assumed to follow Michaelis–Menten kinetics. In Eq. (2) the per capita rate of infection of leptospires satisfies constant per capita production and loss. The periodicity of the model could also be expressed by making the environmental transmission coefficient, γ, and shedding rate, α, functions of time, t, with constant values γ and α, respectively, while the field is occupied and 0 otherwise. This expression of the model would include a Dirac singular measure, which would make it more clear that any solutions to the model are expected to be not only continuous, but also periodic in time. In fact, the solutions can be characterised as Caratheodory solutions (Coddington and Levinson, 1955).

3. Data and parameter values

Climate, farming conditions and local farming practices can have a substantial impact on leptospiral infection. Stocking density, for example, is dependent on land topography (high, hill or flat country) and varies from country to country (Morris, 2013). In New Zealand livestock are grazed predominantly outside, on pasture, and the subtropical climate impacts heavily on free living leptospiral survival. All these factors result in unique conditions for leptospira and as this paper focuses on leptospirosis in New Zealand in particular, where possible, the parameter values used are chosen to reflect local conditions. The model notation and parameter values used are summarised in Table 1.

The parameter values for H, N, α and ρ, used in the model, are either previously published values or are derived from published data. The value for H, the number of leptospires at which transmission rate from the environment is 0.5γ, is taken from a model of leptospirosis by Holt et al. (2006).

The unit for livestock density is the stocking unit (SU), where one stocking unit is equivalent to one 55 kg ewe and her lamb per hectare. The livestock density in New Zealand can range from 0.7 SU ha^{-1} on high country, to 25 SU ha^{-1} on intensive finishing land (Ministry of agriculture and forestry, 2011; Ministry for Primary Industries, 2012; Farmlands Co-operative Society Limited, 2016; Beef and Lamb New Zealand, 2012; Morris, 2013). For simplicity, the lamb density, N, is chosen to be 10 lambs per hectare. Even when ignoring ewes, this figure is within the range above.

Leptospire shedding rate, α, is calculated using various data available in the literature. Unfortunately shedding rate data for sheep are unavailable. However, a New Zealand study found that deer shed leptospires at a concentration between 3×10^3 and 1.7×10^6 leptospires (serovar hardjobovis) per ml of urine (Subharat, 2010). Sheep excrete between 10 and 40 ml of urine per kilogram of body weight per day and lambs weigh on average 38.9 kilograms (Merck Manuals, 2015; Cruickshank et al., 2008). By taking an average of 25 ml of urine per kilogram of body weight per day, each lamb is expected to produce around a litre of urine per day and each infectious lamb sheds between 3×10^6 and 1.7×10^9 leptospires into the environment per day. Not all these leptospires will remain on the surface of the field/grass, some will sink into the soil and not be accessible by the sheep. One would also expect sheep to avoid patches on which there has been recent urination. Therefore, the shedding rate α in the model is set to be less than the number of leptospires shed into the environment by each infectious lamb. A value of 10^3 leptospires is chosen, giving a (scaled) α value of 1.

Several different values of free living leptospire survival times are presented in the literature, ranging from two weeks to several months and even years (Baron, 1996; Shimshony, 2009; Trueba et al., 2004). The leptospire death rate, ρ, used here, is based on Hellstrom and Marshall (Hellstrom and Marshall, 1978). Their study was specific to the Manawatu region of New Zealand and serovar Pomona. Leptospires were found to be culturable and infectious for at least 42 days (Hellstrom and Marshall, 1978). Hence we take $\rho = 1/42$ day^{-1} and denote this value ρ_0 to distinguish it from variable ρ. From a practical stand point, leptospire death rate could be influenced by using antimicrobials to treat the field for infection. This approach does not seem to currently be in use for leptospires, but, as leptospires are sensitive to chemicals, including but not limited to detergents and acids, it may be a viable option (Johnson, 1996; World Health Organization, 2003; Leptospirosis information, 2011). The leptospire death rate is therefore used as a control parameter in the bifurcation diagram. It would be interesting, in future, to consider the role of climate change on leptospire death rate and how this could impact on leptospire infection in livestock. This is, however, beyond the scope of this work.

Data for the environmental transmission coefficient, γ, were not available in the literature and hence the parameter value γ was found by fitting the model to a set percentage of infectious lambs at time of removal. A study of a Waikato, New Zealand abattoir found that approximately 27% of sheep from sheep-only suppliers were shedding leptospires in their urine at time of slaughter (Fang, 2014). The majority of sheep (78%) in this study were lambs, so this percentage is deemed appropriate for use in this model to estimate γ. This was done simply by varying the value of γ until the percentage of infectious lambs at time of removal was 27% (see Fig. 2a). The value of $\gamma = 0.02474$ day^{-1} is denoted γ_0, to distinguish it from other values of γ used.

The initial condition for free living leptospira, L_0, is chosen as the small, but arbitrary, value of 0.01 leptospire units per hectare. This constant is denoted L_0^0.

4. Results

4.1. Numerical results

The system of equations, Eqs. (1)–(3), was solved numerically. Fig. 1 shows the results, using a value of $\gamma = 0.08$ day^{-1}. This is for demonstration purposes, as when starting from the same initial condition, the system converges faster than when using $\gamma = \gamma_0$. Note that the behaviour of the system in years three, four and five indicates a convergence to a limit cycle. This is explored in the following sections.

Fig. 2 shows the behaviour of the system using $\gamma = \gamma_0$, the lower and more realistic value of the transmission coefficient, over a period of 30 years. The system takes a longer time to reach a limit cycle than in the previous example. The proportion of infectious lambs at the end of the year is 27%, as opposed to 100% in Fig. 1.