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A model of Leptospirosis infection in an African rodent to determine risk to humans: Seasonal fluctuations and the impact of rodent control

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Abstract

Human leptospirosis (*Leptospira* spp. infection) is a worldwide public health problem that is of greatest concern for humid tropical and subtropical regions. The magnitude of the problem in these areas is larger because of the climatic and environmental conditions the bacterium face outside their hosts but also because of the frequency of contacts between people and sources of infection. Rodents are thought to play the most important role in the transmission of human leptospirosis. We here model the dynamics of infection in an African rodent (*Mastomys natalensis*) that is thought to be the principal source of infection in parts of Tanzania. Our model, representing the climatic conditions in central Tanzania, suggests a strong seasonality in the force of infection on humans with a peak in the abundance of infectious mice between January and April in agricultural environments. In urban areas the dynamics are predicted to be more stable and the period of high numbers of infectious animals runs from February to July. Our results indicate that removal of animals by trapping rather than reducing the suitability of the environment for rodents will have the greater impact on reducing human cases of leptospirosis.

Keywords: Zoonosis; *Mastomys natalensis*; Epidemiology; Population dynamics; Mathematical model; Tanzania

1. Introduction

Leptospirosis affects all mammals and can spread between domestic pets, livestock, wild animals and humans. In Africa, it is thought that commensal rodents are the most important source of transmission to humans (WHO Leptospirosis Manual, 2003; Dalu and Feresu, 1997; Machangu et al., 1997). Leptospirosis infection in humans presents with symptoms that are similar to that of other better known parasitic, viral and bacterial infections such as malaria, Rift valley fever and brucellosis. Hence it is frequently misdiagnosed and its impact on African communities is largely undocumented.

Perhaps with the exception of Caley and Ramsey (2001), who modelled transmission of letpospirosis in brushtail possums (*Trichosurus vulpecula*), there are no published mathematical models for the spread and maintenance of leptospirosis infection in wildlife. This is not too surprising since so little is understood about

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how it maintains itself in natural populations; whether there is competition between serovars, whether infection or immunity is passed from mother to offspring, what determines survival of leptospires in the environment, and whether animals recover and become immune.

Mathematical models of the type used here (a deterministic model consisting of a set of differential equations) have a long tradition in the study of wildlife diseases (for reviews see Heesterbeek and Roberts, 1995; Barlow, 1995; Swinton et al., 2002). For the majority of models the primary motivation is to predict the impact of intervention by either culling or vaccination (e.g. Roberts and Aubert, 1995) and a universal motivation is a better understanding of the dynamics of infection (e.g. Sauvage et al., 2003).

Here we present a basic model for the dynamics of leptospirosis infection in a common African rodent, the multimammate mouse (*Mastomys natalensis*). Though similar to other models in the literature, the epidemiological characteristics of leptospirosis and the life history of *M. natalensis* have resulted in a model of unique form. The multimammate mouse has long been recognised as a serious agricultural pest (Fiedler, 1988; Leirs et al., 1996) and is hence well studied (Leirs et al., 1990, 1993). The basis for our model is a population dynamics model developed by Leirs et al. (1997) for *Mastomys* populations in maize fields in Tanzania. In crop habitat *M. natalensis* populations undergo predictable seasonal fluctuations but they may also respond to high rainfall and can irrupt to very high densities. Commensal rodent populations are likely to be more stable and we also explore model results when the infection circulates in a population of relatively constant abundance. Seasonality in leptospirosis risk and the potential effects of management interventions were investigated in model simulations.

2. Materials and methods

Our model is a system of differential equations (Appendix A) representing both the changes in total numbers of rodents and in the numbers of rodents carrying leptospirosis. The rodent population is divided into three age classes (juveniles, sub-adults and adults), each of which is further divided into two disease classes (susceptible and infectious). It is assumed in the model that once infected, individuals are chronically infected for their lifetime, and that there is no delay between becoming infected and being infectious. In the absence of evidence to the contrary, we have chosen to ignore the possible occurrence of recovery.

The model includes three potential routes of transmission for leptospirosis; from mother to offspring, direct (sexual) contact, and via the external environment (WHO Leptospirosis Manual, 2003). The relative importance of these routes is unknown and this uncertainty is represented in the model by including parameters that allow their importance to be varied. Direct transmission via sexual contact is modelled as frequency-dependent (Begon et al., 2002) as it is thought that for multimammate mice the frequency of sexual contact is unaffected by population abundance.

There are several differences between the three rodent age classes. Only the adult age-class is able to reproduce and hence transmission via sexual contact only applies to this age-class. Juveniles are generally confined to the nest so infectious juveniles are assumed not to shed leptospires into the environment and susceptible juveniles not to be exposed to free-living leptospires. Juveniles become sub-adults after 3–4 weeks but maturation rate of sub-adults has been found to be sensitive to the amount of rainfall in the previous month as well as the abundance of adults (Leirs et al., 1997). In the model, adult abundance provides a source of density-dependence which essentially determines a carrying capacity and prevents the population from reaching unreasonably high numbers.

A seventh differential equation represents the abundance of leptospires in the external environment. Free-living leptospires are shed in the urine of infectious animals and though the period they survive depends very much on whether they are shed into water or on dry ground, a mean survival time is assumed in the model. The rate at which susceptible sub-adults and adults become infected via free-living leptospires is expected to increase with the abundance of leptospires in the external environment, described by a simple non-linear term so that eventually additional free-living leptospires have a negligible effect on the rate of transmission.

The parameter values associated with *Mastomys* population dynamics can be estimated accurately and seasonal variation in these parameters is also well understood (Leirs et al., 1997). In contrast, there is little information about the leptospire parameters, especially the infection rates, ν_i, and mortality of free-living leptospires, μ. In the absence of directly relevant data, order of magnitude estimates were chosen for the epidemiological parameters (Table 1). It appears that Leptospirosis fails to persist in rodent populations in the absence of an environmental infection source (R. Hartskeerl, personal communication) and indirect transmission, i.e. via free-living leptospires shed by infectious hosts into surface water, has usually been assumed to be the most important transmission route (Ward, 2002; Meites et al., 2004).