Dynamics and control of foot-and-mouth disease in endemic countries: A pair approximation model

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HIGHLIGHTS

- Traditional models of FMD focus on control and dynamics in disease-free settings.
- We analyze long-term dynamics and control of FMD in endemic countries.
- Success of vaccination depends on rates of vaccine and natural immunity waning.
- Prophylactic vaccination performs better that ring vaccination.
- More mathematical models applicable to FMD-endemic countries need to be developed.

ARTICLE INFO

ABSTRACT

Previous mathematical models of spatial farm-to-farm transmission of foot and mouth disease (FMD) have explored the impacts of control measures such as culling and vaccination during a single outbreak in a country normally free of FMD. As a result, these models do not include factors that are relevant to countries where FMD is endemic in some regions, like long-term waning natural and vaccine immunity, use of prophylactic vaccination and disease re-importations. These factors may have implications for disease dynamics and control, yet few models have been developed for FMD-endemic settings. Here we develop and study an SEIRV (susceptible-exposed-infectious-recovered-vaccinated) pair approximation model of FMD. We focus on long term dynamics by exploring characteristics of repeated outbreaks of FMD and their dependence on disease re-importation, loss of natural immunity, and vaccine waning. We find that the effectiveness of ring and prophylactic vaccination strongly depends on duration of natural immunity, rate of vaccine waning, and disease re-introduction rate. However, the number and magnitude of FMD outbreaks are generally more sensitive to the duration of natural immunity than the duration of vaccine immunity. If loss of natural immunity and/or vaccine waning happen rapidly, then multiple epidemic outbreaks result, making it difficult to eliminate the disease. Prophylactic vaccination is more effective than ring vaccination, at the same per capita vaccination rate. Finally, more frequent disease re-importation causes a higher cumulative number of infections, although a lower average epidemic peak. Our analysis demonstrates significant differences between dynamics in FMD-free settings versus FMD-endemic settings, and that dynamics in FMD-endemic settings can vary widely depending on factors such as the duration of natural and vaccine immunity and the rate of disease re-importations. We conclude that more mathematical models tailored to FMD-endemic countries should be developed that include these factors.

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1. Introduction

Foot and mouth disease (FMD) is a highly transmissible viral infection affecting cloven-hoofed animals, including domestic livestock such as cattle, pigs, goats, sheep (Baipolledi et al., 2004; Keeling et al., 2001; Wernery and Kinne, 2012; Ferguson et al., 2001) and some wild animals, e.g. buffaloes. The disease agent of FMD belongs to the *picorna* virus family (Belsham et al., 2011). There are seven known serotypes of FMD virus which vary according to geographical region (Rweyamamu, 1984; Alonso et al., 1992). The serotypes of FMD are classified as (a) European types O, A and C; (b) African types STA 1, STA 2 and STA 3 and (c) Asian type Asia 1 (Davies, 2002; Ding et al., 2013), and there are several (more than 60) subtypes of the virus (Alonso et al., 1992; Anderson et al., 1974; Belsham et al., 2011).

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Vaccination against one serotype does not provide protection against other serotypes. This makes it difficult to control the spread of FMD by vaccination alone and adopting multiple control measures may offer better means of control.

The FMD virus can be found in secretions and excretions from infected animals, including expired air, saliva, milk, urine and semen. The virus is airborne and can also be transmitted through physical contact. Clinical symptoms of FMD include high fever, blisters inside the mouth, raptured feet and stunted growth (Rweyamamu, 1984; Baipoledi et al., 2004; Ferguson et al., 2001; Rae et al., 1999). However, animals rarely die from foot and mouth disease. Upon introduction, FMD virus spreads rapidly within a farm, and interaction between neighboring farms leads to a rapid spread of the disease to several kilometers (up to 6 km) from the source point (Enserink, 2001). Import–export routes also enhance the spread of FMD, potentially resulting in a highly damaging global economic impact.

FMD is one of the most economically important livestock diseases (Belsham et al., 2011; Cottam et al., 2008). Heavy import–export restrictions apply in countries that experience frequent FMD outbreaks (Rae et al., 1999). Thus, the cost–benefit ratio of an investment business in FMD-affected animal species is greatly affected by frequent disease outbreaks. Due to its economic impact, FMD remains the greatest and most feared vesicular diseases in India (Matthew and Menon, 2008). In livestock production, the economic loss due to FMD can be calculated by considering, e.g., milk loss, disease-induced abortions and treatment costs. By the time the 2001 UK FMD outbreak had been stopped, the government had spent nearly GBP 3 billion on the operation of containing and cleaning up after the disease (Thompson et al., 2002). Recent outbreaks in Botswana include in 2002, 2005, 2006, 2007, 2011 and 2012 (Baipoledi et al., 2004; Letshwenyo et al., 2004; Mokopasetso and Derah, 2005).

There is no cure for FMD (Pharo, 2002; Wernery and Kinne, 2012). Infected animals usually recover to a health-compromised status that renders them less profitable. Conventional control measures against FMD are movement restriction; public education; veterinary boundaries; quarantine; vaccination and culling (slaughtering animals in order to reduce the number of susceptible or infectious animals, and hence reduce spread of the disease Barteling, 2002). Two basic forms of vaccination against foot and mouth disease are prophylactic vaccination (pre-outbreak: vaccination carried out prevent introduction of the disease) and ring vaccination (during an outbreak: carried out on farms neighboring infected farms). The Cedivac-FMD Double Oil Emulsion (DOE) vaccines (one of many types of FMD vaccines) confer a duration of immunity of at least 6 months in cattle, sheep and pigs (Chenard et al., 2007; Domenech et al., 2010). Some vaccines can provide prolonged immunity for up to 12 months, depending on, among others, the species affected and the virus serotype. Cattle which have recovered from infection with one of the seven serotypes of the FMD virus remain protected against that serotype for up 6 months to about 5 years, depending on the virus serotype (Doel, 1996). Methods of culling include contagious premises (CP) culling (slaughtering farms based on their proximity to infected farms) and infected premises (IP) culling (slaughtering infected farms).

The availability of data for the 2001 FMD outbreak in the United Kingdom allowed the development of validated epidemiological models, making it possible to explore impacts of various control measures (Tildesley et al., 2001). For instance, Tildesley et al. (2001) used an individual-farm based transmission probability model, capturing spatiality by describing the probability of infection as a function of the distance between susceptible farms and infection source (transmission kernel), and also explored impacts of ring vaccination strategies. Using a stochastic individual farm-based model, Keeling et al. (2003) explored impacts of either

national prophylactic vaccination campaigns, or combinations of reactive (during outbreak) vaccination and culling.

Compartmental models have also been used to study the dynamics and control of foot and mouth disease. In compartmental models, the host population is composed of subdivisions called compartments such that the nature and time rates of transfer from one compartment to another are defined (Brauer, 2006). Each compartment represents the disease status of farms (e.g. susceptible, infectious or recovered). Compartmental models are sometimes referred to as mean-field approximations as they typically assume that members of the host population mix homogeneously (Brauer, 2006). Thus spatial spread of the disease is neglected (Bunwong, 2010), since it is assumed that an infectious farm is equally likely to infect any of the susceptible farms in the population. Ref. (Mushayabasa et al., 2011) adopt this approach to model the spread of FMD and impacts of vaccination, by dividing the population of farms into susceptible (S), vaccinated (V), latently infected (L) and infectious farms (I), and uses it to explore the impacts of births and deaths, culling, and vaccine waning.

Recently a number of foot and mouth disease transmission models have used moment closure approximations (pair approximation models in particular) to capture spatiality implicitly. Parham et al., 2008 design and analyze an SEI (susceptible, exposed but not infectious, infectious) pair approximation model of foot and mouth disease and explore impacts of IP culling and CP culling. They assume that the disease spreads on a network of farms represented by nodes (farms) and edges (links between farms). For many infectious diseases where spatiality is important for transmission and control, including foot and mouth disease, spatially structured models may provide advantages over mean-field approximations such as conventional compartmental models (Parham and Ferguson, 2005; Bauch, 2005). Ferguson et al. (2001) also present and analyze a pair approximation model of foot and mouth disease, employing data from the well-documented 2001 FMD out break in the United Kingdom, and explore impacts of ring culling and ring vaccination (both of which are applied during a single outbreak). In the study of Ferguson et al. (2001), the transmission rate is explicitly defined as a function of both local transmission between connected farms, and long range transmission due to transport since FMD virus can be transported to up to 60 km from the source point.

While mean field approximations are formulated under an assumption that individuals in the host population mix homogeneously, moment closure approximations capture the spatial spread of diseases by modeling states of neighboring members of the host population. This technique provides information about the spatial distribution of disease states on a network by employing pairs, triples, quadruples, and other higher-order correlations as state variables of ordinary differential (Bauch, 2005; Bunwong, 2010). Each ordinary differential equation (also referred to as equation of motion for a state variable) measures the expected rate of change of a state variable by averaging all possible events affecting the state variable (van Baalen, 2000). To do this, the first step is to write the equations of motion for the number of neighboring pairs of individuals or groups of individuals of a given state on a network; these equations will have terms involving triples (Bauch, 2005). The equations of motion for triples will involve quadruples while the equations of motion for quadruples will have terms involving five-order correlations. Essentially the procedure yields an infinite system of ordinary differential equations, each describing rates of change of state variables. However in order to solve the system analytically or using available computer software the system of equations needs to be finite. A closed, manageable system is obtained by truncating the hierarchy at some suitable level by a process known as *moment closure* (Bauch and Rand, 2000; Bauch, 2005; van Baalen, 2000;