Published: November 2017

A model of endemic foot-and-mouth disease in African buffalo

Erin Gorsich - Research Scientist at Colorado State University.
Brianna R. Beechler, Anna E. Jolles and Jan Medlock are faculty in the Department of Biomedical Sciences in the College of Veterinary Medicine at Oregon State University.

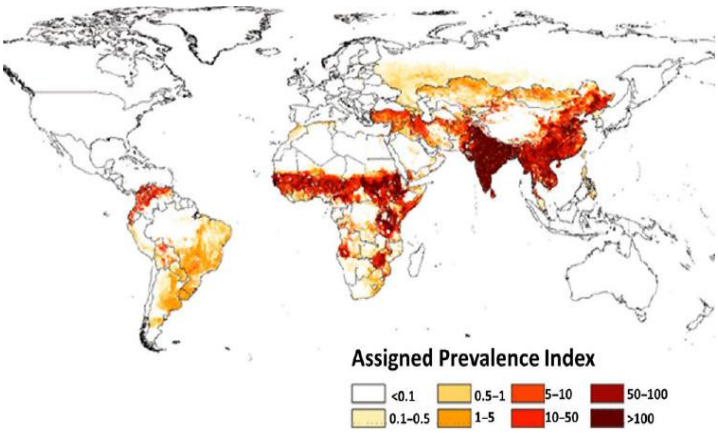
Foot-and-mouth disease (FMD) is one of the most feared transboundary diseases (1). FMD is a rapidly spreading viral infection capable of infecting a range of animals, including livestock. Infection is typically mild; it causes fever and blistering on the animal's hooves and mouth. FMD also has a near-global distribution (2). Figure 1 displays a global map of FMD prevalence in cattle. Fear of FMD, therefore, is primarily driven by the risk of its introduction and spread into non-endemic areas. It is a fear constructed by both economics and production loss. In addition to the direct consequences of infection on production, the economic effects of FMD are also attributable to trade restrictions. Because the World Organization for Animal Health (OIE) classifies countries based on whether FMD is present, only countries free of FMD can export livestock products internationally.

FMD is endemic in many sub-Saharan African countries (3). In South Africa, successful control has eliminated the infection from most of the country. South Africa is recognized by the OIE as FMD free without vaccination. Infection, however, remains in the areas surrounding the Kruger National Park (Figure 1). In this area, African buffalo are the primary wildlife reservoir for FMD. Transmission between buffalo and cattle is believed to occur based on the following evidence. First, transmission from buffalo to cattle has been demonstrated under experimental conditions (4). Second, genetic information has shown that strains identified in buffalo are similar to those found in cattle (5). Third, new FMD infections are more common in cattle that frequently contact African buffalo (6). Understanding how buffalo maintain the infection, when transmission from buffalo is most likely, and why transmission occurs are important to understanding FMD in South Africa.

This article discusses a model-guided research programme in Kruger National Park. We focus on the development and use of an individual-based model that is guiding our field and experimental data collection.

Using individual-based models to study infection persistence

FMD epidemics in livestock are characterized by explosive spread: after the introduction of infection on a farm, the entire farm is rapidly infected. To capture this pattern, models of FMD generally divide individuals into categories based on their disease status (9). Individuals are represented as susceptible to FMD, infected but not yet infectious, infectious, or recovered. Models with this structure, called SEIR



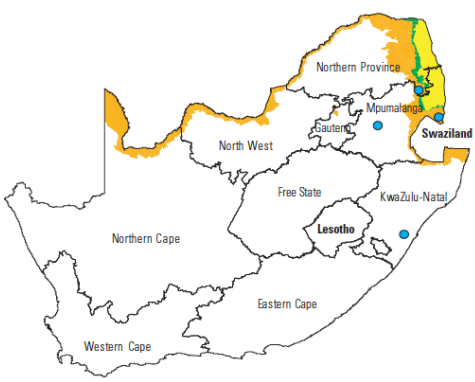


Figure 1. (above) Global distribution of FMD (reproduced from: 7, 8). Prevalence indices were derived from reported incidence rates as well as other indicators of reflecting FMD risk, including expert opinion.
(below) Map of South Africa showing the FMD management zones and outbreak locations (reproduced from: 5). The yellow area indicates the infected zone of Kruger National Park, the green area represents the buffer zone, and the orange area represents the surveillance zone, which extends along the northern and eastern border of South Africa. In these areas, livestock are inspected every 7 or 14 days, respectively, and the movement of animals between control and disease-free areas is prohibited.

(Susceptibles, Exposed, Infectious, Recovered) models, have been successfully used to model a range of rapidly transmitting infections (e.g. measles, pertussis, polio). One property of this type of model is that persistence in small populations is rare (10, 11). Transmission in the early stages of an outbreak is so rapid that most individuals quickly become recovered and few susceptible individuals remain to transmit the infection. As a result, highly contagious pathogens tend to exhibit violent fluctuations, exposing them to greater risk of extinction between outbreaks. Our research programme investigates how FMD, one of the most contagious animal pathogens, overcomes this challenge and persists in populations of its reservoir host, the African buffalo.

To address this question, we built a series of stochastic (e.g. with a random probability distribrution) individual-based models, representing alternative mechanisms of persistence. We used individual-based models because we were interested in the stochastic persistence of FMD. Using this framework, we were able to incorporate randomness in the timing and order of events and uncertainty in timing of infection (e.g. how long is it between when a buffalo is exposed and when they are infectious). We were also interested in quantifying variation between individuals in the timing of infection and the timing of births. Increased variation in either process is known to increase the chance that the pathogen persists (11).

A model-guided fieldwork approach

Our first step was to build a model representing the simplest hypothesis describing FMD, the SEIR model. This model represents rapid transmission and rapid recovery from infection. Over 98% of buffalo have been exposed to FMD, suggesting that the high rate of transmission represented in the model is appropriate. Birthing in African buffalo is seasonal, with most calves being born from December to April. This wide birth pulse may allow FMD to persist because it allows susceptible animals into the population over time. FMD could circulate through each year's population of new susceptible calves, with the latest born calves of one year sparking the new epidemic in the earliest born calves of the following year's cohort. To evaluate this null hypothesis, we analysed the SEIR model and evaluated the conditions allowing persistence.

To parameterize the model, we conducted experimental transmission studies. In these experiments, we housed experimentally infected and naive buffalo together in the same enclosure, and we monitored the timing of transmission and infection. There are three types of FMD, called serotypes, known to circulate within South Africa: South African Territories (SAT) serotypes 1, 2, and 3. We, therefore, repeated this experiment for each serotype. These experimets allowed us to estimate serotype-specific model parameters: how long do buffalo remain infectious and how rapidly is FMD transmitted? They also allowed us to quantify uncertainty in epidemiological parameters to ensure our model predictions robustly account for the challenges inherent to data collection.

The experimental results showed that FMD was transmitted rapidly from acutely infected buffalo and recovery occurred within 4-6 days. Based on this information, model results indicated that FMD would invariably go extinct from buffalo populations within a year or two. In model simulations, FMD only persisted when buffalo were assumed to be infectious for longer than 20 days or in populations larger than 1000 buffalo (Figure 2). This is clearly not the case—which raises the question, what piece of essential biology is represented incorrectly in this model?

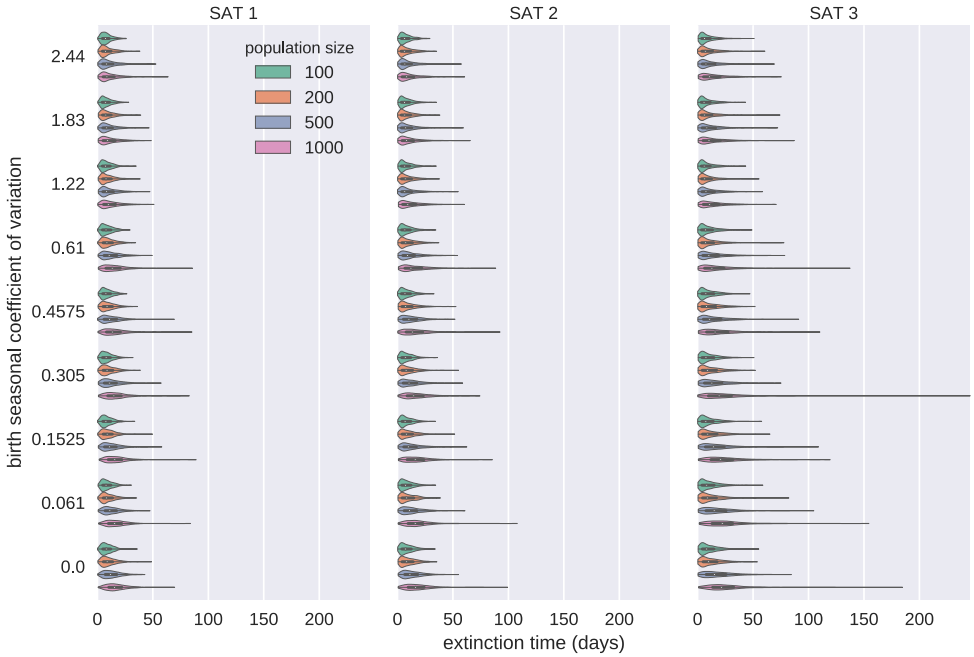


Figure 2. The extinction time for modelled populations shows that persistence is unlikely based on the SEIR model, even at large population sizes and for all serotypes of FMD in South Africa (SAT-1, SAT-2, and SAT-3). Variation in the timing of births among buffalo is represented on the y-axis by a coefficient of variation.

Our second step was to build models representing additional mechanisms of persistence and collect data to quantify and test these mechanisms empirically. One potential mechanism involves buffalo that maintain the infection over longer time

periods. Some studies have reported recovery of FMD virus from buffalo over five years post infection. Therefore, we are quantifying how often and under what conditions do these longer infected buffalo, called carriers, transmit FMD. Another potential mechanism is that buffalo may lose immunity over time. FMD is a rapidly evolving infection so the viral population may change to allow re-infection. We can represent loss of immunity in our model, and we are currently quantifying changes in the virus population in wild buffalo. Models representing these alternative hypotheses provide a clear set of assumptions to inform field and experimental data collection. Experiments to quantify these processes are underway and can be incorporated into our individual-based modelling framework.

In conclusion, our model results suggest that transmission between calf cohorts, as represented in the SEIR model, is highly unlikely to support the persistence of FMD in African buffalo populations. Because the assumptions in this model were used to inform data collection, all epidemiological parameters were estimated from experimental infections. The individual-based modelling approach gave us the flexibility to incorporate both uncertainty in parameter estimates and individual variation into model predictions. It also provided a clear set of assumptions to guide ongoing data collection for our alternative hypotheses.

This work is, therefore, one step in a larger model-guided study on FMD in African buffalo. As we finalize data collection this year, we look forward to further refining our assumptions and clarifying how FMD persists in its wildlife reservoir.

About the FMD-buffalo research team: The FMD-buffalo research team is an interdisciplinary and multinational collaboration. Dr. Jan Medlock and Dr. Anna Jolles lead the modeling work on this project (Oregon State University, OSU). Field-based data collection and disease testing are organized through Kruger National Park's Veterinary Wildlife Services department, Dr. Lin-Mari de Klerk-Lorist, Dr. Louis van Schalkwyk (Department of Agriculture, Forestry and Fisheries, Directorate of Animal Health, State Veterinary Office in Skukuza), Dr. Brianna Beechler (OSU), Dr. Francois Maree, Dr. Katherine Scott (ARC- Onderstepoort Veterinary Institute), and Dr. Eva Perez (The Pirbright Institute).

Erin Gorsich *- Research Scientist at Colorado State University with interests in the ecology and evolution of infectious disease. During her work as a post-doc in the Department of Biomedical Sciences at Oregon State University, Erin studied mathematical models of foot-and-mouth disease.* *eringorsich@gmail.com*

Brianna R. Beechler, Anna E. Jolles *and* ***Jan Medlock*** *are faculty in the Department of Biomedical Sciences in the College of Veterinary Medicine at Oregon State University. Their expertise includes mathematical epidemiology, veterinary medicine, and wildlife disease ecology.*

References:

1. Food and Agriculture Organization of the United Nations Transboundary animal diseases. [http://www.fao.org/emergencies/emergency-types/transboundary-animal-diseases/en/] Accessed 31 October 2017.
2. Sutmoller P, Barteling SS, Olascoaga RC, Sumption KJ. Control and eradication of foot-and-mouth disease. Virus Res. 2003; 91: 101–144.
3. Tekleghiorghis T, Moormann RJM, Weerdmeester K, Dekker A. Foot-and-mouth Disease Transmission in Africa: Implications for Control, a Review. Transbound Emerg Dis. 2016; 63(2): 136–151.
4. Dawe PS, Sorensen K, Ferris NP, Barnett IT, Armstrong RM, Knowles NJ. Experimental transmission of foot-and-mouth disease virus from carrier African. Vet Rec. 1994; 134: 211–215.
5. Bruckner GK, Vosloo W, Du Plessis BJA, Kloeck PELG, Connoway L, Ekron MD, Weaver DB, Dickason CJ, Schreuder FJ, Marais T, Mogajane ME. Foot and mouth disease: the experience of South Africa. Rev Sci Tech OIE. 2002; 21: 751–764.
6. Miguel E, Grosbois V, Caron A, Boulinier T, Fritz H, Cornelis D, Foggin C, Makaya PV, Tshabalala PT, de Garine-Wichatitsky M. Contacts and foot and mouth disease transmission from wild to domestic bovines in Africa. Ecosphere. 2013; 4(4): 51.
7. Knight-Jones TJD, McLaws M, Rushton J. Foot-and-Mouth Disease Impact on Smallholders - What Do We Know, What Don't We Know and How Can We Find Out More? Transbound Emerg Dis. 2017; 64: 1079–1094.
8. Sumption K, Rweyemamu M, Wint W. Incidence and distribution of foot-and-mouth disease in Asia, Africa and South America; combining expert opinion, official disease information and livestock populations to assist risk assessment. Transbound Emerg Dis. 2008; 55(1): 5–13.
9. Pomeroy LW, Bansal S, Tildesley M, Moreno-Torres KI, Moritz M, Xiao N, Carpenter TE, Garabed RB. Data-Driven Models of Foot-and-Mouth Disease Dynamics: A Review. Transbound Emerg Dis. 2015; 64(3): 716-728.
10. Keeling MJ, Grenfell BT. Disease Extinction and Community Size: Modeling the Persistence of Measles. Science. 1997; 275(5296): 65-67.
11. Peel AJ, Pulliam JRC, Luis AD, Plowright RK, O'Shea TJ, Hayman DTS, Wood JLN, Webb CT. The effect of seasonal birth pulses on pathogen persistence in wild mammal populations. Proc Biol Sci. 2014; 281(1786): 20132962.