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MODELING PLAGUE PERSISTENCE IN HOST-VECTOR COMMUNITIES IN CALIFORNIA

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ABSTRACT: Plague is an enzootic disease in the western United States, even though long-term persistent infections do not seem to occur. Enzootic persistence may occur as a function of dynamic interactions between flea vectors and transiently infected hosts, but the specific levels of vector competence, host competence, and transmission and recovery rates that would promote persistence and emergence among wild hosts and vectors are not known. We developed a mathematical model of enzootic plague in the western United States and implemented the model with the following objectives: 1) to use matrix manipulation within a classic susceptible→infective→resistant→susceptible (SIRS) model framework to describe transmission of the plague bacterium *Yersinia pestis* among rodents and fleas in California, 2) to perform sensitivity analysis with model parameters and variables to indicate which values tended to dominate model output, and 3) to determine whether enzootic maintenance would be predicted with realistic parameter values obtained from the literature for *Y. pestis* in California rodents and fleas. The model PlagueSIRS was implemented in discrete time as a computer simulation incorporating environmental stochasticity and seasonality, by using matrix functions in the computer language R, allowing any number of rodent and flea species to interact through parasitism and disease transmission. Sensitivity analysis indicated that the model was sensitive to flea attack rate, host recovery rate, and rodent host carrying capacity but relatively insensitive to changes in the duration of latent infection in the flea, host and vector competence, flea recovery from infection, and host mortality attributable to plague. Realistic parameters and variable values did allow for the model to predict enzootic plague in some combinations, specifically when rodent species that were susceptible to infection but resistant to morbidity were parasitized by multiple poorly competent flea species, including some that were present year-round. This model could be extended to similar vectorborne disease systems and could be used iteratively with data collection in sylvatic plague studies to better understand plague persistence and emergence in nature.

Key words: Community modeling, plague, SIRS model, *Yersinia pestis*.

INTRODUCTION

Yersinia pestis, the agent of plague, is a highly virulent pathogen that persists in poorly understood ecological foci in the western North America, central and Southeast Asia, parts of Africa, South America, and the Middle East. Plague was first introduced into the New World during the Third Pandemic (in the late 19th and early 20th centuries) via infected rats, *Rattus rattus*, and rat fleas, *Xenopsylla cheopis*, through the port of San Francisco, California, USA (Link, 1955). The first human case in Chinatown, San Francisco, in 1900 was followed by epidemics in California in 1907, 1919, and 1924 (Barnes, 1982), with the last pneumonic plague epidemics in the United States in 1924–25 in Los Angeles (Perry and Fetherston, 1997). Simultaneously, *Y. pestis* became established in native rodents in the San Francisco region (Link, 1955), and, as early as 1903, massive epizootics were reported in California ground squirrels (*Spermophilus beecheyi*). The agent of plague was first isolated in California ground squirrels in 1908 in the Berkeley hills in Contra Costa County (McCoy, 1908; Wherry, 1908).

At least 18 rodents species and 27 or more flea species are involved in ongoing enzootic plague cycles in the western United States,

largely independent of the traditional rat-rat flea cycle (Hubbard, 1968; Smith et al., 1998; Gage and Kosoy, 2005). Most cases of *Y. pestis* infection, including those in humans and rodents, are acquired through flea bites, but infections can occur through direct exposure to infectious respiratory and oropharyngeal secretions; through predation, particularly by cats; and through scavenging by rodents, such as *Onychomys leukogaster*, on infected hosts and carcasses (Smith et al., 1998). One theory to account for plague persistence is that unidentified, persistently infected but asymptomatic host species may maintain infection in plague-enzootic communities, whereas lethally susceptible, transiently infected "amplifying hosts" are responsible for most human infections (Pollitzer, 1954). Yet, no persistently infected reservoir hosts have been identified in the western United States. In some situations, fleas may function as de facto reservoirs, because they can retain infection for several months or longer, especially in winter climates (Eskey and Haas, 1940; Gage and Kosoy, 2005). It is likely that the dynamic interactions among hosts and fleas determine whether *Y. pestis* can be maintained in nature; however, it is not known which critical characteristics of these dynamics permit such maintenance.

There are prospects for enormous ecological complexity in the maintenance of the flea-host-*Y. pestis* system. Because *Y. pestis* can spread directly among people in the pneumonic form, can induce fatal disease, and it could be weaponized; it is listed by the US Department of Health and Human Services as a "List A select agent." Additionally, sylvatic plague threatens human health and several endangered and threatened wildlife species, including the black-footed ferret (*Mustela nigripes*) and black-tailed prairie dog (*Cynomys ludovicianus*) (Carter, and Gage, 2000; Cully et al., 2000; Biggins and Godbey, 2003). Yet, not only is there insufficient ecologic knowledge to accurately describe the mechanisms for persistence and periodic re-emergence of plague but also there is no established predictive framework for anticipating the possible consequences of intentional release of *Y. pestis* in regions where the bacteria could persist (Gage and Kosoy, 2005).

Several studies have described modeling approaches to plague dynamics. Some early susceptible→infective→resistant (SIR) plague models only dealt with humans and not rodents or fleas, and they did not allow for hosts to recover or for new susceptible individuals to be introduced into the system (Noble, 1974; Raggett, 1982). A recent model of pneumonic plague also focused on humans, and it did not consider enzootic cycles in nonhuman hosts and arthropod vectors (Gani and Leach, 2004). An excellent model of vectorborne plague was developed focusing on *Y. pestis* infection in humans, *R. rattus*, and *X. cheopis* (Keeling and Gilligan, 2000a, b). Although this model recreated many of the worldwide dynamics observed in human plague outbreaks, little insight was offered at the smaller scale of enzootic plague in wild rodent communities in the western United States.

In this study, we extend traditional vector susceptible→infective→resistant→susceptible (SIRS) models to create a flexible matrix-based community vector SIRS framework, which was used to investigate plague. There were four specific objectives: 1) to use matrix manipulation within a classical SIRS model framework to describe transmission of *Y. pestis* among rodents and fleas in California, 2) to perform sensitivity analysis with model parameters and variables to document which values tended to dominate model output, 3) to manipulate model parameters to determine values that would convert transient epizootic infection to enzootic, and 4) to document predicted outcomes of plague with realistic parameter values obtained from the literature for *Y. pestis* in California rodents and fleas.

MATERIALS AND METHODS

Disease model: single host-single vector system

Plague community dynamics were modeled with a matrix version of the basic Kermack-

McKendrick SIRS model, with SIRS hosts (Kermack and McKendrick, 1927; Bailey, 1982). This community plague model, designated PlagueSIRS, was implemented in R (The R-Development Core Team, http://www.r-project.org); pseudocode for the sequence of events is given in Appendix 1. Discrete-time differential equations coupled host disease transmission dynamics with those of the flea vectors. Host populations are composed of three groups of individuals: susceptibles of size S, infectious I, and resistant R, with

$$N = S + I + R. \tag{1}$$

Flea populations were each separated into susceptibles X, infectious Y, and immunes Z (the latter retained for generality but likely to be rare or lacking in nature):

$$V = X + Y + Z. \tag{2}$$

In a short time interval of 1 day, host individuals move through categories S, I, and R by disease transmission at rate βSY, recovery at rate γI, and death at rates $d_S = d_R$ or d_I (mortality attributable to disease, designated in this article as "mad"). Similar rates apply to fleas, except that after fleas acquire *Y. pestis* infection, there is a substantial latency period during which they are not infective, requiring addition of the vector state E. The rate at which latency shifts to infectivity is ψ, and the mean time in latency is $1/\psi$. The model dynamics are described by the system of differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= bN - \beta SY - d_S S \\
\frac{dX}{dt} &= b_V V - \beta_V XI - d_X X \\
\frac{dI}{dt} &= \beta SY - \gamma I - d_I I \\
\frac{dE}{dt} &= \beta_V XI - \psi E - d_X E \\
\frac{dR}{dt} &= \gamma I - d_R R \\
\frac{dY}{dt} &= \psi E - d_Y Y
\end{aligned} \tag{3}$$

Multiple host-multiple vector system

A plague community contains h host species and v vector species. The community model tracks a vector of host sizes $\mathbf{N} = [N_1 \ldots N_h]$, a vector of S values $\mathbf{S} = [S_1 \ldots S_h]$, and analogous vectors of I, R, X, E, and Y. The community SIRS model is represented below, assuming that host death rates of S and R individuals are similar, X and E flea death rates are similar, and adding the identity matrices (**1**) required for the matrix multiplication:

$$\begin{aligned}
\frac{d\boldsymbol{S}}{dt} &= \boldsymbol{B_H N} - \boldsymbol{S1}\beta\boldsymbol{I} - \boldsymbol{D_S S} \\
\frac{d\boldsymbol{X}}{dt} &= \boldsymbol{B_V V} + {}_{\gamma V}\boldsymbol{Y} - \boldsymbol{X1}\beta_V\boldsymbol{I} - \boldsymbol{D_X X} \\
\frac{d\boldsymbol{I}}{dt} &= \boldsymbol{S1}\beta\boldsymbol{I} - {}_{\gamma}\boldsymbol{I} - \boldsymbol{d_I I} \\
\frac{d\boldsymbol{E}}{dt} &= \boldsymbol{X1}\beta_V\boldsymbol{I} - \psi\boldsymbol{E} - \boldsymbol{D_X E} \\
\frac{d\boldsymbol{R}}{dt} &= {}_{\gamma}\boldsymbol{I} - \boldsymbol{D_S R} \\
\frac{d\boldsymbol{Y}}{dt} &= \psi\boldsymbol{E} - {}_{\gamma V}\boldsymbol{Y} - \boldsymbol{D_Y Y}.
\end{aligned} \tag{4}$$

The 3h+3v-dimensional, nonlinear system of equations was discretized for computer simulations to obtain the model for the survival of susceptible hosts (Nicholson and Bailey, 1935). If infection is distributed as a Poisson process, then $S_i \leftarrow S^* \exp(-\beta Y)$.

Transmission to new hosts can take place from several possible flea species. Let β_{ij} be the transmission rate from vector j to host i; then, the entire host transmission process is as follows:

$$\begin{aligned}
S1\beta Y &= \begin{bmatrix} S_1 \\ S_2 \\ \vdots \\ S_3 \end{bmatrix} [1 \quad 1 \quad \ldots \quad 1] \\
&\begin{bmatrix} \beta_{11} & \beta_{12} & & \beta_{1v} \\ \beta_{21} & \beta_{22} & & \beta_{1v} \\ & & \ddots & \\ \beta_{h1} & \beta_{h2} & & \beta_{hv} \end{bmatrix} \begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_v \end{bmatrix} \\
&= \begin{bmatrix} \beta_{11}S_1Y_1 + \beta_{12}S_1Y_2 + \ldots + \beta_{1v}S_1Y_v \\ \beta_{21}S_2Y_1 + \beta_{22}S_2Y_2 + \ldots + \beta_{2v}S_2Y_v \\ \vdots \\ \beta_{h1}S_hY_1 + \beta_{h2}S_hY_2 + \ldots + \beta_{hv}S_hY_v \end{bmatrix}
\end{aligned} \tag{5}$$

$\boldsymbol{\beta}_V$ is a v^*h matrix analogous to $\boldsymbol{\beta}$ that gives transmission from the jth host to the ith vector.

To transmit a disease from an infective vector j to a susceptible host i, the vector needs to 1) find a host (proportional to aSY, where a is attack rate), 2) be competent to transmit the disease (with vector competency c_{vj}), and 3) want to use the host (with utilization rate u_{ij}). Typical vector-to-host matrix β entries are as follows:

$$\beta_{ij} = ac_{vj}u_{ij}. \quad (6)$$

The host-to-vector matrix β_v has entries of the form:

$$\beta_{vij} = ac_j u_{ji}, \quad (7)$$

where c_j measures the host competency. The lower limit of disease was set by an extinction threshold of one individual; if either infected flea or host numbers went below the threshold (into fractional individuals), the simulation stopped; upper limits were set by host population upper limits (K). Seasonality was incorporated into the model for flea recovery from infection, which is known to be temperature-dependent (indeed, above 27 C, *Y. pestis* may not survive or be transmissible in the flea (Pollitzer, 1954), by Fourier transform.

Host and vector population dynamics

Underlying the disease transmission model is a series of functions that allow for population regulation for each host and vector species, including seasonality and environmental stochasticity. A community consists of h host species, of sizes N_1, N_2, …, N_h with species-specific birth rates (b_i) given in a diagonal matrix:

$$\mathbf{B}_H = \begin{bmatrix} b_1 & 0 & & 0 \\ 0 & b_2 & & 0 \\ & & \ddots & \\ 0 & 0 & & b_h \end{bmatrix}, \quad (8)$$

so that the number of new individuals per host species is as follows:

$$\mathbf{B_H N} = \begin{bmatrix} b_1 & 0 & & 0 \\ 0 & b_2 & & 0 \\ & & \ddots & \\ 0 & 0 & & b_h \end{bmatrix} \begin{bmatrix} N_1 \\ N_2 \\ \\ N_h \end{bmatrix} = \begin{bmatrix} b_1 N_1 \\ b_2 N_2 \\ \\ b_h N_h \end{bmatrix}. \quad (9)$$

Death rates (d_i) are in an analogous diagonal matrix. A stochastic discrete logistic model in small time units gives host population growth and fluctuation:

$$N(t+1) = N(t)(1 + b_i(t) - d_i(t)), \quad (10)$$

where

$$b_i(t) = b_m\left(1 - \frac{N(t)}{K}\right) + \varepsilon_i(t), \quad (11)$$

K_i is the host carrying capacity, b_m is the Malthusian birth rate, and $\varepsilon_i(t) \sim N(0,v_r)$ is the environmental stochasticity term at time t, estimated by regression (May, 1974; Foley, 1997). Seasonality of rodent numbers was incorporated into the model by constraining reproduction to those months described by field data and modeling death via a Fourier function of annual periodicity (Keeling and Gilligan, 2000a). Incorporating an approximation, the transform is as follows:

$$d_i(t) = A_{Hi}\cos(t - t_{peak}) + \bar{d}_i \quad (12)$$

where $d_i(t)$ is the death rate at time t in radians, $\bar{d}_i$ is the mean death rate over the year, A_{Hi} is the amplitude of the host death rate, and t_{peak} is the time of peak mortality. A similar function was used for b_i. For simplicity, environmental stochasticity was included only in birth and not death, which can be done because the model assumes additivity of b+d+ε.

Flea populations, for each species V_1, V_2, …,V_v, depended numerically on the abundance of rodent hosts. The carrying capacity of a vector species j depends on the abundance of each host species i, together with some measure k_{ij} of the vector j's ability to use host species i as a resource. In the absence of interspecific competition among fleas, the carrying capacity of vector j is given by

$$K_{vj} = \sum\nolimits_i k_{ij}N_i. \quad (13)$$

The carrying capacity k_{ij} offered by an individual host i to vector j depends on 1) u_{ij}, the vector's host utilization rate; 2) q_i, host resource quality; and 3) w_i, a flea weighting index. The u_{ij} ranges from 0 (vector j does not use host i) to 1 (the vector can and will fully use the resources available from this host). q_i, the index of the quality of resources a host provides to an average vector, is equivalent to the mean number of fleas of average size on an individual of this host species of average size. w_j, the flea weighting index, is related to the size of the vector (or it could be set as some other measure of the amount of resources an individual vector uses). w_j has a mean of 1 for a "typical" flea species and is close to 1 for most flea species, but it may rise significantly above 1 for large fleas. Then, the carrying capacity pro-

vided by one host to its fleas of species j is shown as follows:

$$k_{ij} = u_{ij} q_i w_j, \quad (14)$$

and the whole carrying capacity for vector species j, which depends on the availability of all of the hosts is as follows:

$$K_{vj} = \sum_i k_{ij} N_i = \sum_i u_{ij} q_i w_j N_i. \quad (15)$$

Density-dependent birth of the jth flea is modeled, with the Malthusian parameter b_{mvj}:

$$b_j(t) = b_{mvj}(1 - V_j/K_{vj}). \quad (16)$$

Then, flea death is

$$d_j(t) = A_{vj} \cos(t - t_{peak}) + \overline{d}_j. \quad (17)$$

The model also was implemented with diagonal matrices designated $\mathbf{B_v}$, $\mathbf{D_v}$; seasonality was incorporated for flea birth and death by Fourier transform.

Parameter estimation and sensitivity analysis

Data were maintained in Excel (Microsoft, Redmond, Washington, USA) and analyzed in R. Data on flea distribution, flea host preferences, and plague transmission dynamics were obtained from the literature and are summarized in Table 1. Data were used as first approximations, to further develop the model, because in many cases, including old literature with very small samples sizes and predictive habitat databases, parameter and variable estimates likely had large confidence intervals. Nevertheless, use of such estimates facilitated investigation to clarify which parameters and variables would require more accurate future estimation.

Life history and habitat association data for rodents were obtained primarily from the California Department of Fish and Game Wildlife Habitat Relationships database (Mayer and Laudenslayer, 1988). Death rates for fleas and rodents were calculated approximately assuming that death times were exponentially distributed with the parameter λ calculated as mean time to death, obtained from the literature. Values for rodent carrying capacities, litter sizes, time windows of reproduction, and numbers of litters per year were obtained from the literature (Mayer and Laudenslayer, 1988; Nowak, 1995). Rodent population time series were obtained from the Center for Population Biology Global Population Dynamics Database (Imperial College, London, UK). The b_m was calculated as r_m–$d(S)$ prorated for the period over which the species reportedly breeds in nature. Assuming a Ricker model of population regulation (Foley, 2000), $r(t)$ was regressed on $N(t)$ to provide estimates of r_m and carrying capacity. v_r was estimated as the noise component in the regression, although this was considered an overestimate, because it includes both environmental stochasticity as well as sampling variation.

The parameters q and w were estimated from reports of the mean flea numbers of rodents (Davis et al., 2002), with w scaled to a maximum value of 3 and a mean of 1. The matrix u was constructed from field data giving the fraction of all flea fauna on each host represented by each flea species. γ (rates of recovery for fleas and rodents) and ψ (rate of movement from latent to active infection in fleas) were estimated as the mean time from the first point at which there was evidence of infection to the first time the flea was infective to rodents (ψ) or the flea or rodent recovered (γ). Vector and host competence were averaged across all published reports of experimental *Y. pestis* infection in that species. If no values were reported, the estimate was used for the most phylogenetically proximal species for which data were available.

Sensitivity analysis was performed to determine which parameters and variables were most responsible for driving observed dynamics, by allowing each parameter, one at a time, to range across very broad possible values for that parameter, as shown in Table 2. All other parameters were fixed corresponding to optimal estimates from literature reviewed as mean values for each parameter. The analysis was run with parameters for a three-host, two-flea community consisting of *Peromyscus maniculatus*, woodrats (*Neotoma fuscipes*), and *S. beecheyi* and the fleas *Aetheca wagneri* and *Oropsylla montana* (Table 3). The following outputs were used as indicators of model results: the mean expected duration of infection in the community (>100 simulation runs) and the expected maximum number of infected hosts. By using output from this exploration, critical values of parameters that would convert epizootic infection to enzootic were determined. Default values were used for all parameter values were except one, as described for sensitivity analysis, whereas the simulation was run until a cutoff for each particular value was found (if at all) where the infection was predicted to be enzootic (defined as infected hosts or fleas for ≥400 days).

To document whether enzootic maintenance would be predicted with realistic parameter values for *Y. pestis* in California rodents and fleas, the model was run with parameter values from the well-studied pla-

TABLE 1. Parameters and variables used in the model PlagueSIRS for simulating plague dynamics.

Abbreviation	Definition	Estimate	Source
H	No. of host species in the community		Davis et al., 2002
V	No. of vector species in the community		Davis et al., 2002
K	Vector of host-carrying capacities	Tables 3, 4, 7	Nowak, 1995; Wildlife and Habitat Data Analysis Branch, 2004
k_{ij}	Composite carrying capacity parameter	Calculated in model from u, q, and w	
N, r_{mi}, r_{mvj}	Species-specific host population size, Malthusian parameter for hosts and fleas	Calculated in model	
b_m	Vector of host maximum birth rates	Tables 3, 4, 7	Linsdale, 1946; Linsdale and Tevis, 1951; Longanecker and Burroughs, 1952; Rutledge et al., 1979; National Center for Ecological Analysis and Synthesis, 2004; Wildlife and Habitat Data Analysis Branch, 2004
Mean no. of litters/yr		Tables 3, 4, 7	Linsdale, 1946; Linsdale and Tevis, 1951; Longanecker and Burroughs, 1952; Rutledge et al., 1979; National Center for Ecological Analysis and Synthesis, 2004; Wildlife and Habitat Data Analysis Branch, 2004
Peak date of birth and window		Tables 3, 4, 7	Linsdale, 1946; Linsdale and Tevis, 1951; Longanecker and Burroughs, 1952; Rutledge et al., 1979; National Center for Ecological Analysis and Synthesis, 2004; Wildlife and Habitat Data Analysis Branch, 2004
b_{mv}	Vector of flea mean daily hatch rates	Daily=0.016	Davis et al., 2002
Peak date, amplitude	Amplitude and peak date of flea hatches	Amplitude=0.016; Table 6	
v_r	Vector of environmental stochasticity affecting hosts	Tables 3, 4, 7	Linsdale, 1946; Linsdale and Tevis, 1951; Longanecker and Burroughs, 1952; Rutledge et al., 1979; National Center for Ecological Analysis and Synthesis, 2004; Wildlife and Habitat Data Analysis Branch, 2004
v_{rv}	Vector of environmental stochasticity affecting fleas	0.01	None
a	Attack rate	0.001	None

TABLE 1. Continued.

Abbreviation	Definition	Estimate	Source
comp	Vector of host competence	0.75 all	McCoy, 1908, 1909, 1911a, b; McCoy and Smith, 1910; McCoy and Chapin, 1912; Eskey and Haas,1940; Holdenreid and Quan, 1956; Marchette et al., 1962a, b; Quan and Kartman, 1962; Quan et al., 1985
compv	Vector of flea vector competence	Tables 6, 8	Eskey and Haas, 1940; Burroughs, 1944, 1947; Wheeler and Douglas, 1945; Holdenreid, 1952; Kartman and Prince, 1956; Kartman, et al., 1958
u	Matrix of relative utilization preferences (scaled 0–1) of flea species for host species	Table 5	Davis et al., 2002
q	Vector of quality of hosts: expected number of fleas on host individuals of each species	Tables 3, 4, 7	Davis et al., 2002
w	Vector of flea species weighting indices	Tables 6, 8	Davis et al., 2002
Ψ	Vector of rates at which latently infected fleas become infective	Tables 6, 8	Eskey and Haas, 1940; Burroughs, 1944, 1947; Wheeler and Douglas, 1945; Holdenreid, 1952; Kartman and Prince, 1956; Kartman et al., 1958
γ	Vector of rates of recovery for each host species	Tables 3, 4, 7	McCoy, 1908, 1909, 1911a, b; McCoy and Smith, 1910; McCoy and Chapin, 1912; Eskey and Haas, 1940; Holdenreid and Quan, 1956; Marchette et al., 1962a, b; Quan and Kartman, 1962; Quan et al., 1985
γ_v, mean, peak date, amplitude	Vector of rates of recovery for each vector species	Peak date 7/1; mean=1/5 for all; Tables 6, 8	Eskey and Haas, 1940; Burroughs, 1944, 1947; Wheeler and Douglas, 1945; Holdenreid, 1952; Kartman and Prince, 1956; Kartman et al., Quan, 1958
$dS=dR$, mean, peak date, amplitude	Vector of death rates of S and R hosts	Peak date 1/1 for all; amp=0.1; Tables 3, 4, 7	McCoy, 1908, 1909, 1911a, b; McCoy and Smith, 1910; McCoy and Chapin, 1912; Eskey and Haas, 1940; Holdenreid and Quan, 1956; Marchette et al., 1962a, b; Quan and Kartman, 1962; Quan et al., 1985
dI="mad"	Vector of death rates of I hosts	Tables 3, 4, 7	Linsdale, 1946; Linsdale and Tevis, 1951; Rutledge et al., 1979
dX, mean, peak date, amplitude	Vector of death rates of X vectors	Tables 6, 8	Eskey and Haas, 1940; Burroughs, 1944, 1947; Wheeler and Douglas, 1945; Holdenreid, 1952; Kartman and Prince, 1956; Kartman et al., 1958

TABLE 1. Continued.

Abbreviation	Definition	Estimate	Source
dY (fleas)="mad"	Vector of death rates of Y vectors.	Tables 6, 8	Eskey and Haas, 1940; Burroughs, 1944, 1947; Wheeler and Douglas, 1945; Holdenreid, 1952; Kartman and Prince, 1956; Kartman et al., 1958

gue-enzootic site at Chuchupate Campground (CG) in Ventura County (Tables 4–6). Chuchupate CG is at 1,890 m on Frazier Mountain in pine (*Pinus* spp.)-oak (*Quercus* spp.) forest. A previous study in Chuchupate CG has documented 20 flea species and 10 rodent species potentially involved in the ecology of plague (Davis et al., 2002).

RESULTS

A vector-SIRS–based simulation model was created to investigate multiple interacting rodent hosts and flea vectors of plague in the western United States. Sensitivity analysis performed for a three-host, two-flea plague community indicated that the expected duration of infection in that community and the maximum number of infected hosts expected in that epizootic were most sensitive to host carrying capacity, attack rate, and host and flea recovery rates (Table 2). Increasing host carrying capacity led to increases both in host and flea numbers, resulting in prolonged duration of infection. This pattern was saturated at high levels of carrying capacity (Figs. 1, 2) and increasing K did not induce permanent enzootic infection at any level. Changing a also did not induce enzootic disease. Very low attack rates did not allow for any disease maintenance, whereas increasing a resulted in an increased epizootic duration up to a plateau value, with a considerable concurrent increase in maximum infected host number. Modifying γ_H, host recovery, had an expectedly important effect. As γ_H was decreased, the duration of infection persistence and maximum number of infected animals both increased until, at low γ_H, enzootic infection was maintained in the simulation. Although not apparent over most values used for γ_V, very low flea recovery rates also had the capacity to convert the epizootic infection to enzootic.

Parameters to which model outcome was relatively insensitive included ψ, u, w, host competence unless a host was completely incapable of transmitting disease, vector competence, mortality attributable to disease (except that at high rates of mortality, there was no enzootic disease), and q. Thus, sensitivity analysis clarified which parameters had the greatest individual impacts on model output and suggested that changes in γ_H and γ_V were most likely to convert transient epizootics to long persistence-time enzootics.

Parameter values supporting a plague-enzootic community were explored using published parameter values for the Chuchupate CG community, allowing a (for which no good estimates were available) to vary in order to observe expected changes in plague persistence. With a universal attack rate (all fleas on all hosts) of 0.01 bites/host/day, plague was enzootic in the community (Fig. 3). Seasonality in rodent and flea numbers was apparent, as were epizootic pulses of plague primarily occurring only in fleas (with only small numbers of infected hosts). The principal rodent and flea species contributing to persistence were woodrats, California ground squirrels, and chipmunks (*Tamias* spp.), with the fleas *A. wagneri* and *M. telchinus*. The features of these hosts contributing to their important roles in plague epizootics included relative resistance to the development of fatal plague (except for ground squirrels) and their ability to support more flea species,

TABLE 2. Results of analysis of the sensitivity of the model PlagueSIRS, measured as changes in expected epizootic duration and maximum infected host number (MIHN), as a function of changes in parameter values. Critical values are the values of each parameter (if any) that permits expected epizootic infection to become persistent in the community.

Parameter	Level	Value	Mean epizootic duration	Change in epizootic duration (%)	Mean maximum infected host no.	Change in MIHN (%)
K	Low	15	75	–25	80	–20
	Default	150	100		100	
	High	1,500	350	250	10	–90
	Critical	None				
a	Low	0.005	0	–100	0	–100
	Default	0.05	100		100	
	High	0.5	100	NC	150	50
	Critical	None				
comp	Low	0.1	0	–100	0	–100
	Default	1	80		80	
	High	NA[c]	NA	NA	NA	NA
	Critical	NA				
compv	Low	0.1	130	–48	40	12.5
	Default	1	250		35	
	High	NA	NA	NA	NA	NA
	Critical	NA				
u	Low	0.08	0	–100	0	NA
	Default	0.8	10		80	
	High	1	100	NC[c]	80	NC
	Critical	None				
q	Low	1	0	–100	0	–100
	Default	10	50		8	
	High	100	50	NC	20	150
	Critical	None				
w	Low	0.5	160	NC	30	–25
	Default	1	160		40	
	High	3	260	62	50	25
	Critical	None				
Ψ	Low	0.01	250	NC	150	NC
	Default	0.1	250		150	
	High	1	250	NC	150	NC
	Critical	None				
γ_H	Low	0.001	persistent	NA	120	71
	Default	0.01	80		70	
	High	0.1	10	–87	5	–93
	Critical	0.05[a]				
γ_V	Low	0.1	250	NC	150	NC
	Default	0.52	250		150	
	High	1	250	NC	150	NC
	Critical	0.01[b]				

[a] The critical value, γ=0.05 induced persistence inconsistently (60% of the runs), compared with no persistent enzootic for higher values of γ.

[b] The critical value, γ_V=0.01 induced persistence inconsistently (10% of the runs), compared with no persistent enzootic for higher values of γ_V.

[c] NA indicates results not applicable, NC indicates no change.

particularly the highly abundant *M. telchinus*. Prolonged duration of infection within individuals did not occur and was not a contributing factor to enzootic plague in the community. When a was increased to 0.1 bites/host/day, plague remained enzootic but apparent stable cycles of infection were disrupted. Reduction of a to 0.009 led

TABLE 3. Parameter values for hypothetical three host-two flea system for sensitivity analysis of the plague simulation.

Host species	K/ha	b_m	v_r	q	dS/day	dI=mad	γ	Litter size	Birth window (mo)	No. litters/yr
N. fuscipes	17.5	0.02	0.4	11.3	0.0042	0.3	0.001	2–3	2–7	1–5
P. maniculatus	17.5	0.02	0.18	10.9	0.006	0.001	0.06	3	3–8	2–4
S. beecheyi	45	0.01	0.26	25	0.0014	0.17	0.001	6–7	5–10	1

Flea species	Peak birth mo	Peak death	$comp_v$	w	ψ	dX	dY=mad	γ_v
A. wagneri	6	12	0.6	1	0.02	0.01	0.05	0.02
O. montana	5	8	0.6	3	0.012	0.015	0.08 (Wheeler and Douglas, 1945)	0.02 (Wheeler and Douglas, 1945)

to a single epizootic of approximately 200-day duration.

DISCUSSION

We present development and exploration of a flexible, matrix-based simulation of a vector-SIRS model for highly complex rodent and flea communities supporting plague in western North America. Unlike most vector-SIRS analytical models, the approach used here has the advantage of offering a framework for inclusion of demographic data for hosts and fleas, expansibility to virtually any size community, and the ability to manage very complex communities without requirements for oversimplification. Exploration of the model indicated that the main features of epizootics, duration and magnitude (i.e., infected host number), were driven by only a few key parameters, a finding that should guide data collection and understanding of natural epizootics in the future. Moreover, simulation of a large plague community documented emergent properties of this ecological system, namely, that indefinite plague persistence was predicted in the highly complex system, even when simplified, three host-two flea systems with very similar parameter values were predicted to go extinct.

The three most important parameter values required to predict epizootic dura-

TABLE 4. Parameter values used in the model PlagueSIRS for rodents in Chuchupate Campground, Ventura County, California.

Species	K/ha	b_m	v_r	q	dS/day	dI=mad	γ	Litter size	Birth window (mo)	No. litters/yr
Chaetodipus californicus	7.5	0.009	0.05	10	0.003	0.01	0.06	3	3–8	2
Dipodomys agilis	7.5	0.03	0.05	10.7	0.003	0.01	0.09	3	1–7	1–2
Microtus californicus	250	0.005	1	12.7	0.0025	0.04	0.06	4	1–12	2–5
Neotoma fuscipes	17.5	0.02	0.4	11.3	0.0042	0.3	0.001	2–3	2–7	1–5
Peromyscus boylii	17.5	0.03	0.18	10.7	0.006	0.04	0.06	3	4–8	1–4
P. maniculatus	17.5	0.02	0.18	10.9	0.006	0.001	0.06	3	3–8	2–4
P. truei	17.5	0.03	0.18	10.6	0.006	0.13	0.01	3	5–9	2
Reithrodontomys megalotis	37.5	0.04	0.49	11	0.012	0.2	0.001	2–4	4–10	14
S. beecheyi	45	0.01	0.26	25	0.0014	0.17	0.001	6–7	5–10	1
T. merriami	12.5	0.01	0.2[a]	11.8	0.0014	0.185	0.007	4	1–6	1

[a] Extrapolated results, poor data availability in literature.

TABLE 5. "*u matrix*", containing values for flea utilization of various rodent species in Chuchupate Campground, Ventura County, California (Davis et al., 2002).

	Flea										
Rodent	*Aetheca wagneri*	*Anomiops falsical*	*A. nudatus*	*Atyph. e.l.*	*Atyph. m.m.*	*Catal. luski*	*Eumol. e. eumolpi*	*E. fornacis*	*Hoplops. anomalus*	*Hystrich. o. linsdalei*	*Malaraeus telchinum*
Dipodomys	0.000	0.000	0.004	0.000	0.000	0.053	0.000	0.000	0.000	0.000	0.000
Microtus	0.005	0.000	0.000	0.000	0.000	0.000	0.000	0.009	0.000	0.071	0.667
Neotoma	0.118	0.913	0.961	0.846	0.680	0.263	0.000	0.026	0.020	0.286	0.140
Peromyscus boylii	0.093	0.000	0.004	0.000	0.000	0.105	0.000	0.000	0.000	0.143	0.032
P. manic	0.760	0.087	0.019	0.154	0.280	0.526	0.000	0.000	0.000	0.500	0.129
P. truei	0.015	0.000	0.000	0.000	0.040	0.000	0.000	0.000	0.000	0.000	0.000
Reithrodonomys	0.005	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.022
Spermophilus	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.980	0.000	0.000
Tamias	0.005	0.000	0.012	0.000	0.000	0.053	1.000	0.966	0.000	0.000	0.011

	Megarth. divisus	*Meringis cummingi*	*Opisodasys nesiotus*	*Orchopeas sexdentatus*	*Oropsylla montana*	*Peromysco. h. adelpha*	*Rhadinop. s. sectilis*	*Thrassis* sp.
Dipodomys	0.000	0.964	0.000	0.000	0.000	0.000	0.063	1.000
Microtus	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Neotoma	0.933	0.000	0.000	0.997	0.024	0.089	0.375	0.000
P. boylii	0.004	0.000	0.333	0.000	0.000	0.311	0.063	0.000
P. manic.	0.064	0.036	0.667	0.003	0.005	0.578	0.438	0.000
P. truei	0.000	0.000	0.000	0.000	0.000	0.022	0.063	0.000
Reithrodontomys	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Spermophilus	0.000	0.000	0.000	0.000	0.967	0.000	0.000	0.000
Tamias	0.000	0.000	0.000	0.000	0.004	0.000	0.000	0.000

tion and magnitude were γ_H, γ_V, and a, the attack rate of fleas on hosts. Reduction in γ_H and γ_V not surprisingly increased the duration of epizootics or induced enzootic disease by essentially increasing reservoir potential in the classical sense of some of the rodents. This interesting finding could help explain some of the differences in the risk of plague in diverse communities where rodent hosts have different γ_H levels. There are estimates of γ_H available in the literature for many California rodents and some fleas. Flea recovery rates in particular can be highly variable because those flea species with a narrow esophagus and proventriculus are more susceptible to blockage with a mat of bacteria and inflammatory debris (and thus more likely to regurgitate infectious material into the host while attempting to feed). Other flea species have greater ability to enzymatically destroy the block and less susceptible anatomic configurations (Perry and Fetherston, 1997). Undoubtedly, more accurate estimates from experimental infection would be valuable for both rodent and flea recovery rates.

Attack rate, for which very little information is available from California systems, was also an important parameter in determining durations of epizootics. This finding is comparable with results from an earlier vector-SIRS model of humans, rats, and fleas that was sensitive to flea search efficiency (Keeling and Gilligan, 2000a). Other vectorborne disease systems also are highly sensitive to attack rate, including the pioneering models of Ross (1928) and MacDonald (1957) showing the nonlinear effect of attack rate of mosquitoes transmitting malaria to humans. The estimation of this parameter from field data likely represents a critically important target for future research.

The earlier vector-SIRS plague model of Keeling was also particularly sensitive to

TABLE 6. Parameter values used in the model PlagueSIRS for fleas in Chuchupate Campground, Ventura County, California.

Species	Peak birth mo	Peak death	$comp_v$	w	ψ	dX	dY=mad	γ_v
Aetheca wagneri	6	12	0.6	1	0.02[a]	0.01[a]	0.05[a]	0.02[a]
Anomiopsyllus falsicalifornicus	4.5	10.5	0.1	0.5	0.02[a]	0.01[a]	0.05[a]	0.02[a]
A. nudatus	3.5	9.5	0.3	1	0.02[a]	0.01[a]	0.05[a]	0.02[a]
Athyphloceras echis longipalpis	12	6	0.3	1	0.02[a]	0.01[a]	0.1 (Eskey and Haas, 1940)	0.02 (Eskey and Haas, 1940)
A. m. multidentatus	10	4	0.3	1	0.02[a]	0.01[a]	0.1 (Eskey and Haas, 1940)	0.02 (Eskey and Haas, 1940)
Catallagia luski	3	9	0.3	1	0.02[a]	0.01[a]	0.05[a]	0.02[a]
Eumolpianus eumolpi eumolpi	7	1	0.6	0.5	0.02[a]	0.01[a]	0.05[a]	0.02[a]
E. fornacis	6	12	0.6	0.5	0.02[a]	0.01[a]	0.05[a]	0.02[a]
Hoplopsyllus anomalus	3	12	0.4	3	0.03	0.01[a]	0.07 (Wheeler and Douglas, 1945)	0.06 (Wheeler and Douglas, 1945)
Hystrichopsylla occidentalis linsdalei	3–7	11	0.6	1	0.02[a]	0.01[a]	0.05[a]	0.02[a]
Malaraeus telchinus	10	4	0.1	0.5	0.105	0.019	0.0038 (Burroughs, 1944)	0.0099 (Burroughs, 1944)
Megarthroglossus divisus	1	7	0.3	3	0.02[a]	0.01[a]	0.05[a]	0.02[a]
Meringis cummingi	6.5	12.5	0.3	1	0.02[a]	0.01[a]	0.05[a]	0.02[a]
Opisodasys nesiotus	7.5	1.5	0.6	1	0.25	0.035	0.076 (Burroughs, 1944)	0.02 (Burroughs, 1944)
Orchopeas sexdentatus	7	1	0.6	1	0.18	0.006	0.08 (Burroughs, 1944)	0.0049 (Burroughs, 1944)
Oropsylla montana	5	8	0.6	3	0.012	0.015	0.08 (Wheeler and Douglas, 1945)	0.02 (Wheeler and Douglas, 1945)
Peromyscoscylla hesperomys adelpha	6	12	0.6	1	0.02[a]	0.01[a]	0.05[a]	0.02[a]
Rhadinopsylla s. sectilis	3	8	0.4	1	0.02[a]	0.01[a]	0.05[a]	0.02[a]
Thrassis aridis	10	4	0.6	1	0.02[a]	0.01[a]	0.05[a]	0.02[a]

[a] Extrapolated results, poor data availability in literature.

changes in the carrying capacity of fleas per rat, the rat's reproductive rate, and the rat's carrying capacity. The model developed in this present study also is sensitive to rodent K: increasing K by orders of magnitude increased the expected epizootic duration but did not, in the three host-two flea system, induce enzootic persistence. This feature may be related to the particular collection of other parameter values used for that system. A previous study in natural plague foci in Kazakhstan documented an abundance threshold in great gerbils, *Rhombomys*

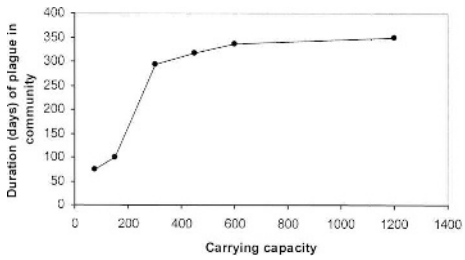

FIGURE 1. Expected dependence of duration of a plague epizootic on *K*, the carrying capacity of the most abundant rodent host. The data were obtained from the model PlagueSIRS with a three rodent-two flea plague community (parameter values given in Table 2).

opimus, above which plague was persistent (Davis et al., 2004). Such a threshold could apply in California as well, although the abundance threshold refers to the actual numbers of animals in the community, whereas the carrying capacity refers to a potential with actual populations often cycling around *K*. Other important differences are that the plague communities in California are highly complex, compared with systems dominated by a single reservoir such as a rat or great gerbil. Although accurate estimates of *K* are difficult to obtain and values are site-specific, some attempt should be made to acquire

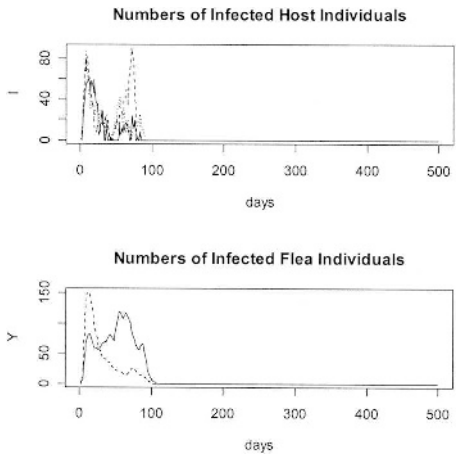

FIGURE 2. Example of model output from PlagueSIRS for a three rodent-two flea plague community with low *K*. *I* = number of infected rodents; *Y* = number of infected fleas.

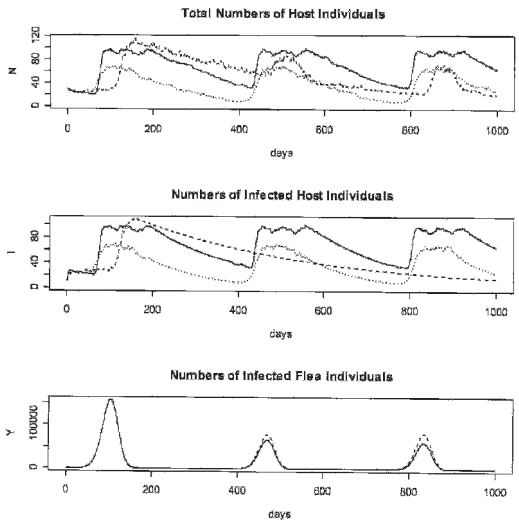

FIGURE 3. Sample model output of simulation PlagueSIRS by using parameter values estimated in Chuchupate CG, Ventura County, California, with 10 rodent species and 20 flea species, with attack rate = 0.005. *I* = number of infected rodents; *Y* = number of infected fleas; *N* = number of rodents total; *V* = total fleas. First and second panels: solid panel = *N. fuscipes*; dotted line = *Tamias* spp.; dashed line = *S. beecheyi*. Third panel: dotted line = *M. telchinus*; solid line = *A. wagneri*.

estimates with reasonable accuracy, although other, possibly more easily estimated, parameters such as γ and a may be more critical.

The structure of PlagueSIRS has advantages of flexibility and expansibility, while focusing on short- and long-term dynamics associated with disease transmission in communities. This model advantage is in contrast to some invasion analysis models, which focus on epidemic thresholds such as $R_0>1$. The matrix method (Diekmann et al., 1990) could offer some insight into the community system, but two difficulties would need to be overcome. First, in reality, *Y. pestis* transmission dynamics must include extensive variability in recovery and transmission parameters to reflect the diverse biology of the hosts and vectors. Because the infection time varies across rodent and flea species, the ***K*** matrix would require considerable adjustment before it could calculate the diverse collection of *I* values

appropriately. Second, to investigate persistence, the ***K*** matrix would need to be made frequency-dependent.

PlagueSIRS has the additional advantages over many vector-SIRS models in realistically representing underlying host and flea population dynamics in the model. This advantage is important because the disease dynamics being studied often occurs over distinctly long periods, a problem that is avoided in some models focusing only on rapid epidemics or disease emergence. In PlagueSIRS, rodent population growth was bounded by a carrying capacity, whereas flea density was given as a function of flea use of specific hosts, abundance of fleas on hosts, attack rates, and seasonal constraints; both rodent and flea dynamics were modified by environmental stochasticity. The earlier model of Keeling used simple flea searching efficiency and an arbitrary flea carrying capacity not explicitly tied to rodent density. Analysis of the model shown here clarifies why population regulation needs to be included in the model, and future model validation with data from field studies should allow for any necessary modifications to the functions predicting host and flea numbers to be incorporated into PlagueSIRS.

It was very interesting how the model represented the enzootic plague community at Chuchupate CG, by using parameter values from the literature. Based on serologic testing of rodents and flea collections, vector control biologists had concluded that plague was enzootic in this region and that three host-flea complexes were important in the local plague ecology, although how these complexes could function as true reservoirs was unclear. These different complexes were 1) California ground squirrel (*S. beecheyi*) and *O. montana/H. anomalous* fleas, 2) Merriam's chipmunk (*Tamias merriami*) and *Eumolpianus* spp. fleas, and 3) dusky-footed woodrats (*N. fuscipes*) and *Orchopeas sexdentatus* and *Anomiopsyllus* spp. fleas. Ground squirrels were generally infested with only two host-specific fleas, whereas other hosts, including deer mice and woodrats, harbored various flea species that they shared with other rodent species. The model recreated enzootic plague with seasonal outbreaks, corresponding to published data (Davis et al., 2002). Hosts with relatively low mortality, including woodrats and chipmunks, were critically important in maintaining enzootic plague, although neither would likely be considered typical reservoirs given the short duration of infection in any individual. Deer mice and voles have been reported previously to be reservoirs for plague (Miles et al., 1957; Goldenberg et al., 1964; Nelson, 1980; Larson et al., 1996). In our model, the most important flea species were *A. wagneri* and *M. telchinus*, the former reported in Chuchupate CG to infest seven different rodent species, especially deer mice (Davis et al., 2002). It was reported that *A. wagneri* is a competent, but not excellent plague vector (Eskey and Haas, 1940). The flea *M. telchinus* is found year-round and feeds on multiple hosts, although with a preference for voles. A pool of this flea species collected from a vole was reported positive for *Y. pestis* in July 1997 in the Chuchupate CG (Davis et al., 2002). Despite that experimental inoculations indicated that *M. telchinum* is a poorly competent vector (Burroughs, 1947), reducing vector competency in the model did not seriously diminish the role of this flea species in modeled epizootics, probably because numbers of this flea are commonly very high. Several flea species that had been thought to be very important in plague ecology played very minor roles in our model, including *O. montana* and *H. anomalus*, probably because they fed on rodents that were so susceptible to disease that they died. Therefore, the host-flea couple could not support anything more than a very transient epizootic. Nevertheless, *O. montana* is important in amplifying plague and particularly in transmitting it to humans, because this flea aggressively

seeks new hosts, including humans, when its preferred host dies (Douglas and Wheeler, 1943; Holdenreid, 1952; Quan et al., 1960; Nelson, 1980; Barnes, 1982; Gage and Kosoy, 2005).

It was interesting that enzootic plague was predicted at Chuchupate, even with similar parameter values to a hypothetical three host-two flea system where plague died out. One possible explanation is that the variability across rodent and flea species in infection dynamics created heterogeneity that is, in some ways, analogous to spatial heterogeneity facilitating longer disease persistence. Specifically, the inclusion of stochasticity into an earlier plague metapopulation model was accompanied by rapid local extinction, which was remedied by the inclusion of spatial structure (Keeling and Gilligan, 2000a, b). Extending the present simulation modeling approach to spatially structured systems would be a logical, although challenging, exercise.

To summarize, a predictive model of plague in complex rodent-flea communities in California clarified key interactions driving plague local extinction or persistence. The described model represents an innovative, highly tractable method of managing ecological complexity typical of communities of multiple hosts and vectors such as occurs in plague but also other vectorborne disease systems such as West Nile virus, granulocytic anaplasmosis, and others. This model also helps establish a framework for ongoing data collection that will allow the model to be refined and ultimately more realistic. This model should be helpful in ongoing surveillance activities and in the event of apparently increased activity that could indicate intentional release.

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APPENDIX 1

Pseudocode for main simulation loop of Plague-SIRS

Main loop (repeat once a day for t_{max} days)

Step 1:

1. Determine season
2. Adjust rodent birth and death rates to season
3. Adjust rodent birth and death rates to density dependence
4. Calculate environmental stochasticity in host and flea birth rates
5. Adjust γ_V to season.

Step 2: Calculate changes in disease states (i.e., transmissions, recoveries, births, and deaths).

Step 3: Adjust numbers in S, I, and R rodents and X, E, and Y fleas by using changes in step 2.

Step 4: Append new S, I, R, X, E, and Y values to history data frame.

LITERATURE CITED

BAILEY, N. 1982. The biomathematics of malaria. C. Griffen, London, UK, 204 pp.

BARNES, A. 1982. Surveillance and control of bubonic plague in the Unites States. Symposium of the Zoological Society of London 50: 237–270.

BIGGINS, D. E., AND J. L. GODBEY. 2003. Challenges to reestablishment of free-ranging populations of black-footed ferrets. Comptes rendus. Biologies 326 (1 Suppl): S104–S111.

BURROUGHS, A. 1944. The flea *Malareus telchinum*, a vector of *P. pestis*. Proceedings of the Society of Experimental Biology and Medicine 55: 10–11.

———. 1947. Sylvatic plague studies. The vector efficiency of nine species of fleas compared with *Xenopsylla cheopis*. Journal of Hygiene 45: 371–396.

CULLY, J. F. JR., L. G. CARTER, AND K. L. GAGE. 2000. New records of sylvatic plague in Kansas. Journal of Wildlife Diseases 36: 389–392.

DAVIS, R. M., R. T. SMITH, M. B. MADON, AND E. SITKO-CLEUGH. 2002. Flea, rodent, and plague ecology at Chuchupate Campground, Ventura County, California. Journal of Vector Ecology 27: 107–127.

DAVIS, S., M. BEGON, L. DE BRUYN, V. S. AGEYEV, N. L. KLASSOVSKIY, S. B. POLE, H. VILJUGREIN, N. C. STENSETH, AND H. LEIRS. 2004. Predictive thresholds for plague in Kazakhstan. Science 304: 736–738.

DIEKMANN, O., J. A. P. HESTERBEEK, AND J. A. J. METZ. 1990. On the definition and the computation of the basic reproductive ratio R0 in models for infectious-diseases in heterogeneous populations. Journal of Mathematical Biology 28: 365–368.

DOUGLAS, J., AND C. WHEELER. 1943. Sylvatic plague studies. II. The fate of *Pasteurella pestis* in the flea. Journal of Infectious Diseases 72: 18–30.

ESKEY, C., AND V. HAAS. 1940. Plague in the western

part of the United States. Public Health Bulletin 254, 83 pp.

FOLEY, P. 1997. Extinction models for local populations. *In* Metapopulation biology, I. Hanski and M. Gilpin (eds.). Academic Press, San Diego, California, pp. 215–246.

———. 2000. Problems in extinction model selection and parameter estimation Environmental Management 26 (1 Suppl): S55–S74.

GAGE, K., AND M. KOSOY. 2005. Natural history of plague: Perspectives from more than a century of research. Annual Review of Entomology 50: 505–528.

GANI, R., AND S. LEACH. 2004. Epidemiologic determinants for modeling pneumonic plague outbreaks. Emerging Infectious Diseases 10: 608–614.

GOLDENBERG, M., S. F. QUAN, AND B. HUDSON. 1964. The detection of inapparent infections with *Pasteurella pestis* in a *Microtus californicus* population in the San Francisco Bay area. Zoonoses Research 3: 1–13.

HOLDENREID, R. 1952. Sylvatic plague studies. VII. Plague transmission potentials of the fleas *Diamanus montanus* and *Polygenis gwyni* compared with *Xenopsylla cheopis*. Journal of Infectious Diseases 90: 131–140.

———, AND S. F. QUAN. 1956. The susceptibility of New Mexico rodents to experimental plague. Public Health Report 71: 979–984.

HUBBARD, C. 1968. Fleas of western North America. Hafner, New York, New York, 533 pp.

KARTMAN, L., AND F. PRINCE. 1956. Studies on *Pasteurella pestis* in fleas V. The experimental plague-vector efficiency of wild rodent fleas compared with *Xenopsylla cheopis*, together with observations on the influence of temperature. American Journal of Tropical Medicine and Hygiene 5: 1058–1070.

———, ———, AND S. F. QUAN. 1958. Studies on *Pasteurella pestis* in fleas VII. The plague-vector efficiency of *Hystrichopsylla linsdalei* compared with *Xenopsylla cheopis* under experimental conditions. American Journal of Tropical Medicine and Hygiene 7: 317.

KEELING, M. J., AND C. A. GILLIGAN. 2000a. Bubonic plague: A metapopulation model of a zoonosis. Proceedings of the Royal Society Biological Sciences Series B 267: 2219–2230.

———, AND ———. 2000b. Metapopulation dynamics of bubonic plague. Nature 407: 903–906.

KERMACK, W., AND A. MCKENDRICK. 1927. Contributions to the mathematical theory of epidemics. Royal Statistical Society Journal 115: 700–721.

LARSON, O., R. SCHWAB, AND A. FAIRBROTHER. 1996. Seasonal occurrence of fleas on deer mice. Journal of Vector Ecology 21: 31–36.

LINK, V. 1955. A history of plague in the United States. Public Health Monographs 26: 1–42.

LINSDALE, J. 1946. The California ground squirrel; a record of observations made on the Hastings natural history reservation. University of California Press, Berkeley, California, 475 pp.

———, AND L. P. TEVIS. 1951. The dusky-footed wood rat; a record of observations made on the Hastings Natural History Reservation. University of California Press, Berkeley, California, 664 pp.

LONGANECKER, D., AND A. BURROUGHS. 1952. Sylvatic plague studies, IX. Studies of the microclimate of the California ground squirrel burrough and its relation to seasonal changes in the flea population. Ecology 33: 488–499.

MACDONALD, G. 1957. The epidemiology and control of malaria. Oxford University Press, Oxford, UK.

MARCHETTE, N., J. BUSHMAN, AND D. PARKER. 1962a. Studies of infectious diseases in wild animals in Utah. IV. A wild rodent (*Peromyscus* spp.) plague focus in Utah. Zoonoses Research 1: 341–361.

———, D. LUNDGREN, P. NICHOLES, J. BUSHMAN, AND D. VEST. 1962b. Studies on infectious diseases in wild animals in Utah. II. Susceptibility of wild mammals to experimental plague. Zoonoses Research 1: 225–250.

MAY, R. 1974. Stability and complexity in model ecosystems. 2nd Edition. Princeton University Press, Princeton, New Jersey, 201 pp.

MAYER, K., AND W. LAUDENSLAYER. 1988. A guide to wildlife habitats of California. California Department of Forestry and Fire Protection, Sacramento, California, 166 pp.

MCCOY, G. 1908. Plague in ground squirrels. Public Health Report 34: 1289–1293.

———. 1909. The susceptibility of gophers, field mice, and ground squirrels to plague infection. Journal of Infectious Diseases 6: 283.

———. 1911a. Studies upon plague in ground squirrels. Public Health Bulletin 43: 7–51.

———. 1911b. Susceptibility to plague of the weasel, chipmunk, and gopher. Journal of Infectious Diseases 8: 42–46.

———, AND C. CHAPIN. 1912. Studies of plague. A plague-like disease and tuberculosis among rodents in California. III Immunity of wild rats (*Mus norvegicus*) to plague infection. IV Susceptibility to a ground squirrel (*Ammospermophilus leucurus* Merriam) to plague. Public Health Bulletin 53: 12–16.

———, AND F. SMITH. 1910. Susceptibility to plague of prairie dog, desert wood rat, and rock squirrel. Journal of Infectious Diseases 7: 374–376.

MILES, V., A. KINNEY, AND H. STARK. 1957. Flea-host relationships of associated *Rattus* and native wild rodents in the San Francisco Bay area of California, with special reference to plague. American Journal of Tropical Medicine and Hygiene 6: 752–760.

NATIONAL CENTER FOR ECOLOGICAL ANALYSIS AND SYNTHESIS. 2004. *Global Population Dynamics*

Database. Vol. 2004, http://cpbnts1.bio.ic.ac.uk/gpdd/. Accessed 20 March 2006.

NELSON, B. 1980. Plague studies in California: the roles of various species of sylvatic rodents in plague. Proceedings of the Vertebrate Pest Conference 9: 89–96.

NICHOLSON, A., AND V. BAILEY. 1935. The balance of animal populations. Proceedings of the Zoological Society London 3: 551–598.

NOBLE, J. 1974. Geographic and temporal development of plagues. Nature 250: 726–728.

NOWAK, R. 1995. Walker's mammals of the world. Johns Hopkins University Press, Baltimore, Maryland, 264 pp.

PERRY, R. D., AND J. D. FETHERSTON. 1997. *Yersinia pestis*—Etiologic agent of plague. Clinical Microbiological Review 10: 35–66.

POLLITZER, R. 1954. Plague. WHO Monograph 22, 698 pp.

QUAN, S. F., AND L. KARTMAN. 1962. Ecological studies of wild rodent plague in the San Francisco Bay area of California. VIII. Susceptibility of wild rodents to experimental plague infection. Zoonoses Research 1: 121–144.

———, V. MILES, AND L. KARTMAN. 1960. Ecological studies of wild rodent plague in the San Francisco Bay area of California. III. The natural infection rates with *Pasteurella pestis* in five flea species during an epidemic. American Journal of Tropical Medicine and Hygiene 9: 85–90.

QUAN, T., A. BARNES, L. CARTER, AND K. TSUCHIYA. 1985. Experimental plague in rock squirrels, *Spermophilus variegatus*. Journal of Wildlife Diseases 21: 205–210.

RAGGETT, G. 1982. Modeling the Eyam plague. Bulletin of the Institute of Mathematical Applications 18: 221–226.

ROSS, R. 1928. Studies on malaria. John Murray, London, UK, 196 pp.

RUTLEDGE, L. C., M. A. MOUSSA, B. L. ZELLER, AND M. A. LAWSON. 1979. Field studies of reservoirs and vectors of sylvatic plague at Fort Hunter Liggett, California. Journal of Medical Entomology 15: 452–458.

SMITH, C., B. WILSON, C. L. FRITZ, C. M. MYERS, J. C. HITCHCOCK, M. MADON, AND S. WERNER. 1998. Review of plague in California. California Morbidity May 1988, 4 pp.

WHEELER, C., AND J. DOUGLAS. 1945. Sylvatic plague studies. V. The determination of vector efficiency. Journal of Infectious Diseases 77: 1–12.

WHERRY, W. 1908. Plague among the ground squirrels. Journal of Infectious Diseases 5: 485–506.

WILDLIFE AND HABITAT DATA ANALYSIS BRANCH. 2004. *California Wildlife Habitat Relationships*, http://www.dfg.ca.gov/whdab/index.html. Accessed 5 January 2005.

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