Description of an epidemic simulation model for use in evaluating strategies to control an outbreak of foot-and-mouth disease

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Objective—To develop a spatial epidemic model to simulate intraherd and interherd transmission of foot-and-mouth disease (FMD) virus.

Sample Population—2,238 herds, representing beef, dairy, swine, goats, and sheep, and 5 sale yards located in Fresno, Kings, and Tulare counties of California.

Procedure—Using Monte-Carlo simulations, a spatial stochastic epidemic simulation model was developed to identify new herds that would acquire FMD following random selection of an index herd and to assess progression of an epidemic after implementation of mandatory control strategies.

Results—The model included species-specific transition periods for FMD infection, locations of herds, rates of direct and indirect contacts among herds, and probability distributions derived from expert opinions on probabilities of transmission by direct and indirect contact, as well as reduction in contact following implementation of restrictions on movements in designated infected areas and surveillance zones. Models of supplemental control programs included slaughter of all animals within a specified distance of infected herds, slaughter of only high-risk animals identified by use of a model simulation, and vaccination of all animals within a 5- to 50-km radius of infected herds.

Conclusions and Clinical Relevance—The FMD model represents a tool for use in planning biosecurity and emergency-response programs and in comparing potential benefits of various strategies for control and eradication of FMD appropriate for specific populations. (*Am J Vet Res* 2003;64:195–204)

Foot-and-mouth disease (FMD) is an economically important livestock disease that is endemic among cloven-hoofed animals in parts of Asia, Africa, and South America.[1] The **FMD virus (FMDV)** can spread rapidly through susceptible livestock populations, often via infected animals that transmit the virus before appearance of clinical signs.[2] Numerous times in various locations throughout the world, hundreds of thousands of animals have been slaughtered to control spread of the disease.[3-6] Trade restrictions imposed by the US government and surveillance efforts of the USDA have successfully prevented reintroduction of FMD into the United States since its eradication in 1929.[7] However, as travel to countries with FMDV-infected livestock continues and livestock and their products from those countries continue to be imported, the potential remains for FMD to be reintroduced into the United States.

The livestock population in California includes approximately 5 million cattle, 1 million small ruminants, and 190,000 pigs.[8] If FMD were to be detected in California, state and federal animal health agencies would impose livestock export restrictions at the borders and begin intense local eradication efforts to minimize transmission and remove affected or exposed animals. Determination of the most appropriate eradication strategy would likely depend on the types of herds infected, density of herds surrounding the index herd, and potential for wildlife exposure. Slaughtering infected herds (referred to as stamping-out) can be an effective eradication strategy in some epidemics[9-12] and would likely be practiced in California in the event of the introduction of FMD.[13,14] Because eradication strategies involving slaughter of only known infected herds have not always been successful, supplemental strategies may need to be considered, including preemptive slaughter of susceptible high-risk herds and the use of vaccines.[13]

Identification of 1 or more effective eradication strategies is needed to improve our preparedness for FMD should it return to the United States. Typically, eradication programs are evaluated after the fact by analyzing epidemiologic data collected during previous eradication efforts. However, contemporary information, such as the likely rates of spread of FMDV and probabilities of secondary transmission in the United States, is not available because FMD has not been in the United States for > 70 years. Even though there

Received June 13, 2002.
Accepted September 12, 2002.
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Supported in part by USDA Animal Health Formula Funds, the USDA-National Research Initiative Competitive Grants Program (grant No. 35204-10173), and collaborative agreements with the California Department of Food and Agriculture and the USDA: Animal Plant Health Inspection Service: Veterinary Services.
The authors acknowledge Drs. Dana Nelson, Dorothy York, Ken Thomazin, Richard Breitmeyer, Phil LaRussa, Paul Ugstad, Tom McKenna and Pam Hullinger for assistance in developing parameter estimates for emergency response to an outbreak of foot-and-mouth disease, and Drs. Derek Belton, Steven Bolin, Christian Griot, Thomas Holt, Martin Hugh-Jones, Paul Kitching, Juan Lubroth, Thomas McKenna, Charles Mebus, John Ryan, Mirzet Sabirovic, Lee Ann Thomas, and Terry Wilson for assistance with estimating the likelihood of transmission of foot-and-mouth disease among herds in California.
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have been recent FMD epidemics in other countries in regions previously free of the disease for > 20 years,[15-17] herd size, herd type, and number of direct and indirect animal contacts among herds in other countries differ widely from those for the United States. Consequently, information obtained from those epidemics about the probabilities of FMDV transmission is unlikely to be applicable to development of appropriate control strategies for FMD for US herds and livestock practices. When information concerning likely outcomes of an outbreak of FMD is unavailable, simulation modeling is 1 tool that can be used to evaluate strategies for disease eradication. Such an approach ideally would use information about location, size, and type of herds and the expected number of direct and indirect animal contacts among the herds that could influence disease transmission. Furthermore, models could be used to simulate epidemics controlled by various eradication strategies to assess and compare projected magnitudes and durations of epidemics.

Numerous models have been developed to simulate FMD outbreaks among livestock populations in developed countries.[18-23] Only recently, however, have mathematical and simulation models been developed to simulate FMDV transmission after considering spatial proximity among herds.[21-23] These models were developed as macro-level tools to predict the size and duration of a nation-wide epidemic, rather than to simulate transmission in a well-defined local area and to assess potential regional eradication strategies prior to an outbreak. To consider appropriate means of controlling an epidemic of FMD in a specific region, a model ideally should consider spatial distances between herds, particularly when eradication strategies being considered, such as vaccination of animals within a 10-km radius of infected herds, have a spatial component (eg, distance). Also, because FMD outbreaks may occur in regions with multiple species, herd sizes, and associated risks of FMDV transmission, a model should consider all herd types and sizes expected to be located in the region and the expected number of contacts among the herds to appropriately estimate FMDV transmission.

The primary objective of the study reported here was to use a computer simulation model to evaluate the potential effectiveness of a mandated (baseline) eradication strategy and 3 additional strategies for eradication of FMD in response to hypothetical epidemics of FMD in a 3-county region of California. The baseline strategy required slaughter of all animals in known FMD-infected herds and imposition of herd quarantines in FMD-affected areas. The 3 supplemental strategies were vaccination of all noninfected animals in herds within a designated distance of each infected herd, preemptive slaughter of all animals in herds within a designated distance of each infected herd, and preemptive slaughter of all animals in the highest-risk herds as determined by use of the model. The goal was to develop practical and scientifically sound strategies to limit local transmission of FMDV should the disease reappear in the United States. The specific purpose of the study was to describe the simulation model and the input parameters considered by the simulation model, which were used to compare the baseline eradication strategy with the 3 supplemental strategies. Results of simulation modeling have been reported in another report.[24]

Materials and Methods

General approach—The general approach was to develop a simulation model that considered herd size, location, FMDV-infection status, and expected direct and indirect contact rates among herds and flocks in a 3-county region of California to allow simulation of hypothetical epidemics of FMD. A series of epidemics was simulated, and epidemics were considered to have been controlled by implementation of a mandated baseline eradication strategy that required slaughter of all livestock in an infected herd as well as restriction on local movement of animals. The baseline strategy also included 2 zones of disease surveillance in the area surrounding each known infected herd (a 10-km infected area and a 20-km surveillance zone). For each infected herd, the model estimated potential herd-to-herd contact sufficient to transmit FMDV to susceptible herds during the simulated outbreak. Models were then simulated for supplemental eradication strategies, and results were examined (or analyzed) to compare the potential effectiveness of each strategy with the baseline strategy.

Type and location of livestock and livestock facilities—Beef, dairy, goat, sheep, and swine herds in Fresno, Kings, and Tulare counties of California were geographically located (**Fig 1**). Herds were categorized on the basis of size and amount of direct and indirect contact activity, as described elsewhere.[25] In 1997, it was estimated that the region contained approximately 462,000 lactating dairy cows, 67,000 beef cows, 614,000 calves and bulls, 124,000 baby pigs and hogs, and 94,000 sheep and lambs.[8] For herds other than dairies, the geographic point location and number of animals in the herd were determined from a livestock survey conducted in September 2000 by use of a global positioning system. Because the precise point location of 70 of the 664 beef herds was not known, locations for those 70 herds were randomly distributed along the eastern portion of the study region, which is populated mainly with beef herds. Size and location of 547 commercial dairies and 29 dairy calf and heifer ranches were determined during a previous survey conducted in 1997. Thirty-eight herds represented the precise locations of

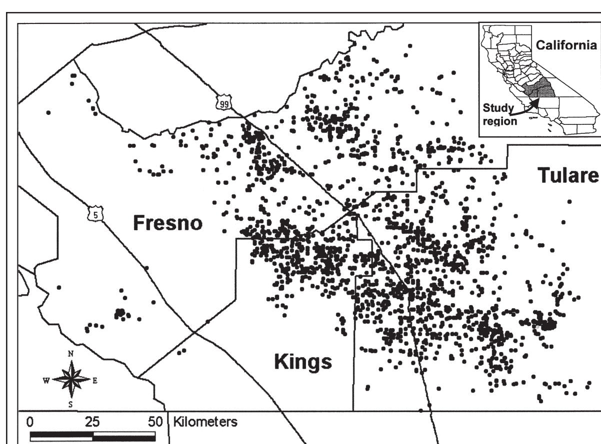

Figure 1—Locations of 2,238 beef, dairy, goat, sheep, and swine herds located in a 3-county region of the southern San Joaquin Valley of California. Precise location of 70 of 664 beef herds was not known; therefore, the location of each of those herds was randomly distributed throughout the eastern portion of the 3-county region.

high school and junior high vocational agriculture farms, many of which were part of the Future Farmers of America organization. Seven hundred eighty-eight herds of any type consisted of < 10 animals and were categorized as backyard herds. Location of 573 student-project (backyard) herds were obtained from the California Statewide 4-H Program and were included along with 215 previously identified backyard herds. Location of 5 sale yards operating within the study region also was included in the model.

Elements and structure of the general model—A computational model was developed that simulated FMDV transmission among herds to enable comparison of the total number of herds affected and the duration of each epidemic for epidemics addressed by various eradication strategies. The model assumed that an entire herd would be slaughtered when FMD was diagnosed in at least 1 animal, which is consistent with recommendations in USDA guidelines.[13] Because many input parameters for the model were expressed as probability distributions and not as point estimates, 1,000 epidemics were simulated for each control scenario to obtain output distributions of the number of herds infected or affected and the duration of each epidemic. Herds were categorized as susceptible, latently infected (not infectious), subclinically infectious, clinically infectious, vaccinated (partially susceptible and partially infectious when infected), or removed (disposed) on the basis of infection status of animals in each herd (**Fig 2**). The subclinically infectious category was considered to occur between the latent and clinically infectious periods, and the sum of the latent and subclinically infectious periods was considered to be the incubation period.[26] Subclinically and clinically infectious herds were considered to remain infectious until removed from the model as a result of slaughter. When a vaccinated herd became infected, the infectiousness of the herd was decreased in proportion with efficacy of the vaccine.

Model parameters and distributions were determined. Time interval for the model was 1 day. Latent and subclinically infectious periods were determined by analysis of data from a controlled study[2] of FMD infection in cattle, sheep, and swine by use of FMDV serotype O_1 that infected herds in the UK during the epidemic of 1967–1968. Herds were considered clinically infected after their subclinical infection period ended, even though only 1 animal in that herd may have had clinical signs. It was assumed that herds in which animals were slaughtered were not restocked during the epidemic; therefore, they could not subsequently become susceptible or infectious.

Distributions of the distance animals were moved to and from a herd, as obtained from a study[25] in which investigators estimated direct and indirect contact rates among herds within a 3-county region of California, were estimated and fit to probability functions. These functions estimated potential spatial transmission of FMDV in the 3-county California region of our study.

Probability of adequate contact without control programs in place—The primary means of FMDV transmission is adequate direct (animal-to-animal) or indirect (people or vehicles) contact between a susceptible herd and an FMDV-infectious herd. For the study reported here, adequate contact was defined as direct or indirect contact between 2 herds such that if 1 herd were infectious and the other susceptible, infection would occur in at least 1 animal in the susceptible herd. Probabilities of herd contact being adequate, however, were unknown; therefore, they were estimated on the basis of responses to an electronic mail survey of 25 internationally recognized FMD experts. Participants resided in 5 countries and 3 continents, and at least 3 had experience working with FMD in countries on 2 continents where FMD is endemic. Experts were asked to provide their opinion on probabilities of transmission for specific scenarios in which a herd in our 3-county study region could become infected by animal movement or by high- or low-risk indirect contact.

High-risk indirect contact was defined as contact by personnel with frequent and close animal contact, such as artificial insemination technicians, hoof trimmers, or veterinarians. Low-risk indirect contact was contact by personnel and vehicles that had infrequent or no live-animal contact during a visit to the premises. For 100 similar scenarios, survey recipients were asked to estimate the minimum, maximum, and most likely numbers of expected occurrences of FMDV transmission. For each question, the survey requested information about the likelihood of transmission from 1 swine herd to another swine herd, from 1 dairy herd to another dairy herd, and between a swine herd and a dairy herd. Survey results for transmission among dairies were used in the model for all nonswine species. Survey responses were characterized by fitting BetaPERT **probability density functions (PDFs)**[27] to the median of the minimum, maximum, and most likely values obtained for each question on the survey. The effects of wildlife and weather on potential transmission of FMDV were excluded from the model because of insufficient data.

Intraherd transmission—Beginning at the time of exposure, the infectiousness of each infected herd was allowed to

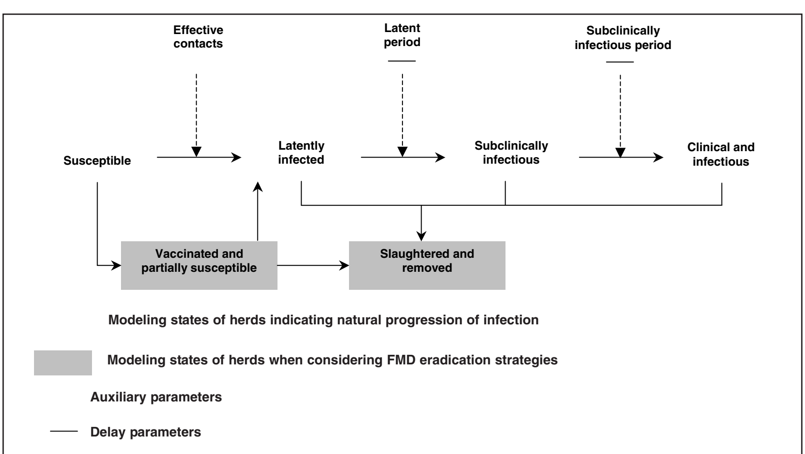

Figure 2—Illustration depicting simulation modeling states, pathways for progression of foot-and-mouth disease (FMD), and additional modeling states when implementation of disease control strategies were considered.

increase over a period of several days. A Reed-Frost epidemic simulation model was used to estimate the proportion of the herd that was infectious during a given time (ie, t) by use of the following equations[28]:

$$L_{t+1} = S_t \left(1 - (1 - \frac{k}{N-1})^{I_t}\right) \quad \text{and}$$

$$I_t = \sum_{i=0}^{t-D} L_i$$

where L_{t+1} is the number of new latently infected animals in the herd at time $t + 1$ and was set equal to 1 at $t = 0$; S_t is the number of susceptible animals in the herd at time t; k is the herd type- and size-dependent number of intraherd adequate contacts per infected animal per day; N is the total number of animals in the herd; I_t is the number of clinically and subclinically infectious animals at time t; L_t is the number of latently infected animals in the herd; and D is the mean duration of the species-specific latent period for the disease. Values for k were estimated by solving the equation for k on the day it was expected that half of the animals within a herd would be infected. The time estimates for half of the herd to become infected were 4 days for swine herds and backyard herds, 9 days for dairy herds, 10 days for sheep or goat herds and beef herds with > 250 cattle, and 14 days for beef herds with < 250 cattle. These estimates were provided through expert opinion.[a] For example, when considering a dairy herd with 125 susceptible animals and a mean latent period of 3.7 days, k was 6.4 adequate contacts generated by each infected animal in a 1-day period. The proportion of animals in the herd that was infected for time t was calculated by dividing I_t for all previous time periods by N. In contrast to results for other herds, infectiousness for sale yards did not increase with time; rather, infectiousness was assumed to be fixed at 0.2, because it was expected that minimal disinfection, if any, would take place in the common areas used to hold animals between days of sales and because we assumed that animals were not retained in a sale yard for more than 24 hours.

Adequate contact—Number of daily adequate contacts from a specific herd to other herds or to a specific herd from other herds was derived for each of the 12 herd types and 3 potential modes of FMDV transmission (ie, direct contact and high- and low-risk indirect contact) by multiplying the expected number of daily contacts for direct contact and for high- and low-risk indirect contacts by the corresponding probability of a contact being adequate and then multiplying that product by the proportion of animals in the herd expected to be infectious. During model simulation, the probability of an adequate contact was determined by Monte-Carlo sampling from the BetaPERT PDFs that estimated the responses provided by the experts to our survey on the potential for FMDV transmission. Consequently, the probability varied for each herd and each time period. Analysis of data previously collected by our laboratory group for the 3-county study area indicated that sale yards typically held 2 or 3 sales each week and involved approximately 56 livestock sellers and 42 buyers. At least 53% of sales were for livestock that moved directly to slaughterhouses where contacts were not made with other herds; therefore, sale yards were considered to have contributed a maximum of 20 ($[1.00 - 0.53] \times 42$) direct contacts/sale day.

Newly infected herds for each time period—The expected number of newly infected herds at time $t + 1$ was calculated by summing the expected number of adequate contacts for all herds subclinically or clinically infectious during the preceding time period. If an adequate contact occurred between an infectious herd and another infected herd or an infected herd that was removed (slaughtered), the contact was not considered to be an effective (susceptible herd becomes infected) contact, because although adequate contact occurred, both herds had already been designated by the model as infected. The number of effective contacts, therefore, was less than or equal to the number of adequate contacts and varied depending on the number of infectious and susceptible herds in the model and the eradication strategy being considered.

FMDV exposure risk—The model used a weighted random selection process to identify susceptible herds at time t that would become latently infected at time $t + 1$. The weights were in proportion to a herd's overall risk of FMDV exposure at time t, where the risk was independently calculated for 3 modes of transmission at each time t by use of the following equation:

$$E_{j,m,t} = \sum_{\substack{i=1 \\ i \neq j}}^{I} C_{s,m,t} \,(1 - F_m[d_{i,j}])$$

where $E_{j,m,t}$ is the risk of exposure to FMDV for herd j for transmission mode m at time t; m is the mode of transmission (direct contact or high-or low-risk indirect contact); I is a vector of subclinically and clinically infectious herds in the model at time t; $C_{j,m,t}$ is the expected number of adequate daily contacts for a susceptible herd via mode m during time t; $d_{i,j}$ is the straight-line distance between herd j and infectious herd i; and $F_m(d_{i,j})$ is the mode-specific cumulative PDF of contact with a herd that is located a specified distance (d) away. Distributions $F_{m = 1 \text{ to } 3}$ represent the fit for frequency distributions of distance of livestock movements for direct contact and of expected distances of high- and low-risk indirect animal contact that were estimated in another study.[25]

Herd-specific exposure risks ($E_{j,m,t}$) were calculated for each herd at each time period and varied according to the number, type, and location of infected herds in the model at time t. Exposure risks for each herd were functions of the modeling parameter $(1 - F_m[d_{i,j}])$, which contributed a heterogeneous risk of FMDV exposure for each herd by adjusting the risk of FMDV exposure on the basis of proximity to infectious herds. Commercial risk analysis software[b] was used to develop cumulative PDFs (ie, F_m) by use of data obtained in another study[25] for the distance livestock were moved and the distance personnel and vehicles traveled during a 3-day period for the 3-county area. Therefore, when 2 similar susceptible herds each had 2 adequate contacts, but 1 herd was located farther from an infected herd, the risk of the herd farther from an infected herd becoming infected was lower than that for the herd nearer to an infected herd.

The model also included constraints that allowed only direct contacts among herds that had a reasonable likelihood of contacting each other. For purposes of restricting livestock movement, all herds were grouped into 1 of 6 categories: backyard, beef, dairy, sheep or goat, swine, and sale yard. Herds within a given category were only at risk of receiving direct contact from infectious herds within the same herd category; however, all herds could have direct contact with a sale yard.

Initiation of model simulation—To initiate an epidemic, a herd within the study region was randomly selected by the model and designated as a subclinically infectious index herd at time 0; all other herds were assumed to be susceptible. For each subsequent time period, the model calculated the number of adequate contacts between infectious herds and susceptible herds by summing values for $C_{j,m,t}$ generated for all infectious herds. During any interval of time, the number of herds that became infected was equal to, at most, the number of adequate contacts weighted by the exposure risk (ie, $E_{j,m,t}$). The model stopped the simulation when no new effective contacts occurred for 14 consecutive days, which approximated the herd infectious period.

Baseline eradication strategy—The 1991 USDA FMD eradication guidelines[13] were considered in the model as the minimum baseline strategy to be used if FMD were introduced into the study region. Those guidelines specify that an infected area, also called a high-risk or protection zone,[29] with a radius of 4.8 to 8.0 km must be established around herds infected with FMDV and that a surveillance zone, formerly called a buffer zone, with a radius of 15 to 40 km must be initiated around the infected herd. However, a revised summary of those guidelines[14] now requires that an infected area of at least 10 km be established around known infected herds, in addition to a surveillance zone. The baseline strategy used in the study reported here included a radius of 10 km for the infected area and a radius of 20 km for the surveillance zone. In accordance with these guidelines, it was assumed that all sale yards within the study region were closed as soon as the baseline eradication strategy was implemented. Furthermore, it was assumed that the baseline eradication strategy would be implemented within 24 hours of diagnosis of FMD (ie, the index case). Movement restrictions required in the baseline eradication strategy were assumed to have varying degrees of effectiveness for decreasing the probability of adequate contacts among herds. The degree of effectiveness of the baseline eradication strategy was estimated by use of information obtained in a second survey conducted of persons expected to have an understanding of probable effectiveness of disease control through restrictions on animal movements. Number of days before the index case was identified in the index herd was assumed to be 21, which was believed to be the approximate delay in diagnosis for the 2001 epidemic of FMD in the United Kingdom. In subsequent sensitivity analyses, however, the delay for implementing the baseline control strategy was varied between 1 and 28 days.

Probability of herd contact after implementation of baseline control strategy—To estimate the likely effectiveness of the baseline eradication strategy for reducing the probability of herd-to-herd contacts, a questionnaire was administered to persons considered to have an understanding of probable effectiveness of disease control through restrictions on animal movements. The questionnaire was administered to volunteers attending the Foreign Animal Disease Committee of the 103rd annual meeting of the United States Animal Health Association and to emergency-response experts working for the state of California or in federal animal health programs. Participants were asked to estimate the percentage decrease in direct and indirect contacts expected to occur within an infected area and within a surveillance zone following implementation of baseline eradication activities. For each epidemic simulated, a new sample was obtained from PDFs by use of Monte-Carlo sampling. The value obtained represented the percentage decrease in expected exposure risk (ie, $E_{j,m,t}$) to herds in the infected area and in the surveillance zone following implementation of baseline eradication activities.

Supplemental eradication strategies—Three supplemental eradication strategies were evaluated by comparing distributions of the number of herds infected or affected and of durations for epidemics during implementation of the mandatory baseline eradication strategy with those distributions during epidemics in which supplemental eradication strategies were applied. The supplemental eradication strategies were to vaccinate all herds within 5, 10, 25, or 50 km of each infected herd; preemptive slaughter all herds within 1, 3, or 5 km of each infected herd; or preemptive slaughter of 1, 5, or 10 of the herds with the highest expected exposure to FMD as determined by results of the model. Because supplemental eradication strategies were only applicable to a subset of herds (eg, those within 25 km of an infected herd), the model considered potential geographic boundaries of each strategy by restricting application of the strategy only to specific herds. For example, when a radius of 25 km for vaccination was considered as a supplemental eradication strategy, herds located outside the 25-km radius were assumed to remain unvaccinated until a diagnosis of FMD was made for a herd within a 25-km radius of those unvaccinated herds.

Herd vaccination strategy—The decision to vaccinate during an epidemic of FMD generally may not be considered until it has been determined that strategies involving slaughter of herds are ineffective.[13] For the model reported here, however, it was assumed that production of FMD vaccine would be initiated as soon as FMD was diagnosed in the United States. The rapidity with which the vaccine would be available would depend on whether stores of viral antigen located at the **North American Vaccine Bank (NAVB)** would match the outbreak strain. Assuming a matching viral antigen was available, it was estimated that transportation of a specimen and preliminary diagnosis at the Foreign Animal Disease Diagnostic Laboratory at Plum Island, NY would require 1 or 2 days, it would require 2 days to determine the viral subtype via use of polymerase chain reaction procedures, it would require 4 days to produce the vaccine and deliver it to the outbreak location, and it would require at least 1 day to administer the vaccine within the initial area designated for vaccination. Therefore, it was assumed that total time from submission of a sample for diagnostic testing to the time of vaccine administration was a minimum of 8 or 9 days. If the virus subtype were not available at the NAVB or a similar international FMD vaccine bank, then the viral antigen would need to be manufactured, and vaccine administration would likely be delayed by at least several weeks. This latter scenario was not considered in the study reported here.

Vaccination with a high-potency vaccine was assumed to elicit sufficient immunologic response to prevent clinical manifestations of FMD in infected animals and to reduce substantial amounts of shedding of FMDV from infected animals within 4 days after inoculation.[30-32] It was assumed that the probability that a susceptible, vaccinated herd would become infected after if was vaccinated at least 4 days previously was the complement of the **vaccine efficacy (*VE*)**, which was calculated as $1 - VE$ for each susceptible herd. On the basis of results of vaccination campaigns in other countries,[33,34] vaccine efficacy was considered to vary from 80 to 90%. When a vaccinated herd did become infected, infectiousness of the vaccinated herd was reduced by the same percentage as the efficacy of the vaccine.

Preemptive herd slaughter strategies—Two supplemental strategies considered use of preemptive slaughter of noninfected high-risk herds. The first strategy was to slaughter all herds within 1, 3, or 5 km of any infected herd. The second strategy was to slaughter 1, 5, or 10 of the highest-risk herds for each infected herd. Highest-risk status was determined by ranking herds on the basis of their herd-specific risk for exposure to FMD (ie, $E_{j,m,t}$) at each time interval. For all strategies, estimates regarding the expected time required for herd slaughter were obtained from estimates provided by the California foreign-animal disease emergency-response experts. Based on those estimations, the time required to complete slaughter of all animals in a typical herd in California varied from 1 to 5 days, depending on herd size and type.

Model programming and statistical analysis—The model was programmed by use of commercially available software[c] and included Monte-Carlo sampling capabilities

Table 1—Number of herds in Fresno, Kings, and Tulare counties of California and expected daily direct and high- and low-risk indirect contacts with other herds

		Direct		Indirect	
Herd type	No. of herds	To herd	From herd	High-risk*	Low-risk*
Backyard†	788	0.060	0.056	0.017	0.846
Beef (< 250 cattle)	583‡	0.013	0.030	0.010	0.721
Beef (≥ 250 cattle)	81	0.013	0.066	0.099	1.421
Dairy (< 1,000 cows)	388	0.086	0.271	0.423	7.322
Dairy (1,000 to 1,999 cows)	127	0.053	0.575	0.800	13.038
Dairy (≥ 2,000 cows)	32	0.066	0.542	0.929	23.640
Dairy calves or heifers (< 250 cattle)	23	0.010	0.023	0.007	0.912
Dairy calves or heifers (≥ 250 cattle)	6	0.562	0.740	0.370	19.775
Goats	62	0.010	0.218	0.007	1.666
Sheep	69	0.066	0.261	0.01	0.998
Swine (< 2,000 pigs)	77§	0.040	0.159	0.099	3.137
Swine (≥ 2,000 pigs)	2	0.007	0.661	0.017	26.670

Direct and indirect contact data were obtained from another study[25] of livestock facilities located within the 3-county area.

*High-risk indirect contacts were artificial insemination technicians, hoof trimmers, and veterinarians, whereas low-risk indirect contacts were other personnel and vehicles. †Backyard herds were herds that consisted of < 10 animals. ‡Includes 70 herds whose exact location was unknown and that were randomly distributed in the eastern half of the study region. §Includes 38 vocational farms that had swine and possibly other livestock species.

Table 2—Type of distribution (probability density function [PDF] parameters) assumed for the pathogenesis and diagnosis of foot-and-mouth disease (FMD) for latent and subclinical infectious periods for herds of swine, sheep, and other species

	Swine	Sheep	Other species
Period	Distribution (parameters)	Distribution (parameters)	Distribution (parameters)
Latent	Normal (μ = 6.0, σ = 0.9)	Pearson5 (α = 15.3, β = 94.7)	Normal (μ = 3.7, σ = 0.8)
Subclinical infectious	Normal (μ = 4.3, σ = 1.9)	Normal (μ = 2.2, σ = 1.1)	Normal (μ = 2.6, σ = 1.1)

Values reported are number of days.
Data were obtained from another study.[2]

developed from commercial software.[d] Mean and median values were calculated for survey responses by use of commercial software for statistical analysis.[e] Distributions and relevant parameters for PDFs that provided the best fit for data on livestock movement and durations of modeling states (eg, latent periods) were obtained by use of the χ^2, Kolmogorov-Smirnov, and Anderson-Darling goodness-of-fit tests at values of $P > 0.05$, using commercial software for fitting distributions.[c] For all analyses, the probability of a type-I error was defined as $P < 0.05$ and was considered to be significant.

Results

Daily contacts—The estimated numbers of daily direct contacts and high- and low-risk indirect contacts for each herd size and type were determined (**Table 1**). Large (≥ 250 cattle) dairy calf and heifer ranches, on average, had the largest number of animal movements (direct contact) to a herd (0.56 direct contacts/d), whereas large (≥ 2,000 pigs) swine operations had the largest number of indirect contacts (26.67 indirect contacts/d).

Duration of latent and subclinical periods—The estimated range of durations of latent and subclinical

Table 3—Type of distribution PDF parameters) assumed for the probability of FMD virus transmission and herd contact distances that were included in an epidemic simulation model

	Swine	Other livestock
Model parameter	Distribution (parameters)	Distribution (parameters)
Transmission probabilities*		
Direct contact	BetaPERT (90, 98, 100)†	BetaPERT (80, 95, 100)
Indirect contact, high-risk‡	BetaPERT (25, 50, 86)	BetaPERT (10, 50, 90)
Indirect contact, low-risk‡	BetaPERT (2, 27.5, 40)	BetaPERT (0.5, 17.5, 35)
Contact distances (km)§		
Direct to facility	Weibull (α = 0.94, α = 30.6)	Weibull (α = 0.94, α = 30.6)
Direct from facility	Weibull (α = 1.35, α = 24.3)	Weibull (a = 1.35, α = 24.3)
High-risk indirect contacts‡	Weibull (α = 0.69, α = 13.7)	Weibull (α = 0.69, α = 13.7)
Low-risk indirect contacts‡	Weibull (α = 1.18, a = 20.7)	Weibull (α = 1.18, α = 20.7)

*Determined on the basis of expert opinions from the analysis of Figure 1. †Values reported for BetaPERT distributions are minimum, most likely, and maximum. ‡High-risk indirect contacts were artificial insemination technicians, hoof trimmers, and veterinarians, whereas low-risk indirect contacts were other personnel and vehicles. §Obtained from results of another study.[2]

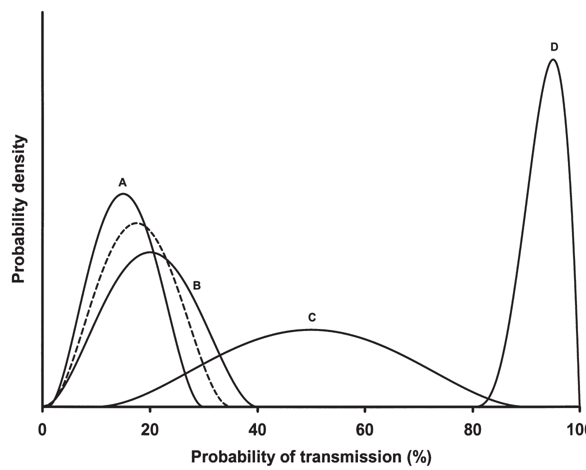

Figure 3—Probability density functions of the probability of transmission of FMD virus between an infectious and a susceptible dairy herd via indirect contact with vehicles (low-risk indirect contact; A), personnel without animal contact (low-risk indirect contact; B), personnel with animal contact (high-risk indirect contact; C), and animal-to-animal direct contact (D). Estimates were obtained from a survey that elicited the opinions of several experts. The dashed line represents the mean value for distributions A and B, which was considered the mean risk of transmission for low-risk indirect contact via vehicles and personnel in the model.

periods estimated for herds of swine, sheep, and other species were calculated (**Table 2**). For example, mean duration of the latent and subclinical periods for beef and dairy cows was 3.7 and 2.6 days, respectively.

Probability of adequate contact without control programs in place—High concordance was evident among the 15 survey respondents with regard to expected probability of transmission by direct contact for transmission among dairies, as indicated by the narrow distribution (minimum, 90; maximum, 100;

Table 4—Epidemic simulation model for evaluating the effectiveness of baseline eradication, vaccination, and preemptive slaughter eradication strategies for an outbreak of FMD

Control measure parameter	Distribution	Reference
Baseline eradication strategy		
Days until FMD diagnosis in index herd	1, 7, 14, 21, 28	Alternative scenarios*
Days required to implement control strategy	1	Expert opinion†
Days from appearance of clinical signs to diagnosis	BetaPert (1, 2, 4)‡	Expert opinion†
Days from diagnosis to slaughter on the basis of No. of animals per herd		
< 250	Uniform (minimum = 1, maximum = 2)	Expert opinion†
250-1999	BetaPert (1, 2, 4)‡	Expert opinion†
≥ 2,000	BetaPert (2, 2.5, 5)‡	Expert opinion†
Radius of infected area (km)	10	Reference No. 14
Radius of surveillance zone (km)	20	Reference No. 13
Percentage decrease in direct contact after implementation of control strategies for:		
Infected area	BetaPERT (60, 95, 100)‡	Analysis of Figure 2
Surveillance zone	BetaPERT (30, 88, 100)‡	Analysis of Figure 2
Percentage decrease in indirect contact after implementation of controls for:		
Infected area	BetaPERT (30, 80, 98)‡	Analysis of Figure 2
Surveillance zone	BetaPERT (25, 60, 95)‡	Analysis of Figure
Vaccination strategy		
No. of days until vaccine was available	4	Model assumption
Radius of vaccination area (Km)	5, 10, 25, 50	Alternative scenarios
Days until vaccine was protective	4	References No. 30–32
Herd-level vaccine efficacy (*VE*) of infection (%)	Uniform (minimum = 80, maximum = 90)	References No. 33 and 34
Percentage reduction in herd infectiousness	1 – *VE*	Model assumption
Preemptive slaughter		
No. of herds with highest exposure	1, 5, 10	Alternative scenarios
All herds within specified radius of an infected herd (km)	1, 3, 5	Alternative scenarios

*Multiple simulations were performed for sensitivity analysis. †Opinions obtained from 10 emergency-response experts familiar with the 3-county region. ‡Values reported for BetaPERT distributions are minimum, most likely, and maximum.

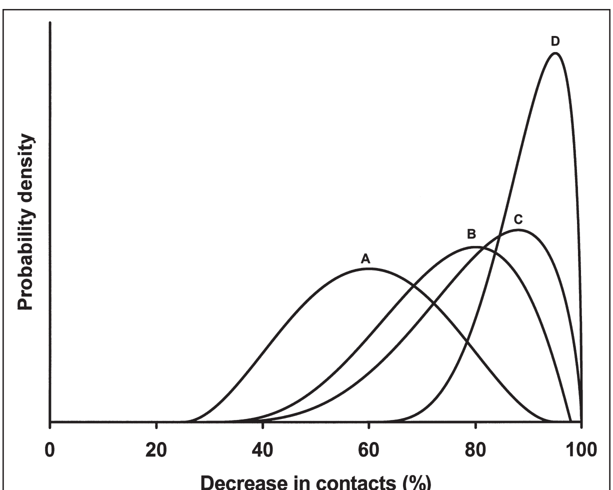

Figure 4—Probability density functions of the expected percentage decrease following implementation of control measures for indirect (A) and direct (B) contact within a surveillance zone and for the percentage decrease in indirect (C) and direct (D) contact in an infected area. Estimates were obtained from a survey that elicited the opinions of several experts.

most likely, 98) (**Table 3**; **Fig 3**). However, there was more variability in the estimated probabilities of transmission by indirect contact. Ranges (maximum minus minimum) for the other parameter estimates were 29, 40, and 80% for low-risk indirect contact with personnel, low-risk indirect contact with vehicles, and high-risk indirect contact, respectively. Most likely values for the probability of transmission among swine herds were 25, 30, 50, and 97.5% when considering low-risk indirect contact by personnel, low-risk indirect contact by vehicles, high-risk indirect contact by animal health personnel, and direct animal contact, respectively.

Probability of herd contact after implementation of baseline control strategy—Minimum, median, and maximum estimates for the 17 participants who responded to the second questionnaire were used to develop BetaPERT PDFs that described distributions of the opinions provided. Most likely percentage response for questions regarding potential reduction of direct contacts indicated a decrease of 95% for direct contacts in an infected area to a decrease of 88% for direct contacts in a surveillance zone (**Table 4**; **Fig 4**). Similarly, most likely percentage response for questions regarding the expected potential reduction in indirect contacts inside a surveillance zone ranged from a decrease of 80% for indirect contacts in an infected area to a decrease of 60% for indirect contacts in a surveillance zone.

Discussion

The model reported here was developed to allow analysis of various eradication strategies for FMD that could be used to slow or prevent transmission of FMDV in a 3-county region in California. Numerous factors that contribute to FMD epidemics make it difficult to predict the size and duration of an epidemic. These factors include the FMDV serotype and its associated host range and infective properties, type and number of index herds, number of direct and indirect animal contacts among herds, geographic distribution of herds, time lag before an initial diagnosis is made, effectiveness of the biosecurity practiced on livestock facilities, weather conditions, exposure of susceptible wildlife to FMDV, eradication strategy used by animal health personnel, cooperation of livestock producers, availability of funds for prompt and fair indemnity payments, ability of animal health personnel to promptly identify infected herds as well as to slaughter affected animals and dispose of the carcasses, and availability of personnel and materials necessary to clean and disinfect infected livestock facilities.

The FMD simulation model reported here accounted for many of these factors; however, the goal was not to predict the size of an epidemic in the 3-county study area if FMDV were to be introduced in that area. Rather, the goal was to evaluate potential eradication strategies. Because the study used a 3-county area and we were unable to estimate potential transmission to and from herds outside the study region, the model should be considered limited to use only for outbreaks in a specified area.

Spatial simulation models have been used to estimate rates of FMDV transmission among feral swine populations,[35,36] and investigators have developed models to analyze cost-effectiveness of alternative eradication and prevention strategies.[19,37-39] However, prior to the epidemic in the United Kingdom in 2001, we are aware of only 1 other study[40] in which investigators considered potential eradication strategies while estimating transmission of FMDV by use of the geographic location of all herds. The model[22] used to provide the estimates in that study was revised during the 2001 FMD epidemic in the United Kingdom and was used as a predictive tool to recommend an eradication policy during the 2001 epidemic. During the epidemic in the United Kingdom, a pseudospatial mathematical model[21] and another fully spatial model[41] also were developed by other investigators with the same goal of evaluating eradication programs for control of FMD.

The simulation model described in the study reported here differs in several ways from other models. Our model included 12 categories for herd size and species and 3 levels of contact risk for each herd category, which enhanced the ability of our model to mimic realistically the manner in which FMDV may be transmitted among various types of herds, particularly those within a study region.[25] Another distinction of the model used in the study reported here was that it did not rely on estimates of effective contact rates derived from the 1967 to 1968 epidemic of FMD in the United Kingdom. In other studies,[18,19,38,42,43] investigators have used the effective contact rates from that epidemic as the basis for their epidemic models, often without describing adjustments for potentially large differences in risk attributable to herd size, herd type, or livestock rearing practices. During development of our model, we instead considered a combination of data obtained during field study and opinions of experts solicited by use of a questionnaire to derive expected adequate contact rates that differed for each herd type and herd size on the basis of its location and expected number of contacts.

Another important aspect of the model reported here was the incorporation of specific herd locations, which have not been included in many FMD simulation models.[18-20] Ideally, a model should account for varying densities of herds within a region to adequately evaluate potential spatial disease transmission and geographically defined control measures, which cannot be accomplished without considering herd location and proximity of herds from each other. Because of strict US privacy laws, comprehensive data on herd location for a region as large as that in our study were not readily available. We were fortunate to have access to a data set that contained the specific location of herds, species, and herd size. Nevertheless, we still had to make some assumptions about the location of some beef herds, because those herds can be moved frequently. Although we included locations of 788 backyard herds, it is likely that some small herds were not documented in the data set. Collection of data on herd location can be expensive; however, collection and maintenance of data on precise location of each herd should be a goal of state and federal animal control agencies in the United States. Access to such data could assist in the rapid identification of herd owners during an outbreak of animal disease or a natural disaster. Information on size and type of herds located throughout New Zealand has been collected,[44] and similar data on livestock census were extremely valuable during the FMD eradication effort in the United Kingdom in 2001.

By considering the specific location, size, and species of each herd, the model also was able to calculate values of the risk for exposure to FMDV for susceptible herds and of the infectiousness for infected herds. At each time period in a simulation, the model recalculated the risk for exposure to FMDV for susceptible herds and the expected number of adequate contacts originating from infected herds. All values were considered independently for 3 potential modes of FMDV transmission (direct contact and high- and low-risk indirect contact) and were adjusted by considering the distance between herds as a function of expected distributions of animal contact. Although computationally intensive, adjustments made on the basis of distance enabled the model to mimic the manner in which FMDV may be spatially transmitted among herds in the study region, which provided a means to analyze specific spatial eradication strategies, such as implementation of an infected area with a radius of 10 km around known infected herds or use of a vaccination strategy within a radius of 25 km of known infected herds.

Distributions of responses of experts to a survey regarding the potential for FMDV transmission by direct and indirect contact were considered in the model reported here. Responses to a question were sometimes highly variable, which led to wide and flat probability distributions (Fig 3), likely reflecting the wide range of potential FMDV transmission scenarios that are realistically possible. It may also reflect a fair degree of uncertainty in our knowledge about FMD transmission. In either situation, more defined probability distributions that are less flat would have lessened uncertainty about model projections. Also, because the survey requested information only about transmission among swine and dairy cattle, results for dairy cattle were used when estimating transmission probabilities among all nonswine species. It is unclear how the application of survey results for transmission among dairy cattle to all nonswine species may have affected the model; however, it is likely that the probabilities of transmission for beef cattle and small ruminants were overestimated.

Estimates of potential percentage decreases in direct and indirect contact among herds within the study region for the assumption that FMD was diagnosed also were obtained from results of a survey of experts. The response rate to our second survey was much higher (85%) than for the initial survey on FMDV transmission (60%); however, analysis of our results indicated that there was a similar large variability for responses, possibly reflecting considerable uncertainty in the expected efficacy of baseline control measures. One important finding, however, was that experts expected 5% (ie, 100% minus 95%) and 12% (ie, 100% minus 88%) of the livestock movements prior to the FMD epidemic to continue within the infected area and surveillance zone, respectively (Table 4). This finding suggested less-than-complete confidence in the willingness of herd owners to adhere to restrictions on livestock movement and in regulatory animal health personnel being able to completely enforce restrictions on livestock movement in controlled areas. The importance of the ability to totally stop animal movement has been illustrated in the Netherlands, where illegal livestock movement may have contributed to delays in eradicating classical swine fever.[45]

When incomplete information is available to assist analysis of a problem, simulation models can be useful tools because they allow incorporation of uncertainty as modeling parameters. By considering all available information, simulation models can assist in finding an acceptable solution to consider "what if"-type questions by consolidating information into relevant parameters and distributions. Results of the model frequently do not yield a unique answer, as would be the result of a deterministic mathematical model; rather, results are reported as distributions that reflect the uncertainty and variability in the information provided.

When applied to FMDV transmission, simulation models that consider information on animal contacts and probability distributions can estimate hypothetical FMDV transmission while incorporating parameters with uncertain and variable information, such as that developed from field studies and opinion surveys of experts. The spatial stochastic epidemic simulation model reported here was developed to facilitate simulation of potential herd-to-herd transmission, allowing evaluation of multiple possible strategies to eradicate FMD prior to an actual outbreak of FMD. Results of comparisons of the use of this model for various control scenarios are reported elsewhere.[24]

[a]Wilson T, USDA, Animal and Plant Health Inspection Service, Veterinary Services, Emergency Services, and the Armed Forces Medical Intelligence Center, Riverdale, Maryland, and Thurmond M, University of California, Davis:Personal communication, 2001.

[b]BestFit, version 2.0, Palisades Corp, Newfield, NY.

[c]Visual Basic, version 6.0, Microsoft Corp, Redmond, Wash.

[d]Risk development kit, version 3.5, Palisades Corp, Newfield, NY.

[e]SAS/STAT, version 8.1, SAS Institute Inc, Cary, NC.

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