Am. J. Trop. Med. Hyg., 66(2), 2002, pp. 186–196

MODELING RELATIONSHIPS BETWEEN CLIMATE AND THE FREQUENCY OF HUMAN PLAGUE CASES IN THE SOUTHWESTERN UNITED STATES, 1960–1997

RUSSELL E. ENSCORE, BRAD J. BIGGERSTAFF, TED L. BROWN, RALPH F. FULGHAM, PAMELA J. REYNOLDS, DAVID M. ENGELTHALER, CRAIG E. LEVY, ROBERT R. PARMENTER, JOHN A. MONTENIERI, JAMES E. CHEEK, RICHIE K. GRINNELL, PAUL J. ETTESTAD, AND KENNETH L. GAGE

Division of Vector-Borne Infectious Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Fort Collins, Colorado; Vector Control Program, New Mexico Environment Department, Santa Fe, New Mexico; Office of Environmental Health and Engineering, Navajo Area, Indian Health Service, Window Rock, Arizona; Vector-Borne and Zoonotic Disease Section, Arizona Department of Health Services, Phoenix, Arizona; Department of Biology, University of New Mexico, Albuquerque, New Mexico; Epidemiology Branch, Headquarters West, Indian Health Service, Albuquerque, New Mexico; Office of Environmental Health and Engineering, Albuquerque Area, Indian Health Service, Albuquerque, New Mexico; Office of Epidemiology, New Mexico Department of Health, Santa Fe, New Mexico

Abstract. The relationships between climatic variables and the frequency of human plague cases (1960–1997) were modeled by Poisson regression for two adjoining regions in northeastern Arizona and northwestern New Mexico. Model outputs closely agreed with the numbers of cases actually observed, suggesting that temporal variations in plague risk can be estimated by monitoring key climatic variables, most notably maximum daily summer temperature values and time-lagged (1 and 2 year) amounts of late winter (February–March) precipitation. Significant effects also were observed for time-lagged (1 year) summer precipitation in the Arizona model. Increased precipitation during specific periods resulted in increased numbers of expected cases in both regions, as did the number of days above certain lower thresholds for maximum daily summer temperatures (80°F in New Mexico and 85°F in Arizona). The number of days above certain high-threshold temperatures exerted a strongly negative influence on the numbers of expected cases in both the Arizona and New Mexico models (95°F and 90°F, respectively). The climatic variables found to be important in our models are those that would be expected to influence strongly the population dynamics of the rodent hosts and flea vectors of plague.

INTRODUCTION

Plague is a zoonotic disease caused by the bacterium *Yersinia pestis.* The natural cycle involves transmission between various rodent species and their fleas. Most human cases result from exposures to infectious flea bites. Smaller numbers of cases are acquired through direct contact with infected animals or, rarely, inhaling infectious materials.[1] During the period of the study (1960–1997), 381 laboratory-confirmed cases of human plague occurred in the United States (mean = 10.0 cases per year, SD = 8.5 cases per year, range = 0–40 cases per year). Two hundred sixty-four (69.3%) of these cases were reported from the southwestern states of Arizona (15.0%) and New Mexico (54.3%). Most of these southwestern cases occurred in two distinct foci, one located in north-central New Mexico and another found in northwestern New Mexico and northeastern Arizona (Plague Section, Centers for Disease Control and Prevention [CDC], Fort Collins, CO, unpublished data).

The number of cases that occur in these southwestern foci fluctuates markedly from year to year (CDC, unpublished data). The reasons for these fluctuations are poorly understood but probably involve factors that affect the likelihood of humans being exposed to infectious fleas. The risk of infectious flea exposure is believed to be highest when plague epizootics decimate populations of certain highly susceptible rodents, forcing infected fleas to seek new hosts to replace those killed by plague. The most threatening epizootics in the Southwest occur among various ground squirrels, prairie dogs, chipmunks, and wood rats.[2,3]

Existing evidence suggests that epizootics occur most frequently when rodent and flea populations are high.[1] Many factors can affect rodent population dynamics, including food availability, disease, and climatic variables, such as precipitation and temperature.[4–12] Seasonal fluctuations in the abundance of certain flea species also have been reported to be correlated with precipitation and temperature changes.[13–17] Additionally, the ability of fleas to transmit *Y. pestis* has been demonstrated to be temperature-dependent, with high temperatures (≥ 81.5°F, ≥ 27.5°C) resulting in reduced rates of transmission.[18–21]

Seasonal shifts in precipitation, humidity and temperature also have been reported to affect the course of plague epidemics.[21,22] However, published attempts to relate the frequency of human plague cases to year-to-year variations in these or other climatic variables are scant and have not examined the effects of multiple climatic variables such as precipitation and temperature. Dubyansky and others[23] analyzed the occurrence of human plague (n = 9) in the Aral-Karakum plague focus of Kazakhstan during the interval 1956–1989. Precipitation amounts were below average for six of the seven years when cases were identified, but had been higher than normal one or two years before the cases occurred. Recently, Parmenter and others[24] demonstrated that human plague cases in New Mexico (n = 215) occurred more frequently following winter-spring periods with above-average precipitation.

In this study, we use Poisson regression to investigate the effects of climatic variables (threshold temperature measures and seasonal precipitation amounts) on the frequency of human plague in one of the two foci mentioned above (northwestern New Mexico and northeastern Arizona). We also discuss the implications of these modeling results for the epidemiology, epizootiology, and prevention of plague in this foci.

MATERIALS AND METHODS

Study area. The study area consisted of a Palmer Drought Region in northwestern New Mexico (New Mexico Region

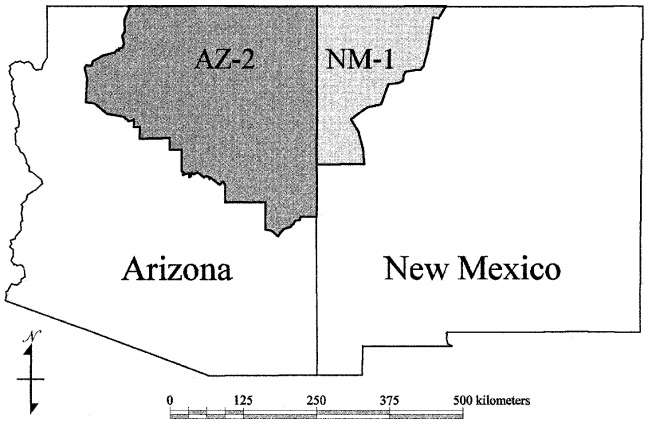

FIGURE 1. Arizona and New Mexico with shaded study areas (Palmer Regions: New Mexico 1 and Arizona 2) used in modeling.

1) and an adjoining Palmer Drought Region in northeastern Arizona (Arizona Region 2). Palmer Drought Regions have been developed by the National Oceanic and Atmospheric Administration (NOAA) for purposes of monitoring drought activity in different areas of the United States, and boundaries generally adhere to regional drainage patterns. Certain climatic data are associated with each Palmer Drought Region, including an estimate of monthly precipitation derived from data collected at many NOAA weather stations throughout the region. The boundaries of the two regions used in our study are shown in Figure 1 (NOAA, unpublished data).

The predominant habitats in each of the two Palmer Regions is Great Basin grassland and Great Basin desert scrub. Much of this semi-arid region has been severely over-grazed, leading to the invasion of woody shrub species and junipers. Pinon-juniper woodland becomes more common as the elevation increases and eventually gives way to ponderosa pine at higher elevations.[25] The mean annual precipitation (1959–1997) in New Mexico Palmer Region 1 is 11.40 inches (289.6 mm), and is 14.96 inches (380.0 mm) for Arizona Palmer Region 2. New Mexico Palmer Region 1 consists of 13,684 square miles (35,442 square km) and a population of 156,701 (11.5 persons per square mile). Arizona Palmer Region 2 consists of 39,777 square miles (103,023 square km) and a population of 106,417 (2.7 persons per square mile) (NOAA, unpublished data). The New Mexico region contains a higher proportion of pinon-juniper woodland than the Arizona region, which is somewhat lower in elevation and contains proportionately more desert scrubland.[25]

Plague cases. Human cases were selected as an indicator of regional plague activity because of the lack of comprehensive and systematic sampling of flea, rodent, and vegetation populations in these regions during the study period. Each case included in the study was laboratory confirmed, according to criteria described elsewhere,[26] and was determined to have been exposed to *Y. pestis* infection at a site within one of the two study areas described above. For the period 1960–1997, a total of 53 cases occurred in Arizona Palmer Drought Region 2 and 45 cases occurred in New Mexico Palmer Drought Region 1, representing 25.7% of all cases reported in the United States during this period. Probable exposure sites were identified from routine case investigation files maintained by CDC. Identification of the probable exposure site for each case was based on travel and activity history, as well as findings of environmental investigations (CDC, unpublished data). The locations in longitude and latitude (rounded to the nearest ten-thousandths of a degree, or about 11 m) of these sites were later determined through site visits and use of Global Positioning System units.

We chose 1960 as a temporal starting point for including cases because this is when investigators began to collect detailed case investigation data in this region. All but one of the 99 cases reported from the study area occurred in the period covered by our study (1960–1997). Inspection of the weekly distribution of cases during this period indicated a gap in the frequency of case onset dates occurring in mid-June (CDC, unpublished data), which also corresponded to a severe dip in mean monthly precipitation.[25] For the purposes of our analysis, a ''plague year'' was defined as occurring from June 16 of a given year through June 15 of the following year; cases were assigned to particular years of occurrence based on their date of illness onset.

Climate data. Monthly precipitation values for each Palmer Drought Region (1959–1997) were obtained from the NOAA. Maximum daily temperature data (1959–1997) were obtained for a centrally located NOAA, National Weather Service (NWS) reporting station in each Palmer Drought Region. Single station data varied within each region primarily as a function of elevation. However, stations exhibited strongly linear relationships making the chosen stations predictive for the designated regions. For Arizona Palmer Drought Region 2, we obtained a complete record for this variable from data for the Winslow Municipal Airport NWS station (35°2′ N, 110°43′ W). For New Mexico Palmer Drought Region 1, maximum daily temperature data were available for the Gallup Municipal Airport NWS station (latitude 35°31′ N, longitude 108°47′ W) for the period 1973–1997. Data were unavailable from the Gallup station prior to 1973, but were available for the Zuni FAA Beacon NWS station (35°4′ N, 108°50′ W) for the period 1959–1972. Zuni station data were not used for the entire period of the study because data were unavailable after 1972. Although no time overlap in data collection occurred between these two stations, weather at the Zuni station was believed to be comparable to that observed at the Gallup site over this period. The two stations are located only 23.4 miles (37.72 km) apart and differ in elevation by only 24 feet (7.3 m). Data for each station were obtained from the NOAA[27] (NOAA, unpublished data). As previously stated (see Study area), precipitation data were obtained from NOAA and were based upon compiled station records within the Palmer Drought Regions.

Missing data. The record of human plague cases is complete, as are the records for regionally compiled precipitation for the two Palmer Drought Regions considered. The records of daily maximum temperatures at the sites above contained a relatively small number of days with missing values. For Arizona Region 2, the total number of missing values, in 38 years, is 21 days (0.15% of total values) and all missing values are from 1996. For New Mexico Region 1, the total number of missing values, in 38 years, is 101 days (0.73%

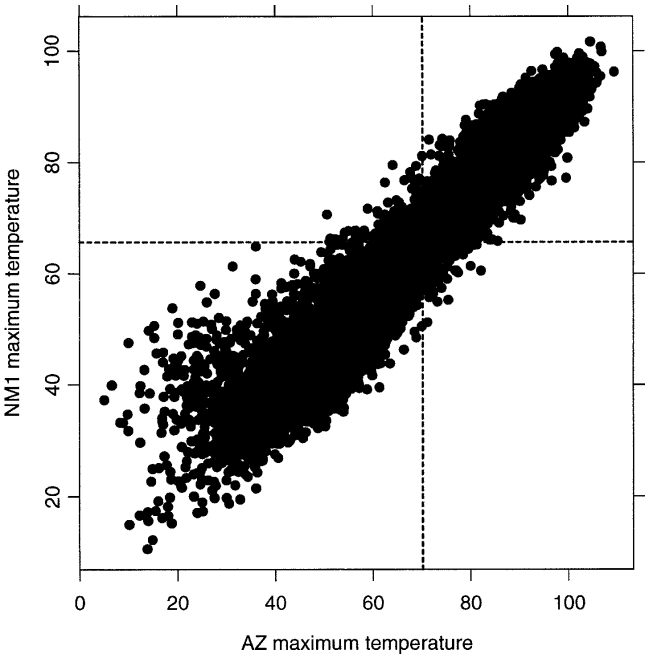

FIGURE 2. Daily maximum temperature relationships for New Mexico Region 1 stations (Gallup and Zuni) and Arizona Region 2 station (Winslow). The dashed lines (-----) mark the mean values for each region.

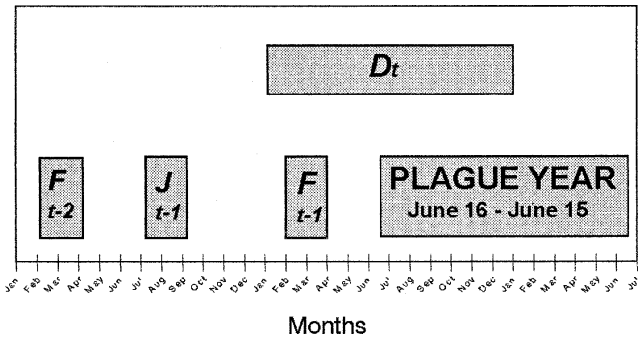

FIGURE 3. Diagram of the temporal relationships between model parameters: F_{t-2} (February–March total precipitation two-year lag), J_{t-1} (July–August total precipitation one-year lag), F_{t-1} (February–March total precipitation one-year lag), D_t^T (degree days in current calendar year at temperature T), and the modeled plague year t.

of the total values) and 91 of those occurred in April–June 1982.

Because we use as covariates the numbers of days in a calendar year above prescribed temperatures, referred to hereafter as ''degree days,'' we must address missing daily maximum temperatures, particularly in the summer months. A strong, reasonably linear relationship for the daily maximum temperatures is apparent between the sites, as can be seen in Figure 2. This can be used to account for missing values in the models described below.

Among the several approaches available for dealing with missing data,[28] we chose multiple imputation. Missing values are imputed (predicted) by using predictive distributions based on a model for relationships observed. These imputes are used in place of the missing values to create a completed data set of daily maximum temperatures. Several different such completed sets are analyzed, and models from these separate analyses are averaged to produce a final model. We used three completed data sets in our analyses. This number has been demonstrated to be sufficient for most analyses,[28] and since the observed relationships in the daily maximum temperatures are so strong (Figure 2), we have confidence that this number of completed data sets is sufficient. The imputations were computed by using the software of Shafer[28] in the statistical computing package S-Plus (S-Plus 4.5 Professional, Release 2, Mathsoft, Inc., Seattle, WA); S-Plus was used for all subsequent statistical modeling.

Statistical modeling. Let N_t be the number of cases of human plague in plague year t, F_t be the sum (inches) of the February and March precipitation for plague year t, and J_t be the sum (inches) of the July and August precipitation for plague year t. For the precipitation covariates, other combinations of months were considered, but the sums for February–March and July–August provided the best fit. Finally, let D_t^T represent the degree days variable for calendar year t and temperature T, i.e., let D_t^T be the number of days in calendar year t above temperature T, for $T = 80$, 85, 90, 95, and 100°F (26.7, 29.4, 32.2, 35, and 37.8°C, respectively). Exploratory analyses suggested that N_t depends on yearly time-lagged values of F_t and J_t, so we included these directly as covariates (see below). Figure 3 illustrates the temporal relationships between the plague year, the time-lagged precipitation variables, and the degree days calendar year.

To model the influence of the covariates F_t, J_t and D_t^T on N_t, we assumed that N_t follows a Poisson distribution with mean λ_t, where

$$\ln \lambda_t = \mu + \beta_0 F_t + \beta_1 F_{t-1} + \cdots + \beta_r F_{t-r} + \theta_0 J_t + \theta_1 J_{t-1} + \cdots + \theta_s J_{t-s} + \delta_{T1} D_t^{T1} + \delta_{T2} D_t^{T2} + \cdots + \delta_{Tq} D_t^{Tq} \quad (1)$$

and μ, $\beta = (\beta_1, \ldots, \beta_r)$, $\theta = (\theta_1, \ldots, \theta_s)$, and $\delta = (\delta_{T1}, \ldots, \delta_{Tq})$ are parameters to be estimated.

The parameters μ, β, θ, and δ were estimated via maximum likelihood by using iteratively weighted least squares.[29] Model selection, that is, the number of lags r of F_t and s of J_t to include, as well as which temperature variables D_t^T are relevant, was carried out by using a combination of the Akaike Information Criterion (AIC) statistic together with analysis of deviance. The AIC statistic is a likelihood-based measure that penalizes models with too many parameters.[30,31] Nested models were used to determine r, s, and the D_t^T by choosing the fit with the smallest AIC, then this model was tuned using analysis of deviance.

The Poisson distributional assumption implies that the variance of N_t is $\mathrm{Var}[N_t] = \lambda_t$. However, several researchers have noted that in practice it is often more reasonable to assume there is more variation than this assumption permits.[29,30,32] Inspection of residual plots led us to consider expanding the model by adding a parameter ϕ such that $\mathrm{Var}[N_t] = \phi\lambda_t$.[29] Under this assumption, we estimated the regression parameters μ, β, θ, and δ in this extended model by using maximum quasi-likelihood, and we estimated ϕ by using a standard moment estimator derived from the Pearson residuals.[29] We performed a score test of the hypothesis H_0: $\phi = 1$ for the stated variance function with methods given by

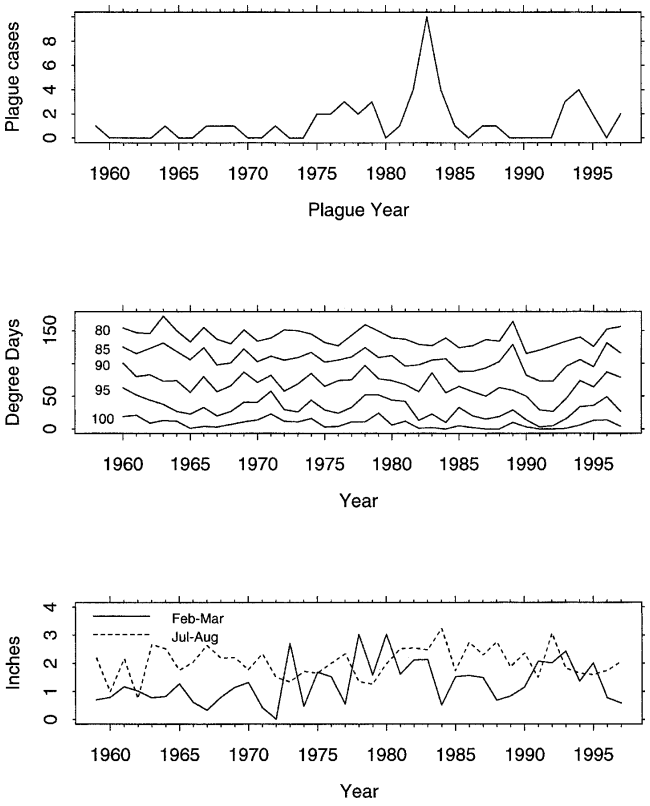

FIGURE 4. Plots of the number of human plague cases by plague year, degree day values, February–March precipitation totals, and July–August precipitation totals for Arizona Palmer Region 2.

Dean.[32] Furthermore, we computed a confidence interval based on a chi-squared approximation[29] to the distribution of this moment estimator.

Models were compared by using asymptotic (quasi-) likelihood ratio tests. Model assumptions were critiqued using residual analyses. In particular a check for serial correlation in the deviance residuals was made, and randomized quantile residual analyses were performed.[33]

Alternative models for N_t are available that mix methods from time series analysis and generalized linear models theory.[30,34–36] These methods were investigated, but the model presented proved the best in both fit and biological interpretation. We therefore refrain from describing other models in detail and will not refer to them in the remainder of the paper.

RESULTS

Arizona Palmer Region 2. Plots of the numbers of human plague cases, February–March and July–August precipitation, and the number of days above 80, 85, 90, 95, and 100°F for Arizona Palmer Region 2 are given in Figure 4. Visible similarities between the series exist, though the nature of the relationships is not obvious. Preliminary analyses suggested that no more than four annual lags of F_t and J_t were necessary to consider. Fitting the model in Equation 1 to these data resulted in the minimum AIC model containing F_t at lags 1 and 2, J_t at lags 0 and 1, along with D_t^T for temperatures 90, 95, and 100°F. The estimates of the coefficients and their standard errors are reported in Table 1. Table 1 also provides the analysis of deviance results for the fitted coefficients with the asymptotic χ^2 P values to test the hypotheses that the associated coefficients are 0, given all the preceding variables are in the model. The coefficient for J_t is not significant ($P = 0.65$), given the values for F_{t-1} and F_{t-2}, and when the model is re-fit without J_t, the P value for the test that the coefficient of D_t^{100} equals 0 is 0.11, also not significant. These two coefficients' joint contribution to the fit were evaluated by comparing it (using the likelihood ratio test) to the sub-model containing the remaining variables only ($P = 0.08$). Since these two variables did not contribute significantly to the fit, we retained the simpler model containing only the other five variables, resulting in the final model for Arizona Region 2 given in Table 2 and shown in Equation 2; their standard errors and the analysis of deviance for this model are also given in Table 2.

$$\ln \lambda_t = -5.90 + 0.68\, F_{t-1} + 0.66\, F_{t-2} + 0.61\, J_{t-1} + 0.06\, D_t^{90} - 0.05\, D_t^{95} \quad (2)$$

Overdispersion was not apparent, since the residual deviance of 30.40 for the final model was slightly less than the residual degrees of freedom (31). The point estimate for ϕ in the extended (quasi-likelihood) model, in which $\mathrm{Var}[N_t] = \phi\lambda_t$, was 0.89. The score test of the hypothesis $\phi = 1$ yielded a P value of 0.72 and a 95% confidence interval (CI) for ϕ of 0.57 − 1.58. Based on these results, we retained the strict Poisson model with $\mathrm{Var}[N_t] = \lambda_t$.

Figure 5 presents a plot of the fitted values and 95% CI for λ_t from the final model along with the observed numbers of cases. The fitted values follow the observed values well, with the fitted curve closely tracking the relatively large spike in cases observed in plague year 1982 (June 16, 1982–June 15, 1983).

TABLE 1
Minimum Akaike Information Criterion model and analysis of deviance for Arizona Palmer Region 2

Coefficient	Estimate	Standard error	Degrees of freedom (df)	Deviance	Residual df	Residual deviance	P
Null (μ)	−4.95	1.73			36	82.85	
β_1	0.74	0.22	1	11.05	35	71.80	0.001
β_2	0.86	0.24	1	14.11	34	57.69	<0.001
θ_0	−0.66	0.42	1	0.21	33	57.47	0.65
θ_1	0.61	0.38	1	7.08	32	50.39	0.01
δ_{90}	0.08	0.02	1	13.22	31	37.16	0.003
δ_{95}	−0.12	0.04	1	8.11	30	29.05	0.004
δ_{100}	0.11	0.06	1	3.64	29	25.42	0.06

TABLE 2
Final model and analysis of deviance for Arizona Palmer Region 2

Coefficient	Estimate	Standard error	Degrees of freedom (df)	Deviance	Residual df	Residual deviance	*P*
Null (μ)	−5.90	1.42			36	82.85	
β_1	0.68	0.22	1	11.05	35	71.80	0.001
β_2	0.66	0.22	1	14.11	34	57.69	<0.001
θ_1	0.61	0.36	1	7.29	33	50.40	0.01
δ_{90}	0.06	0.01	1	12.72	32	37.68	<0.0001
δ_{95}	−0.05	0.02	1	7.28	31	30.40	0.01

Analysis of the residuals indicated no serious violations of the remaining modeling assumptions. Although auto-correlation was observed in the response series N_t, none was apparent in the deviance residuals. While the model's output closely fitted the value of nine cases observed in plague year 1982, this value does not exert undue influence on the fit since there is a corresponding spike in the covariates, particularly the difference between the degree days' variable for temperatures 90°F and 95°F for this same year.

New Mexico Palmer Region 1. The analysis here closely followed that for Arizona Palmer Region 2, and the final model is seen to have a similar form. Figure 6 contains plots of the numbers of human cases, February–March precipitation, July–August precipitation, and the degree days' series for New Mexico Palmer Region 1. As in Arizona Palmer Region 2, general patterns may be spotted here, though not all are obvious. The fit of the original model to these data with minimum AIC contained F_t at lag 2, along with D_t^T for temperatures 85°F, 90°F, and 100°F. The coefficient for D_t^{100} was not significant ($P = 0.21$) given that the other variables are in the model, and the analysis of deviance for the fit without D_t^{100} is given in Table 3.

The coefficient for D_t^{85} is not significant ($P = 0.36$), given that F_{t-2} is in the model, while that for D_t^{90} is significant, given that the previous two are in the model. The likelihood ratio test was used to evaluate the contribution of D_t^{85} to the fit with both F_{t-2} and D_t^{90} in the model, yielding a P value for this comparison of 0.02. We therefore retained D_t^{85}, resulting in the final model for New Mexico Palmer Region 1 that contains the coefficients listed in Table 3 and shown in Equation 3.

$$\ln \lambda_t = -3.69 + 1.40F_{t-2} + 0.06D_t^{85} - 0.06D_t^{90} \quad (3)$$

As shown in Table 3, the residual deviance for the fit is

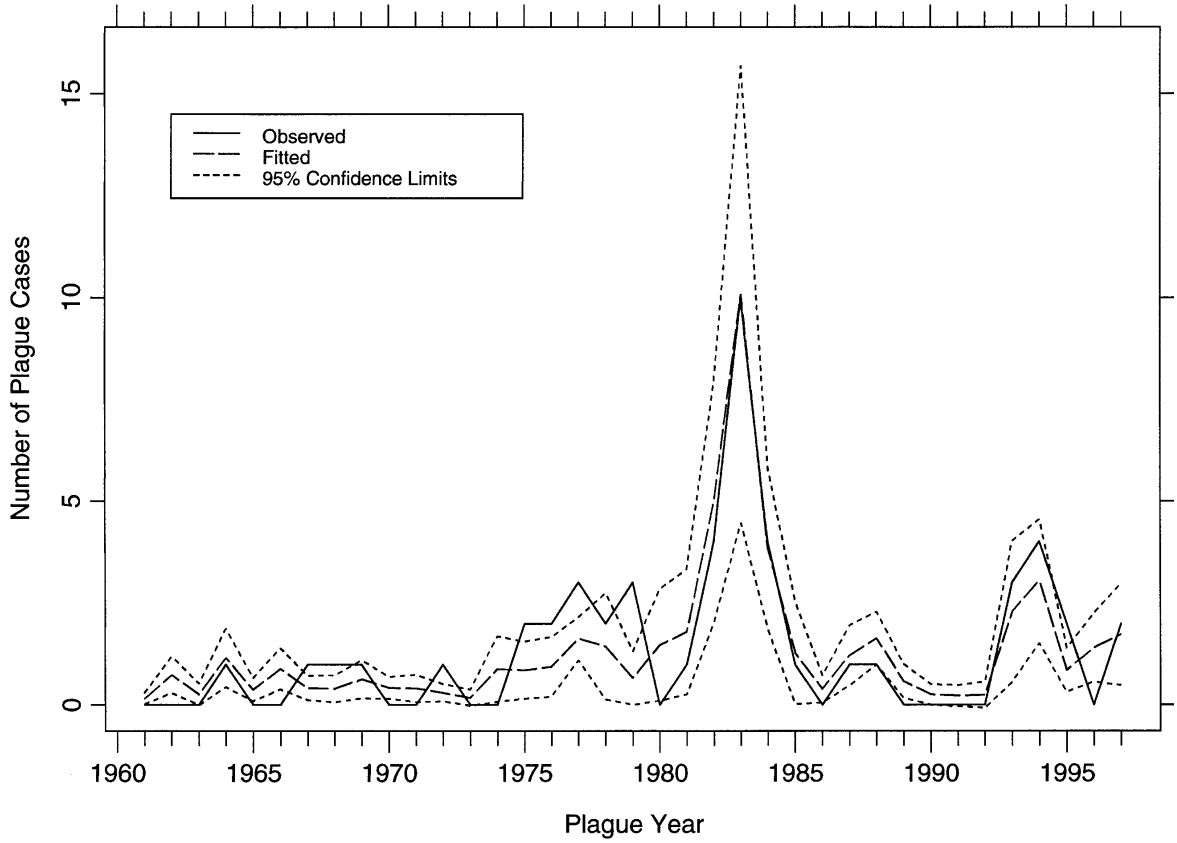

FIGURE 5. Arizona Palmer Region 2 model fit showing observed (actual) numbers of cases (solid line) and fitted (model output) numbers of cases (dashed line) for plague years 1960–1997. Upper and lower 95% confidence limits for the mean function are also shown.

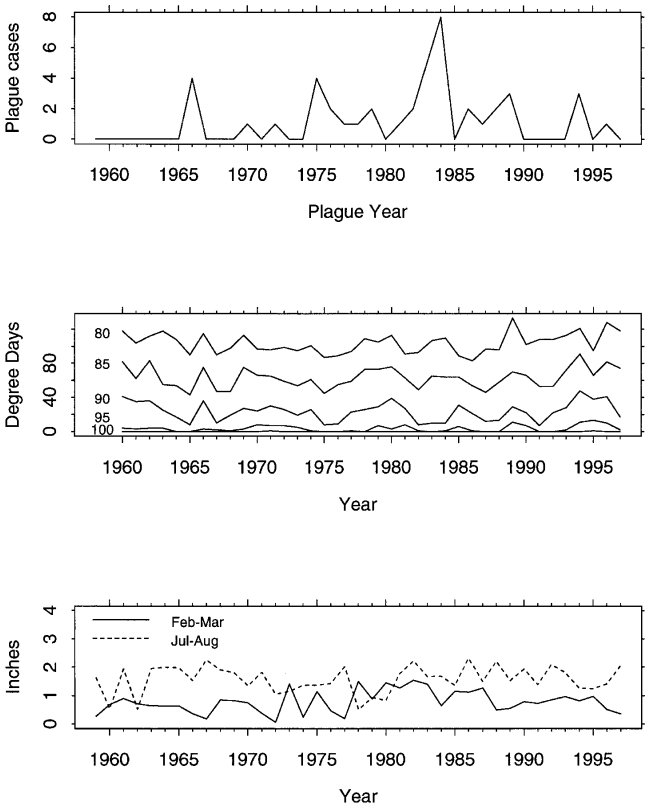

FIGURE 6. Plots of the number of human plague cases by plague year, degree day values, February–March precipitation totals, and July–August precipitation totals for New Mexico Palmer Region 1.

53.14 on 33 degrees of freedom, suggesting the presence of overdispersion. By refitting the model using maximum quasilikelihood and the variance function $\mathrm{Var}[N_t] = \phi\lambda_t$, we estimated ϕ as 1.61 with a 95% CI = 1.05–2.80. The score test of the hypothesis H_o: $\phi = 1$ yielded a P value of 0.02, also indicating significant overdispersion. We therefore corrected the standard errors for the parameter estimates in Table 3 by inflating them by $\sqrt{1.61}$ (square root of variance = standard deviation); this correction is incorporated in the corrected standard errors in Table 3, and updated analyses of deviance P values from the appropriate F-test are also given there. Residual analyses indicated no serious violations of the model assumptions.

Figure 7 presents a plot of the fitted values and 95% CIs for λ_t from the final model along with the observed number of cases. Clearly, this fit is not as good as that for Arizona Palmer Region 2, as reflected numerically in the large residual deviance. While the major spike was picked up by the model, the remaining spikes were not fitted as well.

In an effort to improve the fit, we expanded the final models by including interactions between the precipitation and temperature variables; however, none of these expanded models significantly improved the model fits.

DISCUSSION

The influence of climatic events on the incidence of vector-borne and zoonotic disease in humans has recently been the subject of an increasing number of studies and much speculation.[24,37–42] Our models indicated a close relationship between the frequency of human plague cases in the southwestern United States and values for certain climatic variables. Time-lagged (two-year lags) precipitation for the months of February and March strongly influenced the outputs of both models, where more precipitation was associated with larger numbers of expected cases. One-year lag effects for precipitation in February–March and July–August also were important in the Arizona model. Temperature-related covariates were particularly important for fitting the models to the observed case data, and differences between certain degree days' covariates ($D_t^{90} - D_t^{95}$ for Arizona and $D_t^{85} - D_t^{90}$ for New Mexico) appeared to be key contributors to the fit of both models. As shown in plots of these variables (standardized) for the Arizona and New Mexico study areas, the shape of the difference variable closely followed the observed numbers of cases and was particularly noticeable during the 1982 and 1983 plague years, when large spikes occurred in the number of reported plague cases (Figures 8 and 9). These observations suggest that the numbers of plague cases will be relatively high when summer temperatures are relatively cool and time-lagged values for February–March precipitation are high.

While it is clearly beyond the scope of our paper to imply causality, consideration of the biological plausibility of our findings is important. Our modeling results could be explained by many factors, including the effects of climate on rodent and flea populations. Unusual climatic events have been reported to be associated with large fluctuations in rodent populations.[8,12,43–46] Variations in temperature and precipitation are known to affect the growth of plant[5,47–49] and insect[50–53] populations, both of which are important food sources for rodents in the Southwest.[54–56]

At least some lag time can be expected to occur between the appearance of favorable environmental conditions and the occurrence of rodent population increases or increased

TABLE 3

Minimum Akaike Information Criterion, final model, and analysis of deviance for New Mexico Palmer Region 1, with corrected standard errors

Coefficient	Estimate	Standard error	df *	Deviance	rdf †	Residual deviance	P	Corrected standard error	Corrected P
Null (μ)	−3.69	1.13			36	83.34		1.43	
β_2	1.39	0.41	1	18.68	35	64.66	<0.01	0.52	<0.01
δ_{85}	0.06	0.02	1	1.37	34	63.29	0.24	0.02	0.36‡
δ_{90}	−0.06	0.02	1	10.15	33	53.14	<0.01	0.02	0.02

* df = degrees of freedom.
† rdf = residual degrees of freedom.
‡ Parameter included based on results of tests for interdependence.

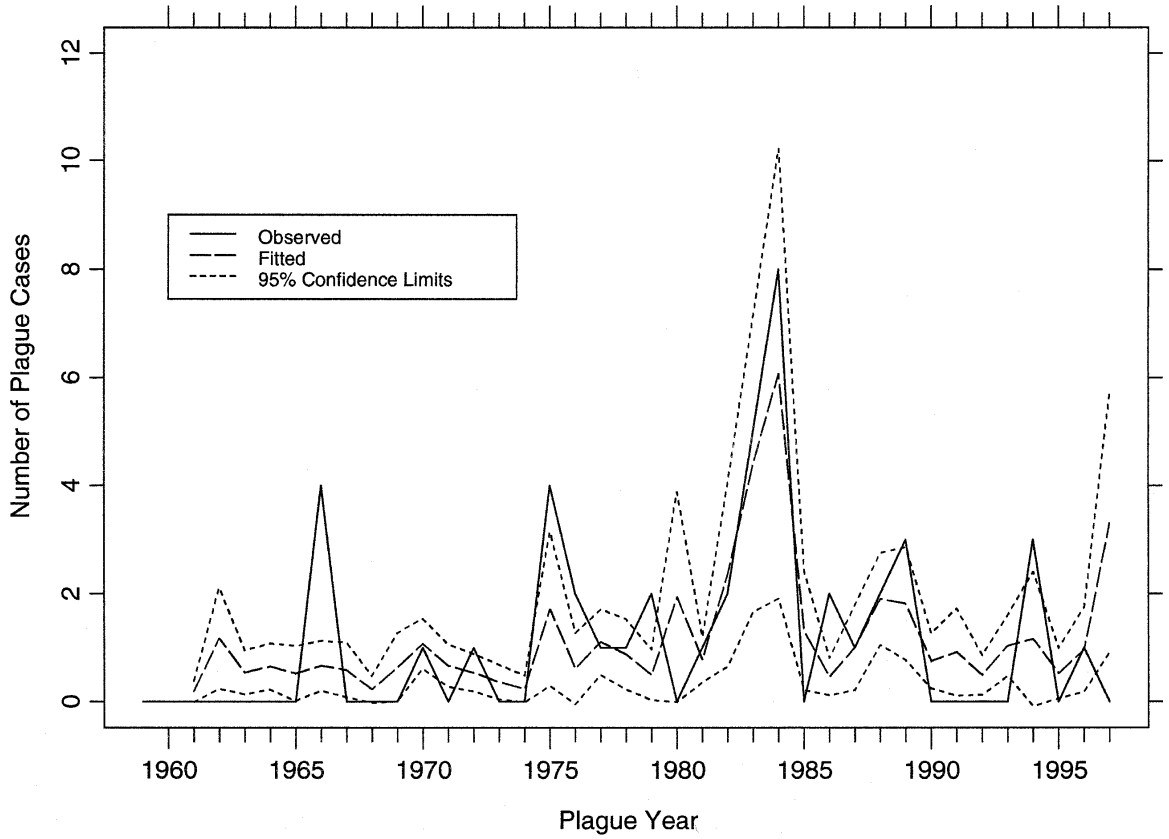

FIGURE 7. New Mexico Palmer Region 1 model fit showing observed (actual) numbers of cases (solid line) and fitted (model output) numbers of cases (dashed line) for plague years 1960–1997. Upper and lower 95% confidence limits for the mean function are also shown.

levels of plague transmission among these animals. However, the actual length of these lags will vary among different rodent species, depending upon the time to sexual maturity, litter size, number of litters that can be produced per year, gestation period, and the types of foods consumed.[8,12] Regardless of the reasons for any observed lags in rodent population responses, they could be epidemiologically significant and might explain the importance of the lagged precipitation values in our models. In the Southwest, the frequency of human cases is closely associated with epizootic activity among certain highly susceptible hosts of plague, particularly ground squirrels (*Spermophilus* spp. and *Ammospermophilus* spp.) and prairie dogs (*Cynomys* spp.)[1,2] (CDC, unpublished data). These epizootic hosts have relatively low reproductive rates compared to likely enzootic hosts, such as mice (*Peromyscus* spp.),[57–59] and more than one breeding season might be required for their populations to reach sufficient densities to support widespread epizootic transmission of *Y. pestis.*

It is also possible that the two-year time lag between precipitation events and the observed increases in human cases is related to factors affecting the spread of plague from enzootic hosts to those involved in the epizootic cycle of the disease. If one assumes that the rate of plague transmission among rodents is at least partially density dependent, it is reasonable to expect that as the densities of partially resistant enzootic hosts populations increase, so will the likelihood of plague spreading to more highly susceptible epizootic hosts, such as ground squirrels and prairie dogs. Although mice can exhibit a rapid numerical response to favorable environmental conditions, at least some lag time will occur before mouse densities reach the point where spread to epizootic hosts is likely. In central New Mexico, rodent populations have been shown to increase following periods of increased moisture, but peak populations typically lag the precipitation by 2–12 months.[12] These values are consistent with the results of the models reported here, and with the results of Parmenter and others[24] on precipitation and plague across New Mexico.

Threshold temperature variables exerted both positive and negative influences on the models' outcomes. Unlike the effects of the precipitation variables, however, those related to temperature were not time-lagged. It is possible that moderately high temperatures, as indicated by an increased number of degree days above the lower threshold temperature values (90°F in Arizona and 85°F in New Mexico), result in earlier onsets of seed germination or the seasonal growth and reproduction of important plant species. Moderately high temperatures also could positively affect the survival or timing of reproduction among the rodent hosts and flea vectors of plague, or accelerate the growth and development of fleas. Conversely, the survival or reproduction of rodents or fleas might be negatively impacted when the number of degree days above the higher temperature thresholds (95°F in Arizona and 90°F in New Mexico) increases. This should be particularly true for fleas, which are susceptible to desiccation during hot, dry conditions.[60] The ability of fleas to transmit plague also has been shown to be temperature-re-

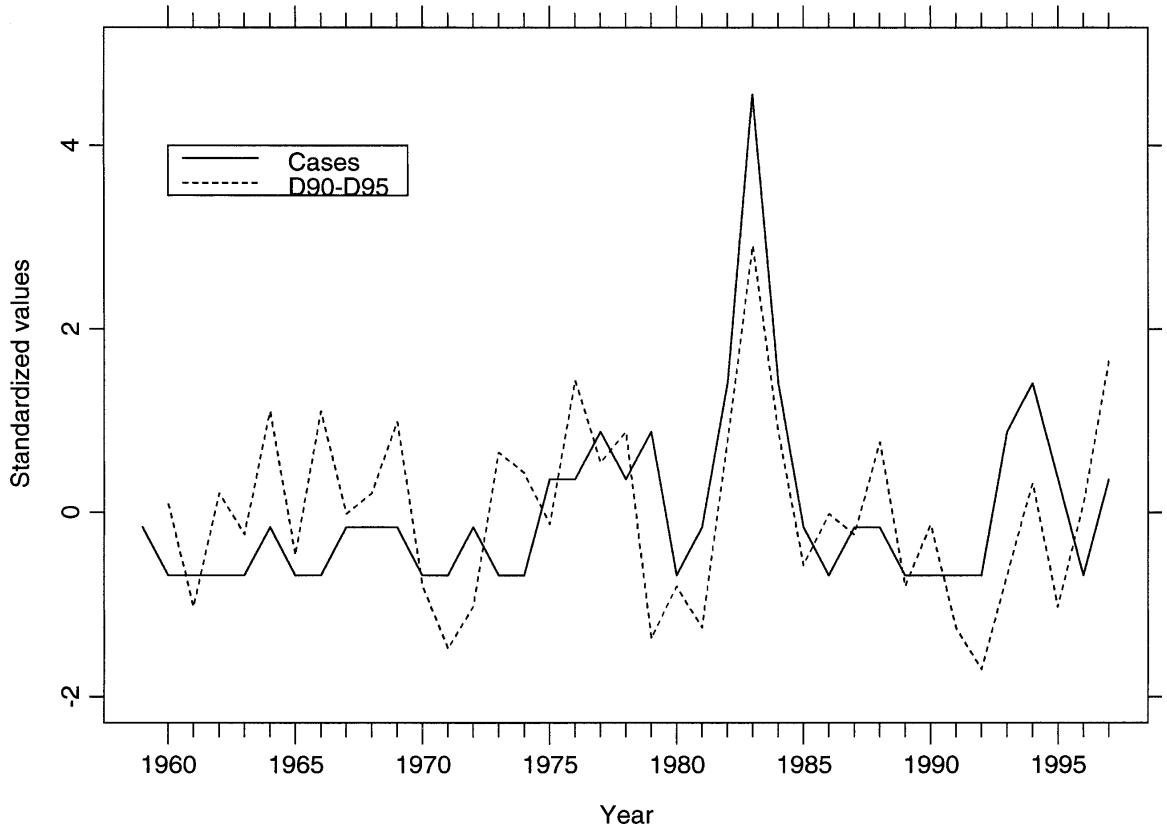

FIGURE 8. Standardized degree day differences ($D_t^{90} - D_t^{95}$) and standardized numbers of human plague cases for Arizona Palmer Region 2, 1960–1997.

lated, with prolonged exposures to temperatures above 81.5°F leading to a decreased proportion of fleas being ''blocked'' and, therefore, infectious.[21] Regardless of the mechanism for these temperature effects, other researchers have noted that hot, low-humidity conditions can result in cessation of epidemics or epizootic plague activity in some regions of Vietnam, India, and other plague-affected areas.[22,60,61]

The slight ecologic differences between the two Palmer Regions might explain the differences observed in the two models. New Mexico Region 1 has a higher percentage of pinon-juniper cover than Arizona Region 2, which contains a higher proportion of desert scrubland. These vegetative differences could result from variations in soils, groundwater availability, precipitation, temperature or other factors. New Mexico Region 1 lies primarily to the east and north of the Chuska Mountains and the Zuni Uplift, which might create a slight ''rainshadow'' effect and reduce the amount of precipitation falling from storms that sweep into the region from the Pacific Ocean to the west and southwest. The New Mexico region receives almost 24% less annual precipitation than its Arizona counterpart, which for the reasons described above, could be expected to influence the diversity, abundance, and survival of rodent and flea populations. The effect of climatic factors on these two regions also could affect the temporal appearance of rodent food sources or the timing and duration of periods favorable for the survival of adult fleas.

The modeling goals were to investigate relationships between climate and the temporal distribution of plague cases and to summarize these relationships succinctly with biologically plausible statistical models. The model-fitting procedure used reflects these goals, as selection criteria were based solely on fit, rather than on prediction. Use of the models for prediction is limited by these criteria, and because computation of the models' outputs for a given plague year requires concurrent temperature data, making direct, lead-time computation impractical. Development of predictive models that include both precipitation and temperature might still be possible, however, if sufficient improvements are made in the reliability of long-range seasonal temperature forecasts. It also might be possible to improve the fit of the models or their ability to be used in a predictive manner by incorporating other variables, such as humidity, rodent population data, greenness indices derived from remote sensing, or human land use and activity patterns. Regardless of which additional variables might be included, the close fit between the models' outputs and the observed numbers of cases suggests that the identified climatic variables account for much of the temporal variation noted in the frequency of human plague.

Despite the close fit of the models to the observed frequency of human plague in our study areas, several limitations to the interpretation of the modeling should be considered. The models considered are relatively complex for the length of data series available. The numbers of cases also were limited by occurrence of the disease, though our methodology's precision is mainly dependent on the number of

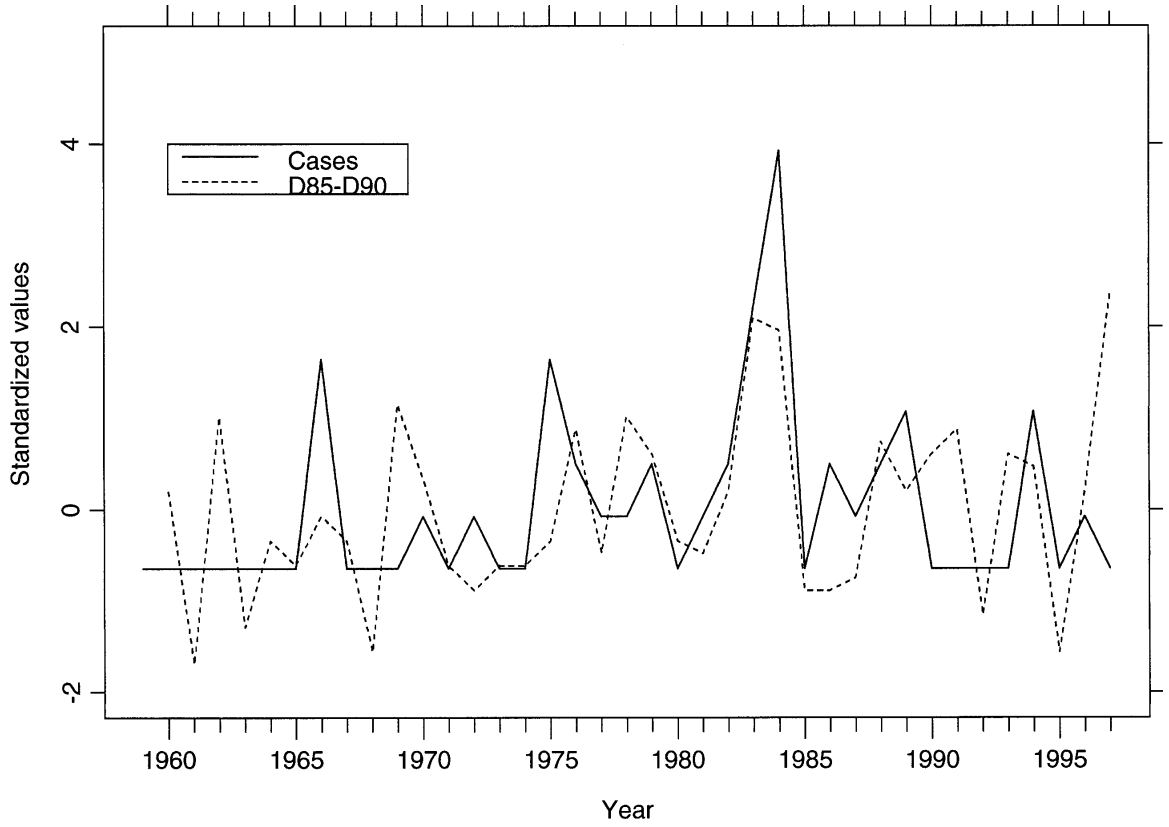

FIGURE 9. Standardized degree day differences ($D_t^{85} - D_t^{90}$) and standardized numbers of human plague cases for New Mexico Palmer Region 1, 1960–1997.

years observed. Aggregation of the data into a single model was considered, but model fit was sacrificed presumably due to local variations in the ecology and epidemiology of plague in both regions.

In conclusion, the close fit between the outputs of the models and the observed frequencies of human plague cases in our study suggests that precipitation and temperature strongly influence the epidemiology and epizootiology of plague in the American Southwest. The models described in this paper also can serve as a basis for further investigations of the actual mechanisms underlying the effects of temperature and precipitation on the transmission of plague among the rodent hosts and flea vectors of plague. Understanding how these climatic variables influence the ecology of plague in the two study areas also might help explain why the models for each region varied slightly. The climatic variables identified as being most important for fitting the models to the observed frequency of human cases are ones that are biologically relevant and can affect rodent and flea population dynamics. When favorable climatic conditions (mild summer temperatures and time-lagged increases in late winter precipitation) occur, they can be expected to lead to increased reproduction and survival rates among rodents and fleas. As populations of rodent hosts and flea vectors increase, so will the likelihood of epizootic transmission and the risk of human exposures to infectious fleas or animals. Although our current models are not intended to be predictive, it might be possible to develop similar ones that are predictive through the use of existing time-lagged precipitation data and long-range forecasts for summer temperatures. Attainment of such a goal should increase our ability to target limited plague prevention resources toward those situations where they are most likely to result in significant reductions in human plague risk.

Acknowledgments: We acknowledge those individuals from the Centers for Disease Control and Prevention, Indian Health Service, Arizona and New Mexico State Health Departments, and local health departments who participated in the epidemiologic and laboratory investigation of the plague cases included in this study. We also thank Dr. Larry Lèon (Environmental Risk Analysis, San Mateo, CA) for sharing his software for fitting Markov time series of counts and for helpful discussion, M. Samuel McCown (National Oceanic and Atmospheric Administration, National Climate Data Center, Asheville, NC) for assistance in climate data acquisition and interpretation, and Dr. Michael Kosoy (Centers for Disease Control and Prevention, Fort Collins, CO) for translating Russian articles on plague.

Authors' addresses: Russell E. Enscore, Brad J. Biggerstaff, John A. Montenieri, and Kenneth L. Gage, Division of Vector-Borne Infectious Diseases, Centers for Disease Control and Prevention, PO Box 2087, Fort Collins, CO 80522-2087. Ted L. Brown and Pamela J. Reynolds, Vector Control Program, New Mexico Environment Department, 525 Camino de los Marques, Suite 4, Santa Fe, NM 87501. Ralph F. Fulgham, Office of Environmental Health and Engineering, Navajo Area Indian Health Service, PO Box 9020, Window Rock, AZ 86515. Robert R. Parmenter, University of New Mexico, Department of Biology, 167 Castetter Hall, Albuquerque, NM 87131. David M. Engelthaler and Craig E. Levy, Arizona Department of Health Services, 3815 Black Canyon Highway, Phoenix, AZ 85015. James E. Cheek, Epidemiology Section, Indian Health Service Headquarters West, 5300 Homestead Road NE, Albuquer-

que, NM 87110. Richie K. Grinnell, Office of Environmental Health and Engineering, Nashville Area Indian Health Service, 711 Stewarts Ferry Pike, Nashville, TN 37214-2634. Paul J. Ettestad, New Mexico Department of Health, Division of Epidemiology, 1190 St. Francis Drive, Santa Fe, NM 87501.

Reprint requests: Russell E. Enscore, Division of Vector-Borne Infectious Diseases, Centers for Disease Control and Prevention, P.O. Box 2087, Fort Collins, CO 80522-2087.

REFERENCES

1. Gage KL, 1998. Plague. Colier L, Balows A, Sussman M, eds. *Topley & Wilson's Microbiology and Microbial Infections.* Volume 3. *Bacterial Infections.* Ninth edition. New York, NY: Oxford University Press, 885–903.
2. Barnes AM, 1982. Surveillance and control of bubonic plague in the United States. *Symp Zool Soc Lond 50:* 237–270.
3. Gage KL, Ostfeld RS, Olson JG, 1995. Nonviral vector-borne zoonoses associated with mammals in the United States. *J Mammalogy 76:* 695–715.
4. Beatley JC, 1969. Dependence of desert rodents on winter annuals and precipitation. *Ecology 50:* 721–724.
5. Beatley JC, 1976. Rainfall and fluctuating plant populations in relation to distributions and numbers of desert rodents in southern Nevada. *Oecologia 24:* 21–42.
6. Brown JH, Reichman OJ, Davidson DW, 1979. Grainvory in desert ecosystems. *Annu Rev Ecolog Systemat 10:* 201–228.
7. Boutin S, 1990. Food supplementation experiments with terrestrial vertebrates: patterns, problems, and the future. *Canad J Zool 68:* 203–220.
8. Meserve PL, Yunger JA, Gutierrez JR, Contreras LC, Milstead WB, Lang BK, Cramer KL, Herrera S, Lagos VO, Silva SI, Tabilo EL, Torrealba MA, Jaksic FM, 1995. Heterogeneous responses of small mammals to an el nino southern oscillation event in northcentral semiarid Chile and the importance of ecological scale. *J Mammalogy 76:* 580–595.
9. Leirs H, Verhagen R, Verhagen W, Mwanjabe P, Mbise T, 1996. Forecasting rodent outbreaks in Africa: an ecological basis for *Mastomys* control in Tanzania. *J App Ecol 33:* 937–943.
10. Brown JH, Valone TJ, Curtain CG, 1997. Reorganization of an arid ecosystem in response to recent climate change. *Proc Natl Acad Sci USA 94:* 9729–9733.
11. Jones CG, Ostfeld RS, Richard MP, Schauber EM, Wolff JO, 1998. Chain reactions linking acorns to gypsy moth outbreaks and Lyme disease risk. *Science 279:* 1023–1026.
12. Ernest SKM, Brown JH, Parmenter RR, 2000. Rodents, plants, and precipitation: spatial and temporal dynamics of consumers and resources. *Oikos 88:* 470–482.
13. Ryckman RE, Lindt CC, Ames CT, Lee RD, 1954. Seasonal incidence of fleas on the California ground squirrel in Orange County, California. *J Econ Entomol 47:* 1070–1074.
14. Parker DD, 1958. Seasonal occurrence of fleas on antelope ground squirrels in the Great Salt Lake Desert. *J Econ Entomol 51:* 32–36.
15. Ryckman RE, 1971. Plague vector studies: part II. The role of climatic factors in determining seasonal fluctuations of flea species associated with the California ground squirrel. *J Med Entomol 8:* 541–549.
16. Schwan TG, 1986. Seasonal abundance of fleas (Siphonaptera) on grassland rodents in Lake Nakuru National Park, Kenya, and potential for plague transmission. *Bull Entomol Res 76:* 633–648.
17. Lindsay LR, Galloway TD, 1997. Seasonal activity and temporal separation of four species of fleas (Insecta: Siphonaptera) infesting Richardson's ground squirrels, Spermophilus richardsonii (Rodentia: Sciuridae), in Manitoba, Canada. *Canad J Zool 75:* 1310–1322.
18. Bacot AW, Martin CJ, 1924. The respective influences of temperature and moisture upon the survival of the rat flea (*Xenopsylla cheopis*) away from its host. *J Hyg 23:* 98–105.
19. Kartman L, Prince FM, 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. *Am J Trop Med Hyg 5:* 1058–1070.
20. Kartman L, 1969. Effect of differences in ambient temperature upon the fate of *Pasteurella pestis* in *Xenopsylla cheopis. Trans R Soc Trop Med Hyg 63:* 71–75.
21. Cavanaugh DC, 1971. Specific effect of temperature on transmission of the plague bacillus by the Oriental rat flea, *Xenopsylla cheopis. Am J Trop Med Hyg 20:* 264–273.
22. India Plague Commission, 1908. Reports on plague investigation in India, XXXI: On the seasonal prevalence of plague in India. *J Hyg 8:* 266–301.
23. Dubyansky MA, Dubyanskaya LD, Bogatyrev SK, 1992. The relationship between the amount of atmospheric precipitations and the probability for humans to contract plague in a natural focus of infection (Russian). *Zh Mikrobiol Epidemiol Immunobiol 9–10:* 46–47.
24. Parmenter RR, Yadav EP, Parmenter CA, Ettestad P, Gage KL, 1999. Incidence of plague associated with increased winter-spring precipitation in New Mexico. *Am J Trop Med Hyg 61:* 814–821.
25. Brown DE, 1994. *Biotic Communities: Southwestern United States and Northwestern Mexico.* Salt Lake City, Utah: University of Utah Press.
26. Centers for Disease Control and Prevention, 1997. Case definitions for infectious conditions under public health surveillance. *MMWR Morb Mortal Wkly Rep 46 (No. RR-10):* 25–26.
27. France L, 1998. National Oceanic and Atmospheric Administration, National Climate Data Center. *Surface Land Daily Cooperative Summary of the Day.* Technical Paper. Asheville, NC: Publication no. TD-3200.
28. Schafer JL, 1997. *Analysis of Incomplete Multivariant Data.* London: Chapman & Hall.
29. McCullagh P, Nelder JA, 1989. *Generalized Linear Models.* Second edition. London: Chapman & Hall.
30. Fahrmeir L, Tutz G, 1994. *Multivariate Statistical Modeling Based on Generalized Linear Models.* New York: Springer-Verlag.
31. Venables WN, Ripley BD, 1997. *Modern Applied Statistics with S-Plus.* Second edition. New York: Springer-Verlag.
32. Dean CB, 1992. Testing for overdispersion in Poisson and binomial regression models. *J Am Stat Assoc 87:* 451–457.
33. Dunn KP, Smyth GK, 1996. Randomized quantile residuals. *J Comput Graph Stat 5:* 236–244.
34. Zeger SL, Qaqish B, 1988. Markov regression models for time series: a quasi-likelihood approach. *Biometrics 44:* 1019–1031.
35. Zeger SL, 1998. A regression model for time series counts. *Biometrika 75:* 621–629.
36. Léon LF, Tsai CL, 1998. Assessment of model adequacy for Markov regression time series models. *Biometrics 54:* 1165–1175.
37. Cook GC, 1992. The effect of global warming on the distribution of parasitic and other infectious diseases. *J R Soc Trop Med 85:* 688–690.
38. Epstein, PR, Chikwenhere GP, 1994. Environmental factors in disease surveillance. *Lancet 343:* 1440–1441.
39. Reeves WC, Hardy JL, Reisen WK, Milby MM, 1994. Potential effect of global warming on mosquito-borne arboviruses. *J Med Entomol 31:* 323–332.
40. Gubler DJ, 1998. Resurgent vector-borne diseases as a global health problem. *Emerg Infect Dis 4:* 442–450.
41. Bi P, Wu X, Zhang F, Parton KA, Tong S, 1999. Seasonal rainfall variability, the incidence of hemorrhagic fever with renal syndrome, and prediction of disease in low-lying areas of China. *Am J Epidemiol 148:* 276–281.
42. Engelthaler DM, Mosley DG, Cheek JE, Levy CE, Komatsu KK, Ettestad P, Davis T, Tanda DT, Miller L, Frampton JW, Porter R, Bryan RT, 1999. Climatic and environmental patterns associated with Hantavirus Pulmonary Syndrome, Four Corners Region, United States. *Emerg Infect Dis 5:* 87–94.
43. Brown JH, Zeng Z, 1989. Comparative population ecology of eleven species of rodents in the Chihuahuan desert. *Ecology 70:* 1507–1525.

44. Ortega JC, 1990. Reproductive biology of the rock squirrel (*Spermophilus variegatus*) in southeastern Arizona. *J Mammalogy 71:* 448–457.
45. Jimenez JE, Feinsinger P, Jaksic FM, 1992. Spatiotemporal patterns of an irruption and decline of small mammals in north-central Chile. *J Mammalogy 73:* 356–364.
46. Ellis LM, Crawford CS, Molles MC Jr, 1997. Rodent communities in native and exotic riparian vegetation in the middle Rio Grande valley of central New Mexico. *Southwestern Naturalist 42:* 13–19.
47. Went FW, 1979. Germination and seedling behavior of desert plants. Goodall DW, Perry RA, eds. *Arid-Land Ecosystems.* Cambridge, UK: Cambridge University Press, 477–489.
48. Ludwig JA, 1986. Primary production variability in desert ecosystems. Whitford WG, ed. *Pattern and Process in Desert Ecosystems.* Albuquerque, NM: University of New Mexico Press, 5–17.
49. Bock CE, Bock JH, 1997. Shrub densities in relation to fire, livestock grazing, and precipitation in a Arizona desert grassland. *Southwestern Naturalist 42:* 188–193.
50. Cloudsley-Thompson JL, 1991. *Ecophysiology of Desert Arthropods and Reptiles.* New York: Springer-Verlag.
51. Leather SR, Walters KFA, Bale JS, 1993. *The Ecology of Insect Overwintering.* Cambridge, UK: Cambridge University Press.
52. Somme L, 1995. *Invertebrates in Hot and Cold Environments.* New York: Springer-Verlag.
53. Stauffer TW, Whitman DW, 1997. Grasshopper oviposition. Gangwere SK and Muralirangan MC, eds. *The Bionomics of Grasshoppers, Katydids and Their Kin.* Wallingford, UK: CAB International, 231–280.
54. Gashwiler JS, 1979. Deer mouse reproduction and its relationship to the tree seed crop. *Am Midland Naturalist 102:* 95–104.
55. Hall LS, Morrison ML, 1998. Responses of mice to fluctuating habitat quality II. A supplementation experiment. *Southwestern Naturalist 43:* 137–146.
56. Morrison ML, Hall LS, 1998. Responses of mice to fluctuating habitat quality I. Patterns from a long-term observational study. *Southwestern Naturalist 43:* 123–136.
57. King JA, 1968. *The Biology of Peromyscus.* Stillwater, OK: The American Society of Mammalogists.
58. Millar JS, 1989. Reproduction and development. Kirkland GL and Lane JN, eds. *Advances in the Study of Peromyscus (Rodentia).* Lubbock, TX: Texas Tech University Press, 169–232.
59. Poland JD, Quan TJ, Barnes AM, 1994. Plague. Beran GW, ed. *CRC Handbook of Zoonoses* Second edition. Boca Raton, FL: CRC Press, 93–112.
60. Cavanaugh DC, Marshall JD, 1972. The influence of climate on the seasonal prevalence of plague in the Republic of Vietnam. *J Wildl Dis 8:* 85–93.
61. Pollitzer R, 1954. *Plague.* World Health Organization Monograph Series No. 22. Geneva: World Health Organization.