Interannual Variability of Human Plague Occurrence in the Western United States

Explained by Tropical and North Pacific Ocean Climate Variability

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Abstract. Plague is a vector-borne, highly virulent zoonotic disease caused by the bacterium Yersinia pestis. It persists in nature through transmission between its hosts (wild rodents) and vectors (fleas). During epizootics, the disease expands and spills over to other host species such as humans living in or close to affected areas. Here, we investigate the effect of large-scale climate variability on the dynamics of human plague in the western United States using a 56-year time series of plague reports (1950–2005). We found that El Niño Southern Oscillation and Pacific Decadal Oscillation in combination affect the dynamics of human plague over the western United States. The underlying mechanism could involve changes in precipitation and temperatures that impact both hosts and vectors. It is suggested that snow also may play a key role, possibly through its effects on summer soil moisture, which is known to be instrumental for flea survival and development and sustained growth of vegetation for rodents.

INTRODUCTION

Plague is a disease caused by the bacterium Yersinia pestis. Humans may accidentally become infected when bitten by plague-infectious flea vectors or when handling plague-infected hosts.1–3 Unless quickly treated with antibiotics, the disease is fatal to humans.3,4 Plague is circulating and/or persisting in many populations of small mammals and other wildlife species in diverse biotopes around the world.5 Human-plague cases occur regularly in the western United States.6 Plague was first introduced to the United States in San Francisco during the last pandemic (1899), most likely by a merchant ship arriving from Hong Kong, China.6–7 Ultimately, transmission among native rodents and their fleas resulted in an eastward spread of the disease and the establishment of discontinuous plague foci across the western United States6,8 as far east as the 100th meridian.8,9 Within 10 years, plague had spread from urban rats to wild rodents such as sciurid, sigmodontine, or microtine rodents living in surrounding rural areas.7 Climate factors are known to regulate both host and vector abundances.10–14 Small mammal population dynamics are controlled by both intrinsic and extrinsic factors, where the latter includes contemporary and past local temperature and precipitation,10,11,14–20 Fleas spend the majority of their life cycle in the environment and thus, are affected by surrounding conditions, notably by temperature and humidity changes.21–23 During plague epizootics, the abundance of these hosts and the prevalence of Y. pestis in them, as well as the numbers of active fleas,24 are high.25–27 At such times, the disease expands spatially, increasing the chances of infection for ecologically associated species or humans and their domestic animals.9 Earlier studies have consistently shown that these scenarios happen while local climatic conditions are favorable to both hosts and vectors,28,29 possibly because of a cascade of events involving above-normal precipitation and mild temperatures.29,30

The specific combination of rodent and flea species responsible for plague maintenance and amplification in the United States varies markedly across the region.9 It is, therefore, desirable to develop means of understanding and predicting the current occurrence of human plague and how this may change with possible climatic changes that are independent of the particular rodents and fleas involved. Earlier studies had concluded that there was no significant association between human-plague occurrence and large-scale climate variability,29 and this conclusion has been widely accepted in World Health Organization (WHO) reports and other sources.2,28,31–36 At interannual scales, climate variability over the western United States is primarily characterized by two modes of fluctuations, with a spatial imprint extending outside this limited region: the Pacific Decadal Oscillation (PDO; decadal time periods)37 and El Niño Southern Oscillation (ENSO; 3- to 4-year time periods).38 Positive (respectively [resp.]; negative) PDO and ENSO (El Niño; resp. La Niña) phases are both associated with wetter (resp.; drier) and milder climate over the western United States. A variety of ecosystems have been shown to respond to either or both of these climate fluctuations.37,38 Recently, it was shown that the number of human cases in this region is linearly linked to PDO and the number of abnormally hot days,40 but both PDO and ENSO are responsible for the spatially coherent and predictable climate anomalies in this region.37,41–42 These large-scale climate indices are known to be efficient predictors of ecological processes in other systems, including rodent population dynamics and demographic rates.43–46 In this study, we examine the associations between climate anomalies driven by PDO and ENSO and the dynamics of human plague and discuss the mechanisms that might underlie such associations. Specifically, we focus our discussion on one link in the cascade hypothesis, namely the effect of precipitation and temperature patterns (as captured by PDO and ENSO) on primary production (i.e., rodents host food availability as captured by the normalized difference vegetation index [NDVI] index) in the plague areas. Finally, we look at the possible effects of climate change on plague dynamics.

MATERIALS AND METHODS

Data. Plague data. We used annual counts of human plague cases in the counties of exposure, available from 1950 to 2005. We considered all 105 counties (distributed across 13 states) reporting at least one plague case over the study period. No
correlation exists between plague outbreak frequency and population density at the county level. The largest human-plague outbreaks typically occur in primarily rural counties with close to median population density (73/km²). Plague counts are adjusted by county population density to produce county-level human-plague time series compatible with climate. Population density, \( D_{(c,y)} \), for county \( c \) in year \( y \) is given as \( D_{(c,y)} = \frac{\text{population}_{(c,y)}}{\text{area}_{(c)}} \) and is based on linearly interpolated population censuses for each county performed every 10 years by the US Census Bureau (http://www.census.gov/). The adjusted plague time series \( P_{(c,y)} \) is calculated as \( P_{(c,y)} = \frac{P_{(c,y)}}{D_{(c,y)}} \). The raw \( \hat{P} \) and adjusted plague time series exhibit a strong correlation (correlation = 0.92; \( \hat{P} \) value < 0.001) (Supplemental Figure S1, available at www.ajtmh.org.). The data reveal a period of increased mean infection during 1970–1988, with an overall peak of 40 human cases around 1983.

**Climate data.** Our analyses use sea surface temperature (SST) averaged over the so-called NINOn3.4 region (5°S–5°N; 170–120°W) for the same time window (1950–2005). We calculated the standard deviation (SD) for this index and considered three different phases for ENSO: El Niño (index > 1 SD), neutral (−1 SD < index < 1 SD), and La Niña (index < −1 SD). The strongest ENSO signal in precipitation over the southwestern United States is observed in late winter to early spring (i.e., when local precipitation has been documented by Parmenter and others29 to be important for plague hosts and vectors). Values for the PDO index were obtained from http://jisao.washington.edu/data_sets/). Both ENSO and PDO are characterized by high persistence through the fall and winter until early spring. March values for these indices are representative of recent conditions as well as a measure of springtime climate forcing, which, as we shall see, is very important for summertime plague. Figure 1B and C depicts the time series of March PDO and March NINOn3.4.

Extensive temperature and precipitation records are freely available (NCDC, 2003, http://www.ncdc.noaa.gov/oa/ncdc.html) for thousands of available meteorological stations in the United States. From these records, we chose a network of the 100 stations with the highest quality data (defined as those with the fewest missing data and the highest proximity to plague counties) (Figure 2) to build proxies for monthly temperature and precipitation regimens across the western United States.

**NDVI data.** The NDVI\(^{64} \) data cover the study area (100–125°W, 30–45°N) in a 0.25° resolution grid of monthly composite values compiled over the period 1982–1998. This is roughly the time period over which advanced very high resolution radiometer (AVHRR) data from Pathfinder are available with concomitant solar zenith angle and view zenith angle (and relative azimuth) so that a Fourier-Adjusted, Sensor and Solar Zenith Angle-Corrected, Interpolated, Reconstructed (FASIR) can be constructed (O. S. Los, personal communication). NDVI is an index of the light absorbed by chlorophyll and thereby, a derived measure of primary production. In arid zones with a simple vegetation structure, NDVI reflects variation in ground chlorophyll and vegetation coverage when snow cover is absent. For data documentation, see http://islscp2.sesda.com/ISLSCP2_1/data/vegetation/.

**Wavelet analyses.** In nature, non-stationary processes are common, and increasing evidence suggests the importance of transient dynamics in ecological processes.\(^{50–53} \) Epidemiological time series are typically noisy, complex, and strongly non-stationary.\(^{54} \) Wavelet analyses provide powerful tools for analyzing such signals.\(^{55–58} \) It is indeed well-suited to dealing with transient relationships between two signals (e.g., climate interaction with the dynamics of an epidemic). Wavelet analysis performs a time-frequency (f) decomposition of the signal and allows one to follow the evolution of the different frequency components as time progresses. We used wavelet analysis and its bivariate extensions, wavelet cross-spectrum and wavelet coherency,\(^{56} \) to analyze the plague data and their statistical relationships with the climatic time series (PDO and ENSO).

The statistical significance of the univariate and bivariate analyses was assessed using \( \beta \) surrogates.\(^{59} \) This approach accounts for the autocorrelation structure of the original time series by assuming an underlying 1/f model for its power spectrum. Contrary to white noise and autoregressive processes, it reproduces the relative distribution of the whole range of frequencies in the signal and thus, accounts for the dominance of low frequencies often found in ecological time series. All of the computations were done using R version 2.4 (www.Rproject.org) on the basis of the wavelet libraries developed by Cazelles and others.\(^{60,54,55} \)

**RESULTS**

**PDO and ENSO affect precipitation and primary production in the western United States.** PDO exhibits coherent positive correlations with late winter/early spring precipitation throughout the area.\(^{55,42,60,64} \) Consistent positive precipitation anomalies occur in late winter to spring when PDO is high (i.e., above 1 SD); this pattern is most marked when El Niño events combine with positive PDO. Conversely, a low PDO/La Niña combination results in below normal precipitation (Figure 3). Snow anomalies (measured as the amount of water precipitated on days when the daytime temperature is below freezing) are also higher during El Niño(PDO positive phases (Supplemental Figure S2, available at www.ajtmh.org). NDVI is a good indicator of yearly food availability for small mammals living in semi-arid areas.\(^{62–63} \) Yearly maximum NDVI, a proxy for yearly maximum food available for small mammals,\(^{64,65} \) reveals above- and below-mean values between 1982 and 1998. NDVI above-mean years coincide with above-mean total precipitation (Figure 1). In the Four Corners region plateau, NDVI spatial anomalies during El Niño/positive PDO years are consistently above normal (120–150% in 1983, 1987, 1992, and 1998) and below normal during the La Niña(PDO negative year (60–80% in 1989). This pattern is less consistent in the Pacific and Northwest areas (Figure 3).

**PDO and ENSO significantly explain the temporal variability of plague cases.** To explore human-plague patterns across the whole region, we used the spatial sum of all population density-scaled human cases (Figure 1A and Supplemental Figure S3, available at www.ajtmh.org) (a measure we refer to as the plague time series; see also plague occurrences in consecutive time windows). Plague outbreaks occur predominantly during positive phases of PDO; the number of population-adjusted human-plague occurrences is, on average, 4.4 during positive PDO phases and 0.9 during negative phases (or respective plague anomalies of 138% against 59%; \( P < 0.05 \) (Table 1). The correlation between the plague time series and the ENSO index alone is, however, generally not significant. Looking more carefully, periods of high plague occurrence seem to occur when El Niño events coincide with a positive PDO.
phase (e.g., 1959, 1983, 1987, and 1992). Conversely, decreases in plague cases after La Nina events are accentuated if they occur during PDO negative phases (36% versus 52%; $P < 0.05$) (Table 1).

Because the strong autocorrelation at lag one in the plague time series ($r_{[\text{plague}_t, \text{plague}_{t-1}]} = 0.72; P < 0.001$) might lead to an overestimation of the tested significance of the associations measured in Table 1, we carried out a wavelet analysis of the plague time series and cross-wavelet analysis of both PDO/ENSO and plague case numbers. We tested significances against 1,000 bootstrapped time series with similar frequency spectra (i.e., a dominance of low frequency; see Materials and Methods). The plague time series shows interannual cycles with periods of 7–8 years and 3–4 years that are most marked from the mid-1970s to the late 1980s after a major PDO shift (Figures 1B and 4). This is not inconsistent with the time periods generally associated with PDO and ENSO. To test a plague ENSO association conditional to PDO, we computed
In our data, we indeed find a trend to higher elevation/latitude, but this trend may have started in the 1980s (Supplemental Figure S5, available at www.ajtmh.org) and is not significant; the use of exposure-site data for cases rather than county-level data could provide more specific conclusions to be made on the possible role of climate change on what locations will have the greatest amounts of human-plague activity in the future, but such analyses are outside the scope of the current study.

**DISCUSSION**

In our efforts to identify a region-wide, system-independent link between climate and the occurrence of human-plague cases in the western United States, we found that ENSO and PDO patterns, especially in combination, can be related—first, to climatic variables in the United States known to be important in determining the probability of human plague, and second, to the number of human-plague cases themselves. We showed that the years that had both high numbers of plague cases and high precipitation coincide with above-mean values of NDVI. We also noted that recent rises in temperature associated with reductions of the snow pack and its persistence correspond to anomalously low numbers of plague cases.

**Significant association between large-scale climate variability and plague.** In an earlier study, Parmenter and others showed that local precipitation in winter and spring significantly increased the number of human-plague cases in New Mexico. These authors tried but were unable to find significant links between plague and ENSO, the dominant mode of Pacific-sector climate variability. They concluded, therefore, that local, not large-scale, climate drives plague dynamics. Several reasons may have led to this conclusion, including the use of an overaggregated index of ENSO (i.e., mean from October to May of the Southern Oscillation Index [SOI]) that is not the most relevant for North American precipitation anomalies (SST averaged over the so-called NINO3.4 region [5S–5° N; 170–120° W] is more relevant for well-documented reasons). Additionally, the North Pacific decadal climate variability (i.e., PDO) also exerts a direct influence on North American climate, sometimes enhancing and sometimes obscuring ENSO teleconnections. In this context, the clearest link is between PDO and plague levels in the west. The present study proposes a mechanistic explanation for this link by showing the existence of spatio-temporal coherent anomaly patterns in surface temperature and precipitation associated with PDO. This result is consistent with the dominance of PDO over ENSO regarding the storm-track position. Seasonal climate anomalies over North America exhibit strong variability between years characterized by the same ENSO phase and are caused largely by modulation by PDO. Earlier studies did not take this into account and were unable to find links between southwestern plague and ENSO. El Nino (resp., La Nina) signals to North American climate are strongest and most spatially coherent and predictable when El Nino (resp., La Nina) occurs during the positive (resp., negative) phase of PDO. Therefore, Los Niños consistently results in fairly mild winters and above-normal precipitation if occurring during the positive phase of PDO (i.e., in 1955, 1966, 1983, 1987, 1992, 1993, and 1998), whereas La Nina events result in coherent dry and above-normal hot climate over the western United States, especially if occurring during the negative PDO phase.
Accordingly, we found that El Niño events occurring during positive PDO excursions are related to high plague counts and that La Niña events occurring during negative PDO consistently led to low plague values (Table 1). A notable exception is the most recent El Niño event, which was not followed by increased plague numbers (i.e., in 1998 [positive PDO]); the same was true, to a lesser extent, in 2003 (neutral PDO), but see discussion of climate change for further information.

Wavelet analysis enabled us to better determine the transient associations between PDO/ENSO and the plague time series. The coherency analysis and cross-wavelet spectrum of PDO and plague confirmed that both signals are significantly coherent over the total study period (Figure 4). Furthermore, a notable exception is the most recent El Niño event, which was not followed by increased plague numbers (i.e., in 1998 [positive PDO]); the same was true, to a lesser extent, in 2003 (neutral PDO), but see discussion of climate change for further information.

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available for small mammals increases in the onset years of NDVI anomalies (Figures 1E and 3), suggesting that the food positive precipitation anomalies corresponded to positive anomalies. El Niño/PDO positive years inducing coherent larger scales, we extended our precipitation analysis to NDVI.

In assessing whether this general scheme was consistent at spatial scales between primary production and hosts abundance; likewise, serological or flea sampling would be necessary to confirm whether increased rodent densities led to higher plague prevalence among hosts populations—a link that may not be simple or direct. In the absence of these elements, we can neither accept nor reject with certainty the hypothesis that rodents were part of a trophic cascade that drove the dynamics of plague.

Potential mechanisms to explain the association between human plague and climate variability. We have shown that the number of human-plague cases exhibits large-scale coherent positive correlations with late winter to spring precipitation (Supplemental Figure S6, available at www.ajtmh.org). Although yet to be proven for plague, the cascade hypothesis provides us with a possible platform from which to understand the effects of climate variability on the plague system in the United States. Including those conducted in the United States, in some instances, lead times for rodent population increases have been quite short. In the case of Sin nombre virus (a type of hantavirus), which, like plague, is a rodent-associated zoonosis, these short lead times resulted in enhanced virus transmission soon after the period of enhanced precipitation. Rodent densities are known to be associated, through bottom-up processes, with increased precipitation in relatively dry areas where it may be limiting. Obviously, rodent data would be necessary to confirm the correlation at interannual scales between primary production and hosts abundance; likewise, serological or flea sampling would be necessary to confirm whether increased rodent densities led to higher plague prevalence among hosts populations—a link that may not be simple or direct. In the absence of these elements, we can neither accept nor reject with certainty the hypothesis that rodents were part of a trophic cascade that drove the dynamics of plague.

Plague activity also reflects flea dynamics and activity. Variations in humidity and temperature indirectly impact flea density and geographical distribution. Excessively high temperatures reduce flea survival, early-stage development, reproduction rates, and fleas’ ability to transmit the disease, and thus, overall plague activity, which is expressed in the temperature-modulated cascade hypothesis. Metabolic rates are higher and survival is lower when temperature increase or humidity is below a certain threshold. In fact, temperature and humidity together affect fleas. Rodent flea stages occurring off the host (i.e., all stages but fed fleas) are sensitive to variations of the host environment and particularly, to burrow microclimatic conditions. The macroclimate to which humans are exposed is not necessarily the best indicator of these conditions. In burrows, soil moisture could be a better indicator of humidity, because it affects fleas, rather than above-ground measures of humidity. Contrary to air (above-ground) and burrow temperatures that exhibit strong coherent correlations, burrow humidity depends more on past rainfall and soil type than on the humidity of the air outside the burrow. In this study, we have described how seasonal precipitation is instrumental in understanding the association between PDO/ENSO and human plague. Precipitation in winter and early spring mainly falls as snow in the elevated plague areas. Soil moisture is well-predicted by snow accumulation...
and the timing of the snow melt. The strong positive correlation between winter and early spring precipitation and plague reinforces the hypothesis that the effect of snow cover on summertime soil humidity is crucial for plague activity.

Likely decrease of plague activity in response to increased temperatures associated with climate change. The West naturally undergoes multidecadal fluctuations between wet and dry periods associated with PDO, but previous studies suggest that the region has been losing snow in favor of relatively more rain and earlier snowmelt across a broad region of mountainous western North America. Minimum (i.e., nighttime) temperatures, increasing since 1990, are related to reduced volume and persistence of the snow pack. Although global anthropogenic signals are often difficult to separate from natural climate variability at this regional scale and early stage of climate change, it has recently and convincingly been done for this region. The observed regional trends of decreasing snow/rain ratio, and warmer spring and summer seasons are consistent with climate-model projections. These changes, which are because of both natural and anthropogenic causes, influence summertime soil moisture in the western United States. Moreover, warmer temperature can dry the soil directly by enhancing evaporation, whereas dry soil, in turn, promotes warmer nighttime temperature. These trends, if they continue and intensify as projected, will likely lead to decreased soil humidity and increased temperatures as a result of the direct and indirect (e.g., through hydrology feedbacks) effects of global warming. This could decrease flea survival and reproduction rates and therefore, reduce the number of active fleas. Global warming is expected to continue and accelerate, which almost undoubtedly will result in increasingly unfavorable conditions for fleas and decreased primary production in the spring and summer; thereby, this will lead to less-favorable conditions for large increases in rodent populations and the occurrences of plague epizootics among these animals. Based on this reasoning and the results of our study, we suggest that human plague in the southwestern United States is likely to decrease over the coming decades. Nevertheless, in places like New Mexico where human-population expansion into the wildland–urban interface is expected to continue and where humans typically contract plague during epizootics in rodents, plague exposure and risk could still increase on a local basis.

Also, this overall decrease in plague can be expected to still be punctuated by episodic outbreaks as a result of natural climate variability for decades to come. At this time, we cannot determine how ENSO and PDO variability or their influences on southwestern climate will change in response to global warming. However, we may reasonably assume that the persistence of the fall/winter PDO and ENSO into the next spring will continue to provide simple probabilistic means for projecting the severity of the next summer’s plague season. This study provides information needed for developing probabilistic forecast models of seasonal plague risks. One such model would be based on simple PDO and ENSO persistence as well as long-term temperature trends. If based on the observed/ extrapolated values of PDO and ENSO in the fall, the forecast model could involve long lead times, up to three seasons ahead. At shorter lead times (e.g., one season ahead), a more skillful model describing relationships between human plague and climate can be based on observed precipitation patterns (amount and type) and spring temperatures that would implicitly include natural and anthropogenic signals.

Note: Supplemental figures are available at www.ajtmh.org.

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