Climate Change Effects on Plague and Tularemia in the United States

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ABSTRACT

Plague and tularemia are serious zoonotic diseases endemic to North America. We evaluated spatial patterns in their transmission in view of changing climates. First, we tested whether observed shifts since the 1960s are consistent with expected patterns of shift given known climate changes over that period. Then, we used general circulation model results summarizing global patterns of changing climates into the future to forecast likely shifts in patterns of transmission over the next 50 years. The results indicate that these diseases are indeed shifting in accord with patterns of climatic shift, but that overall geographic shifts will likely be subtle, with some northward movement of southern limits and possibly northward movement of northern limits as well. Key Words: Tularemia—Plague—Climate change—Spatial patterns—Disease transmission.

INTRODUCTION

GLOBAL CLIMATE CHANGE is affecting environmental conditions worldwide, creating new situations in which biological species are distributed—warmer climates at higher latitudes, shorter and milder winters, extreme conditions at low latitudes, etc. (Karl et al. 1996, Hulme et al. 1999a, 1999b, Magnuson 2001, Francou et al. 2003, Kunkel 2003) (Fig. 1). Early commentaries anticipated distributional shifts and phenological changes with warming climates (Emanuel et al. 1985, Peters and Darling 1985, Dobson et al. 1989, Schneider 1989), and such effects are now being seen in many species and biological communities worldwide (Parmesan et al. 1999, Walther et al. 2002, Cresswell and McCleery 2003, Crozier 2003, Parmesan and Yohe 2003).

Considerable discussion has focused on the potential for global climate change also to af-

fect distributions of pathogens and disease transmission (Martens et al. 1995, Hayes and Hussain 2000, Kovats et al. 2001, Harvell et al. 2002, Hay et al. 2002, Hunter 2003). The thought is that warming climates may permit poleward expansion of disease transmission (e.g., malaria and dengue northward into Europe and the United States) and/or changes in timing and seasonality.

Plague (*Yersinia pestis*) and tularemia (*Francisella tularensis*) are relatively rare zoonotic diseases endemic in North America. In both cases, transmission is at least partially via arthropod vectors (fleas, ticks, or flies), and transmission to humans is relatively rare. Nonetheless, hundreds of human cases of each disease have been recorded over the past half-century, and the ecology and natural history of their transmission is an active field of research (Levy and Gage 1999, Parmenter et al. 1999, Enscore et al. 2002). Climate change-related effects on these

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diseases, nonetheless, have not been documented for transmission patterns of either disease to date.

In this article we present a geographic analysis of the spatial distribution of plague and tularemia cases over the past five decades. Specifically, we note a northward-shifting pattern in the actual occurrences of human cases of each disease. Given potentially confounding human socioeconomic correlates (e.g., shifting patterns of hunting and land use), we then test the hypothesis that these shifts are (or are not) consistent with ongoing climatic shifts in the region. The result is a clear association suggesting that climate change effects are indeed shifting

these two zoonotic diseases northward in North America.

METHODS

Occurrence data

National surveillance data for human plague and tularemia cases have been compiled by the U.S. Public Health Service since before 1960. Physicians and laboratories report suspect or probable cases to state or local health officials according to local laws or regulations; states report cases to the Centers for Disease Control and Prevention (CDC) through the National
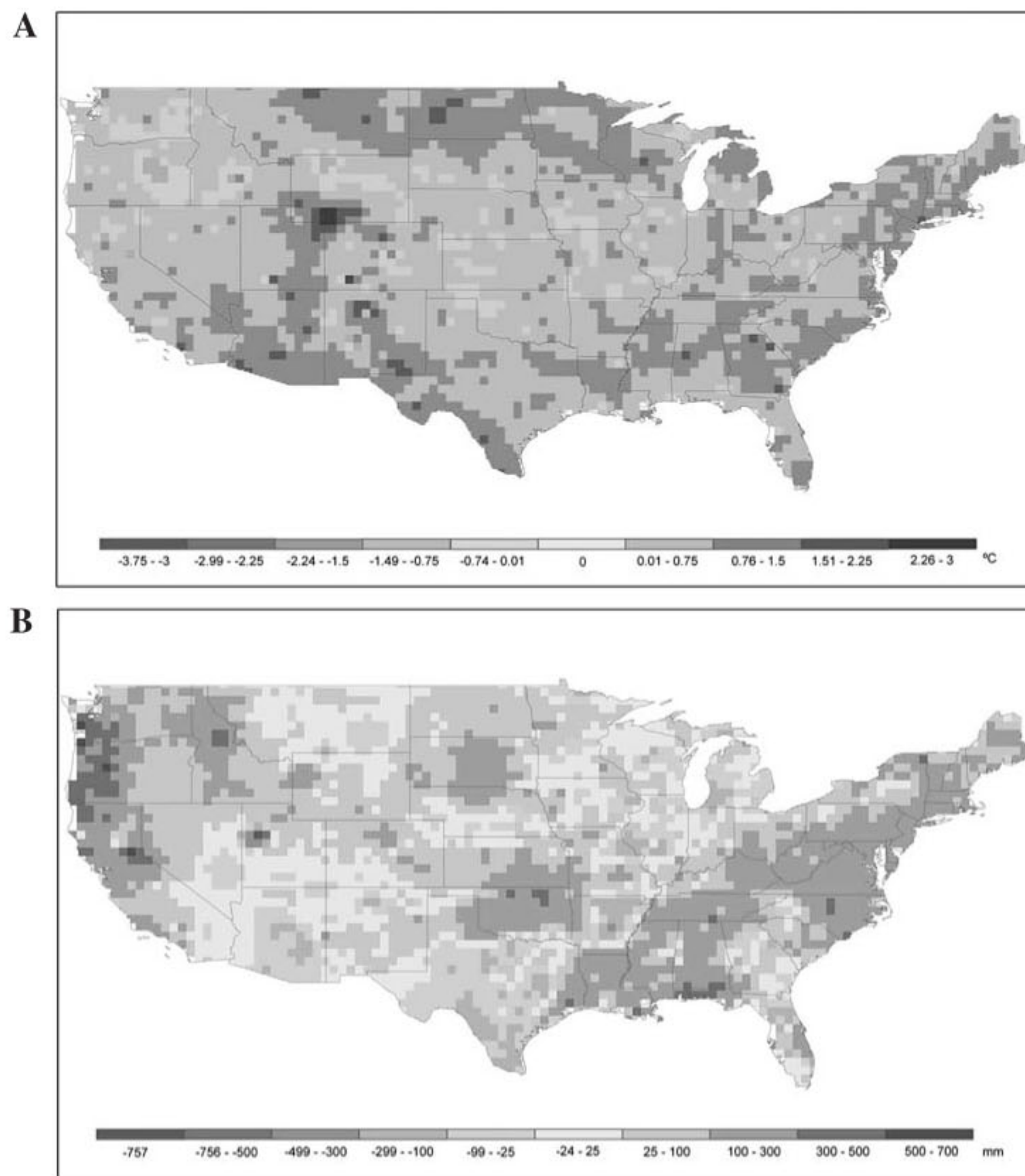
FIG. 1. Change of mean temperature (**A**) and annual precipitation (**B**), obtained by subtracting the mean value for the 1965–1969 period from the mean value for the 1995–1999 period.

Notifiable Diseases Surveillance System (NNDSS). At present, for plague, a confirmed case is defined as a clinically compatible illness with isolation of *Y. pestis* from a clinical specimen or fourfold or greater change in serum antibody titer to *Y. pestis* F1 antigen. A confirmed case of tularemia is defined as a clinically compatible illness with isolation of *F. tularensis* in a clinical specimen or a fourfold or greater change in serum antibody titer to *F. tularensis* antigen. Although uniform national surveillance case definitions were not formally adopted until 1990, definitions of confirmed cases did not change appreciably over the period covered by this study. Tularemia reporting was officially discontinued in 1995–1999; however, cases continued to be reported during that period at a steady rate. Underreporting occurs with all diseases, but it tends to be less pronounced with severe illnesses such as plague; consistent underreporting does not interfere with comparisons over time or across jurisdictions. Because studies of these two diseases north and south of the United States have been few (Leighton et al. 2001, Humphreys and Campbell 1947, Varela and Vásquez 1954), we restricted our analyses to the lower 48 United States. Although Farlow et al. (2005) distinguished between types of tularemia (A1, A2, B), because sample sizes of subtyped isolates of tularemia are few, we analyzed all tularemia cases together. The total number of cases included in this study was 393 for plague and 6051 for tularemia (Table 1).

Because occurrence data were in the form of counties in which cases occurred, it was necessary to take this imprecision into account in the development of ecological niche models. Previous efforts have attempted to use polygon-based occurrence data by means of assigning the geographic coordinates of centroids of polygons to each occurrence (Peterson et al. 2004). However, given large differences in size of counties across the United States, we were concerned that these differences might introduce biases into the modeling process.

We used a more computationally intensive approach that has been developed only recently (Peterson et al. 2006). We plotted 25 random points within each county polygon in which cases occurred (when multiple cases oc-

curred in single counties, 25 random points were generated for each case, Fig. 2). The random points were numbered from 1 to 25, creating in effect 25 sets of random points representing the counties in which cases occurred. This randomization approach represents small counties very precisely (i.e., with little spatial variation) and large counties with more spatial variation in position of points.

Environmental data

We assembled half-decade-specific environmental data sets for model development. The
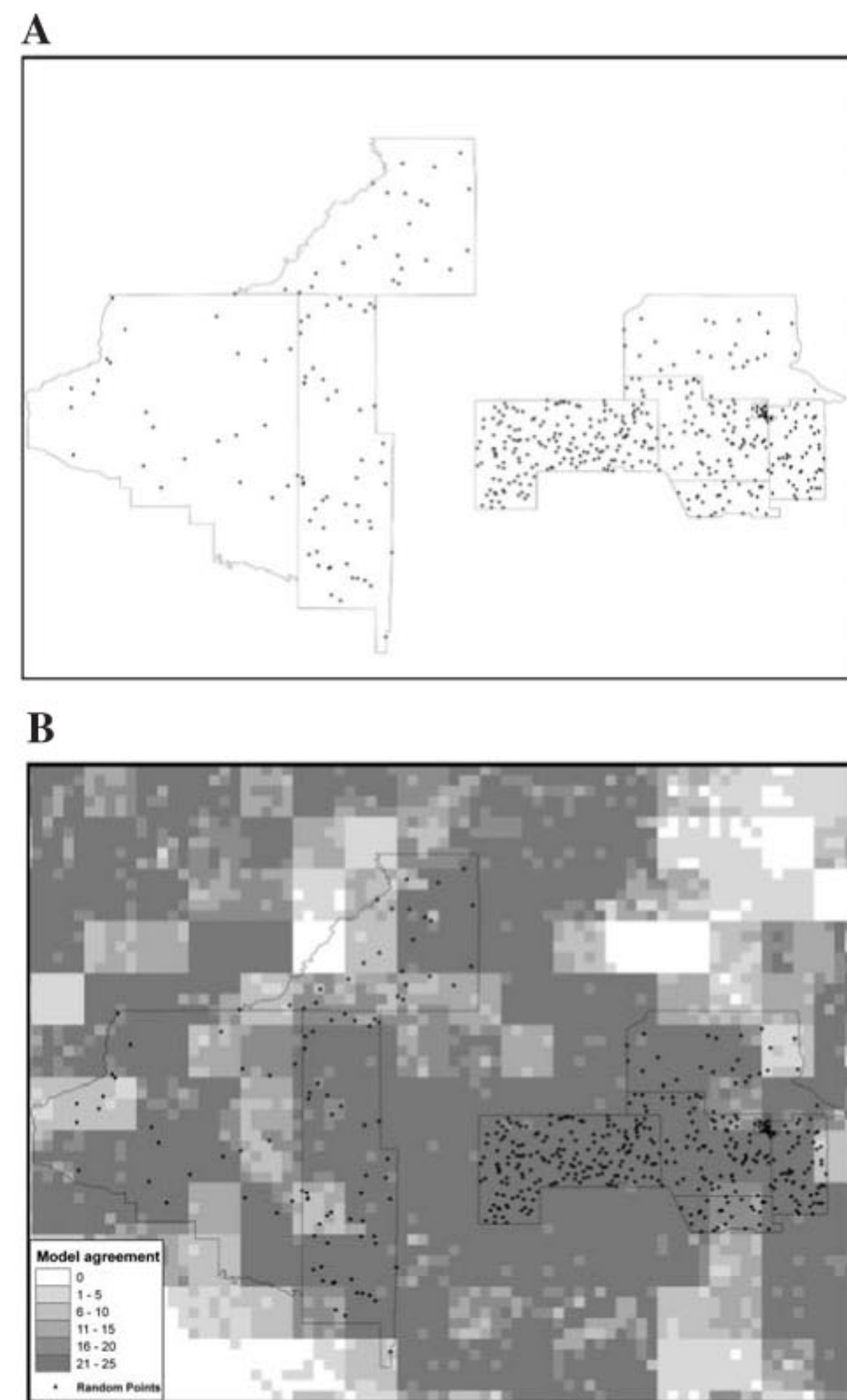
FIG. 2. Illustration of methodology for treating polygon-based occurrence data in algorithms that ordinarily require point-based data as inputs. (**A**) County outlines and 25 random points per case occurring in each county (note that some counties have greater densities owing to the occurrence of multiple cases). (**B**) Model prediction based on these points showing ramp of model agreement in predicting presence (dark area) versus absence (white).

bulk of the environmental information consisted of monthly summaries of climatic information (precipitation, mean temperature, maximum temperature, minimum temperature, actual evapotranspiration, potential evapotranspiration, moisture surplus, moisture deficit) drawn from Feddema (2006). We averaged these variables across (i.e., within) 5-year periods from 1965 to 2003 to provide half-decade summaries of changing climates. In addition to the climate variables, we included four variables summarizing topographic characteristics, including elevation, slope, aspect, and compound topographic index (USGS 2001). All variables were resampled to 0.1° resolution for analysis.

Ecological niche modeling (ENM)

The algorithm used for generating ENMs was the Genetic Algorithm for Rule-Set Prediction (GARP) (Stockwell and Noble 1992, Stockwell and Peters 1999). GARP is an evolutionary-computing method that builds ENMs based on non-random associations between known occurrence points for species and sets of GIS coverages describing the ecological landscape. Occurrence data are used by GARP as follows: 50% of occurrence data points are set aside for an independent test of model quality (extrinsic testing data), 25% are used for developing models (training data), and 25% are used for tests of model quality internal to GARP (intrinsic testing data). Distributional data are converted to raster layers, and by random sampling from areas of known presence (training and intrinsic test data) and areas of "pseudoabsence" (areas lacking known presences), two data sets are created, each of 1250 points; these data sets are used for rule generation and model testing, respectively.

The first rule is created by applying a method chosen randomly from a set of inferential tools (e.g., logistic regression, bioclimatic rules). The genetic algorithm consists of specially defined operators (e.g., crossover, mutation) that modify the initial rules, and thus the result are models that have "evolved"—after each modification, the quality of the rule is tested (to maximize both significance and predictive ac-

curacy), and a size-limited set of best rules is retained. Because rules are tested based on independent data (intrinsic test data), performance values reflect the expected performance of the rule, an independent verification that gives a more reliable estimate of true rule performance. The final result is a set of rules that can be projected onto a map to produce a potential geographic distribution for the species under investigation. We analyzed each half-decade period 25 times, once for each of the 25 random-point representatives of each case in that time period. Following recent best-practices recommendations (Anderson et al. 2003), for each of these time-period × representative point combinations, we developed 25 replicate random-walk GARP models and filtered out 96% based on consideration of error statistics, as follows. The "best subsets" methodology consists of an initial filter removing models that omit (omission error = predicting absence in areas of known presence) heavily based on the extrinsic testing data, and a second filter based on an index of commission error (= predicting presence in areas of known absence), in which models predicting very large and very small areas are removed from consideration. Specifically, in DesktopGARP, we used a "soft" omission threshold of 20%, and 20% retention based on commission considerations; the result was a final "best" prediction for each species. In sum, in the process of developing this report, we developed 25 replicate models for each of 25 suites of random representative points for each of seven half-decade time periods for each of the two diseases, for a total of 8750 GARP models.

Testing hypotheses of climate change

The focus of this analysis is on assessing possible roles of changing climates in determining spatial distributions of plague and tularemia cases in the United States. As such, for each half-decade-specific model described above, we projected the ENM rule set to all other half-decade time periods. Our test of consistency of range shifts with climate change consisted of assessing predictivity among time periods—e.g., how well the model for 1965–1970 was able

to predict the distribution of the disease in 1985–1990, and so forth—among all combinations of time periods.

Once again, the polygon-based nature of the occurrence data forced us to use novel methodologies. For each combination of time periods, we overlaid the counties in which cases of each disease occurred on the prediction from the "other" time period, and tallied the number of counties that had some area predicted present within their extents (e.g., 20 of 24 counties holding occurrences predicted in some part present by the model). Then, to assess the degree to which this degree of coincidence is better than that expected by chance, we used the following randomization test to characterize random expectations. For each intertemporal prediction to be tested, if N_t cases of a particular disease occurred in the time period being predicted, we chose 100 sets of N_t counties at random with

replacement from the entire lower 48 states for tularemia, and the lower 48 United States west of 100° longitude for plague, and repeated the measurement of coincidence with predictions for each set. We compared the observed coincidence with this distribution of random expectations; the probability of a given observation was taken as its position in the randomized distribution.

Future projections

Because no future climate scenarios were available to match the time-specific climate data described above, we repeated our analyses with a simpler data set for which future scenarios are available. We used five climatic parameters and four topographic parameters (maximum, minimum, and mean monthly temperatures; solar radiation; precipitation; slope;
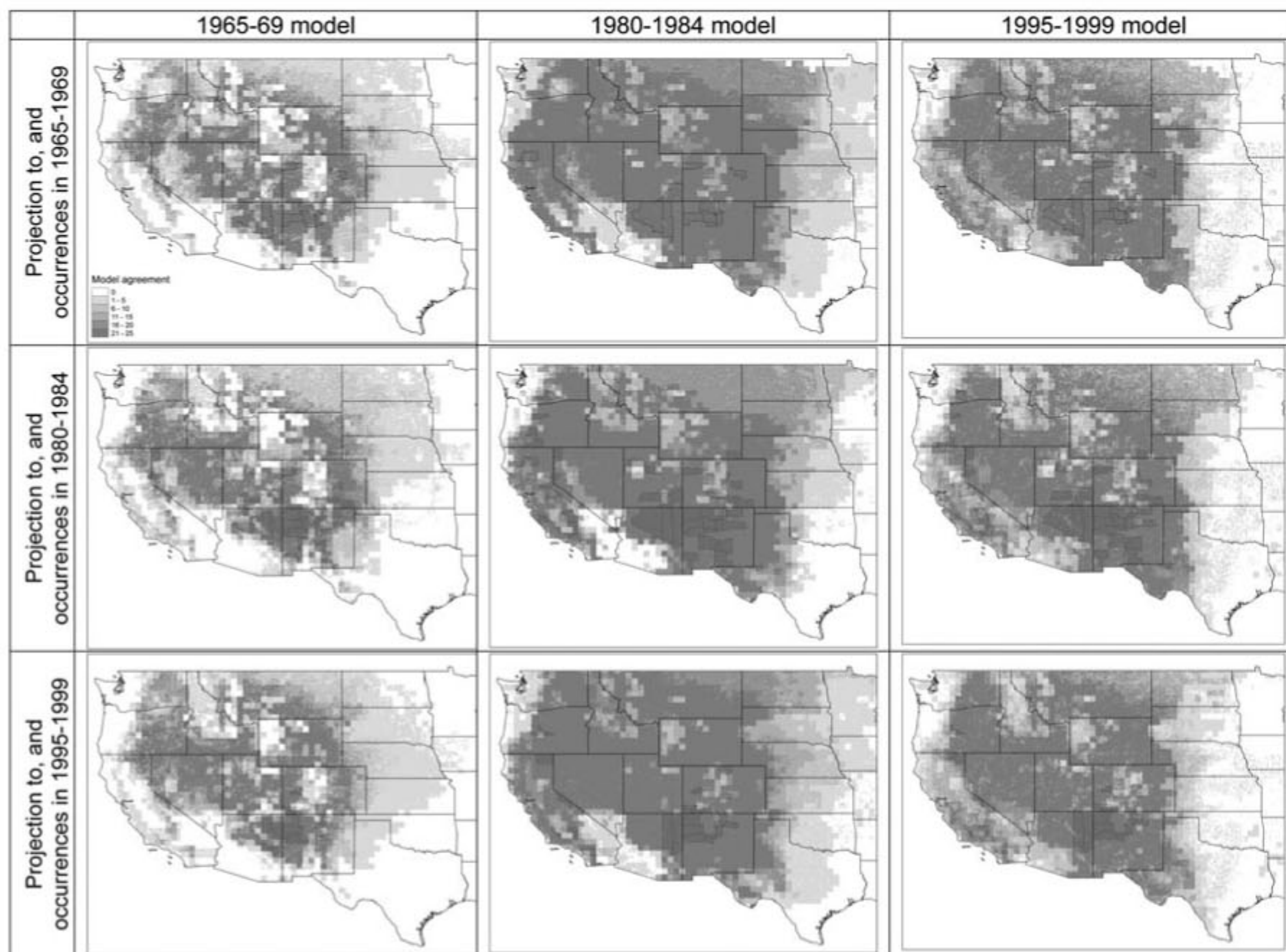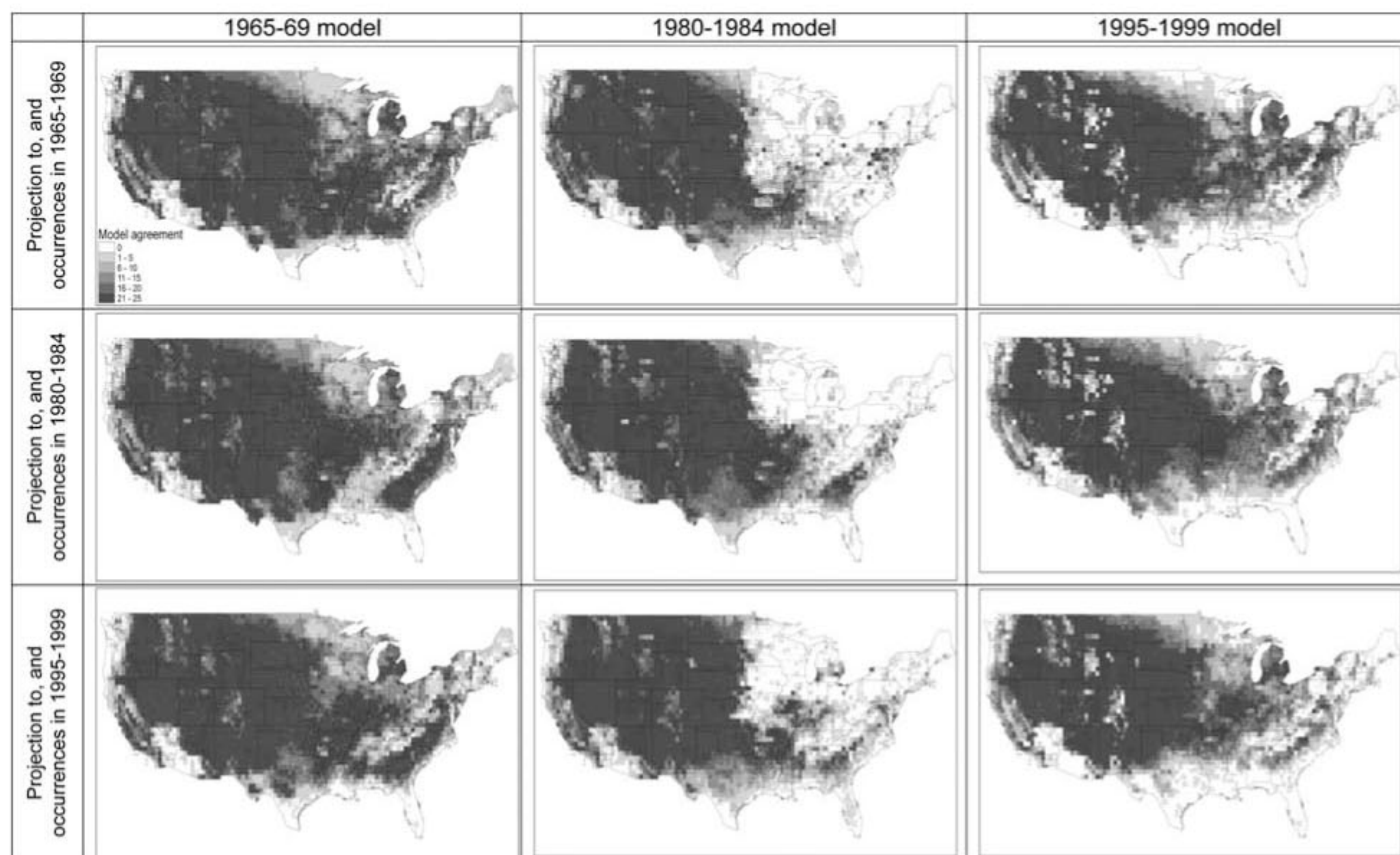

FIG. 3. Plague occurrences and model projections for 1965–1969, 1980–1984, and 1995–1999. Each column represents models developed based on plague cases from a particular time period, and each row represents the climatic conditions to which the models were projected, and the counties of occurrence in those time periods.

FIG. 4. Tularemia occurrences and model projections for 1965–1969, 1980–1984, and 1995–1999. Each column represents models developed based on tularemia cases from a particular time period, and each row represents the climatic conditions to which the models were projected, and the counties of occurrence in those time periods.

aspect; and compound topographic index) drawn from a different climatic data set (New et al. 1997). Ecological niches were characterized using climatic variables for the period 1961–1990 (New et al. 1997), and topographic data (slope, aspect, compound topographic index) were obtained from the Hydro-1K dataset (USGS 2001), all resampled to 0.1° resolution for analysis.

To predict future potential distributions, we used two general circulation models (GCMs) that outline future climates: those of the Hadley Centre (HadCM3) (Pope et al. 2002) and the Canadian Center (CGCM1) (Flato et al. 1999). From each GCM, we analyzed two emissions scenarios: the B2 scenario, which is a relatively conservative estimate of climate change, and the A2 scenario, which is more extreme in the climates reconstructed. As they are based on a 30-year average around 2055, our models do not take into account potential effects of increased climate variability (El Niño events, in

particular) on species' distributions. Because these future climate data are provided at a very coarse spatial resolution of 2.5° × 3.75°, we calculated expected changes in temperature (°C) and precipitation (mm) under each scenario from the relatively coarse raw model results; these expected changes were applied to the original IPCC current climate data layers to provide a final pixel resolution of ~30 × 30 km for future-climate data layers.

TABLE 1. DISTRIBUTION OF REPORTED CASES FOR
PLAGUE AND TULAREMIA THAT WERE INCLUDED
IN ANALYSES ACROSS THE SEVEN TIME PERIODS

Time period	Plague	Tularemia
1965–1969	24	970
1970–1974	26	816
1975–1979	79	782
1980–1984	121	1394
1985–1989	58	909
1990–1994	49	723
1995–1999	36	457

TABLE 2. SUMMARY OF PREDICTIONS AMONG TIME PERIODS FOR PLAGUE

		Model						
		65–69	70≠74	75–79	80–84	85–89	90–94	95–99
Projection	65–69	13/14 9–0	10/14 9–0	10/14 7–0	14/14 12–0	13/14 10–0	13/14 9–0	13/14 11–0
	70–74	10/15 8–0	14/15 9–0	14/15 15–8	13/15 14–3	13/15 10–0	13/15 12–0	14/15 12–0
	75–79	21/36 13–0	27/36 14–0	34/36 14–0	31/36 30–0	27/36 24–0	24/36 19–0	31/36 25–0
	80–84	24/42 14–0	27/42 15–0	36/42 11–0	40/42 31–0	32/42 23–0	31/42 20–0	34/42 24–0
	85–89	21/37 16–0	22/37 16–0	31/37 28–0	32/37 32–1	33/37 27–0	30/37 23–0	30/37 24–0
	90–94	22/34 12–0	31/34 13–0	30/34 26–0	31/34 25–0	28/34 20–0	31/34 22–0	30/34 20–0
	95–99	16/22 14–0	17/22 9–0	20/22 15–0	21/22 18–0	18/22 11–0	18/22 13–0	21/22 15–0

Information presented includes #occ/totcase, followed by maxrnd − numgr, where #occ = the number of county occurrences correctly predicted by the model, totcase = total number of cases in that time period, maxrnd = maximum value observed in any of the randomizations (i.e., random selection of the same number of counties), and numgr = the number of randomizations in which the random coincidence exceeded the observed (note that this last number, divided by 100, would be an approximate probability level for the test of significance of coincidence of model predictions with observed case distribution).

RESULTS

Observed changes

The half-decade climate data sets developed in this study indeed captured the essence of a changing—warming—climate (Fig. 1). Visible in these anomaly maps is not just the general warming trend continentwide, but also regional changes in precipitation patterns. As such, the ecological landscape in which plague and tularemia are distributed is indeed changing, motivating the present analyses.

The raw, county-level occurrence data for each time period for the two diseases show northward shifts. Across the four decades covered by this study, the southern border of tularemia distributions shifted approximately the north–south length of Louisiana, or about 600

TABLE 3. SUMMARY OF PREDICTIONS AMONG TIME PERIODS FOR TULAREMIA

		Model						
		65–69	70≠74	75–79	80–84	85–89	90–94	95–99
Projection	65–69	221/401 160–0	111/401 84–0	175/401 128–0	107/401 101–0	30/401 18–0	67/401 73–0	126/401 125–0
	70–74	171/307 112–0	111/307 68–0	140/307 101–0	71/307 86–41	53/307 25–0	43/307 43–54	88/307 103–8
	75–79	189/318 120–0	103/318 68–0	165/318 102–0	107/318 91–0	48/318 17–0	59/318 53–0	124/318 99–0
	80–84	239/445 152–0	147/445 88–0	233/445 152–0	226/445 133–0	87/445 36–0	96/445 67–0	207/445 135–0
	85–89	104/342 190–2	63/342 65–1	181/342 142–0	74/342 83–7	146/342 87–0	66/342 77–28	86/342 99–14
	90–94	81/295 85–1	93/295 55–0	57/295 86–97	80/295 81–1	39/295 21–0	68/295 63–0	84/295 75–0
	95–99	139/222 82–0	93/222 51–0	146/222 75–0	91/222 68–0	26/222 12–0	49/222 37–0	113/222 71–0

Information presented is as in Table 2.

km. The number of plague cases increased in the 1970s and 1980s but declined again by the late 1990s; it did not show clear geographic trends. The ENM-based interpretations of these case data similarly reflected shifts even more plainly; moving across the four decades of the analysis, a northward shift becomes clear (Figs. 3 and 4). The northern border of the distribution of the two diseases is less clear, as fewer or no data were available from Canada, and both diseases reach at least narrowly into Canada.

Model-based tests

Because geographic shifts in disease incidence can occur for a variety of reasons, we explored the consistency of the observed shifts in plague and tularemia with climate-change expectations. That is, we used the ENM results to posit what the shifts would look like were they to be climate-change driven, and we then as-

sessed whether actual (observed) patterns were consistent with those expectations (Peterson and Shaw 2003). In general, the approach was (1) training an ENM based on one time period, (2) projection to another time period, (3) overlay of known disease occurrences for that "other" time period, and (4) performance of a randomization test to assess whether the observed degree of coincidence of prediction and independent test data is greater than random expectations; we conducted such tests for all reciprocal predictions between all seven time periods for both diseases.

The result of these intertemporal analyses was a clear indication of consistency of observed patterns with climate change expectations. Tables 2 and 3 summarize intertemporal predictions and tests for both plague and tularemia: for tularemia, 35 of 42 intertemporal predictions (83.3%) were statistically significantly better than random expectations, and for plague, 41 of 42 (97.6%) were significantly bet-
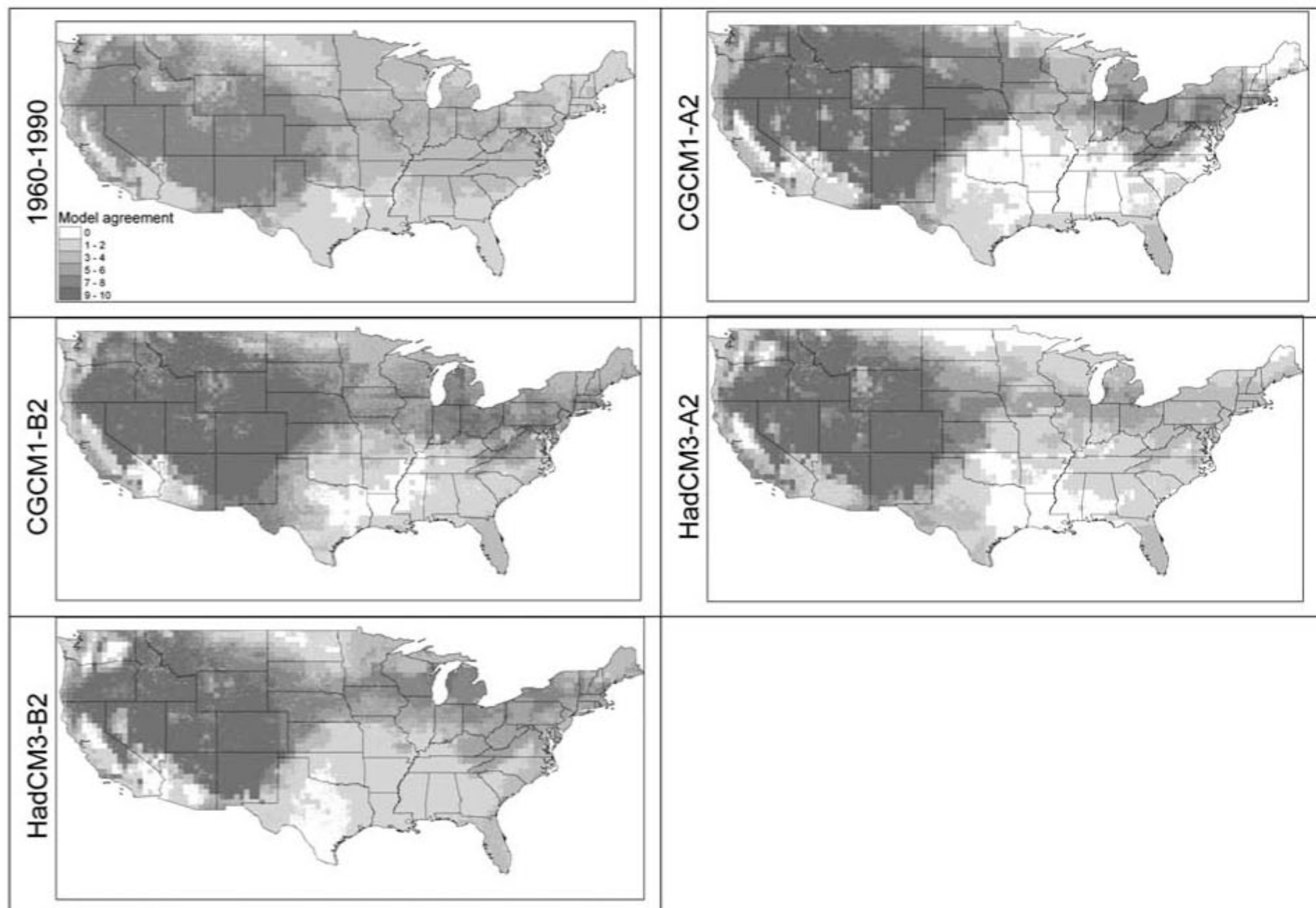

FIG. 5. Present-day plague model projected to 2055 using based on four scenarios of changing climates: CGCM1–A2, CGCM1–B2, HadCM3–A2, and HadCM3–B2.

ter than random expectations. Most important, we observed no tendency for model predictivity to decline with increasing time differential; that is, predictivity across four decades was as high as that between adjacent time periods.

Predictions

The tests presented above suggest strongly that observed shifts in plague and tularemia distributions may be a result of shifts of pathogen, vector, or host distributions following climate change. Using somewhat different environmental data sets (perforce), we explored the implications of climate change-caused shifts for likely future distributions of plague and tularemia (Figs. 5 and 6). In the case of tularemia, reduced incidence may be expected in the central-south of the United States (e.g., Louisiana, Mississippi), and greater incidence may be expected in the northern tier of states (e.g., Michigan to North Dakota). For plague, while New Mexico (the present heart of plague transmission in the United States) is not predicted to see much change, we do

see increased potential for transmission in Wyoming and Idaho.

DISCUSSION

The approach

The techniques used in this study are experimental in nature, and their implications are only beginning to be explored. In the realm of biodiversity science, these techniques have now been applied to a variety of geographic and taxonomic situations (Thomas et al. 2004), and some general tendencies are beginning to emerge (Peterson 2003, Thuiller et al. 2005). More important, a few quantitative tests of the ability of such models to anticipate real phenomena are beginning to appear (Martínez-Meyer et al. 2004, Araujo et al. 2005, Martínez-Meyer and Peterson 2006); these tests and, we hope, more that will be developed, can provide important benchmarks for interpretation and understanding of model predictions.
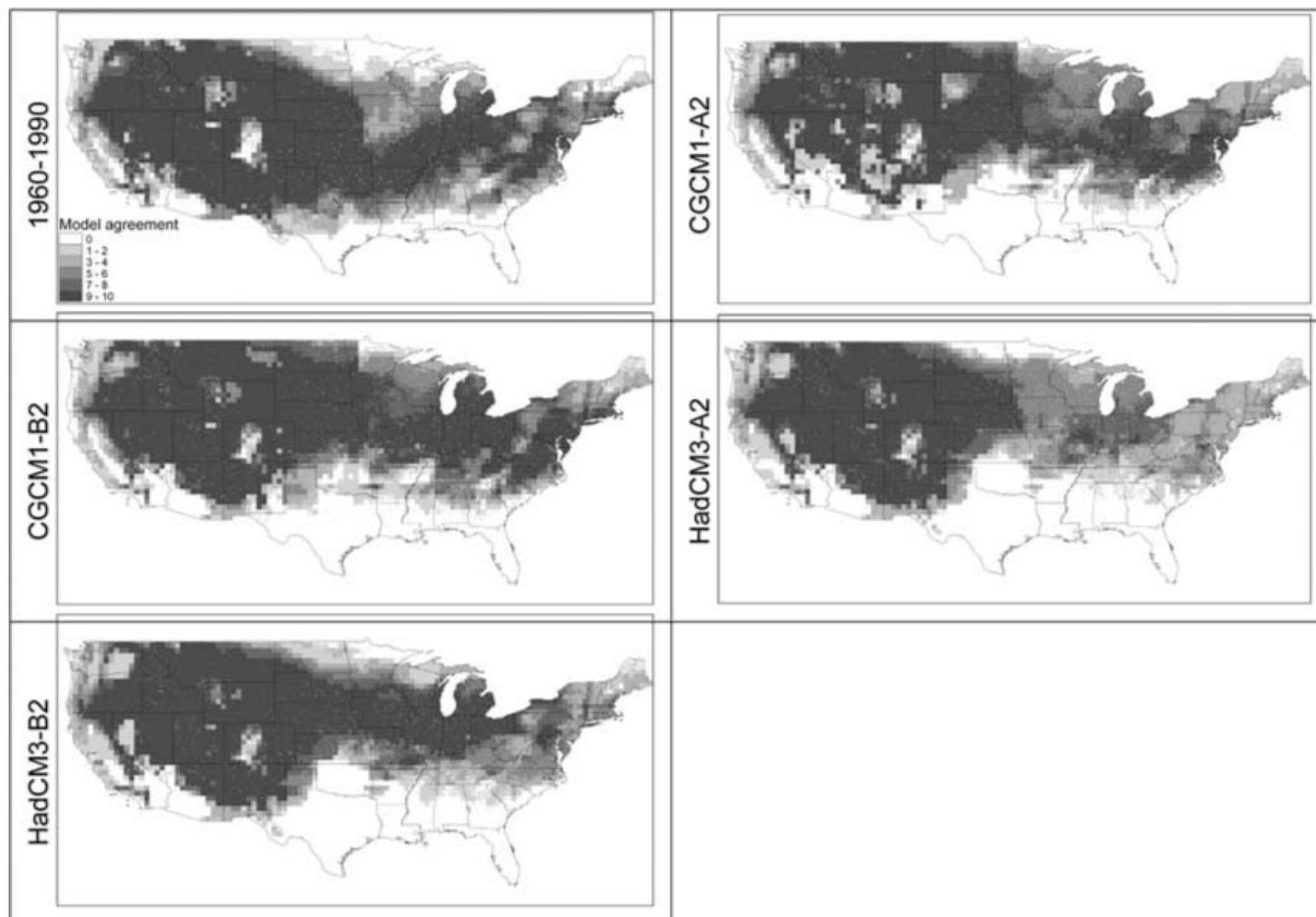

FIG. 6. Present-day tularemia model projected to 2055 using based on four scenarios of changing climates: CGCM1–A2, CGCM1–B2, HadCM3–A2, and HadCM3–B2.

With regard to disease transmission, our results represent one of very few such applications. In a previous study, one of us analyzed spatial distributions of sandfly vectors of leishmaniasis in southern Brazil, and made predictions of which species should be increasing in abundance in key regions—these predictions have seen some preliminary indications of support (Peterson and Shaw 2003). Clearly, these techniques can and should be applied to a broader variety of disease systems, particularly in situations in which tests of model predictions are possible.

These models have several limitations (Austin et al. 1990, Guisan and Zimmermann 2000, Hirzel et al. 2002, Soberón and Peterson 2005). Obviously, the spatial resolution of the occurrence data and environmental data limits the spatial resolution possible in resulting maps. The environmental data in particular are often of coarse resolution, particularly when future projections across changing climates are involved. Finally, true errors in model development can lead to inaccurate predictions, in which environmental conditions not appropriate for the species are included or those appropriate for the species are excluded. It is thus clear that the ENM methodology requires refinement and testing, to make clear when limitations are reached, and when caution is merited in interpretation.

The implications of this study regarding future risk of human cases of plague and tularemia are more difficult to define. Human tularemia cases are relatively rare, generally confined to rural settings, and influenced by individual behaviors, such as hunting (for sport or for subsistence). In contrast, human plague cases may occur not only in rural areas but also in plague-enzootic areas experiencing suburbanization and new housing construction (Barnes 1982, Craven et al. 1994). Human plague cases in these areas are likely to be acquired in peridomestic environments, particularly those located in habitats preferred by plague-susceptible rodents or that provide man-made sources of food or shelter for these animals. Geographic shifts in the frequency or distribution of the pathogens could increase, decrease, or leave unchanged the overall frequency of disease. Nevertheless, the shifts and changes expected and outlined based on our results could result in shifts in disease activity that would require action on the part of local health officials to reduce risks to public health.

Although the CDC does not collect data on human plague or tularemia in Mexico and Canada, evidence of infections has been identified in western U.S. counties bordering both Canada and Mexico. Although tularemia is well known in Canada, distributions of plague north and south of the western United States are not well characterized. Direct evidence of *Y. pestis* infections also has been identified in Canadian rodents and rodent-consuming carnivores (Humphreys and Campbell 1947, Leighton et al. 2001). Humphreys and Campbell (1947) described a likely case of human plague in a Canadian mink rancher who had been handling ground squirrels. A single Mexican prairie dog was reported positive for *Y. pestis* infection based on the identification of bipolar staining bacteria in tissue samples (Varela and Vasquez 1954), but the true status and distribution of *Y. pestis* in Mexico remains unknown. The shifts identified in this study would suggest that Canada may see a greater incidence, and Mexico a lower incidence, of these diseases, particularly where tularaemia is concerned.

CONCLUSIONS

This study has used a combination of GIS and ecological niche modeling techniques to clarify evidence for climate change-mediated range shifts in plague and tularemia in North America. We emphasize the need for clarity in how far such model-based tests should be interpreted—we have demonstrated that observed patterns are *consistent with* climate change causation, but we have not presented a definitive test of this hypothesis. On the basis of this association, we go on to explore likely shifts over coming decades in these two disease systems. Such more convincing work will have to await more detailed data sets, and perhaps even experimental manipulation. Still, this approach is now seen to be quite useful in testing hypotheses regarding disease transmission and its spatial and temporal distributions.

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