Rego RF, Moraes LR, Dourado I. Diarrhoea and garbage disposal in Salvador, Brazil. Trans R Soc Trop Medi Hyg. 2005;99:48–54.

Stiratelli R, Laird N, Ware JH. Random-effects models for serial observations with binary response. Biometrics. 1984;40:961–971.

Trostle JA, Hubbard A, Scott J, et al. Raising the level of analysis of food-borne outbreaks. Epidemiology. 2008;19(3):384–390.

Tumwine JK, Thompson J, Katua-Katua M, et al. Diarrhoea and effects of different water sources, sanitation and hygiene behaviour in East Africa. Trop Med Int Health. 2002;7:750–756.

Wallace D, Wallace R. A plague on your houses: How New York was burned down and national public health crumbled. New York: Verso; 1998.

Wallace R. A Synergism of plagues: "Planned shrinkage," contagious housing destruction, and AIDS in the Bronx. Environmental Research. 1988;47(1):1–33.

WHO. Persistent diarrhoea in children in developing countries: Memorandum from a WHO meeting. Bulletin of the World Health Organization. 1988;66:709–717.

A12

CLIMATE, WIND STORMS, AND THE RISK OF VALLEY FEVER (COCCIDIOIDOMYCOSIS)

Heidi E. Brown,[47] *Andrew C. Comrie*,[48] *James Tamerius*,[49] *Mohammed Khan*,[50] *Joseph A. Tabor*,[51] *and John N.* ***Galgiani***[52]

Introduction

Valley fever (coccidioidomycosis) is a Western Hemisphere disease, having been found in several South American, Central American, and North American countries (Laniado-Laborin, 2007). For the most part, the areas endemic for *Coccidioides* spp. are rural areas of low population densities. However in the United States there are exceptions such as Bakersfield in Kern County, California

[47] Heidi E. Brown, Ph.D., M.P.H.; Assistant Professor, University of Arizona; Mel and Enid Zuckerman College of Public Health; Division of Epidemiology and Biostatistics; 1295 N. Martin Ave.; Tucson, AZ 85724.

[48] Andrew C. Comrie, Ph.D.; Professor, University of Arizona; School of Geography & Development; 409 Harvill Building; Tucson, AZ 85721.

[49] James Tamerius, Ph.D.; Assistant Professor, University of Iowa; Department of Geographical and Sustainability Sciences; 316 Jessup Hall; Iowa City, IA 52245.

[50] Mohammed Khan, M.S.P.H.; Epidemiologist; Infectious Disease Epidemiology and Surveillance; Office of Infectious Disease Services; Arizona Department of Health Services; 150 N. 18th Ave. Suite 140; Phoenix, AZ 85007.

[51] Joseph A Tabor, Ph.D., M.P.H.; Assistant Professor, University of Arizona; Mel and Enid Zuckerman College of Public Health; Division of Community, Environment and Policy; 1295 N. Martin Ave.; Tucson, AZ 85724.

[52] Corresponding author: John N Galgiani, M.D.; Professor, University of Arizona College of Medicine; Director, Valley Fever Center for Excellence; PO Box 245215; Tucson, AZ 85724.

(population nearly one million), and populations surrounding Phoenix in Maricopa County and Tucson in Pima County of Arizona whose combined populations are approximately five million. The total number of infections reported from endemic states (Arizona, California, Nevada, New Mexico, and Utah) in 2011 were 10-fold greater than in 1998 (CDC, 2013). That the case rates for these populations have also increased eight-fold indicates that the rise is not simply due to population growth. In this report, we review some of the factors that are responsible for these changes with particular attention to how weather patterns may influence infection rates.

The Problem of Valley Fever

Coccidioidomycosis is a systemic fungal infection caused by *Coccidioides* spp. Spores (arthroconidia) of the fungus that develop in the soil of endemic regions are aerosolized by wind or mechanical disturbance of endemic soil. Inhalation of an arthroconidium into the lungs of a human or another mammal can initiate a respiratory infection. It is estimated that 150,000 such infections annually occur in U.S. residents. The consequences of infection range from no apparent illness in 60 percent of infections, to a self-limited community-acquired pneumonia in another 35 percent. The remaining 5 percent result in a variety of progressive, even life-threatening, complications, either in the lungs or outside of the chest if the fungus travels through the bloodstream to other organs such as the brain, bones, and skin (Figure A12-1). Since two-thirds of all U.S. infections occur in Arizona, the Arizona Department of Health Services (ADHS) has been investigating the overall impact of this problem to the state. A questionnaire survey of newly diagnosed patients with valley fever in 2007 (Tsang et al., 2010) demonstrated the severe consequences associated with infection:

- Illness lasted an average of 6 months.
- 75 percent of employed persons stopped working, half missing 2 or more weeks.
- 40 percent were hospitalized.

In a more recent report, hospital costs alone in 2012 amounted to over $100 million.[53] This, taken with outpatient care costs and lost productivity, suggests that the economic impact of valley fever on Arizona is easily several hundred million dollars annually. In California for 2000 through 2011, hospital costs were greater than $2 billion (Sondermeyer et al., 2013).

[53] See http://azdhs.gov/phs/oids/epi/disease/valley-fever/documents/reports/valley-fever-2012.pdf (accessed December 2, 2013).

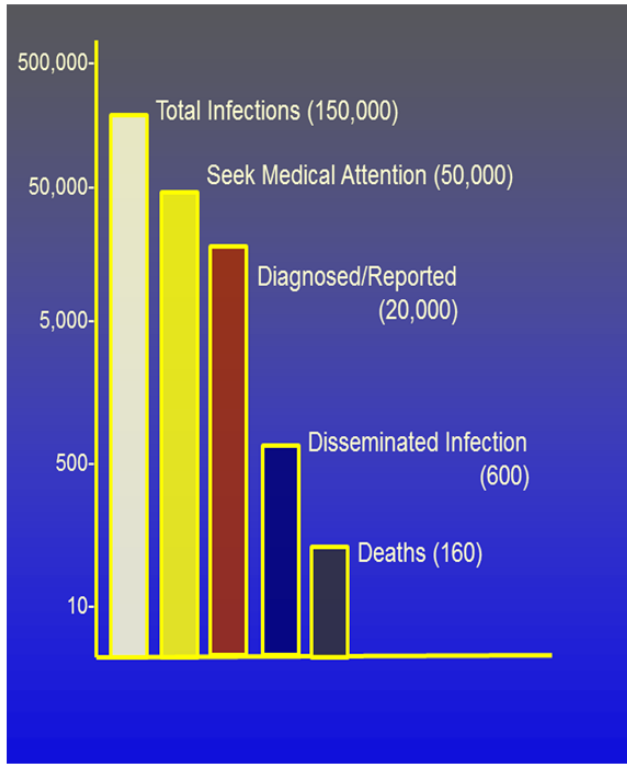

FIGURE A12-1 Coccidioidomycosis. Estimated numbers of total annual U.S. infections with *Coccidioides* spp. and resulting clinical consequences.
SOURCE: Courtesy of Galgiani, 2013.

How Passive Surveillance May Affect Reported Numbers of Valley Fever Infection

There is no question that the nationally reported annual number of patients with coccidioidomycosis has progressively increased since the 1990s. This has been noted in several reports in recent years (CDC, 1996, 2003; Chen et al., 2011; Hector et al., 2011; Leake et al., 2000; Park et al., 2005; Sunenshine et al., 2007; Tsang et al., 2010), but the most recent Centers for Disease Control and Prevention report (CDC, 2013) gives this trend much needed visibility in both the medical community and the general media, which reported on this story nationally. Headlines such as "Valley Fever Cases Skyrocket" and "Valley Fever Cases Are at Their Highest Numbers in Nearly Two Decades" dotted news stories for more than a week following the CDC report. There have been 111,717 cases of coccidioidomycosis reported to the CDC from 1998 through 2011. Arizona

was responsible for 66 percent of these infections and California for 31 percent. Nearly all of the remaining infections were reported from New Mexico, Utah, and Nevada. The annual number of valley fever cases in Arizona and California are shown in Figure A12-2. Case rates reported by the CDC are prevalence estimates based on the general population and not the susceptible population as are disease incidence rates. Care needs to be used when comparing reported case rates between different parts of the country since they do not take into account the proportion of previously infected (now immune) individuals (Tabor and O'Rourke, 2010).

Notably absent from these numbers is representation from Texas, well known to be endemic along its western border (Edwards and Palmer, 1957). There are no reports of coccidioidomycosis from Texas because it is not a reportable disease in that state, underscoring one of the limitations of the National Notifiable Disease Surveillance System (NNDSS): state reporting to NNDSS is voluntary. In addition to missing information from Texas, underreporting by some or many of the nonendemic states is likely as well.

Beyond state reporting decisions, several other surveillance factors need to be met for a patient's infection to be incorporated into the overall case tally. First, only persons sick enough to seek medical care will be included. Second, a clinician needs to consider the diagnosis and order the necessary tests. Third, the tests need to have sufficient sensitivity and specificity to enable the correct diagnosis.

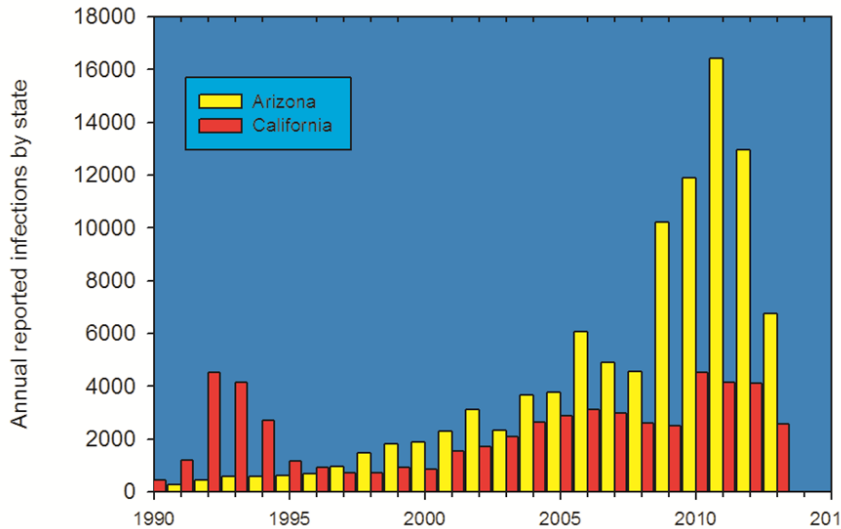

FIGURE A12-2 Annual coccidioidomycosis. Numbers of cases of coccidioidomycosis reported to the CDC by Arizona and California from 1990 through 2013.
SOURCE: Courtesy of Galgiani, 2013.

Fourth, once diagnosed, the infection must be reported to public health authorities. How completely the second, third, and fourth of these steps is conducted has a direct effect on the resulting estimates of disease activity.

Physician awareness of valley fever is variable even within the endemic regions. For example, in a survey by the ADHS, Arizona clinicians were asked about their knowledge, attitudes, and practice with respect to valley fever (Chen et al., 2011). Only 12 percent of respondents indicated they had learned medicine in Arizona schools and 47 percent had no clinical training in Arizona prior to starting practice here. Moreover, 40 percent lacked confidence in diagnosing a coccidioidal infection. In another study of two physician group practices, only 2–13 percent of patients with community-acquired pneumonia were evaluated for *Coccidioides* infection (Chang et al., 2008). These relatively recent studies strongly suggest that the actual number of patients seeking care for valley fever infections is greatly underreported. Moreover, if clinicians improve their capacity for detecting new coccidioidal infections, their changed practices have the potential of significantly increasing the number of reported cases.

Although available serologic tests are effective in diagnosing patients with widespread and long-standing infection, false negatives are common among newly infected patients with disease limited to the lungs. In one study, standard serologic testing missed such infections in about half of first sera tested (Wieden et al., 1996). Improving the sensitivity of clinical testing is under active investigation, and progress in this area could significantly change the number of reported cases. For example, in 2009 a major clinical laboratory in Arizona began using a more sensitive test as indicative of infection. As a result the number of reported cases to the state nearly doubled (Hector et al., 2011).

A puzzling observation in the 2013 CDC report is the disproportionate increase in reported coccidioidomycosis among females in Arizona. The percentage of females with coccidioidomycosis before 2009 was 44 percent, but since 2009 this has risen to 55 percent. One possible explanation for this shift comes from a pair of studies conducted by the University of Arizona Campus Health (Lundergan et al., 1985; Stern and Galgiani, 2010). In their 1985 report, women comprised 44 percent of valley fever cases, but in 2010, females comprised 56 percent of infected scholarship athletes. Between these two studies, screening serologic tests for coccidioidomycosis at Campus Health changed from the less sensitive standard coccidioidal serology (immunodiffusion tests) to the more sensitive enzyme-linked immunoassays (EIAs) (Wieden et al., 1996). This was the same change that was made in 2009 by the major Arizona clinical laboratory mentioned above. Women at the University of Arizona, on average, were found to have lower complement fixation titers (Lundergan et al., 1985), raising the plausible possibility that the increased statewide percentage of females with valley fever could be due to the increased sensitivity of EIAs to lower levels of anticoccidioidal antibodies in women. Certainly further studies are needed to clarify these findings.

Reporting newly diagnosed patients with coccidioidomycosis may not always be complete. For example, although clinicians are required to report new coccidioidomycosis, it may be difficult because of busy schedules. In contrast, if reporting is asked of the clinical laboratory that identifies the positive test, the likelihood of reporting is much greater. In Arizona, the reporting responsibilities were shifted in 1997 to include laboratory reporting, and it is possible that some of the increase in the ensuing years was due to that change.

Relationship Between Weather Patterns and Valley Fever Infections in Arizona

Despite several surveillance considerations just described, none adequately account for the episodic increases seen in California in 1993 and 1994 or in Arizona in 2011 (Figure A12-2). Weather factors such as wind, precipitation, and heat may provide an explanation. The 37 percent increase in Arizona cases in 2011 highlights the interaction of valley fever and weather with the co-occurrence of several spectacular dust storms, known as haboobs. These haboobs were so severe and so directly affecting the urban Phoenix area that time-lapse video footage featured prominently on national evening news programs.[54] As early as 1940, Smith described the relationship between seasonal weather patterns and valley fever incidence: the lowest incidence occurs during the wet seasons; incidence increases with the onset of the dry weather of spring and early summer; the peak season follows the hot summer and increased winds of fall. Smith (1940) also described human activity (harvesting) as an exposure risk. It bears noting, however, that the strength of the association varies across populations and time periods.

Wind is an important factor to generate aerosols of *Coccidioides* spores. For example, in December 1977, a major Santa Anna wind swept across the Central Valley of California, resulting in cases of valley fever in distant, nonendemic areas such as the San Francisco Bay Area (Flynn et al., 1979). In Kern County there were 120 excess cases in the following 3 months (Pappagianis and Einstein, 1978). That was with a Kern County population of approximately 400,000 of which three quarters were likely immune because of prior infection and therefore not susceptible to new infection. In contrast, the Phoenix area population downwind to the July 2011 haboobs was 10 times larger, and three-quarters were likely to be susceptible because of the large in-migration population. Simple extrapolation using these figures results in a prediction of an excess 3,600 infections in the months following July. However, this prediction was not borne out. As shown in Figure A12-3, the week-to-week numbers of reported valley fever cases for the three major urban areas within the endemic region (Maricopa, Pima, and Pinal Counties) were strikingly stable with no apparent increase in cases in the months following the first major July storm.

[54] See http://www.cbsnews.com/2100-201_162-20094755.html (accessed December 2, 2013).

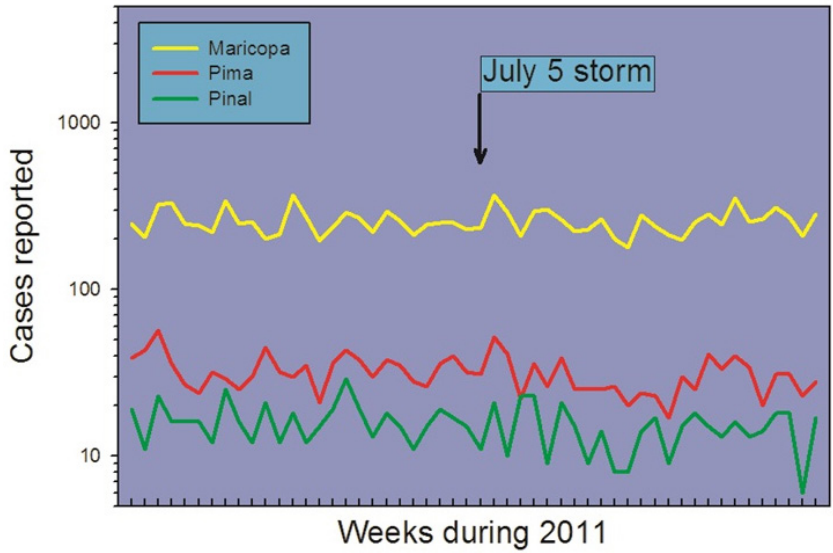

FIGURE A12-3 Dust storms have little effect on Arizona case rates. Weekly reported cases of coccidioidomycosis in selected Arizona counties for 2011.
SOURCE: Courtesy of Galgiani, 2013.

There are at least three possible explanations for how these 2011 observations in the Phoenix area could be so different from what was observed in California in the 1977 storm. First, the California storm occurred in the winter, a time when infections are minimal in Kern County. Therefore, with very low background numbers of cases, the excess cases were very apparent. In contrast, the Phoenix storms occurred when many cases normally are reported. Thus, it is possible that there in fact were excess cases that could not be detected by the passive surveillance that is in place. Second, summer haboobs, although exceptionally spectacular, usually last only a matter of hours. It very well may be that these very short-term peak concentrations and exposures of coccidioidal spores in the air cannot be detected from case reporting due to the attenuating effects of variable disease onset and reporting time. The spores, being 3–5 microns in size, may require only slight turbulence to be lifted from the soil surface into the air. Figure A12-4 is a hypothetical representation of such a situation to illustrate that if spores are being picked up on a regular basis the overall area under the curve for spore density might only slightly be increased from exceptional but brief dust storms. Third, haboobs in the Phoenix area are generally associated with summer thunderstorms, but in different locales across central and southern Arizona they may possess different amounts and types of dust. Much of the dust in and around Phoenix may come from disturbed agricultural and urban land—neither

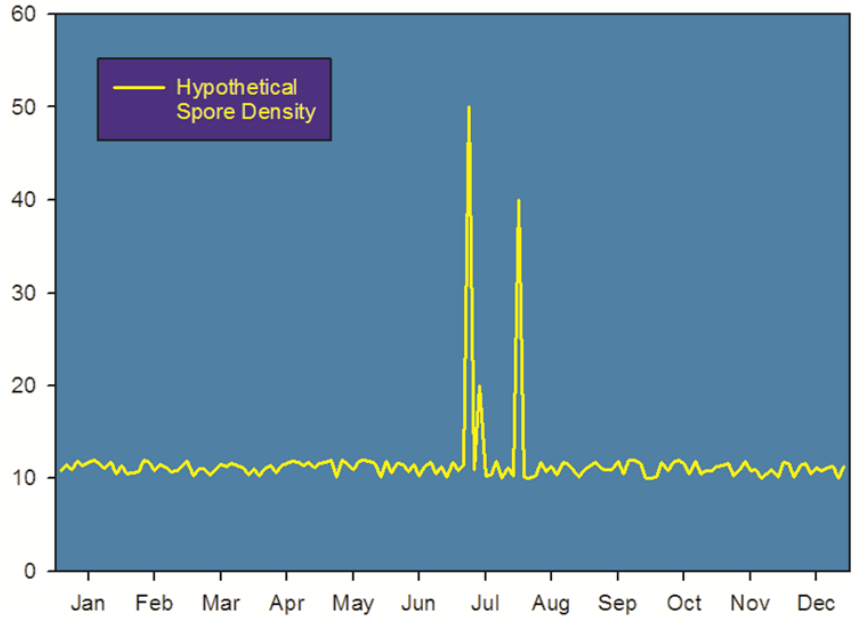

FIGURE A12-4 How dust storm contribution on spore density could be minimal. Hypothetical contribution of episodic wind storms to ambient atmospheric spore density if only small breezes are sufficient to produce an aerosol.
SOURCE: Courtesy of Galgiani, 2013.

of which represents the natural desert soils that *Coccidioides* spp. are thought to favor. Thus the path that these storms cover may largely determine the exposure risk they pose to downwind populations.

Although it is difficult to show a causal relationship between wind storms and the 2011 increase in valley fever cases, a recently developed model shows a strong relationship at seasonal time scales between precipitation patterns and the year-to-year changes in valley fever cases in Arizona. In particular, winter precipitation promotes fungal growth in the soil (Hugenholtz, 1957), and increased precipitation during this period seems to be related to increased incidence of valley fever the following summer and fall (Comrie, 2005; Kolivras and Comrie, 2003; Smith et al., 1946; Tamerius and Comrie, 2011). High summer precipitation, conversely, has a negative effect on incidence, perhaps by reducing the chances of aerosolized spores (Kolivras and Comrie, 2003). Tamerius and Comrie (2011) used data from 1995 through 2006 for rainfall and cases in the Arizona counties of Maricopa and Pima to develop a precipitation-driven model of valley fever cases. They reasoned that the overall trend evident in Figure A12-2 of increasing cases over that period was not climate related and removed the trend to reduce biasing any association between weather and reported cases. Using

an autocorrelation statistical procedure, they were then able to define a primary coccidioidal exposure season of August through March. By examining rainfall patterns before and during these exposure seasons, these authors identified two countervailing relationships. First, the magnitude of rainfall during the winter was positively correlated with the number of reported infections the following season. Second, higher rain amounts during an exposure season resulted in fewer reported infections. Combining these two relationships in a single model during the training period resulted in a correlation coefficient of 0.83 for Maricopa data and 0.73 for Pima County. In preparation for this workshop, this model was updated to the present period for Maricopa County. The model was also used to estimate disease activity backward to 1950 (hindcasting) using historical precipitation data. With the hindcasting, there are no surveillance data available for the majority of this period to validate the accuracy of the results.

Updating the model for Maricopa County The model was updated to investigate the predictive power of winter precipitation and valley fever exposure using current data (1995–2013). The greatest challenge with these data was the aforementioned changes in case definition, reporting, and testing around 2009 that led to a doubling of cases: from under 5,000 to over 10,000 (Nguyen et al., 2013). As in the original publication, the case data were adjusted to estimate exposure dates rather than date of diagnosis or report. Monthly reported incidence (number of cases per 100,000) for each was calculated by dividing the number of cases in Maricopa County by the U.S. Census Bureau estimated annual population for the county. As previously, the data were detrended for the period January 1995–February 2009 by removing the best-fit linear regression (i.e., modeling the residuals). To adjust for the change in the case definition and reporting, the median incidence was subtracted out for the period from March 2009–March 2013. While this standardizes the two distinct periods, the variance for the latter period (2009–2013) is greater and creates difficulty when comparing incidence across study periods. Finally, seasonal incidence was calculated by summing across months during the exposure season (August–March).

Monthly precipitation totals for the grid points in which the Maricopa National Weather Service Station locations fall were acquired from the Oregon State PRISM (Parameter-elevation Regressions on Independent Slopes Model) climate mapping system (http://prism.oregonstate.edu/index.phtml, last accessed December 2, 2013) and averaged for use in the model. The previously identified regression coefficients were applied on the data to estimate the number of exposures per month for the primary exposure season (August–March). There is concordance between the predictions from the model and the observed reported cases for the exposure seasons (Figure A12-5). The model fits relatively well, though it errs in 1998, 2008, 2009, and 2010 (i.e., predicts high when the exposures are low or vice versa). Note that the means of the detrended (observed) time series and the modeled time series have been standardized (forced to equal) for comparison.

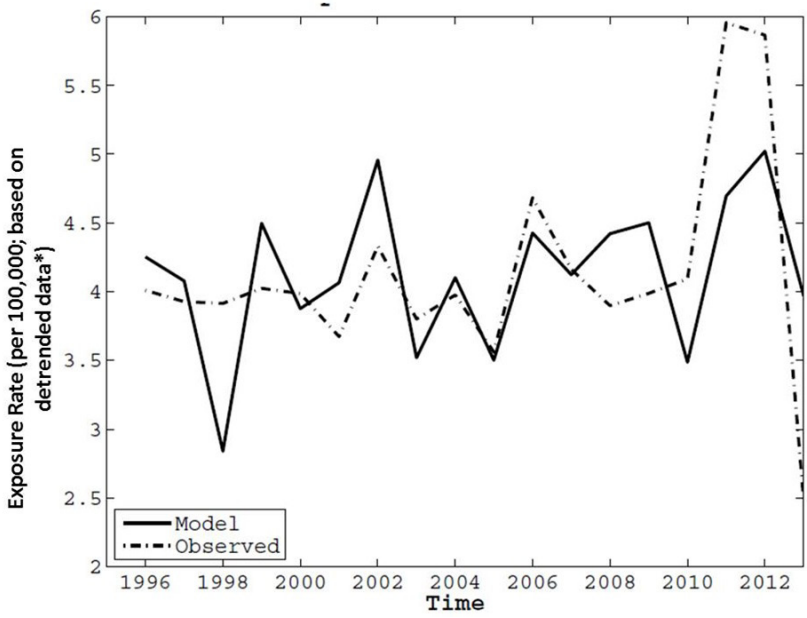

FIGURE A12-5 Model results (1996–2013). Comparison of modeled versus the predicted exposure rates based on October–December precipitation prior to the exposure season and concurrent exposure season (August to March) precipitation. The solid line indicates the model exposure rate and the dashed line the observed rate.

* Tamerius and Comrie, 2010.

SOURCE: Courtesy of James Tamerius.

Hindcasting (1950 through 2013) To estimate the number of cases back in time, we also applied the model to a precipitation time series beginning in 1950 using the same PRISM-based precipitation data for one location, Maricopa County (downloaded from http://www.cefa.dri.edu/Westmap). The model was applied in order to estimate the number of cases that might have been expected in the past. The outcome of this model is the estimated exposure rate for the primary exposure period (August–March) per 100,000.

Average case numbers predicted by the model for the periods 1950–1979 and 1908–2009 are shown in Figure A12-6. The dashed line indicates the time period for which data were available and upon which the original model was built (Tamerius and Comrie, 2011), and the solid line indicates the predictions. Unlike observed temperature increases, the Southwest has not experienced shifting trends in precipitation for the past 110 years (Hoerling et al., 2013). Our precipitation-based model similarly does not appear to indicate any significant change in the predicted seasonal exposure.

Finally, in addition to wind and precipitation, heat and human behavior also play a role the incidence of valley fever. Evidence suggests temperature has a

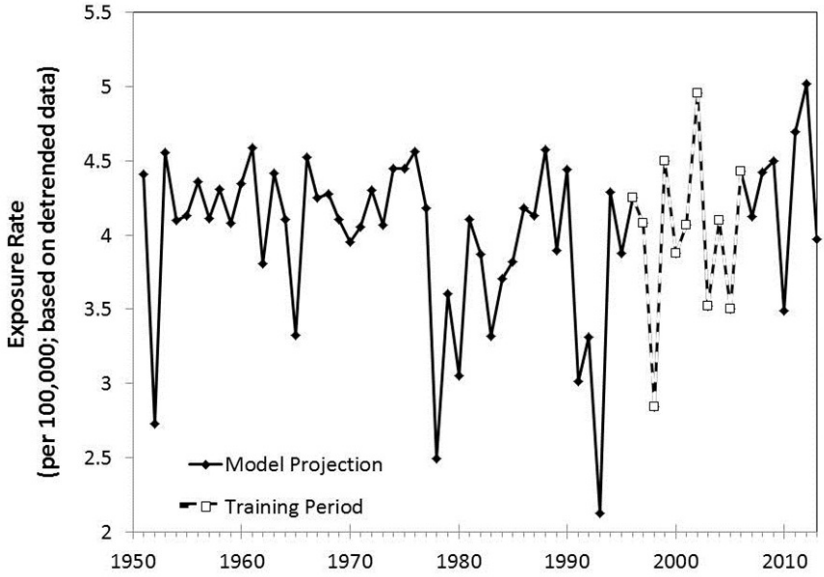

FIGURE A12-6 Hindcasting estimates (1950–2013). Modeled coccidioidal exposure in Maricopa County during August–March for the years 1950 through 2012. The model training period, 1995–2006, is shown as a dashed line while the prediction is a solid line. SOURCE: Courtesy of Andrew Comrie.

role in regulating competition between fungal species. Laboratory experiments showed *Coccidioides* spp. are well adapted to the arid environment, tolerating extreme heat and a wide range of humidity levels (Friedman et al., 1956). High heat and sun is proposed to have a sterilizing effect on soils that may provide a competitive advantage for *Coccidioides* spp. over other soil fungi (Duran et al., 1973; Hugenholtz, 1957; Maddy, 1965). Heat is also thought to facilitate the aerosolization of spores by drying soils. All of these external forces acting upon the fungus are further affected by host behavior. Human or other animal activity such as digging, excavating, and other soil disrupting activities may result in cases outside the climate-driven seasonality (Converse and Reed, 1966; Maddy, 1965). This is further supported by work in Kern County, California, where weather has only a weak association with incidence—the authors attribute human behavior to the observed disease trends in their area (Talamantes et al., 2007; Zender and Talamantes, 2006).

Future Approaches to Better Understand the Effects of Environmental Change on Risk of Coccidioidomycosis

Current knowledge of *Coccidioides* ecology is based mostly on pre-1970 studies and, more recently, inferred from reported human cases that are aggregated

at the county level (Baptista-Rosas et al., 2007; Comrie, 2005; Tamerius and Comrie, 2011). Spatial and temporal precision is low when relying on reported case data, whereas the alternative of analyzing environmental samples collected precisely is expensive and problematic. Indeed, our accumulated understanding about the environmental biology and ecology of *Coccidioides* spp. is largely incomplete, due to specific challenges in identifying the fungus in its natural state. Improvements in PCR detection and direct plating isolation methods for environmental samples are needed in order to replace the standard method of induced infections in laboratory mice (Barker et al., 2012). Here we briefly summarize the literature and identify a pathway to completing this ecological puzzle.

Geographic distribution Much groundwork for identifying environmental correlates of *Coccidioides* spp. habitat was performed in the 1940s and 1950s. Researchers like Maddy (1958) showed an association between valley fever incidence and the lower Sonoran life zone, though subsequent research expanded the endemic zone more broadly. Epidemiological evidence led researchers to believe exposure was inhalational, often windborne (Emmons, 1942a; Smith et al., 1946), despite difficulty recovering *Coccidioides* spp. from the air (Ajello et al., 1965; Anderson, 1958; Converse and Reed, 1966). Weather was also found to play a role in identifying endemic regions that shared a characteristic wet period followed by a dry period with blowing winds (Hugenholtz, 1957; Maddy, 1958; Smith et al., 1946). The association with precipitation patterns has been borne out in modern times as well (Kolivras and Comrie, 2003; Park et al., 2005; Stacy et al., 2012; Tamerius and Comrie, 2011; Zender and Talamantes, 2006).

Rodents and microhabitat Ideas regarding the role of animals in the evolution of *Coccidioides* spp. has been inconsistent. Some researchers have concluded that infected animals, like humans, are accidental hosts to the fungus (Cummins et al., 1929; Pulford and Larson, 1929), while others have proposed a role for the animal carcass as a medium for fungal growth within the soil (Emmons, 1942b; Emmons and Ashburn, 1942). While the mechanism is unknown, there is significant evidence that rodents play a prominent role in the saprophytic phase of this fungus. For example, although the fungus is notoriously difficult to recover from soil (Greene et al., 2000), soil samples collected near animal burrows are often positive for the fungus (Barker et al., 2012; Eulalio et al., 2001; Maddy, 1959, 1965).

Challenges and Future Work

While considerable strides were made in those early years of research on valley fever, Ajello (1967) concluded that "the ecology of these fungi, i.e., the study of their relationship to their environment, is rather superficial and scanty." This sentiment holds today: "ecology of the pathogen, *Coccidioides*, remains obscure" (Barker et al., 2012). Recent outbreaks of coccidioidomycosis in eastern

Washington and northern Utah (Mardo et al., 2002; Marsden-Haug et al., 2013), far outside of known endemic areas, illustrate our poor understanding of these fungi's ecologies. The outbreaks could be due to soil disturbances in isolated patches of *Coccidioides* spp. or due to range expansion. Genetic analyses have shown that valley fever is caused by *C. immitis* in central/southern California and a genetically related, but distinct *C. posadasii* in southern Arizona, Texas, and Mexico (Barker et al., 2007; Fisher et al., 2002). Consideration of differences among these two fungal species will likely help further elucidate distinctions and nuances in the range and habitat of these fungi. However, the difficulty in locating areas of infected soil—which, as noted, may be related to burrowing animals, soil salinity (Ajello, 1967; Friedman et al., 1956), soil type (Maddy, 1958), and vegetation (Egeberg, 1953; Swatek, 1970)—continues to stymie accurate exposure tracking. From a public health standpoint, it is this latter aspect—more narrowly defining exposure risk—that will be critical in reducing the impact of this disease.

Currently, soil samples must be collected in the field, transported to the laboratory, and mouse models exposed to the potentially contaminated soil (Barker et al., 2012; Levine and Winn, 1964; Maddy, 1965) in order to identify *Coccidioides* spp. This is a labor- and cost-intensive method for identifying possible sources and does not lend itself well to large-scale risk mapping. Sorely needed is a means to quickly and accurately identify the microhabitat wherein this fungus thrives.

Conclusions

In this paper, we discuss trends in occurrence of valley fever in the United States. Of note are the challenges this disease presents to prevention efforts: reporting issues, changes in diagnostics and detection, changes in surveillance, and limited tools for assessing risk. We provide an updated version of a precipitation-driven model that fits well for Maricopa County, Arizona. We end with a discussion of the ecology of this disease of the American Southwest and the challenges facing improvements to disease control.

The increase in the number of reported cases and interest following these reports have generated a justifiable spotlight on this disease. As physicians' awareness of the disease increases, there will likely be an increase in testing for valley fever. Accordingly, reported incidence of this disease will likely increase. While improving our capacity to describe the burden of this disease, these increases will be a result of enhanced case identification rather than changes in susceptibility or exposure. In all likelihood, individual patient outcomes will be improved by accurate and earlier diagnosis; however, these changes will not translate into valley fever prevention.

Currently, a serious impediment to prevention is a lack of knowledge about the ecological processes that modulate the presence of *Coccidioides* spp. in the environment. Ecological research is needed that examines the relationships

between the occurrence of *Coccidioides* spp. and soil moisture, soil temperature, and rodent populations. Defining the habitat of this pathogen (identifying specific soils, areas, regions) would enable the identification of risk related to specific human activities or periods of time; possibilities for developing treatment of landscapes to reduce fungal proliferation; and early warning for protection against aerosols (e.g., knowing that sufficient strength winds are blowing across known endemic soils). Until a means to detect the pathogen in the soil is discovered, we are left with broad and sometimes conflicting studies on the risk of acquiring valley fever from the environment.

Also needed is the exploration into the etiological relationships for spore exposure. Not all dust contains viable spores. Many validated models exist for predicting dispersal and exposure of airborne particulates, but not for predicting when and where viable *Coccidioides* spp. spores are entrained into the air from the soil surface. Likely predictors for airborne dispersal and exposure are soil surface temperature, soil surface moisture, vegetative cover, and UV exposure from the sun. Once these ecological and etiological questions can be answered then actionable occupational and land use practices can be identified for disease prevention.

References

Ajello, L. 1967. Comparative ecology of respiratory mycotic disease agents. *Bacteriological Reviews* 31(1):6-24.

Ajello, L., K. Maddy, G. Crecelius, P. G. Hugenholtz, and L. B. Hall. 1965. Recovery of *Coccidioides immitis* from the air. *Sabouraudia* 4(June):92-95.

Anderson, A. A. 1958. New sampler for the collection, sizing, and enumeration of viable airborne particles. *Journal of Bacteriology* 76(5):13.

Baptista-Rosas, R. C., A. Hinojosa, and M. Riquelme. 2007. Ecological niche modeling of *Coccidioides* spp. in western North American deserts. *Annals of the New York Academy of Sciences* 1111:35-46.

Barker, B. M., K. A. Jewell, S. Kroken, and M. J. Orbach. 2007. The population biology of coccidioides: Epidemiologic implications for disease outbreaks. *Annals of the New York Academy of Sciences* 1111:147-163.

Barker, B. M., J. A. Tabor, L. F. Shubitz, R. Perill, and M. J. Orbach. 2012. Detection and phylogenetic analysis of *Coccidioides posadasii* in Arizona soil samples. *Fungal Ecology* 5:13.

CDC (Centers for Disease Control and Prevention). 1996. Coccidioidomycosis—Arizona, 1990-1995. *Morbidity and Mortality Weekly Report* 45:1069-1073.

CDC. 2003. Increase in coccidioidomycosis—Arizona, 1998-2001. *Morbidity and Mortality Weekly Report* 52(6):109-112.

CDC. 2013. Increase in reported coccidioidomycosis—United States, 1998-2011. *Morbidity and Mortality Weekly Report* 62:217-221.

Chang, D. C., S. Anderson, K. Wannemuehler, D. M. Engelthaler, L. Erhart, R. H. Sunenshine, L. A. Burwell, and B. J. Park. 2008. Testing for coccidioidomycosis among patients with community-acquired pneumonia. *Emerging Infectious Diseases* 14(7):1053-1059.

Chen, S., L. M. Erhart, S. Anderson, K. Komatsu, B. Park, T. Chiller, and R. Sunenshine. 2011. Coccidioidomycosis: Knowledge, attitudes, and practices among healthcare providers—Arizona, 2007. *Medical Mycology* 49(6):649-656.

Comrie, A. C. 2005. Climate factors influencing coccidioidomycosis seasonality and outbreaks. *Environmental Health Perspectives* 113(6):688-692.

Converse, J. L., and R. E. Reed. 1966. Experimental epidemiology of coccidioidomycosis. *Bacteriological Reviews* 30(3):678-695.

Cummins, W. T., J. K. Smith, and C. H. Halliday. 1929. Coccidioidal granuloma, an epidemiologic survey, with a report of 24 additional cases. *Journal of the American Medical Association* 93:1046-1049.

Duran, F., Jr, G. W. Robertstad, and E. Donowho. 1973. The distribution of *Coccidioides immitis* in the soil in El Paso, Texas. *Sabouraudia* 11(2):143-148.

Edwards, P. Q., and C. E. Palmer. 1957. Prevalence of sensitivity to coccidioidin, with special reference to specific and nonspecific reactions to coccidioidin and to histoplasmin. *Diseases of the Chest* 31:35-60.

Egeberg, R. O. 1953. Coccidioidomycosis: Its clinical and climatological aspects with remarks on treatment. *Transactions of the American Clinical and Climatological Association* 65:116-126.

Emmons, C. W. 1942a. Coccidioidomycosis. *Mycologia* 34:452-463.

Emmons, C. W. 1942b. Isolation of coccidioides from soil and rodents. *Public Health Reports* 57:109-111.

Emmons, C. W., and L. L. Ashburn. 1942. The isolation of *Haplosporangium parvum* n. sp. and *Coccidioides immitis* from wild rodents. Their relationship to coccidioidomycosis. *Public Health Reports* 57:1715-1727.

Eulalio, K. D., R. L. de Macedo, M. A. Cavalcanti, L. M. Martins, M. S. Lazera, and B. Wanke. 2001. Coccidioides immitis isolated from armadillos (*Dasypus novemcinctus*) in the state of Piaui, northeast Brazil. *Mycopathologia* 149(2):57-61.

Fisher, M. C., G. L. Koenig, T. J. White, and J. W. Taylor. 2002. Molecular and phenotypic description of *Coccidioides posadasii* sp nov., previously recognized as the non-California population of *Coccidioides immitis*. *Mycologia* 94(1):73-84.

Flynn, N. M., P. D. Hoeprich, M. M. Kawachi, K. K. Lee, R. M. Lawrence, E. Goldstein, G. W. Jordan, R. S. Kundargi, and G. A. Wong. 1979. An unusual outbreak of windborne coccidioidomycosis. *New England Journal of Medicine* 301(7):358-361.

Friedman, L., C. E. Smith, D. Pappagianis, and R. J. Berman. 1956. Survival of *Coccidioides immitis* under controlled conditions of temperature and humidity. *American Journal of Public Health* 46:1317-1324.

Greene, D. R., G. Koenig, M. C. Fisher, and J. W. Taylor. 2000. Soil isolation and molecular identification of *Coccidioides immitis*. *Mycologia* 92(3):406-410.

Hector, R. F., G. W. Rutherford, C. A. Tsang, L. M. Erhart, O. McCotter, K. Komatsu, S. M. Anderson, F. Tabnak, D. J. Vugia, Y. Yang, and J. N. Galgiani. 2011. Public health impact of coccidioidomycosis in California and Arizona. *International Journal of Environmental Research and Public Health* 8(4):1150-1173.

Hoerling, M. P. D., K. Wolter, J. Lukas, J. Eischeid, R. Nemani, B. Leibmann, and K. E. Kunkel. 2013. Present weather and climate: Evolving conditions. In *Assessment of climate change in the Southwest United States*, edited by G. J. Garfin, R. Merideth, M. Black, and S. LeRoy. Washington, DC: Island Press. Pp. 74-100.

Hugenholtz, P. G. 1957. Climate and coccidioidomycosis. In *Proceedings of Symposium on Coccidioidomycosis, Phoenix, AZ.* Atlanta: Public Health Service Publication No. 575. Pp. 136-143.

Kolivras, K. N., and A. C. Comrie. 2003. Modeling valley fever (coccidioidomycosis) incidence on the basis of climate conditions. *International Journal of Biometeorology* 47(2):87-101.

Laniado-Laborin, R. 2007. Expanding understanding of epidemiology of coccidioidomycosis in the Western Hemisphere. *Annals of the New York Academy of Sciences* 1111:19-34.

Leake, J. A., D. G. Mosley, B. England, J. V. Graham, B. D. Plikaytis, N. M. Ampel, B. A. Perkins, and R. A. Hajjeh. 2000. Risk factors for acute symptomatic coccidioidomycosis among elderly persons in Arizona, 1996-1997. *Journal of Infectious Diseases* 181(4):1435-1440.

Levine, H. B., and W. A. Winn. 1964. Isolation of *Coccidioides immitis* from soil. *Health Laboratory Science* 1:29-32.

Lundergan, L. L., S. S. Kerrick, and J. N. Galgiani. 1985. Coccidioidomycosis at a university outpatient clinic: A clinical description. In *Coccidioidomycosis. Proceedings of the Fourth International Conference*, edited by H. E. Einstein and A. Catanzaro. Washington, DC: National Foundation for Infectious Diseases. Pp. 47-54.

Maddy, K. T. 1958. The geographic distribution of *Coccidioides immitis* and possible ecologic implications. *Arizona Medicine* 15:178-188.

Maddy, K. T. 1959. A study of a site in Arizona where a dog apparently acquired a *Coccidioides immitis* infection. *American Journal of Veterinary Research* 20:642-646.

Maddy, K. T. 1965. Observations on *Coccidioides immitis* found growing naturally in soil. *Arizona Medicine* 22:281-288.

Mardo, D., R. A. Christensen, N. Nielson, S. Hutt, R. Hyun, J. Shaffer, C. Barton, G. Dowdle, M. Mottice, C. Brokopp, R. Rolfs, and D. Panebaker. 2002. Coccidioidomycosis in workers at an archeologic site—Dinosaur National Monument, Utah, June-July 2001. *Archives of Dermatology* 138(3):424-425.

Marsden-Haug, N., M. Goldoft, C. Ralston, A. P. Limaye, J. Chua, H. Hill, L. Jecha, G. R. Thompson, 3rd, and T. Chiller. 2013. Coccidioidomycosis acquired in Washington State. *Clinical Infectious Diseases* 56(6):847-850.

Nguyen, C., B. M. Barker, S. Hoover, D. E. Nix, N. M. Ampel, J. A. Frelinger, M. J. Orbach, and J. N. Galgiani. 2013. Recent advances in our understanding of the environmental, epidemiological, immunological, and clinical dimensions of coccidioidomycosis. *Clinical Microbiology Reviews* 26(3):505-525.

Pappagianis, D., and H. Einstein. 1978. Tempest from Tehachapi takes toll or coccidioides conveyed aloft and afar. *Western Journal of Medicine* 129:527-530.

Park, B. J., K. Sigel, V. Vaz, K. Komatsu, C. McRill, M. Phelan, T. Colman, A. C. Comrie, D. W. Warnock, J. N. Galgiani, and R. A. Hajjeh. 2005. An epidemic of coccidioidomycosis in Arizona associated with climatic changes, 1998-2001. *Journal of Infectious Diseases* 191(11):1981-1987.

Pulford, D. S., and E. E. Larson. 1929. Coccidioidal granuloma; report of a case treated by intravenous dye, colloidal lead, and colloidal copper, with autopsy observations. *Journal of the American Medical Association* 93:1049-1056.

Smith, C. E. 1940. Epidemiology of acute coccidioidomycosis wth erythema nodosum. *American Journal of Health* 30:600-611.

Smith, C. E., R. R. Beard, H. G. Rosenberger, and E. G. Whiting. 1946. Effect of season and dust control on coccidioidomycosis. *Journal of the American Medical Association* 132(14):833-838.

Sondermeyer, G. L., D. Gilliss, F. Tabnak, and D. Vugia. 2013. Coccidioidomycosis-associated hospitalizations, California, USA, 2000-2011. *Emerging Infectious Diseases* 19(10):8.

Stacy, P. K., A. C. Comrie, and S. R. Yool. 2012. Modeling valley fever incidence in Arizona using a satellite-derived soil moisture proxy. *GIScience and Remote Sensing* 49(2).

Stern, N. G., and J. N. Galgiani. 2010. Coccidioidomycosis among scholarship athletes and other college students, Arizona, USA. *Emerging Infectious Diseases* 16(2):321-323.

Sunenshine, R. H., S. Anderson, L. Erhart, A. Vossbrink, P. C. Kelly, D. Engelthaler, and K. Komatsu. 2007. Public health surveillance for coccidioidomycosis in Arizona. *Annals of the New York Academy of Sciences* 1111:96-102.

Swatek, F. E. 1970. Ecology of *Coccidioides immitis*. *Mycopathologia et Mycologia Applicata* 40(1-2):3-12.

Tabor, J. A., and M. K. O'Rourke. 2010. A risk factor study of coccidioidomycosis by controlling differential misclassifications of exposure and susceptibility using a landscape ecology approach. *Science of the Total Environment* 408(10):2199-2207.

Talamantes, J., S. Behseta, and C. S. Zender. 2007. Statistical modeling of valley fever data in Kern County, California. *International Journal of Biometeorology* 51(4):307-313.

Tamerius, J. D., and A. C. Comrie. 2011. Coccidioidomycosis incidence in Arizona predicted by seasonal precipitation. *PLoS One.* 6(6):e21009.

Tsang, C. A., S. M. Anderson, S. B. Imholte, L. M. Erhart, S. Chen, B. J. Park, C. Christ, K. K. Komatsu, T. Chiller, and R. H. Sunenshine. 2010. Enhanced surveillance of coccidioidomycosis, Arizona, USA, 2007-2008. *Emerging Infectious Diseases* 16(11):1738-1744.

Wieden, M. A., L. L. Lundergan, J. Blum, K. L. Delgado, R. Coolbaugh, R. Howard, T. Peng, E. Pugh, N. Reis, J. Theis, and J. N. Galgiani. 1996. Detection of coccidioidal antibodies by 33-kDa spherule antigen, *Coccidioides* EIA, and standard serologic tests in sera from patients evaluated for coccidioidomycosis. *Journal of Infectious Diseases* 173:1273-1277.

Zender, C. S., and J. Talamantes. 2006. Climate controls on valley fever incidence in Kern County, California. *International Journal of Biometeorology* 50(3):174-182.

A13

ZOONOTIC DISEASE RISKS ASSOCIATED WITH TRADE AND MOVEMENT OF ANIMALS

*Nina **Marano***,[55] *Adam J. Langer*,[55] *G. Gale Galland*,[55] *Nicole J. Cohen*,[55] *Emily Lankau*,[56] *Ashley Marrone*,[55] *David McAdam*,[55] *Casey Barton Behravesh*,[57] *and Nicki Pesik*[55]

Globalization of the market for live animals and animal products—combined with human behaviors and preferences for the exotic—are ever-growing risk factors for the translocation of zoonotic diseases to the United States from parts of the world where they are endemic or exist in a reservoir state. Why is there global trade in animals? Animals and animal products are transported across borders for many reasons. They are used for exhibitions at zoos; scientific education, research, and conservation programs; food and nonedible products; for the pet trade; and in the case of companion animals, tourism and immigration. The United States is one of the world's largest consumers of imported wildlife and wildlife products. A recent analysis showed that during 1999–2010, over 80 million vertebrate species were imported to the United States, including 2 million mammalian species; of these, 46 percent were rodent species (Romagosa, 2010; CDC, unpublished data).

In the United States, there is a network of federal, state, and local agency regulations in place to prevent the transmission of diseases carried by animals that could be harmful to humans, other animals, or the environment. There are five U.S. federal agencies whose authorities pertain to movement of live animals: the

[55] Division of Global Migration and Quarantine, U.S. Centers for Disease Control and Prevention.
[56] LandCow Consulting.
[57] Division of Foodborne, Waterborne, and Environmental Diseases, U.S. Centers for Disease Control and Prevention.