Operational Guidelines (version 1.0) for Geological Fieldwork in Areas Endemic for Coccidioidomycosis (Valley Fever)

by

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Abstract

Coccidioidomycosis (Valley Fever) is a disease caused by the inhalation of the arthroconidia (spores) of *Coccidioides immitis*, a fungus that lives in the soils of southwestern United States. Although large numbers of people are exposed to the arthroconidia and are consequently infected**,** very few individuals contract the more serious forms of the disease. Earth scientists working in field areas where *Coccidioides immitis* is endemic have an increased risk of becoming infected. Because field operations often disturb the upper surface of the ground**,** they may inhale large numbers of arthroconidia. This also increases their risk of developing more severe forms of the disease. Any other occupations or activities that create dusty conditions in endemic areas also have increased risk of infection.

Risk management strategies can lower the incidence of infection and also reduce the numbers of arthroconidia inhaled thereby decreasing the chances of developing more serious disease. Dust control, by utilizing dust masks, and dust prevention, by limiting ground disturbing activities, are the primary weapons against infection. However, infection risk can also be lowered by conducting fields studies in the winter months; avoiding sites favorable for *Coccidioides immitis* growth; seeking prompt medical treatment if flu-like or respiratory illness occur during, or within a few weeks following, fieldwork; getting a coccidioidin skin test to determine susceptibility to the disease; and by educating all members of the field party about the possibilities and consequences of infection.

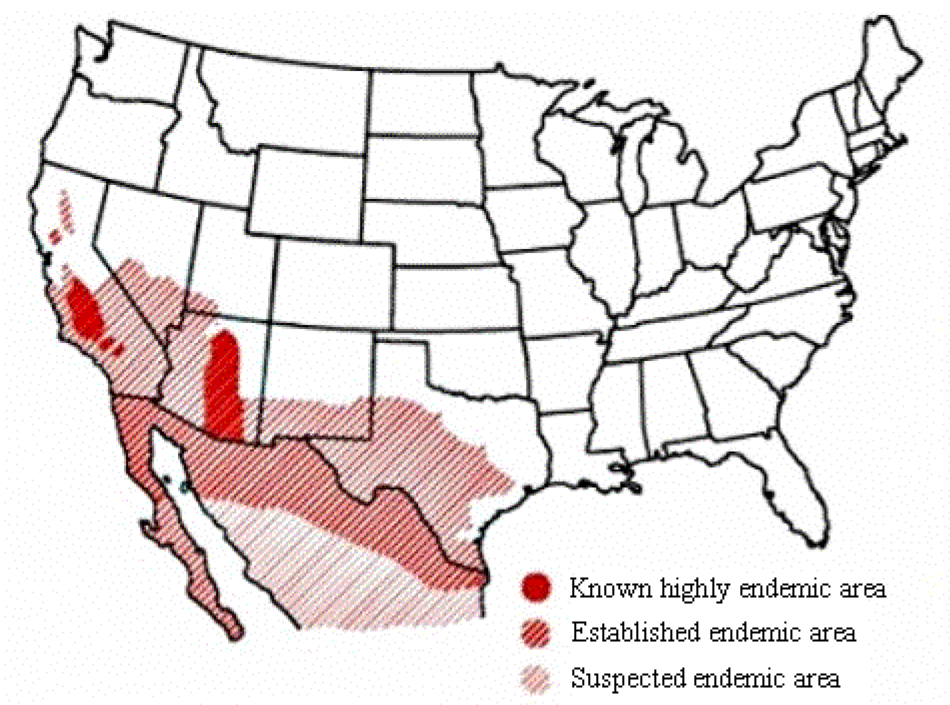
Introduction

The purpose of this report is to present operational guidelines that will lower the risk of contracting coccidioidomycosis for individuals who work outdoors in areas where the disease is endemic. Coccidioidomycosis (or as it is sometimes called, Valley Fever) is an infection usually caused by the inhalation of (rarely by traumatic introduction through the skin) arthroconidia (spores) of the soil inhabiting fungus *Coccidioides immitis.* The disease may occur in any individual residing, visiting, or even passing through endemic areas. While this report is directed at earth scientists it also applies to other occupations involving outdoor activity in dusty conditions (e.g. farming, ranching, construction, archaeology, soil scientist, etc.). However, specific occupation is not as important in determining infection risk as is the amount of time spent outdoors and involvement in activities that expose an individual to dusty conditions or to intensive contact with soils. This report also applies to many outdoor recreational pursuits (e.g.. gardening, landscaping, equestrian, biking, hiking etc.). The recommendations made here are based on information available to date on the habitat of *Coccidioides immitis.* This information may change as new data are currently being collected by ongoing studies at the University of Arizona and by the U.S. Geological Survey that are focused specifically on the habitat of *C. immitis*. This paper does not discuss medical treatments for the disease, however, the authors do utilize knowledge about the ailment to help individuals apply strategies that will lower their risk of becoming infected. Definitive discussions of the medical aspects and treatments of coccidioidomycosis may be found in Einstein and Johnson, (1993) and Galgiani, (1993).

Endemic areas

Rapid population growth, greater numbers of recreational visits and activities, and continued stationing of military personnel for active training in the deserts of the southwestern U.S. place an increasingly large unexposed population within endemic areas. These demographic changes, coupled with increasing numbers of individuals with suppressed immune systems due to the ongoing AIDS epidemic, and the growing use of immunosuppressing medical therapies are of concern to public health officials (Galgiani, 1992, 1993, 1999; Rush and others, 1993; Pappagianis and others, 1993).

Figure 1. Endemic regions of *C. immitis* in the United States and northern Mexico
Courtesy of the Valley Fever Americas Foundation, Bakersfield, California



In the conterminous United States *C. immitis* is endemic in parts of Arizona, California, New Mexico, Nevada, Texas, and Utah (fig. 1). Outside of the United States it is endemic in parts of Argentina, Brazil, Colombia, Guatemala, Honduras, Mexico, Nicaragua, Paraguay, and Venezuela. With some exceptions endemic areas are generally arid to semiarid with low to moderate rainfall (5 to 20 inches), mild winters, and long hot seasons. The Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia declared in 1993 that coccidioidomycosis was epidemic in parts of California (Kern County) and also issued a warning to physicians nationwide to watch for the disease in patients who may have become infected while traveling in endemic areas. The CDC also listed coccidioidomycosis as an example of one of the important emerging disease threats to the Nation and has called for expanded studies of the disease (Bryan, and others, 1994).

In endemic areas, recognized cases of coccidioidomycosis are under-reported (Lundergan and others, 1985, p. 53; Galgiani, 1992, p. 100). In 1957 it was shown that, in infected individuals, the disease resulted in an average of 33 to 35 lost work days (Scogins, 1957). Pappagianis (1980) estimated that the overall annual cost to the nation was one million person-days of labor. A review by the CDC (Goodman, 1994) of the medical records in Kern County, California showed that coccidioidomycosis accounted for approximately $66 million in direct costs of hospitalization and outpatient care during the period 1991-1993. Infection rates for humans vary throughout the endemic areas. In 1966 long-term residents in Arizona (several years) showed the following infection rates by county; Apache 13%, Cochise 37%, Coconino 5%, Gila 48%, Graham 60%, Greenlee 40%, Maricopa 71%, Mohave 57%, Pima 72%, Pinal 76%, Santa Cruz 40%, Yavapai 14%, Yuma 26% (Converse and Reed, 1966, p. 682, fig. 4).

Character of the Disease

Arthroconidia of *C. immitis* can be released into the air when soils are disturbed by natural or anthropogenic means. Inhalation of the arthroconidia into the lungs of an appropriate host can cause primary infection. Once in the lung the arthroconidia change into a spherule form and reproduce efficiently by endosporulation causing relatively rapid growth and increased infection (Galgiani, 1993; Einstein and Johnson, 1993). Primary coccidioidomycosis is limited to the lesions in the lungs with symptoms that may include fever, chills, night sweats, chest pains, cough, appetite loss, and muscle and joint aches. Symptoms usually clear within a few weeks. Disseminated coccidioidomycosis occurs when the disease spreads to sites in the body other than the lungs and can involve any organ with the exception of the gastrointestinal tract which is rarely involved (Einstein and Johnson, 1993). Disseminated forms of the disease are more severe and have a variety of symptoms. Involvement of a vital organ can lead to death.

Most people who are long-term residents (several years) in areas where *C. immitis* is present are exposed to the arthroconidia of the fungus and are consequently infected. About 60 percent of the people infected are asymptomatic, their exposure to the infection being reflected only by a positive coccidioidin skin test. Most symptomatic cases result in primary infection with relatively mild cold or influenza-like symptoms for which only about 10 percent of the people seek medical attention; however, in some cases there may be pneumonia. In about 1 percent of those infected, *C. immitis* disseminates elsewhere in the body beyond the pulmonary system with much more serious, and at times, fatal results (Pappagianis and others, 1993). Early diagnosis and treatment of coccidioidomycosis is of value in managing primary infections and is essential in most cases of disseminated disease (Galgiani, 1999). Pregnant women, African-Americans, Filipinos, and possibly Asians, Hispanics, and Native Americans have higher rates of dissemination of the disease (Pappagianis and others, 1979; Einstein and Johnson, 1993). Coccidioidomycosis is often severe and life threatening in patients whose immune systems have been compromised. The disease is capable of lying dormant in some infected individuals for years, becoming active and opportunistic only when the immune system is weakened by other conditions (Cuellar and others, 1993). In addition to humans the disease affects many species of domestic and wild animals including burros, cattle, dogs[1] , horses, sheep, swine, bats, coyotes, mountain lions, rodents, sea otters, and reptiles (Reed and others, 1994; Pappagianis, 1988).

New infections are frequently seasonal and appear to be related to several factors including humidity, rainfall, sunlight, temperature, and wind conditions (Smith and others, 1946; Egeberg, 1953; Pappagianis, 1988). Rates of infection are highest during hot dry spells that follow cooler rainy seasons and rates often spike following large dust storms (Pappagianis, 1988). Other new infections are related to ground-disturbing activities with consequent exposure to soil and dust, such as construction, mining, agriculture, archaeological excavations, military maneuvers, recreational activities, etc.(Johnson, 1981; Pappagianis, 1983). Laboratory studies have shown that as few as 10 arthroconidia are sufficient to cause an infection in dogs and monkeys (Converse and Reed, 1966) and it has been suggested that even a single arthroconidia could be responsible for infection in humans (Bulmer, 1979; Galgiani, 1993). Many severe infections in animals and humans are related to inhaling aerosols containing high doses of arthroconidia derived from sites where *C. immitis* is present in the soils (Converse and Reed, 1966; Pappagianis, 1988). Once an individual has been infected by *C. immitis*, even mild cases, and is skin-tested positive, immunity to additional infection by *C. immitis* is developed (Fiese, 1958, pp 92-97; Galgiani, 1999).

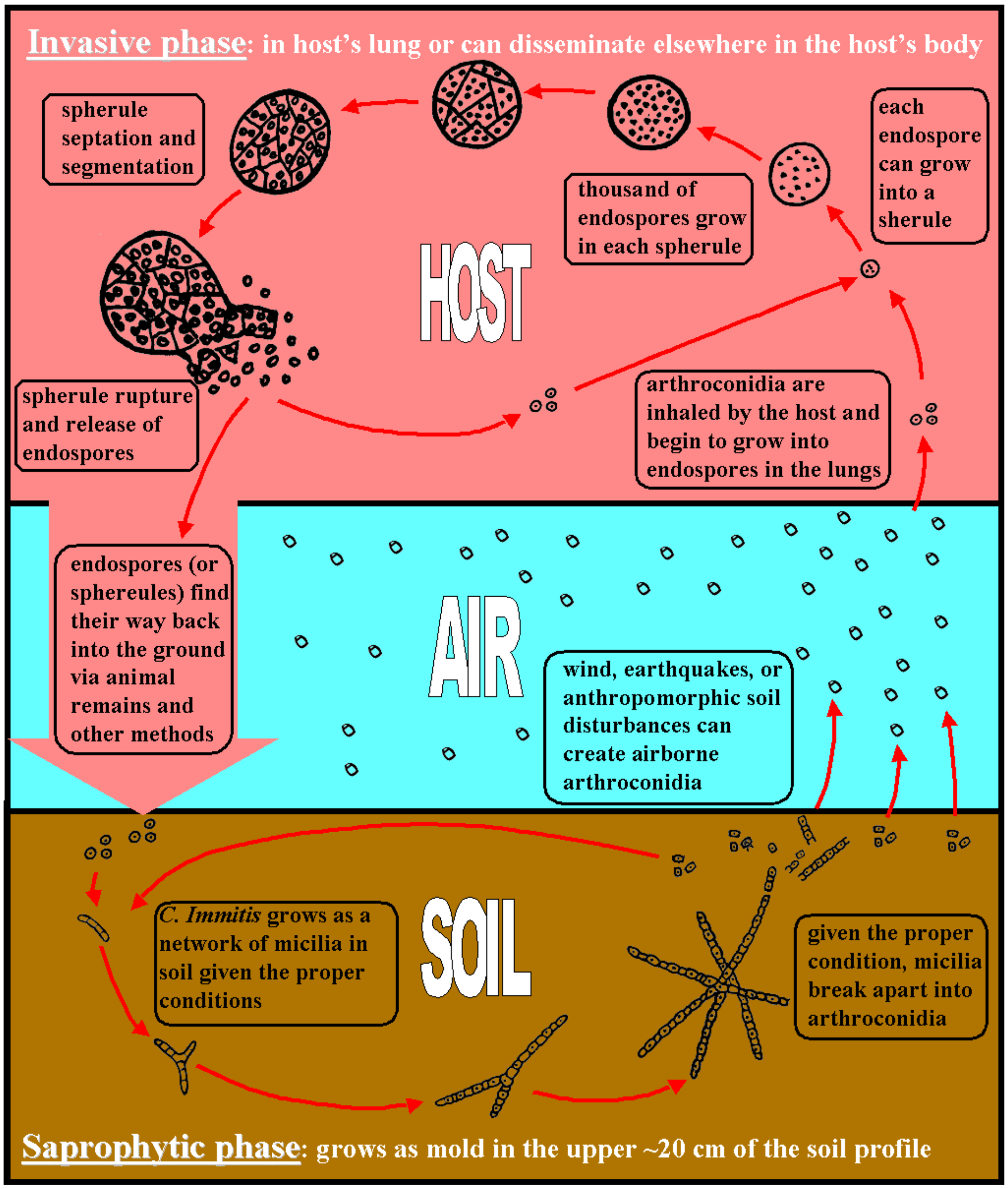
Habitat of *C. immitis*

C. immitis grows in the upper (5 - 20 cm) horizons of soils in endemic areas (fig. 2). This saprophytic phase of the fungus is characterized by branching segmented hyphae that form a network of mycelium. As the fungus matures, arthroconidia, 2 to 5*u*m in size, are formed as barrel shaped, rectangular segments of the hyphae. Given the right environmental conditions, alternate arthroconidia undergo autolysis leaving the viable arthroconidia which are easily separated by soil disturbance (natural or anthropogenic) and consequently easily dispersed by the wind. Arthroconidia are also very buoyant and may be readily moved by sheet-wash water during rainstorms only to be concentrated in fine sedimentary material some distance from the initial growth site. Under suitable environmental conditions the arthroconidia can germinate to form new hyphae and mycelium, which can repeat the cycle. However, numerous studies suggest that *C.*

[1] Dogs are very prone to infection because of their habit of sniffing the ground and frequent deep inhalation of air in rodent burrows. Once infected many dogs develop severe forms of the disease which most often necessitates euthanasia (Davidson and Pappagianis, 1994).

immitis does not readily colonize outside of existing growth sites. The reasons for this are not completely understood but may be associated with the sensitivity of the fungus to environmental factors and competition from other soil inhabiting organisms (Swatek, 1975; Pappagianis, 1980, 1988).

Figure 2. Life cycle of *C. immitis*



If the airborne arthroconidia are inhaled by an appropriate host (humans, animals, even reptiles) the invasive phase of *C. immitis* is initiated (fig. 2). In tissue the arthroconidia transform into spherules 10 to 80 *u*m in diameter which when mature are internally divided into endospores that are 2 to 5 *u*m in diameter. The mature spherules then rupture and the endospores are released into the surrounding tissue thereby spreading the infection locally, or at times, into other organs by disseminating outside of the respiratory system. The invasive phase may end with the death of the host or by the expulsion of spherules outside of living tissue by sputum, pus, or exudates. If this occurs in an acceptable environment then the spherules (or endospores) will germinate and hyphae and mycelium will be developed and the saprophytic phase will again be initiated (Fiese, 1958). In some cases both mycelia and spherule forms of *C. immitis* have been observed in tissue and sputum (Fiese, 1958, p. 34-35).

The presence of *C. immitis* in specific areas is determined by direct sampling of soils, identification of positive skin and serologic tests in non-mobile human populations, and recognition of the infection in humans and animals (mostly dogs). Several authors have noted that these occurrences or growth sites are relatively restricted in size, with individual sites ranging from several tens to several hundreds of square meters (Maddy and Crecelius, 1967; Egeberg and others, 1964; Swatek, 1975; Pappagianis, 1980, 1988). Although some growth sites have been identified, their distribution and recognition throughout the entire endemic area of the southwestern U.S. is poorly known.

Laboratory and site specific field studies have shown that many physical, chemical, climatic, and biological factors influence the growth of *C. immitis* in the soil and the consequent development and deployment of arthroconidia (Fiese, 1958; Sorensen, 1964; Swatek, 1975; Pappagianis, 1988). Key factors include, amount and timing of rainfall and available moisture (humidity), temperature, soil texture, alkalinity, salinity and types of water-soluble salts, organic content of soils, and degree of exposure to sunlight and ultraviolet light. Others that may be important are the presence of marine sedimentary rocks, presence of borates, soil chemistry, presence of specific vegetation types, inclusion within the Lower Sonoran Life Zone, competition with other fungal and/or plant species, presence of Indian middens, and presence of rodent burrows and middens (Maddy, 1957; Egeberg, 1962; Pappagianis, 1988). Many of the above mentioned factors are closely interrelated and the influence on the presence and/or growth of *C. immitis* by any combination of, or single factor, is an intricate balance that varies both in time (season) and in response to changes in the physical, chemical, and biological environment at any given location.

Risk Management Strategies

Because ambient airborne *C. immitis* arthroconidia may be present anywhere within endemic areas, absolute prevention of infection is virtually impossible, and, as no effective vaccine for coccidioidomycosis is currently available, consideration of risk management strategies seems prudent. Some of these methods may not be practical for individuals who are not involved closely with soils, aerosols, or other materials derived directly from *C. immitis* growth sites; however, earth scientists doing fieldwork in endemic areas can lower their risk of infection by following strategies appropriate for their own particular activities.

Education of individuals and institutions about the disease is the first step in developing risk management strategies and it is to that end this report is directed. General information brochures on coccidioidomycosis may be obtained from the American Lung Association of Arizona (2819 E. Broadway Blvd., Tucson, AZ, 85716), the California Department of Health Services (2151 Berkeley Way, Berkeley, CA, 94704), and The Valley Fever Center for Excellence (Mail Stop 111, 3601 S. 6th Ave., Tucson, AZ, 85723).

The factors listed below, all of which increase the chance of infection, are associated with the probability of inhaling *C. immitis* arthroconidia and must be considered in a risk management strategy.

1) Residence within endemic areas; longer times increases risk
2) Travel within endemic areas; again longer time increases risk
3) No previous history of infection as shown by a negative coccidioidin skin test; (successful recovery from coccidioidomycosis, even mild cases, imparts immunity to further infection)
4) Exposure to dust containing arthroconidia, as a result of incidental circumstances, occupation, recreation, or life style
5) Duration of time spent outdoors
6) Duration of time spent in dusty conditions (inhalation of larger numbers of arthroconidia has been associated with more severe cases of coccidioidomycosis)
7) Activities (and duration of time) that involve intensive contact with soils in endemic areas
8) Exposure to fomites derived from endemic areas

In addition to the above it is also important to consider the risk factors associated with development of the more serious disseminated forms of the disease as listed below:

1) A compromised immune system (HIV/AIDS, organ transplants, diabetes, chemotherapy, etc.)
2) African-American, Filipino, or other Asian heritage (possibly also Hispanic and native American)
3) second and third trimester of pregnancy
4) male gender

For those earth scientists living in or assigned to work in endemic areas several strategies should be considered to lower the risk and severity of infection by *C. immitis* arthroconidia. A coccidioidin skin test should be done to determine prior exposure to the disease. Those who test negative indicating no prior exposure should be more diligent in adopting risk reducing strategies and should seek medical treatment early in the course of flu-like illnesses that may develop a few weeks following fieldwork in endemic areas. Those who test positive are unlikely to become reinfected and probably only need to use extra precautions when exposed to intensive contact with soils in highly infective areas (i.e. rodent burrows in known *C. immitis* growth sites). Individuals who are at a higher risk of developing disseminated disease, especially the immunosuppressed, may be wise to a) limit fieldwork in endemic areas, b) completely avoid locations containing favorable *C. immitis* growth sites and, c) avoid dust producing activities.

Infections by *C. immitis* frequently have a seasonal pattern with infection rates that generally spike in the first few weeks of hot dry weather that follow extended milder rainy periods. In California infection rates are generally higher during the hot summer months especially if weather patterns bring the usual winter rains between November and April. The normal weather pattern in Arizona is a winter rainy season in December, January, and February followed by hot dry weather and also a summer monsoon season in July and August again followed by hot dry weather. Thus in Arizona infection rates are often higher in spring, then decrease during the summer monsoons and increase again in autumn, with highest rates often occurring in November, and finally decreasing to the lowest rates during the winter rainy season. Numerous studies have suggested the connection between above average rainfall during the winter and spring and higher infection rates the following summer (Smith and others, 1946; Maddy, 1965, Pappagianis, 1988). Increased moisture is believed to provide a longer period for growth of *C. immitis* and consequently greater production of arthroconidia which, with the onset of dry, hot, windy weather creates infective conditions for susceptible hosts (Maddy, 1965). During rainfall, dust and arthroconidia are washed from the air and wetting of the soil decreases the opportunity for spores to become airborne thereby creating less infective conditions. The seasonal character of infections should be considered in risk management strategies and earth scientists should whenever possible schedule fieldwork in endemic areas during the winter rainy periods when infection rates are generally lowest.

Clearly, dust-control measures are the main defense against infection. However it is important to note that dust itself is only an indicator that *C. immitis* arthroconidia may be airborne in a given area and that some dust clouds may be completely free of arthroconidia. Arthroconidia of *C. immitis* have slow settling rates in air due to their small (2*u*m - 5*u*m) size, low terminal velocity (0.003 cm/sec), and possibly also due to their buoyancy, barrel shape and commonly attached empty hyphae cell fragments (Gregory, 1973; Dimmick, 1965; Lacey, 1981). Thus arthroconidia, whose size is well below the limits of human vision, may be present in air that appears relatively clear and dust free. Such ambient, airborne arthroconidia with their low settling rates can remain aloft for exceedingly long periods and be carried hundreds of kilometers from their point of origin (Table 1).

Table 1

Time of flight and range of distances of particles moving in moderately strong winds (15 m/sec.). Modified from Chorley and others, 1984

Particle type	Diameter (mm)	Fall Velocity (cm/sec)	Flight time (maximum)	Transportation distance (max.)
clay	0.001	0.00824	9-90 years	4-40 x 10^6 km
C. immitis arthroconidia	0.002-0.005	0.003	?	?
silt	0.01	0.824	8-80 years	4-40 x 10^2 km
very fine sand	0.10	82.4	0.3-3 sec.	46-460 meters

Arthroconidia may also become airborne by hitchhiking rides on larger dust or sand sized particles. Large dust storms, at times carrying arthroconidia of *C. immitis*, in California and Arizona have long been noted for creating epidemic conditions (Smith and others, 1946). More recently dust clouds resulting from the January 17, 1994, earthquake in California are believed to be responsible for outbreaks of coccidioidomycosis from eastern Ventura County to the western San Fernando Valley (Pappagianis and others, 1994; Schneider and others, 1997; Jibson and others, 1998). Viability of fungi spores in the atmosphere depends on several factors including temperature, desiccation, radiation (especially in the ultraviolet wave lengths), and how robust individual types of spores are when placed in different environments (Gregory, 1973; Lacey, 1981). How long airborne *C. immitis* arthroconidia remain infective for humans is unknown but laboratory experiments suggest that *C. immitis* arthroconidia are hardy (Friedman and others, 1956; Pappagianis, 1988) and thus may be viable in the atmosphere for extended periods. Weather patterns with associated strong winds can carry arthroconidia great distances and coupled with their robust viability can spread infection well outside of recognized endemic areas. For example, in 1977 strong winds (gusts to 160 km/hr) centered in Kern County, California (located in the southern San Joaquin Valley) scoured topsoil to depths of 15 cm creating a dust cloud that reached elevations of approximately 1500 meters. The storm carried *C. immitis* arthroconidia 500 km north to the vicinity of Sacramento, California (an area not considered endemic for *C. immitis*) (Flynn and others, 1979). The dust spread over an area of about 87,000 km^2 reaching Sacramento about 20 hours after the start of the storm in Kern County and infecting as many as 7,000 people in Sacramento County (Pappagianis and Einstein, 1978; Flynn and others, 1979, p. 360).

There are many ways to avoid and control dusty conditions during field operations, although some may not be practical for certain operations. Few methods (perhaps none) are 100 percent effective. Following are suggestions for reducing infection risk by limiting exposure to dust in endemic areas:

1) Avoid working outdoors during windy conditions
2) If possible use machinery with enclosed cabs and utilize air conditioning
3) Use air conditioning in field vehicles
4) Avoid unnecessary digging or soil disturbance
5) Use dust masks; Although the use of dust masks for protection against the inhalation of *C. immitis* arthroconidia has not been scientifically evaluated, their application by workers in dusty conditions is strongly recommended. Several types of masks are available that have been proven to be very effective against dust particles as small as 0.4 microns in size, which is several times smaller than *C. immitis* arthroconidia. Masks capable of filtering particles as small as 0.4 microns should provide nearly total protection if fitted properly and conscientiously utilized during dusty operations. Manufactures instructions must be followed and it should be noted that mustaches or beards may prevent a mask from making an airtight seal against the face and thus may allow unfiltered dust to be inhaled.
6) Wet soils before digging or collecting samples (a small backpack weed sprayer containing water may be useful)
7) camp and sleep upwind of known or suspected *C. immitis* growth sites or dusty areas
8) avoid sandy campsites; camp on vegetated areas as much as possible
9) sterilize soil or rock samples by heating them to 60^0C for thirty minutes which will kill *C. immitis*
10) Use fungicides to kill *C. immitis* (Elconin and others, 1967) but be aware that they are only effective on the soil surface and possibly to a depth of 0.5 cm

Don't take *C. immitis* arthroconidia home with you or unwittingly expose other individuals to infection by fomites from endemic areas. Many cases of coccidioidomycosis have occurred as a result of exposure to contaminated materials derived from endemic areas (Albert and Sellers, 1963).

1) wash and sterilize rocks, soils, fossils, vegetation, or other sampled material before removing it from the field to the laboratory
2) keep field vehicles washed, and clean interiors by using water (do not create dust by sweeping or vacuuming interiors)
3) remove dusty clothing after fieldwork and store in closed plastic bags until washed
4) clean field equipment before returning to the home, office or laboratory

The distribution of *C. immitis* within endemic areas is not uniform and growth sites are commonly small (a few tens of meters) and widely scattered. Known sites appear to have some ecological factors in common suggesting that certain physical, chemical, and biological conditions are more favorable for *C. immitis* growth. Avoidance, when possible, of sites favorable for the occurrence of *C. immitis* is a prudent risk management strategy. Listed below are ecologic factors and sites favorable for the occurrence of *C. immitis*:

1) Rodent burrows (often a favorable site for *C. immitis,* perhaps because temperatures are more moderate and humidity higher than on the ground surface)
2) Old (prehistoric) Indian campsites near fire pits
3) Areas with sparse vegetation and alkaline soils
4) Areas with high salinity soils
5) Areas adjacent to arroyos (where residual moisture may be available)
6) Packrat middens
7) Upper 30 cm of the soil horizon, especially in virgin undisturbed soils
8) Sandy well aerated soil with relatively high water holding capacities

Sites within endemic areas less favorable for the occurrence of *C. immitis* include:

1) Cultivated fields
2) Heavily vegetated areas (e.g. grassy lawns)
3) Higher elevations (above 7,000')
4) Areas where commercial fertilizers (e.g. ammonium sulfate) have been applied
5) Areas that are continually wet
6) Paved (asphalt or concrete) or oiled areas
7) Soils containing abundant microorganisms
8) Heavily urbanized areas where there is little undisturbed virgin soil

In summary, because arthroconidia of *C. immitis* can occur anywhere within endemic areas, or even possibly a few hundred kilometers outside of endemic areas, (given windy, dusty conditions as documented above) 100 percent protection against infection is impossible. However earth scientists conducting field studies within endemic areas can limit their risk of becoming infected and most likely, reduce the severity of the disease in those that do become infected by; 1) scheduling fieldwork during winter months; 2) avoiding activities (if possible) in areas most favorable for *C. immitis* occurrences; 3) utilizing dust control methods when appropriate; 4) having a coccidioidin skin test and, if test is negative, exerting additional caution while working in dusty conditions; 5) seeking prompt treatment of flu like or respiratory illness that occur during, or a few weeks following, fieldwork and also informing their physician about possible exposure to *C. immitis* arthroconidia; and 6) educating all members of the field party about the disease. Those individuals at high risk of developing severe disseminated disease should carefully evaluate the necessity of conducting field studies within endemic areas, however, it should be remembered that the large majority of individuals infected suffer no or very minor symptoms and that the severe disseminated form of the disease occurs in less than one percent of those exposed.

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